Comparative Effectiveness Review
Number 258

Diagnostic Errors in the Emergency Department: A Systematic Review

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of healthcare in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new healthcare technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see https://effectivehealthcare.ahrq.gov/about/epc/evidence-synthesis.

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If you have comments on this systematic review, they may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $5,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

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Diagnostic Errors in the Emergency Department: A Systematic Review

Structured Abstract

Objectives. Diagnostic errors are a known patient safety concern across all clinical settings, including the emergency department (ED). We conducted a systematic review to determine the most frequent diseases and clinical presentations associated with diagnostic errors (and resulting harms) in the ED, measure error and harm frequency, as well as assess causal factors.

Methods. We searched PubMed®, Cumulative Index to Nursing and Allied Health Literature (CINAHL®), and Embase® from January 2000 through September 2021. We included research studies and targeted grey literature reporting diagnostic errors or misdiagnosis-related harms in EDs in the United States or other developed countries with ED care deemed comparable by a technical expert panel. We applied standard definitions for diagnostic errors, misdiagnosis-related harms (adverse events), and serious harms (permanent disability or death). Preventability was determined by original study authors or differences in harms across groups. Two reviewers independently screened search results for eligibility; serially extracted data regarding common diseases, error/harm rates, and causes/risk factors; and independently assessed risk of bias of included studies. We synthesized results for each question and extrapolated U.S. estimates. We present 95 percent confidence intervals (CIs) or plausible range (PR) bounds, as appropriate.

Results. We identified 19,127 citations and included 279 studies. The top 15 clinical conditions associated with serious misdiagnosis-related harms (accounting for 68% [95% CI 66 to 71] of serious harms) were (1) stroke, (2) myocardial infarction, (3) aortic aneurysm and dissection, (4) spinal cord compression and injury, (5) venous thromboembolism, (6/7 – tie) meningitis and encephalitis, (6/7 – tie) sepsis, (8) lung cancer, (9) traumatic brain injury and traumatic intracranial hemorrhage, (10) arterial thromboembolism, (11) spinal and intracranial abscess, (12) cardiac arrhythmia, (13) pneumonia, (14) gastrointestinal perforation and rupture, and (15) intestinal obstruction. Average disease-specific error rates ranged from 1.5 percent (myocardial infarction) to 56 percent (spinal abscess), with additional variation by clinical presentation (e.g., missed stroke average 17%, but 4% for weakness and 40% for dizziness/vertigo). There was also wide, superimposed variation by hospital (e.g., missed myocardial infarction 0% to 29% across hospitals within a single study). An estimated 5.7 percent (95% CI 4.4 to 7.1) of all ED visits had at least one diagnostic error. Estimated preventable adverse event rates were as follows: any harm severity (2.0%, 95% CI 1.0 to 3.6), any serious harms (0.3%, PR 0.1 to 0.7), and deaths (0.2%, PR 0.1 to 0.4). While most disease-specific error rates derived from mainly U.S.-based studies, overall error and harm rates were derived from three prospective studies conducted outside the United States (in Canada, Spain, and Switzerland, with combined n=1,758). If overall rates are generalizable to all U.S. ED visits (130 million, 95% CI 116 to 144), this would translate to 7.4 million (PR 5.1 to 10.2) ED diagnostic errors annually; 2.6 million (PR 1.1 to 5.2) diagnostic adverse events with preventable harms; and 371,000 (PR 142,000 to 909,000) serious misdiagnosis-related harms, including more than 100,000 permanent, high-severity disabilities and 250,000 deaths. Although errors were often multifactorial, 89 percent (95% CI 88 to 90) of diagnostic error malpractice claims involved failures of clinical decision-making or judgment, regardless of the underlying disease present. Key process failures were errors in

diagnostic assessment, test ordering, and test interpretation. Most often these were attributed to inadequate knowledge, skills, or reasoning, particularly in "atypical" or otherwise subtle case presentations. Limitations included use of malpractice claims and incident reports for distribution of diseases leading to serious harms, reliance on a small number of non-U.S. studies for overall (disease-agnostic) diagnostic error and harm rates, and methodologic variability across studies in measuring disease-specific rates, determining preventability, and assessing causal factors.

Conclusions. Although estimated ED error rates are low (and comparable to those found in other clinical settings), the number of patients potentially impacted is large. Not all diagnostic errors or harms are preventable, but wide variability in diagnostic error rates across diseases, symptoms, and hospitals suggests improvement is possible. With 130 million U.S. ED visits, estimated rates for diagnostic error (5.7%), misdiagnosis-related harms (2.0%), and serious misdiagnosis-related harms (0.3%) could translate to more than 7 million errors, 2.5 million harms, and 350,000 patients suffering potentially preventable permanent disability or death. Over two-thirds of serious harms are attributable to just 15 diseases and linked to cognitive errors, particularly in cases with "atypical" manifestations. Scalable solutions to enhance bedside diagnostic processes are needed, and these should target the most commonly misdiagnosed clinical presentations of key diseases causing serious harms. New studies should confirm overall rates are representative of current U.S.-based ED practice and focus on identified evidence gaps (errors among common diseases with lower-severity harms, pediatric ED errors and harms, dynamic systems factors such as overcrowding, and false positives). Policy changes to consider based on this review include: (1) standardizing measurement and research results reporting to maximize comparability of measures of diagnostic error and misdiagnosis-related harms; (2) creating a National Diagnostic Performance Dashboard to track performance; and (3) using multiple policy levers (e.g., research funding, public accountability, payment reforms) to facilitate the rapid development and deployment of solutions to address this critically important patient safety concern.

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Executive Summary

Main Points

- Overall diagnostic accuracy in the emergency department (ED) is high, but some patients receive an incorrect diagnosis (~5.7%). Some of these patients suffer an adverse event because of the incorrect diagnosis (~2.0%), and some of these adverse events are serious (~0.3%). This translates to about 1 in 18 ED patients receiving an incorrect diagnosis, 1 in 50 suffering an adverse event, and 1 in 350 suffering permanent disability or death. These rates are comparable to those seen in primary care and hospital inpatient care.
- We estimate that among 130 million emergency department (ED) visits per year in the United States that 7.4 million (5.7%) patients are misdiagnosed, 2.6 million (2.0%) suffer an adverse event as a result, and about 370,000 (0.3%) suffer serious harms from diagnostic error. Put in terms of an average ED with 25,000 visits annually and average diagnostic performance, each year this would be over 1,400 diagnostic errors, 500 diagnostic adverse events, and 75 serious harms, including 50 deaths per ED. Although overall error and harm rates are derived from three smaller studies conducted outside the United States (in Canada, Spain, and Switzerland, with combined n=1,758), study methods were prospective and rigorous. All three were conducted at university hospitals, and, for the two studies used to estimate harms, about 92 percent of clinicians under study at those institutions had full training or formal certification in emergency medicine.
- Five conditions (#1 stroke, #2 myocardial infarction, #3 aortic aneurysm/dissection, #4 spinal cord compression/injury, #5 venous thromboembolism) account for 39 percent of serious misdiagnosis-related harms, and the top 15 conditions account for 68 percent. Variation in diagnostic error rates by disease are striking (range 1.5% for myocardial infarction to 56% for spinal abscess, with the other thirteen falling between 10% and 36%). Stroke, the top serious harm-producing disease, is missed an estimated 17% of the time. Among these 15 diseases, myocardial infarction is the only one with false negative rates near zero (1.5%), well below the estimated average rate across all diseases (5.7%).
- For a given disease, nonspecific or atypical symptoms increase the likelihood of error. For stroke, dizziness or vertigo increases the odds of misdiagnosis 14-fold over motor symptoms (those with dizziness and vertigo are missed initially 40% of the time).
- Variation in diagnostic error rates across demographic groups is present and sometimes fairly large in magnitude. The effect of age is heterogeneous and disease-specific (e.g., younger age increases risk of missed stroke 6.7-fold, while older age increases risk of missed appendicitis). Female sex and non-White race were often associated with important (20–30%) increases in misdiagnosis risk; although these disparities were inconsistently demonstrated across studies, being a woman or a racial or ethnic minority was generally not found to be "protective" against misdiagnosis (i.e., was neutral at best).
- Variation in diagnostic error rates across specific hospital EDs is wide. Methods of measuring diagnostic errors in the ED are highly variable. However, even when similar methods are used, measured diagnostic error rates vary up to 100-fold across hospitals. In individual studies, missed cases varied by hospital for subarachnoid hemorrhage (0% to 100%), myocardial infarction (0% to 29%), and appendicitis (1% to 16%). Error rates are usually found to be lower in academic/teaching hospitals, but it is unknown if this is an effect of increased availability/intensive use of diagnostic technologies or other factors.

- Root causes of ED diagnostic errors were mostly cognitive errors linked to the process of bedside diagnosis. Malpractice claims associated with serious misdiagnosis-related harms involved failures of clinical assessment, reasoning, or decision making in about 90 percent of cases. Similar findings were seen in incident report data. These issues are not unique to the ED—they are seen across clinical settings, regardless of study method.
- The strongest, most consistent predictors of ED diagnostic error were individual case factors that increased the cognitive challenge of identifying the underlying disorder, with nonspecific, mild, transient, or "atypical" symptoms being the most frequent.
- Our findings are tempered by limitations in the underlying evidence base, including issues related to data sources, measurement methods, and causal relationships. Nevertheless, overall diagnostic error and misdiagnosis-related harm rates are consistent with what has been found in other clinical settings (e.g., primary care and inpatient).

Background and Purpose

The National Academy of Medicine (NAM) has called diagnostic error a "blind spot" for modern medicine and improving diagnosis a "moral, professional, and public health imperative."[1] Diagnostic errors occur across all clinical settings, but the ED is thought to be a high-risk site for diagnostic error.[2-7] The scope of this evidence review, commissioned by the Agency for Healthcare Research and Quality, was limited to the ED setting.

The key decisional dilemma for this evidence review is "What are the most common and significant medical diagnostic failures in the ED, and why do they happen?" We conducted a systematic review to determine the following: (1) What clinical conditions are associated with the greatest number and highest risk of ED diagnostic errors and associated harms? (2) Overall and for the clinical conditions of interest, how frequent are ED diagnostic errors and associated harms? and (3) Overall and for the clinical conditions of interest, what are the major causal factors associated with ED diagnostic errors and associated harms?

Methods

We employed methods consistent with those outlined in the Agency for Healthcare Research and Quality Evidence-based Practice Center Program Methods Guidance (https://effectivehealthcare.ahrq.gov/topics/cer-methods-guide/overview), and we described these in the full report. Our searches covered publication dates from January 2000 to September 2021. We included research studies and targeted grey literature reporting diagnostic errors or misdiagnosis-related harms in EDs in the United States or other developed countries with comparable ED care. Two reviewers independently screened search results for eligibility, serially extracted data regarding common diseases, error/harm rates, and causes/risk factors, and independently assessed risk of bias of included studies. We synthesized results for each question and extrapolated U.S. estimates. When possible, to describe uncertainty, we present 95 percent confidence intervals (CIs); otherwise, we present plausible range (PR) bounds for key estimates.

Results

We identified 19,127 abstracts, screened 1,455 full text studies, and included 279 studies that addressed Key Questions 1, 2, and 3. The top 15 individual diseases associated with the greatest number of serious misdiagnosis-related harms in the ED, in rank order, were (1) stroke, (2) myocardial infarction, (3) aortic aneurysm and dissection, (4) spinal cord compression and

injury, (5) venous thromboembolism, (6/7 – tie) meningitis and encephalitis, (6/7 – tie) sepsis, (8) lung cancer, (9) traumatic brain injury and traumatic intracranial hemorrhage, (10) arterial thromboembolism, (11) spinal and intracranial abscess, (12) cardiac arrhythmia, (13) pneumonia, (14) gastrointestinal perforation and rupture, and (15) intestinal obstruction. Together, they accounted for 68 percent (95% CI 66 to 71) of all serious harms from diagnostic error in the ED. Grouped by organ system, neurologic diseases were the top category (34%). Disease-specific error rates were lowest for myocardial infarction (1.5%) and highest for spinal abscess (56%). Relative to myocardial infarction, stroke, the top serious harm-producing missed diagnosis, was missed approximately 10-fold more often (17%), despite having comparable disease incidence.

An estimated 5.7 percent (95% CI 4.4 to 7.1) of all ED visits will have at least one diagnostic error. The overall (not disease-specific), per ED visit, potentially preventable diagnostic adverse event rates were estimated as follows: any harm severity 2.0 percent (95% CI 1.0 to 3.6), serious misdiagnosis-related harms (i.e., permanent, high-severity disability or death) 0.3 percent (PR 0.1 to 0.7), and misdiagnosis-related deaths 0.2 percent (PR 0.1 to 0.4). For each misdiagnosis-related death, it is estimated that there are roughly 0.41 (PR 0.27 to 0.60) ED patients suffering non-lethal, permanent, serious disability. If generalizable to all US ED visits (130 million, 95% CI 116 to 144), these rates translate to 7.4 million (PR 5.1 to 10.2) ED diagnostic errors annually; 2.6 million (PR 1.1 to 5.2) diagnostic adverse events with preventable harms; and 371,000 (PR 142,000 to 909,000) serious misdiagnosis-related harms, including more than 100,000 permanent, high-severity disabilities and 250,000 deaths.

Although errors were often multifactorial, 89 percent (95% CI 88 to 90) of diagnostic error malpractice claims involved failures of clinical decision making or judgment, regardless of the underlying disease present. Key process failures were errors or delays in bedside diagnostic assessment, laboratory or imaging test ordering, and test interpretation. Most often these were attributed to inadequate clinical knowledge, skills, or reasoning, particularly in "atypical" or otherwise subtle case presentations. Unsurprisingly, "obviousness" predicted correct diagnosis and "subtlety" predicted incorrect diagnosis. Subtle diagnostic situations included diseases in the "wrong" age groups; transient, milder, non-specific, or atypical symptoms; and finding second, third, or fourth problems in patients who were very ill (e.g., polytrauma).

Strengths and Limitations

Overall, the evidence supported answers to all three Key Questions, including most subquestions. We were able to identify the top 15 diseases associated with serious misdiagnosis-related harms (Key Question 1), the frequency of errors and harms both overall and for many of these specific diseases (Key Question 2), and the chief causes of and risk factors for these errors (Key Question 3). Results for Key Question 1 relied heavily on two large studies (one of medical malpractice claims, the other incident reports). Although there are clear biases in malpractice claims, there was a high degree of concordance between claims and incident reports with respect to diseases causing serious harms. Overall (i.e., not disease-specific) error and harm rates for Key Question 2 relied heavily on three studies from centers outside the United States which were given greater weight relative to the larger body of literature because of rigorous, prospective methods. Preventable harm rate estimates derived from two studies conducted at academic centers (1 in Canada, 1 in Switzerland) at which about 92 percent of ED clinicians under study had formal training in emergency medicine. The Canadian study measured preventable harms by requiring a high-bar standard on record review—at least two of three independent raters with emergency medicine training had to agree that the adverse event was causally related to the

diagnostic error and preventable with a level of certainty of at least 5 on a 6-point Likert scale. The Swiss study assessed deaths as an outcome among admitted patients and found a 2.3-fold increase in mortality with a 4.8 percent absolute difference (8.6% of those initially misdiagnosed in the ED ultimately died versus 3.8% of those correctly diagnosed). Estimated misdiagnosis-related mortality from the Canadian study (0.2%, PR 0.1 to 0.4) was bolstered by similarity to the mortality estimate calculated from the two Western European studies (PR 0.2% to 0.3%) and preventable deaths due to inpatient diagnostic errors (~0.2% based on a prior systematic review). Studies of disease-specific error rates were sufficient for meta-analysis (n=6) or at least point estimates (n=6). Causal factors were extensively studied, but too heterogeneously categorized for overall meta-analysis. The causal and risk factor literature was strongest for patient and illness characteristics and relatively weaker on clinician characteristics, fixed systems factors, and dynamic systems factors. Discrepant results were mostly attributable to differences in research methods across studies, including study design, inclusion or exclusion criteria, diagnostic error definitions, and heterogeneity in classifying disease diagnoses and causal factors. Specific gaps identified for each question, with potential remedies, are described in the full report.

Implications and Conclusions

The ED is one of the most challenging clinical settings to practice medicine. That just 5.7 percent of patients would be misdiagnosed, just 2.0 percent would suffer some sort of adverse event as a result, and just 0.3 percent of patients would suffer serious harms from diagnostic error is a testament to the skill and capability of practicing emergency physicians. It should be remembered that not all diagnostic errors are preventable and attempting to prevent some errors may lead to undesirable, unintended consequences that could adversely impact patients. Nevertheless, substantial variability in diagnostic error rates by disease, presenting symptoms, demographic groups, and specific hospitals suggests there remains room for improvement in diagnostic performance that could benefit many patients. Scalable solutions to enhance bedside diagnostic processes are needed, and these should target the most commonly misdiagnosed clinical presentations of key diseases causing serious harms.

Future research should emphasize areas in which data are suboptimal or lacking. For decision making in the United States, overall diagnostic error and harm rates should be confirmed in U.S.-based studies using rigorous, prospective methods. Diagnostic error measurement and reporting should be standardized for both internal and external benchmarking purposes, including public accountability. More research is needed on the burden of diagnostic errors and harms related to diseases with less immediate and severe consequences, pediatric ED diagnostic errors and harms, and the causal contributions of modifiable systems factors amenable to policy intervention such as ED overcrowding, which may increase the risk of diagnostic error). This should also include study of potential unintended consequences of solutions designed to address these errors, since harms from overuse of diagnostic tests or false positives are also a concern.

Policy changes to consider based on findings from this review include: (1) standardizing measurement and research results reporting to maximize comparability of measures of diagnostic error and misdiagnosis-related harms[1, 8, 9]; (2) creating a National Diagnostic Performance Dashboard[10] to track performance (analogous to the Dartmouth Atlas Project for utilization of healthcare services[11]); and (3) using multiple policy levers (e.g., research funding, public accountability, payment reforms)[1] to facilitate the rapid development and deployment of solutions to address this critically important patient safety concern. Resources applied should be commensurate with the measured public health burden, which is likely substantial.

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Introduction

Background

Diagnostic errors represent a source of iatrogenic harms whose adverse impact on patients may exceed the total morbidity and mortality from all other medical errors combined.[1] The number of diagnostic errors each year in the United States is estimated to be at least 12 million but could be an order of magnitude higher.[1] Estimates for the number of Americans seriously harmed each year as a result of diagnostic error (so-called "misdiagnosis-related harms"[2]) range from approximately 40,000 to 10 million,[1] but the most plausible values are likely in the hundreds of thousands.[3] Misdiagnosis-related harms range from none to serious (i.e., permanent disability or death). Costs to the U.S. healthcare system may exceed $100 billion per year.[4]

Despite their toll on patients and society, diagnostic errors remain largely invisible. This is mostly because diagnostic errors are rarely evident at the time when they occur and only surface later, often when they are discovered by another clinician or after misdiagnosis-related harms have occurred. Furthermore, diagnostic errors are variably defined, difficult to measure, and not routinely tracked as part of patient safety or quality improvement initiatives. The National Academy of Medicine (NAM) defines diagnostic error as "the failure to (a) establish an accurate and timely explanation of the patient's health problem(s) or (b) communicate that explanation to the patient."[5] Notably, this definition (which is used in this report) does not require a care process failure (e.g., a specific clinical reasoning "mistake" on the part of an individual clinician) and is agnostic with respect to any resulting harms or their preventability. Furthermore, it does not elaborate on the words "accurate" or "timely," nor does it draw distinctions between false negative and false positive errors or specify how management differences might be used inferentially in assessing the "correctness" of diagnostic decision-making. There is no clear consensus on how to define "diagnostic error" at this deeper level,[6] but some authors focused on emergency department (ED) diagnosis have made important attempts to do so. For example, a Swiss group examining diagnostic errors among admitted ED patients divided differences between ED and final hospital discharge diagnoses into those that were deemed, in their view, not to represent ED diagnostic errors (ED diagnosis was somewhat underspecified or a complication not present at the time of the ED visit later became the primary inpatient diagnosis) and those that were considered diagnostic errors (ED missed a second, more important diagnosis or ED diagnosis was qualitatively incorrect).[7] There is even less certainty about how best to capture communication failures between ED clinician and patient, and very few studies have sought to address this aspect of diagnostic error definitions.[8] Whenever possible, we relied on the NAM definition of diagnostic error (e.g., to differentiate diagnostic errors from diagnostic errors with adverse events or harms), but we also relied, as necessary, on individual study-based operational definitions, including more granular determinations of error, harms, and preventable harms that were used in the included studies.

Diagnostic errors occur across all medical settings. Overall diagnostic error rates are not known, but a commonly cited figure is that 10-15 percent of medical diagnoses are wrong.[9] Hospital autopsy studies tend to corroborate this figure, with estimated major error rates of 8 percent to 24 percent, even after accounting for selection bias in what deaths undergo autopsy.[10] On sheer volume alone, most diagnostic errors happen in ambulatory clinic settings, where diagnostic errors are estimated to affect 6.3 percent of primary care encounters, translating to more than 12 million Americans suffering errors each year.[11] Because this figure is based largely on studies that searched retrospectively for adverse events (e.g., unplanned revisits), the true

error rate is likely higher, but the rate of misdiagnosis-related *harms* in primary care is likely lower and closer to 0.1% (calculated as 187/212,165 from Singh et al., 2013).[12] Diagnostic adverse event rates (defined similarly to misdiagnosis-related harms) are estimated to occur in 0.7% of hospitalizations[3]; that this adverse event rate would be higher than in primary care makes sense, given the higher intensity of illness present among hospitalized patients.

There are approximately 130 million ED visits each year[13] at the roughly 5,000 EDs in the United States.[14] The ED is believed to be a high-risk site for diagnostic error,[15-20] but error rates are highly variable by disease[1] and symptom presentation.[21, 22] Diagnostic error rates for myocardial infarction, for example, are impressively low at about 1 to 2 percent[1] (in part due to the availability of electrocardiograms and a reliable lab test [i.e., troponin assays]), but delays in diagnosing spinal abscess occur in up to 75 percent of such encounters in the ED.[23] Diagnostic error rates for stroke, a condition that tends to be more reliant on bedside diagnosis, are approximately 4 percent for those presenting with weakness but approximately 40 percent for those presenting with dizziness or vertigo.[21] Most misdiagnosed patients do not suffer significant adverse events. However, even if preventable misdiagnosis-related harm rates in the ED were as low as approximately 0.1 percent (n=13 of 13,495 ED visits),[24] with 130 million ED visits per year in the United States,[13] this would translate to approximately 125,000 ED patients harmed each year. Perhaps most importantly, there is evidence that error and harm rates are highly variable across individual EDs—for example, one epidemiologic study found that rates of missed myocardial infarction varied from 0 to 29 percent across hospitals[25] while another found that rates of missed appendicitis varied from 1 to 16 percent, with higher error rates correlating strongly with higher harm rates.[26]

There are many reasons why the ED may be the most challenging clinical setting for diagnosis. The breadth of clinical presentations is extremely wide, with dozens of common symptoms caused by thousands of possible diseases. Patients seen in the ED frequently have dangerous underlying conditions causing their symptoms, but the manifestations may be vague or atypical. Patients are often seen early in the natural history of their disease presentation (sometimes just minutes or hours after the onset of symptoms), so "obvious" features may not yet have developed, and diagnoses may be highly uncertain. ED physicians usually have no prior relationship with their patients, and information at the time of evaluation is often incomplete (e.g., patients may not provide accurate information on past medical history or medications; the history of present illness may not be clear, as with altered mental status). Many EDs have limited access to specialty consultants or advanced diagnostic tests, such as magnetic resonance imaging (MRI). The ED environment is often fast-paced, chaotic, and distraction-rich, increasing cognitive load for clinicians.[27] Finally, the goal of ED care is often not to make a firm diagnosis, but instead to make a diagnosis-informed management decision about immediate on-site testing, treatment, or hospitalization, and generally to do so in a matter of hours. The asymmetry of false negative versus false positive diagnostic errors often factors heavily in such considerations—an "undercall" (discharging a patient with a dangerous disease) is generally viewed as less desirable than an "overcall" (admitting a patient without a dangerous disease). As a result, some forms of diagnostic "error" (e.g., symptom-only diagnoses or false positive overcalls among admitted patients) may simply reflect goals and context of care.

Understanding more about the frequency, contexts, and causes of ED diagnostic error offers a springboard for both research and operational quality improvement efforts aimed at reducing or eliminating preventable misdiagnosis-related harms. For example, if 15 specific diseases account for two-thirds of the serious harms from ED diagnostic error, then these diseases can become top

targets for solutions both at the institutional level and nationally. If stroke is diagnosed well among patients with unilateral weakness but poorly among patients with dizziness, local clinical pathways and national guidelines for diagnosing dizziness could be developed. If local hospital diagnostic performance benchmarks are better than the overall average ED performance nationally but lag for aortic dissection, then that disease can be made the focus of a new local quality improvement program. Thus, this report offers decision-makers at every level (individual clinicians, ED directors, hospital safety officers, national policy makers, etc.) critical insights about diagnostic failures. It provides a detailed view of what is known, as well as what is not known, about ED diagnostic errors and misdiagnosis-related harms.

Purpose and Scope of the Systematic Review

Although diagnostic errors are known to occur across all clinical settings, the scope of this evidence review, commissioned by the Agency for Healthcare Research and Quality, was limited to the ED. The key decisional dilemma for this evidence review is "What are the most common and significant medical diagnostic failures in the ED, and why do they happen?" We conducted a systematic review to determine the most frequent diseases and clinical presentations associated with diagnostic errors (and resulting harms) in the ED, measure error and harm frequency, as well as assess causal factors and identify risk predictors for these errors.

Methods

Review Approach

We followed the methods outlined in the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews.[28] We reported this systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.[29]

The topic was nominated by a member of the AHRQ Learning Health System (LHS) panel and AHRQ developed the topic of this systematic review. We further refined the Key Questions (KQs) with input from Key Informants and representatives from AHRQ, the LHS panel, and the Center for Quality Improvement and Patient Safety (CQuIPS). The KQs were posted on AHRQ's website for public comment between October 2 and October 23, 2020.

We recruited a Technical Expert Panel (TEP) to review the draft protocol. With the feedback from the TEP and representatives from AHRQ, the LHS panel, and CQuIPS, we finalized the protocol and posted it on the AHRQ Effective Health Care Program's website (www.effectivehealthcare.ahrq.gov). We also registered the protocol on PROSPERO (CRD42021225828).

Key Questions

KQ 1: What clinical conditions are associated with the greatest number and highest risk of emergency department (ED) diagnostic errors and associated harms?

a. What diseases or syndromes are associated with the greatest total number and the highest risk of diagnostic errors or misdiagnosis-related harms?
b. Do results vary based on the severity of any resulting misdiagnosis-related harms (e.g., death or permanent disability, as opposed to less serious harms)?
c. What are the most common clinical presenting symptoms or signs associated with diagnostic errors or misdiagnosis-related harms in the ED?
d. Do the most common clinical presenting symptoms or signs associated with diagnostic error or misdiagnosis-related harms vary by disease or syndrome?

KQ 2: Overall and for the clinical conditions of interest, how frequent are ED diagnostic errors and associated harms?

a. On a per-visit or symptom-specific basis, what is the rate of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms?

b. On a per-disease/syndrome basis, what is the rate of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms?
c. Approximately how many patients does this equate to nationally in the United States?
d. Are there clear commonalities or differences across clinical conditions in the frequency or risk of ED diagnostic errors or misdiagnosis-related harms?

KQ 3: Overall and for the clinical conditions of interest, what are the major causal factors associated with ED diagnostic errors and associated harms?

a. What are the most frequent causes identified?
b. Do causes identified differ based on severity of harms?
c. Do different causes have differential impact on patient outcomes (i.e., harms)?
d. Overall and for each clinical condition:
    i. Are patient characteristics (e.g., age, gender, race/ethnicity, language, socioeconomic status/income, health literacy) associated with errors/harms?
    ii. Are illness characteristics (e.g., symptom type, clinical presentation, mode of arrival) associated with errors/harms?
    iii. Are clinician characteristics (e.g., provider type, training background, experience level, prior disciplinary action) associated with errors/harms?
    iv. Are facility or health system characteristics (e.g., region, ED patient volumes or discharge fraction, teaching status, access to imaging, access to or type of electronic health record system) associated with errors/harms?
    v. Are context-specific systems factors (e.g., at the time of the error—high ED patient volume or severity of illness, night or weekend shift, provider fatigue, change of shift/handoff) associated with errors/harms?
e. Are there significant commonalities or differences among causes of ED diagnostic errors or associated harms across clinical conditions?

Prospectively analyzed subgroups and covariates (as appropriate to the individual KQs) included the following:

- Studies conducted in United States versus those not conducted in the United States

- Children (<18 years) versus adults (18+ years); adults <65 years versus adults 65+ years (KQ1 only)
- General versus specialty EDs (e.g., psychiatric, eye and ear) (KQ1 only)
- ED discharges versus admissions versus transfers (KQ1 only)
- Epoch in which studies were reported (2000 to 2010 versus 2011 to 2021) (KQ2 only)
- ED clinician training: physicians versus advanced practice providers; physicians who are trained versus physicians who are not trained in emergency medicine; trainees (residents) versus fully trained physicians; and years of experience (KQ2 only)

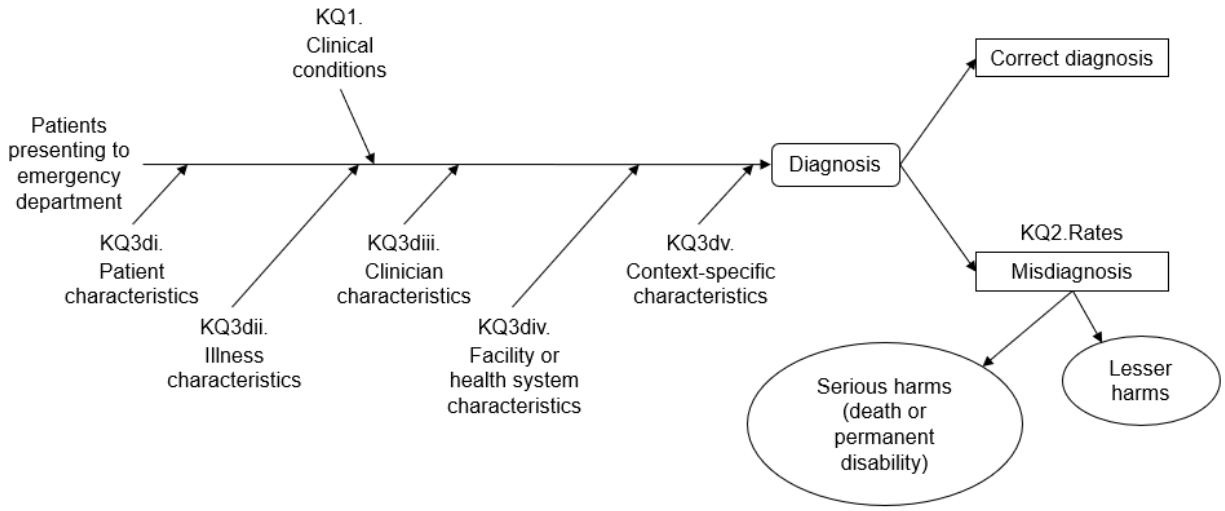
Based on prior research and discussions with Key Informants, we defined clinical conditions of interest to be vascular events (stroke, myocardial infarction, venous thromboembolism [especially pulmonary embolism], aortic aneurysm and dissection, arterial thromboembolism [especially mesenteric ischemia]); infections (sepsis, meningitis and encephalitis, spinal abscess, pneumonia, endocarditis, and appendicitis); and selected fractures.[1, 16, 17, 30, 31] Additional conditions deemed likely relevant to pediatric populations included testicular torsion, necrotizing enterocolitis, and sudden cardiac death/arrythmias/congenital heart disease.[15, 32] Additional conditions deemed likely relevant to pregnant populations included ectopic pregnancy and preeclampsia/eclampsia.[16, 33, 34]

The National Academy of Medicine (NAM) defines diagnostic error as "the failure to (a) establish an accurate and timely explanation of the patient's health problem(s) or (b) communicate that explanation to the patient."[5] We used this definition for diagnostic error, while recognizing that many studies only address either accuracy or timeliness, not effectiveness of communication with patients. We relied on this definition to determine "diagnostic error" regardless of whether authors of included studies used this terminology or other language (e.g., diagnostic delay, diagnostic discrepancy). We use the term "misdiagnosis" in this review as synonymous with "diagnostic error" (though we recognize not all authors or studies do the same).[6] Misdiagnosis-related harms are defined as harms resulting from the delay or failure to treat a condition actually present, when the working diagnosis was wrong or unknown (delayed or missed diagnosis [false negative]), or from treatment provided for a condition not actually present (wrong diagnosis [false positive]).[1, 2, 17] We use the terms "misdiagnosis-related harms" and "diagnostic adverse events" interchangeably. We considered *serious* misdiagnosis-related harms to include death or permanent disability (i.e., scores of 6 to 9 on the National Association of Insurance Commissioners [NAIC] Severity of Injury Scale).[35] Recognizing that definitions of *preventable* harms are variable,[36] we relied on the definitions and determinations of preventability that were used in the included studies or on measured differences in outcomes between groups (e.g., mortality among those correctly versus incorrectly diagnosed).

Analytic Framework

Figure 1 provides a diagram of the analytic framework we used for the KQs.

Figure 1. Analytic framework for diagnostic errors in the emergency department



KQ = Key Question

Data Sources and Study Methods

As outlined by Shojania in 2010, there are numerous potential data sources and methods for institutions to monitor patient safety and quality.[37] No perfect data sources or analytic approaches exist, and this is especially true for diagnostic errors. It is usually necessary to rely on multiple data sources and different methods to gain a more comprehensive view of patient safety and quality.[37] Data sources may be disease-agnostic (any disease) or disease-specific (one single disease or a group of diseases – e.g., major cardiovascular events). Disease-agnostic studies were used to answer the bulk of KQ1 and parts of KQ2 (chiefly KQ2a, KQ2c focused on overall ED diagnostic error rates) and KQ3 (chiefly KQ3a focused on the most frequent root causes). Disease-specific studies were used to answer the bulk of KQ2 (specifically the large KQ2b section on disease-specific error and harm rates) and the bulk of KQ3 (chiefly the large KQ3d section on specific risk factors for diagnostic error) and minor parts of KQ1 (chiefly KQ1d focused on the most common clinical presenting symptoms by disease). Data sources and their associated analytic methods may be numerator-only (no explicitly defined source population from which they were drawn, so valid error/harm rates cannot be calculated) or numerator-denominator (explicitly defined source population, so valid error/harm rates can potentially be calculated). Typical numerator-only data derive from malpractice claims and incident reports; typical numerator-denominator data derive from retrospective case-control studies that begin with an outcome event (e.g., a hospitalization) or cohort analyses (whether retrospective, prospective, or mixed [so-called "ambispective"]) that begin with an exposure (e.g., an ED visit). For KQ1, disease-agnostic data sources are needed, but numerator-only data are sufficient. For KQ2, both data sources are needed, but numerator-denominator data are required. For KQ3, either data source can be used, and numerator-only data are sufficient. The relationship between different data sources and the KQs answered is shown in Appendix Table A-1.

From a diagnostic testing perspective, a medical diagnosis is a judgement or an interpretation of a disease or condition in a patient. There are two fundamental reasons for error. The first reason is a systematic tendency for a diagnosis to deviate from the true value or reference

standard, which is called bias. The absence of bias is accuracy (sometimes called "validity"). The second reason is the propensity for a diagnosis to show scattered deviation from the true value, which is called random error. The absence of random error is precision (sometimes called "reliability"). Diagnostic accuracy is the closeness of the diagnosis to the reference standard or "truth" and diagnostic precision is the inter-observer agreement or repeatability of the test (in this case, a clinical diagnosis). Studies of diagnostic error in radiology, pathology, or other image-based fields are readily able to assess clinical precision because the specific clinical artifact that is the subject of diagnosis (radiograph, histopathology slide, etc.) can be re-examined by a second clinician without loss of fidelity. However, studies of diagnostic error in the ED (or any other clinical practice setting involving a typical, multi-faceted patient encounter) rarely, if ever, can do so—the full clinical counter (as experienced by the first clinician) cannot readily be reproduced. Thus, the ED-based studies assessed in KQ2 (error rates) nominally focus on diagnostic accuracy (relative to some reference standard [presumed] "true" diagnosis), not diagnostic precision (relative to a second "equivalent" observer). Accordingly, precision (in the inter-rater or test-retest reliability sense) plays only a minor role in this report and only at a "meta" level—specifically, some research studies report the measurement precision of assessing clinical accuracy (e.g., if chart review was performed by two independent human raters judging the presence or absence of a diagnostic error, misdiagnosis-related harm, or preventable harm). However, it should also be noted that judgments of diagnostic error (often called "inaccuracy") usually do not help us distinguish between systematic (bias) and unsystematic (random) error.

Study Selection

We searched the following databases for primary studies from January 2000 through September 2021: MEDLINE®, Embase™, and Cumulative Index to Nursing and Allied Health Literature (CINAHL®). We developed a search strategy for MEDLINE, accessed via PubMed®, based on an analysis of medical subject headings (MeSH®) and text words from eligible studies identified *a priori*. Our search strategy is presented in Appendix A. Our search was peer-reviewed by a medical librarian with experience in developing literature searches in the field of diagnostic errors. To supplement the electronic searching, we used a variety of forward and backward searching techniques, which included hand searching the reference lists of included articles and relevant reviews. We used tools, such as the "Similar Articles" or "Cited By" features in PubMed, Web of Science, or Google Scholar for the forward searching. The backward searching was limited to studies published in 2000 or later.

We conducted grey literature searches to identify data and studies not reported in the published literature, to assess for publication and reporting bias, and to inform future research needs. Studies identified through grey literature searches were considered for inclusion into the review under two conditions: (1) if they were a source of a unique study that met inclusion criteria and provided enough methodologic detail to assess risk of bias or (2) if they could be matched to an original publication that had been included in the review and the grey literature reported on an outcome not reported in the original publication. We reviewed malpractice claims reports from major medical liability insurance carriers or similar risk management entities. We reviewed any material that was submitted through the Supplemental Evidence and Data for Systematic Reviews (SEADS) portal.

Two independent reviewers screened each abstract. Both reviewers needed to agree that any article to be excluded met at least one of the exclusion criteria. We tracked and resolved differences between reviewers regarding abstract inclusion or exclusion through consensus

adjudication. Dr. Newman-Toker did not participate in screening. We used DistillerSR database (Evidence Partners Inc., Ottawa, Canada) to conduct and manage screening.

Articles promoted on the basis of the abstract screen underwent another independent screen by two reviewers using the full-text article. We tracked and resolved differences between reviewers regarding article inclusion or exclusion through consensus adjudication.

Table 1 lists our inclusion and exclusion criteria using the Perspective, Population, Setting, Phenomenon, Environment, Timing, Findings, and Study (PerSPEcTiF) framework.

Table 1. Inclusion and exclusion criteria

PerSPEcTiF	Inclusion Criteria	Exclusion Criteria
Perspective	N/A	N/A
Population	Populations with a condition with the greatest number and highest risk of misdiagnosis in the ED (KQ2, KQ3)	N/A
Setting	Studies conducted in the ED or studies that have a reasonable prospect of including data about ED physician or APP diagnostic accuracy	No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy (e.g., about pre-hospital accuracy, ED resident training or education, reliability study of a diagnostic screening tool for a specific disease)
Phenomenon	Diagnostic error* Misdiagnosis-related harms† Serious misdiagnosis-related harms (death or permanent disability [NAIC scale 6-9])	N/A
Environment	United States, Canada, United Kingdom, Western Europe, Australia, New Zealand	Studies conducted outside these countries
Timing	At least 50% of the patients were seen in the year 2000 or later	More than 50% of the patients were seen prior to the year 2000
Findings	List of key clinical conditions accounting for the majority of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms (KQ1) Frequency of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms overall and for key clinical conditions (KQ2) Root causes or patient, illness, clinician, fixed facility or health system characteristics, or dynamic, context-specific systems factors that are associated with diagnostic errors/harms (KQ3)	N/A
Study	We included studies regardless of language. We included published, peer-reviewed studies with original data and ≥50 ED patients studied. We included relevant reports from major medical liability insurance carriers or similar risk management entities, even if these were not peer-reviewed publications.	We excluded case reports or small case series with <50 ED patients. We excluded studies with no original data (e.g., reviews, simulation studies). We excluded studies using qualitative research methods that do not rely on specific patient data (e.g., physician focus groups about the general causes of diagnostic error). We excluded meeting abstracts.

APP = advanced practice provider (e.g., advanced practice nurse or physician's assistant); ED= Emergency department; KQ = Key Question; N/A = not applicable; NAIC = National Association of Insurance Commissioners

* The National Academy of Medicine defines diagnostic error as "the failure to (a) establish an accurate and timely explanation of the patient's health problem(s) or (b) communicate that explanation to the patient."[5] We used this definition for diagnostic error, while recognizing that many studies only address either accuracy or timeliness, not effectiveness of communication with patients. We relied on this definition to determine "diagnostic error" regardless of whether authors of included studies used this terminology or other language (e.g., diagnostic delay, diagnostic discrepancy). We use the term "misdiagnosis" in this review as synonymous with "diagnostic error" (though we recognize not all authors or studies do the same).

† Misdiagnosis-related harms are defined as harms resulting from the delay or failure to treat a condition actually present, when the working diagnosis was wrong or unknown (delayed or missed diagnosis [false negative]), or from treatment provided for a condition not actually present (wrong diagnosis [false positive]).[1, 2, 17]

As noted above in Data Sources and Study Methods, we searched for a mix of disease-agnostic (any disease) and disease-specific (one single disease or group of diseases – e.g., major cardiovascular events) studies. The search strategy was designed to capture both sorts of studies. However, disease-specific studies could only be identified by pre-specifying these diseases as part of the search strategy. Based on preliminary knowledge of the literature, we proposed *a priori* the following conditions to be included in the disease-specific component of the search strategy: stroke, myocardial infarction, venous thromboembolism, aortic aneurysm and dissection, arterial thromboembolism, sepsis, meningitis and encephalitis, spinal abscess, pneumonia, endocarditis, appendicitis, and selected fractures. Additional conditions were added to expand the search based on input from Key Informants and the TEP. Additional conditions deemed likely relevant to pediatric populations included testicular torsion, necrotizing enterocolitis, and sudden cardiac death/arrythmias/congenital heart disease. Additional conditions deemed likely relevant to pregnant populations included ectopic pregnancy and preeclampsia/eclampsia. While screening the full-text articles, we included all disease-agnostic studies meeting our other entry criteria, but we excluded disease-specific studies that did not include populations with at least one of these named conditions. We did not exclude studies based on condition during screening of abstracts.

We included studies if they were conducted in the United States, Canada, United Kingdom, Western Europe, Australia, or New Zealand. If studies were conducted in these countries and also other countries but the results were not separated by country, we contacted the authors. We excluded the study if we received no response from the authors. We considered Western European countries to be Austria, Belgium, Cyprus, Denmark, Finland, France, Germany, Greece, Ireland, Italy, Luxembourg, Malta, Netherlands, Norway, Portugal, Spain, Sweden, and Switzerland.[38] These nations or regions (Western Europe) were chosen in consultation with Key Informants and the TEP to reflect countries with roughly comparable systems of ED care to those found in the United States, in order to maximize representativeness of the final results for U.S.-based ED care. Much less is known about the scope and nature of diagnostic errors in developing nations, but access to basic diagnostic testing resources is very limited in many low- and middle-income countries.[39, 40] As a result, diagnostic delays for life-threatening diseases can be substantial,[41, 42] so studies from these other countries were excluded by design.

Data Extraction and Risk of Bias Assessment

We created standardized forms for data extraction and pilot tested them. Each article underwent double review by the study investigators for data abstraction. The second reviewer confirmed the first reviewer's abstracted data for completeness and accuracy. We formed reviewer pairs to include personnel with both clinical and methodological expertise. Authors of included studies were excluded from extracting or assessing their own studies.

For all articles, the reviewers extracted information on general study characteristics (e.g., study design, data source, study period, country); study participants (e.g., population, age, sex, race/ethnicity, whether they were admitted to the hospital or discharged); the type of clinician (e.g., physician versus advanced practice provider); if the clinician was trained in emergency medicine or not (and the level of training or experience); the definition of diagnostic error; the method of ascertainment of outcomes, and the outcome results, including measures of variability. To the extent possible, we also looked for other variables that had been previously associated with diagnostic error as suspected causal factors (e.g., rural versus urban ED location, night/weekend, ED discharge fraction, socioeconomic status, whether an interpreter was used).

The reviewer entered all information from the article review process into a DistillerSR database (Evidence Partners Inc., Ottawa, Canada). Reviewers entered comments into the system whenever applicable. We used the DistillerSR database to maintain the data and to create detailed evidence tables and summary tables. We contacted the authors of the included studies for additional data, if necessary.

We assessed the risk of bias by tailoring (as recommended by best practice) the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool.[43] The QUADAS-2 tool assesses the risk of bias in four domains: patient selection, index test, reference standard, and flow and timing. We instructed reviewers to consider the index test to be the initial diagnosis, usually from the ED, and the reference standard to be the final diagnosis or whatever the initial diagnosis was being measured against. Two reviewers independently evaluated the risk of bias of each study. Differences between reviewers were resolved by consensus adjudication.

Data Synthesis and Analysis

We organized the report by KQ and then by condition, where appropriate to the KQ's structure. For each KQ, we created a set of detailed evidence tables containing all information extracted from eligible studies. We conducted meta-analyses when there were sufficient data (i.e., at least two studies) and studies were sufficiently homogenous with respect to key variables (e.g., population characteristics, condition, provider type, and data source/study design). For the purposes of KQ1, we defined two sets of top-ranked diseases: (1) based on frequency among all diagnostic errors in the ED (independent of harm severity) and (2) based on frequency among diagnostic errors leading to serious harm outcomes (permanent disability or death), as judged by original study authors and methods. We also analyzed malpractice payout ranks.

Heterogeneity was tested using a standard chi-square test using a significance level of alpha less than or equal to 0.10. We also examined heterogeneity across studies using an I-square statistic, and considered a value greater than 50 percent to indicate substantial heterogeneity.[44]

We calculated a mean error rate or serious misdiagnosis-harm rate by using a random-effects model with the DerSimonian and Laird formula in settings of low heterogeneity[45] or with appropriate analyses when there was higher heterogeneity.[46]

We considered study heterogeneity before all quantitative, meta-analytic syntheses were conducted. For example, we excluded from the primary analysis of KQ1's most frequent clinical conditions any results from exclusive, specialty EDs (e.g., eye and ear), since specialty EDs are non-representative with respect to the spectrum of clinical conditions. Likewise, we did not combine the error frequencies found in incident reports (i.e., reports that do not include a denominator) with reports of true error rates (i.e., reports that do include a denominator) in calculating overall error rates in the ED. Where specific studies used heterogeneous methods to define or capture diagnostic error in ways that might impact the measured results, we sought to

include in our synthesis the studies most likely to have both internal and external validity and described these specific choices for readers.

The error and harm rates, which are the focus of KQ2, may have been expressed differently in different studies. There was segregation in many studies between disease "present" and disease "absent" patients. Some studies presented results conditioned on the presence or absence of true disease (sensitivity/specificity), while others presented results conditioned on the presence or absence of the ED diagnosis rendered (positive/negative predictive value). To make the results as clear and informative as possible, we tried to synthesize the following parameters across disease-specific studies, as permitted by the types of data that were available:

- false negative rate (1-sensitivity) (denominator is disease present)
- false positive rate (1-specificity) (denominator is disease absent)
- false discovery rate (1-positive predictive value) (denominator is diagnosis label present)
- false omission rate (1-negative predictive value) (denominator is diagnosis label absent)
- total diagnostic error rate (1-accuracy for all patients [disease and non-disease])
- overall cohort-based rates of errors and harms per ED visit (e.g., 2 per 10,000 visits)

We used the metaprop command in Stata to meta-analyze these rates since they are technically proportions (see Appendix A for details on calculating the rates). We used the Freeman-Tukey double arcsine transformation to calculate the pooled estimate.[47] We used the exact binomial method to calculate the confidence intervals.[48]

We extrapolated to U.S. national estimates arithmetically. To estimate the total number of ED diagnostic errors per year, we multiplied total annual U.S. ED visits (based on Centers for Disease Control and Prevention data) by the best estimate of overall diagnostic error rate from KQ2. To estimate the total number of diagnostic adverse events, we multiplied total annual U.S. ED visits by the overall diagnostic adverse event rate from KQ2. To estimate the total number of serious misdiagnosis-related harms, we used two different methods. For the first method, we multiplied the total number of diagnostic adverse events by the serious harm proportion derived from KQ1 (using incident report data rather than malpractice claims). For the second method, we multiplied total annual U.S. ED visits by the misdiagnosis-related mortality rate from KQ2 to estimate misdiagnosis-related deaths; we multiplied misdiagnosis-related deaths by the disability-to-death ratio from KQ1 (incident reports) to estimate misdiagnosis-related serious, permanent disability before adding the two values (deaths plus severe disability) to get a total serious harms estimate.

For estimates of uncertainty in extrapolated values, we used 95 percent confidence intervals based on source data, where appropriate. For mathematical products, we were not able to provide statistically valid 95 percent confidence intervals since this would require statistical modeling techniques (e.g., Monte Carlo simulation) that were beyond the scope of the report. Instead, plausible range estimates were calculated by multiplying the lower bounds of corresponding confidence intervals together to get a lower plausible range bound and, similarly, by multiplying the upper bounds of corresponding confidence intervals together to get an upper plausible range bound. The impact of using this method is that plausible ranges are wider than corresponding 95 percent confidence intervals would be (i.e., they *overstate* the uncertainty).

For KQ3, we did not anticipate being able to aggregate mathematically specific key causal factors or risk predictors for diagnostic errors and serious misdiagnosis-related harms. Therefore, we used a high-level approach to synthesizing key causal factors into "cognitive" (e.g., faulty knowledge) and "systems" (e.g., technical or organizational issues) factors, which are often used to classify causes in the diagnostic error literature.[49] We grouped risk predictors for diagnostic

error as patient, illness, clinician, fixed facility or health system characteristics, or dynamic, context-specific systems factors. We then described common themes identified in each category.

We used STATA statistical software (Intercooled, version 14.2, StataCorp, College Station, TX) for all meta-analyses. We used STATA statistical software (Intercooled, version 16.1, StataCorp, College Station, TX) for confidence intervals in national extrapolations.

Studies that were not amenable to pooling were summarized qualitatively.

Grading the Strength of the Body of Evidence

We graded the strength of evidence (SOE) by adapting an evidence grading scheme recommended by the Guide for Conducting Comparative Effectiveness Reviews.[50] We assessed the bodies of evidence about diagnostic errors and serious misdiagnosis-related harms for each condition for KQ2.

We considered the number of studies, their study designs, the study limitations (i.e., risk of bias and overall methodological quality), the directness of the evidence to the KQ, the consistency of study results, the precision of any estimates of effect, the likelihood of reporting bias, other limitations, and the overall findings across studies. Based on these assessments, we assigned an SOE rating as being either high, moderate, low, or insufficient evidence to estimate an effect. In accordance with AHRQ guidance for describing treatment effects,[51] we used qualifying language when stating conclusions (i.e., "probably" for conclusion statements with Moderate SOE and "may" for conclusion statements with Low SOE). When evidence was inadequate to draw conclusions, we used 'no studies found' or 'insufficient,' as appropriate per current guidance.[52, 53]

Peer Review and Public Commentary

Experts in diagnostic errors and emergency medicine, and individuals representing stakeholder and user communities were invited to provide external peer review of this systematic review. AHRQ and an associate editor also provided comments. The peer-reviewed draft report was posted on the AHRQ website for 4 weeks to elicit public comment. We addressed all public reviewer comments, revising the text as appropriate, and documented everything in a disposition of comments report that will be made available 3 months after AHRQ posts the final systematic review on the Effective Health Care (EHC) website.

Results

Description of Included Evidence

We retrieved 19,127 unique citations from our searches (Appendix B). After screening all abstracts and 1,455 full-text studies, we included 279 studies. Appendix C provides a list of the articles excluded during the full-text screening. Details of the included articles, including our assessment of their risk of bias, are provided in the Evidence Tables in Appendix D. Our strength of evidence tables, which present details regarding our confidence in the estimates of the rate of diagnostic errors, can be found in Appendix D, Tables D-6 through D-8. The results of our grey literature search are presented in Appendix Table B-1.

Of the included studies, 41 listed the distribution of diseases associated with diagnostic error or misdiagnosis-related harms, 160 reported the rate of diagnostic error, and 185 examined the causes of diagnostic error. Five studies were randomized controlled trials[54-58] and the remainder were observational studies. Studies were conducted in the United States (n=137), Western Europe (n=85), Canada (n=28), the United Kingdom (n=14), Australia (n=12), or in multiple countries (n=3). Sixty-four studies were published before 2011 and 215 were published in 2011 or later. The majority of studies identified were disease-specific. Thus, relatively fewer studies were available to answer Key Question (KQ) 1, and answers to KQ2 and KQ3 included aggregation of literature on a per-disease basis.

Key Question 1. Distribution of Diseases

Key Points

- The top 20 diseases associated with diagnostic errors in the emergency department (ED) (independent of harm severity), in approximate rank order, were fracture, stroke, myocardial infarction, appendicitis, venous thromboembolism, spinal cord compression and injury, aortic aneurysm and dissection, meningitis and encephalitis, sepsis, traumatic brain injury and traumatic intracranial hemorrhage, arterial thromboembolism, lung cancer, ectopic pregnancy and ovarian torsion, pneumonia, testicular torsion, gastrointestinal perforation and rupture, spinal and intracranial abscess, open and non-healing wounds, cardiac arrhythmia, and intestinal obstruction (with or without hernia). It is likely that this list of misdiagnosed diseases is strongly skewed by reporting bias towards diseases that, when missed, lead to more serious harms and false negatives (as opposed to false positives).
- Missed fractures are the ED diagnostic errors most commonly reported in malpractice claims and incident reports, but the level of harm associated with most missed fractures is lower than that for missed major medical and neurologic events. Detection bias for radiographic misdiagnosis (which is more easily confirmed than other types of diagnostic error) likely contributes to their high frequency in claims and incident reports, but, even if overrepresented, they are still likely quite common given the high incidence of fractures.
- The top 15 diseases associated with the greatest number of serious misdiagnosis-related harms in the ED, in rank order, were (1) stroke, (2) myocardial infarction, (3) aortic aneurysm and dissection, (4) spinal cord compression and injury, (5) venous thromboembolism, (6/7 – tie) meningitis and encephalitis, (6/7 – tie) sepsis, (8) lung cancer, (9) traumatic brain injury and traumatic intracranial hemorrhage, (10) arterial

thromboembolism, (11) spinal and intracranial abscess, (12) cardiac arrhythmia, (13) pneumonia, (14) gastrointestinal perforation and rupture, and (15) intestinal obstruction. The top 3 conditions account for an estimated 28 percent of all serious harms from ED diagnostic error, while the top 8 account for 52 percent and the top 15 for 68 percent.

- The so-called "Big Three" disease categories (vascular events, infections, and cancers) account for an estimated 72 percent of all ED diagnostic errors resulting in serious misdiagnosis-related harms. However, major vascular events (42%) and infections (23%) substantially outnumber cancers (8%) in the ED clinical setting. Misdiagnosed trauma (11%), particularly craniospinal trauma linked to neurological injury, is also common.
- The top 5 organ systems with diseases linked to serious diagnostic error are neurologic (including stroke) (34%), cardiovascular (23%), pulmonary (8%), gastrointestinal (7%), and hematologic (including venous thromboembolism) (7%). Taken together, these account for an estimated 79 percent of all serious misdiagnosis-related harms in the ED.
- Among children in the ED, the distribution of misdiagnosed diseases is likely substantially different, with missed infections and fractures dominating over missed vascular events. Unusual conditions such as Kawasaki disease may be frequent among misdiagnosed diseases, although robust data from multiple sources are lacking.

Summary of Findings

There were 41 studies pertinent to Key Question (KQ) 1. Among these were 40 studies that reported on the most common diagnostic errors among patients presenting to the ED.[16, 17, 31, 59-96] There were 18 "numerator only" studies (including five based on malpractice claims,[17, 71, 84, 95, 96] two based on incident reports,[16, 31] and two based on mixed data sources[80, 90]) and 23 "numerator and denominator" studies" (20 cohort studies and 3 cross-sectional studies). Heterogeneity in disease categorization across studies hampered cross-study comparisons and meta-analysis.

When considering all diagnostic errors, including those that produce minimal patient harm, relatively little is known about the overall distribution of symptoms or diseases involved. This is because studies of diagnostic error distribution that address all diseases (i.e., not disease-, symptom-, or discipline-specific) generally rely on a triggering adverse event to identify cases (e.g., repeat visit or hospitalization, incident report, malpractice claim). Thus, more is known about disease distribution for diagnostic errors that result in adverse events, and little is known about the subset that result in minimal or minor harms. With that caveat noted, the top 20 individual diseases associated with diagnostic errors (independent of harm severity), in approximate rank order, were found to be fracture, stroke, myocardial infarction, appendicitis, venous thromboembolism, spinal cord compression and injury, aortic aneurysm and dissection, meningitis and encephalitis, sepsis, traumatic brain injury and traumatic intracranial hemorrhage, arterial thromboembolism, lung cancer, ectopic pregnancy and ovarian torsion, pneumonia, testicular torsion, gastrointestinal perforation and rupture, spinal and intracranial abscess, open and non-healing wounds, cardiac arrhythmia, and intestinal obstruction (with or without hernia). It is likely that this list of misdiagnosed diseases, derived from two large "numerator-only" studies (one malpractice-based and one incident report-based), is strongly skewed by reporting bias towards diseases that, when missed, lead to serious harms. It is also likely that the list is skewed towards false negatives (as opposed to false positives). Finally, it may also be partly skewed towards errors likely to be confirmed in hindsight by radiographic review, including both fractures and lung cancer, and skewed away from common conditions that may be frequently misdiagnosed (e.g., migraine[97]), but go unaccounted. The top 15 individual diseases associated

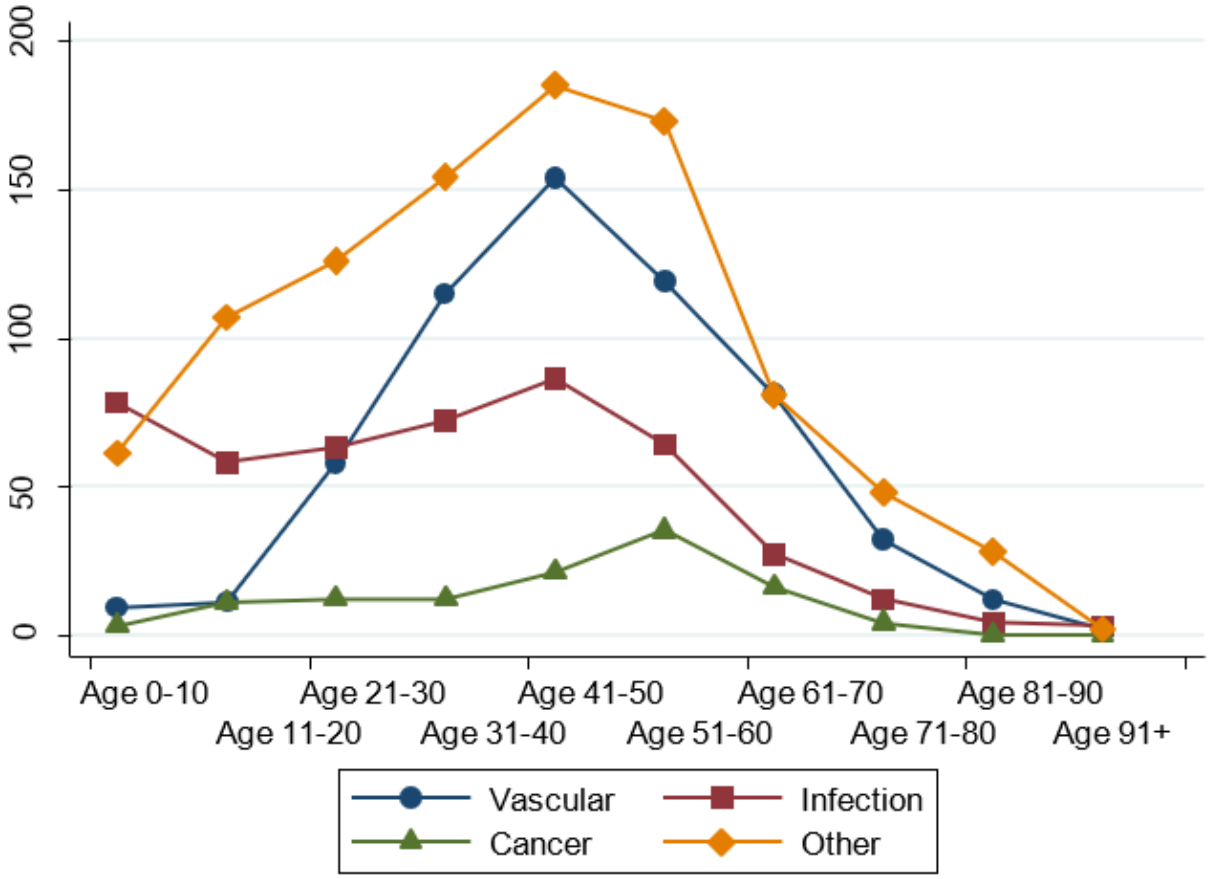
with serious misdiagnosis-related harms, in rank order, were found to be (1) stroke, (2) myocardial infarction, (3) aortic aneurysm and dissection, (4) spinal cord compression and injury, (5) venous thromboembolism, (6/7 – tie) meningitis and encephalitis, (6/7 – tie) sepsis, (8) lung cancer, (9) traumatic brain injury and traumatic intracranial hemorrhage, (10) arterial thromboembolism, (11) spinal and intracranial abscess, (12) cardiac arrhythmia, (13) pneumonia, (14) gastrointestinal perforation and rupture, and (15) intestinal obstruction. The top 3 conditions account for an estimated 28 percent (95% confidence interval (CI) 26 to 30) of all serious harms from diagnostic error in the ED, while the top 8 account for 52 percent (95% CI 49 to 55) and the top 15 for 68 percent (95% CI 66 to 71). This list is much more likely to be representative, because malpractice claims and incident reports, although clearly biased towards more severe adverse events, are likely fairly representative of the cases with poor health outcomes (i.e., serious harms). Fractures (#1 any severity) and appendicitis (#4 any severity) do not make the serious-harm list, since most associated harms are low- or medium-severity, not high-severity. It is possible that lung cancer is still overrepresented because the "proof" of error found in chest radiographs may be a key factor that helps ascertain the presence of an error or, alternatively, increases the odds of legal action.

Data were sparse with respect to the most commonly misdiagnosed clinical presentations (symptoms, signs, or syndromes). One small study based on malpractice claims (n=62) found that abdominal pain, trauma, and neurological symptoms topped the list.[95] The largest study of malpractice claims[17] found that neurological diseases were the most common, which implies that neurological symptoms are probably highly prevalent among malpractice claims. The relative frequency of misdiagnosed symptoms obviously varies by disease (e.g., stroke does not present with abdominal pain, and mesenteric ischemia does not present with headache). Multiple studies from the review demonstrated a strong link between specific symptoms and specific misdiagnosed diseases. Among these were dizziness/vertigo (strongly associated with missed ischemic stroke); headache (associated with missed ischemic stroke, subarachnoid hemorrhage, raised intracranial pressure, cerebral venous sinus thrombosis, and meningitis)[21, 64, 81]; abdominal pain (associated with missed myocardial infarction, aortic pathology, cancer, appendicitis, intestinal disorders, and ovarian pathology, among others)[60, 68, 70, 73, 76, 98]; and back pain (associated with missed spinal abscess and other causes of spinal cord compression, as well as other myelopathic disorders).[81, 99]

Regarding prospectively defined subgroups, data were insufficient to determine whether disease distributions meaningfully differed between the United States and countries outside the United States. Unsurprisingly, the spectrum of diseases seen in specialty EDs differed dramatically from that seen in general EDs. For example, key missed conditions in "eye" or "eye and ear" EDs leading to patient harm included uveitis and retinal detachment. There were fewer studies of admitted patients and only a subset identified the distribution of missed diseases; differences in disease groupings and result reporting made direct comparisons challenging.

The absolute frequency of malpractice claims of different diseases varies over the age spectrum (Figure 2). Among pediatric populations, dangerous diseases are, overall, less common than in adults, and, accordingly, serious misdiagnosis-related harms are also less common.[17] In particular, vascular events are less common than in adults, and missed fractures and infections (including missed appendicitis) predominate. Nevertheless, missed strokes and childhood cancers remain important causes in children, particularly older children. Missed testicular torsion may also be an important cause of misdiagnosis-related harms in the pediatric ED population. Child abuse is an important condition that is likely underrepresented in diagnostic error malpractice claims (see Representativeness of Malpractice Claims Data for Disease Distribution, below).

Figure 2. Age distribution of "Big Three" and other (non-Big Three) diseases among diagnostic error malpractice claims (any severity)*



* Emergency department-only subset of data from "Big Three" malpractice study (Newman-Toker et al., 2019[4]) via contact with authors

Key Question 1a. What diseases or syndromes are associated with the greatest total number and the highest risk of diagnostic errors or misdiagnosis-related harms?

For disease-agnostic data on diagnostic errors, major data sources are malpractice claims (numerator-only), incident reports (numerator-only), and stimulated chart reviews based on systematically identified unexpected or adverse outcome events (numerator-denominator). Systematic follow-up of patients, conducted routinely or as part of a prospective study, generally provides the strongest data (because contemporaneous data can be gathered, independent of the clinical record) but is rarely available. Malpractice claims are routinely captured by risk insurers, labeled as diagnostic error-related, and then thoroughly analyzed, making them a rich source of information on the distribution of diseases (KQ1) and causes (KQ3) of diagnostic error. Incident reporting systems sometimes permit labeling of incidents as a diagnostic error-related[100]; at the institutional level, their value is principally in identifying unexpected errors or latent risks, but regional or national incident reporting systems can also be used to identify the distribution of diseases (KQ1) and causes (KQ3) of diagnostic error.

There were nine studies[16, 17, 31, 59, 71, 80, 90, 95, 96] that addressed KQ1a directly for all diagnostic errors, reporting on a total of 5,817 diagnostic errors. The two largest studies, one a large, United States-based review of a national malpractice claims database (Newman-Toker, 2019[17]) and the other a large, United Kingdom-based review of a national incident reporting system (Hussain, 2019[16]) together represented 78 percent of the total number of diagnostic error cases (n=4,561 of 5,817). These two studies organized their categories in similar enough fashion to present results together (Table 2). In particular, Newman-Toker et al. used the Agency for Healthcare Research and Quality's standardized coding schema from the Clinical Classifications Software[101] to aggregate diagnosis codes into clinically sensible and comparably granular categories (something not done by most diagnostic error studies). Data provided by the original authors permitted reaggregation of data using the standardized coding schema for more than just the "Big Three" categories emphasized in the original report (i.e., the "non-Big Three" category was categorized here using the original method to identify comparably granular categories across all diagnostic error groups). They also provided further detail broken down by severity of harm to patients, enabling comparison of diseases causing higher- versus lower-severity harm to patients when misdiagnosed. Table 3 reports the diseases in rank order that cause serious misdiagnosis-related harms, as determined from the largest, most detailed study of ED malpractice claims (Newman-Toker, 2019).[17]

Missed fractures appear to be the ED diagnostic errors most commonly reported in malpractice claims and incident reports,[16, 31, 71, 80, 90] but the level of harm associated with most missed fractures is generally lower than that for missed major medical and neurologic events.[17] As a result, though they top the list of diagnostic errors identified (Table 2), they are not among the top 15 clinical conditions associated with serious misdiagnosis-related harms to patients (Table 3).

Table 2. Frequency of diagnostic errors from the two largest studies of all emergency department diagnostic errors

Condition (Listed in Estimated Rank Order From Mean Frequency Across Malpractice Claims and Incident Reports)*	U.S. Malpractice Claims % (n) [Rank] (n=2,273†)[17]	U.K. Incident Reports % (n) [Rank] (n=2,288)[16]	Mean % (n) [Estimated Rank]‡ Across Malpractice and Incident Reports
Fracture*	8.3% (188)* [2]	44.0% (1,007) [1]	26.2% (1,195) [1]
Stroke	9.4% (213) [1]	10.4% (237) [2]	9.9% (450) [2]
Myocardial infarction	6.0% (136) [3]	7.0% (161) [3]	6.5% (297) [3]
Appendicitis	5.0% (114) [5]	0.7% (17) [7]	2.9% (131) [4]
Venous thromboembolism	3.6% (81) [7]	2.0% (45) [4]	2.8% (126) [5]
Spinal cord compression/injury	5.3% (120) [4]	-	2.6% (120) [~3-6]‡
Aortic aneurysm/dissection	3.8% (86) [6]	0.8% (18)§ [6]	2.3% (104) [7]
Meningitis/encephalitis	3.1% (71) [8]	0.5% (11) [9]	1.8% (82) [8]
Sepsis	3.1% (70) [9]	-	1.5% (70) [~9-10]‡
TBI/traumatic intracranial hemorrhage	2.7% (62) [10]	-	1.4% (62) [~10-11]‡
Arterial thromboembolism	1.9% (44) [12]	0.7% (15) [8]	1.3% (59) [~11-13]‡
Lung cancer	2.5% (56) [11]	-	1.2% (56) [~10-13]‡
Ectopic pregnancy/ovarian torsion£	1.1% (25)£ [20]	1.4% (31)£ [5]	1.2% (56) [~12-14]‡
Pneumonia	1.9% (43) [13 tie]	0.3% (8) [10]	1.1% (51) [~13-16]‡
Testicular torsion	1.9% (43) [13 tie]	-	0.9% (43) [~15-17]‡
Gastrointestinal perforation/rupture	1.7% (39) [15]	-	0.9% (39) [~9-17]‡
Spinal & intracranial abscess	1.6% (37) [16]	-	0.8% (37) [~15-19]‡
Open/non-healing wound	1.6% (36) [17]	-	0.8% (36) [~13-20]‡
Cardiac arrhythmia	1.4% (32) [18]	-	0.7% (32) [~17-20]‡

Intestinal obstruction (+/- hernia)	1.1% (26) [19]	-	0.6% (26) [~15-20]‡
OTHER	33.0% (751)	32.3% (738)	32.6% (1,489)
TOTAL ERRORS	**100.0% (2,273)**	**100.0% (2,288)**	**100.0% (4,561)**
Acute abdomen (not aortic aneurysm)¥	*3.6% (82)*	*2.6% (59)§*	*3.1% (141)*

TBI = traumatic brain injury; U.K. = United Kingdom; U.S. = United States

* The category schemas across the two studies were similar but not identical. Results were combined, whenever possible, to match (e.g., pulmonary embolism plus deep vein thrombosis in Hussain combined to match the venous thromboembolism row of Newman-Toker). Where no matching could be performed, the absence of data is marked by a "-". Note that in the malpractice claims, there were 255 total fractures (11.2% of all diagnostic claims). Among these, the 188 non-craniospinal (157 limb fractures, 16 facial, 13 torso, 2 unnamed location) fractures are listed under "fractures" in the first row of the table. The remaining 67 craniospinal fractures were mostly accompanied by traumatic neurologic injuries (which also occurred in the absence of fractures), so those with fractures are incorporated into other rows with the corresponding traumatic injuries to the central nervous system --- 58 vertebral fractures, mostly with associated spinal cord injury (29 cervical, 15 thoracic, 11 lumbosacral, 3 unnamed location) and 9 skull fractures, mostly with associated traumatic intracranial hemorrhage.

† Data are drawn from the single largest malpractice claims-based analysis of ED diagnostic errors. Data in the original manuscript[17] were presented as combined across clinical settings (inpatient, ED, and clinic), but the original authors were able to provide data to the systematic review team on the ED-only subgroup for analysis.

‡ Estimated ranks for the conditions near the top of the rankings are far more certain than those listed near the bottom. Of those listed in the Top 8, only spinal cord compression/injury might be higher than #6 based on the two studies summarized. This category in the malpractice data includes vertebral fractures with spinal cord compression/injury; if the incident report data grouped that type of injuries as "fractures" then this would likely elevate spinal cord compression/injury up to a rank of #4 and potentially as high as #3 (if 18% or more of fractures reported were associated with spinal cord injury). By contrast, rankings from #9 to #20 are less certain. Most of these categories were available in Newman-Toker (U.S. malpractice claims) but not in Hussain (U.K. incident reports). Because these conditions could have been represented in the "Other" category of Hussain (or, in some cases, the "acute abdomen" category), the value carried forward from Newman-Toker represents a minimum value (i.e., assumes "0" from Hussain). Hussain reported their lowest single-disease value as n=8 for pneumonia; therefore, we made the simplifying assumption that no individual disease could have had more than n=7 within the "Other" category in Hussain (unless it was a disease likely to have caused an acute abdomen, in which case it could have been more [see footnote labeled "§" for explanation]). Thus, the range of estimated ranks shown in this last column reflect the possibility of various conditions "leapfrogging" up the rankings if there were a maximum plausible number of cases in "Other" or "Acute abdomen" of Hussain.

§ Hussain et al. report 77 cases of "acute abdomen" in their Table 1. They also report 18 cases of abdominal aortic aneurysm rupture in the manuscript text. Although not explicitly stated in the original manuscript, we assume here that these abdominal aortic aneurysm ruptures were included among the 77 cases grouped under the heading "acute abdomen," since the study's main table reports individual (ungrouped) events with 'n' less than 18, and no row for aortic aneurysm is listed in their Table 1. They did not list aortic dissection cases, so there could be some of these in the Hussain "Other" or "Acute abdomen" categories, but, most likely, there would have been 7 or fewer of these (as per the discussion in the previous footnote, labeled '‡'). We have subtracted these 18 cases from 77 to get n=59 residual acute abdomen (not abdominal aortic aneurysm) cases in Hussain to avoid double counting of cases for the purposes of disease rankings.

£ In Newman-Toker, ectopic pregnancies (n=19) were combined with ovarian torsion (n=6). In Hussain, only ectopic pregnancies were listed.

¥ The "acute abdomen" line is not a specific condition, so it is not listed in rank order with the individual diseases but instead is placed after the Total row. For data from Newman-Toker, the acute abdomen combines four categories (gastrointestinal perforation/rupture, intestinal obstruction, diverticulitis, peritonitis). Note that for the purposes of the Total row, the 59 cases from Hussain have been added to the "Other" diseases presented in Hussain (n=679) to get a new "Other" total of 738.

The list of top diagnostic errors independent of harm severity (i.e., any severity), as seen in malpractice claims and incident reports, is shown in Table 2 above. Fractures, stroke, myocardial infarction, appendicitis, and venous thromboembolism top the list. A reporting bias towards more severe outcomes almost certainly impacts this list (see "Representativeness of Malpractice Claims Data for Disease Distribution," below). It is unknown whether ascertainment and reporting biases linked to radiographic misdiagnosis (which is more easily confirmed and contested than other types of diagnostic error) lead to fractures being further overrepresented in malpractice claims or incident reports, but their high annual incidence (2 million ED cases per year in the United States, as of 2020, according to the National Electronic Injury Surveillance System [NEISS][102]) makes it likely that, even if overrepresented, they are still quite common. Additional information on possible overrepresentation of fractures is provided in the section below entitled, "Representativeness of Malpractice Claims Data for Disease Distribution."

What remains unknown when considering "all" diagnostic errors is the frequency of other misdiagnoses that are likely to be as or more common than fractures, yet less transparent. There is some evidence that certain non-radiographic errors causing lower-severity harms are probably grossly underrepresented in both absolute terms and relative to fractures. For example, there are now nearly 5 million ED visits for dizziness and vertigo in the United States annually. Based on known disease distributions, it is probable that more than 1 million of these patients have benign inner ear causes (mostly benign paroxysmal positional vertigo [BPPV] and vestibular neuritis). Diagnostic error rates for these benign conditions have been estimated to be over 80 percent.[103, 104] [A recently completed randomized clinical trial (AVERT NCT02483429), too new to be included in our search, found an 87 percent error/non-diagnosis rate for these disorders for the ED clinical team (with just 9 of 68 cases correctly diagnosed using all available data including neuroimaging and clinical consultation results) versus 26 percent error/non-diagnosis rate for a specialist (with 50 of 68 correctly diagnosed using only a brief history and eye movement recordings from the ED visit).][105] Thus, the total number of misdiagnosed benign inner ear cases is likely to exceed 800,000 per year, with more than 500,000 clearly preventable. By contrast, fractures are probably missed less than 5 percent of the time (see KQ2), so, given an estimated 2 million ED fractures per year in the United States from NEISS, the absolute number of missed fractures is likely to be fewer than 100,000 per year (and probably only about 20,000 per year, given the most likely estimate of the false negative rate for fractures is about 1% [see KQ2]). Despite over an order of magnitude more ED missed cases than fractures, inner ear diseases such as BPPV do not appear in any malpractice claim- or incident report-based "top 10" lists (while fractures routinely occupy the top-ranked spot in such lists, as they do in Table 2). There is no way to know how many other similar diagnostic error problems exist in the ED yet are not currently being tracked or reported, but it is probable that other commonly misdiagnosed diseases are missing (e.g., migraine[97]).

It strengthens and corroborates the evidence from both sources shown in Table 2 that the percentages for the two most common dangerous diseases (stroke and myocardial infarction) are nearly the same between these two data sources (U.S. malpractice claims[17] and U.K. incident reports[16]), and, although absolute frequencies differed (especially for fractures and appendicitis), the relative disease frequency rank order was fairly similar for the top 8 listed conditions. Appendicitis was the third most commonly identified condition after stroke and myocardial infarction in the U.S. claims-based study (Newman-Toker, 2019[17]), but harms were low- to medium-severity in 94 percent of cases, such that it was not part of the top 15 diseases associated with serious harms (Table 4). The serious harm frequency for appendicitis of 0.5 percent in the U.S. claims-based study (Newman-Toker, 2019[17]) was quite similar to the 0.7 percent in the U.K. incident report-based study (Hussain, 2019[16]). This would seem to suggest that the U.K. incident reporting system pulls for higher-severity harm events, similar to malpractice claims. However, the serious harm proportion in the U.K. incident report-based study (Hussain, 2019[16]) was much lower than in the U.S. claims-based study (Newman-Toker, 2019[17]) (15% versus 59%), suggesting otherwise. Also, the proportion of fractures (which are generally of lower severity) was much higher in the U.K.-based study. It is unclear whether these differences are methodological or real.

Table 3. Most common individual conditions causing serious misdiagnosis-related harms reported in ED malpractice claims*

Condition (Top 15 Ranked Diseases Based on Proportion of High-Severity Harm Malpractice Claims Cases) [Rank Based on Total Claim Payouts of Any Severity; Total Payout $ for This Condition, % of All Payouts n=2,273]	High-Severity Harm† Cases - % of Total (n) (% Death, % Disability)	Low-/Medium-Severity Harm† Cases - % of Total (n)
#1 Stroke [#1; $60M, 10.8%]	13.5% (179) (29, 71)	3.6% (34)
#2 Myocardial infarction [#3; $37M, 6.6%]	8.3% (110) (76, 24)	2.7% (26)
#3 Aortic aneurysm/dissection [#7; $25M, 4.5%]	6.1% (81) (89, 11)	0.5% (5)
#4 Spinal cord compression/injury [#2; $44M, 7.8%]‡	5.4% (72) (N/A)‡	5.1% (48)
#5 Venous thromboembolism [#9; $20M, 3.5%]	5.1% (68) (94, 6)	1.4% (13)
#6 Meningitis/encephalitis [#4; $34M, 6.1%]	4.7% (62) (52, 48)	0.9% (9)
#6 Sepsis [#8; $25M, 4.5%]	4.7% (62) (78, 22)	0.8% (8)
#8 Lung cancer [#10; $17M, 3.0%]§	3.9% (51) (56, 44)	0.5% (5)
#9 TBI/traumatic intracranial hemorrhage [#6; $27M, 4.8%]‡	3.6% (48) (N/A)‡	1.5% (14)
#10 Arterial thromboembolism [#16; $8M, 1.5%]	2.8% (37) (51, 49)	0.7% (7)
#11 Spinal/intracranial abscess [#5; $29M, 5.2%]	2.6% (34) (18, 82)	0.3% (3)
#12 Cardiac arrhythmia [#12; $11M, 2.0%]‡	2.2% (29) (N/A)‡	0.3% (3)
#13 Pneumonia [#11; $14M, 2.6%]	2.1% (28) (93, 7)	1.6% (15)
#14 Gastrointestinal perforation/rupture [#15; $10M, 1.7%]‡	1.6% (21) (N/A)‡	1.9% (18)
#15 Intestinal obstruction (+/- hernia) [#18; $6M, 1.0%]‡	1.4% (19) (N/A)‡	0.7% (7)
Top 15 Diseases (subtotal) [#1-12, 15-16, 18; $367M, 65%]	68.1% (901) (N/A)‡	22.6% (215)
OTHER£ (subtotal) [#13, 17, 19-42+; $194M, 35%]	31.9% (422) (N/A)‡	77.4% (735)
TOTAL HARMS†	**100% (1,323) (59, 41)**	**100% (950)**

ED = emergency department; N/A = not available; TBI = traumatic brain injury

* Data are drawn from the single largest malpractice claims-based analysis of ED diagnostic errors (n=2,273 from 2006-2015). Data in the original manuscript[17] were presented as combined across clinical settings (inpatient, ED, and clinic), but the original authors were able to provide data to the systematic review team on the ED-only subgroup for analysis. The other three general malpractice claims studies were all substantially smaller (sample sizes of 50, 65, 242) and analyzed data in a way that was non-comparable for a meta-analytic summary.[71, 95, 96] Although the data in this table reflect only a single, large study, the malpractice claims database from which these analyses derive (CRICO Comparative Benchmarking System) is a data source that is highly representative of U.S. malpractice claims. The data set includes 20 member insurers that contribute their malpractice claims for coding and comparative analysis and together represent about 30% of all claims in the United States.; cases come from all 50 states plus Washington, D.C. and Puerto Rico, and the overall distribution of cases in the database closely mirrors the findings from the National Practitioner Data Bank, which includes all claims (see original manuscript[17] [specifically Appendix A2]).

† Harm severity was defined on the National Association of Insurance Commissioners (NAIC) Severity of Injury Scale, a recognized industry standard. NAIC severity codes are organized on a nine-point scale ranging from 0 (legal issue only) to 9 (death). High-severity harms are grouped according to a standard low-medium-high schema that aggregates NAIC codes 6–9 as representing permanent, serious morbidity with mortality. Specifically, this includes as "high-severity" the following NAIC scores: 6 – permanent, significant injury (e.g., deafness, loss of single limb, loss of eye, or loss of one kidney or lung); 7 – permanent, major injury (e.g., paraplegia, blindness, loss of two limbs, or brain damage); 8 – permanent, grave injury (e.g., quadriplegia, severe brain damage, lifelong care, or fatal prognosis); and 9 – death, including fetal/neonatal death when the mother suffers lesser direct harm. In this report, we use the term "serious misdiagnosis-related harms" as synonymous with "high-severity" harms (i.e., NAIC scale scores 6-9).

‡ In response to feedback from reviewers and public commenters, the team re-analyzed source data from the study to delve more deeply into "non-Big Three" subcategories (i.e., other than vascular events, infections, and cancers). Raw data were recoded using the same basic approach taken in the original manuscript (i.e., based on Agency for Healthcare Research and Quality Clinical Classifications Software) (for additional details, see original manuscript[17] [specifically Appendix A3]). The result was 5 new conditions in the top 15 diseases that were not part of the original list of diseases that, when missed, lead to high-severity harms—spinal cord injuries, traumatic brain injuries, cardiac arrhythmias, gastrointestinal perforations, and intestinal obstructions. Because this analysis was performed in the final stage of the report, it was not possible to break down the proportion of death versus permanent disability for these conditions. Other conditions ranked outside the top 15 associated with high-severity harms included brain/spinal tumors (#16, 1.4%), fractures (#17, 1.3%), necrotizing fasciitis (#18, 1.2%), poisoning/toxicity (#19, 1.2%), and endocarditis/myocarditis (#20, 1.0%). Every other condition represented <1% of all high-severity harm malpractice claims.

§ Lung cancer was not one of the prespecified conditions, but, in this study of malpractice claims, it was the eighth ranked disease in terms of frequency of serious misdiagnosis-related harms, so is listed here among the top 15. As discussed in the text, lung cancer may be overrepresented in ED malpractice claims. It also likely reflects a very different type of ED diagnostic error than the others, since many cases likely reflect missed incidental lung nodules on imaging that eventually led to patient harm through diagnostic delay,[106] rather than immediate failures to diagnose acute, dangerous causes of symptomatic disease.

£ Non-craniospinal fractures (n=188, mostly limb fractures [n=157] – see Table 2 footnote "*" for additional details) are included

as part of "OTHER." They represent a substantial proportion of low/medium severity harm cases (18.0%, n=171/950), but a much smaller proportion of high-severity harm cases (1.3%, n=17/1,323). In this classification schema, vertebral fractures (n=58) appear as part of the grouping "spinal cord compression/injury" and skull fractures (n=9) appear as part of the grouping "TBI/traumatic intracranial hemorrhage." Craniospinal fractures are much more often associated with high-severity harms (52.2%, n=35/67) compared to non-craniospinal fractures (9.0%, n=17/188) ($P < 0.0001$).

Table 4. Proportion of misdiagnosis-related harms attributable to "Big Three" diseases reported in ED malpractice claims, broken down by high-severity versus low-/medium-severity harms*

Category	Condition (Diseases Grouped by "Big Three" Categories and Total Harms Broken Down by Organ System)	High-Severity Harm* Cases - % of Total (n)	Low-/Medium-Severity Harm* Cases - % of Total (n)
Big Three Disease Category Breakdown	**Big Three† (subtotal)**	**72.0% (952)**	**38.4% (365)**
	Vascular events	***41.5% (549)***	***10.9% (104)***
	Stroke	*13.5% (179)*	*3.4% (32)*
	Myocardial infarction	*8.3% (110)*	*2.7% (26)*
	Aortic aneurysm/dissection	*6.1% (81)*	*0.5% (5)*
	Venous thromboembolism	*5.1% (68)*	*1.4% (13)*
	Arterial thromboembolism	*2.8% (37)*	*0.7% (7)*
	OTHER vascular events	*5.6% (74) (each ≤ 2.2%)*	*2.2% (21)*
	Infections	***22.5% (298)***	***25.6% (243)***
	Meningitis/encephalitis	*4.7% (62)*	*0.9% (9)*
	Sepsis	*4.7% (62)*	*0.8% (8)*
	Spinal & intracranial abscess	*2.6% (34)*	*0.3% (3)*
	Pneumonia	*2.1% (28)*	*1.6% (15)*
	Necrotizing fasciitis	*1.2% (16)*	*0.5% (5)*
	OTHER infections	*7.3% (96) (each ≤ 1.0%)*	*21.4% (203)*
	Cancers	***7.9% (105)***	***1.9% (18)***
	Lung cancer	*3.9% (51)*	*0.5% (5)*
	OTHER cancers	*4.1% (54) (each ≤ 0.8%)*	*1.4% (13)*
	Non-Big Three† (subtotal)	**28.0% (371)**	**61.6% (585)**
	Trauma	***11.3% (149)***	***33.8% (321)***
	Other	***16.8% (222)***	***27.8% (264)***
	TOTAL HARMS	**100% (1,323)**	**100% (950)**
Major Organ System Breakdown	**Top 5 Organ Systems**	**78.6% (1040)**	**45.1% (428)**
	Neurologic (including stroke)	*34.1% (451)*	*14.9% (142)*
	Cardiovascular (not including stroke)	*22.8% (302)*	*6.1% (58)*
	Pulmonary	*7.6% (100)*	*3.1% (29)*
	Gastrointestinal	*7.1% (94)*	*18.8% (179)*
	Hematologic (including VTE)	*7.0% (93)*	*2.1% (20)*
	All Other Organ Systems‡	**21.4% (283)**	**54.9% (522)**
	TOTAL HARMS	**100% (1,323)**	**100% (950)**

VTE = venous thromboembolism

***** Data sources and definitions are the same as in Table 3.

† The "Big Three" diseases refer to vascular events, infections, and cancers, which, together, account for approximately three-fourths of all serious misdiagnosis-related harms in malpractice claims (Newman-Toker et al., 2019).[17]

‡ The top "other" organ system was musculoskeletal/joints, accounting for 3.5% (n=46/1,323) of high-severity harms and 25.7% (n=244/250) of low-/medium-severity harms. Note that craniospinal fractures with neurological injury are listed as "neurologic."

The largest and most comprehensive study evaluating severity of patient harms from diagnostic error is Newman-Toker, 2019.[17] This was a U.S.-based malpractice claims study (not restricted by age or disease, and representing nearly 30% of all U.S. national claims during the study period from 2006-2015) which found misdiagnosed stroke as the leading cause of serious misdiagnosis-related harms (i.e., severe disability or death), followed by myocardial infarction, aortic aneurysm/dissection, spinal cord compression/injury, venous thromboembolism, meningitis/encephalitis, sepsis, lung cancer, traumatic brain injury/traumatic intracranial

hemorrhage, arterial thromboembolism, spinal/intracranial abscess, cardiac arrhythmia, pneumonia, gastrointestinal perforation/rupture, and intestinal obstruction +/- hernia (Table 3).[17] As is apparent from Tables 3 and 4 (and the differences between these and Table 2), the list of conditions responsible for different severity harms is only partially overlapping. The top-ranked 15 conditions causing serious harm account for 68.1 percent of the high-severity harms but only 22.6 percent of the lower-severity harms. Fractures and appendicitis, which are commonly mentioned (particularly in studies of diagnostic errors in children), do not make the top 15 associated with high-severity harms despite being major contributors to lower-severity harms.

The so-called "Big Three" disease categories (vascular events, infections, and cancers) account for an estimated 72 percent of all ED diagnostic errors resulting in serious misdiagnosis-related harms. However, major vascular events (42%) and infections (23%) substantially outnumber cancers (8%) in the ED clinical setting. Misdiagnosed trauma (11%), particularly craniospinal trauma linked to neurological injury, is also common. The top 5 organ systems with diseases linked to serious diagnostic error are neurologic (including stroke) (34%), cardiovascular (23%), pulmonary (8%), gastrointestinal (7%), and hematologic (including venous thromboembolism) (7%). Taken together, these account for an estimated 79 percent of all serious misdiagnosis-related harms in the ED (Table 4).

Total malpractice claim payouts may be important for prioritization at the institutional level. The range across the top 10 most costly diseases (including claims of any severity, 2006-2015) was from $17 million for lung cancer (#10 in payouts) to $60 million for stroke (#1 in payouts) (Table 3). Four other neurological conditions led to disproportionately high payouts when missed, causing their payout-based rank to rise above their high-severity harm frequency-based rank—spinal cord compression/injury (from #4 to #2, $44M), meningitis/encephalitis (from #6 to #4, $34M), spinal and intracranial abscess (from #11 to #5, $29M), and traumatic brain injury/traumatic intracranial hemorrhage (from #9 to #6, $27M). Taken together, these five neurological conditions accounted for 30 percent of high-harm ED cases (ranks #1, 4, 6, 9, 11) and 35 percent of total payouts (ranks #1, 2, 4, 5, 6). Most (8 of 10) of the medical conditions making up the remainder of the top conditions associated with serious harm had lower payout ranks than their frequency ranks for high-severity harms. This suggests neurological injuries led to worse patient outcomes (and, in particular, a higher proportion of severely disabling outcomes, as expected).

We reviewed other published malpractice claims reports and grey literature reports from major medical liability insurance carriers or similar risk management entities (Appendix Table B-1). Only one provided data on claims specific to the ED setting and used a roughly comparable disease categorization process (Troxel, 2014).[96] These results, published in a quarterly report by The Doctor's Company, found that 58 percent of their ED claims (n=242/414) were diagnosis-related. They did not stratify their findings based on harm severity and listed only the top six conditions (fracture 13%, stroke 13%, myocardial infarction 5%, meningitis 5%, appendicitis 2%, spinal abscess 2%); nevertheless, the list appears to be quite similar to results obtained from the 9.3-fold larger CRICO Comparative Benchmarking System database analysis (n=2,273).

The U.K. incident report study (Hussain, 2019) reported that among 877 (38%) of cases with sufficient data to assess outcome severity, the distribution was no harm (20%), mild harm (52%), moderate harm (14%), severe harm (4%), and death (10%).[16] Among 128 cases with severe harm or death, frequent diagnoses included abdominal aortic aneurysm (n=18, 14%), intracranial bleed (a subtype of stroke) (n=15, 12%), and pulmonary embolus (n=8, 6%). This top three of high-severity misdiagnosis-related harms presented by Hussain et al. matches three of the top five

conditions from the high-severity U.S. malpractice claims. Myocardial infarction did not make the Hussain top-harms list, despite being substantially ahead of aortic aneurysm and pulmonary embolus on the overall (regardless of harm severity) frequency list from Hussain. This could indicate that serious harm from myocardial infarction is overrepresented among U.S. malpractice claims (see below on "Representativeness of Malpractice Claims Data for Disease Distribution").

A smaller incident report study (Okafor 2016) found similar overall disease distributions to those from malpractice claims shown in Table 4. The proportion of claims attributable to the "Big Three" (both high-severity and low-/medium-severity) is 58 percent (Table 4). When cases reported in Okafor (n=214) are tabulated and classified into the "Big Three" disease categories, together these three groups accounted for 55 percent of incident reports (33% vascular, 21% infection, 1% cancer, 45% other).[31] These overall similarities across studies, study teams, and methods further bolster the validity of findings presented in Tables 2 through 4.

Differences in Disease Distribution by Prespecified Subgroups

We attempted to assess whether disease distributions differed by prespecified subgroups for KQ1. These included comparison between U.S.-based and non-U.S. based studies; patient age group (children younger than 18 years of age versus adults aged 18 years or older; and, within the adult population, adults younger than 65 years of age versus adults aged 65 years or older); ED type (general versus specialty ED [e.g., psychiatric, eye and ear]); and ED disposition (ED discharges versus admissions versus transfers).

Differences by Country of Study Origin

We identified 6 studies conducted in the United States[17, 31, 59, 90, 95, 96] and 3 studies conducted outside of the United States.[16, 71, 80] Unfortunately, it was not possible to draw any strong conclusions based on country of study origin because very few studies addressed disease distribution in directly comparable ways. As described above and shown in Table 2, there were strong similarities in the disease distributions between U.S. malpractice claims and U.K. incident reports, at least for the most commonly identified errors and harms. It was noteworthy that the one non-U.S. study of closed claims, based out of the Netherlands, found 78 percent of cases to be associated with missed fractures or related musculoskeletal injuries[71]; this was substantially higher than what was found in U.S.-based studies, where fractures or other traumatic injuries represented just 10 to 20 percent of cases.[17, 95, 96] It is unknown whether this apparent difference relates to differences in study methodology or to international differences in the mechanisms for malpractice claims to be filed.

Differences by Patient Age Group

We identified one study conducted among pediatric populations,[90] none among adult populations, four among multiple age groups or populations not restricted by age,[17, 59, 80, 96] and four among populations where the patient age was unclear or not reported.[16, 31, 71, 95] While meta-analytic comparisons were hampered by study differences in design and reporting, there were clear differences in disease distribution by age group. These were most clearly illustrated in the largest U.S.-based malpractice claims study, as shown above in Figure 2 and below in Table 5.

Table 5. Variation in diagnostic error malpractice claims (any severity) by patient age decile*

Decade of Life	Vascular	Infection	Cancer	Other	TOTAL†
Age 0-10	9 (1.5%)	78 (16.7%)	3 (2.6%)	61 (6.3%)	151 (7.1%)
Age 11-20	11 (1.9%)	58 (12.4%)	11 (9.6%)	107 (11.1%)	187 (8.7%)

Decade of Life	Vascular	Infection	Cancer	Other	TOTAL†
Age 21-30	58 (9.8%)	63 (13.5%)	12 (10.5%)	126 (13.1%)	259 (12.1%)
Age 31-40	115 (19.4%)	72 (15.4%)	12 (10.5%)	154 (16.0%)	353 (16.5%)
Age 41-50	154 (26.0%)	86 (1%)	21 (18.4%)	185 (19.2%)	446 (20.9%)
Age 51-60	119 (20.1%)	64 (13.7%)	35 (30.7%)	173 (17.9%)	391 (18.3%)
Age 61-70	81 (13.7%)	27 (5.8%)	16 (14.0%)	81 (8.4%)	205 (9.6%)
Age 71-80	32 (5.4%)	12 (2.6%)	4 (3.5%)	48 (5.0%)	96 (4.5%)
Age 81-90	12 (2.0%)	4 (0.9%)	0 (0%)	28 (2.9%)	44 (2.1%)
Age 91+	2 (0.3%)	3 (0.6%)	0 (0%)	2 (0.2%)	7 (0.3%)

* Emergency department-only subset of data from "Big Three" malpractice study (Newman-Toker et al., 2019[17]) via contact with authors.

† Column totals add up to less than 2,273 because some patients had unknown age.

There are fewer ED diagnostic error-related malpractice claims among children (<18 years old, 13%) than among adults (18 years or older, 87%). This is mainly because there are fewer pediatric ED patients (about 30 million, 20-25%[107]) than adult ED patients (about 100 million, 75-80%). However, this incompletely accounts for the difference. Table 5 shows that there are proportionately fewer claims per age decile for those ages 0-20 (8%) versus for those ages 21 and older (11%). When considering adults ages 21-60 (for whom age-related mortality has not appreciably reduced the general population),[108] the difference is even larger (17%, ratio about 2:1 for claims in adults versus children). A similar difference in the epidemiology of malpractice claims per population has been reported previously (for all claims, not restricted to diagnostic errors or ED care) using the National Practitioner Data Bank, which showed 5.6 claims per 100,000 population for children versus 10 claims per 100,000 for adults (ratio about 2:1 for claims in adults versus children),[109] so is unlikely to represent a bias in CRICO data. Although all malpractice claims are less frequent in pediatric populations, the plurality (48%) of claims are still diagnosis related (as in adults), and 58 percent occur in the ED setting.[110] Although this absolute frequency difference between children and adults could be accounted for by a lower likelihood of a lawsuit being brought when the patient is a child, this seems highly improbable; if anything, one would suspect just the opposite, since legal actions are disproportionately sought when the severity of adverse outcomes is greater[111] (as would be the case for a child who might otherwise have a "full life to live" were it not for a devastating medical misdiagnosis). The greater likelihood of a lawsuit being brought when the claimant is a child is supported by data from the National Practitioner Data Bank showing higher payouts in pediatric than adult cases, with the highest payouts occurring among the youngest children and the lowest payouts among the oldest adults.[109] Some specific data on the relative frequency of claims, such as those related to lung cancer misdiagnosis in the ED, appear to confirm the general suspicion of a higher likelihood that cases will be brought when patients are younger (see Representativeness of Malpractice Claims Data for Disease Distribution, below).

This leaves two possible explanations—either (a) diagnostic errors are less frequent among children (e.g., because they have less medical comorbidity, so are less "complex") or (b) harms are less frequent among children (e.g., because they are less often impacted by life-threatening diseases or are more medically resilient when such diseases are present). The rate of diagnostic errors in pediatric acute care settings (5.0%)[112] is close to that estimated for the aggregate ED setting (5.7%, see KQ2), suggesting explanation "a" is less likely. Explanation "b" makes sense and corresponds best to the data shown in Figure 2, which show that diagnostic error claim frequency roughly mirrors the relative prevalence of dangerous disease groups in children versus adults (higher prevalence of infections and lower prevalence of vascular events and cancer). Thus, to summarize, there appear to be fewer total (absolute) misdiagnosis-related harms among

children, most likely because they are fewer in number (total population), visit the ED less frequently, and less often have a dangerous underlying cause; there is less evidence to support the contention that the rate of diagnostic errors is lower or that harms occur less frequently (or are less severe) when a misdiagnosis occurs and an underlying dangerous cause is present.

Overall, among children, vascular events are less prevalent than in adults while missed fractures and infections (including missed appendicitis) tend to predominate.[17, 90] As shown in Table 5 with results by age decile, the largest malpractice claims-based study (Newman-Toker, 2019) found that infections accounted for 52 percent in the 0-10 age group and 31 percent in the 11-20 age group. Authors grouped fractures with "other" diseases, but a review of source data from the authors found that, among children under age 18, fractures accounted for just 9 percent (n=25 of 269) of diagnostic error malpractice cases of any harm severity and 7 percent (n=4 of 54) of those resulting in high-severity harms. In a smaller study of pediatric diagnostic error malpractice claims, 24 percent (n=12 of 50) were fractures.[84] Studies in pediatric populations using other methods showed some degree of concordance (i.e., a relative preponderance of infections), but were not directly comparable because of differences in design and disease categories. One cohort study of patients admitted from the ED, in particular, from Children's Hospital (Boston, Massachusetts) looking at 10 predefined conditions (notably not including fracture) found the most common of the 10 diseases (regardless of error) were appendicitis (53%), pancreatitis (14%), and sepsis (10%) (n=2,151).[82] However, the most frequent diagnostic errors (total n=67) occurred with Kawasaki disease (25 percent diagnostic errors [n=17 of 67]; 9% of cases [n=194 of 2,151]), followed by pancreatitis (24% diagnostic errors; 14% of cases) and septic arthritis (18% of diagnostic errors; 8% of cases). The list of diagnostic error frequency after that was appendicitis (10%), sepsis (9%), stroke (including cerebral venous sinus thrombosis) (6%), ovarian torsion (4.5%), and hemolytic uremic syndrome (3%). The diseases with the highest ratio of diagnostic error proportion to overall prevalence were hemolytic uremic syndrome, stroke, and Kawasaki disease. Since this study was conducted at a quaternary care referral center and the age ranges of patients included was not reported, it is unclear the extent to which results are representative of all ED diagnostic errors among children.

Differences by ED Type

We identified two studies conducted in specialty EDs: one an eye and ear ED[79] and one an orthopedics ED for minor injuries.[83] The remainder were general EDs or did not report the ED type. Given the limited number of studies in specialty EDs, no meta-analysis could be performed. However, as expected, the distribution of diagnostic errors differed dramatically from those seen in general EDs. Unsurprisingly, missed conditions at the "eye and ear" ED leading to patient harm included uveitis, retinal detachment, and corneal abrasion, while all the diagnostic errors at the orthopedic ED were reported to be musculoskeletal.

Differences by ED Disposition

Although data are limited, the distribution of diseases frequently misdiagnosed in admitted patients may be distinct from that among discharged patients. For disease-specific studies, patients admitted were usually "overcalls" (e.g., false positive diagnosis of a dangerous disease such as migraine mistaken for stroke) while patients discharged were "undercalls" (e.g., false negative diagnosis of a dangerous disease such as stroke, misattributed to inner ear disease). However, this is what would necessarily be expected from a disease-specific study by design, so does not speak directly to any possible differences in disease distribution.

We identified only two disease-agnostic studies that addressed diagnostic error among patients admitted via the ED, both European.[62, 75] The first, from Spain, found 42 errors among 669 admissions (6.3%) with the most frequent misdiagnoses being infections (pneumonia, bronchitis, and tuberculosis) and vascular events (pulmonary embolism and heart failure).[75] The second, from Switzerland (Peng, 2015), looked at a specific subset of patients presenting to the ED with non-specific symptoms and modest illness severity (Emergency Severity Index scores of 2 or 3).[62] They found 309 ED diagnostic errors among 573 admissions (54%), only 53 of which were corrected during the hospitalization, with the others discovered through follow-up. This high rate of error may have been due to differences in error definition (based on 30-day follow-up rather than end of hospitalization) or, more likely, a function of the narrowly defined "non-specific symptoms" cohort included in the Swiss study. Among the 309 errors, 211 were coded as "missed" diagnoses in the ED, while others were listed as secondary diagnoses in the ED but were later determined to be primarily responsible for the initial clinical presentation. The most frequent correct final diagnoses (n missed/n total) were urinary tract infection (26/49), electrolyte disorders (19/40), pneumonia (12/37), functional impairment (30/34), renal failure (20/33), malignant neoplasm (14/32), heart failure (14/26), intoxications (16/24), dementia (13/23), depression/anxiety (17/20), orthostasis (10/19), and dehydration (8/17).

Representativeness of Malpractice Claims Data for Disease Distribution

It is known that malpractice claims data represent a biased sample of cases, so it is then reasonable to consider whether bias(es) might influence the distribution of diseases represented in this report. In particular, claims are known to be biased towards higher-severity harms[17]; this is self-evident from Tables 3 and 4, since high-severity harms are relatively rare, yet among the malpractice cases there are more high-severity harm cases than low- and medium-severity harm cases combined. This is further reinforced by the much higher fraction of high-severity harms in the malpractice claims than in the large incident report study described above (58%[17] versus 15%[16]). It is uncertain what additional biases may be at work, but results from the systematic review do suggest that some specific biases in the malpractice claims data may be present.

It has previously been suggested that diseases with tangible clinical artifacts from the encounter (e.g., radiographs showing missed incidental findings, such as a lung nodule on chest X-ray) make it easier to bring a legal action, leading to overrepresentation of cancer cases in claims, which does appear to be the case in primary care settings.[17] It is possible that this may partially account for the relatively high number of lung cancer cases among ED claims, particularly given the high frequency of obtaining chest imaging in the ED (relative to other types of imaging likely to disclose cancers of the breast, prostate, colon, or other malignancies).

It is unknown the extent to which the same bias might lead to overrepresentation of fractures among ED claims. As mentioned above, there are about 2 million ED cases of fractures per year in the United States, as of 2020, according to the NEISS.[102] With a maximum plausible error rate of 5 percent and a more probable estimate of about 1 percent (see KQ2, Fractures), there are likely no more than 100,000 missed ED fractures per year and probably closer to 20,000 per year in the United States. By contrast, there are an estimated 800,000 strokes and likely 400,000 transient ischemic attacks (TIA) each year in the United States; with a meta-analytically summarized error rate of 17% (see KQ2), this suggests there are roughly 200,000 missed cerebrovascular events annually. In Table 2, fractures outnumber strokes 1.3-fold in U.S.-based malpractice claims and 4.2-fold in U.K.-based incident reports. It is hard to imagine how this discrepancy can be explained other than to suggest missed fractures are overrepresented relative

to missed strokes in these data sets. One possible cause, alluded to in the prior paragraph, is the presence of verifiable evidence of the diagnostic error through re-examination of radiographs.

Given that only 1.5 percent of myocardial infarctions are missed, it is possible that missed heart attacks may also be overrepresented in malpractice claims relative to their population prevalence. In terms of population annual incidence, heart attacks and strokes are very similar in the United States,[113] and the rate of missed stroke (17%) is roughly an order of magnitude higher than that for heart attacks, yet there are only 1.5-fold more strokes in claims than there are heart attacks. We speculate here that the rationale could be that "standard of care" expectations are now so high for heart attacks that any missed case probably crosses the legal threshold for care to be considered "sub-standard." Alternatively, missed strokes could be underrepresented for the opposite reason—because successful legal claims may be infrequent when overall misdiagnosis rates are high (e.g., stroke manifesting with clinical dizziness or vertigo, where error rates are estimated to be roughly 40%,[21, 103, 114-116] yet claims cases are fewer than expected[117]). In such cases, if the "standard of care" is effectively to miss (rather than detect) a stroke, a course of legal action may be pursued less often or only infrequently lead to a paid claim. If malpractice data are used to track diagnostic error rates or disease distributions, it will be important to conduct further research into the types, direction, magnitude, and frequency of such biases.

Age-related biases are also a possibility, at least for some diseases. Figure 2 and Table 5 show that the peak age of incidence of missed cancer in malpractice claims is 51-60 years of age, and most of this reflects lung cancer (46% of 122 cases) with the next most common being brain/spinal tumors (19%), hematologic malignancies (8%), and colorectal cancer (7%). However, the peak incidence of cancer cases is 65-74 years, with 71 percent of cases occurring over age 65.[118] If the principal mechanism by which lung cancer is missed in the ED is via missed incidental lung nodules on chest X-ray,[106, 119] then there is no specific reason why this should occur with greater frequency in younger patients than older ones—if anything, they should have less lung pathology that interferes with radiographic interpretation. This suggests a likely age bias to file a legal claim when the patient is younger, rather than older. It is unknown whether this sort of bias may explain some of the skewed distribution in Figure 2 and Table 5 towards more claims among younger and middle-aged patients, who have a lower incidence of dangerous diseases relative to their older counterparts; the alternative explanation is that misdiagnosis is more frequent because younger patients are not thought likely to have dangerous diseases (e.g., stroke).[64] Child abuse (non-accidental trauma) is a special case in which misdiagnoses are unlikely to result in malpractice claims, even if the underlying problem does result in serious harm to the child, since the abuser (often a parent) is unlikely to draw attention to the underlying cause via a legal claim. Also see KQ1, Differences by Patient Age Group, for additional consideration of potential biases related to pediatric claims.

Other biases could be at work that are not readily apparent from the available literature. For example, disadvantaged or vulnerable populations (e.g., those who are differently abled, racial or ethnic minorities, lower health literacy, lower socioeconomic status, prisoners, immigrants) might be more likely to be misdiagnosed and less likely to file a legal claim. However, we could find no specific evidence to suggest that this would likely impact the distribution of diseases for KQ1. In particular, it is important to note that there was close alignment between the list of diseases from malpractice claims and those reported in diagnostic safety incidents (Table 2), which argues fairly powerfully against a major disease maldistribution based on claims data.

Key Question 1b. Do results vary based on the severity of any resulting misdiagnosis-related harms (e.g., death or permanent disability, as opposed to less serious harms)?

Twelve out of 40 studies reported misdiagnosis-related harms.[16, 17, 31, 61, 74, 75, 80, 83, 86, 87, 89, 92] Many of these studies (6 out of 12) did not report harms related to specific disease categories but rather across all diseases in the cohort.[16, 31, 61, 75, 80, 92] As described above, the clearest data on this point come from a single, large, U.S.-based malpractice claims study.[17] It is clear from the data presented in Tables 2 and 3 that the distribution of diseases responsible for serious misdiagnosis-related harm differs from those responsible for any misdiagnosis-related harm. Serious harms are caused disproportionately by missed vascular events and severe infections, while less severe harms are caused disproportionately by "non-Big Three" diseases (Table 4), including fractures and some infections with fewer high-severity adverse outcomes when missed (e.g., appendicitis).

The same malpractice claims study also provides evidence that, among those with serious misdiagnosis-related harms, the distribution of underlying diseases in those suffering death differs somewhat from the distribution of underlying diseases in those suffering permanent disability. Specifically, the top three causes of death are myocardial infarction, aortic aneurysm or dissection, and venous thromboembolism. By contrast, the top three causes of permanent, serious disability are stroke, spinal cord compression/injury, and meningitis/encephalitis. This pattern is expected, with serious adverse outcomes from major cardiovascular disease principally being death and those from major neurologic disease principally being permanent disability.

Key Question 1c. What are the most common clinical presenting symptoms or signs associated with diagnostic errors or misdiagnosis-related harms in the ED?

In malpractice claims, the top clinical presentations associated with diagnostic error may be neurological symptoms, abdominal pain, and trauma, but data are sparse.[72, 95] A high frequency of neurological symptoms is made more likely by the fact that diseases affecting the central nervous system are the most common diseases associated with serious misdiagnosis-related harms (34% of all ED serious harms, representing the #1 organ system involved [Table 4]). In addition, based on studies of specific diseases, it appears likely that the most common symptoms associated with misdiagnosis vary substantially by disease[21, 63, 64, 77, 94] and also by age group.[78, 94]

Key Question 1d. Do the most common clinical presenting symptoms or signs associated with diagnostic error or misdiagnosis-related harms vary by disease or syndrome?

In addition, based on studies of specific diseases, it appears likely that the most common symptoms associated with misdiagnosis vary substantially by disease[21, 63, 64, 77, 94] and also by age group.[78, 94] As clarified in KQ3, "atypical" symptoms for a given disease consistently increase risk for diagnostic error. Table 6 highlights the most common "atypical" presenting symptoms and related misdiagnosed diseases identified in this analysis, by symptom. Table 7 highlights the most common "atypical" symptoms, by disease. We found limited data on the relationship between presenting symptoms and harms, other than to note that those with "atypical" symptoms often have milder forms of disease, leading to the "misdiagnosis is protective" paradox (KQ2).

Table 6. Most common "atypical" presenting symptoms and related misdiagnosed diseases

Atypical Presenting Symptoms*	Final Diagnosis After Delay or Missed Diagnosis
Abdominal pain	Myocardial infarction,[65, 76] aortic aneurysm/dissection,[68, 73] appendicitis, diverticulitis, ovarian disease, gallbladder pathology, cancer[60, 70]
Altered mental status/confusion	Stroke,[64, 66, 67, 85, 88] sepsis[67, 94]
Back Pain	Spinal abscess or other spinal cord compression, myelitis, aortic aneurysm/dissection[68, 81]
Dizziness/vertigo	Stroke[64, 66, 69, 87, 88]
Dyspnea/shortness of breath	Myocardial infarction,[65, 76] aortic aneurysm/dissection[68, 73]
Fatigue/malaise/generalized weakness	Myocardial infarction,[65] stroke,[64, 66] sepsis[94]
Fever	Sepsis,[78, 93, 94] aortic aneurysm/dissection (aortitis)[68]
Gait disturbance	Stroke[64, 66, 85, 87]
Headache	Stroke,[64, 66, 69, 87, 88, 91] (other diseases with headaches as a more "typical" presentation include subarachnoid hemorrhage, meningitis/encephalitis, raised intracranial pressure, and giant cell arteritis[81])
Nausea/vomiting	Stroke,[64, 66, 87] appendicitis,[60, 70] myocardial infarction[65, 76]
Syncope/fall	Myocardial infarction,[65] aortic aneurysm/dissection,[68, 73] venous thromboembolism, stroke[64, 66, 69, 87, 88]

* Symptoms are listed in alphabetical order since the literature review did not support a relative placement in the list.

Table 7. Most common dangerous conditions presenting with "atypical" symptoms

Diagnosis	Atypical Presenting Symptoms
Stroke[64, 66, 69, 85, 87, 88, 91]	Headache, dizziness/vertigo, altered mental status/confusion, gait disturbance, nausea/vomiting
Myocardial infarction[65]	Syncope/fall, nausea/vomiting, fatigue/malaise/generalized weakness, altered mental status/confusion, dyspnea
Aortic aneurysm and dissection[68, 73]	Fever (aortitis), no pain or mild pain, abdominal pain, syncope, dyspnea, back pain
Sepsis[78, 93, 94]	Weakness/fatigue, altered mental status (elderly), fever (children)

Key Question 2. Rates of Diagnostic Errors

Key Points

- We estimate a weighted average overall diagnostic error rate of 5.7 percent (95% CI 4.4 to 7.1) per ED visit. The overall representativeness of this estimate for ED care is uncertain, but the figure is not outside the range expected based on disease-specific error rates.
- Variation in diagnostic error rates by disease were striking with the lowest per-disease diagnostic error rate seen for myocardial infarction (false negative rate 1.5%) and the highest seen for spinal abscess (false negative rate 56%). Most of the top harm-producing dangerous diseases are initially missed at rates of 10 to 28 percent, and there is roughly an inverse relationship between annual disease incidence and diagnostic error rates.
- An estimated overall misdiagnosis-related harm rate of 2.0 percent (95% CI 1.0 to 3.6) per ED visit comes from one rigorous, prospective study. Retrospective trigger-based studies included many more ED visits and often reported much lower rates, but this was almost certainly due to systematic under-ascertainment from retrospective methods.
- An estimated overall misdiagnosis-related death rate of 0.2 percent (plausible range [PR] 0.1 to 0.4) per ED visit comes from the same prospective study. This value is corroborated by estimates derived from another high-quality prospective study of admitted ED patients, which found an absolute mortality increase of 4.8 percent (2.4-fold

relative increase) and, when combined with data on preventable deaths measured among ED discharges, yields a similar blended total mortality rate estimate (0.19% to 0.29%).

- We estimated an overall serious misdiagnosis-related harms rate of 0.3 percent (PR 0.1 to 0.7) by averaging the results of two arithmetic calculations (one based on the proportion of adverse events that are serious and the other based on the mortality rate per ED visit combined with the ratio of disability to death among those with serious harms). This estimate reflects the combination of permanent, high-severity morbidity plus mortality.
- Data on disease-specific health outcomes associated with diagnostic error were limited, and many were incorrectly reported as null effects (or even "protective" effects) without proper severity matching (or adjustment) from the time of initial clinical presentation. Nevertheless, our meta-analysis found an increase in mortality associated with diagnostic error for aortic dissection (21%, 95% CI 6 to 37) and individual studies reported increases for stroke, venous thromboembolism, and arterial thromboembolism (mesenteric ischemia).
- If generalizable to all ED visits in the United States (130 million), best available evidence suggests there are over 7 million ED diagnostic errors, over 2.5 million diagnostic adverse events with preventable harms, and over 350,000 serious misdiagnosis-related harms, including more than 100,000 serious, permanent disabilities and 250,000 deaths. This is equivalent to a diagnostic error every 18 patients, a diagnostic adverse event every 50 patients, a serious harm (serious disability or death) about every 350 patients, and a misdiagnosis-related death about every 500 patients. Put in terms of an average ED with 25,000 visits annually and average diagnostic performance, each year this would be over 1,400 diagnostic errors, 500 diagnostic adverse events, and 70 serious harms, including 50 deaths.

Summary of Findings

Relatively less is known about the overall diagnostic error rate than the misdiagnosis-related harms rate. This is because studies of diagnostic error frequency that seek to address all diseases (i.e., are not disease-, symptom-, or discipline-specific) generally rely on a triggering adverse event to identify cases (e.g., repeat visit or hospitalization, incident report, malpractice claim). Thus, more is known about frequency for diagnostic errors that result in adverse events, and far less is known about the frequency of those that result in minimal or minor harms.

Nevertheless, we estimate a weighted average overall diagnostic error rate of 5.7 percent (95% CI 4.4 to 7.1) per ED visit by combining the error rate among ED discharges (4.1%) from a case-control study at a large university hospital in Spain with the error rate among ED admissions (12.3%) from a rigorous, prospective study at a university hospital in Switzerland. The overall representativeness of this estimate for U.S. ED care is uncertain, but the figure is not outside the range expected based on disease-specific error rates found in KQ2b, which range from 1 to 2 percent (fractures, myocardial infarction) to 56 percent or more (spinal abscess). Additionally, the 4.1 percent estimate for the ED diagnostic error rate is correctly situated within the spectrum of error and harm rates—diagnostic errors among admitted patients with "non-specific" symptoms [i.e., where there is a high degree of diagnostic uncertainty] (54%) >> diagnostic errors among all admitted patients (12%) >> diagnostic errors among treat-and-release discharges (4%) > diagnostic errors resulting in adverse events (2%) >> diagnostic errors resulting in serious harms, including death or permanent disability (0.3%). Finally, the overall error rate of 5.7% is comparable to that found in rigorous U.S.-based studies of other frontline

care settings (e.g., 6.3% overall diagnostic error rate in U.S.-based primary care clinics).[11] Thus, in light of all the relevant evidence, we believe it is appropriate to report and rely on this result.

Methodological approaches used in most of the identified studies tend to bias towards ***underestimation*** of diagnostic errors and misdiagnosis-related harms. These include (1) lack of systematic follow-up on discharged patients who do not return (including out-of-hospital deaths); (2) failure to account for hospital or health system crossovers (i.e., return to a different hospital or health system); (3) narrow definitions of diagnostic error that *(i)* limit to specific diagnostic process failures discernable from chart review, *(ii)* categorize as treatment-related the mismanagement of patients on the basis of an incorrect diagnosis, or *(iii)* do not include failures in communicating diagnoses to patients; and (4) failure to adjust for initial case severity, a key confounder, when assessing adverse outcomes due to diagnostic delay.

The last issue of initial case severity adjustment is crucially important to assessing adverse health outcomes from diagnostic error and calls into question the results of any study that fails to do so.[1] Some studies in the review failed to adequately address case mix severity, potentially leading to erroneous inferences that delays in diagnosis do not have a deleterious impact on patient outcomes (or even benefit patients – the "misdiagnosis is protective" paradox).[1] This problem occurs because illness severity is often a confounder (i.e., is causally linked to both the risk of misdiagnosis and the risk of a bad health outcome). Patients with *higher* initial case severity are *less* likely to have favorable clinical outcomes and also generally *less* likely to be misdiagnosed (because patients with more advanced or more serious disease tend to have more obvious clinical features that are easier to diagnose). Patients with *lower* initial case severity are *more* likely to have favorable clinical outcomes and also generally *more* likely to be misdiagnosed (because patients with earlier or milder disease tend to have less obvious clinical features that are more challenging to diagnose). An observational study that directly compares a population of all correctly diagnosed and all incorrectly diagnosed patients will generally find that initial case severity is higher in the correctly diagnosed population, skewing health outcomes for these patients in an unfavorable direction. This effect will tend to nullify the unadjusted, measured impact of diagnostic error or even reverse it ("misdiagnosis is protective" paradox).[1] When cases of similar severity at initial presentation are compared, the impact of misdiagnosis can be properly determined. When early presentations with lower initial severity are missed at first contact, early treatment opportunities are squandered, so outcomes for these untreated patients become closer to those who initially presented later in the illness course with higher severity. In such cases, early intervention could potentially have yielded better outcomes, but this fact will often be obscured if a study compares outcomes unadjusted for initial case severity.

There were insufficient data to assess overall error and harm rates by prospectively defined subgroups. For disease-specific studies, there were no clear differences between studies conducted in United States versus those not conducted in the United States. The one disease-specific study which included both U.S.-based and European EDs and compared diagnostic performance directly across continents found slightly longer diagnostic delays for aortic dissection patients in North America, where 12 of 14 sites were U.S.-based.[68] There were no clear differences based on the epoch in which studies were reported (2000 to 2010 versus 2011 to 2021), although comparisons were limited to just a few diseases based on data availability. The one study which explicitly assessed temporal trends for cardiovascular misdiagnosis in U.S.-based EDs (2006-2014, using Medicare data) found no significant trends for myocardial infarction or aortic dissection and a *rising* trend (increased false negative diagnostic errors) over time for ruptured aortic aneurysm, subarachnoid hemorrhage, and ischemic stroke.[120] Insufficient

data were available to assess the impact of ED clinician training on overall measured rates of diagnostic error or misdiagnosis-related harms. The impact of training background and clinical experience varied by study and disease, as reported in the sections analyzing KQ3.

Key Question 2a. On a per-visit or symptom-specific basis, what is the rate of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms?

Twenty-nine studies reported on per-visit or clinical presentation-specific rates of diagnostic error or harms.[54, 56, 58, 72, 74, 75, 121-143] There was significant methodological heterogeneity across studies in defining diagnostic errors, any harms, or serious harms, which made synthesis challenging. Most of the rates reported are underestimates, since few studies reported a systematic regional inquiry into returns to other hospitals or health systems, and hospital crossovers after ED misdiagnosis can occur in more than one third of cases.[144, 145]

Per-Visit Overall ED Diagnostic Error Rates

We use the term "overall" ED diagnostic error rates to refer to rates measured across presenting symptoms and clinical problems (as opposed to those that are symptom-, disease-, or discipline-specific). Although many studies reported on "diagnostic error" rates, they were mostly misdiagnosis-related harm rates, since they used an adverse event trigger to focus their search for errors. Only two studies addressed diagnostic error (as opposed to adverse events) systematically – one among ED patients who were discharged and the other among ED patients who were admitted to the hospital. These two studies are described below. In aggregate, the weighted average estimated ED diagnostic error rate is 5.7 percent (Moderate strength of evidence [SOE]).

We found just one study that systematically measured overall per-visit diagnostic error rates among patients *discharged* from the ED.[137] This study (Nuñez, 2006) was based in a large, university hospital in Spain and began by using an adverse event trigger (72-hour unscheduled returns for the same chief complaint) to identify cases and assess diagnostic errors (which external, masked reviewers defined as a discrepancy between initial and final diagnoses).[137] Study investigators then purposively sampled from the remaining visits (patients who did not return) to create a comparable population on factors likely to impact diagnostic error rates. Exclusion criteria were "age <14 years, obstetric/ gynecological emergencies, erroneous referral, voluntary withdrawal, and incomplete or unavailable data in the medical records at the hospital or health center." Of 32,523 eligible patients during a four-month period in 2004, there were 250 unscheduled 72-hour returns; among these study investigators found a diagnostic error rate of 20 percent (Nuñez, 2006, Table 2, including footnote). The control group "consisted of 250 patients who did not return; these comprised the next consecutive patient after each case in an attempt to balance cases and controls with respect to the influence of the attendance team, patient census, day of the week, work shift, and other external factors." Among the control group, the study investigators found a diagnostic error rate of 4 percent. Thus, diagnostic errors were 5-fold enriched among patients with 72-hour returns, but because the unscheduled return rate was very low at 0.8 percent of all visits (n=250/32,523 visits), the estimated total diagnostic error rate for the discharged ED population was very close to 4 percent. Authors did not report the admission fraction; however, given the small number of unscheduled returns (n=250), an admission fraction anywhere between 1 and 50 percent would produce a weighted average diagnostic error rate of 4.1 to 4.2 percent (with 4.1% being the value for a typical admission fraction of 10-15%). This

likely represents a "floor" (minimum) rate estimate because diagnostic errors were based solely on chart review and not systematic patient follow-up. Methodologically, the control group schema was strong with respect to the risk of diagnostic errors in those with unscheduled returns versus those without, but the absolute error rate is of uncertain representativeness even for this individual ED. For example, if every diagnostic error was attributable to a single clinician who was intermittently on call, then the matched population would track that individual's diagnostic error rate, rather than the average diagnostic error rate for the entire ED.

One high-quality prospective study was identified that examined overall diagnostic error rates and misdiagnosis-related mortality among patients *admitted* from the ED.[7] The study was a prospective observational study of 755 consecutive ED patients at a university-affiliated tertiary care facility in Switzerland. They used the primary hospital discharge diagnosis as the reference standard for the final correct diagnosis. They used a rigorous and moderately reliable (kappa 0.54) process of classifying diagnostic differences that only counted clinically meaningful discrepancies for the main analysis of the primary outcomes (hospital length of stay and mortality). They found diagnostic differences in 42 percent of cases (n=319 of 755) and considered these meaningful discrepancies in 12 percent of cases (n=93 of 755). Although the authors demurred labelling these as errors (focusing on "error" as a process failure), these events meet the National Academy of Medicine (NAM) definition of a diagnostic error used in this report, regardless of whether an explicit, preventable failure occurred during the diagnostic process. Diagnostic errors were associated with longer hospital stay (mean 10.3 versus 6.9 days; Cohen's d 0.47; 95% confidence interval 0.26 to 0.70; $P = 0.002$) and increased patient mortality (8.6% [n=8] versus 3.8% [n=25]); OR 2.40; 95% confidence interval 1.05 to 5.5 $P = 0.038$). Note that no post-hospital follow-up was performed, so the authors concluded that their estimates were likely minimum estimates (i.e., some additional diagnostic errors were presumably not captured by the inpatient team and therefore unaccounted for in the study results). The authors defend this approach well, but it is apparently more common than one might expect for the inpatient team to convert a correct ED diagnosis into an incorrect one, as found in one study that focused on the subset of patients with non-specific symptoms at higher risk for diagnostic error.[62] Whether this is a "floor," "ceiling," or intermediate estimate therefore remains unknown.

Per-Visit Overall ED Misdiagnosis-Related Harm Rates

There were seven studies that assessed overall per-visit misdiagnosis-related harm rates, referred to in most of the studies as diagnosis-related adverse events, or similar terminology (Table 8).[7, 24, 72, 131, 137, 141, 143] Only three of these studies were high-quality, prospective studies (Nuñez, 2006[137]; Calder, 2010[131]; Hautz, 2019[7]) and just one included both those discharged and admitted from the ED, in addition to systematic patient follow-up (Calder, 2010).[131] The prospective studies found adverse events and deaths at rates one to two orders of magnitude higher than those found in the various retrospective cohorts identified by revisit triggers. The retrospective studies are likely to represent substantial underestimates, given under-ascertainment as a consequence of design.

Table 8. Overall per-visit ED misdiagnosis-related harm rates

Author, Year	ED Cohort, Patient Ages, Exclusions,* Study Years	Outcome Trigger	Country (Number, Type, Annual Volume of ED[s])	Misdiagnosis-Related Adverse Event Rate†	Misdiagnosis-Related Death Rate†
Aaronson, 2018[141]	ED discharges, all ages‡, no exclusions, 2012-2015	72-hour returns	U.S. (n=1, academic, 100,000)	0.012% (48 of 413,167)	0.00073% (3 of 413,167)
Calder, 2010[131]	ED discharges/admissions from high-acuity areas (ESI triage level 1-3), adults (18+), with patient-level exclusions, 2004	Systematic follow-up (97%) of "flagged outcomes"	Canada (n=2, academic, 112,000 combined)	2.0% (10 of 503)§	0.20% (1 of 503)§
Calder, 2015[24]	ED discharges/admissions, likely adults£, excluded those admitted for more than 7 days, 2010	7-day returns plus other mechanisms	Canada (n=2, academic, 134,000 combined)	0.11% (15 of 13,495)	0.0074% (1 of 13,495)
Hautz, 2019[7]	ED admissions to internal medicine, adults (18+), with patient-level and specialty exclusions, no specified date range	Hospital admission (consecutive)	Switzerland, (n=1, academic, 45,000)	NR	4.8% (8.6% of cases [8 of 93] minus 3.8% of controls [25 of 662])
Heitmann, 2016[143]	ED discharges, all ages, excluding "minor casualty," 2014	30-day returns for an identical complaint	Denmark (n=1, regional, 15,000)	1.6% (11 of 688 discharges¶)	Not reported
Nuñez, 2006[137]	ED discharges, older teens/adults (14+)‡, excluding obstetric/ gynecologic emergencies, 2004	72-hour unscheduled returns for the same complaint plus a control sample of those who did not return	Spain (n=1, academic, 115,000)	NR	1.2% (3 of 250 unscheduled returns); 0% (0 of 250 controls); blended rate (weighted average) estimate ~0.13-0.25%¥
Vanbrabant, 2009[72]	ED discharges managed by general internal medicine, adults (16+)‡, specialty exclusions, 2006-2007	72-hour returns	Belgium (n=1, academic, 50,000)	0.21% (20 of 9,511)	0% (0 of 9,511)
SUMMARY	-	-	-	2.0% (95% CI 1.0-3.6) (Moderate SOE)	0.20% (plausible range 0.1-0.4)€ (Moderate SOE)

CI = confidence interval; ED = emergency department; ESI = Emergency Severity Index; NR = not reported; strength of evidence = SOE; U.S. = United States

* Exclusions were as follows, by study (listed alphabetically). Aaronson – "No exclusions." Calder (2010) – "We excluded patients if they met any of the following criteria: cognitive impairment due to an organic brain process or major psychiatric illness and no available substitute decision maker; critically ill or in too much distress to be capable of informed consent; unable to complete a telephone interview in English or French (or their substitute decision maker was unable); discharged home and did not have a telephone or otherwise unavailable for follow-up 2 weeks later (as determined at enrollment)." Calder (2015) – "All patients having an ED encounter between 9 May and 13 June 2010 were eligible for the study… This could include patients admitted on the index visit but who were discharged prior to the 7-day evaluation period." Hautz – "Patients were excluded if admitted to the internal medicine for palliative care or for social reasons or if admitted to internal medicine for reasons of age, comorbidities, or surgical ward crowding." Heitmann – "Patients only seen in the minor casualty room were excluded from the survey." Nuñez – "age <14 years, obstetric/ gynecological emergencies, erroneous referral, voluntary withdrawal, and incomplete

or unavailable data in the medical records at the hospital or health center." Vanbrabant – "medical problems (non-trauma patients) and who are not referred to a specific department (cardiology, gastroenterology, hepatology, …)."
† All but three studies used only triggered event analyses to identify diagnostic errors/harms, so patients who suffered diagnostic errors without a subsequent adverse event (e.g., short-term hospitalization post treat-and-release ED discharge) went uncounted. In those studies using trigger-based case reviews, all patients identified necessarily suffered adverse events (at a minimum, an ED revisit) and some of these were associated with clinical harm to the patient, including, in some cases, death. Permanent morbidity was not reported as an outcome in any of these studies.
‡ Aaronson – Age not reported in the study, but based on site-specific data, it appears that all ages are treated at this hospital (https://www.massgeneral.org/children/emergency-medicine). Calder (2015) – Age not mentioned in the methods; low end of interquartile range is reported as 31 years, making it more likely that patients considered were adults. Nuñez – Age range not explicitly described in the Methods, per se, but authors listed "exclusion criteria were age <14 years..." and results indicated "median age 45 years (5–95th percentiles 18–85, range 14–97)." Vanbrabant – Age stated as "adult patients (> 16 years old)."
§ Calder (2010) – Management errors due to treatments applied related to inaccurate diagnoses were considered management errors, and not counted as diagnostic errors, so these are "floor" (minimum) estimates. Adverse events deemed preventable by study authors included one patient who died of an aortic dissection and another who suffered "permanent disability" from a missed myocardial infarction (the severity of this disability was not graded by study authors).
£ Calder (2015) – "The study used our institution's Patient Safety Learning System. The Patient Safety Learning System is an electronic system designed to help identify and manage adverse events. It incorporates data from the following sources: (1) voluntary incident reporting from front line healthcare workers; (2) prospective surveillance by clinical observers; (3) morbidity and mortality rounds; and (4) electronic triggers such as those described by the Institutes of Health (e.g., transfer to intensive care unit). For the purpose of this study, we used the Patient Safety Learning System's capability to electronically capture all return ED visits within 7 days and analysed [*sic*] these for adverse events. This created a comprehensive and automated electronic trigger. In this study, we did not use voluntary incident reporting as a data source." Note that incorrect management pursuant to an incorrect diagnosis was not counted as a diagnostic error, but as a management error—"A management issue was defined as a suboptimal management plan despite accurate diagnosis or based on an inaccurate diagnosis."
¶ In Heitmann, those admitted at the original ED visit had a lower ED revisit rate after hospital discharge, but since these were post-inpatient diagnostic errors, they are not included here.
¥ In Nuñez, there were 250 unscheduled returns and 250 "control" cases sampled from ED discharges without returns. Deaths among the control group were not expressly mentioned, but it appears there were none in this small sample. This could be because of the much lower diagnostic error rate among non-returns (5-fold lower) and just 3 deaths among those who did return. However, assuming a mortality risk of 0% in this group understates the case, and the 95% upper confidence bound on 0% for n=0/250 extends up to 1.5% (which is probably too high, given the death risk among returns was measured at 1.2%). If the probability of death among control patients ***suffering a diagnostic error*** is roughly proportional to the probability of death among the unscheduled returns ***suffering a diagnostic error*** (i.e., 6% mortality among diagnostic errors [n=3/50]), then the estimated average risk of death among all ED discharges would be ~0.25%. If the probability of death is half as high among non-returning diagnostic errors, then the estimate is ~0.13%. Both values assume an admission fraction of about 10-15% of patients, but the results would change little based on this parameter, across a range of plausible admission fractions (e.g., 1% to 50%). For example, with a 50% admission fraction, the estimates would be ~0.26% and ~0.14% instead of ~0.25% and ~0.13%.
€ The plausible range is defined based on a multiplication factor of +/- 2-fold (see text for justification).

As noted above, we identified only one high-quality study that assessed overall diagnostic adverse event rates for both admitted and discharged patients with a prospective design using systematic follow-up (Calder, 2010).[131] They enrolled adult patients (≥18 years of age) from high-acuity areas of the ED (Emergency Severity Index triage level 1-3) during random shifts at two university-affiliated hospitals in Canada in 2004. They excluded patients deemed incapable of informed consent (cognitive impairment or major psychiatric illness; critically ill or in distress) or unable to complete 2-week phone follow-up (non-English/French speaker, no telephone, or expected to be unavailable). Of 518 enrollees (369 treat-and-release ED visits and 134 hospital admissions), an impressive 97 percent had a follow-up assessment, with 2 patients withdrawing and 13 lost to follow-up (at equal rates among those discharged versus admitted). They looked for prespecified "flagged outcomes" including deaths, hospital complications, returns, healthcare visits, and new, worsening, or persistent symptoms. They found 22 percent of both discharged and admitted groups had flagged outcome events, which were then assessed via chart review. They found 43 of 107 flagged outcomes represented preventable adverse events and classified 10 of these as diagnostic in nature. Thus, the authors found 2.0 percent (n=10 of 503, 95% CI 1.0 to 3.6) of ED patients enrolled suffered preventable diagnostic adverse events.

However, treatment errors pursuant to inaccurate diagnoses were considered management adverse events, rather than being counted as diagnostic adverse events; furthermore, events had to be deemed causally related and preventable with a certainty of at least 5 on a 6-point Likert scale by at least 2 of 3 reviewers. Also, this study was conducted at an academic hospital, and teaching hospitals are known to have lower diagnostic error rates for some conditions (see KQ3). Therefore, this represents a "floor" estimate. One of the 10 patients died of a delayed diagnosis of aortic dissection (rate 0.20%, 95% CI 0.005 to 1.1). Although the severity of the morbidity was not fully quantified, one additional patient was noted to have suffered "permanent disability" from a missed myocardial infarction (rate 0.20%, 95% CI 0.005 to 1.1).

There were four retrospective studies that reported overall per-visit harm rates. All but one (Heitmann, which used the longest revisit window) found much lower rates than the prospective study (Table 8).[24, 72, 141, 143] These studies all used triggered chart reviews at single institutions, with the trigger being an ED revisit or short-term hospitalization (<72 hours to <30 days), and none used regional health information exchange or insurance claims-based follow-up to ascertain health events. This means that diagnostic errors were not generally counted towards the totals if they (a) were not discovered until after the time window; (b) did not prompt further care within the time window; (c) were discovered at an outpatient clinic visit, rather than via an ED revisit or hospitalization; (d) prompted care at another hospital or health system; or (e) resulted in an out-of-hospital death. Furthermore, all studies used chart review procedures that required reviewers to gauge whether care was "appropriate" or diagnostic errors "preventable," further reducing the estimates. Such chart reviews are limited by the data recorded, which tend to be systematically incomplete and biased away from relevant details in cases where diagnostic errors have occurred.[104, 145, 146] This group of studies systematically underestimates harms, and likely does so by a wide margin, given much higher rates in studies not limited by under-ascertainment.

The four trigger-based studies examining returns after ED discharge were each conducted at single institutions (total of 5 EDs, with ED annual visit volumes ranging from 15,000 to 100,000) (Table 8).[24, 72, 141, 143] Trigger event time windows varied from 72 hours to 30 days, reducing direct comparability across studies. The all-cause return rates ranged from 2.0-2.9 percent at 72 hours, 4.4-6.8 percent at 7 days, and 11 percent at 30 days, suggesting a fairly comparable rate of overall ED returns across studies. However, these returns were at lower absolute rates than those reported using U.S. state-level data (7.5 percent at 72 hours and 22.4 percent at 30 days),[147] perhaps suggesting an academic/teaching hospital bias in the reported studies.[148] The proportion of ED returns attributed to diagnostic error varied from 0.6 to 14.2 percent, with a weighted mean of 1.0 percent (n=94 of 9,277). The overall rate of diagnostic adverse events (returns attributed to diagnostic error) per original ED visit varied over 100-fold across studies (i.e., across hospitals) from 0.01 percent at a large tertiary care ED in the United States to 1.6 percent at a small regional ED in Denmark, with a weighted mean of 0.022 percent (n=94 of 436,861). It was unclear the extent to which these reflected real differences between institutions as opposed to methodological differences in time windows, inclusions, or outcome definitions. Regardless, the rate of diagnostic adverse events in the one high-quality, prospective study (2.0%) is 92-fold higher than the weighted mean from the five retrospective studies (0.022%).

Misdiagnosis-related deaths per ED visit were reported in three of four retrospective studies,[24, 72, 141] ranging from 0 to 0.007 percent, with a weighted mean of 0.0009 percent (n=4 of 436,173). On an institutional basis in these three studies (representing 4 EDs), each ED would see between 1 and 5 misdiagnosis-related deaths annually (based on their reported ED volumes). Since these studies conducted no systematic searches for out-of-hospital or out-of-hospital-

network deaths and the single largest study (Aaronson, 2018, representing 94% of the patients synthesized) used 72-hour returns, rather than 7-day returns, this is, again, likely a substantial underestimate. The rate of misdiagnosis-related deaths in the one high-quality, prospective study (0.2 percent, n=1 of 503) is 217-fold higher than the weighted mean from the three retrospective studies (0.0009 percent). Although the rate of 0.2 percent is based on just a single death (so is imprecise, with a wide 95% CI 0.005 to 1.1), the value is the best estimate from this study and matches data from other sources. However, the confidence interval from the Calder study alone is implausibly wide. Based on data from other sources, we have assigned a +/- 2-fold plausible range to the 0.2 percent estimate (0.1% to 0.4%). This range bound comports well with other available data relevant to estimates of serious misdiagnosis-related mortality (details below in "Plausibility of Mortality Estimates from Higher Quality Studies").

Plausibility of Mortality Estimates From Higher Quality Studies

U.S. data based on deaths post ED discharge from Medicare (where ascertainment of death is nearly complete) suggest that, at least for patients over age 65, the 7-day death rate among non-hospice patients treated and released with non-lethal ED diagnoses is 0.12 percent (n=12,375 of 10,093,678),[148] equating to about 1 death per 833 ED treat-and-release visits. This value is 134-fold higher than what was found in the retrospective, trigger-based studies with incomplete ascertainment of deaths and just 1.6-fold off from the 0.2 percent measured in the one high-quality, prospective study that identified the one death among 503 patients (Calder, 2010). It is also a value that fits within the plausible range we have defined (0.1% to 0.4%).

We can compare this death rate to that found in the other high-quality prospective study, which examined only admitted patients (Hautz, 2019). Using a strong design, the increased mortality associated with diagnostic error was 4.8 percent (8.6% of cases [8 of 93 incorrectly diagnosed] minus 3.8% of controls [25 of 662 correctly diagnosed]). In the United States, ED admitted patients constitute 12.4 percent of ED visits (n=16.2 million of 130.0 million in 2018).[13] Thus, if misdiagnosis-related deaths *only* occurred among admitted ED patients (not those discharged), the overall misdiagnosis-related mortality rate would be 0.07 percent. If the death rate among those discharged were the same as in Nuñez, 2006, the overall blended (weighted average) rate for all ED visits would be 0.19-0.29 percent. These values also fit within the plausible range we have defined (0.1% to 0.4%).

We can further assess the plausibility of a 0.10-0.40 percent death rate based on the proportion of total post-ED deaths it represents. The overall 30-day death rate after an ED visit is 3.0 percent for patients of any age group (from a population-based Danish study)[149]; this is likely a reasonable proxy for U.S.-based ED deaths, since the U.S.-based 30-day mortality rate is 4.6 percent among Medicare beneficiaries,[150] and mortality is naturally expected to be higher among this older cohort that represents approximately 1 in 5 ED visits.[151] If the misdiagnosis-related death rate is 0.10 to 0.40 percent and the overall death rate is 3.0 percent, then the proportion of deaths attributable to diagnostic error (misdiagnosis-related deaths) would be 3.3 to 13.3 percent. This range is quite plausible, given that a systematic review of misdiagnosis-related deaths estimated the combined Goldman Class I/II diagnostic error rate for an average, modern, U.S.-based hospital that autopsied 100% of its deaths would be 8.4% (95% CI 5.2-13.1). Death among hospitalized patients is often due to severe, untreatable diseases that were correctly diagnosed in the ED (in obviously sick individuals), while this is not likely to be the case for those who die unexpectedly after ED treat-and-release discharge. Thus, even though the likelihood of death is much higher among hospitalized patients than discharged patients, the proportion of deaths that are attributable to ED misdiagnosis among those who die after ED treat-and-release is expected

to be *higher* than the proportion of deaths attributable to ED misdiagnosis among those who die during a post-ED hospitalization (see Role of Hospitalization and Discharge Fraction, below). The point estimate of 0.2 percent mortality corresponds to roughly 6.7 percent of deaths being attributed to diagnostic error, so, if anything, the 0.2 percent estimate may be slightly low.

Misdiagnosis-Related Permanent Disability Estimates

The rate of non-lethal yet serious misdiagnosis-related harms (i.e., permanent disability, rather than mortality) was not systematically reported in these particular studies. The Calder, 2010 study did not expressly quantify morbidity, but one patient (0.2%, 95% CI 0.005 to 1.1) "suffered permanent disability as a result of a missed inferior wall myocardial infarction."[131] The largest ED malpractice study in our review found that disabling outcomes (National Association of Insurance Commissioners scale score of 6-8, equivalent in severity to the loss of one arm or one eye [level 6], paraplegia or blindness [level 7] or quadriplegia or severe brain damage [level 8]) account for 41 percent (n=545/1,323) of high-severity harm outcomes; similarly, the largest incident report study found that disabling outcomes accounted for 29 percent (n=37/128) of high-severity harm outcomes. Thus, the number of serious harms is expected to be approximately 1.4- to 1.7-fold higher than the mortality rate. There are known differences in the relative proportions of disabling morbidity versus mortality by disease (e.g., aortic aneurysm and dissection 89% mortality and 11% permanent disability versus stroke 29% mortality and 71% permanent disability [Table 3][17]), these findings indicate it is insufficient to monitor death alone to assess poor overall health outcomes from diagnostic error or prioritize diagnostic error problems for intervention. Among the top 15 diseases identified in KQ1, serious misdiagnosis-related harms are known to disproportionately represent disabling morbidity (rather than mortality) for several neurological conditions including spinal and intracranial abscess (82% disability versus 22% mortality), stroke (71% disability versus 29% mortality), and meningitis and encephalitis (48% disability versus 52% mortality).[17] The same is likely true for other neurological conditions in the top 15 (e.g., spinal cord compression/injury and traumatic brain injury). Given that the organ system most often involved in diagnostic errors leading to serious harms is the nervous system (34%, Table 4), mortality alone will be a particularly poor health outcome proxy and will tend to substantially understate these individual diseases and total, serious misdiagnosis-related harms.

Role of Hospitalization and Discharge Fraction

Only one study assessing per-visit diagnostic harm rates reported on both treat-and-release (discharged from the ED) and hospitalized (admitted from the ED) fractions with respect to subsequent ED returns. The study was conducted at a 15,000 visit per year regional hospital in Denmark. Heitmann et al., 2016 found that 1.6 percent of ED discharges and 0.3 percent of patients admitted to a hospital ward via the ED returned within 30 days due to a diagnostic error, and almost all of these (in both subgroups) returned within 7 days.[143] This likely indicates that hospital admission serves as a clinical safety net for patients who are initially misdiagnosed, and comports with U.S. Medicare data showing that EDs with very high discharge fractions (proportion of patients sent home on any given day) are more susceptible to diagnostic errors associated with short-term, unexpected patient deaths.[148] This also comports with the findings from Hautz et al., 2019 in which 12.3 percent of patients admitted via the ED were found to have clinically important diagnostic discrepancies during their hospital stays.[7]

However, an unrelated Swiss study (Peng, 2015) of ED patients with non-specific symptoms who were admitted to a tertiary care hospital found 9 percent of ED diagnoses were corrected during the inpatient stay while, remarkably, 4 percent of ED diagnoses were converted from

correct to *incorrect* diagnoses by the inpatient team. Diagnoses were assessed based on 30-day follow-up review of clinical records.[62] While the overall impact of hospitalization was still to increase diagnostic accuracy over and above the initial admitting ED diagnosis, the high rate of conversion to an incorrect diagnosis could potentially cast doubt on whether inpatient diagnoses are always a good proxy reference standard for a final correct diagnosis. However, this particular population of patients was selected for a set of symptoms that predispose to diagnostic error, so it is probably not representative of the overall impact of inpatient care on diagnostic accuracy.

Differences in Estimation Based on Study Design

Prospective methods are likely to identify substantially more frequent diagnostic errors, diagnostic adverse events, and serious misdiagnosis-related harms than is possible using trigger-based retrospective chart review methods. Methodological reasons for this are detailed in the sections above. The strongest empiric evidence supporting these methodological contentions comes from a study group headed by the same lead author that published two non-overlapping studies using different methods (Calder, 2010; Calder, 2015) (see also Table 8).[24, 131] Both studies were conducted at the same two university-based hospital EDs in Ottawa, Canada. The more recent study used a triggered chart review process based on 7-day ED returns and other indirect methods of case capture to find a 0.11 percent diagnostic adverse event rate and a 0.0074 percent misdiagnosis-attributable death rate among 13,495 ED visits. The earlier study used systematic ascertainment in a small, random sample of ED patients (n=503) to determine a 2.0 percent diagnostic adverse event rate (18-fold higher) and a 0.20 percent misdiagnosis-attributable death rate (27-fold higher). It is also important that, in both Calder studies, management errors pursuant to incorrect diagnoses were counted as management errors, rather than diagnostic ones, suggesting that even these latter figures are likely "floor" estimates. Similar evidence has been published previously with respect to missed fractures in trauma patients—when Enderson and colleagues changed the study design from retrospective to prospective, the incidence of missed traumatic fractures increased from 2 to 9 percent.[152]

Additional evidence comes from studies of patients who do not return for care, who are also at risk of diagnostic error, but go uncounted in most trigger-based studies. As described above, one trigger-based study (Nuñez, 2006) reported on a matched control population of patients who did not return to the ED.[137] If the 250 sampled patients who did not return are representative of the broader ED population at that hospital, then 96 percent of all diagnostic errors occur in patients who do not return to the ED, and are therefore missed by trigger-based studies.

Finally, studies with insurance-based death ascertainment are likely to have much greater event capture than those based on revisits to the same hospital, because hospital crossovers are enriched among diagnostic error cases (37% of cases rather than 25%).[145] One study with such a design found misdiagnosis-related death rates—0.12 percent (n=12,375 of 10,093,678)[148]—to be much closer to those seen in the high-quality, prospective study (0.2%). Taken in aggregate, these findings suggest that real-world per-visit diagnostic error and misdiagnosis-related harm rates are likely substantially higher than currently reported in much of the medical literature.

Per-Symptom ED Diagnostic Error and Harm Rates

Appendix Table B-2 shows included studies reporting on symptom-specific rates of diagnostic error. Six studies reported on rates of diagnostic error among **polytrauma** patients.[121, 125, 127, 128, 130] Wilner et al. focused on *pediatric patients* and reported an 8 percent rate of delayed diagnosis of injury as well as a 0.3 percent rate of clinically significant delayed diagnoses.[130] The

remaining five studies focused on *adult populations*, had varying definitions of diagnostic delay, and reported delayed diagnosis rates ranging from 0.2 to 40.3 percent.

Kornblith et al. reported that 16.9 percent of patients **'found down'** had a late-identified injury/medical diagnosis.[123] Sun et al. reported a 4 percent rate of diagnostic delay among patients presenting with **syncope/near-syncope**.[135]

Royl et al. reported a 44 percent rate of diagnostic error for patients seen in the ED with **dizziness** and for whom a neurology consult was sought. The rate of harm ranged 5 to 6 percent for patients that had a primary diagnosis changed from a benign to a serious condition, and for patients that had one serious primary diagnosis replaced with another serious condition.[129] Moeller et al reported a 17 percent discordance between the emergency clinicians' diagnosis and the final diagnosis and a 19 percent discordance between ED trainees' diagnosis and the final diagnosis among patients that received a neurology consult for **any neurological complaint**.[134]

Two studies reported on misdiagnosis rates among patients presenting with **headache**.[122, 140] Miller et al. included *adult and pediatric* patients and reported a 1.7 percent rate of missed intracranial diagnoses.[140] Dubosh et al. focused on *adult populations* and reported a 0.5 percent rate of serious misdiagnosis-related harms. Dubosh et al. also reported a 0.2 percent rate of serious misdiagnosis-related harms for adults presenting with **atraumatic back pain**.[122]

Four studies reported on misdiagnosis rates among patients presenting with **abdominal pain**.[58, 126, 138, 139] Gallager and Osterwalder focused on *adult populations*. Gallager et al. reported a 14.1 percent rate of misdiagnosis among abdominal pain patients receiving morphine and 14.6 percent among patients not receiving morphine.[58] Osterwalder et al. reported a 5.6 percent rate of misdiagnosis and 1.7% rate of patients requiring surgery.[139] Saaristo et al. reported on *adult and pediatric* populations, and found the misdiagnosis rate to be 3.3 percent rate; 0.7 percent of the patients with abdominal pain required hospitalization, and 0.06 percent needed immediate surgery.[138] Crosby et al. focused on *pediatric patients* and reported a misdiagnosis rate of 1 percent among surgeons, and of 0.3 percent among emergency medicine clinicians. Crosby also reported a 1.6 percent and 0 percent rate of misdiagnosis for **testicular pain** among surgeons and emergency clinicians, respectively, and equal rates of misdiagnosis for **minor head trauma** at 0.3 percent across the providers types.[126] Freedman et al reported a 0.28 percent rate of misdiagnosis among pediatric patients with **constipation**.[142]

Two studies reported on misdiagnosis rates of adults presenting with **dyspnea**.[54, 136] Ray et al. focused on *older adults* (65 years and older) and reported a misdiagnosis rate of 20 percent.[136] Pirozzi reported on all *adults* and found the rate of misdiagnosis to be 5 percent when using point-of-care ultrasound, and 50 percent when not using point-of-care ultrasound (their definition of a misdiagnosis was a discordance between the initial and final ED diagnosis).[54]

One study reported on rates of misdiagnosis among adults presenting with **'low-risk' chest pain;** they found a 0.5 percent rate of missed or delayed acute coronary syndrome among control patients, and 0% among intervention patients randomized for patient and clinician to receive print-out information on their acute coronary syndrome risk assessment.[56]

One study reported on rates of **infection** misdiagnosis among *older adults* (age 65 years and older); they found an 18.4 percent false discovery rate in the ED.[124]

Two studies reported on rates of misdiagnosis among patients receiving **radiological imaging**.[132, 133] Chung et al. reported a 2 percent misdiagnosis rate for patients receiving torso imaging that were read by radiology residents during off-hours; 0.3 percent of the cases resulted in a change in management or call back to the ED, and no cases resulted in serious harm.[132] Filippi et al. reported a 7.2 precent misdiagnosis rate of neurological magnetic resonance

imagine (MRI) being read by radiology residents off-hours; 4.2 percent of the cases resulted in harm.[133]

Key Question 2b. On a per-disease/syndrome basis, what is the rate of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms?

When interpreting rates shown in the sections that follow, the meanings for these rates (technically, proportions, but more commonly referred to as "rates") are as follows, using the exemplars of myocardial infarction, pneumonia, and appendicitis (data from Table 9):

- **False negative rate** (1-sensitivity) of 1.5 percent means that patients who DO have myocardial infarction are missed (not promptly diagnosed) 1.5 percent of the time, which is nominally independent of the prevalence of myocardial infarction;
- **False omission rate** (1-negative predictive value) of 0.2 percent means those said NOT to have myocardial infarction actually DO have myocardial infarction 0.2 percent of the time, which is dependent on the overall prevalence of myocardial infarction (i.e., for a given *sensitivity*, the false omission rate will be lower with *lower* disease prevalence);
- **False positive rate** (1-specificity) of 24 percent means that patients who do NOT have pneumonia are misdiagnosed (called pneumonia) 24 percent of the time, which is nominally independent of the prevalence of pneumonia;
- **False discovery rate** (1-positive predictive value) of 7 percent means those said TO have appendicitis actually do NOT have appendicitis 7 percent of the time, which is dependent on the overall prevalence of appendicitis (i.e., for a given *specificity*, the false discovery rate will be lower with *higher* disease prevalence).

The first two rates are related to false negatives, while the second two rates are related to false positives. The first and third (which are based on sensitivity and specificity, respectively) can be thought of as reflecting diagnostic accuracy "in principle." The second and fourth (which are based on negative and positive predictive values, respectively) can be thought of as reflecting diagnostic accuracy "in practice." False negative and false positive rates are more readily compared and aggregated across studies, because they are nominally[153] prevalence independent. However, since prevalence of high-acuity illnesses such as myocardial infarction is likely to be relatively comparable across various EDs, the false omission and discovery rates are also likely to be reasonably compared and aggregated across studies with similar designs (inclusion criteria, diagnostic reference standards, outcome definitions, and outcome event ascertainment). More meaningful heterogeneity is expected for false omission and false discovery rates across settings with marked differences in disease prevalence (e.g., stroke in a pediatric versus adult ED).

A commonly used method for identifying rates of diagnostic adverse events was the Symptom-disease Pair Analysis of Diagnostic Error (SPADE) approach.[145] SPADE is a clinically valid, methodologically sound, statically robust,[154] and operationally viable[155] method of identifying misdiagnosis-related harms from electronic health record or billing/administrative data, without the requirement of manual chart review (although chart review can inform root cause analysis if so desired). Most often the diagnostic adverse event examined is a subsequent short-term hospitalization for a dangerous disease, although mortality and other outcomes can also be assessed; sometimes an observed minus expected rate is calculated to account for the epidemiologic base rate of the disease in question. Because it relies on an adverse event, SPADE estimates more closely reflect the misdiagnosis-related harm rate and will generally identify

substantially lower rates than the true diagnostic error rate (since only a subset of missed cases result in a short-term adverse events). SPADE can use either a look-back (case-control) or look-forward (cohort) architecture. The SPADE look-back approach (diseases to symptoms) works backwards from dangerous diseases (hospitalizations) to identify statistically anomalous (above baseline) patterns of antecedent symptomatic visits (ED treat-and-release with an incorrect, "benign" diagnosis). The look-back approach identifies specific symptoms or other clinical features (e.g., demographics) that increase risk for misdiagnosis, given the patient has the target disease; it also allows calculation of the false negative rate (and sensitivity) among those with the target disease. The SPADE look-forward approach (symptoms to diseases) works forwards from symptomatic ED visits with benign treat-and-release diagnoses to identify statistically anomalous (above baseline) patterns of subsequent hospitalizations for dangerous diseases. The look-forward approach, for a given symptom, identifies specific diseases that are misdiagnosed at excess rates, accounting for real-world prevalence; it permits calculation of the false omission rate (and negative predictive value) among those said not to have the target disease.

Overall, we identified 128 studies which addressed ED diagnostic error rates for 12 of the diseases prespecified in our study protocol. The number of studies was not distributed evenly by disease, with by far the most for stroke. There were many more studies of false negatives than false positives. The majority of false negative-related studies examined the initial ED false negative rate (1-sensitivity) among all patients hospitalized with a dangerous disease; almost all either conducted a detailed chart review to identify misdiagnoses or used a look-back SPADE approach for recent prior treat-and-release visits in large administrative databases. A few looked at the false omission rate (i.e., labelled as disease absent when it was present, calculated as 1-negative predictive value) among all patients discharged with a particular symptom, generally via look-forward SPADE approach, relying on a subsequent hospitalization or similar trigger. Almost all of the false positive-related studies looked at the false discovery rate (i.e., labelled as disease present when it was absent, calculated as 1-positive predictive value) in admitted patients, rather than the false positive rate (1-specificity) which would require data on all patients without the target disease (including those who were discharged from the hospital).

Variation in diagnostic error rates by disease were striking, with the lowest per-disease diagnostic error rates being for myocardial infarction (pooled false negative rate of 1.5%), and most of the remaining key dangerous diseases initially missed at rates of 10 to 36 percent (Table 9). There appears to be a roughly inverse relationship between annual disease incidence and diagnostic error rates, although myocardial infarction is clearly a low outlier in this regard (Figure 3). The highest per-disease diagnostic error/harm rates were almost certainly for spinal abscess (56% false negative rate, n=66 of 119), but per-disease error rates were derived from a single, high-quality study which was ultimately excluded from the final analysis because ED cases could not be separated from those missed in ambulatory care clinics, and the relative proportion seen in the ED remained unknown (despite successful outreach to study authors). The result is mentioned here because the findings were roughly comparable to those found in an older, fully ED-based study that found a 75 percent false negative rate (n=47 of 63).[23] That study, which included cases from 1992 to 2002, was excluded from the systematic review because more than half of the cases were presumed to fall prior to the study period (2000 to 2021) and no subgroup analysis was provided describing the more recent cases included in the study. It is also relevant to the validity of this estimated rate that spinal abscess is a rare disease, with fewer than 20,000 cases per year in the United States; it would be difficult for such a rare

condition to make the top 15 list of serious misdiagnosis-related harms in ED malpractice claims if errors were not frequent or subsequent serious misdiagnosis-related harms not the norm.

Effects of diagnostic error on health outcomes, as reported, were mixed, including some studies that identified null effects or even paradoxically "protective" effects of misdiagnosis[156] after failing to adequately case mix adjust based on initial severity of illness. Nevertheless, increases in misdiagnosis-related mortality were synthesized for aortic dissection (21% relative increase) and reported in individual studies for stroke (ischemic stroke and subarachnoid hemorrhage), venous thromboembolism, and arterial thromboembolism (mesenteric ischemia).

Table 9. Summary of per-disease diagnostic error rates

Harm Rank*	Prespecified Disease	Estimated Annual Incidence (Rank)	False Negatives	False Positives
1	Stroke	952,000 (5)	FNR 17%† (any type) • 12% (SAH) • 15%† (ischemic) • 14%† (younger, 15-60yo) • 6-21% (CVT) • 38% (TIA) • 40% (delayed‡) FOR 0.2% (dizziness) FOR 0.2% (headache)	FPR N/A FDR 21%† (any type) • 4% (tPA-treated) • 10%† (hemorrhage) • 10%† (ischemic) • 49%† (TIA)
2	Myocardial infarction	1,242,000 (4)	FNR 1.5%† (missed‡) FNR 26% (delayed‡) FOR 0.2% (chest pain or dyspnea discharges)	FPR N/A FDR 14%†
3	Aortic aneurysm and dissection	96,000 (9)	FNR 36%† FOR N/A	FPR N/A FDR 5%
5	Venous thromboembolism	320,000 (6)	FNR 20%† FOR N/A	FPR N/A FDR N/A
6/7 (tie)	Meningitis and encephalitis	47,000 (10)	FNR 22% FOR 0.01% (headache discharges)	FPR N/A FDR N/A
6/7 (tie)	Sepsis	1,345,000 (3)	FNR 10%† (*excludes Morr*[157]) FOR 0.44% (altered mental status or FED discharges)	FPR N/A FDR N/A
10	Arterial thromboembolism	173,000 (8)	FNR 15% (≥24hrs) FNR 38% (≥6hrs) FOR N/A	FPR N/A FDR N/A
11	Spinal abscess	14,000 (11)	FNR 56%§ FOR 0.1% (back pain)	FPR N/A FDR N/A
13	Pneumonia	1,469,000 (2)	FNR 14% FOR 9%	FPR 24%£ FDR 34%£
-	Appendicitis	318,000 (7)	FNR 0.2-5% (<18yo) FOR N/A	FPR N/A FDR 7%†
-	Fractures	1,990,000 (1)	FNR 1% FOR N/A	FPR N/A FDR N/A
-	Testicular torsion	2,600 (12)	FNR 5% FOR N/A	FPR N/A FDR 7%

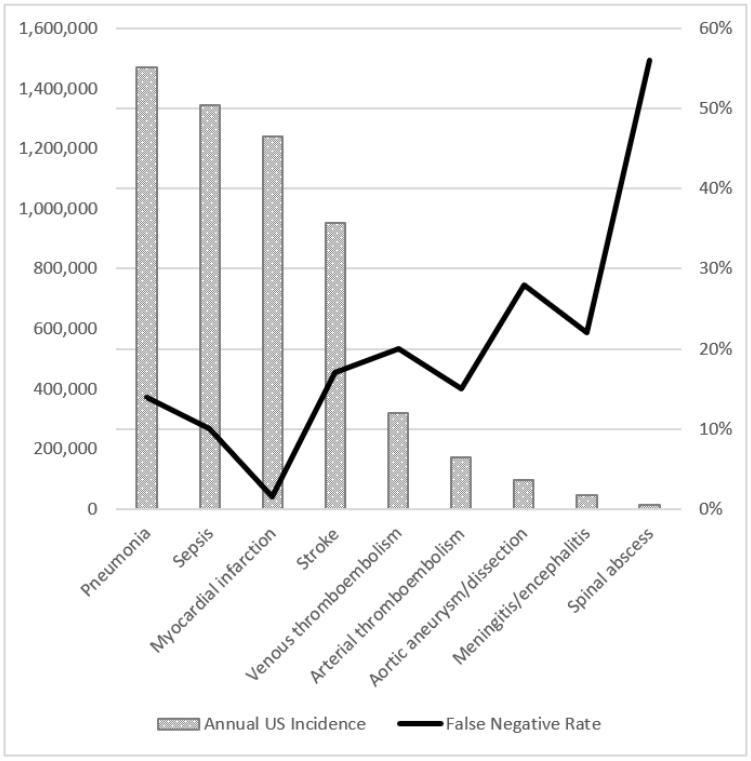
CVT = cerebral venous thrombosis; ED = emergency department; FED = fluid and electrolyte disturbance; FDR =false discovery rate (1-positive predictive value); FNR =false negative rate (1-sensitivity); FOR = false omission rate (1-negative predictive value); FPR = false positive rate (1-specificity); N/A = not available; SAH = subarachnoid hemorrhage; TIA = transient ischemic attack; tPA = tissue plasminogen activator; yo = year old

* The 'Harm Rank' is based on the frequency of high-severity misdiagnosis-related harms from Key Question 1, from most (rank #1) to fewest (rank #13). Cardiac arrhythmias (#12) are not listed because there were no studies found. Spinal cord compression and injury (#4), lung cancer (#8), traumatic brain injury and traumatic intracranial hemorrhage (#9), gastrointestinal perforation and rupture (#14), and intestinal obstruction (#15) were not included in the original, prespecified disease-specific searches, so no rate information is available. Those searched but below rank #15 are simply denoted by "-" and are listed in alphabetical order.

† Pooled result from current meta-analysis.

‡ Here we use the term "delayed" diagnoses to refer to patients who are admitted from the ED with incorrect diagnoses and only discovered later in the hospitalization diagnosed correctly. This is as opposed to our use of the term "missed" diagnoses to refer to patients discharged from the ED with incorrect diagnoses. It is noteworthy that the rate of error appears to be higher among admitted patients, suggesting perhaps that ED clinicians are focused more on correct disposition than correct diagnosis. Note also that "missed" myocardial infarction diagnoses for this calculation were derived from studies using methods that more closely approximate the subset of false negatives associated with misdiagnosis-related harms, rather than all false negatives; nevertheless, data from a large, prospective randomized trial conducted in the United States in 1993[22] suggests the stated 95 percent confidence range (1-2%) likely captures both the diagnostic error rate and the misdiagnosis-related harm rate (for details see text in the section below on Myocardial Infarction: False Negatives).
§ The study reporting a spinal abscess miss rate of 56 percent (n=66 of 119) was excluded at the full text review stage because the proportion of cases seen in the ED (as opposed to ambulatory clinic settings) could not be verified (it was otherwise eligible for the review). The estimate comes from a recent national database analysis and is consonant with false negative rates from prior ED-based studies (excluded based on year of study), so it is included here. Davis et al., 2004, found diagnostic delays in 75 percent (n=47/63) overall, including 68 percent (n=43/63) with multiple ED visits.[23]
£ The high false positive rate and false discovery rate for pneumonia is based on a study that looked at patients who were pneumonia suspects but may have had conditions that presented similarly (e.g., congestive heart failure). The false positive rate for a "general" non-pneumonia ED population would be far lower, but no studies addressed this issue directly.

Figure 3. Relationship between annual U.S. incident cases of disease and estimated ED miss rate



ED = emergency department; KQ = Key Question
Shown are 9 of the top 15 diseases associated with serious misdiagnosis-related harms in the ED from KQ1. The other six are omitted because we lack false negative rates. One (cardiac arrhythmia) we found no data, while five (spinal cord compression and injury, lung cancer, traumatic brain injury and traumatic intracranial hemorrhage, gastrointestinal perforation and rupture, and intestinal obstruction) were not included in the original, prespecified disease-specific search (because they were recognized only after completing the final analysis for KQ1). Counts for mean annual disease cases derive from the National Inpatient Sample, 2012-2014 (*Newman-Toker, unpublished*). The graph reveals an inverse relationship between annual disease incidence and estimated false negative diagnostic error rates for major medical and neurological conditions. However, the relationship is imperfect, with myocardial infarction diagnostic rates substantially lower than those for pneumonia, sepsis, and stroke, which have comparable annual incidence. Note that this relationship may not hold for all conditions, including testicular torsion, which likely has an annual U.S. incidence of fewer than 3,000 cases yet only a 5 percent estimated false negative rate.[158] This suggests that disease-specific factors such as "degree of diagnostic difficulty" are important variables in determining the overall likelihood of a diagnostic error; such diagnostic difficulty may result from genuinely ambiguous presentations or lack of expertise.

Stroke

We identified 50 studies (28 of these U.S.-based) that reported on the rate of diagnostic errors and/or misdiagnosis-related harms among over 1.9 million patients with cerebrovascular events.[55, 64, 66, 69, 85, 87, 88, 120, 122, 144, 159-198] Studies varied significantly in the methodological approach, definitions to assess diagnostic errors, target populations, and inclusion/exclusion criteria. Most of the studies had a low risk of bias. However, 22 studies had an unclear or high risk of bias in terms of patient selection,[177, 179, 182, 194] the reference standard,[165, 167-169, 177-179, 181, 182, 186, 188, 195, 198] or the patient flow.[160, 161, 163, 176, 182, 189, 195, 196]

Stroke: False Negatives

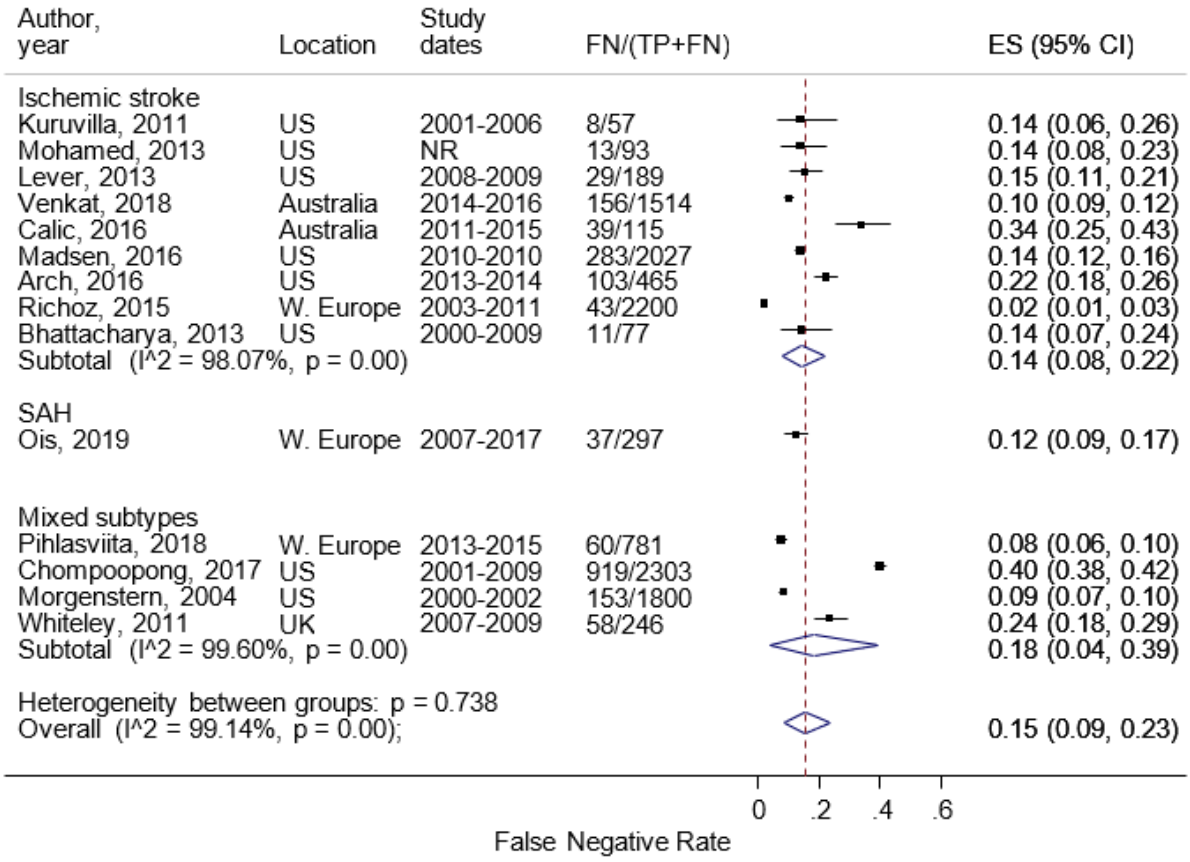
Twenty-three studies reported on the false negative rate (1-sensitivity) for stroke.[64, 66, 87, 88, 120, 122, 159, 160, 169, 171, 173-175, 177-181, 183, 186, 194-196] Fourteen of these were sufficiently comparable to conduct a meta-analysis (Figure 4).[66, 85, 87, 88, 159, 160, 171, 178, 179, 181, 183, 186, 194, 196] After contacting the authors, two of these were largely overlapping (Morgenstern, 2004 and Kerber, 2006 [dizziness subgroup]), so we excluded Kerber, 2006 from this meta-analysis. The pooled false negative rate was 15 percent (95% CI 9 to 23; I-squared 99%), with no clinically meaningful or statistically significant heterogeneity based on whether the study included only ischemic stroke, focused on subarachnoid hemorrhage, or had a mixed population that included ischemic strokes and intracranial hemorrhages (high SOE for false negative rate). The highest estimate (false negative rate 40%, 95% CI 38 to 42) was from a large U.S.-based study of patients (n=2303) admitted from the ED with non-stroke diagnoses who were discharged from the hospital with strokes of mixed subtypes, including transient ischemic attack (Chompoopong, 2017).[85] Authors acknowledged the limitation that some cases may have involved strokes occurring during hospitalization (i.e., not present at the time of admission). The lowest estimate (false negative rate 2%, 95% CI 1 to 3) was from a large Swiss study of patients (n=2200) of only ischemic strokes derived only from patients admitted to the stroke unit or intensive care units (Richoz, 2015).[186] Focusing on strokes admitted to stroke or intensive care tends to inflate diagnostic accuracy and reduce estimates of diagnostic error. Authors acknowledged the limitation that their estimate may have been low because some strokes may never have been detected; their methods note that MRI was not routinely performed—"Systematic diffusion-weighted MRI is not performed in all patients with new neurologic disease in our ED." In a severity-adjusted analysis, they found worse outcomes and greater mortality.

We further analyzed false negatives excluding any studies with strong case selection filters likely to bias estimates away from the true overall cerebrovascular false negative rate (Figure 5). For this analysis, we excluded 2 studies selecting on case features that confer higher illness severity, which tends to bias towards lower error rates (Richoz, 2015 [stroke unit/intensive care unit admissions][186]; Pihlasviita, 2018 [stroke code activations for possible thrombolysis][183]). We also excluded 5 studies selecting on case features known to increase false negative risk—3 studies selecting only for younger stroke patients ages 16-50 (Kuruvilla, 2011[171]; Mohamed, 2013[178]; Bhattacharya, 2013[160]) and 2 studies selecting on case features linked to posterior circulation stroke (Kerber, 2006 [dizziness][168]; Calic, 2016 [cerebellar stroke location][87]). The resulting false negative rate point estimate (17%, 95% CI 9 to 27) was slightly higher than the overall point estimate prior to removing these potentially biased studies (15%, 95% CI 9 to 23), but each point estimate fell well within the other's 95 percent confidence interval. The 17 percent estimate shown in Figure 5 (low selection bias) is more likely to be representative of the real-world ED rate. Because most studies did not capture missed strokes among ED treat-and-release

patients or account for missed TIAs (which have higher error rates), this estimate is likely conservative.

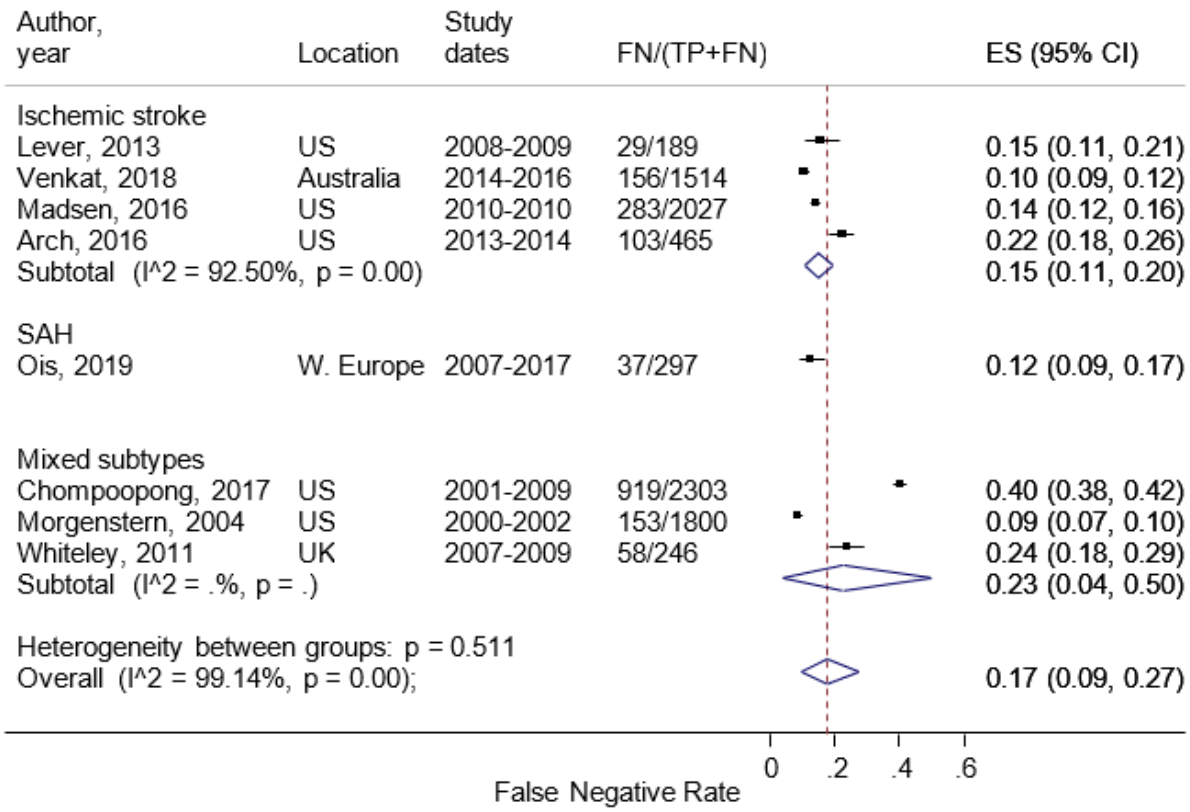
Most of the studies did not compare diagnostic accuracy for TIA to that for acute ischemic stroke, but Whiteley, 2011 provided data that permitted such a calculation. Their results suggest that TIAs are more often missed than ischemic strokes (false negative rate 37.8% [n=14/37] for TIA versus approximately 20.8% [n=41/197, assuming equal proportion of hemorrhages among missed cases as overall], p=0.025). However, Morgenstern found that TIA did not predict greater odds of a false negative (odds ratio [OR] 1.02, 95% CI 0.71 to 1.46).

Figure 4. False negative rate for stroke in the emergency department by stroke subtype



CI = confidence interval; ES = effect summary (false negative rate); FN = number of false negatives; SAH = subarachnoid hemorrhage; TP = number of true positives; U.S. = United States; W. = Western

Figure 5. False negative rate for stroke among studies with low selection bias, by stroke subtype



CI = confidence interval; ES = effect summary (false negative rate); FN = number of false negatives; SAH = subarachnoid hemorrhage; TP = number of true positives; U.S. = United States; W. = Western

Stroke False Negatives: Younger Patients

Three studies included younger adult populations of stroke cases (16 to 50 years) and reported on missed cerebrovascular accidents. The pooled false negative rate of cerebrovascular accidents was 14 percent (95% CI 10 to 19, I-squared 0%).[160, 171, 178] All three studies found higher rates of misdiagnosis among younger patients (either <35 or <40 years of age) within their already "young stroke" cohorts. Another study investigated delayed diagnosis of stroke specifically among children <18 years of age and reported that 65 percent of cases were diagnosed ≥6 hours after hospital arrival and 23 percent were diagnosed after 24 hours.[177] So, although the measured rate of 14 percent for patients aged 16 to 50 is nominally lower than the overall false negative rate for stroke of 17 percent obtained from other studies, this may be artifactual and related to methods or other inter-study differences.

A study using SPADE methods (which assesses misdiagnosis-related harms, rather than diagnostic error rates, per se, since detection is based on diagnostic adverse/unexpected events), found that patients 18 to 44 years of age were 6.7-fold more likely to suffer a missed opportunity antecedent to a stroke hospitalization than their older counterparts ages 75 and above (3.98% vs. 0.59% with $P < 0.001$ for differences across age groups).[64] The same study reported (in its supplemental "Appendix 2") limited details on those under age 18, but, compared with those 18 and over, the odds of a misdiagnosis appeared to be greater. Specifically, the observed to expected ratio for antecedent ED treat-and-release visits for headache prior to a stroke hospitalization were 1.9-fold enriched for adults and 11.0-fold enriched for children.

Included studies did not permit a meta-analytic assessment of the overall rate of stroke misdiagnosis in pediatric populations, but available studies do seem to suggest that younger age is a strong risk factor for diagnostic error and associated adverse events, with the youngest patients (who have the lowest overall risk of stroke) having the highest risk of being missed.

Stroke False Negative: Special Stroke Subtypes (Subarachnoid Hemorrhage)

Three studies reported on false negatives in patients with subarachnoid hemorrhage. A prospective cohort study (n=401) from Western Europe reported 26 percent missed subarachnoid hemorrhage diagnosis, although the cohort included cases misdiagnosed outside of the ED, and the false negative rate in the ED was lower (12%) than the aggregate rate.[181] When adjusted for initial case severity (i.e., restricting to patients with mild initial clinical presentations [Hunt and Hess grade 1 or 2], who comprised 59% of all cases), misdiagnosed patients had a 3.89-fold increased odds (95% confidence interval 1.9 to 8.0) of a poor clinical outcome. Two studies used look-back SPADE-style methods to assess diagnostic adverse events (i.e., the subset of false negative cases requiring hospitalization after an initial misdiagnosis). One retrospective cohort study reported 3.5 percent missed cases (observed minus expected ED visits within the last 45 days for patients ultimately hospitalized with subarachnoid hemorrhage) using Medicare data.[120] Another study reported a 5.4 percent miss rate for subarachnoid hemorrhage based on retrospective data from ED visits in the 14 days prior to hospital admission but, importantly, demonstrated wide variability across institutions (false negative rates ranged from 0-100% across 147 EDs); they found a paradoxical "misdiagnosis is protective" association between missed diagnosis and better health outcomes using crude (unadjusted) 30-day mortality, but were not able to adjust for initial case severity due to the lack of clinical details, leaving unanswered the question of whether earlier diagnosis may have actually improved outcomes in this cohort.[195]

Stroke False Negative: Special Stroke Subtypes (Dissection, Cerebral Venous Thrombosis)

One study reported that 3.1 percent of patients with cervicocephalic dissection were treated-and-released from the ED in the prior 14 days with related symptoms.[175] Two studies included cases with cerebral venous thrombosis: one reported 3.6 percent misdiagnosis. They found longer length of hospital stay among misdiagnosed cases, but no unfavorable outcome (again, unadjusted for initial case severity). They also did a chart review on a smaller group of patients with cerebral venous thrombosis and found 6 percent missed diagnosis.[174] The other study reported 20.8 percent diagnostic error rate among cerebral venous thrombosis cases, using the "Safer Dx" Instrument.[173] Without adjusting for initial case severity, they found worse health outcomes among cases without a diagnostic error compared to those with a diagnostic error (28.6 versus 0%, $P = 0.05$),[173] again reflecting the apparent "misdiagnosis is protective paradox." One study of stroke in polytrauma patients found that 11 of 192 patients (5.7%) had acute ischemic strokes, all of which were initially missed (and no neurologic consultations were obtained initially, despite neurologic findings being noted in four cases); the underlying cause for acute ischemic stroke was discovered by neurovascular imaging to be craniocervical dissection in six cases (two carotid artery, four vertebral artery); median time to diagnosis was 2 days (range 0 to 5).[198]

Stroke False Negatives: Symptom—Specific Populations (Dizziness and Headaches)

Stroke patients presenting with dizziness or headache symptoms are prone to be missed. Dizziness increases the odds of misdiagnosis 14-fold over motor symptoms, and those with dizziness and vertigo are missed initially in an estimated 40 percent of cases.[21] A large,

population-based stroke surveillance program in Texas used ED chart review by neurologists (including hospitalization and imaging results) to validate stroke diagnoses, demonstrating that 46 out of 1629 (2.8%) of those with a presenting complaint of dizziness were strokes and 16 (35%) were misdiagnosed in the ED.[168] The same study found that only 5 of 15 cases with isolated dizziness admitted as stroke TIA from the ED were validated as stroke (i.e., false discovery rate of 67%). A second study from the same Texas cohort followed ED patients with dizziness who initially received a non-stroke diagnosis for a median period of 347 days, reporting a stroke incidence rate of 13.2 per 1000 person years (1.32%); this study found that most of that risk occurred in the first 48 hours after ED treat-and-release.[169] A separate U.S.-based study found that stroke hospitalizations were enriched in the 30 days following an ED dizziness discharge, with a false omission rate of 0.3 percent for these diagnostic adverse events; the 180-day cumulative incidence of a major vascular event or death was 0.93 percent.[170]

Isolated ED headaches appear to be a risk factor for misdiagnosis of both ischemic stroke and intracranial hemorrhage (both intracerebral and subarachnoid).[64] A U.S.-based study found that among cases with an ED visit because of headache, 0.3 percent had ischemic stroke and 0.4 percent had any cerebrovascular disease within 1 year.[176] Similarly, a single-site study in the United States with regional follow-up showed that 0.6 percent of patients discharged with a benign headache diagnosis from ED had subsequent cerebrovascular disease hospitalization within 1 year.[144] Another U.S.-based study using state-level data found that stroke cases were enriched in the 30 days following an ED headache visit, with a false omission rate of 0.2 percent (n=4,253 of 2,101,081 headache discharges) (high SOE for false omission rate).[81]

Stroke False Negatives: Impact on Care and Outcomes

Multiple studies demonstrated cases who missed acute stroke interventions because of an initial missed or delayed diagnosis, including younger patients.[88, 159, 171, 183, 194] In one large study of 2,027 confirmed acute ischemic strokes, 1.1 percent of misdiagnosed cases did not receive tissue plasminogen activator, despite being eligible; as expected, the number of cases eligible for tissue plasminogen activator was smaller in the misdiagnosed group than the correctly diagnosed group.[88] However, another study reported that in 22 percent of misdiagnosed ischemic stroke cases, the error resulted in missed or delayed tissue plasminogen activator administration.[159] This rate was slightly higher in community hospitals compared to academic centers, although the difference was not statistically significant. With regards to possible harms, misdiagnosed cases were readmitted within the next 60 days almost twice as often as correctly diagnosed cases.[159]

Using Medicare data and a SPADE-style look-back approach (reflecting diagnostic adverse events), the false negative rate antecedent to stroke hospitalization (defined as observed minus expected prior ED visits) was reported to be 4.1 percent (95% CI 4 to 4.2) within the last 45 days and 3.7 percent (95% CI 3.7 to 3.8) within the last 30 days.[120] These cases reflect potential missed opportunities to have prevented major stroke after minor stroke or TIA.

Four studies, one from Australia and three from Western Europe, reported on missed ischemic and hemorrhagic strokes among 5,130 patients and analyzed stroke functional outcomes or mortality. The pooled rate of missed ischemic and hemorrhagic strokes was 7 percent (95% CI 3 to 14, I-squared 98%).[181, 183, 186, 194] Using chart review (and an analysis unadjusted for initial severity), an Australian study found no association between missed diagnosis and worse outcome, but a subgroup of misdiagnosed cases who were admitted under non-neuro service showed worse functional outcomes (Modified Rankin Scale score ≥3, 80% versus 41%, $P < 0.0001$) and greater in-hospital mortality (15% versus 4%, $P = 0.002$) when compared to those admitted under the neurology service that was robust to adjustment for initial

stroke severity.[194] Using chart review (and an analysis unadjusted for initial severity), a study from Finland found that 0.8% of misdiagnosed cases could have possible or likely worsened outcome, but no deaths were attributed to misdiagnosis.[183] A Swiss registry-based study with prospective data collection (Richoz, 2015) found in a multivariate, adjusted analysis (which included initial stroke severity) that *favorable* outcomes were 4.8-fold *less* likely and *mortality* 4.3-fold *more* likely among those with misdiagnosed acute ischemic strokes.[186] As noted in the subarachnoid hemorrhage section above, when adjusted for initial case severity (limiting to Hunt and Hess Grade 1 or 2, n=236), misdiagnosed subarachnoid hemorrhage patients with an initially mild clinical presentation had a 3.89-fold increased odds (95% CI 1.9 to 8.0) of a poor clinical outcome.[181]

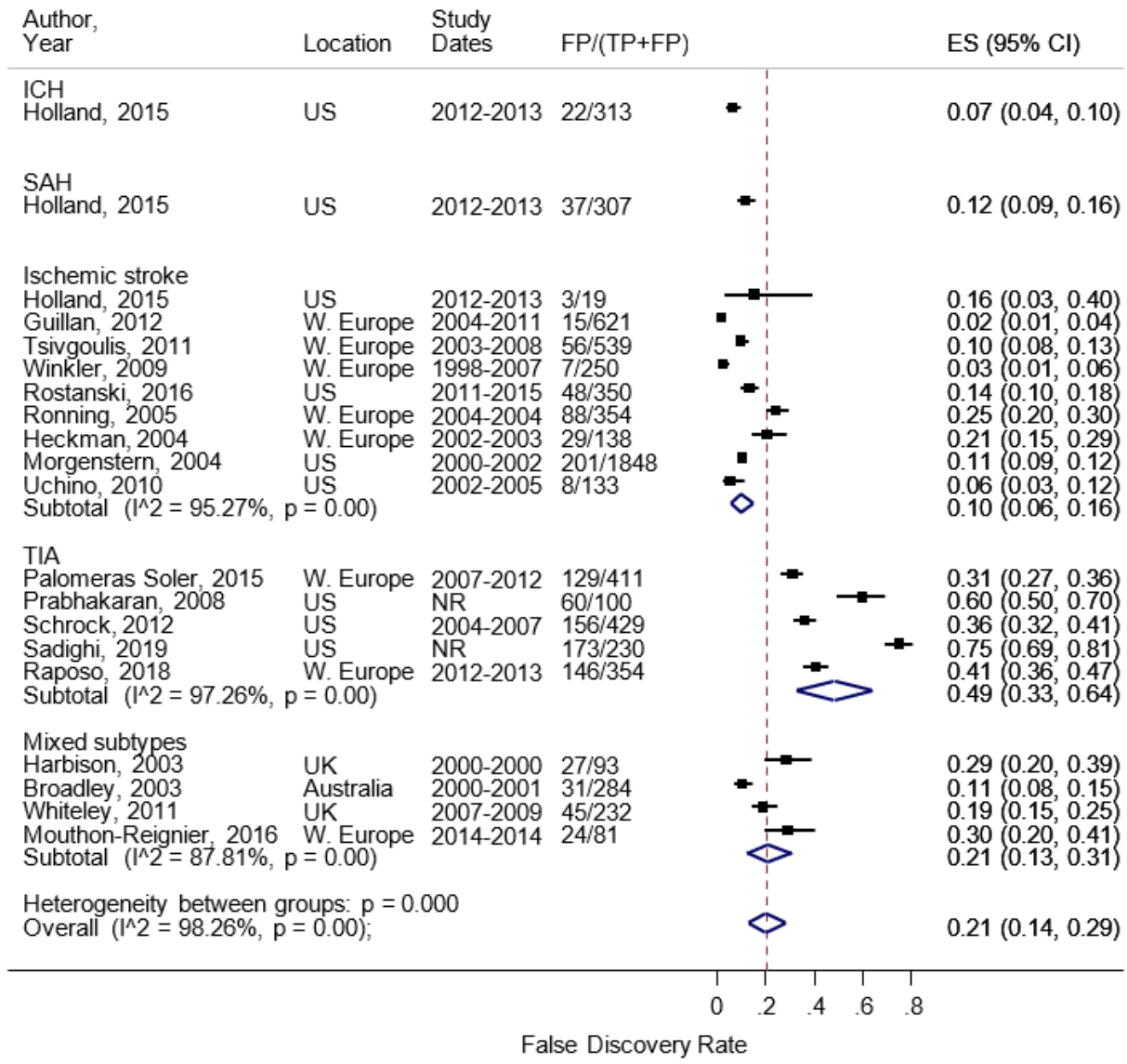
Stroke: False Positives

Nineteen studies reported on the false discovery rate (1-positive predictive value) for strokes.[69, 161, 164-168, 179, 180, 182, 184, 185, 187, 190-193, 196, 197] After contacting the authors, two of these were largely overlapping (Morgenstern, 2004 and Kerber, 2006 [dizziness subgroup]), so we excluded Kerber, 2006 from this meta-analysis. We have analyzed these by stroke type (Figure 6). The pooled false discovery rate was 21 percent (95% CI 14 to 29), but there was clinically meaningful and statistically significant heterogeneity based on stroke subtype. The most obvious difference was that TIAs were falsely positive at a much higher rate (49%, 95% CI 33 to 64) than ischemic strokes (10%, 95% CI 6 to 16) or brain hemorrhages (10%, 95% CI 7 to 12) (high SOE for false discovery rate). These differences are not surprising, since it is much more challenging to correctly diagnose TIA than completed stroke. The small differences between ischemic stroke, subarachnoid hemorrhage, and intracranial hemorrhage (Holland, 2015 in Figure 6) may be explained by frequent use of computed tomography (CT) scans (often obtained in the ED for neurological symptoms), which are substantially more sensitive for detection of hemorrhages than ischemic strokes.[199] Patients treated with thrombolysis using tissue plasminogen activator were false positives less frequently (erroneous treatment 3.9%, n=13/331).[183]

A single U.S.-based study reported on stroke false discovery rate in the pediatric population by investigating stroke alerts (activated when patient presents with symptoms or signs suggestive of stroke or TIA, prompting rapid neurology stroke evaluation). They found that in 74.2 percent of pediatric stroke alerts, the correct diagnosis was not stroke or TIA. Given the design of this study, the high rates are unsurprising, since stroke alert calls are similar to requesting a neurology consultation for suspected stroke, rather than assigning a diagnosis, per se.[172] Nevertheless, this high rate could also potentially reflect (a) a lower threshold for ordering a stroke consultation among children with neurological symptoms, (b) generally low stroke prevalence among children, or (c) increased probability of a false positive misdiagnosis.

As with false negatives, false positives appear to be disproportionately common among patients presenting to the ED with dizziness and vertigo—one included study from Western Europe found 31 percent of benign ear causes were initially misdiagnosed as stroke.[129]

Figure 6. False discovery rate (referred/admitted) for stroke in the emergency department by stroke subtype



CI = confidence interval; ES = effect summary (false discovery rate); FP = number of false positives; ICH = intracranial hemorrhage; SAH = subarachnoid hemorrhage; TIA = transient ischemic attack; TP = number of true positives; U.K. = United Kingdom; U.S. = United States; W. = Western

Stroke Misdiagnosis: Imaging-Focused Studies

We identified five studies that focused heavily on imaging aspects of stroke, including studies of imaging timeliness, radiology accuracy, and the relationship between use of CT and the likelihood of misdiagnosis. A U.S.-based study reported that only 11.5 percent of patients with suspected stroke received a head CT scan within 25 minutes and the remainder (88.5%) received delayed imaging workup.[188] Two studies focused on radiology accuracy for accuracy of vascular imaging reads. One reported missed intracranial aneurysm diagnosis in initial radiology resident reads in 13 percent of cases with subarachnoid hemorrhage caused by intracranial aneurysms.[55] The other reported 20 percent of large vessel occlusions are missed on initial

radiology read among cases with ischemic stroke caused by large vessel occlusion.[162] They found that radiologists not subspecializing in neuroradiology were more likely to miss large vessel occlusions compared to neuroradiologists (OR 5.6; 95% CI 1.1 to 29.9; $P = 0.04$).

Two other studies focused on the link between head CT scan use and the likelihood of a missed stroke diagnosis. Both found ED treat-and-release visits resulting in non-cerebrovascular diagnoses were more likely to be followed by a stroke hospitalization after *negative* CT scans than among patients *without* CT scans. A SPADE-style regional study in Canada looked into subsequent strokes among a group of patients who had been discharged from ED with a peripheral vertigo diagnosis and had undergone head CT in that visit. They found that the frequency of stroke occurrence within 30, 90, and 365 days was 0.29 percent, 0.41 percent, and 0.60 percent, respectively. These rates were all higher versus a propensity-score matched control group who had not undergone head CT during their ED visit (0.15%, 0.20%, and 0.36%, respectively) (OR 2.27 for likelihood of 30-day stroke hospitalization [95% CI, 1.12–4.62]).[163] A U.S.-based study assessed the risk of future stroke among older patients (60 to 89 years of age) discharged from the ED who had neurological symptoms but were not given a diagnosis of stroke or TIA. They divided these patients into four groups based on presence of symptoms suggestive of stroke or TIA and whether head CT was performed in the ED. The groups were symptom absent/CT absent, symptom present/CT absent, symptom absent/CT present, and symptom present/CT present. The 1-year risk of stroke occurrence was highest in the symptom present/CT present group (2.54%), compared with symptom absent/CT present (1.09%), symptom present/CT absent (0.69%), and symptom absent/CT absent (0.54%) groups. Additionally, the symptom present/CT present group also had a higher risk of stroke occurrence within the shorter 30- and 90-day periods, when compared to other groups.[189] These studies suggest that ED clinicians may be accurately risk-stratifying patients at higher risk for stroke, but may then be falsely reassured that a negative head CT scan has "ruled out" ischemic stroke.

Stroke: Summary

There is a large body of evidence on diagnostic accuracy for stroke in the ED. Results are heterogeneous, but generally in predictable ways. False negatives are much more common than with other similarly prevalent diseases (see Myocardial Infarction, below). The overall measured false negative diagnostic error rate is 17 percent, with errors being most frequent for TIAs, next for acute ischemic strokes, and last for intracranial hemorrhages. Error rates are strongly influenced by presenting clinical symptoms, with "typical" unilateral motor and sensory symptoms or signs being protective against error and "atypical" or otherwise non-specific symptoms (e.g., dizziness or headache) substantially increasing risk of false negatives. As a result, patients with posterior circulation strokes are much more likely to be missed, as are those with lower stroke scale severity scores. Similarly, the degree of diagnostic difficulty (and resulting error rate) is increased when patients are themselves "atypical" (especially those under age 40 or without vascular risk factors) or there are distracting case features (e.g., polytrauma[198]). CT scans appear to provide false reassurance that ischemic strokes have been "ruled out," increasing the risks of false negative diagnostic errors. Functional outcomes and mortality are worse among those misdiagnosed when patients of similar stroke severity are considered, but this effect is typically masked or even reversed ("misdiagnosis is protective paradox") when cases are left unadjusted for initial stroke severity. Poor outcomes are 4- to 5-fold more frequent when lower severity strokes are initially missed. The overall measured false positive diagnostic error rate is 21 percent, with these errors also most frequent for TIAs, next for acute ischemic strokes,

and last for intracranial hemorrhages. False positives are also probably more common among those with atypical or non-specific symptoms (e.g., dizziness) and among younger patients.

Myocardial Infarction

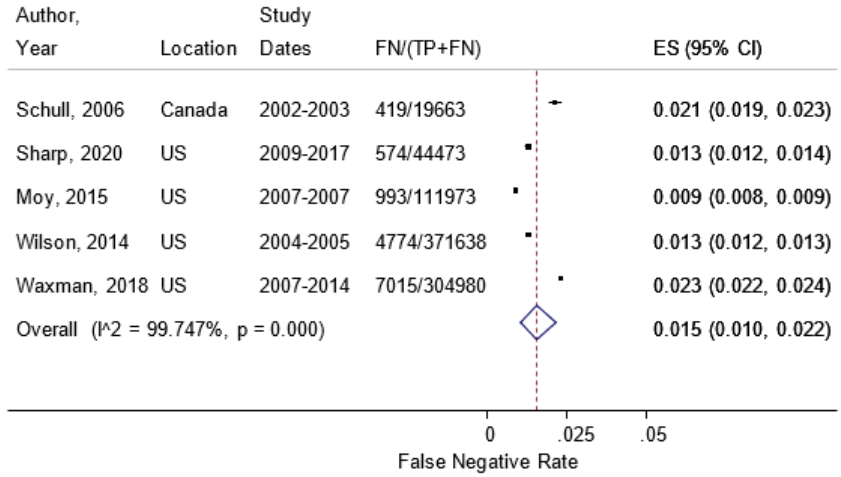
We identified 15 studies that reported on the rate of diagnostic errors among 869,711 patients presenting with myocardial infarction to the ED.[25, 63, 65, 77, 120, 200-209] The risk of bias of included studies was generally low.

Myocardial Infarction: False Negatives

Six studies[25, 63, 77, 120, 202, 206] assessed diagnostic false negative rates for myocardial infarction in routine ED practice, five of which used variations of the SPADE method, look-back approach, based on recent ED treat-and-release visits antecedent to a hospitalization for confirmed myocardial infarction.[145] All were based on either regional or insurance-based capture of both hospitalizations and antecedent ED visits. A meta-analysis was conducted to synthesize those five similarly designed studies[25, 63, 77, 120, 202] and estimated a false negative rate of 1.5 percent (95% CI 1.0 to 2.2; I-squared 99.7%; Figure 7; high SOE for false negative rate). These studies indicate that very few patients who are ultimately hospitalized with myocardial infarction are discharged from the ED in the 7 to 30 days prior. They do not address patients whose myocardial infarctions may have been mild or silent, never requiring hospitalization. Thus, these studies more closely reflect misdiagnosis-related harm rates than diagnostic error rates, per se.

We can assess the relationship between the measured harm rates and false negative diagnostic error rates from a large (n=10,689), U.S.-based prospective, randomized trial with 99 percent follow-up of patients, which did not meet our entry criteria because it was conducted in 1993.[22] That study (Pope, 2000), which used serial measurement of creatinine kinase myocardial band (CK-MB) as the biomarker, found the missed myocardial infarction rate was 2.1 percent (95% CI 1.1 to 3.1). Even in the oldest study included in our meta-analysis (Schull, 2006, patients 2002-2003), troponin tests were available around-the-clock at 55 percent of 153 EDs responding to a study survey (survey response rate 89.5%, n=153 of 171).[25] Given the advances in diagnostic testing for myocardial infarction between the time of the Pope et al. study and the studies included in our meta-analysis, it would be expected that missed myocardial infarction rates in the ED would have fallen (i.e., would be below the 2.1% rate identified in the 1993 randomized trial). Accordingly, a measured misdiagnosis-related harm rate of 1.5 percent in our meta-analysis is probably quite close to the false negative diagnostic error rate for myocardial infarction, at least in absolute terms. If the true myocardial infarction false negative diagnostic error rate is 2 percent, then even though the error rate is 25 percent higher in relative terms, the absolute difference is just 0.4 percent. Thus, diagnostic error and harm rates for myocardial infarction appear to be low enough that the gap between the two values is at the level of rounding error.

Figure 7. False negative rate (initially discharged) for myocardial infarction in the emergency department



CI = confidence interval; ES = effect summary (false negative rate); FN = number of false negatives; TP = number of true positives; U.S. = United States

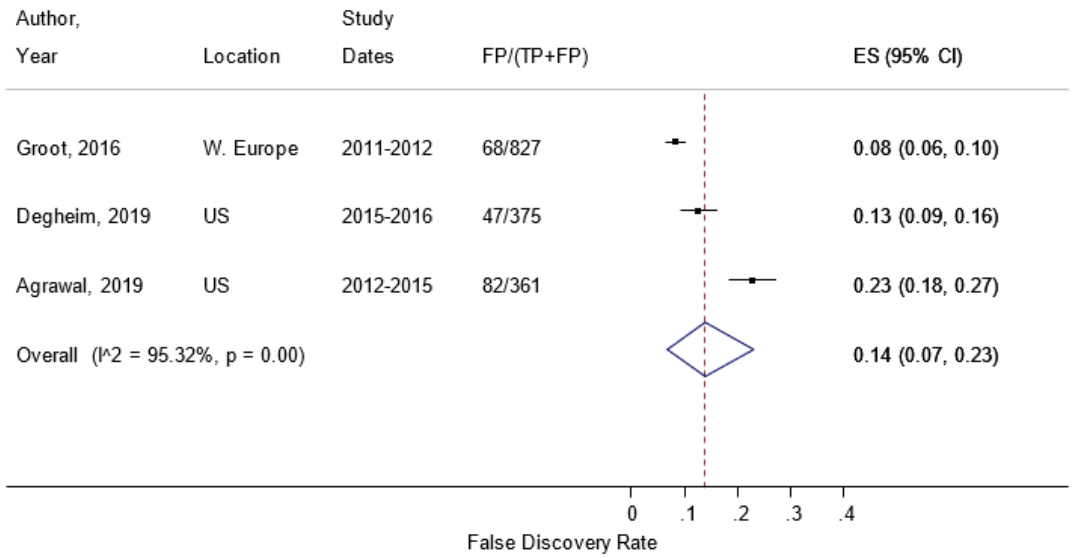
The sixth and final study (Graff, 2006) also began with a cohort of patients hospitalized for myocardial infarction, but addressed patients admitted, rather than discharged, from the ED. They found that 25.6 percent of myocardial infarction patients were admitted with a non-acute coronary syndrome diagnosis.[206] These were mostly other cardiac diagnoses (17.6%) with respiratory diagnoses next (4.7%) and a small proportion of all other diagnoses (3.3%). Patients admitted with non-specific chest pain or coronary artery disease diagnoses were classified with more specific acute coronary syndrome admitting diagnoses (acute myocardial infarction and unstable angina) in the three-fourths of patients who were "correctly" diagnosed on admission (i.e., ED admitting diagnoses were underspecified). The authors found that the non-acute coronary syndrome admitting diagnoses ("diagnostic delay") were associated with substantially lower quality care (substantially fewer evidence-based therapies applied, including 17% as opposed to 39% undergoing cardiac catheterization) than their counterparts with myocardial infarction who had no delay in diagnosis. Taken together with the meta-analytic results shown in Figure 7, this suggests that EDs are only rarely "missing" heart attacks outright, but diagnostic delays among admitted patients are perhaps substantially more frequent.

One SPADE look-forward study reported that among 325,088 patients who were discharged from the ED with a diagnosis of chest pain or dyspnea, 508 (0.2%) returned to the hospital and were diagnosed with a myocardial infarction (high SOE for false omission rate).[77] In one additional prospective study of 1114 patients admitted to three academic ED chest pain units, 991 were discharged after a negative chest pain work up and 0.4 percent developed acute coronary syndrome within 45 days.[210] Finally, a Canadian population-based study looked at 498,291 patients aged 40 years old or older who presented to an ED with chest pain and were discharged after assessment. Overall, 0.7 percent of patients were hospitalized within 30 days for myocardial infarction or unstable angina and 0.2 percent died. This study also demonstrated that higher ED volume was associated with significantly lower adjusted OR for mortality or acute coronary syndrome at 30 days.[211]

Myocardial Infarction: False Positives

Three studies assessed the diagnostic false discovery rate for myocardial infarction in routine ED practice.[201, 207, 209] All three focused on false positive ST-elevation myocardial infarction, using patients referred for immediate cardiac catheterization who were determined not to be having ST-elevation myocardial infarction (STEMI). A meta-analysis produced a false discovery rate of 14 percent (95% CI 7 to 22; I-squared 95%; Figure 8; low SOE for false discovery rate) based on those three studies. No evidence on heterogeneity due to country, recruiting period, or clinician training could be detected due to the small number of included studies.

Figure 8. False discovery rate (cardiac catheterization) for acute STEMI in the emergency department



CI = confidence interval; ES = effect summary (false discovery rate); FP = number of false positives; STEMI = ST-elevation myocardial infarction; TP = number of true positives; U.S. = United States; W. = Western

Myocardial Infarction: Other Studies

Three studies assessed the diagnostic accuracy of specific symptoms for myocardial infarction, such as chest pain and atypical symptoms.[65, 200, 203] One study assessed the diagnostic accuracy of 80-lead electrocardiogram (ECG).[205] Two studies assessed diagnostic delay including the door-to-balloon time and door-to-reperfusion time.[204, 208]

Myocardial Infarction: Summary

In general, the evidence on diagnostic accuracy for myocardial infarction is limited but fairly homogeneous. Large studies consistently show that just 1 to 2 percent of patients hospitalized for myocardial infarction were recently treated and released from the ED. Diagnostic accuracy for myocardial infarction patients admitted but not initially characterized as having an acute coronary syndrome is lower, with delays in diagnosis in up to one fourth of cases that potentially contribute to lower-quality care based on evidence-based guidelines. The false discovery rate for STEMI is 14 percent among patients referred for immediate cardiac catheterization, but the number of studies was small and their results heterogeneous.

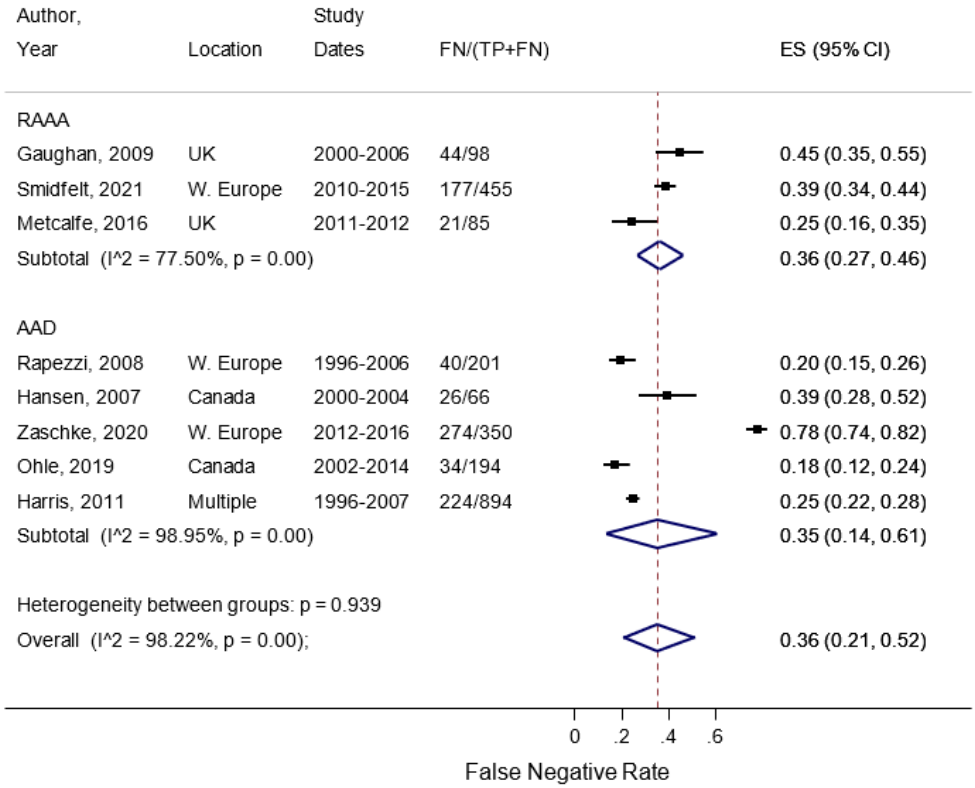
Aortic Aneurysm and Dissection

Twelve studies with an unclear- or low-risk of bias reported on the rate of misdiagnosis among at least 37,638 patients with aortic aneurysm or dissection.[68, 73, 89, 120, 212-219] Two studies likely had overlapping study populations as they both included patients with ruptured abdominal aortic aneurysm from the same region of Sweden during similar time periods[216, 219]; we included the most recent study in the analysis.[219]

Aortic Aneurysm and Dissection: False Negatives

We pooled eight studies that reported on missed or delayed diagnoses among patients with ruptured abdominal aortic aneurysm[89, 213, 219] or acute aortic dissection[68, 73, 89, 214, 218, 219] (n=1,799). The estimated false negative rate was 36 percent (95% CI 21 to 52; I-squared 98%; Figure 9; moderate SOE for false negative rate). Studies differed in their definitions of missed or delayed diagnoses. Five studies compared patients who were correctly diagnosed in the ED or at initial presentation with those who were misdiagnosed.[89, 213, 214, 218, 219] Two of these studies provided strict criteria for a correct diagnosis. Ohle et al. classified patients as missed diagnosed if they were not diagnosed within the ED, if they received treatment for an alternate diagnosis in the ED, or if they re-presented at an ED within 14 days of initial visit.[218] Smidfelt et al. considered patients as correctly diagnosed if aortic aneurysm was mentioned in the medical chart by the ED, if the patient was referred by the ED for an acute CT scan for aortic aneurysm, or if the patient received a laparotomy for suspected ruptured abdominal aortic aneurysm.[219] Two other studies used time to diagnosis to determine patients who had a short versus long diagnostic time.[68, 73]

Figure 9. False negative rate (diagnostic delay) for aortic aneurysm or dissection in the emergency department



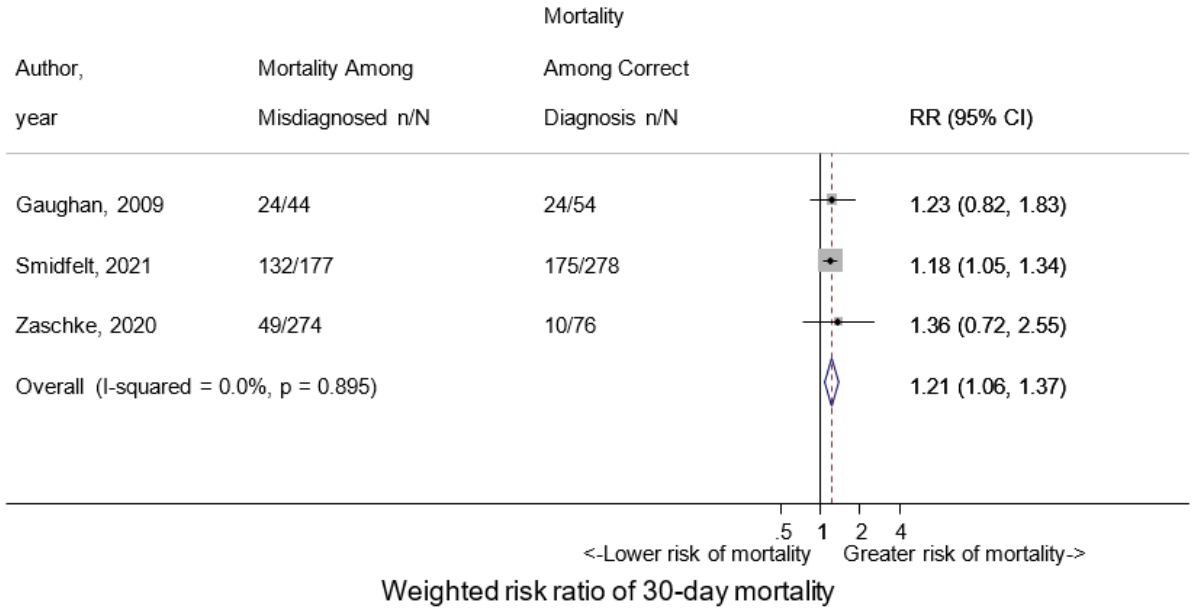
AAD = acute aortic dissection; CI = confidence interval; ES = effect summary (false negative rate); FN = number of false negatives; RAAA = ruptured abdominal aortic aneurysm; TP = number of true positives; U.K. = United Kingdom; W. = Western

We were unable to include three studies in the meta-analysis due to differences in study design and differences in defining missed diagnoses. One was a retrospective cohort that reported a false negative rate of 0 percent among those who received a focused cardiac ultrasound by an emergency physician and 43 percent among those who did not.[212] Another study reported a misdiagnosis rate of 24 percent among patients transferred to a referral center, including 15 percent of patients misclassified type of acute aortic syndrome (aneurysm called dissection, dissection called aneurysm, or error in type of dissection).[215] Using Medicare data and SPADE-style methods, the false negative harm rate for diagnosis (defined as observed minus expected prior ED visits in advance of a related hospitalization) was reported as 3.4 percent (95% CI 2.9 to 4.0) for ruptured abdominal aortic aneurysm and 4.5 precent (95% CI 3.9 to 5.1) for aortic dissection.[120]

Three studies reported on the association between misdiagnosis and 30-day mortality.[213, 216, 217] Pooling these three studies in a meta-analysis suggests a greater risk of 30-day mortality among those who were misdiagnosed than among those who were correctly diagnosed with aortic aneurysm and dissection (risk ratio [RR] 1.21; 95% CI 1.06 to 1.37; I-squared 0%; Figure 10). In addition to these unadjusted results, one study (Smidfelt, 2021) reported an even greater increased risk for mortality among those who were misdiagnosed when adjusted for age, sex, serum creatinine, and first-recorded systolic blood pressure of 90 mmHg or less (adjusted OR 1.83; 95% CI 1.13 to 2.96). The last of these is a proxy for initial case severity (those with low initial blood pressure were misdiagnosed in 28% vs. 44%, $P = 0.001$), and, as expected, when

adjusted for initial severity (which often confounds the relationship between diagnostic error and misdiagnosis-related harms), the impact of diagnostic delay on mortality increases.

Figure 10. Association between initial emergency department delay in diagnosis of aortic aneurysm or dissection and 30-day mortality



CI = confidence interval; RR = risk ratio

Aortic Aneurysm and Dissection: False Positives

One study reported a misdiagnosis rate of 24 percent among transfers, including 9 percent of patients being misclassified as having an aneurysm or a dissection when they did not (low SOE for false discovery rate).[215] A recent study of 1,762 emergency transfers for acute aortic syndrome was identified during the final report review (after the period of the systematic search).[220] The study found 188 patients misdiagnosed (134 of these referred by ED physicians), including 84 of the 188 had suspected rupture or dissection they did not have (5% false discovery rate, n=84/1,762); all misdiagnoses were attributed to misinterpretation of imaging studies. Taking the two studies together, the estimated false discovery rate was 5 percent (n=93/1,862).

Venous Thromboembolism

Five studies with a low-risk of bias reported on the rate of misdiagnosing venous thromboembolism (N=13,459 patients).[54, 221-224] All of the studies, except one,[224] were conducted outside of the United States.

Venous Thromboembolism: False Negatives

Three studies included patients (n=2,757) with a final diagnosis of pulmonary embolism and reported on the number of patients with a delayed diagnosis, which was defined as a diagnosis 7 days after the onset of symptoms[221, 223] or a diagnosis between 24 hours and 30 days after an ED presentation.[222] Pooling these three studies in a meta-analysis yielded a false negative rate of 20 percent (95% CI 17 to 24; Figure 11; moderate SOE for false negative rate).[221-223] Heterogeneity was not significant (I-squared 43%). Limiting the meta-analysis to only studies that were

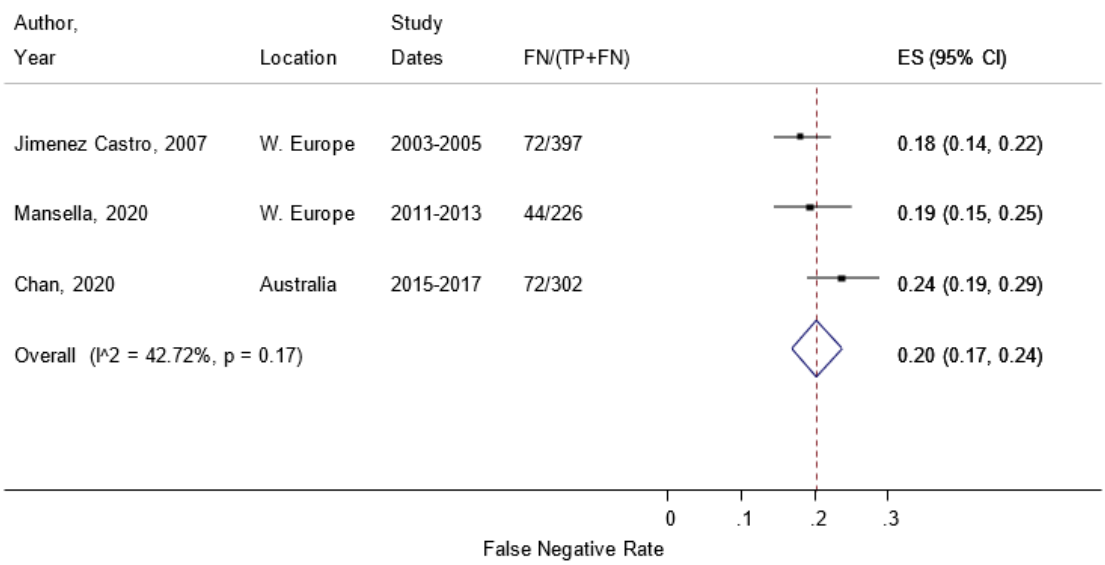
conducted after 2010 yielded a pooled false negative rate of 22 percent (95% CI 18 to 25),[222, 223] indicating no change over time.

We did not include one study in this analysis because of the heterogeneity in study design. This study recruited patients with undifferentiated dyspnea and randomized them to receive immediate or delayed point of care ultrasound.[54] The sensitivity and specificity of detecting acute pulmonary embolism in the ED were 89 percent and 100 percent, respectively, with immediate point-of-care ultrasound and 83 percent and 100 percent, respectively, with delayed ultrasound.

A second study was not included in this analysis because of heterogeneity in study design. This study was a retrospective interrupted time series evaluating age-adjusted dimer in patients over the age of 50 suspected of having pulmonary embolism (D-dimer ordered, chest related complaints, and no ultrasound order). The primary outcome was use of advanced diagnostic imaging and secondary outcome was diagnosis of pulmonary embolism within 30 days with age-adjusted D-dimer demonstrating a sensitivity of 95.2 percent and specificity of 68.6 percent.[224]

Two studies reported the mortality associated with a delayed diagnosis of pulmonary embolism.[221, 222] One study reported no difference in all-cause mortality at 3 months between those with a delayed (>7 days from symptom onset) versus timely diagnosis (unadjusted OR 0.9; 95% CI 0.4 to 2.0).[221] This study showing no difference failed to adjust for baseline initial case severity, and patients diagnosed in timely fashion were clearly sicker at baseline (e.g., oxygen saturation <60 mmHg at presentation, 57 versus 42%, $P = 0.03$). The other study reported a significantly higher inpatient mortality rate among those with a delayed diagnosis (between 24 hours to 30 days after ED presentation) compared to those with an early diagnosis (unadjusted OR, 45.3; 95% CI 13.2 to 153.4).[222]

Figure 11. False negative rate (diagnostic delay) for pulmonary embolism in the emergency department



CI = confidence interval; ES = effect summary (false negative rate); FN = number of false negatives; TP = number of true positives; W. = Western

Meningitis and Encephalitis

Meningitis and Encephalitis: False Negatives

We identified one study that reported the rate of diagnostic error among 521 children, aged 30 days to 5 years, who were diagnosed with meningitis or septicemia.[93] The study conducted a SPADE-style look back analysis to examine if children hospitalized with meningitis or septicemia in Ontario, Canada had ED treat-and-release ED visit(s) prior to their admission. The study reported 114 (21.9%) of the 521 children had prior treat-and-release ED visits with a median return time of 24.5 hours (low SOE for false negative rate). Although the authors reported no significant difference in the health outcomes among children who had repeated ED visit versus those who were admitted on the first ED visit, they failed to adjust for initial case severity, which likely confounds the finding.

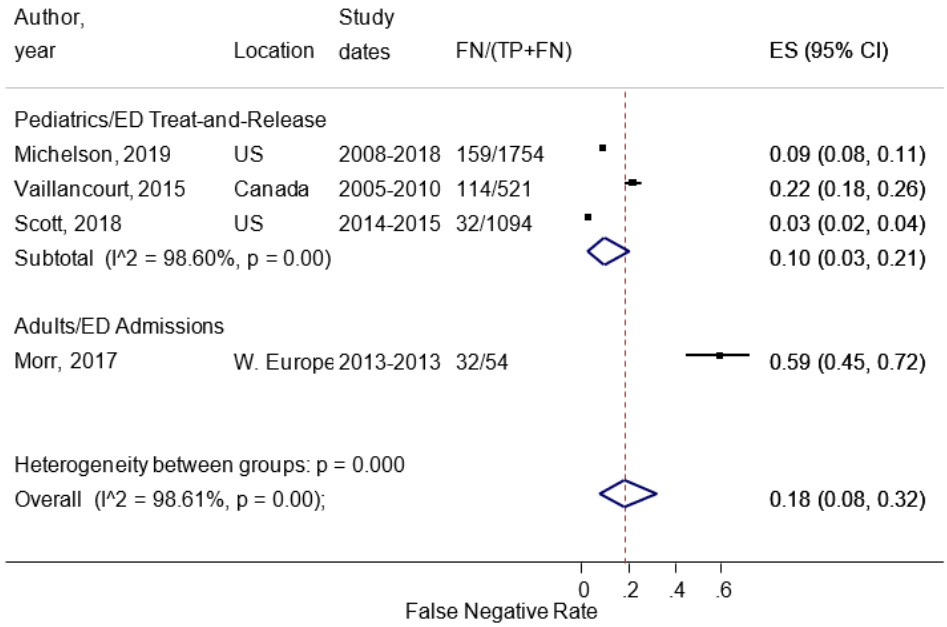
Sepsis

We identified four studies that reported on the rate of diagnostic errors among 3,479 patients presenting to the ED and later diagnosed with sepsis.[93, 156, 157, 225] All the studies were retrospective cohort studies (three of the four using SPADE-style look-back analyses in large electronic data sets) to identify missed diagnoses at ED or discrepancy in diagnosis between ED and inpatient. Only one study (Morr, 2017) was performed among adults (over 18 years of age). This study focused on review of consecutive hospital admissions from the ED to an internal medicine service; the case records were systematically assessed for evidence of infection, sepsis, and severe sepsis, and the authors reported on lack of recognition of sepsis or severe sepsis.[157]

Sepsis: False Negatives

The pooled false negative rate among sepsis patients was 18 percent (95% CI 8 to 32; I-squared 99%; Figure 12; moderate SOE for false negative rate). Subgroup analysis by age showed a significant difference in rate of misdiagnoses among patients under 18 years of age (10%; 95% CI 3 to 21) versus those over 18 years (59%; 95% CI 45 to 72), with rates significantly higher among adults than children. However, the lone adult study (Morr, 2017) used very different methods than the studies in children, focusing on incorrect severity assessment among ED patients admitted with infections, rather than missed opportunities to diagnose infection among ED treat-and-release visits that were followed by sepsis hospitalizations. The Morr, 2017 paper refers to “ED discharge letters” but in the methods section they note that “All medical patients receive a detailed discharge letter upon transfer from the ED to the wards.”; this seems to clarify that the patients are all admitted via the ED, rather than admitted after having been treated and released previously from the ED. Thus, it is likely that the apparent difference in false negatives by age group is methods-related, rather than age-related. It is unsurprising that the rate of ED treat-and-release followed by sepsis hospitalization would be lower than the rate of correctly diagnosed infection requiring admission in which severity (i.e., sepsis) was under-recognized in the ED. Thus, the more generalizable false negative rate is likely 10 percent, rather than 18 percent. Two studies assessed impact of missed diagnosis on health outcomes (30-day mortality), and no significant difference was observed.[93, 156] Both studies failed to adequately adjust for initial case severity in performing their analyses of adverse health outcomes.

Figure 12. False negative rate for sepsis in the emergency department



CI = confidence interval; ED = emergency department; ES = effect summary (false negative rate); FN = number of false negatives; TP = number of true positives; U.S. = United States; W. = Western

Arterial Thromboembolism

Arterial Thromboembolism: False Negatives

We identified two studies that reported on the rate of false negatives for acute mesenteric ischemia.[226, 227] One study assessed delayed diagnosis of acute mesenteric ischemia among 72 cases presenting to the ED.[226] Time to surgical consult was ≥24 hours in 15.3 percent of patients (low SOE for false negative rate). Delay in consultation was associated with increased odds of death, although the result was not statistically significant (severity-adjusted OR 3; 90% CI 0.69 to 13; $P = 0.11$). Time to operation was ≥6 hours in 37.9 percent of cases (n=22 of 58 undergoing operations). Delay in operation was associated with a statistically significant increased odds of death (severity-adjusted OR 3.7; 90% CI 1.1 to 12; $P = 0.04$). After excluding cases for whom care was withdrawn (i.e., eliminating very high-severity cases that fared very poorly, thereby focusing on milder cases) and again adjusting for illness severity, mortality was substantially increased for both delay in consultation (9.4-fold increased, $P = 0.03$) and delay in operation (4.9-fold increased, $P = 0.04$). This again shows that illness severity adjustment is essential for determining the full negative health impact of diagnostic delay, which is understated when illness severity is not considered. The second study focused on radiographic misdiagnosis among 95 patients with 97 acute mesenteric ischemia events.[227] Acute mesenteric ischemia was incorrectly diagnosed by the on-call radiologist in 14 of these 97 cases (14%).

Spinal and Intracranial Abscess

One study included as part of the review (Dubosh, 2020) addressed missed spinal abscess among 1,381,614 ED discharges for back pain, enabling assessment of the false omission rate.[81] Two others addressed missed cases (false negative rate) in all-comers with spinal abscess but

were excluded during the full-text review stage; the nature of these exclusions (described below) is such that they are unlikely to invalidate the study findings, so results are presented here.

Spinal and Intracranial Abscess: False Negatives

One study identified as part of the review examined the frequency of missed spinal and intracranial abscess among ED patients treated and released with "benign" back pain diagnoses.[81] In a large retrospective cohort study (look forward method) from six U.S. states, Dubosh et al. found that the most common missed neurologic condition among treat-and-release visits for back pain was intraspinal abscess (46% of missed neurologic conditions among those hospitalized within 30 days were for intraspinal abscess). The absolute rate of 30-day returns for a subsequent hospitalization (including in-hospital mortality) with spinal abscess was 0.1 percent (n=1,320/1,381,614) of "benign" back pain treat-and-release visits from the ED (high SOE for false omission rate). This false omission rate corresponds to one missed spinal abscess for every 1,047 "benign" back pain ED discharges.

One detailed study of missed spinal abscess cases drawn from a large national clinical data repository through the Veterans Administration was captured but excluded from the review at the full text stage solely because it admixed ambulatory clinic care and ED cases; the authors were contacted, but they were unable to provide a breakdown of the number of cases that were ED based (*personal communication*). If results from that study are applicable to ED missed spinal abscess, the misdiagnosis rate for spinal abscesses is estimated to be 56 percent (n=66/119).[228] Pre-defined missed "red flags" in misdiagnosed cases (n=66) were unexplained fever (n=57), focal neurologic deficits with progressive or disabling symptoms (n=54), active infection (n=54), immunosuppression (n=36), intravenous drug use (n=20), prolonged use of corticosteroids (n=16), unexplained weight loss (n=13), back pain duration greater than 6 weeks (n=13), and a history of cancer (n=9). Among misdiagnosed cases (n=66), the mean number of pre-defined missed "red flag" signs was 4.9, which was higher than the mean of 4.3 in those correctly diagnosed ($P = 0.03$). Diagnostic process failures resulted from: 1) the provider-patient encounter (n=60 with missed red flags [information not gathered during history and physical examination] or inappropriate action [ordering tests] after identifying red flags); 2) the subspecialty consultation process (n=51 in which the provider did not believe referral was required or an appropriate expert was not consulted); 3) patient-related delays (n=17 in which the patient did not show up for a follow-up visit); 4) provider-related delays (n=11 in which the provider took too much time to follow-up test results); and 5) radiographic misdiagnosis (n=5 in which the MRI report was not read accurately and was believed to be non-serious). The level of misdiagnosis-related harms identified was of high severity, with the potentially preventable results of diagnostic delay being death (n=8), severe harm (n=32), moderate harm (n=25), mild harm (n=1), and no harm or unknown (n=0).

Pneumonia

We identified two studies that reported the rate of diagnostic error among 293 patients who were diagnosed with pneumonia.[136, 229] Neither study addressed all ED patients with pneumonia. One study reported on community-acquired pneumonia among patients 65 years or older with acute respiratory failure[136]; the other study reported on round pneumonia among patients under 19 years of age.[229]

Pneumonia: False Negatives

The first study was a prospective observational study at a University hospital in Paris, France (Ray, 2006).[136] This was a well-designed study that looked at ED diagnostic accuracy rigorously, but in the specific population of elderly patients with acute respiratory failure (n=514), a subset of whom had community-acquired pneumonia (n=181). All patients were admitted for an extensive hospital-based diagnostic evaluation. In this narrowly defined patient population, the authors described ED physician diagnostic accuracy for pneumonia as follows (value [95% CI]): sensitivity 0.86 [0.80–0.90], specificity 0.76 [0.71–0.80], positive predictive value 0.66 [0.59–0.71], negative predictive value 0.91 [0.87–0.93], total diagnostic accuracy 0.79 [0.75–0.82]. These values correspond to a false negative rate of 14 percent, a false positive rate of 24 percent, a false discovery rate of 34 percent, and a false omission rate of 9 percent (low SOE for all measures of diagnostic accuracy).

Pneumonia: False Positives

As noted above, the Ray, 2006 study found a false positive rate of 24 percent and false discovery rate of 34 percent. The second study was a retrospective review of radiology cases of round pneumonia conducted at a large tertiary care Children's hospital in Cincinnati (Kim, 2007).[229] Although not mentioned explicitly in the report, it was assumed that the majority of cases would have initially presented via the ED. The authors, on review of the cases, found "three patients (2.6%, three of the initially identified 112) who were originally suspected to have round pneumonia and were later shown to have other diagnoses." No further details were provided (including whether the errors occurred in ED patients), but it appears these were errors in radiographic interpretation. This would correspond to a false discovery rate of 2.6 percent, but it is highly improbable that this corresponds well to overall ED diagnostic accuracy.

Appendicitis

We identified eight studies that reported the rate of diagnostic error of appendicitis among 7,351 patients.[225, 230-236] Two studies assessed diagnostic error as part of a prospective assessment of different diagnostic imaging in the ED.[230, 231] Three studies conducted a retrospective analysis.[225, 232, 233] Two studies examined diagnostic outcome changes before and during the coronavirus (SARS-CoV-2) disease 2019 (COVID-19) outbreak.[234, 235] One study examined missed diagnostic opportunities at the ED using a look-back method.[236] All approaches may have high risk of biases due to inclusion criteria and sampling.

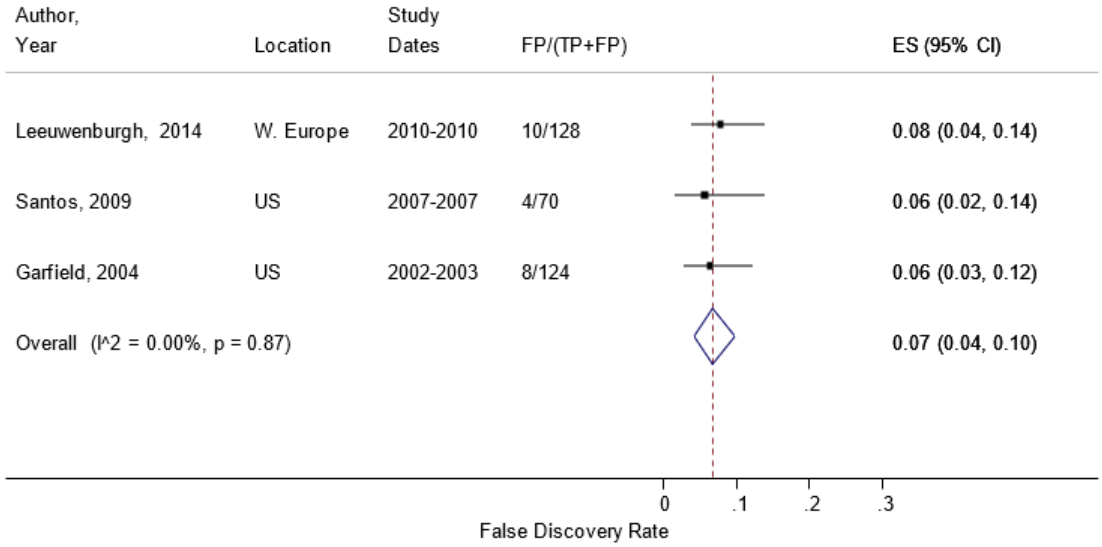
Appendicitis: False Negatives

Of those with a final diagnosis of appendicitis, misdiagnosis rates ranged from 0.2 to 4.8 percent in pediatric studies (moderate SOE for false negative rate).[225, 233, 236-238] The false negative rate was 2.9 percent among patients under 18 years of age.[225] The false negative rate in an unrelated study among patients 17 years of age and older was 30.8 percent, but this study used a very different method and focused only on missed cases using point-of-care ultrasound.[233] That said, an older study (from prior to the study period) which compared younger and older presentations of appendicitis appears to corroborate the notion that diagnostic delays in older adults are more common than among children, with contributions from both the "patient interval" (from symptoms to presentation) and "clinician interval" (from presentation to diagnosis) delay components—the result appears to be a higher rate of complications and greater mortality.[239] This difference is not necessarily unexpected, given that appendicitis in older patients is both less common and more atypical ("wrong" age group for the illness).

Appendicitis: False Positives

The pooled false discovery rate for appendicitis diagnoses in the ED was 7 percent (95% CI 4 to 9; I-squared, 0%; Figure 13)[230-233] (moderate SOE for false discovery rate). The studies included a combination of prospective and retrospective cohorts. However, case selection due to inclusion criteria for certain studies limited their generalizability. False positive diagnoses of appendicitis may result in harm by subjecting patients to unnecessary surgical procedures.

Figure 13. False discovery rate for appendicitis in the emergency department



CI = confidence interval; ES = effect summary (false discovery rate); FP = number of false positives; TP = number of true positives; U.S. = United States; W. = Western

During the COVID-19 outbreak, Somers et al. showed that the false discovery rate decreased from 26.1 percent to 2.5 percent.[234] This observation might have been due to changes in patient illness seeking behavior during the pandemic—since volumes were lower, perhaps only those who experienced more severe symptoms or more advanced illness might have ended up seeking care in the ED, making the mix of diagnoses more "obvious." However, Willms et al. showed no difference in the false discovery rate before and during the COVID-19 outbreak.[235]

Fractures

We identified 17 retrospective or prospective studies (4 in the United States[240-243]) that reported on the rate of diagnostic errors and/or misdiagnosis-related harms among 138,551 patients with fractures.[74, 83, 121, 240-253] Studies varied significantly in the methodological approach, definitions to assess diagnostic errors, target populations, and inclusion/exclusion criteria. Most of the studies had a low risk of bias. The retrospective design in most of the studies makes it difficult to know the true rate of diagnostic error. When Enderson and colleagues changed the study design from retrospective to prospective the incidence of missed traumatic fractures increased from 2 to 9 percent.[152] Studies tended to emphasize delay in diagnosis as an endpoint, while clinically meaningful delays affecting outcomes were far fewer in number.

Fractures: False Negatives

Fourteen studies reported on the false negative rate for fractures in the ED.[83, 84, 121, 240-244, 246-248, 250-253]

In an ED that evaluates adults and children, a total of 350 false-negative errors occurred in 28,904 fractures (1.2%). The sites most often missed in children were elbow (29%) and wrist (21%); in adults, it was the foot (17%), as well as the pelvis and hip (37%) in elderly patients.[248] Spine fractures (shown in KQ1 to be more harmful) accounted for just 6.2 percent of missed cases. In a second study of 5,879 patients who presented to an ED, 40 patients had a false negative fracture (0.7%). The missed fractures were in the ankle or foot (28%, n=11), lower arm (22%, n=9), hand and fingers (22%, n=9), hip (10%, n=4) and miscellaneous (18%, n=7).[246]

However, miss rates varied widely across studies (from 0.02 to 40%), depending on study design, definitions, or included populations. In one study that compared initial radiology resident reads to those of attending radiologists in a tertiary care ED, just 19 out of 81,201 images (0.02%) were classified as a missed fractures.[241] In patients with minor trauma, 7 of 4,025 patients (0.2%) had a missed fracture when evaluated in an outpatient clinic.[251] In patients with fractures at a specialty orthopedics ED who had imaging read only by an orthopedic surgeon versus a radiologist, the incidence of false-negative fractures was 293 out of 13,561 (2.2%).[83] In another study, 51 of 304 limb or pelvis X-rays had discrepancies between ED clinical notes and the final radiology report (17%), although only 15 (5% of the total) were deemed clinically significant.[250] In a study of ED ankle X-rays, 61 out of 2947 (2%) were considered major discrepancies that changed management.[253] Among polytrauma patients, rates of delayed diagnosis of injury ranged from 2 to 40 percent, with the most common of these being fractures (moderate SOE for false negative rate).

Fracture False Negatives: Polytrauma

In patients with polytrauma, rates of missed secondary fractures are generally higher than in the general ED population, despite multiple trauma surveys searching for injuries. In polytrauma patients presenting to one trauma center 12 percent (n=172 of 1,416) suffered delayed diagnoses of injury; the majority of these were extremity fractures, given that these patients received CT scans of the head, chest, and pelvis as the primary focus of their initial trauma survey for injuries. The incidence of false-negative extremity fractures (in order of the proportion delayed) was hand (54%, n=39 of 72), foot (38%, n=23 of 61), tibia (21%, n=11 of 53), fibula (18%, n=4 of 22), ankle (15%, n=7 of 47), humerus (15%, n=13 of 88), radius (10%, n=11 of 109), patella (8%, n=2 of 26), ulna (8%, n=8 of 96), clavicle (6%, n=12 of 196), scapula (4%, n=6 of 127), femur (2% , n=3 of 134), and cruris (2%, n=2 of 86).[121] The importance of ongoing reassessment in polytrauma patients was emphasized. In severe trauma cases requiring CT of the whole body, 39 of 375 patients (10%) had a missed injury, of which 85% could be detected on a second read. This study suggested that a second read in the setting of quality assurance would be helpful to minimize missed fractures.[252] In another study in a non-United States trauma center, 64 missed injuries (the majority of which were fractures) were detected in 58 patients out of 1,187 patients seen (4.9% of patients).[245] There was a delay in diagnosis of fracture in a pediatric trauma center in 44 of 1,056 patients (4%) who presented with trauma.[240] There were eight fractures out of 76 pediatric trauma patients (11%) that were missed: two were of the spine, two were of the head and face, two were in the upper limb, and two were in the lower limb.[247] In a large pediatric trauma center, 62 of 2,316 (2%) patients had a missed fracture, the majority of which were upper and lower extremity injuries.[249] In another pediatric trauma center, 18 of 196 (9%) were classified as delayed diagnosis of fracture, one of which required surgical treatment.[243] In one study from Spain, 49 of 122 (40%) had delayed diagnosis of injury, and the most frequently missed injury was fracture (43%).[74]

Fracture False Negatives: Abuse

In pediatric patients with a delay in diagnosis of abuse, 54 of 258 patients (21 percent) were falsely classified as a non-abuse fracture.[244]

Fractures: False Positives

Four studies reported on the rate of false positive diagnoses of fractures.[83, 246, 249, 253] Twenty-one of 61 misdiagnosed fractures in adult ED patients were false positives (34% of fracture diagnostic errors).[246] Among 13,561 ED patients with minor trauma whose X-rays were not reviewed by an attending radiologist, 337 misdiagnosed fractures were identified (2.5%); of these, 44 (13%) had false-positive fractures.[83] Sixty-five of 125 incorrect fracture diagnoses in pediatric skeletal radiographs were false positives (52%).[249] Ten of 81 major discrepancies in ED ankle radiographs were false positives (12%).[253] We were unable to draw strong conclusions about the rate of false positive fracture diagnoses because of concerns with study limitations and methodological heterogeneity. Nevertheless, a sizable minority of diagnostic errors related to fractures are likely to be false positive (12-52%) rather than false negative diagnoses.

Fractures: Other Studies

One study used a machine-learning algorithm to improve clinician detection of fractures from a sensitivity of 80.8 to 91.5 percent and a specificity of 87.5 to 93.9 percent. The authors suggested this technique could allow expert knowledge to be delivered remotely to generalists.[242]

Testicular Torsion

We identified two studies (one in the United States and one in Canada) that reported on the rate of diagnostic errors and/or misdiagnosis-related harms among 262 patients with testicular torsion.[254, 255] One study was a retrospective review evaluating doppler ultrasound as a means of detecting testicular torsion.[254] The other study was a retrospective chart review of ED patients who underwent detorsion and orchiopexy or orchiectomy (2005-2015).[255]

Testicular Torsion: False Negatives

Both studies reported false-negative errors.[254, 255] In one study evaluating doppler ultrasound, three out of 46 patients with a false negative had absent or diminished flow, 18 had an absence of arterial waveform, 29 had heterogeneous echotexture, and 15 had an absence of doppler flow.[254] All of the tests had a positive predictive value of 91 percent or higher; none of the test findings had negative predictive values greater than 40 percent. In the other study, the initial miss rate overall was 6 percent (n=12 of 208) and 13 percent among patients with a delayed presentation (n=12 of 94). Among the 12 initially misdiagnosed, 11 were missed in the ED, which corresponds to an ED false negative rate of 5 percent. Delayed presentations were more likely to report isolated abdominal pain, have developmental disorders, or report a history of genital trauma.[255] Chan et al., 2019 focused on testing delays and radiographic errors, while Bayne et al., 2017 enabled an estimate of ED false negative rate (n=11 of 208 total cases, all in the "delayed presentation" subgroup [n=94]). Among patients with testicular torsion, 5.3 percent (95% CI, 2.7% to 9.3%) are initially misdiagnosed in the ED (low SOE for false negative rate).

Testicular Torsion: False Positives

One study had three false-positive patients among 46 patients: one with absent or diminished flow, one with heterogeneous echotexture, and one with abscess of doppler flow.[254] This corresponds to a 7 percent false discovery rate. We are unable to draw a conclusion about the

rate of false positive diagnoses of testicular torsion because of our concerns with study limitations and the imprecise results from a single study.

Other Conditions

We did not find any studies meeting our inclusion criteria that reported on the ED diagnostic error rate for endocarditis, necrotizing enterocolitis, sudden cardiac death, arrythmias, congenital heart disease, ectopic pregnancy, or pre-eclampsia/eclampsia.

Key Question 2c. Approximately how many patients does this equate to nationally in the United States?

Each year in the United States there are 130 million ED visits.[13] Given the best estimates outlined in the sections above, it is likely that there are over 7 million ED diagnostic errors, over 2.5 million diagnostic adverse events involving preventable harms, and over 350,000 serious misdiagnosis-related harms, including more than 100,000 serious, permanent disabilities and over 250,000 deaths (Table 10). The studies of general (not disease-specific) diagnostic errors on which these estimates are based were not explicit about the breakdown of false negative versus false positive errors, but used methods related to diagnostic discrepancy, so should have included both types of error (including both "undercalls" and "overcalls" of dangerous diseases). Since there was no explicit search described for the adverse effects of false positive diagnoses (e.g., complications from invasive diagnostic tests or adverse health outcomes from treatment for incidental, yet unimportant, findings), it is presumed that the misdiagnosis-related harms reflect only those related to false negatives for those whose dangerous underlying diseases were missed.

Although these estimates may seem high, they are on par with what has been estimated for harms from inpatient diagnostic error (250,000 harms out of 36 million hospitalizations), based on systematic review data.[3] Furthermore, if we use the high-quality, prospective study (Hautz, 2019) of ED admissions (which did not look at discharged patients) to estimate errors and harms, we get numbers that corroborate these figures. There are 16.2 million hospital admissions each year in the United States via the ED.[13] If we combine that with a 12.3 percent error rate and 4.8 percent misdiagnosis-related death rate,[7] we get 2 million diagnostic errors and 97,000 deaths among patients hospitalized via the ED. Using the ratio of disability to death shown in Table 10, that corresponds to about 136,000 serious harms. These are included among the total of more than 350,000 estimated in Table 10, since the diagnostic adverse event rate and mortality include both discharged and admitted patients. It seems plausible that roughly one third of the serious harms from ED diagnostic error would occur among admitted patients (who are lower in number [12.4% of ED visits end in admission[13]] but higher in risk), with the rest among those treated and released (who are higher in number [87.6% of ED visits end in discharge[13]] but lower in risk).

Table 10. U.S. national estimates for ED diagnostic adverse events, serious morbidity, and death

Parameter	Best Estimate (95% CI or Estimated PR*)
Total Annual ED Visits (n)	130,000,000[13] (95% CI 116,000,000 to 144,000,000)
Diagnostic Error Rate (%)	5.7%[7, 137†] (aggregate† 95% CI 4.4% to 7.1%)
Diagnostic Errors (n)	**7,370,000 (PR 5,140,000 to 10,200,000)**
Diagnostic Adverse Event Rate (%)	2.0%[131] (95% CI 1.0% to 3.6%)
Diagnostic Adverse Events (n)	**2,600,000 (PR 1,110,000 to 5,230,000)**
Serious Harm Proportion (%)	14.6%[16] (95% CI 12.3% to 17.1%)
Serious Harms Method #1 (n)	**379,000 (PR 137,000 to 895,000)**
Serious Harms Rate Method #1 (%)	**0.3% (PR 0.1% to 0.7%)**
Misdiagnosis-Related Mortality Rate (%)	0.20%[131‡] (PR 0.10% to 0.40%)
Misdiagnosis-Related Deaths (n)	258,000 (PR 115,000 to 574,000)

Parameter	Best Estimate (95% CI or Estimated PR*)
Disability-to-Death Ratio	0.41[16§] (95% CI 0.27 to 0.60)
Misdiagnosis-Related Serious Disability (n)	105,000 (PR 31,000 to 345,000)
Serious Harms Method #2 (n)	**363,000 (PR 146,000 to 919,000)**
Serious Harms Rate Method #2 (%)	**0.3% (PR 0.1% to 0.7%)**
Average Serious Harms (Method #1-#2)	**371,000 (PR 142,000 to 909,000)**
Average Serious Harms Rate (Method #1-#2)	**0.3% (PR 0.1% to 0.7%)**

Abbreviations: CI = confidence interval, ED = emergency department, PR = plausible range

* Shown are a mix of true 95% CIs (based on source data, where appropriate) and plausible range values. For total ED visits, the 95% CI is based on standard errors provided in the source data. For proportions and ratios (error rate, adverse event rate, serious harm proportion, disability-to-death ratio), the 95% CIs are based on the source sample sizes using the "cii prop" command in Stata/IC v16.1 (College Station, Texas). For the mathematical products shown (e.g., diagnostic errors [n] = total annual ED visits [n] x diagnostic error rate [%], we are not able to provide statistically valid 95% CIs since this would require statistical modeling techniques (e.g., Monte Carlo simulation) that are beyond the scope of the report. Instead, plausible range estimates are provided by simply multiplying the lower bounds of corresponding CIs together to get a lower plausible range bound and, similarly, by multiplying the upper bounds of corresponding CIs together to get an upper plausible range bound. Note that the impact of using this method is that plausible ranges are wider than corresponding 95% CIs would be (i.e., they *overstate* the uncertainty). Note that all values shown are calculated using unrounded estimates, but then are rounded to no more than three significant digits.

† The diagnostic error rate was calculated as the weighted average of three measured rates from two studies—the error rate **(a)** ***among ED discharges who returned*** (20% [n=50/250] from Nuñez, 2006; representing 0.8% [n=250/32,523] of ED visits and an estimated 0.9% [n=250/28,481] of presumed ED discharges in Nuñez, using a discharge fraction estimate from the ED of 87.6% [using data from the Centers for Disease Control and Prevention's National Center for Health Statistics, 2018[13]]); **(b)** ***among ED discharges who did not return*** (4% [n=10/250] from Nuñez, 2006; representing 99.2% of ED visits and an estimated 99.1% of ED discharges in Nuñez); and **(c)** ***among ED admissions*** (12.3% [n=93/255] from Hautz, 2019; representing an estimated 12.4% of ED visits in the United States[13]). The "aggregate" 95% CI is calculated using the aggregated sample across the two studies (n=1,255 [i.e., 500 in Nuñez, 755 in Hautz]) by using the blended rate (weighted average) to infer a "numerator" (i.e., 1,255 x 5.7% = 71).

‡ The uncertainty bounds around the misdiagnosis-related mortality rate are based on a plausible range of +/- 2-fold. Uncertainty from the cited study (Calder, 2010) by 95% CI would be wider, but other studies suggest this is a more appropriate PR estimate. For example, Nuñez, 2006 found 3 deaths (1% of 250) among their unscheduled returns who were initially misdiagnosed. Using the same method described for weighted average calculation for the diagnostic error rate, this corresponds to a point estimate of 0.25% among ED discharges, and an overall death rate of 0.29% (using data from Hautz for admitted patients). Further rationale for the estimated PR bounds is found in the text for Key Question 2a ("Plausibility of Mortality Estimates from Higher Quality Studies").

§ The disability-to-death ratio reflects an estimate of how many serious harm disabilities would be expected per ED death. From Hussain et al. (U.K.-based incident report study), this was 0.41 (n=37:91). From Newman-Toker et al. (U.S.-based malpractice claims study), this was 0.70 (n=545:778). We chose the more conservative estimate, since permanently disabling outcomes may be overrepresented among malpractice claims (e.g., an outcome of quadriplegia may be more likely to result in a lawsuit than an outcome of death). However, if instead incident reports underrepresent disabling outcomes, then the point estimate (Method #2) of annual disabling harms would be higher (181,000) and the total serious harms also correspondingly higher (439,000).

These estimates are equivalent to a diagnostic error every 18 patients, a diagnostic adverse event every 50 patients, a serious harm (serious disability or death) about every 350 patients, and a misdiagnosis-related death about every 500 patients. Put in terms of an average ED with 25,000 visits annually and average diagnostic performance, each year this would be over 1,400 diagnostic errors, 500 diagnostic adverse events, and 75 serious harms, including 50 deaths (Table 11). This translates to 10 patients harmed and more than 1 death or disability each week.

Table 11. Estimated "typical" ED frequency of diagnostic errors and misdiagnosis-related harms

Parameter	Per Year	Per Month	Per Week	Every Nth Patient Visit
Total Annual ED Visits (n)	25,000	2,083	481	-
Diagnostic Errors (n)	1,418	118	27	18
Diagnostic Adverse Events (n)	500	42	10	50
Serious Harms Method #1 (n)	**73**	**6.1**	**1.4**	**343**
Diagnosis-Related Deaths (n)	50	4.1	1.0	503
Diagnosis-Related Disabilities (n)	20	1.7	0.4	1,237
Serious Harms Method #2 (n)	**70**	**5.8**	**1.3**	**358**
Average Serious Harms (n)	**71**	**6.0**	**1.4**	**350**

ED = emergency department

Key Question 2d. Are there clear commonalities or differences across clinical conditions in the frequency or risk of ED diagnostic errors or misdiagnosis-related harms?

The most striking commonality across all conditions is that mild, non-specific, or atypical symptoms substantially increase the frequency or risk of diagnostic errors and harms; this is elaborated further in the KQ3 section on Illness Characteristics. There is also evidence across diseases that the temporal profile of adverse events after missed major vascular events and infections is one of initially high risk followed by exponential decline over time (elaborated below as it relates to temporal risk windows and optimizing measurement).

The clearest difference across conditions is that, among dangerous diseases, myocardial infarction appears to stand alone as a "shining star" example for which ED miss rates have been reduced to a near-zero level. Even there, however, delays in admitted patients may still represent an area for improvement, and the false discovery rate is 14 percent. Fractures and appendicitis, both less likely to cause serious misdiagnosis-related harms than the other conditions assessed, are also missed at fairly low rates. By contrast, rates of misdiagnosis for neurologic symptoms and neurologic diseases appear to be higher than for most general medical symptoms and diseases. Unsurprisingly, death is the most common serious harm from missed general medical diseases while disability is the most common serious harm from missed neurologic diseases.

ED Treat-and-Release Discharges Versus Hospital Admissions

There is direct evidence that diagnostic errors are more frequent among patients discharged than admitted. Heitmann et al., 2016 found that 1.6 percent of ED discharges and 0.3 percent of patients admitted to a hospital ward via the ED returned within 30 days due to a diagnostic error, and almost all of these (in both subgroups) returned within 7 days.[143] This likely indicates that hospital admission serves as at least a partial clinical safety net when there is diagnostic uncertainty or error, and comports with U.S. Medicare data showing that EDs with very high discharge fractions (proportion of patients sent home on any given day) are more susceptible to diagnostic errors associated with short-term, unexpected patient deaths.[148]

For both stroke and myocardial infarction there was evidence that patients admitted with the wrong ED diagnoses were more frequent than patients misdiagnosed and discharged. Chompoopong, 2017 began with a cohort of patients hospitalized for stroke and found that 40 percent were admitted initially from the ED with non-stroke diagnoses.[85] Graff, 2006 began with a cohort of patients hospitalized for myocardial infarction and found that 25.6 percent were admitted initially from the ED with non-acute coronary syndrome diagnoses.[206] These rates are much higher than the overall false negative diagnosis rates among patients who are discharged (17% for stroke, 1.5% for myocardial infarction). This may suggest that ED clinicians are (appropriately) focused more on correct disposition than correct diagnosis, per se.

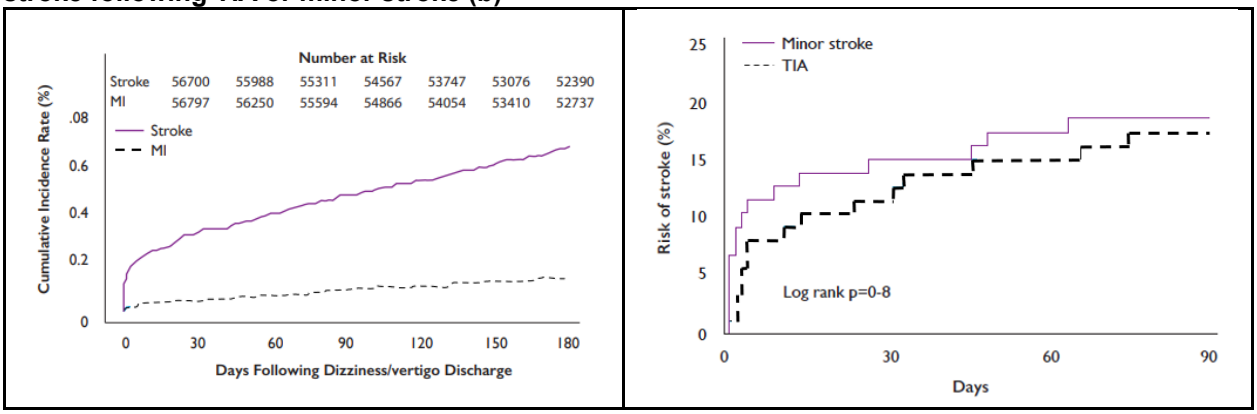
There also appears to be evidence that false negatives for dangerous diseases, particularly among those discharged from the ED, are generally less common than false positives (Table 9). Some false negatives are associated with significant adverse outcomes (including death), but we presume that false positives (i.e., those who undergo diagnostic testing for the dangerous disease in question via hospital admission but are found instead to have some more benign underlying cause) are generally less dangerous for patients. This would seem to suggest that ED clinicians

are weighting their diagnostic decision-making tradeoffs appropriately based on asymmetry of outcomes (i.e., dangerous diseases are worse to "undercall" than to "overcall").

Temporal Profile of Diagnostic Adverse Events/Harms

It has been shown previously that the short-term risk of adverse events following a false negative (missed) dangerous disease in the ED follows a characteristic temporal profile. The initial risk is at its peak, then exponentially declines towards a linear base rate over days to months, depending on the specific disease. We identified studies in our review showing this pattern for stroke,[64, 81, 120, 144, 170] myocardial infarction,[63, 77, 120] aortic aneurysm/dissection,[120] multiple vascular events combined,[120] sepsis,[78, 93, 94, 256] meningitis,[81, 93] and spinal abscess.[81] Unsurprisingly, the temporal profile of returns after a missed case seems to mirror the underlying disease biology and natural history, as shown in Figure 14 for stroke.

Figure 14. Cumulative incidence of stroke hospitalizations post ambulatory (ED or other) treat-and-release as "benign dizziness" (a)* and cumulative incidence curve for natural history of major stroke following TIA or minor stroke (b)†



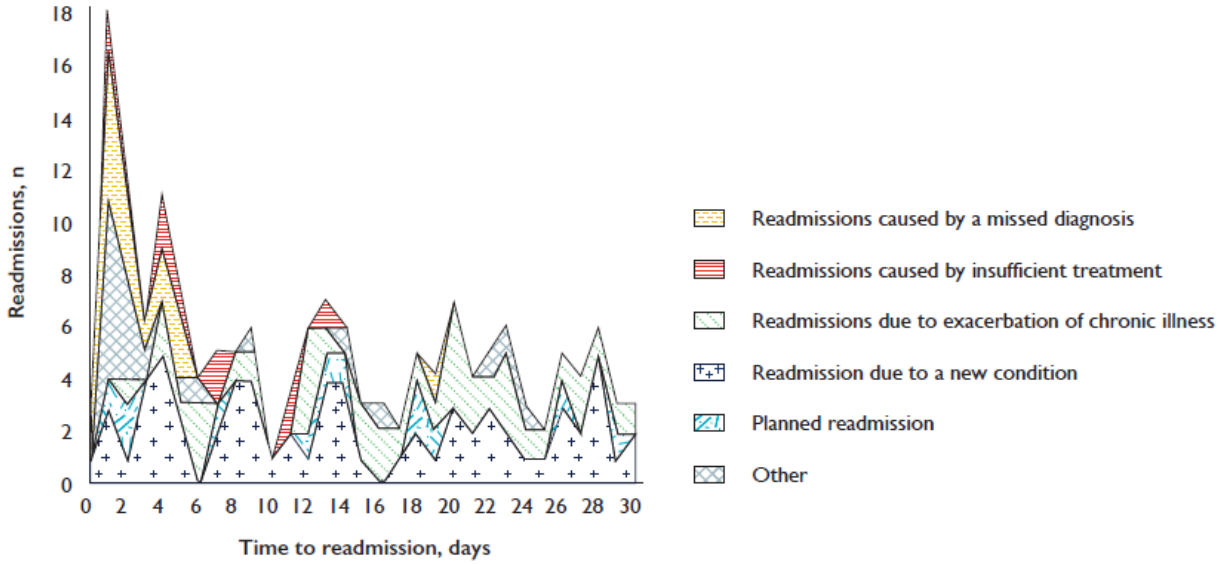
ED = emergency department; MI = myocardial infarction; TIA = transient ischemic attack

Source: Adapted from Coull AJ, Lovett JK, Rothwell PM. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: implications for public education and organisation of services. BMJ (Clinical research ed). 2004 Feb 7;328(7435):326. doi: 10.1136/bmj.37991.635266.44. PMID: 14744823. Used with permission.

* Heart attack (myocardial infarction) returns are shown as a "control" comparator. Data are from Kaiser Permanente.[257]
† Data are from the population-based Oxford Vascular Study as adapted from Coull et al.[258]

This appears to be true, more generally, of diagnostic adverse events in the ED. Specifically Heitmann et al. also showed that most returns linked back to chart review-detected diagnostic errors occur in the first week (Figure 15). This comports with data from the large administrative and electronic health record data studies alluded to above that use symptom-disease pairs ("SPADE" methods),[145] which have found that short-term rehospitalizations occurring at rates statistically above baseline for missed dangerous vascular events and infections occur dominantly in the first month and disproportionately in the first week after ED discharge. This indicates that 72-hour or 7-day revisits are expected to be an enriched source to detect diagnostic error, but that absolute error rates will be substantially underestimated using very short revisit windows for analysis (e.g., 72-hour returns, which are commonly utilized).

Figure 15. Nature of short-term ED revisits



ED = emergency department; SPADE = Symptom-disease Pair Analysis of Diagnostic Error

Source: Adapted from Heitmann MG, Sarwary M, Larsen JJ, et al. Readmittance rates within seven days are preferable in quality measuring of emergency departments. Danish Medical Journal. 2016 Sep;63(9). PMID: 27585528. Used with permission.

Note: The graph clearly demonstrates that return visits related to diagnostic errors (dots) tend to occur predominantly in the first week after ED discharge. Multiple studies using different designs (SPADE methods) have found similar revisit distribution curves for diagnostic error cases.

It should be noted that this temporal profile has also been demonstrated for all ED revisits (without regard to underlying cause for the revisit). Using data from the Agency for Healthcare Research and Quality's Healthcare Cost and Utilization Project (HCUP) family of databases,[259] Rising et al. found that 31 percent of ED visits were followed by a revisit within 1 year (3-day revisit rate 7.5%; 30-day revisit rate 22.4%).[147] The modeled cumulative hazard for revisits showed exponential growth over roughly the first 14 days, followed by a linear rise thereafter (best approximated by a double-exponential model, with excellent fit, $R^2 = 0.9997$). The authors concluded that the optimal balance between capturing "excess" acute revisits and "expected" revisits would be achieved by using a 9-day return window for quality measurement, rather than the more typically used 72-hour window. However, for diagnostic error detection, relevant windows likely vary in disease-specific fashion.

Key Question 3. Causes of Diagnostic Errors

Key Points

- Diagnostic error causes were often multifactorial, but cognitive errors dominated across data sources. In malpractice claims, nearly 90 percent of cases involved failures of clinical decision-making or judgment, regardless of the underlying disease present. In incident reports, key process failures were errors in diagnostic assessment, test ordering, and test interpretation which were usually attributed to inadequate clinical knowledge, skills, or reasoning, particularly in "atypical" clinical cases.
- Disease-specific studies addressed a mix of predictors, the most common of which were patient demographics (especially age, sex, and race) and illness characteristics (especially

symptom type, illness severity, and mode of arrival). Fewer studies addressed clinician characteristics, facility characteristics, or dynamic, context-specific systems factors. There was substantial heterogeneity in the effects of these predictors across diseases and studies, with variability in results partially explained by methodological differences.

- The effect of age was heterogeneous and disease-specific (e.g., younger age increases risk of missed stroke while older age increases risk of missed appendicitis) and sometimes large in magnitude. Female sex and non-white race were often associated with important (20-30%) increases in misdiagnosis risk; although these disparities were inconsistently demonstrated across studies, being a woman or a racial or ethnic minority was generally not found to be "protective" against misdiagnosis (i.e., was neutral at best).
- Atypical or non-specific symptoms were the strongest and most consistent predictors of increased risk for a missed diagnosis across diseases studied. For undiagnosed serious medical illnesses, less severe presentations and less urgent modes of arrival increased misdiagnosis risk; for multi-trauma patients, the reverse was true—more, rather than less, severe presentations increased misdiagnosis risk.
- Other notable predictors of misdiagnosis included care provided by less experienced clinicians, at non-teaching hospitals, with high ED discharge fraction, and during off hours. The diagnostic performance gap with academic (teaching) EDs having lower false negative rates than community (non-teaching) EDs was a fairly consistent finding, but it is unknown whether lower academic false-negative rates were achieved through greater overall diagnostic accuracy or by favoring overutilization, leading to arbitrarily greater admission fractions and resulting in higher false-positive rates.
- One overarching commonality across causes was that degree of difficulty in assessing a clinical presentation for a specific disease was a critical factor—"obviousness" predicted correct diagnosis and "subtlety" predicted incorrect diagnosis. "Subtle" situations include diseases in the "wrong" age groups; non-specific, milder, or atypical symptoms; and finding second, third, or fourth problems in patients who are very ill (e.g., polytrauma).

Summary of Findings

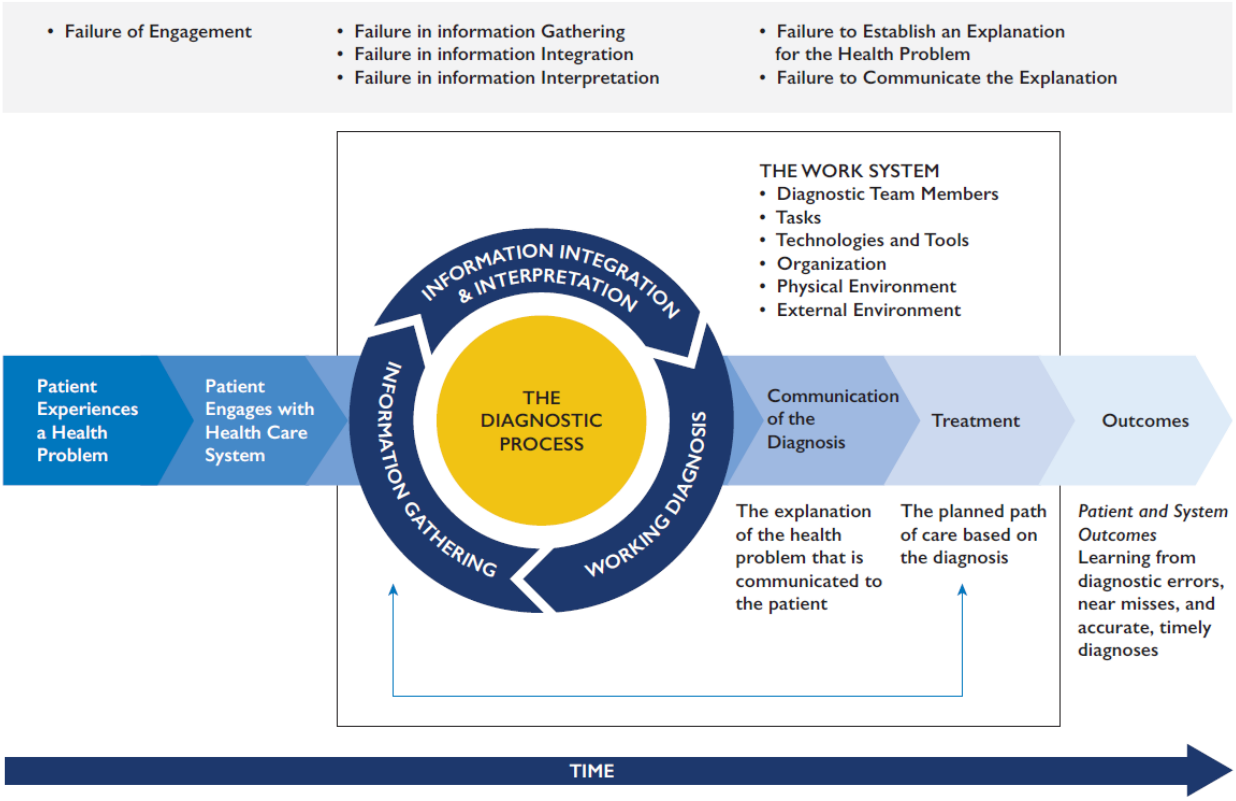
Key Question 3a. What are the most frequent causes identified?

When considering causes of diagnostic error, these can be framed either as "predisposing factors" (e.g., atypical illness presentation, off hours), "root causes" (e.g., clinical judgment failure, communication failure), or diagnostic "process steps" (e.g., failure during clinical information gathering, test ordering, or test interpretation). In most studies, only one of these frameworks was adopted. The majority of disease-specific studies focused on predisposing factors (often referred to as "predictors" or "risk factors"). By contrast, the majority of cross-cutting (not disease-specific) studies focused on root causes, or, less often, diagnostic process steps. Sometimes root causes were framed explicitly using the "cognitive" versus "systems" versus "mixed" factors, but other times studies applied their own or pre-existing taxonomies to describe the underlying root causes. We identified no studies that attempted to drill down further into the cognitive psychology of cognitive error (e.g., types of decision-making heuristics or associated cognitive biases at play). Even when studies focused on diagnostic process steps such as those found in the NAM report *Improving Diagnosis in Healthcare* (see Figure 16), relatively few focused on either (a) the patient-facing aspects of delays in engaging the healthcare system at the outset or (b) effective communication of the diagnosis to the patient.

The most robust data on the relative frequencies of overall root causes came from the large malpractice claims study from the United States (Newman-Toker, 2019) and the incident report study from the United Kingdom (Hussain, 2019) that formed the basis of the analysis of the most frequent diseases associated with diagnostic error (KQ1, Table 2).

Newman-Toker et al. broke down the causes into one of 11 major categories (Figure 17). There was an average of 2.4 cause categories identified per case, and these were dominated by clinical judgment factors (present in 89% of cases), regardless of the underlying disease involved (vascular events 93%, infections 89%, cancers 75%, other diseases 87%). This study used data from a large malpractice risk insurer that routinely conducts a standardized case evaluation process. According to the published study, "relevant factors in each case are abstracted based on a complete review of the medical and legal case file including case summaries, medical record data, depositions, and legal proceedings. Cases are reviewed and coded by experienced clinical taxonomy specialists (typically registered nurses with at least 10 years of quality or risk management experience), who abstract data using a multi-tiered coding taxonomy." It is unknown whether this process might systematically underrepresent certain causal features (e.g., certain fixed or dynamic systems factors), but findings were consistent with prior literature on diagnostic error causes found in non-claims sources from both the ED and other frontline care settings.[31, 49, 260] It was also face valid that the distribution of causes was similar for vascular events and infections, but slightly different for cancer (Figure 17). In a further analysis by Newman-Toker et al., among 55 more granular (i.e., more "split" rather than more "lumped") causes, 7 of the top 10 were clinical judgment factors (Table 12).

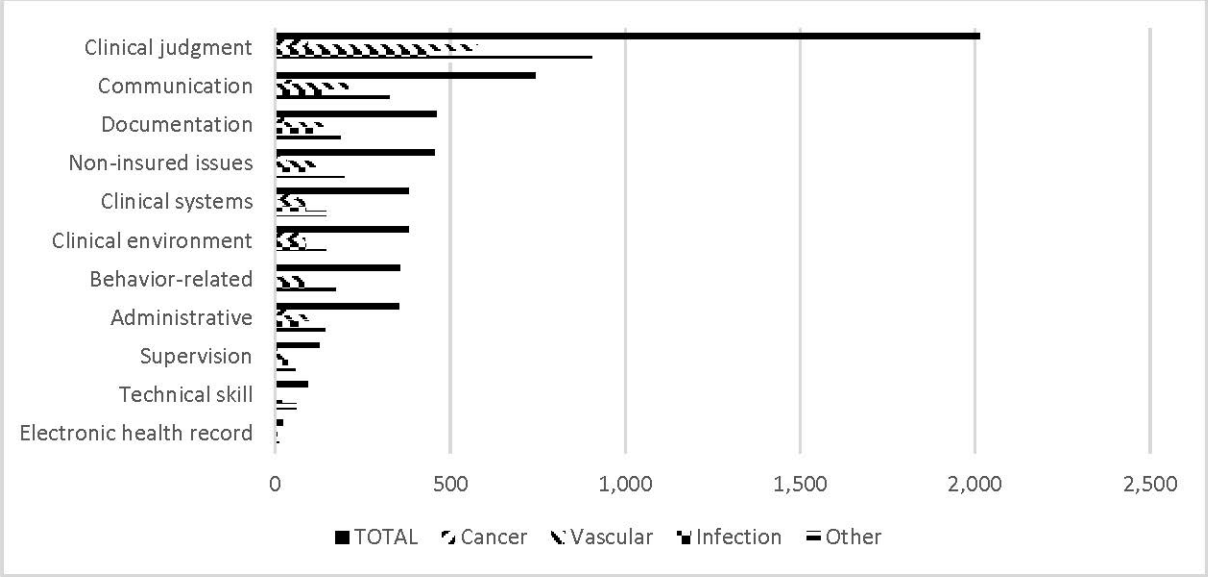
Figure 16. Diagnostic process steps where failures can occur that contribute to diagnostic errors



Source: Adapted from National Academies of Science Engineering and Medicine. Improving Diagnosis in Health Care.

Washington, DC: The National Academies Press; 2015. https://www.nap.edu/catalog/21794/improving-diagnosis-in-health-care#rights. Used with permission.

Figure 17. Root causes of emergency department diagnostic errors overall and by disease category



Data derive from a large U.S.-based malpractice claims study (Newman-Toker, 2019); the mean number of cause categories identified per case was 2.4, so the number of causes exceeds the number of cases (n=2,273). Note that even among cancer misdiagnoses, clinical judgment factors were the most common; however, the distribution of causes was less heavily weighted towards clinical judgment factors, as might be expected (e.g., failures related to communication or clinical systems might play a more significant causal role, as with an incidental finding of a lung nodule on chest X-ray not being communicated back to the patient or their primary care provider).

Hussain et al. provided fewer details on root causes, but the message was similar—"Both the wrong and delayed diagnoses had largely common themes for contributory incidents, including: insufficient assessment (32%); inappropriate response to diagnostic imaging/investigations (25%); and failure to order diagnostic imaging/investigations (8%)… In all diagnostic error reports, the most common contributory factors (identified in 1577 reports, 69%) related to staff or human factors: "inadequate skill or knowledge"; "mistake", "missed task or job to do" (e.g., checking diagnostic test results); and "failure to follow protocol"." Overlapping causes were not described, but these clinician-focused cognitive causes accounted for 70-90 percent of all cases in which contributory factors were available.

A smaller incident report study by Okafor et al. also found that most diagnostic errors (n=214) were associated with multiple causes (2.9 causes per case [n=615/214]), but cognitive factors still predominated.[31] They described 317 cognitive factors (52%), 192 system-related factors (31%), and 106 illness or patient factors they referred to as "non-remedial" (17%). Cognitive factors were faulty information verification (21%, n=130), faulty information processing (16%, n=97), faulty data gathering (10%, n=61), and faulty knowledge (5%, n=29). System-related factors were inefficient process (13%, n=77), high workload (11%, n=66), handoff/communication problem (5%, n=28), and insufficient resources/poor equipment (3%, n=21). Illness factors were atypical presentation (5%, n=33), complicated medical history (3%, n=19), and rare presentation (1%, n=7). Patient factors were "limited historian" (5%, n=33), language barrier (2%, n=10), and psychiatric issues or non-adherence (1%, n=4). The top 5

causes (faulty information verification, faulty information processing, inefficient process, high workload, and faulty data gathering) accounted for 70 percent of all causes identified.

Table 12. Top contributing factors to emergency department diagnostic error in malpractice claims*

Contributing Factors	N	%
Failure/delay in ordering diagnostic test	869	9.7%
Lack of/inadequate patient assessment with premature discharge	808	9.0%
Narrow diagnostic focus in patient assessment with failure to establish differential diagnosis	770	8.6%
Failure to appreciate and reconcile relevant signs, symptoms, or test results	606	6.8%
Failure/delay in obtaining a consultation or referral	570	6.4%
Misinterpretation of diagnostic test studies (e.g., X-rays)	521	5.8%
Issues related to lack of health insurance	455	5.1%
Inadequate communication among providers regarding the patient's condition	396	4.4%
Off-hours care (weekend, night shift, or holiday)	317	3.5%
Inadequate history or physical examination	250	2.8%
All other contributing factors (n=45)	3,441	38.4%

* Data derive from a large U.S.-based malpractice claims study (Newman-Toker, 2019).

Representativeness of Malpractice Claims Data for Root Causes

It is known that malpractice claims data represent a biased sample of cases, so it is then reasonable to consider whether bias(es) might influence the root causes of diagnostic error identified. As described above, it was clear from ED incident report studies (e.g., Hussain 2019,[16] Okafor 2016[31]) that the spectrum of root causes identified is quite similar to that found in ED malpractice claims studies—mostly cognitive errors related to bedside diagnostic decision-making (especially clinical examination, test ordering, or integration of test results into diagnostic reasoning). What is not known is whether both malpractice claims and voluntary incident reports might be biased towards cases with cognitive errors by physicians. This question cannot be easily addressed by retrospective studies relying on chart review, since most potential root causes must be inferred (i.e., they are not actually captured or recorded). Nor can it be addressed by diagnostically oriented, experimental vignette-based studies (which only assess for cognitive errors). To address this question rigorously, one would need a cohort study or clinical trial that prospectively captured all potential root causes and then assessed diagnostic errors and root causes. We found no such studies, so this remains an unanswered scientific question.

Key Question 3b. Do causes identified differ based on severity of harms?

The only information we were able to identify on this issue comes from Newman-Toker, 2019. Clinical judgment factors accounted for roughly the same 89 percent of cases resulting in high-severity (serious) harms as in the lesser-severity harm cases.

Key Question 3c. Do different causes have differential impact on patient outcomes (i.e., harms)?

We were not able to identify any studies that addressed this question.

Key Question 3d. Overall and for each clinical condition, are the following characteristics associated with errors/harms?

The three main sources for variation in a diagnostic "test" (in this case a clinical diagnosis rendered by the ED care process) are the patient, the testing process, and the observer (i.e., diagnostician). Variation contributes to bias and random error. Diagnosticians are not only the

observers who make diagnoses but also are part of the testing process (e.g., by obtaining clinical history or performing a physical examination). As part of our study method for this report, we prospectively defined characteristics and factors that have been shown to impact diagnostic errors in prior studies (Table 13) and used these to abstract data from included studies. Individual clinicians were rarely the subject of research on diagnostic error, so variation at the level of clinicians reflects "average" characteristics among a pool of clinicians within a given study.

One high-quality, prospective study looked across conditions at predictors of diagnostic "discrepancy" (which met the definition of diagnostic error used in this report) among consecutive patients admitted to the hospital via the ED. Hautz, 2019 found that the only factor that predicted diagnostic error was the diagnosing ED physician's assessment that the patient presented atypically for the diagnosis assigned (OR 3.04; 95% CI 1.33 to 6.96; $P = 0.009$).[7] They found no evidence that patient characteristics (age, gender), other illness characteristics (triage category, specific chief complaint, diagnostic category), clinician characteristics (gender, experience), dynamic systems factors (ED overcrowding, noise), or diagnostic process factors (perceived diagnostic difficulty, confidence in the diagnosis) predicted diagnostic error.

Table 13. Prospectively defined potential predictors or risk factors for diagnostic error

Patient Characteristics	Illness Characteristics	Clinician Characteristics*	Fixed Systems Factors	Dynamic Systems Factors
• Age • Sex • Race • Ethnicity • Language • SES/income • Health literacy • Health insurance	• Mode of arrival • Illness severity (e.g., triage intake level) • Symptom type • 'Atypical' presentation • Comorbidities • Tests ordered	• Provider type/role (including consultants) • Training background • Clinical experience (including training level) • History of disciplinary action • Provider fatigue	• Geographic region • Population density • Ownership/business model • Delivery/payment model • Teaching status • Access to EHR/EHR type • Access to consultants • Access to testing • Average ED volume/annual visits • Average ED discharge fraction • Average inpatient occupancy rate	• Off hours presentation • Handoffs • Same-day ED staffing • Same-day ED crowding • Same-day ED illness severity • Same-day ED discharge fraction • Incomplete ED visit

ED = emergency department; EHR = electronic health record; SES = socioeconomic status
* Clinician characteristics could be considered fixed or dynamic systems factors, but they are treated separately in this section. Provider fatigue is both a clinician characteristic and a dynamic systems factor but is reported with clinician characteristics.

Patient Characteristics

We identified 108 studies that reported the effect of one or more patient characteristics on diagnostic error. We report the impact of patient characteristics separately by condition. Across conditions, the impact of **age, sex, race, and ethnicity** were reported far more often than the impact of **language, socioeconomic status/income, health literacy, or health insurance**.

The most common patient factors studied in relation to the misdiagnosis of **stroke** were age, sex, and race. Older age was associated with a lower risk of misdiagnosis[64, 88, 171, 183] and patients with missed stroke were younger than the correctly diagnosed cases.[160, 164, 174, 175, 186, 187, 192, 195] However, several studies found no age-difference in the time to evaluation for stroke.[161, 185, 188, 261] Women were more likely to be misdiagnosed[64, 164, 175, 183, 192, 262] and have a longer time of evaluation.[185, 188, 261] Black[64, 174, 188, 262] and Hispanic[64, 262] patients were also at increased risk of misdiagnosis. Some studies reported no difference by race or ethnicity.[160, 179]

Twenty studies reported on patients' characteristics and missed or delayed diagnosis of **myocardial infarction**. Studies reported mixed results on the effect of age on myocardial

infarction misdiagnosis. Age was significantly associated with decreased risk,[25, 63, 201] increased risk,[77, 204, 206, 263, 264] or no effect on myocardial infarction misdiagnosis.[120, 202, 205, 209, 265, 266] Three studies reported higher risk of misdiagnosis of myocardial infarction among female patients,[120, 264, 267] One study found even among patients who presented with cardiac chest pain and cardiac troponin > 99th percentile, women were less likely to be diagnosed with MI, to undergo cardiac catheterization, or to be using evidence-based medications within 90 days of discharge.[267] The rest of the studies reported no effect by sex on misdiagnosis of myocardial infarction.[25, 63, 202, 204, 205, 208, 209, 265, 268-270] There were mixed results on the effect of race on misdiagnosis of myocardial infarction. Some studies reported an increased risk among African American patients,[63, 77, 202] while others reported no significant effect of race on myocardial infarction misdiagnosis.[120, 206, 208, 209, 266, 271] Several studies found no effect by ethnicity,[63, 77, 120, 202] or socioeconomic status.[25, 63, 77, 202] Due to concern for delayed STEMI treatment among women and older patients, one study aimed to assess the performance of a physician-blinded prehospital activation system for STEMI in comparison with standard systems with physician involvement. In the standard system, female sex and age > 75 were independent predictors of treatment delay in hospitals with and without a prehospital notification system. By contrast, with implementation of a physician-blinded prehospital notification system, there was no difference in treatment delay by age and there was a smaller gap in treatment delay among women.[264]

Eight studies reported on the effect of age, sex, race, and drug abuse on accuracy diagnosing **aortic aneurysm and dissection**. Studies showed conflicting results about the effect of age on diagnostic delay or missed diagnosis of aortic aneurysm and/or dissection. Some studies reported significant decreased or increased risk of diagnostic delay among older age patients,[73, 120, 214] while others reported no significant effect of age on delayed or missed diagnoses.[68, 216-218] Two studies reported increased risk of diagnostic delay among female patients,[120, 219] others reported no significant difference among male or female patients on missed or delayed diagnosis of aortic aneurysm and/or dissection.[68, 73, 216-218] Other studies reported no effect of race or drug abuse on delayed or missed diagnosis of aortic aneurysm and/or dissection.[68, 120, 217] None of the studies on risk of delays in aortic dissection diagnosis found a statistically significant difference between those with a history of Marfan's syndrome and those without,[68, 73, 217] although the presence of a known history was, if anything, protective (median time from presentation to diagnosis 2.2 hours for those with a known history versus 4.5 hours for those without, $P = 0.066$[68]).

We identified one study that reported on the effect of patient characteristics on diagnostic errors among 521 patients under 5 years of age presenting to the ED and later diagnosed with **sepsis or meningitis**.[93] Compared to 30-90 day-old children, older age children (age 91 days-2 years and >2 to 5 years) experienced higher odds of missed diagnosis of sepsis or meningitis in the ED (OR 2.56; 95% CI 1.49 to 4.41 and OR 2.26; 95% CI 1.17 to 4.35, respectively).[93]

Two studies assessed clinical and patient characteristics associated with delayed diagnosis of **appendicitis**.[236, 272] There was no effect of age (among children) or sex on delayed diagnosis of appendicitis in either study. Race, ethnicity and insurance status could not be studied in relation to diagnostic delay due to significant differences in these characteristics between the case and control group and was not assessed in the other study.[236, 272] Michelson et al., 2021 found 63 percent of children had a delayed diagnosis of appendicitis, of which 76.8 percent were deemed possible or probable missed opportunities to improve diagnosis.[272] In comparison with children who received a timely diagnosis, patients with delayed diagnosis of appendicitis had longer hospital length of stay, higher rates of perforation, and a higher likelihood of undergoing two or more abdominal surgeries (OR 8.0; 95% CI, 2.0 to 70.4).[272] Lastunen et al. 2021 found that

among patients with uncomplicated appendicitis on initial CT, age greater than 60 years was independently associated with progression to complicated appendicitis at the time of operation.[273] Although we did not find any included studies that directly addressed older age (i.e., adult presentations) as a risk factor for misdiagnosis in appendicitis, cross-study differences suggested that it might be a risk factor. In one study, the false negative rate among patients 18 years of age and under was 2.9 percent.[225] In an unrelated study, the false negative rate among patients 17 years of age and older was 30.8 percent.[233] Although this latter study used a very different method and focused only on missed cases using point-of-care ultrasound,[233] an older study (from prior to the study period), which directly compared younger and older patients with appendicitis, appears to corroborate older age as a risk factor. In that older study, diagnostic delays among older adults were more common than among children, with contributions from both "patient interval" (from symptoms to presentation) and "clinician interval" (from presentation to diagnosis) delay components—the result appears to be a higher rate of complications and greater mortality.[239]

Nine studies reported on the distribution of age and sex among patients with diagnostic errors related to **fractures**. However, the effect of age or sex on misdiagnosis of fractures was not quantified in any of the studies.

Three studies reported about patient characteristics and delayed diagnosis of **testicular torsion**.[254, 255, 274] These studies focused on patient-related delays prior to seeking care (known as the "patient interval" in studies of cancer) as it related to delay in definitive therapies and clinical outcomes. Chan et al., 2019 found that patients with testicular torsion who underwent orchiectomy had significantly longer prehospital pain duration compared with those who underwent testicular salvage (18.75 versus 3.56 hours; $P = 0.003$).[254] For patients who underwent orchiectomy, in-hospital time intervals were not significantly different than those who underwent testicular salvage. Bayne et al., 2017 found that patients in the delayed presentation group were 4 times more likely to have a developmental, cognitive, or social disorder than patients in the acute presentation group (10.6 versus 2.6%; $P = 0.02$). Half of the patients in the delayed group reported having autism spectrum disorder. Patients reporting a history of recent genital trauma were twice as likely to present in the delayed vs acute setting (14.9 versus 7%; $P = 0.07$). Misdiagnosed patients were younger and weighed less than those correctly diagnosed in the acute setting (9.9 years versus 12.9 years; $P = 0.006$; 42.6 kilograms versus 59.2 kilograms; $P = 0.01$). All boys who were misdiagnosed eventually underwent orchiectomy compared with 24.6 percent of those correctly diagnosed in the acute period ($P < 0.0001$).[255] One study reported on potentially avoidable testis loss in the setting of delayed diagnosis and treatment of cryptorchidism.[274] Despite international guidelines which recommend surgical exploration and orchidopexy prior to 18 months of age, the authors found 60% of the patients were above this age when they presented with preventable cases of testicular torsion. Further, there was significant delay (over 6 hours) from symptom onset to presentation to the ED in 72 percent of patients, which was associated with higher rates of orchidectomy (56% versus 23% in those who arrived within 6 hours; $P = 0.04$). There was not a significant effect of age on the duration of delay in ED presentation, and the effect of sex was not quantified.[274]

One study looked at rates of concordance and discordance between ED diagnosis and discharge **diagnosis across all International Classification of Diseases (ICD)-10 codes** and found no difference by age or sex.[275] Another study focused on delays (including diagnostic delays) due to difficulty obtaining intravenous access (DIVA).[276] Patients with DIVA (or 3.1% of the population) were more likely to be female, black and were more often triaged to a higher

acuity track. Throughout the ED, DIVA was associated with delays in median time to completion of lab testing, intravenous fluid and contrast administration, pain medication administration and delayed admission and discharge orders.

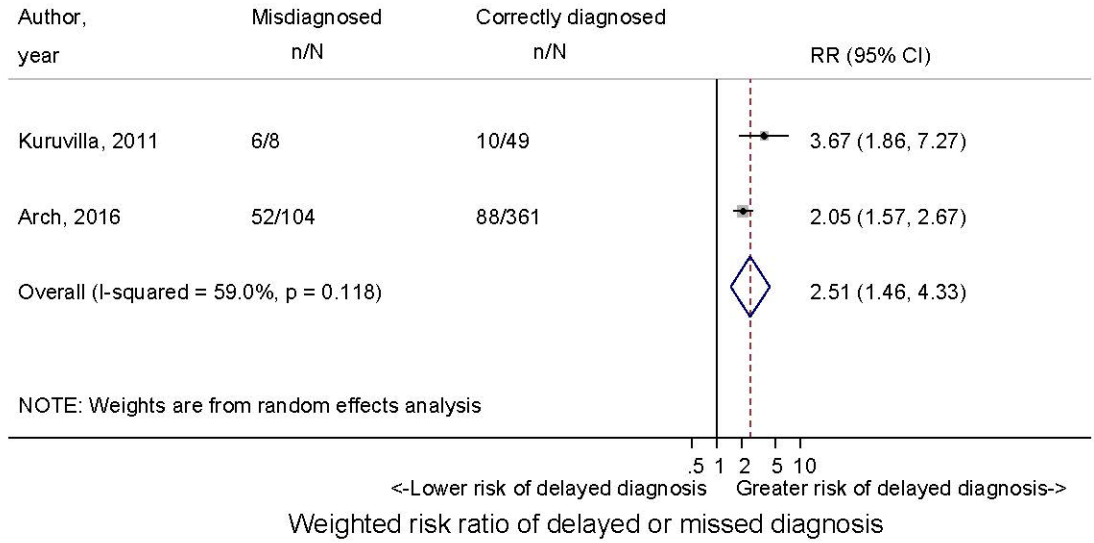
Illness Characteristics

We identified 120 studies that reported on the effect of one or more illness-related factors on diagnostic error in the ED. Most of the studies had a low risk of bias and/or low concerns for applicability. However, 12 studies had concerns with patient selection[58, 160, 177, 179, 194, 200, 244, 266, 271, 272, 277, 278] and 19 studies had concerns with the reference standard.[176-179, 186, 188, 195, 208, 213, 244, 267, 272, 275, 279-284] We report the impact of illness characteristics separately by condition. The illness characteristics most studied were **symptom type and illness severity,** followed by **mode of arrival and diagnostic tests ordered**. **Atypical presentations** were the strongest and most consistent predictors of increased risk for a missed diagnosis. **Comorbidities** were often studied as outcome predictors (e.g., mortality), but generally not in relation to diagnostic error, apart from polytrauma, where comorbidities tended to increase the risk of missing a second disease.

Thirty-one studies reported on **stroke**, including five prospective cohorts, 18 retrospective cohorts, eight registries, two case-control studies, and one cross-sectional study that reported on the illness-related causes of diagnostic error among patients presenting to the ED. We meta-analyzed two studies, including 522 patients, indicating an increased risk of misdiagnosis in posterior circulation stroke (RR 2.51; 95% C, 1.46 to 4.33; I-squared 59%; Figure 18).[159, 171] Three other studies also confirmed the increased risk of misdiagnosis in posterior circulation stroke but were not included in the meta-analysis because of study design, and lack of sufficient information.[87, 186, 194] Atypical presentation[66, 87, 88] and non-specific symptoms,[184] dizziness,[69, 159, 194] altered mental status,[88, 194] and loss of consciousness,[88, 194] syncope,[194] headache,[69] involuntary movement,[69] and having a negative Face-Arm-Speech-Time test were associated with increased risk of misdiagnosis.[161, 194] Compared to the correctly diagnosed stroke patients, misdiagnosed cases had a tendency to present without focal neurological deficits[69, 88, 183, 186, 194] and with lower clinical severity as judged by the following: (a) ED triage resuscitation/emergency category,[194, 195] (b) the National Institutes for Health Stroke Scale (NIHSS) score for ischemic stroke/TIA,[164, 179, 183, 192, 197, 262, 285] (c) the ABCD2 score for TIA,[69, 184, 185] and (d) the Hunt and Hess and Fisher scale scores for subarachnoid hemorrhage.[181] By contrast, the presence of unilateral weakness or numbness were protective against misdiagnosis.[88] A retrospective review of an acute stroke registry found a bimodal NIHSS distribution among missed stroke cases, indicating that very severe cases may also be at risk of misdiagnosis (e.g., due to presentation in stupor/coma from basilar artery occlusion).[186] Mode of arrival by emergency medical services/ambulance also decreased delayed/missed diagnosis of stroke.[160, 185, 188, 261, 262] MRI was performed equally often among misdiagnosed and correctly diagnosed cases,[184, 194] but with longer delays among the misdiagnosed.[194] Unsurprisingly, stroke-specific sequences such as diffusion-weighted MRI and neurovascular imaging were used less frequently among misdiagnosed cases.[184] Whether or not ED patients with neurologic complaints had symptoms highly suggestive of TIA/stroke (e.g., aphasia or weakness), the use of head CT portended increased risk of subsequent stroke.[189] Similarly, having a head CT scan at the index visit for headache was associated with an increased risk of subsequent cerebrovascular event[91, 176]; however, one study showed that a reduction in the use of head CT scan in ED visits for headache had no effect on the rate of death or subsequent cerebrovascular events.[140] Two studies assessed delayed diagnosis of ischemic stroke/TIA among pediatric patients (n=181).[177, 286] They found no effect for the type of first

contact with the medical sector, pediatric NIHSS, level of consciousness, symptoms, or the location of the brain lesion. One study looked systematically for ischemic stroke among polytrauma cases brought to a trauma center and found 11 acute ischemic strokes among 192 patients (5.7%)—none were detected initially and none had neurologic consultation obtained at initial trauma triage (100% missed); the median time to diagnosis was 2 days (range 0-5).[198] These studies all point to greater miss rates in case presentations with a higher degree of diagnostic difficulty (transient, milder, non-specific, or atypical symptoms[21]).

Figure 18. Risk ratio of misdiagnosis among people who have posterior circulation stroke



CI = confidence interval; RR = risk ratio

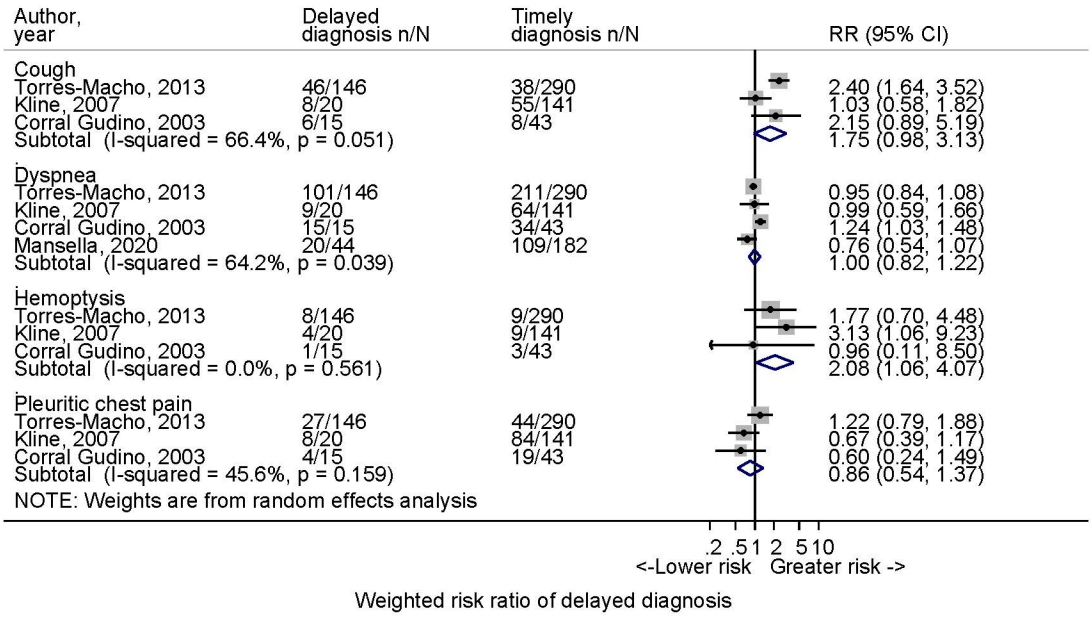
We identified 11 studies on myocardial infarction, including two registries, two prospective cohorts and seven retrospective cohorts that reported on the illness-related causes of diagnostic error among patients presenting to the ED. Meta-analysis was not possible because of differences in the definitions of the risk factors and diagnostic error. The rate of misdiagnosis was lower among patients with chest pain[65, 209, 266] and more severe triage levels.[25, 287] However, one study found no difference in the median door-to-balloon time between patients with and without angina pectoris[265] and another study found no difference in the percentage of triage delay between triage levels.[266]

We identified 12 studies on aortic aneurysm/aortic dissection, including two registries, one randomized controlled trial, and nine retrospective cohorts that reported on the illness-related causes of diagnostic error among patients presenting to the ED. Meta-analysis was not possible because of missing data and differences in the definitions of the potential risk factors among these studies. Misdiagnosed cases were more likely to present with atypical symptoms,[68, 73] dyspnea,[73, 217] systolic blood pressure of above 105 mmHg,[68, 73, 216] or clinical features resembling myocardial infarction, including angina pectoris,[217] positive troponin,[73, 288] and acute coronary syndrome-like findings on ECG.[73] Cases who underwent CT scan had less diagnostic delay than those who did not.[68, 73]

We identified five studies with a low or unclear risk of bias on pulmonary embolism, including one prospective cohort and four retrospective cohorts that reported on the illness-related causes of diagnostic error among patients presenting to the ED with pulmonary

embolism. We included three studies (655 patients), reporting on hemoptysis, cough, and pleuritic chest pain,[278, 289, 290] and four studies (881 patients) reporting on dyspnea[222, 278, 289, 290] in a meta-analysis (Figure 19). The risk of misdiagnosis increased with the presence of hemoptysis (RR 2.08; 95% CI 1.06 to 4.07; I-squared 0%) and cough (RR 1.75; 95% CI 0.98 to 3.13; I-squared 66.4%), decreased slightly with pleuritic chest pain (RR 0.86; 95% CI 0.54 to 1.37; I-squared 45.6%), and was not related to dyspnea at the index visit (RR 1.00; 95% CI 0.82 to 1.22; I-squared 64.2%). One study reporting an increased risk of delayed diagnosis in the absence of dyspnea was not included in the meta-analysis because of the unclear number of misdiagnosed patients.[223] In addition, two studies reported on syncope in the clinical presentation of PE.[278, 289] Kline et al., reported syncope at a higher rate among those diagnosed within 48 hours after leaving the ED (delayed) than patients diagnosed while in the ED at the initial presentation.[278] However, Torres et al., found syncope at a similar rate among ED diagnosed patients and those sent home with a wrong diagnosis, but less frequently among patients diagnosed with PE during hospitalization.[289] Compared to the correctly diagnosed patients with pulmonary embolism, misdiagnosed cases were less likely to have D-dimer tested in the initial work-up[222, 289] and more likely to present with pulmonary infiltrates on chest X-ray.[289, 290]

Figure 19. Risk ratio of pulmonary embolism misdiagnosis in patients presenting with cough, dyspnea, hemoptysis, or pleuritic chest pain



CI = confidence interval; RR = risk ratio

We identified five or fewer studies on other conditions in the ED, where meta-analysis was not possible because of different definitions or statistical measures, or the limited number of reports on each risk factor.

Across these studies, higher triage severity increased misdiagnosed injuries in pediatric or adult trauma patients.[74, 127, 130, 243, 291] However, clinical and triage severity decreased sepsis misdiagnosis among children[93] and adults.[157]

Typical symptoms such as isolated scrotal pain for testicular torsion[255] and right lower quadrant abdominal tenderness for appendicitis[272, 292] decreased misdiagnosis. However, atypical presentation, as in isolated abdominal pain for testicular torsion[255] and lack of abdominal pain or

abdominal pain accompanied by constipation for appendicitis[292] increased misdiagnosis. Imaging on first presentation by a single sonography or CT scan decreased diagnostic delay of testicular torsion.[293, 294] The studies on preoperative imaging for appendicitis were inconclusive. In two reports, CT scan or sonography was performed less frequently among adults with missed appendicitis at index visit than those with a same-day diagnosis.[272, 292] One study showed no change in the rate of negative appendectomy (i.e., false positive diagnosis of appendicitis) but a delay to surgery with preoperative imaging,[295] while another study indicated that preoperative imaging reduced the false discovery rate from 10 percent to 3 percent.[296]

Clinician Characteristics

We identified 30 studies, including one randomized controlled trial, three prospective cohorts and 17 retrospective cohorts, two case-control studies, five cross-sectional studies, one registry, and one case series that reported on clinician characteristics associated with diagnostic error among patients presenting to the ED. Most of the studies had a low risk of bias and/or low concerns for applicability. However, five studies had concerns with patient selection[132, 194, 200, 266, 297] and five studies had concerns with the reference standard.[186, 202, 281, 298, 299] The sources of heterogeneity between studies were differences in the definitions of the clinician factors, study design, and patient selection. **Provider type and clinical experience (including training level)** were the most frequently reported factors. Most studies were limited by a retrospective design that made it difficult to evaluate some potential risk factors such as clinician **fatigue**.

Numerous studies addressed accuracy of diagnosing patients based on **provider type**. For strokes, Arch found that neurological consultation was strongly associated with fewer diagnostic errors (35% [n=20/55] of missed cases were seen by a neurologist, while 95% [n=213/225] of correctly diagnosed cases were seen by a neurologist, $P < 0.001$).[159] These numbers correspond to a false negative rate of 9 percent (n=20/233) for neurologists which is roughly half of the estimated overall error rate in the ED shown in KQ2 (which includes multiple studies that gave "credit" to correct ED diagnoses employing neurological consultation); however, authors did not report results on a per-symptom or case-mix adjusted basis, so these results could potentially be confounded by indication (i.e., neurologists might have been consulted disproportionately in obvious cases and they might not have fared so well in subtle cases). Richoz found that "ED physicians were a little less than twice as likely as neurologists or neurologists in training to miss the right diagnosis."[186] Importantly, this was in cases where the ED initially missed the diagnosis (among 43 initially missed strokes by ED physicians, 33 underwent neurological consultation without suspicion for stroke by the ED, and 14 of these were correctly diagnosed as stroke by the neurologist); however, the neurologist also caused the misdiagnosis in four cases suspected to represent strokes by the ED clinician.[186] In two multivariable models, Morgenstern found point estimates that neurology consultation (obtained in just 8.6% of stroke cases) cut diagnostic error by 34 to 51 percent, but results were imprecise and confidence intervals overlapped with no difference.[179] Venkat found that neurology service admission (versus non-neurology service) was associated with lower rates of stroke misdiagnosis (non-neurology admissions were 11% of correctly diagnosed vs. 35% of misdiagnosed cases, $p < 0.001$).[194] Liberman found that, in cerebral venous sinus thrombosis, fewer misdiagnosed patients had neurology consultations, but the result was not statistically significant (81.8% among misdiagnosed vs. 95.2% among correctly diagnosed, $P = 0.19$).[173] Yi found that access to telestroke video consultations did not reduce false positive transfers for mechanical thrombectomy for large vessel occlusions causing stroke.[285] In summary, studies that assessed neurologist accuracy found that neurologists

generally missed fewer strokes than ED clinicians, but neurologists also missed strokes (even sometimes when ED clinicians correctly suspected them). There was also clear evidence of opportunities for improvement by ED clinicians in stroke diagnosis. Vaghani found a large number of patients who presented with red flags and multiple stroke risk factors did not undergo appropriate ED diagnostic evaluation, and processes failures related to the patient–provider encounter (history and physical examination) were the most frequent cause of diagnostic errors.[300] However, one study of ED patients with suspected acute stroke found that formal use of bedside diagnostic stroke scales improved ED clinician sensitivity for detecting stroke over ED clinical impression alone (76% clinical impression vs. 83% using Recognition of Stroke In the Emergency Room (ROSIER) [P = 0.005]; use of the Face Arm Speech Test [FAST] scale by ED clinicians was not statistically different than use of ROSIER by ED clinicians 81% FAST vs. 83% ROSIER [P = 0.39]).[196] Results were said to be similar whether the scales were performed by a physician or nurse. This suggests that relatively simple interventions might be helpful.

For potential surgical conditions, surgeons were less likely to miss ruptured aortic aneurysm than internists.[219] However, compared to emergency physicians, surgeons were more likely to misdiagnose common surgical complaints in the pediatric ED including head trauma, testicular pain, and abdominal pain.[126] Data suggest that early recognition of diseases such as testicular torsion needing emergent treatment are sometimes delayed and/or missed; in these cases absence of early surgical consultation was deemed to be the main cause.[274, 301]

For radiographic diagnoses, specialists in radiology generally provided more accurate diagnoses, and subspecialists were the most accurate when interpreting images in their own subspecialty. ED clinicians (non-radiologists) had significantly higher error rates compared to radiologists and radiology residents when interpreting ED imaging.[299] In acute stroke patients, neuroradiologists missed fewer large vessel occlusions on CT angiography than non-neuroradiologists.[162] However, subspecialty radiologists who interpreted ED imaging outside their area of expertise had diagnostic error rates similar to radiology residents.[299] Radiologists were less likely to miss acute mesenteric ischemia on CT imaging of patients with acute abdominal pain if clinicians had suspected the diagnosis prior to CT referral.[227] In patients with fractures who had imaging read only by an orthopedic surgeon (without attending radiology backup during the visit), the incidence of false-negative fractures was 2.2 percent,[83] which is slightly higher than that generally reported for radiologists (see KQ2 fractures).

Multiple studies addressed accuracy of diagnosing patients at the bedside based on **clinical experience, including training level**. Less clinical experience of ED clinicians showed a trend towards increased stroke misdiagnosis (≤6 years of experience OR 1.20; 95% CI 0.80 to 1.75)[69] but was not identified as a predictor of missed myocardial infarction.[202] A stroke study "found no significant difference in diagnostic accuracy between neurologists and trained neurology residents."[183] Radiology residents were more prone to diagnostic error than attendings in the diagnosis of stroke,[162] subtle pelvic fractures[130] and interpreting CT scan,[132] CT angiography,[55] and MRI.[133] Nevertheless, one large study comparing "off hours" initial radiology resident reads to those of attending radiologists (n=81,201) found diagnostic errors in just 0.2 percent.[241] Earlier year of residency in radiology was associated with greater risk of MRI misinterpretation.[133] Although radiology residents had overall suboptimal sensitivity (87%) for detecting intracranial aneurysms on head CT angiography in subarachnoid hemorrhage patients, there was no clear benefit to overall diagnostic accuracy based on year of residency training.[55]

We identified one study assessing **training background** which found that hospitals with a greater proportion of emergency medicine board certification among their ED clinicians was

associated with fewer missed diagnoses of myocardial infarction (median 0.3% [interquartile range 0 to 1.15] for hospitals in the top quartile versus median 2.0% [interquartile range 0 to 33.33] for hospitals in the bottom quartile of emergency medicine board certification).[202]

We did not find studies that addressed a clinician's history of **disciplinary action** as a predictor. We also did not find studies that addressed clinician **fatigue** as a predictor.

Fixed Systems Factors

Fixed systems factors were those that would generally not change on a given day or at a given visit for a specific patient. We identified 21 studies that reported on fixed facility or health systems factors that were associated with diagnostic errors/harms.[25, 63, 64, 78, 93, 156, 160, 178, 188, 189, 195, 202, 208, 244, 253, 281, 302-305] We identified six studies that reported on both fixed and dynamic factors.[25, 63, 64, 93, 188, 195] Nine studies took place in the United States,[63, 64, 78, 156, 160, 178, 188, 189, 202] seven studies took place in Canada,[25, 93, 195, 211, 244, 303, 304] three studies took place in the United Kingdom or Western Europe,[253, 281, 302] and two studies were based in Australia.[208, 305]

Twelve studies reported on the association between a facility's **teaching status and rates of misdiagnosis**.[25, 63, 64, 78, 93, 178, 188, 189, 193, 195, 202, 302] Schull et al, 2006, Cifra et al., 2020, and Rosenman et al., 2020 found no association between teaching status and myocardial infarction, sepsis, and stroke misdiagnosis respectively.[25, 78, 189] All other studies found significantly lower odds of misdiagnosis at academic centers.

Five studies reported on variation by **U.S. geographic region** in rates of misdiagnosis.[63, 64, 78, 202, 303] Moy reported significantly higher odds of myocardial infarction misdiagnosis in the Midwest relative to the Northeast.[63] Wilson reported significantly lower rates of myocardial infarction misdiagnosis in the Mid-Atlantic, West, South, Central, and Mountain regions of the country.[202] Newman-Toker reported non-significantly lower rates of stroke misdiagnosis in the Northeast relative to the Midwest, South, and West.[64] Cifra reported significantly higher odds of sepsis misdiagnosis in California, Florida, and Massachusetts relative to New York.[78] Cheong reported on geographic variation in Canada, and found the West had significantly higher odds of appendicitis misdiagnosis that relative to the Maritime region.[303]

Five studies reported on **facility ownership/business models**.[63, 64, 78, 160, 202] Moy, Newman-Toker, and Cifra found no association between facility ownership and rates of myocardial infarction and stroke misdiagnoses respectively.[63, 64, 78] Wilson found that public hospitals had higher odds of myocardial infarction misdiagnosis relative to private hospitals.[202] Bhattacharya found non-significantly higher rates of correctly diagnosed strokes among young adults presenting to primary stroke centers (PSC) relative to non-PSCs.[160]

Four studies reported on the association between **population density** and rates of misdiagnosis.[63, 64, 202, 208] Moy and Wilson found a significant association between lower population density and higher rates of myocardial infarction misdiagnosis.[63, 202] Williams also reported an increased rate of myocardial infarction misdiagnosis in rural regions of Australia, but did not report on significance.[208] Newman-Toker found that small metropolitan regions had lower odds of stroke misdiagnosis relative to large metropolitan areas; the effect size was small but statistically significant.[64]

Four studies reported on the association between **average ED volume/annual number of visits** and diagnostic accuracy.[64, 78, 93, 211] Ko, in a study following approximately 500,000 Canadian adults with treat-and-release ED visits for chest pain, found that EDs with higher annual volumes of chest pain complaints had significantly lower rates of myocardial infarction/unstable angina hospitalizations and death in the 30 days following those treat-and-

release ED encounters.[211] This trend continued until the ED volume reached 1400 annual visits—once volumes exceeded 1400 annual chest pain visits, there was no longer a significant reduction in the rates of acute coronary syndrome hospitalizations or death relative to the lower-volume EDs. Newman-Toker found that lower-volume EDs had significantly higher odds of stroke misdiagnosis, and that moderate-volume EDs had non-significantly higher odds of stroke misdiagnosis relative to high-volume EDs.[64] Cifra found that rates of pediatric sepsis misdiagnosis were significantly higher in lower-volume EDs.[78] Vaillancourt did not find a significant association between ED volume and the rate of pediatric sepsis misdiagnosis.[93]

Two studies reported on **access to electronic health records**.[78, 304] Cifra found that hospitals' accuracy decreased non-significantly when diagnosing pediatric sepsis if the hospital had fully implemented electronic health records.[78] Gouin found that emergency physicians' diagnostic accuracy increased non-significantly with use of digital versus conventional radiography viewing using a Picture Archiving and Communications System (PACS).[304]

Two studies reported on **access to testing**.[63, 202] Both studies found that access to cardiac catheterization facilities reduced risk of myocardial infarction misdiagnosis, but the findings in the Wilson study were not statistically significant.[202] The Wilson study also found a significant benefit to diagnostic accuracy from being at what was classified as a "high-tech" hospital.[202]

Two studies reported on **average ED discharge fraction**.[63, 64] Newman-Toker found that higher discharge fractions were associated with increased risk of stroke misdiagnosis.[64] Likewise, Moy found that higher discharge fractions were associated with significantly higher odds of myocardial infarction misdiagnosis.[63] Both studies were compatible with findings from a large Medicare-based study (outside the systematic review) which found that unexpected deaths (associated with apparent diagnostic errors) within 7 days of an ED treat-and-release visit were increased at EDs with higher discharge fractions. In that study, hospitals in the lowest quintile of admission fraction from the ED had the highest rates of early death—3.4 times higher (0.27% versus 0.08%) than hospitals in the highest quintile of admission fraction—despite serving healthier populations, as measured by overall 7-day mortality among all comers to the ED.[148]

Two studies reported on **average inpatient occupancy rates** influencing misdiagnosis rates.[63, 64] Newman-Toker found that occupancy rates did not affect rates of stroke misdiagnosis.[64] Moy found significantly *lower* rates of myocardial infarction misdiagnosis among hospitals with *higher (classified as "medium" or "high" relative to "low")* occupancy rates.[63] The implications of this finding are uncertain.

One study reported on **access to consultants**.[93] Vaillancourt found that hospitals with access to pediatric consultations improved accuracy among children with meningitis or sepsis.[93]

We did not identify any studies that evaluated the association between **delivery or payment models** and rates of misdiagnosis.

Dynamic Systems Factors

Dynamic, context-specific systems factors were those that might change on a given day or at a given visit for a specific patient. We identified 17 studies that reported on dynamic, context-specific systems factors.[25, 63, 64, 88, 92, 93, 122, 127, 162, 183, 188, 195, 208, 253, 265, 285, 286] Seven studies took place in the United States,[63, 64, 88, 122, 188, 265, 285] five studies took place in the United Kingdom or Western Europe,[92, 127, 162, 183, 253] three studies took place in Canada,[25, 93, 195] and two studies took place in Australia.[208, 286]

Sixteen studies reported on the rates of misdiagnosis during **off-hours**.[25, 63, 64, 88, 92, 93, 127, 162, 183, 188, 195, 208, 253, 265, 285, 286] Newman-Toker reported significantly increased odds of stroke

misdiagnosis during off-hours.[64] Muhm also reported increased cases of misdiagnosis in polytrauma cases during off-hours though did not report on significance.[127] Rose reported suspected stroke patients had more *rapid* access to immediate CT scans during *off* hours.[188] Parikh, Schull, Daverio, and York reported mixed results.[25, 253, 265, 286] Moy, Vermeulen, Fasen, Williams, Pihlasviita, Madsen, Yi, Mirete, and Vaillancourt reported no effect.[88, 92, 93, 162, 183, 195, 208, 285]

We identified two studies that reported on the relationship between **same-day ED crowding** and rates of misdiagnosis and found mixed results.[63, 64] Unexpectedly, Moy[63] found that *high* levels of same-day ED crowding were associated with *lower* risk of misdiagnosis (OR 0.78, $P = 0.009$), but this appears to have been a univariable analysis that might have been confounded by other factors (e.g., high same-day ED admission fraction, which was not measured, but in a similar analysis for stroke[64] was strongly protective against error). Although Newman-Toker[64] did not find an association between same-day ED crowding and odds of stroke misdiagnosis, there was an increased risk of stroke misdiagnosis among **incomplete ED visits** (e.g., patient left against medical advice), suggesting that incomplete diagnostic assessments may be more important than crowding, per se (though it is expected that overcrowding is likely to increase incomplete ED visits). We identified one study that reported on the relationship between **same-day ED discharge fraction** and rates of misdiagnosis which found a strong association, with higher discharge fraction on the day of the visit (top quintile versus bottom quintile) increasing the odds of a misdiagnosis 6.3-fold ($P < 0.001$).[64] We found no studies that assessed the association between **handoffs**, **same-day ED staffing**, or **same-day ED illness severity** and misdiagnosis rates, but the Okafor 2016 incident report study did note inadequate or failed handoffs (5% of all causes) and high workload (11% of all causes) as contributing factors.[31]

Key Question 3e. Are there significant commonalities or differences among causes of ED diagnostic errors or associated harms across clinical conditions?

The clearest and most consistent causal connections across conditions are that (1) most ED diagnostic errors happen at the bedside and disproportionately involve cognition and clinical judgement as root causes; (2) illness characteristics are a strong and consistent predictor of diagnostic error—"obviousness" predicts correct diagnosis and "subtlety" predicts incorrect diagnosis; and (3) the final common pathway for false negatives in patients with dangerous underlying diseases is failure to order tests or consultations, resulting in inappropriate discharge from the ED. It is the second of these that merits additional consideration here, because some heterogeneity in results identified in the systematic review can be explained via the interaction between illness characteristics and other characteristics (e.g., patient demographics).

Atypical or non-specific symptoms were among the strongest and most consistent predictors of increased risk for a missed diagnosis across diseases. On the one hand, this is almost a truism—***clinicians do not miss diagnoses when they are obvious, they miss them when they are subtle***. On the other hand, it is a deeply complex problem, because "subtlety" comes in multiple forms: (a) **low prevalence/ pre-test probability/ base rate** (e.g., hemiplegia is caused by stroke more than half the time; dizziness is caused by stroke just 3 to 5 percent of the time); (b) **degree of difficulty** (e.g., it may be intrinsically harder to perform the bedside HINTS eye movement exam to differentiate stroke from inner ear disease[306-308] than to order a troponin level to identify myocardial infarction); (c) **training/ background knowledge/ familiarity/ expertise** (e.g., training in emergency medicine focuses more on critical care neurology than on what has been

called “acute diagnostic neurology” the medical discipline concerned with the initial assessment, diagnosis, management, and referral of patients presenting with new neurologic symptoms that are not obviously due to serious, life-threatening neurologic diseases . . . but might be.”[309]; thus, the varied presentations of stroke may be more challenging to sort out than heart attacks).

An interesting twist on the issue of atypical case presentations is how it interacts with other predictors, leading to seemingly contradictory findings that are, in fact, internally consistent. For example, the effect of age is heterogeneous and disease-specific (e.g., younger age increases risk of missed stroke while older age increases risk of missed appendicitis). However, it is likely that these findings are largely explained by atypicality because the disease is occurring in the “wrong” patient population. Stroke is a disease of the elderly, so younger patients with stroke are atypical (and therefore more likely to be misdiagnosed). Likewise, appendicitis is a disease of the young, so older patients with appendicitis are atypical (and therefore more likely to be misdiagnosed). The same applies to illness severity, again with seemingly contradictory findings. For undiagnosed serious medical illnesses, less severe presentations and less urgent modes of arrival increase misdiagnosis risk; for multi-trauma patients, the reverse is true—more, rather than less, severe presentations increase misdiagnosis risk. Again, context is crucial—in the case of undiagnosed serious medical illnesses, higher severity is a “signal” that makes diagnosis easier, but in the case of polytrauma, higher severity is “noise” that makes diagnosis (of the subtle hand fractures, for example) harder or less pressing.

Achieving equity in diagnosis by addressing racial and other diagnostic health disparities is of recognized importance to achieving diagnostic excellence.[310] Not all studies found an increased risk of diagnostic error with female gender or non-white race, but no studies that normalized for baseline risk of having the target disease found these demographic factors to be protective. In general, most studies that found an association with gender, race, or ethnicity, found a 20 to 30 percent increased risk of diagnostic error for women and minorities. The remaining studies showed null effects. Heterogeneity in data presentation made it challenging to perform meta-analysis to estimate an average health disparity-related effect, and the role of implicit or explicit bias was not directly measured. Much of the apparent heterogeneity in results for demographic predictors may stem from confusion about the inferences to be drawn from different study designs. The look back method speaks to the relative risk or odds of a misdiagnosis conferred on a patient based solely on their gender or race, while the look forward method estimates the absolute risk of a misdiagnosis based on a mix of disease and misdiagnosis prevalence. Because ED clinicians are likely to calibrate their decision-making to baseline disease prevalence, this may contribute to some proportion of the demographic disparities seen in diagnosis, if actual disease prevalence is lower among women or minorities (see Discussion for additional details). Disparities in diagnosis should be a focus of future research, and special care should be taken to ensure that rigorous epidemiologic and statistical methods are used to address this concern, since incorrect methods can lead to erroneous inferences.

It was noteworthy that testicular torsion was one of the few conditions which focused heavily on risk factors that increased the “patient interval” (time prior to engaging the healthcare system). In particular, studies assessed whether the patient was cognitively impaired or developmentally delayed. While this does occur for other conditions (e.g., delays in seeking stroke care are linked to memory impairment, health literacy, and race),[311-313] it may be that the symptom of testicular pain is particularly challenging for young boys to share with their parents, leading 6 percent of patients (n=12 of 208) to hide their symptoms for more than 24 hours.[255]

Fewer studies addressed clinician characteristics, facility characteristics, and dynamic, context-specific systems factors. Results were heterogeneous, but notable predictors of misdiagnosis in some studies included care provided by less experienced clinicians, at non-teaching hospitals, with high ED discharge fraction, and during off hours.

Discussion

Findings in Relation to the Decisional Dilemmas

The key decisional dilemma for this evidence review is "What are the most common and significant medical diagnostic failures in the emergency department (ED), and why do they happen?" This report summarizes current best evidence as it relates to the nature, frequency, and causes of diagnostic error in the ED. It provides the first comprehensive look at current best evidence related to ED diagnostic error and fills key gaps in prior understanding. The report's findings offer new insights into which clinical problems should be targeted for solutions, how the impact of those solutions might be measured, and what types of interventions are most likely to succeed.

Key Question (KQ) 1: What clinical conditions are associated with the greatest number and highest risk of ED diagnostic errors and associated harms?

Although limited by biases in the data towards diseases causing more severe harms when missed, the top 20 individual diseases associated with diagnostic errors (independent of harm severity), in approximate rank order, were found to be fracture, stroke, myocardial infarction, appendicitis, venous thromboembolism, spinal cord compression and injury, aortic aneurysm and dissection, meningitis and encephalitis, sepsis, traumatic brain injury and traumatic intracranial hemorrhage, arterial thromboembolism, lung cancer, ectopic pregnancy and ovarian torsion, pneumonia, testicular torsion, gastrointestinal perforation and rupture, spinal and intracranial abscess, open and non-healing wounds, cardiac arrhythmia, and intestinal obstruction (with or without hernia). It is likely that this list of misdiagnosed diseases, which derive from two large "numerator-only" studies (one malpractice-based and one incident report-based), is strongly skewed by reporting bias towards diseases that, when missed, lead to serious harms. It is also likely that the list is skewed towards false negatives relative to false positives; many "benign" diseases that do not cause immediate threat to life or limb are likely missed in far higher total numbers than most of these disorders. Finally, it may also be partly skewed towards errors likely to be confirmed in hindsight by radiographic review, including both fractures and lung cancer.

Best available evidence indicates that the top 15 individual diseases associated with the greatest number of serious misdiagnosis-related harms in the ED, in rank order, were (1) stroke, (2) myocardial infarction, (3) aortic aneurysm and dissection, (4) spinal cord compression and injury, (5) venous thromboembolism, (6/7 – tie) meningitis and encephalitis, (6/7 – tie) sepsis, (8) lung cancer, (9) traumatic brain injury and traumatic intracranial hemorrhage, (10) arterial thromboembolism, (11) spinal and intracranial abscess, (12) cardiac arrhythmia, (13) pneumonia, (14) gastrointestinal perforation and rupture, and (15) intestinal obstruction. These data derive from a large, nationally representative study of malpractice claims in the United States[17] and are bolstered by corroborating data from a similarly large, nationally representative incident reporting system in the United Kingdom[16]; together these two studies represent 78 percent of the diagnostic error cases analyzed for KQ1 (n=4,561 of 5,817). These results are further bolstered by results from a recent malpractice study that was not included in the report, because it was identified after completion of our grey literature search. This was a report on ED diagnostic errors from The Doctor's Company which also identified stroke as the top category, stating, "The top categories for final diagnosis among the settled claims differed slightly. The highest

classification remained cerebrovascular disease, but at a larger percentage (18 percent)."[314] Unsurprisingly, spinal abscess, myocardial infarction, aortic aneurysm and dissection, arterial thromboembolism, and sepsis all also appeared among the top missed conditions. It is possible that missed myocardial infarctions and lung cancers may be overrepresented in malpractice claims, so their ranks could be overstated. However, it is also likely that this is a relatively unbiased list of diseases leading to serious misdiagnosis-related harms. The source data (which are organized by the final, correct diagnosis) likely reflect almost entirely false negatives, but this is probably still an accurate reflection of serious misdiagnosis-related harms. Put differently, death or permanent disability is probably a rare outcome among patients with non-life- or limb-threatening diseases mistaken for dangerous ones (e.g., migraine mistaken for stroke and leading to excess imaging and hospital admission). Nevertheless, complications (including death) can certainly occur, especially when invasive procedures are involved, such as when surgery is performed because of a false positive appendicitis diagnosis.[315] The precise frequency of such adverse outcomes is unknown, but it is likely that such cases would appear in medicolegal claims with equal or greater odds relative to false negative diagnoses of dangerous illnesses, since the legal claim must present evidence that the patient's outcome would have differed but for the diagnostic error, and this is more easily proven for a patient whose misdiagnosis is a false positive (i.e., "healthy" without the disease) who suffers a complication from treatment for an incorrect diagnosis than for a patient whose misdiagnosis is a false negative (i.e., "sick" with the disease) who suffers from the disease itself.

Taken together, these 15 diseases account for an estimated 68 percent of all serious harms from diagnostic error in the ED. The so-called "Big Three" disease categories (vascular events, infections, and cancers), in their totality, account for an estimated 72 percent of all ED diagnostic errors resulting in serious misdiagnosis-related harms. However, major vascular events (42%) and infections (23%) substantially outnumber cancers (8%) in the ED clinical setting. Pediatric populations have fewer high-severity harms than adults and, unlike adults, more infections than vascular events; less is known about the ranks of specific disease distributions.[17]

When considering ED diagnostic errors of mixed severity, missed fractures are the most frequent conditions reported in malpractice claims and incident reports.[16, 31, 71, 80, 90] However, the level of harm associated with most missed fractures is generally lower than that for missed major medical and neurologic events,[17] so they are not among the more common causes of serious misdiagnosis-related harms to patients. Perhaps more importantly, they may be overrepresented in claims as well as incident reports due to ascertainment and reporting biases, perhaps related to the relative ease with which radiographic misdiagnosis can be documented (i.e., using the tangible artifact of the radiograph), even well after the fact (see KQ1a above for details). Epidemiologic data suggest that other diagnostic errors (e.g., for conditions producing lower-severity harms and unaccompanied by radiographs) are likely far more frequent than fractures yet go unaccounted for in malpractice claims or incident reports. For example, missed diagnoses of inner ear diseases are likely an order of magnitude more frequent than fractures, yet do not appear on "top ten" lists of the most commonly missed conditions (see KQ1a). Missed appendicitis is also commonly noted in such reports, but data on frequency are conflicting.

The most commonly misdiagnosed clinical presentations may be abdominal pain, trauma, and neurological symptoms (e.g., dizziness, headache, back pain). However, data are sparse.

Gaps filled: Prior to this report, there was a clear evidence gap regarding the most frequent diseases missed in the ED, and data from different sources appeared conflicting. Best available evidence regarding the most frequent causes of serious misdiagnosis-related harms has now been

synthesized, and clearly points to missed vascular events and infections as the principal causes, with stroke the undisputed leader in total serious harms, particularly permanent disability. Just 15 diseases likely account for more than two-thirds of all serious harms; this means that eliminating preventable patient harms from ED diagnostic error is more tractable than previously imagined.

Gaps identified: A number of gaps were identified in preparing this report. These are described below in the section on Strengths and Limitations (Evidence subsection).

KQ2: Overall and for the clinical conditions of interest, how frequent are ED diagnostic errors and associated harms?

Although based on just a few higher-quality studies less likely to be impacted by systematic under-ascertainment bias, best available evidence indicates that an estimated 5.7 percent (95% confidence interval [CI] 4.4 to 7.1) of all ED visits will have at least one diagnostic error. The overall (not disease-specific), per ED visit, potentially preventable diagnostic adverse event rates were estimated as follows: any harm severity 2.0 percent (95% CI 1.0 to 3.6), serious misdiagnosis-related harms (i.e., permanent, high-severity disability or death) 0.3 percent (plausible range [PR] 0.1 to 0.7), and misdiagnosis-related deaths 0.2 percent (PR 0.1 to 0.4). For each misdiagnosis-related death, it is estimated that there are roughly 0.41 (PR 0.27 to 0.60) ED patients suffering non-lethal, permanent, serious disability. If generalizable to all U.S. ED visits (130 million), that translates to over 7 million ED diagnostic errors, over 2.5 million diagnostic adverse events with preventable harms, and over 350,000 serious misdiagnosis-related harms, including more than 100,000 serious, permanent disabilities and 250,000 deaths. This is equivalent to a diagnostic error every 18 patients, a diagnostic adverse event every 50 patients, a serious harm (serious disability or death) about every 350 patients, and a misdiagnosis-related death about every 500 patients. Put in terms of an average ED with 25,000 visits annually and average diagnostic performance, each year this would be over 1,400 diagnostic errors, 500 diagnostic adverse events, and 75 serious harms, including 50 deaths. These estimates corroborate the National Academy of Medicine (NAM) position that improving diagnosis is a "moral, professional, and public health imperative."[5]

The overall preventable diagnostic adverse event rate of 2.0 percent and misdiagnosis-related death rate of 0.2 percent both come from the only high-quality, prospective study to look at diagnostic adverse events using systematic phone and chart review follow-up on 503 patients both discharged and admitted from the ED. The death rate from such a small study is necessarily imprecise, but supported by corroborating, indirect evidence from other sources, including the other high-quality prospective study of mortality (see report text of KQ2 for elaboration). Retrospective trigger-based studies included many more ED visits (sometimes hundreds of thousands) and often revealed substantially lower rates, but this was almost certainly due to systematic under-ascertainment, as described in the report text for KQ2. Estimates of diagnostic adverse events varied more than 100-fold across studies (i.e., across hospitals) from 0.01 percent at a large, U.S.-based tertiary care ED to 1.6 percent at a small regional ED in Denmark. It is unknown how much of this high degree of variation is real versus study design related.

Variation in diagnostic error rates by disease were striking, with the lowest per-disease diagnostic error rate being for myocardial infarction (false negative rate 1.5%), well below the estimated average diagnostic error rate across all diseases (5.7%). Most of the top harm-producing dangerous diseases are initially missed in the ED at rates of 10 to 36 percent, but spinal abscess is likely the principal high outlier with 56 percent missed initially. There is roughly an inverse relationship between annual disease incidence and diagnostic error rates,

although myocardial infarction is clearly a low outlier. Among the diseases producing frequent death or disability, myocardial infarction stands alone as an exemplar for which ED miss rates have been reduced to a near-zero level, and its rank in malpractice studies may be overstated.

Gaps filled: Prior to this report, there was a clear evidence gap regarding the frequency of diagnostic errors and misdiagnosis-related harms, and data from different sources were highly variable and difficult to compare. Importantly, specific studies identified during the review strongly point to a high degree of systematic under-ascertainment of both errors and harms in the most common types of retrospective studies. Best available evidence regarding the frequency of diagnostic errors and harms both per ED visit and per disease case has now been synthesized. Evidence clearly points to a large public health burden of ED diagnostic errors and rates of diagnostic error for most dangerous diseases that offer a fair amount of "room for improvement." We also present the first meta-analytically supported data on increased mortality from diagnostic error. Finally, demonstrating what appears to be large inter-ED variability in diagnostic error rates suggests many errors are likely remediable, rather than "the price of doing business."

Gaps identified: A number of gaps were identified in preparing this report. These are described below in the section on Strengths and Limitations (Evidence subsection).

KQ3: Overall and for the clinical conditions of interest, what are the major causal factors associated with ED diagnostic errors and associated harms?

Best available evidence indicates that cognitive errors dominate. Although errors were often multifactorial, nearly 90 percent of cases involved failures of clinical decision-making or judgment, regardless of the underlying disease present. Key process failures were errors in diagnostic assessment, test ordering, and test interpretation. Most often these were attributed to inadequate clinical knowledge, skills, or reasoning, particularly in "atypical" cases.

Atypical presentations, non-specific symptoms, and diseases that seem "out of place" (e.g., stroke in a younger patient or appendicitis in an older patient) were among the strongest and most consistent predictors of increased risk for a missed diagnosis across diseases. In other words, ***clinicians do not miss diagnoses when they are obvious, they miss them when they are subtle***. Therefore, solution-making to eliminate preventable harms from diagnostic error must be focused entirely on subtler disease presentations, not obvious ones. For example, it is thoroughly insufficient to attempt to tackle missed stroke in the ED by strengthening existing stroke treatment pathways and reducing door-to-needle times for administration of thrombolytic therapies. Instead, it is essential to create mechanisms that rapidly identify patients with subtle stroke symptoms which are prone to be missed (e.g., dizziness and headaches), in order to bring such patients into stroke treatment pathways so they too may benefit from prompt therapy (e.g., dual antiplatelet therapy for early secondary prevention, which, if applied in the first 24 hours, lowers risk of major stroke after minor stroke or transient ischemic attack by 34% over the next 21 days[316]).

Taken together, this suggests that interventions to reduce harm from ED diagnostic error must directly tackle problems in bedside diagnostic skills and clinical reasoning for atypical presentations of the 15 diseases producing the most harm. If substantial headway is to be made, we must develop system-wide solutions to address these cognitive problems.[2] Options fall into three basic mechanisms that all target increasing the availability of diagnostic expertise:

(1) enhance the expertise of ED clinicians through deliberate practice training and feedback;
(2) support ED clinicians' decision-making through teamwork, including access to experts;
(3) minimize cognitive load by deploying technologies that digitally encapsulate expertise.

Because diagnostic expertise is deeply problem-specific,[317] these broadly construed solutions will need to be individually tailored on a symptom- and disease-specific basis (i.e., modular).

Achieving equity in diagnosis by addressing diagnostic health disparities is of acknowledged importance to achieving diagnostic excellence.[310] Studies that normalized for baseline risk of having the target disease often found an association with gender, race, or ethnicity, with a roughly 20 to 30 percent increased risk of diagnostic error for women and minorities.

Gaps filled: Prior to this report, there was a clear evidence gap regarding the overall causes of diagnostic errors and misdiagnosis-related harms in the ED, including both root causes and contextual risk factors. Clear results here point to a high frequency of cognitive errors in cases with subtle or atypical clinical presentations. This identifies a clear target for systems-based interventions that target cognitive error—increase the availability of diagnostic expertise at the point of care for dangerous diseases with a known high rate of misdiagnosis-related harms.

Gaps identified: A number of gaps were identified in preparing this report. These are described below in the section on Strengths and Limitations (Evidence subsection).

Strengths and Limitations

Evidence

Overall, the evidence available supported answers to all three Key Questions, including a majority of the sub-questions. On KQ1 (diseases), the literature was relatively strong for diseases causing more severe harms but fairly weak on the disease distribution for lower-severity errors. On KQ2 (frequency), the literature was strong on false negatives but relatively weak on false positives. Estimates for overall error and harm rates were drawn principally from three smaller studies (combined n=1,758), none U.S.-based, but these were the only studies that did not restrict patients by disease and still conducted systematic patient follow-up to minimize under-ascertainment of diagnostic errors. There is reason to believe that both the overall and disease-specific results generalize to U.S.-based EDs (see Applicability Section). On a disease-specific basis, literature about error frequency was strongest for stroke, myocardial infarction, and aortic aneurysm and dissection; weaker for venous thromboembolism, meningitis and encephalitis, sepsis, arterial thromboembolism, spinal abscess, pneumonia, appendicitis, fractures, and testicular torsion; and absent for endocarditis, necrotizing enterocolitis, sudden cardiac death, arrythmias, congenital heart disease, ectopic pregnancy, and pre-eclampsia/eclampsia. On KQ3 (causes), the literature was strongest for patient and illness characteristics and relatively weaker on clinician characteristics, fixed systems factors, and dynamic systems factors. Overall, there is a relative paucity of literature on diagnostic errors among pediatric ED populations. More studies are warranted, including research on how the distribution of diseases (KQ1), rates of diagnostic error (KQ2), and causes/risk factors (KQ3) differ from those in adult patients. Specific gaps identified for each question with potential remedies are described below for each KQ.

The list of diseases under consideration for the overall search and, specifically, KQ2, was prespecified on the basis of prior literature and informed by the use of a TEP and Key Informant interviews. This approach was chosen because, in the timeframe for conducting the work, it was not possible to complete the KQs "in series" (i.e., to do KQ1 first and then start the search anew for KQ2 and KQ3). Thus, this was the only methodologically feasible approach. This represents a limitation (particularly as relates to the list of diseases assessed in KQ2). We have assessed the impact of this limitation through the final results derived from KQ1, and the impact appears to have been modest. The prespecified list appears to have been fairly complete vis-à-vis the most

common causes of misdiagnosis-related harms—for example, in the largest incident report study of ED diagnostic errors (n=2,288) (which was not used to determine the prespecified list), all top 12 conditions found in that study (Hussain et al., Table 1[16]) appeared in our prespecified list. No other conditions identified in that study had higher individual frequency, and, collectively, all of those other conditions combined accounted for just 30 percent of the total incidents reported (n=679/2,288) (i.e., our list embraced more than 70% of the total incident reports related to diagnostic error and all of the top conditions). Our prespecified list included searches for error rates for 14 of the top 20 diseases identified in malpractice claims and 10 of the top 15 associated with the largest number of serious misdiagnosis-related harms. While some conditions (particularly those affecting children) may have been underrepresented (e.g., missed child abuse/non-accidental trauma), we found no evidence to suggest that using a prespecified list based on prior literature, Technical Expert Panel and Key Informant interviews appreciably affected our results. However, because of the constrained focus on the most common conditions, we do not have data on misdiagnosis of less common conditions that may nevertheless be of importance to ED clinicians (non-accidental trauma, necrotizing fasciitis, compartment syndrome, brain tumors, obstructive hydrocephalus, ovarian torsion, post-partum hemorrhage, etc.); this is a limitation. We also do not know whether exclusion of smaller studies (n<50) by design influenced results.

Most studies did not directly address issues surrounding measurement of diagnostic error (e.g., validity, reliability, determination of causes, preventability, or attribution of harms). In clinical practice, many disease reference standards are insufficiently understood, developed, and implemented, so diagnosticians often disagree on final patient diagnoses. To the extent that manual chart reviews were used to identify errors, original studies are likely to suffer from problems of poor chart documentation,[318, 319] low inter-rater reliability,[320, 321] and hindsight bias.[322] The problem of author bias in choice of definition or method of measurement (e.g., specialists [or diagnostic error "advocates"] determining ED misdiagnosis and favoring more lax definitions of error/harm, or the reverse, with ED clinicians favoring more stringent definitions) is difficult to ascertain. Our use of the NAM definition of diagnostic error mitigates some of these concerns, since there is less subjectivity inherent in a diagnostic label change (e.g., discharged with "musculoskeletal chest pain" returns with "aortic dissection" within 24 hours) than in the determination of preventability, which is known to be highly subjective.[320] Also, many included studies used stringent measurement protocols or objective statistical methods (e.g., Symptom-disease Pair Analysis of Diagnostic Error [SPADE][145]). Nevertheless, poorly standardized or low-reliability measurements are important limitations.

Gaps in Evidence for KQ1—Diseases Associated With Diagnostic Error/Harm

- The literature on diagnostic error is dispersed and challenging to aggregate. A concerted effort should be made to standardize reporting language in studies that address diagnostic error and harms (e.g., by creating an extension to the Standards for Reporting of Diagnostic Accuracy Studies [STARD] reporting guidelines[323]) and improve meta-data tagging of relevant studies by the National Library of Medicine.
- Differences in disease classification, categorization, and granularity (i.e., lumping versus splitting) powerfully influence frequency rankings. This hampers synthesis across studies, so standardized reporting categories and definitions should be adopted. This could be accomplished using the Agency for Healthcare Research and Quality (AHRQ)

standardized coding schema from the Clinical Classifications Software,[101] as was used in the study that defined the top 15 above.

- Data on the conditions most often misdiagnosed in the ED, independent of outcome severity, remain uncertain—fractures are common but probably overrepresented relative to other lower harm-severity illnesses, while other common conditions are probably more frequently misdiagnosed based on epidemiologic data (e.g., benign inner ear disorders), yet go underreported. This would ideally be addressed through nationally representative mechanisms of annually tracking ED diagnostic error, using existing mechanisms such as AHRQ's Healthcare Cost and Utilization Project (HCUP) family of databases[259] or the Centers for Disease Control and Prevention's National Center for Health Statistics.[324] In such a process, special attention should be paid to differences in conditions between children and adults, since less is known about pediatric diagnostic error distribution. Some diseases relevant to children were not identified in our preliminary search or through our Technical Expert Panel and Key Informant interview processes, so were not explicitly assessed in our protocol (e.g., ovarian torsion,[82] child abuse,[325-328] brain tumors); these may be important to future inquiries.
- The special case of child abuse (which was not incorporated into our study design but was identified during the review/comment period for the report) highlights an important gap around recognition of diagnostic errors for diseases that may be intentionally concealed, rather than surfaced, as problems. The Centers for Disease Control and Prevention have estimated that nearly 1 in 7 children suffer abuse and neglect, resulting in 1,750 deaths in the United States in 2020.[329] One older study of 173 abused children under age 3 with head injuries found 54 (31%) were not recognized by physicians (across settings) as non-accidental injuries; among these, 15 (28%) were reinjured after the misdiagnosis.[330] A more recent, multi-center, ED-based study in the Netherlands found that EDs complying with screening guidelines for child abuse were 4-fold more likely to detect cases (0.3% versus 0.1%, $P < 0.001$), suggesting that many missed cases are likely detectable.[331] Because abusive parents are highly unlikely to file a malpractice claim for an ED missed diagnosis of abuse, malpractice data will grossly underrepresent this condition. The same is likely to be true for other forms of abuse (e.g., missed spousal abuse, elder abuse), certain socially unacceptable conditions (e.g., missed cases of illicit drug use or dependence), or factitious disorders (e.g., missed Munchausen syndrome). Furthermore, individuals may be more likely to seek care at different EDs,[332] limiting the utility of single institutions to detect missed cases (e.g., via chart review). For these populations and disorders, special efforts must be made to identify misdiagnoses using alternative data sources and methods.
- Data on the symptoms or clinical presentations most often misdiagnosed are sparse. This is a problem because solution-making for diagnostic error requires a focus on clinical presenting symptoms, rather than diseases (because patients attend the ED with new or troubling symptoms, and the diagnostic process must then focus efforts on identifying the underlying causes). This should be rectified by leveraging existing coding architectures, such as that provided by the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10), "Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified (R00-R99).[333]" This could be accomplished via modified billing requirements (e.g., the Centers for Medicare &

Medicaid Services could require all encounters billed from the ED, regardless of final disposition, to be tagged permanently with a standardized symptom-based code).

Gaps in Evidence for KQ2—Frequency of Diagnostic Error/Harm

- Diagnostic accuracy and error rate terminology should be standardized for reporting purposes (e.g., by creating an extension to the STARD reporting guidelines[323]). More research should be done to assess systematic differences between prevalence-independent measures (false negative rate, false positive rate) and prevalence-dependent measures (false omission rate, false discovery rate), particularly since most of the literature is mixed-and-matched in this regard (i.e., focused on either false negative rates [sensitivity] or false discovery rates [positive predictive value], but not on false positive rates [specificity], false omission rates [negative predictive value], or total accuracy). The impact of study design on different diagnostic accuracy parameters should be assessed.
- Methodological approaches used in most of the identified studies tend to bias towards underestimation of diagnostic errors and misdiagnosis-related harms by one to two orders of magnitude. The literature is heavily weighted towards retrospective administrative studies that use variable definitions, differing time windows for outcome assessment, and fall short on ascertainment because of incomplete outcome event data. New measurement approaches are needed, including those that capitalize on regional or insurance-based assessment of adverse events such as hospitalizations and deaths. It may be necessary to rigorously develop statistical inflation factor estimates that facilitate adjustment of retrospective study results to match prospectively obtained rates. Time windows should be standardized and based on appropriate empiric evidence.[143, 147]
- Data on disease-specific health outcomes associated with diagnostic error were limited, and many were incorrectly reported as null effects (or even "protective" effects) without proper severity matching (or adjustment) from the time of initial clinical presentation. A guide to proper analysis (including initial case severity adjustment) to assess the adverse health outcomes of diagnostic error should be developed and disseminated by AHRQ.
- More research should be done to assess preventability of harms from diagnostic errors, since there is moderate inter-rater variability in clinician ratings of preventability.[320]
- More research should be done on the magnitude and severity of false positive diagnostic errors in the ED, since most of the studies identified focused on false negatives.
- More research should be done to understand the biases present in both malpractice claims and incident report data. For example, diagnostic error rates for myocardial infarction are just 1.5 percent, yet there are nearly as many claims and incidents as there are for stroke, which affects a similar number of patients but is misdiagnosed 10-fold more often. Likewise, sepsis affects more patients overall than stroke and is probably missed at slightly lower rates (meaning there are expected to be a similar numbers of misdiagnosed cases), yet there are many fewer claims and incident reports for sepsis. It is unknown how much of these differences relate to true outcome differences across diseases versus the disease-specific probability that a malpractice claim or incident report is filed.
- More research should be done to measure diagnostic error rates among admitted patients, since we identified few studies of this type, but there were more errors than expected (e.g., a 12% error rate correlated with a 2.4-fold increase in mortality[7] and frequent missed myocardial infarction among patients admitted with other diagnoses). It is possible that these errors account for one third of all ED-related serious harms.

- More research should be done to assess the relationship between admission fraction and diagnostic error rates, including total diagnostic accuracy (particularly with respect to academic versus non-academic status). It appears that, at least in some studies, academic teaching hospitals have lower diagnostic error rate (among those discharged) but a higher admission fraction than non-teaching hospitals. Because individual studies rarely address both false negatives and false positives together, it is unknown whether overall diagnostic performance or accuracy (i.e., area under the receiver operating characteristic curve) at teaching hospitals is actually better or they are simply making different disposition decisions by trading off false negatives (fewer discharged missed cases of dangerous diseases) in favor of false positives (more patients with unnecessary hospitalizations).
- More research should be done to assess the utilization and cost implications of diagnostic error, including both those treated and released from the ED and those admitted to the hospital. Relatively few studies addressed this issue in rigorous ways.

Gaps in Evidence for KQ3—Causes of Diagnostic Error/Harm

- Analysis and reporting of risk factors for (or causes of) diagnostic error in the current literature is highly variable. Much of the heterogeneity in results for demographic predictors (e.g., gender or race) may stem from confusion about the inferences to be drawn from different study designs that either look back from hospitalized patients with a given disease or look forward among patients with a given symptom (see KQ3). Reporting should be standardized (e.g., by creating an extension to the STARD reporting guidelines[323]) so that health equity in diagnosis can be accurately measured. The root causes of measured diagnostic disparities should be examined, including the role of implicit or explicit bias towards women, minorities, or other vulnerable populations. Research should be done to assess the contribution of (nominally correct) prevalence-based decision-making on the part of ED clinicians to diagnostic health disparities. Other patient characteristics reflecting marginalized status[334] (e.g., members of religious minorities; lesbian, gay, bisexual, transgender, and queer [LGBTQ+] persons; persons with disabilities; persons who live in rural areas; and persons otherwise adversely affected by persistent poverty [including homelessness] or inequality) or the presence of marginalizing co-morbidities (e.g., mental health or substance use disorders[335, 336] or obesity) that may increase the risk of diagnostic error are understudied and deserve further equity-related research. To summarize, measuring health equity in diagnosis should be a key focus of future research, and special care should be taken to ensure that rigorous epidemiologic and statistical methods are used to address this concern, since incorrect methods can lead to erroneous inferences.
- We found relatively few studies that assessed the impact of clinician characteristics, fixed system characteristics, and dynamic system characteristics. There were relatively few studies that addressed potentially important predictors related to ED clinicians (e.g., training background, years of clinical experience, history of disciplinary action, fatigue), fixed systems factors (e.g., access to consultants, access to tests, delivery system/payment models), and dynamic systems factors (e.g., ED staffing, ED workload, crowding, handoffs, discharge fraction). These are important areas for future study, since they may be used to identify high-risk individuals, sites, or practices that could be targets for remedial action. For example, the path to closing the measured diagnostic performance gap between community and academic EDs (with lower false negatives at teaching

centers) is unclear; to guide solution-making, it would be very helpful to know whether lower false negative rates at academic centers reflect greater total diagnostic accuracy (lower false negatives and *lower* false positives) or a merely a lower threshold for further diagnostic testing and admission (lower false negatives and *higher* false positives).[337]

- We found no studies included in the review that considered how teamwork directly impacted the risk of diagnostic error for better or worse (e.g., involvement of patients, trainees, advanced practice providers (APPs), ED nurses, allied health professionals, or specialists; typical ED team composition; or team cohesion and dynamics). Recent studies suggest that ED diagnostic accuracy can be improved through the direct engagement of specialist consultants as part of the diagnostic team caring for ED patients.[338] It would also be valuable to know whether engaging ED nurses in support of ED clinician diagnosis by promoting adherence to guidelines, protocols, or pathways would improve diagnostic accuracy or outcomes for patients (as demonstrated previously in other areas of patient safety).[339] Likewise it would be valuable to know whether findings from vignette-based trials showing that medical students make more accurate diagnoses when working in teams than when working alone[340] also apply to routine, real-world ED care delivery, as implied by one recent study that focused on systematic physician cross-checking in the ED.[341]
- We found few studies that addressed whether patients themselves affected ED diagnostic errors for the worse (e.g., via delayed recognition of the problem as part of the "patient interval" in diagnosis [see KQ3 results regarding testicular torsion]) or for the better (e.g., via proposed patient-facing strategies to prevent diagnostic error or mitigate resulting harms[5, 342]). Further study is needed to assess the impact on diagnosis-related health outcomes of delayed (or rapid) disease recognition by patients themselves; the role of directly engaging patients as part of the diagnostic team[343]; and more effective methods for shared diagnostic decision making as part of "patient-centered diagnosis.[344]"
- We found limited evidence on the distribution of causes based on harm severity and no evidence of whether certain error causes were more likely to result in patient harm. It would be helpful for future studies to report the relationship between causes and harms to determine whether specific causal factors are more important targets in reducing harms.

Review

Neither the study team nor the TEP prospectively identified five conditions that ultimately appeared among the 15 most harmful conditions identified as part of KQ1. As a result, spinal cord compression and injury (#4), lung cancer (#8), traumatic brain injury and traumatic intracranial hemorrhage (#9), gastrointestinal perforation and rupture (#14), and intestinal obstruction (#15) were not included in the original, prespecified disease-specific searches related to KQ2 and KQ3. Thus, rates are not available. It is likely that the causes of missed lung cancer differ somewhat from the studied vascular events and infections. Cognitive errors are likely to have been errors in interpreting radiographs (missed lung nodules) and systems errors are likely to have been errors in communication or handoffs for follow-up of incidental findings.

Applicability

The majority of patient populations studied are likely applicable to a typical U.S.-based adult ED population. However, the relative paucity of pediatric studies suggests that caution should be

exercised when extrapolating results to children/pediatric EDs. Studies were disproportionately conducted in academic hospital settings. There is some evidence that such hospitals have lower diagnostic error rates but higher admission fractions; non-teaching hospitals may have lower admission fractions and higher diagnostic error rates.[148] This means that non-teaching hospitals may experience higher error rates than those listed above in KQ2; however, there is no specific reason to believe results from KQ1 or KQ3 do not apply. As noted in the section on Strengths and Limitations (Evidence subsection), outcome measures were neither homogeneous nor consistently reported across studies. This was principally an issue for KQ2 (rates) and, to a lesser extent, KQ3 (causes). Nevertheless, we believe we were able to combine studies appropriately and summarize both rates and causes where evidence supported meta-analysis.

Despite sourcing key portions of the data for KQ2 (rates) from a small number of studies conducted in countries outside the United States, we believe the results apply to U.S.-based EDs. Point estimates for overall error and harm rates were drawn from three studies based outside the United States (Canada, Spain, and Switzerland, with a combined n=1,758), but these were the only higher-quality studies found that conducted systematic patient follow-up to minimize under-ascertainment of diagnostic errors. The overall estimated ED diagnostic error rate of 5.7 percent was far lower than the measured false negative rates for the top serious harm-producing diseases other than myocardial infarction (range 10-56%, Table 9), and 9 of the 12 disease-specific rates included U.S.-based studies (not pulmonary embolus, meningitis, or pneumonia). The measured overall harm and death rates derived from a single, well-designed, prospective Canadian study. Although that study excluded "less urgent" and "non urgent" cases (which may artificially inflate the estimated mortality rate), the study was also conducted at an academic institution, diagnostic errors resulting in mistreatment were classified as treatment errors, and the methods used for determining a preventable diagnostic adverse event (minimum certainty of 5 on a 6-point Likert scale by at least 2 of 3 emergency medicine reviewers) was very stringent (all of which may artificially reduce the estimated mortality rate). Because the measured mortality rate and range triangulate well with estimates from the two European studies, a nationally representative U.S.-based source (Medicare data on short-term deaths post ED treat-and-release with a "benign" diagnosis[148]), and benchmarking from autopsy data in relation to ED error (see KQ2 Plausibility of Mortality Estimates From Higher Quality Studies), we believe they are likely representative.

The misdiagnosis-related death and total serious harms rate can be compared to the estimated rates for inpatient care. A prior systematic review by Gunderson et al.[3] found a total diagnostic adverse event rate of 0.7 percent in hospital inpatients. One of the studies cited in that review (Zwaan, 2010) found 29 percent of these hospital-based diagnostic errors resulted in death (and another 26% were associated with persistent disability at hospital discharge). Combining these results suggests the inpatient misdiagnosis-related mortality rate is roughly 0.2 percent (and the inpatient serious misdiagnosis-related serious harm rate is roughly 0.4 percent). These hospital-based estimates comport well with the ED serious harm rates estimated in this evidence report. The diagnostic adverse event rate in the hospital (from the prior review) is lower than the ED (in this review) while the serious harm rate in the hospital is higher than the ED. This makes sense since hospital care is permitted more time and greater diagnostic resources (i.e., it is expected that errors would be less frequent), but harm severity is higher because patients are sicker.

Because there are known differences between ED training and certification in the United States and other countries that might influence applicability, we reached out to study authors to determine the training background of ED clinicians from these three studies. The study from Spain (Nuñez, 2006) used to estimate the diagnostic error rate among treat-and-release

discharges differed the most from U.S. ED practice—because there is no emergency medicine training pathway, ED clinicians were trained as a mix of internists, surgeons, and family physicians. The study from Switzerland (Hautz, 2019) used to estimate the diagnostic error rate among admitted patients and to triangulate mortality was closer to U.S. ED practice. There were 33 different attending ED physicians, all with a primary degree in internal/hospital medicine, and 26 of 33 (78.8%) had further formal specialization in emergency medicine. Mean professional experience was 11 years since graduation (range 6-25 years) and mean experience in emergency medicine was 6 years (range 1-25). The study from Canada (Calder, 2010) used to estimate diagnostic adverse event and mortality rates was very similar to U.S. ED practice. All attendings (estimated by study authors as n≈55) had training or certification in emergency medicine. The majority (estimated by that study's authors at ~80%) underwent a 5-year emergency medicine training program (which is longer than the 3 to 4 years of emergency medicine training typical in the United States), while the minority (estimated by that study's authors at ~20%) underwent a 1-year emergency medicine certification program following 2 years of family medicine training. Thus, from the two studies used to estimate harms, about 92 percent (n≈81/88) had specific training and certification in emergency medicine, and 50 percent (n≈44/88) had more training in emergency medicine than would be typical in a U.S.-based emergency medicine residency.

While the referral architecture by which patients attend EDs likely differs across countries (including some included as part of our review), we found no evidence that studies conducted in comparable, disease-specific populations outside the United States had substantively different results than those conducted in U.S.-based EDs. Comparison across studies within each disease did not demonstrate any systematic differences in diagnostic error rates between U.S.-based and non-U.S.-based EDs. The one disease-specific study which included both U.S.-based and European EDs and compared diagnostic performance directly across continents found slightly longer diagnostic delays for aortic dissection patients in North America when compared to Europe; from the list of investigators included in the registry, 12 of 14 North American sites were U.S.-based institutions and the other two were in Canada, while the European sites were from seven countries, including Spain and Switzerland.[68] Thus, there is reason to believe that the error and harm rate estimates are either representative of U.S. ED performance or perhaps low.

Given that this systematic review spans studies from more than two decades, there are naturally applicability concerns regarding recency of estimates. We found no clear differences based on the epoch in which studies were reported (2000 to 2010 versus 2011 to 2021), although comparisons were limited to just a few diseases based on data availability. The one study which explicitly assessed temporal trends for cardiovascular misdiagnosis in U.S.-based EDs (2006-2014, using Medicare data) found no significant trends for myocardial infarction or aortic dissection and a ***rising*** trend (increased false negative diagnostic errors) over time for ruptured aortic aneurysm, subarachnoid hemorrhage, and ischemic stroke.[120] Thus, we believe that the disease-specific error rates, despite in some cases being more than a decade old, are either representative of current U.S. ED performance or, for some diseases, perhaps low.

Implications for Clinical Practice, Education, Research, or Health Policy

Although not all diagnostic errors or associated harms are preventable, we believe that the current report outlines a clear path forward towards eliminating those misdiagnosis-related harms in the ED that are preventable—(1) it identifies the diseases with the greatest burden of misdiagnosis-related harms, permitting prioritization; (2) it clarifies which clinical presentations

have the greatest opportunity for improvement, focusing improvement efforts and delineating diagnostic performance benchmarks to assess progress; and (3) it pinpoints the common root causes and contexts, defining the nature and scope of appropriate solutions, and explaining why modular solutions are more likely to work than general ones. Limitations of the report included reliance on a few high-quality studies for the list of diseases (KQ1a) and overall error/harm rates (KQ2a) as well as inconsistent methodology across studies (including issues related to data sources, measurement methods, and causal relationships).

Several policy recommendations flow directly from the report's findings and the documented limitations in the evidence base: (1) standardizing measurement and research results reporting to maximize comparability of measures of diagnostic error and misdiagnosis-related harms[5, 345, 346]; (2) creating a National Diagnostic Performance Dashboard to track performance (analogous to the Dartmouth Atlas Project for utilization of healthcare services[347]); and (3) using multiple policy levers (e.g., research funding, public accountability, payment reforms)[5] to facilitate the rapid development and deployment of solutions to address this critically important patient safety concern. The first flows from the lack of standardized measurement of diagnostic error and harms identified by the systematic review. The second derives from the lack of adequate national benchmarking and lack of comparability of measurement across EDs identified in this systematic review. The third derives directly from the overall public health scale and scope of the problem identified by the review. These interventions will require the application of new resources, and the magnitude of such resources should be commensurate with the large public health burden.

Considerations for Clinical Practice and Policy

Challenges Facing ED Diagnostic Safety and Quality

Discussing diagnostic errors can feel overwhelming for clinicians, educators, researchers, and policymakers alike. Clinically there is already a long list of things required for patient safety and quality, so addressing diagnostic errors feels like "one more thing." ED physicians do not routinely receive performance feedback, so may be mis-calibrated as to their diagnostic accuracy,[116] raising internal doubts about the magnitude of this as a safety problem. Skepticism related to the role of hindsight bias in retrospective studies further fuels such doubts.[322] Diagnostic competence is also deeply personal for physicians and tied to their sense of identity as a clinician,[348] likely more so than medication errors from bad handwriting or patient falls in the hospital. Especially for older ED physicians in the United States, the historical struggle for recognition of Emergency Medicine as its own discipline has fostered a degree of "hyper-independence"[309] that may feel threatened by discussions of diagnostic error which link back to insufficient diagnostic expertise as a potential cause. For educators, there is already too much to teach and too little time to teach it. It seems hard to know even where to begin with diagnostic errors, since they happen for all symptoms and all diseases, and our present modes of education appear to be insufficient to the task.[349] For researchers, this is a complex, multi-faceted problem that does not lend itself well to reductionist methods or precise outcome measurement. For policymakers, this is a deeply technical area where scientific consensus is often lacking, solutions appear to be few in number[342, 350] (and too narrowly constructed), and the best course of action may seem to be inaction. It is also self-evident that fixing diagnostic errors will be difficult—had it been easy, it would have been done long ago. There would have been no need for an over 400-page report in 2015 from the NAM, entitled Improving Diagnosis in Healthcare,[5] describing this multi-faceted, "wicked problem"[351] (in the technical sense[352]), nor need for the

current report. Lastly, any attempts to fix the problem carry an associated risk of unintended consequences. For example, EDs have often been criticized for the overuse of diagnostic tests—an emphasis on diagnostic error has the potential to increase testing among low-risk patients, increasing costs, adding radiation exposure or other diagnostic test-related risks, and leading to more incidental findings that themselves adversely impact patient wellbeing.[353] Some of our findings suggest that, at least for myocardial infarction, the balance may already have shifted in the direction of test overuse, excess workups, and diagnostic overcalls (see KQ2). Furthermore, ED overuse of increasingly sensitive diagnostic tests now risks overdiagnosis[354, 355] of mild forms of illness where, despite a correct diagnosis, harms (physical, psychological, or financial) may ultimately outweigh treatment benefits (e.g., sub-segmental pulmonary embolism[354]).

Concerns Over ED Diagnostic Test Overuse Due to a Focus on Diagnostic Safety

In considering implications for clinical practice and policy, it is important to examine the apparent tension between test underuse and test overuse as it relates to diagnostic errors. A common concern is that a focus on false negatives will drive diagnostic test overuse and more false positives (as well as adverse impacts of greater testing such as risks, incidental findings, and costs). For example, concern over missed stroke in ED dizziness appears to be driving increased use of neuroimaging.[306, 356] Head computed tomography (CT) is the primary neuroimaging modality used to search for stroke in ED dizziness,[357] and there is strong evidence that CT overuse in ED dizziness presentations is increasing radiation exposure and healthcare costs without improving diagnosis of stroke or other neurologic diseases.[163, 357-359] Conversely, the argument is often made that a focus on cost containment and care efficiency will drive test underuse and more false negatives. For example, there are legitimate concerns that downward financial pressure on use of magnetic resonance imaging (MRI) in back pain presentations[360] may increase the risk of missed spinal abscess, which requires spine imaging for diagnosis. But this "tradeoff" scenario assumes that (a) current practice optimally applies existing diagnostic methods, (b) innovations in diagnosis do not occur, and, therefore (c) the only way to influence diagnosis is to alter the threshold for ordering existing tests (e.g., by lowering the threshold and testing patients at very low risk for the target disease). This premise then leads to the (often) erroneous conclusion that diagnosis is a "zero sum game" and the only choice is to "pick your poison" between more false negatives (favor specificity, sacrifice sensitivity) and more false positives (favor sensitivity, sacrifice specificity).[337] However, this is generally a false dichotomy, since current practice often fails to apply basic diagnostic methods (e.g., proper history-taking and neurologic examination in patients with back pain at risk for spinal abscess[228]) and innovations that actually improve diagnosis (e.g., via better education or training, new clinical pathways, novel diagnostic tests, enhanced teamwork in diagnosis, greater access to specialists, or improved feedback and calibration) will almost always increase both sensitivity and specificity at any given decision threshold. The result is then fewer false negatives ***and*** fewer false positives, sometimes even at a lower total cost.[337, 361]

Implications for Solutions To Reduce Diagnostic Error and Associated Harms

In pursuing new solutions to tackle ED diagnostic errors, the first question that any chief quality officer, risk management professional, or policymaker should ask is whether there are cross-cutting (non-problem-specific) solutions that could be implemented immediately in the ED

(e.g., a diagnostic "time out" for clinicians to reflect on their own diagnostic process[362] or tools that help patients summarize their symptoms[363]). Although this would seem to be the quickest way to solve the problem of ED diagnostic error, there is some evidence to suggest that general solutions like this are unlikely to work. Our KQ3 findings indicate that cognitive errors in diagnostic reasoning predominate as causes. Monteiro et al. have nicely summarized the extensive body of evidence that diagnostic expertise is deeply problem-specific in their 2020 review article aptly subtitled "The enduring myth of generalisable skills."[317] Our KQ2 findings also support this position, given that ED clinicians are clearly quite accurate in diagnosing myocardial infarction, but far less accurate with other dangerous diseases. Our KQ3 findings further bolster this position, given that clinical symptoms which are "atypical" are the most consistent risk factors for misdiagnosis, within a given disease. Put differently, being expert at diagnosing heart attack in patients with chest pain does not confer the same expertise in diagnosing stroke in patients with dizziness; the converse is also true. As a result, all solutions will likely need to be tailored on a symptom- and disease-specific basis (i.e., modular).

Target diseases should be prioritized based on (a) the overall share of misdiagnosis-related harms (particularly high-severity harms), (b) higher absolute error or harm rates (i.e., with ample opportunity for improvement), (c) variability in diagnostic performance (including known health disparities or variation by organization, site, or provider), and (d) availability or cost-effectiveness of promising solutions. This approach to prioritization reflects an emphasis on public health needs while balancing societal costs and benefits. There is a value judgment to be made when comparing more frequent but less severe harms (as with missed fractures) to those that are less frequent but more severe (as with missed stroke). From a purely utilitarian standpoint, the aggregate societal disutility in these two categories of diagnostic error may be similar, but our personal experience with patients who have suffered diagnostic errors is that they care more about permanent, severe harms than temporary, milder ones, even if the latter are more frequent. Therefore, we believe that prioritization on the basis of high-severity harms (KQ1, Table 3) makes both the most public health sense and the most patient-centered sense. Nevertheless, solutions targeting very high-frequency errors may also be warranted.

Just 15 diseases likely account for more than two-thirds of the serious misdiagnosis-related harms in the ED, so these should certainly become the initial priority focus. Only one of these is missed at rates near zero—myocardial infarction stands alone with a miss rate of 1.5 percent. While there may still be room for improvement among admitted patients, trying to further reduce missed heart attacks in the ED may prove challenging.[77] Instead, we should leverage the prior successes in deploying chest pain clinical pathways for diagnosis of acute coronary syndromes to serve as a model for how to improve diagnosis for other symptoms and diseases. That process took decades of focused research on heart attack diagnosis,[364] followed by concerted quality improvement efforts to improve diagnosis through care process redesign,[365] including partnering with specialists from a relevant discipline (cardiology) to achieve optimal outcomes.[366] Lessons learned should now be extended to other diseases in the top 15.

A strong next candidate for targeted diagnostic safety and quality initiatives, based on results of this systematic review and priority-setting approaches described above, would be to construct clinical pathways for dizziness to identify strokes. Improving diagnosis of strokes in dizziness is a top priority for ED clinicians,[356] and a clinical practice guideline for acute dizziness diagnosis is currently under development by the Society for Academic Emergency Medicine.[367] Dizziness now leads to nearly 5 million ED visits per year, at a cost of over $10 billion.[115] Dizziness and vertigo are "atypical" stroke symptoms relative to the more familiar (and obvious) unilateral

weakness or inability to speak. Strokes presenting with dizziness are missed 40 percent of the time,[21] leading to an estimated 45,000 to 75,000 missed strokes.[115] Brief bedside physical exam techniques that look closely at eye movements (known as "HINTS"[368]) have been shown to have greater accuracy (sensitivity) than MRI in this specific context.[307, 368-370] Current evidence shows that many ED physicians are unfamiliar, uncomfortable, or inexpert in using these bedside techniques.[306, 307] This creates an opportunity for diagnostic quality improvement. Our results show that more diagnostic expertise is needed. This could be accomplished by enhancing ED physician expertise via scalable education techniques such as virtual patients,[349] supporting ED clinicians through access to dizziness experts via telehealth,[338] or leveraging devices (including mobile phones) married to algorithms that digitally encapsulate expert interpretive knowledge about these findings.[371, 372] One could envision that similar quality initiatives might target other symptom-disease pairs such as abdominal pain (aortic aneurysm/dissection, mesenteric ischemia), altered mental status (sepsis, meningitis/encephalitis), or back pain (spinal abscess).

Implications for Operational Quality Measurement and Benchmarking

A recent issue brief from AHRQ outlines the full palette of options for operational measurement of diagnostic errors.[373] Below, based on ED measurement needs derived from our systematic review and meta-analysis, we offer specific suggestions from among the list of possibilities mentioned in that brief. We divide these into methods that are disease-specific and those that are disease-agnostic. We also note measures that are "numerator only" (i.e., they are all "events" and the precise population from which these events are drawn is ill-defined) and briefly summarize the use of each data type considering findings from this report. These are followed by some general recommendations on measurement based on our findings. Because no single measurement method can address all types of diagnostic errors, ED diagnostic errors should be tracked using a portfolio of metrics that include the following:

1. **Disease-Specific Data Sources/Metrics for Diagnostic Error**. Disease-specific measurement facilitates targeted quality improvement efforts and assessment of their impact. These measures should be used to address symptoms, diseases, or symptom-disease pairs that are either common or frequently misdiagnosed.
    a. **SPADE (Symptom-disease Pair Analysis of Diagnostic Error)[145]** - We identified multiple studies using SPADE or related methods for missed stroke,[64, 120, 155] myocardial infarction,[63, 77, 120] aortic aneurysm/dissection,[120] sepsis,[78, 93, 94, 256] and meningitis,[93] but it can be applied to any acute disease which confers excess short-term risk of an adverse clinical outcome when left untreated after an initial treat-and-release visit. The look back method (from diseases to symptoms) can be used to discover clinical presentations (often "atypical" ones) at high risk of misdiagnosis, as well as other risk factors for misdiagnosis, such as age, gender, or race. The look forward method (from symptoms to diseases) can be used to measure absolute rates of misdiagnosis-related harms and monitor performance in response to diagnostic improvement initiatives. SPADE is a clinically valid, methodologically sound, statically robust,[154] and operationally viable[155] method of identifying misdiagnosis-related harms from electronic health record or billing/administrative data—importantly, without the requirement of manual chart review (although chart review can inform root cause analysis if so desired). However, SPADE relies on detecting adverse events. From the studies we identified, these are relatively infrequent

(typically less than 1 percent of treat-and-release cases), so stable measurement generally requires thousands of encounters. That means that at a medium to large-sized ED, relatively common symptoms (e.g., abdominal pain, chest pain, dizziness, headache, back pain) can be mined using SPADE for misdiagnosis-related harms linked to more common dangerous diseases such as stroke, myocardial infarction, sepsis, or pneumonia using a rolling 6- to 12-month window. Smaller hospitals or rarer diseases generally require longer assessment time windows. Also, related symptoms[77, 256] or diseases[120] can be aggregated to increase the sample size. If insufficient data are available for stable measures, SPADE can be used as an electronic trigger mechanism to identify cases for manual chart review.

b. **Change from ED admitting diagnosis to final hospital discharge diagnosis** - We found many studies that measured false positives among patients admitted to the hospital for a specific target disease. For example, this included studies of the rate at which admissions to a medical unit with suspected myocardial infarction turned out to be incorrect or the rate at which the cardiac catheterization lab consulting service was activated unnecessarily. These studies tended to focus on overutilization of clinical services or hospital admission. This method is likely to be more helpful in assessing overall diagnostic accuracy for a given disease if paired with a search for false negatives, at least among admitted patients (e.g., admission for "fall" that turns out to be a missed myocardial infarction). This involves a search for when the ED admitting diagnosis differs from the final hospital discharge diagnosis for a given dangerous disease, as done retrospectively for myocardial infarction using Medicare data[206] and in robust prospective fashion by Hautz et al., 2019 across medical conditions.[7] Even more robust would be to combine this with 30-day disease-specific hospitalizations after ED treat-and-release for a more complete capture of false negatives, although we did not identify any disease-specific studies that combined these sorts of data.

c. **Unannounced standardized patients[374] ("secret shoppers")** - Although no studies of this type were identified in our review, standardized "fake" patients can be used to assess diagnostic quality for specific symptoms or diseases in clinical practice.[375] This approach decreases the variance in measurement, allowing very direct comparisons, down to the individual ED clinician level. However, the effort and expense required makes this an option that should be reserved for very high-stakes scenarios (e.g., pay-for-performance benchmarking for diagnosis of a specific clinical presentation).

2. **Disease-Agnostic Data Sources/Metrics for Diagnostic Error.** Disease-agnostic measurement facilitates inquiry into overall error and harm trends but is less actionable. These measures should be used to track the impact of broad interventions likely to affect the overall diagnostic error rate (e.g., change in staffing model or access to specialists) and, when possible, as a general benchmarking tool to compare across institutions.

   a. **Malpractice claims** (numerator only) - At most institutions, ED claims are readily captured and thoroughly analyzed. Based on this review, claims should be presumed to be both biased towards dangerous diseases and to substantially underrepresent total errors, but also to be mostly representative of diagnostic errors resulting in serious harms (barring perhaps overrepresentation of heart attacks and radiographically determined misdiagnoses). Tracking changes in the frequency or severity of claims in response to diagnostic improvement interventions may work for more common

conditions in claims (e.g., stroke) or using long-term averages over time for less common ones, but the latter may be impacted by other secular trends.

b. **Incident reports** (numerator only) - These are most useful if there is a structured mechanism for identifying the incident as a diagnostic error and concerted efforts are made to encourage reporting by clinicians.[100, 339, 376] This includes physicians (who rarely report but are best positioned to report on diagnostic issues),[376] as well as other team members such as nurses (who routinely report but do not routinely view diagnostic errors as within the scope of their reporting duties[100, 339, 376]). Their value is principally in identifying unexpected errors or latent risks. Incident reports can be combined with similar data (e.g., patient complaints, autopsy, morbidity and mortality rounds cases[377, 378]). Incident reports can be enhanced and made more informative via the use of common formats that permit aggregation of data at the local, regional, or national levels.[379] The AHRQ Common Formats for Event Reporting (CFER) now include a special common format for Diagnostic Safety event reporting (CFER-DS) that has recently been developed for use by patient safety organizations (PSOs).[379, 380] The CFER-DS (and all of the other AHRQ Common Formats) are available in the public domain to encourage their widespread adoption. An entity does not need to be listed as a PSO or working with one to use the Common Formats. However, it should also be noted that the Federal privilege and confidentiality protections only apply to information developed as patient safety work product by providers and federally listed PSOs working under the Patient Safety and Quality Improvement Act of 2005.

c. **Electronic triggers for ED treat-and-release visits (unplanned revisits or outcomes)** - Electronic triggers represent an important mechanism for identifying potential diagnostic adverse events that then trigger manual chart review. After case review and confirmation as diagnostic errors, the rate can be tracked over time for any changes. Typical triggers include short-term revisits, hospitalizations, or adverse patient outcomes (e.g., non-hospice death), if available. Based on our review, 72 hours provides an enriched sample but will substantially underestimate totals. The range of reasonable time frames is estimated at 7 to 30 days, but it appears 14 days is sufficient to capture the majority of adverse events following diagnostic errors. Ideal ascertainment time windows are likely disease-specific in relation to natural history.

d. **Electronic triggers for ED admissions (unplanned escalation in care or change in treating service)** - Typical triggers include intensive care unit transfers after routine (ward) admission, transfer of admitting service (e.g., from medicine to neurology), or adverse patient outcomes (e.g., in-hospital death). Because our review found that diagnostic errors are enriched among admitted patients and associated with both hospital mortality and increased length of stay, it would not be unreasonable to screen any chart with a change in diagnosis from ED admitting diagnosis to hospital discharge for diagnostic errors, as in Hautz et al., 2019.[7]

e. **Routine or sampled follow-up outreach to patients (e.g., Leveraging Patient's Experience to improve Diagnosis [LEAPED][8])** - Although methods for determining diagnostic error using routine or sampled patient follow-up contact are still being optimized, feasibility has recently been established.[8, 381] Our review identified very few studies assessing failures in communicating diagnoses to patients (which are also defined as diagnostic errors by the NAM). Direct patient outreach post-visit is likely the only method by which diagnostic errors due to communication failures with

patients can be ascertained. If follow-up is obtained very early (e.g., less than 72 hours), communication failures will predominate. If follow-up is obtained later (e.g., 30 days), it is likely that both communication failures and diagnostic accuracy can be captured. Such later phone calls are likely to serve as an important source of information regarding diagnostic errors with less severe consequences, including temporary harms, which our review found were poorly captured by existing methods.

3. **General Recommendations for Measuring Diagnostic Error.** Below are general insights about measurement derived from our systematic review of the literature.
    a. **False negatives and false positives** - It would be optimal to measure all four aspects of diagnostic accuracy (true positives, true negatives, false positives, false negatives). This permits calculation of all accuracy statistics – sensitivity (false negative rate), specificity (false positive rate), negative predictive value (false omission rate), positive predictive value (false discovery rate), and total diagnostic accuracy (total diagnostic error). However, doing so requires combining multiple types of data, and we found no studies that did this. This can be done more easily for a single disease than for all diseases simultaneously.
    b. **Balancing measures** – Diagnostic process improvements (e.g., through use of new or different test batteries, structured clinical pathways, or teamwork in diagnosis) that increase total diagnostic accuracy will generally lead to reductions in both false negatives and false positives.[337] However, one potential ED clinician response to concerns over (false negative) diagnostic errors is to simply "do more of the same" by changing their personal threshold for ordering diagnostic tests; this tends to produce diagnostic test overuse and excessive hospital admissions, rather than more accurate diagnosis.[337] All diagnostic error-related measures should be accompanied by balancing measures that address rates of diagnostic test utilization and hospitalization.
    c. **Outcome ascertainment** - Optimal outcome ascertainment involves prospective data collection, as seen in the few very high-quality studies of diagnostic error on which our overall error and harm estimates are most heavily based. Ideally, this would be built into the process of routine care—systematically recording presenting symptoms, admitting diagnoses, discharge diagnoses, plus follow-up events and outcomes. With modern electronic health records, EDs can generally secure all but the last of these data points. Systematic ascertainment of outcomes is a crucial addition. All errors requiring chart review should be analyzed using diagnosis-specific root cause analysis procedures (e.g., specialized diagnostic error fishbone diagram[382]).
    d. **Pitfalls in measurement** - Based on the review, we identified several pitfalls in measurement that some studies failed to address, leading to heterogeneity, apparently conflicting results, and, in some cases, false conclusions.
        i. **Finding discrepant diagnoses versus errant processes:**[6] The literature is admixed with studies that examine diagnostic errors very differently. A key aspect is whether studies require only an incorrect diagnosis label (or even a communication failure despite the correct label, as in the NAM's definition), mandate some identifiable diagnostic process failure, require preventability, or only consider it an error when outcomes were judged to have been impacted. As expected, the highest frequency of errors will be measured when a label failure is all that is required and the lowest when resulting harms must have been judged by clinicians to have been preventable. However, as demonstrated nicely by Hautz,

2019, even a label failure (regardless of process) is associated with 2.4-fold increased mortality and 3.4-day increased hospital length of stay.[7] Thus, even without ascertaining diagnostic process failures, label failures alone portend worse outcomes. This suggests that identifying label failures (which is easier and has greater inter-rater reliability than identifying process failures[7]) is preferable as a starting point for measuring errors from a quality improvement standpoint. It also suggests that studies or results should not be directly compared when different definitions are used. We recommend using the NAM definitions, which reflect all diagnosis label failures as errors, without regard to process.[5]

ii. **Counting errors versus harms**: When assessing post-treat-and-release ED returns or hospitalizations, it is incorrect to label these "diagnostic errors" because they are actually *misdiagnosis-related harms*. The severity of harms may be judged minor (e.g., temporary inconvenience and loss of confidence in the healthcare system[383]), but they still represent harms. Furthermore, many patients who suffer diagnostic errors "get lucky" temporarily (i.e., suffer no short-term consequences of the diagnostic error), but these patients are nevertheless at risk of delayed harms from lack of secondary prevention. For example, mislabeling a transient ischemic attack as "benign positional vertigo" may prevent the patient from getting secondary stroke prophylaxis. Untreated, 10 to 20 percent of such patients will suffer a major stroke in the subsequent 90 days,[113, 258, 384] but even if the patient is one of the fortunate ones who do not have a major stroke in that time frame, the diagnostic error may nevertheless prevent the patient from being recognized as needing long-term stroke prophylaxis or risk factor modification.

iii. **Tracking hospital crossovers**: Not all patients return to the same hospital (or even health system) when they develop new or worsening symptoms after having been treated and released from an initial ED. This means there is systematic under-ascertainment of diagnostic adverse events (e.g., subsequent hospitalizations) when out-of-network crossovers are not considered. One estimate using a regional health information exchange found that 25 percent of patients who visit the ED more than once will cross over to another hospital or health system.[385] When patients are misdiagnosed, they may be more likely to return to a different ED than if they were correctly diagnosed.[145] One study included in our review found a 37 percent crossover rate.[195] The importance of this for measurement is that hospitals should recognize that their true misdiagnosis-related harm rate could be more than 1.5-fold higher than measured using intra-hospital data. The implication for national benchmarking, payment incentives, and other high-stakes accountability initiatives is that data sources that capture out-of-network follow-ups are critical to ensure comparability of case ascertainment. Potential data sources include (a) insurance-based billing data such as Medicare, (b) linkable state-level data such as AHRQ's State Emergency Department Databases (SEDD)[386] and State Inpatient Databases (SID),[387] or (c) regional health information exchanges such as Maryland's Chesapeake Regional Information System for our Patients (CRISP).[388]

iv. **Including morbidity in addition to mortality**: From this review, we estimate that 29 to 41 percent of the serious misdiagnosis-related harms from ED diagnostic error are permanently disabling, rather than lethal. This means that

mortality statistics alone will understate the total by 1.4- to 1.7-fold and diseases that confer a high rate of morbidity relative to mortality will be underrepresented in summaries of mortality. In particular, this includes neurologic diseases with a high proportion of serious harms that are morbid but not mortal—spinal abscess (82%), stroke (71%), and meningitis (48%). It is expected that untreated neurologic disorders tend to produce more permanent disability than death (and this likely includes two other top 15 neurologic conditions associated with serious misdiagnosis-related harms for which we were unable to ascertain the breakdown of morbidity versus mortality (i.e., spinal cord compression and injury; traumatic brain injury and traumatic intracranial hemorrhage)). Given that the organ system most often involved in diagnostic errors leading to serious harms is the nervous system (34%, Table 4), mortality alone will be a particularly poor health outcome proxy and will tend to substantially understate both individual diseases and total harms.

v. **Controlling for initial severity ("misdiagnosis is protective paradox")**: Illness severity is often a confounder of the relationship between diagnostic error and health outcomes for patients (i.e., is causally linked to both the risk of misdiagnosis and the risk of a bad health outcome). An observational study that directly compares a population of all correctly diagnosed and all incorrectly diagnosed patients will generally find that initial case severity is higher among the correctly diagnosed population, skewing health outcomes for these patients in an unfavorable direction. This effect will tend to nullify the unadjusted, measured impact of diagnostic error or even reverse it ("misdiagnosis is protective" paradox).[1] We found a number of studies which failed to control for initial case severity and, as a result, drew erroneous inferences about lack of impact of diagnostic error on patient outcomes. No measures of this type should be considered valid unless appropriate statistical controls (e.g., matching or adjustment) are used to account for initial case severity or its proxies.

vi. **Addressing preventability of harms**: There is moderate inter-rater variability in clinician ratings of preventability.[320] This issue is more complex for diagnostic errors than treatment errors because there is dual uncertainty—first, whether the diagnostic errors themselves can be prevented and, second, whether treatments for the diagnosed underlying diseases would prevent any associated untoward outcomes. Although combined diagnosis-treatment studies are recommended by the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) group as ideal, this two-step link from diagnosis to health outcome is rarely assessed when diagnostic interventions are put to the test.[389, 390] The strongest evidence of preventability of harms will come from prospective (preferably randomized) studies that measure the health outcomes of interventions to improve diagnosis and that demonstrate both greater diagnostic accuracy and a link between that greater accuracy and improved patient outcomes. Absent this level of rigor, measurements of inter-institutional variability (adjusted for likely confounders) may be a good proxy for preventability, with lower-performing institutions striving to match outcomes from higher-performing institutions.

vii. **Differences in causal inferences based on different denominators**: In the same way that inferences about error rates may differ dramatically depending on the

denominator used (e.g., false negative rate [denominator all with disease] versus false omission rate [denominator all at-risk patients]), the same is true for causal inferences. For example, much of the apparent heterogeneity in our KQ3 results for demographic predictors likely stems from confusion about the inferences to be drawn from different study designs. For example, one study showed that being a woman or a minority is a risk factor for misdiagnosis of heart attack when looking back from heart attack admissions to antecedent treat-and-release ED visits, but not when looking forward from chest pain discharges to subsequent heart attack hospitalizations.[77] These results seem conflicting, but they are not. The reason for this difference is as follows. The look back method normalizes overall risk for heart attacks by starting with heart attack hospitalizations as the denominator; this, in turn, allows investigators to assess the impact of gender or race on the likelihood of misdiagnosis, given equal baseline risk of the underlying disease. However, the look forward method uses chest pain discharges as the denominator; here the distribution of heart attacks is uneven by gender and race, with the largest number of heart attacks being among white men. Since the impact of disease prevalence is greater than the impact of misdiagnosis risk, the result is that white men are more likely to return having had their heart attack initially missed. Thus, the look back method speaks to the relative risk or odds of a misdiagnosis conferred on a patient based solely on their gender or race, while the look forward method estimates the absolute risk of a misdiagnosis based on a mix of disease and misdiagnosis prevalence. Because ED clinicians are likely to calibrate their decision-making to baseline disease prevalence, this may contribute to some proportion of the demographic disparities seen in diagnosis. Since that proportion is unknown, additional research should be done to assess the impact of prevalence-based reasoning on demographic disparities in diagnosis.

4. **Approaches to Measurement at the Institutional Level**. No single measurement method or individual measure will suffice. A "portfolio" approach is needed. A one-size-fits-all approach is unlikely to be equally appropriate for all institutions. Offered below are a few different ways that an institution might choose to approach measuring diagnostic errors.
    a. **Tailored-risk portfolio**: An institution with limited measurement resources and a need to convince institutional leadership of the return on investment for measuring diagnostic errors might take a tailored-risk approach. This could begin with numerator-only measures (e.g., malpractice claims or incident reports) to identify specific symptoms or diseases which have been a known source of institutional risk. These could then spark a disease-specific approach to measurement such as SPADE for those clinical presentations, with balancing measures related to false positives and resource utilization (e.g., test frequency, hospital admission rates, false discovery rate). After addressing one or more diseases and showing improvement, the entire process could be repeated to identify current risks and then address new conditions.
    b. **Top-harms portfolio**: An institution with intermediate measurement resources and institutional recognition of the importance of diagnostic error might develop a local dashboard for the top conditions generally causing the greatest misdiagnosis-related harms from "undercalls" (i.e., false negatives with dangerous diseases)—**top five most harmful vascular events** (stroke, myocardial infarction, aortic aneurysm and

dissection, venous thromboembolism, arterial thromboembolism) plus **top five most harmful infections** (meningitis/encephalitis, sepsis, spinal/intracranial abscess, pneumonia, necrotizing fasciitis). They could (i) use SPADE look-back metrics to identify high-risk clinical presentations, (ii) design interventions to address the most pressing of these, and (iii) measure impact of these interventions using SPADE look-forward metrics. They could use balancing measures related to false positives and resource utilization (e.g., test frequency, hospital admissions, false discovery rate) for each of these high-harm diseases to address "overcalls" (i.e., false positive diagnoses of dangerous diseases or inappropriate resource use in pursuit of those diseases).

c. **Comprehensive portfolio**: An institution with more substantial measurement resources and leadership support to pursue institutional diagnostic excellence might combine the tailored-risk and top-harms portfolio approaches (*described above*) with systematic sampling of patient feedback (e.g., using LEAPED[8]) and systematic use of disease-agnostic e-triggers to identify (i) 7-day hospital admissions after ED treat-and-release visit to identify additional high-risk diseases or clinical presentations and (ii) unplanned escalation in care or change in treating service for admitted patients. Taken together, this comprehensive approach would address almost all potential opportunities to improve diagnostic performance in pursuit of diagnostic excellence.

5. **High-Stakes Measurement for Accountability, Payments, and National Benchmarking.** Based on the results of this review, high-stakes, cross-institutional comparisons require greater standardization and efficiency than can be achieved using most of the available data sources and methods listed above.

   a. **Data source (likely Medicare or HCUP databases)**: While integrated health plans (e.g., Kaiser Permanente, Intermountain Healthcare, and Geisinger Health System) and the Veterans Administration have electronic medical record data sources that are fairly complete and comparable within their respective systems, there are no such data sets for all hospitals nationally. Currently, the most promising data for high-stakes measurement in the United States are from Medicare beneficiaries, since Medicare billing data are gathered in fairly consistent fashion, from a relatively unbiased sample of older patients, at almost all U.S. hospital EDs. They are unconstrained by health system crossovers or geographic boundaries, and they incorporate death data. They do not, however, represent children, so cannot be used to assess pediatric diagnostic error. They also represent only a subset of ED cases (roughly 24 percent in 2018[391]), which means the sample size for some hospital-level analyses will need to sacrifice temporal resolution for smaller hospitals. It is possible that with greater state-level engagement in maintaining linkable ED visit (SEDD) and hospitalization (SID) patient databases that these two obstacles can be overcome, and the preferred data source would then likely become the AHRQ family of HCUP databases (though integration with the national death index for out-of-hospital mortality would be an important addition to increase capture of important outcomes). Both data sources would benefit by the addition of ongoing health-related quality of life (HRQoL) metrics, but implementation of this could prove cumbersome. An alternative would be for the Centers for Disease Control and Prevention to adapt the National Hospital Ambulatory Medical Care Survey (NHAMCS) to include short-term patient follow-up from their nationally representative sample of ED visits.

b. **Measurement method (likely SPADE)**: We found no methods of measurement other than SPADE using a statistically robust approach to measuring diagnostic error without the reliability challenges and high costs faced by triggered manual chart review or routine patient follow-up assessment (e.g., phone calls at 30 days). This appears to be the most promising method currently available for achieving valid, high-stakes measurement that can easily incorporate case mix severity adjustments or propensity score case matching.[163] Missed cancer (including lung cancer) may require alternative monitoring methods, since the temporal risk profile of adverse events after a lung cancer misdiagnosis are very different than those after a missed vascular event or infection, making it less readily amenable to current SPADE methods.
c. **Disease metrics (Top 10+ for Serious Misdiagnosis-Related Harms)**: A reasonable place to start for national ED quality measurement would be to create metrics for the **top five most harmful vascular events** (stroke, myocardial infarction, aortic aneurysm and dissection, venous thromboembolism, arterial thromboembolism) and **top five most harmful infections** (meningitis/encephalitis, sepsis, spinal/intracranial abscess, pneumonia, necrotizing fasciitis). Diseases most appropriate to pediatric misdiagnosis, such as appendicitis and testicular torsion, could be added if the data source were changed to one that was not age restricted (i.e., if it were not Medicare data). Standardized ICD code sets for each disease could be derived from the Elixhauser system used by AHRQ in its Clinical Classifications Software,[101] with appropriate modification to match the diseases in question (as done recently by Newman-Toker, et al.[17]). Ideally these measures would be endorsed by Emergency Medicine specialty societies (e.g., American College of Emergency Physicians, Society for Academic Emergency Medicine) and national quality and safety organizations (e.g., National Quality Forum, The Joint Commission).
d. **National Diagnostic Performance Dashboard**: AHRQ, other government bodies (e.g., Centers for Disease Control and Prevention's National Center for Health Statistics[324]), or non-governmental organizations could monitor the overall epidemiology and variability of diagnostic performance (specifically, diagnostic outcomes, which can be adjusted for case mix severity) across the nation (analogous to the Dartmouth Atlas Project for utilization of healthcare services[347]). For the 10+ diseases noted above, disease-specific metrics could be combined into a National Diagnostic Performance Dashboard. For simplicity, this might initially use only a look-back approach and ignore specific symptoms (as done recently by Waxman, et al[120]). Later, for greater precision and monitoring of diagnostic quality and safety performance, ICD symptom code sets could be added for the most common ED symptoms. This would allow realization of the full potential of SPADE analysis, using both look-back (identifying high-risk presentations and disparities in diagnosis) and look-forward (measuring absolute harm rates and monitoring impact of solutions) approaches, which have been shown to vary substantially by hospital (e.g., for acute myocardial infarction, where misdiagnosis-related adverse event rates varied 3.3-fold from 0.6% to 1.9% across individual EDs, $P < 0.001$[77]) and permit observed minus expected analysis to detect statistically valid excess adverse events above the base rate.[256] The purpose of a national monitoring mechanism would be multiple: (i) providing a benchmarking tool for individual institutional ED performance; (ii) monitoring national diagnostic quality and safety (e.g., temporal trends and health

disparities) to help guide policy decisions; (iii) assessing the impact of major policy interventions (e.g., payment reforms that incentivize better diagnostic performance).

Research Recommendations

Specific research recommendations related to KQ1, KQ2, and KQ3 may be found in the sections above entitled "Gaps in Evidence," but a high-level summary is provided here. For KQ1, the diseases most often misdiagnosed but causing lesser or longer-term harms are poorly understood. Research is needed to better understand the most common less-harmful conditions misdiagnosed other than fractures (e.g., inner ear diseases, migraine headaches). More research is also needed to better characterize the diseases associated with diagnostic error in pediatric ED settings and specialty EDs, where there are many fewer studies. For KQ2, large U.S.-based studies using rigorous, prospective ascertainment are needed to validate that estimated error rates reflect current U.S. ED diagnostic performance, but these should be deliberately designed to assess the extent to which less rigorous but easier methods of measurement can serve as valid proxies. Special attention should be paid to further assessing the relative frequency (and absolute total rates) of harm (and estimated preventable harm) among discharged versus admitted patients, and among false negatives versus false positives in each of these groups. False positive diagnostic errors should be a key research focus, given the relative paucity of studies addressing this issue. For KQ3, more research needs to be done to clarify the extent to which structural factors (particularly those that could be induced to change by payment mechanisms) are strong predictors of diagnostic error and harms. For example, these might include ED discharge fraction, staffing patterns (e.g., volumes per clinician, routine availability of consultants), and access to specialized imaging or diagnostic laboratory tests. Additional work should be done to better elucidate the relationship between clinician mental models of disease prevalence and implicit bias towards specific demographic groups (e.g., women and minorities). It is unknown how much of the health disparity seen with diagnostic errors can be attributed to true prevalence effects with appropriate clinical risk assessments, perceived (yet false) prevalence estimates, versus fundamental bias; some of these closely related effects may only be readily differentiated using experimental methods, as seen in many cognitive psychology experiments. Reporting of research on diagnostic errors should be standardized, probably with an extension to the existing STARD reporting guidelines focused on diagnostic error-related studies.

Conclusions

This report summarizes current best evidence regarding the nature, frequency, and causes of ED diagnostic errors. Our review findings are tempered by limitations in the underlying evidence base, including issues related to data sources, measurement methods, and causal relationships. Nevertheless, its contents are relevant to patients, ED clinicians, quality officers, risk management professionals (and professional liability insurers), educators, and policymakers, among others. **The results and conclusions presented herein should be viewed through the lens of opportunity for quality improvement and increased diagnostic safety for ED patients, rather than as an indictment of current ED care or ED clinicians. It is acknowledged that the ED is a particularly challenging setting in which to practice medicine, and many factors contribute to diagnostic errors that occur there**.

Despite this, we estimate that 1 of every 18 patients is misdiagnosed in the ED, one of every 50 suffers a diagnostic adverse event, and about 1 of every 350 patients is seriously harmed as a consequence of diagnostic error. Put in terms of an average ED with 25,000 visits annually and

average diagnostic performance, each year this would be over 1,400 diagnostic errors, 500 diagnostic adverse events, and 75 serious harms, including 50 deaths. This translates to 10 patients harmed and more than 1 death or disability each week at an average-sized ED. New insights for the field generated by this report include the following:

1. Just 15 diseases likely account for more than two-thirds of serious misdiagnosis-related harms in the ED, making the problem of diagnostic error more tractable than previously imagined. Among these ten diseases, myocardial infarction is the only one with miss rates near zero (1.5%), well below the estimated average diagnostic error rate across all diseases (5.7%). The field should seek to replicate these successes for other high-harm diseases (which currently have estimated miss rates of 10-56%), modeling new interventions after the successful multi-pronged approaches to ED diagnosis of chest pain and acute coronary syndromes. Target diseases should be prioritized based on (a) the overall share of high-severity harms, (b) higher absolute error or harm rates (i.e., with opportunity for improvement), (c) variability in diagnostic performance (including known health disparities or variation by organization, site, or provider), and (d) availability or cost-effectiveness of promising solutions. Missed stroke in patients presenting with dizziness, which ranks high on all four criteria (stroke is #1 cause of harm; rate of missed stroke in dizziness is 40%; variability is documented based on hospital characteristics; and solutions have been demonstrated in clinical trials), is likely the top target.
2. We estimate that each year in the United States there may be more than 7 million diagnostic errors and 350,000 patients who are permanently disabled or die due to diagnostic error. Methods of measuring diagnostic errors in the ED are highly variable, but, even when similar methods are used, diagnostic error rates vary up to 100-fold across individual hospitals. More than any other finding, this variability indicates that opportunities for diagnostic quality improvement exist. Diagnostic error measurement and reporting should be standardized for both internal and external benchmarking purposes, including public accountability. This report proposes approaches to standardizing measurements and measurement pitfalls to avoid. When quantifying serious misdiagnosis-related harms, it is imperative to measure both mortality ***and*** morbidity to fully represent adverse health outcomes for patients. In doing so, great care should be taken to avoid the known trap of the "misdiagnosis is protective" paradox[1] by using clinically appropriate, statistically valid adjustments for initial case severity. Solutions should be designed to address both false negatives and false positives, and all measurement and reporting of diagnostic error should be accompanied by balancing measures that monitor diagnostic test utilization and hospital admission rates.
3. Root causes of ED diagnostic errors are disproportionately cognitive in nature and mainly happen at the bedside. Those resulting in serious misdiagnosis-related harms involve failures of clinical assessment, reasoning, or decision-making in roughly 90 percent of cases. The strongest, most consistent predictors of ED diagnostic error are case factors that increase the cognitive challenge of identifying the underlying disorder, with "non-specific," "atypical," or "milder" symptoms being the most frequent. This suggests that system-wide, scalable solutions need to be developed to tackle cognitive problems, and that these solution sets must be targeted to address not the most common clinical presentations of key diseases of interest but the ***most commonly misdiagnosed*** clinical presentations of key diseases of interest. This is a tractable approach because epidemiologic studies using the SPADE look-back method have shown that only a

handful of symptoms account for the majority of missed clinical presentations for any one disease[64, 77, 94]—in other words, these are what might be called "typical" atypical cases or recurring diagnostic pitfalls.[392] To support reliable delivery of enhanced diagnostic expertise at the bedside, solution sets should capitalize on training, teamwork, and technology. Interventions and tools should be tailored to specific symptoms/diseases, then organized as modules. For example, stroke diagnosis could be bolstered to explicitly identify posterior circulation strokes among patients with dizziness and vertigo (one of the key symptoms conferring the greatest risk of misdiagnosis). This might include (a) scalable ***training*** tools using virtual patient cases[349]; (b) enhanced ***teamwork*** via clinical pathways that incorporate rules to determine need for specialty consultation[338] or engage nurses and other allied health professionals more effectively in the diagnostic process[339, 343, 393]; and (c) computer-based decision support using point-of-care ***technology***.[371, 372] All of these solutions should be subjected to rigorous outcomes research to assess any benefits to improved diagnosis or unintended consequences (e.g., test overuse).

Future research should emphasize areas in which data are lacking, such as the burden of diagnostic errors and harms related to diseases with less immediate and severe consequences, pediatric ED diagnostic errors and harms, and the causal contributions of systems factors potentially amenable to policy intervention. Importantly, large, prospective studies are needed to validate current diagnostic error rate estimates, as well as to help develop valid proxy measures that are more readily and routinely acquired for operational measurement. A key focus of research should be to define symptoms and diseases for which diagnostic errors and associated harms can realistically be mitigated and to measure the real-world impact of interventions and strategies in reducing these errors and harms. Policy changes to consider based on findings from this review include: (1) standardizing measurement and research results reporting to maximize comparability of measures of diagnostic error and misdiagnosis-related harms[5, 345, 346]; (2) creating a National Diagnostic Performance Dashboard to track performance (analogous to the Dartmouth Atlas Project for utilization of healthcare services[347]); and (3) using multiple policy levers (e.g., research funding, public accountability, payment reforms)[5] to facilitate the rapid development and deployment of solutions to address this critically important patient safety concern. Resources applied should be commensurate with the large public health burden.

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Abbreviations and Acronyms

AHRQ	Agency for Healthcare Research and Quality
APP	Advanced practice provider
BPPV	Benign paroxysmal positional vertigo
CFER-DS	Common Formats for Event Reporting – Diagnostic Safety
CI	Confidence interval
CINAHL®	Cumulative Index to Nursing and Allied Health Literature
COVID-19	Coronavirus (SARS-CoV-2) disease 2019
CQuIPS	Center for Quality Improvement and Patient Safety
CRISP	Chesapeake Regional Information System for our Patients
CT	Computed tomography
DIVA	Difficult intravenous access
ECG	Electrocardiogram
ED	Emergency department
EHC	Effective Health Care
EPC	Evidence-based Practice Center
ES	Effect summary
FAST	Face Arm Speech Test
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
HCUP	Healthcare Cost and Utilization Project
ICD	International Classification of Diseases
KQ	Key Question
LEAPED	Leveraging Patient's Experience to Improve Diagnosis
LHS	Learning Health System
MeSH®	Medical subject headings
MI	Myocardial infarction
MRI	Magnetic resonance imaging
NAIC	National Association of Insurance Commissioners
NAM	National Academy of Medicine
NEISS	National Electronic Injury Surveillance System
NHAMCS	National Hospital Ambulatory Medical Care Survey
NIHSS	National Institutes for Health Stroke Scale
OR	Odds ratio
PACS	Picture Archiving and Communications System
PerSPEcTiF	Perspective, Population, Setting, Phenomenon, Environment, Timing, Findings, and Study
PR	Plausible range
PSO	Patient safety organization

QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies
ROSIER	Recognition of Stroke In the Emergency Room
RR	Relative risk
SEADS	Supplemental Evidence and Data for Systematic Reviews
SEDD	State Emergency Department Databases
SID	State Inpatient Databases
SOE	Strength of evidence
SPADE	Symptom-disease Pair Analysis of Diagnostic Error
STARD	Standards for Reporting of Diagnostic Accuracy Studies
STEMI	ST-elevation myocardial infarction
TEP	Technical Expert Panel
TIA	Transient ischemic attack
TOO	Task Order Officer

Appendix A. Methods

Data Sources and Study Methods

A breakdown of data types and sources used for each Key Question (KQ) is shown in Table A-1. Exact KQs are re-iterated below for clarity.

Table A-1. Breakdown of data types and sources by Key Question

Key Question (KQ)	Primary Versus Secondary Focus of That KQ*	Disease-Agnostic Studies (No Methods-Based Restriction on Disease Inclusions)	Disease-Specific Studies (Methods-Based Restriction by Disease or Category)	Numerator-Only Studies (Malpractice Claims, Incident Reports, Case Series)	Numerator-Denominator Studies (Cohort, Cross-Sectional, Randomized Trials)
KQ1a (most common diseases associated with errors or harms)	**Primary**	*Allowed*: **REQUIRED** *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: **NONE†**
KQ1b (variation in disease distribution by harm severity)	Secondary	*Allowed*: **REQUIRED** *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: **NONE**
KQ1c (most common symptoms linked to errors or harms)	Secondary	*Allowed*: **REQUIRED** *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes
KQ1d (variation in most common symptoms by disease)	Secondary	*Allowed*: yes *Available*: **NONE**	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes
KQ2a (disease-agnostic ED rate of diagnostic errors or harms)	**Primary**	*Allowed*: **REQUIRED** *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: **NO** *Available*: N/A	*Allowed*: **REQUIRED** *Available*: yes
KQ2b (disease-specific ED rate of diagnostic errors or harms)	**Primary**	*Allowed*: yes *Available*: **NONE**	*Allowed*: yes *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: **REQUIRED** *Available*: yes
KQ2c (total estimated ED errors and harms in the US)	Secondary	*Allowed*: **REQUIRED** *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: **NO** *Available*: N/A	*Allowed*: **REQUIRED** *Available*: yes
KQ2d (variation in risk of error or harm by disease, other factors)	Secondary	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: **REQUIRED** *Available*: yes
KQ3a (most frequent causes of diagnostic errors or harms)	**Primary**	*Allowed*: **REQUIRED** *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: **NONE†**
KQ3b (variation in error causes by harm severity)	Secondary	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: **NO**	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: **NONE**
KQ3c (variation in harm severity by error causes)	Secondary	*Allowed*: yes *Available*: **NONE**	*Allowed*: yes *Available*: **NONE**	*Allowed*: yes *Available*: **NONE**	*Allowed*: yes *Available*: **NONE**
KQ3d (risk factors or predictors of diagnostic error or harms)	**Primary**	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes	*Allowed*: **NO** *Available*: N/A	*Allowed*: **REQUIRED** *Available*: yes
KQ3e (commonalities in error causes across diseases)	Secondary	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes	*Allowed*: yes *Available*: yes

KQ = Key Question; N/A = Not Applicable

***** Each KQ had sub-questions that represented either a primary or secondary focus for that KQ. Those with a primary focus were ones of greatest importance to the report's goals and deemed likely to be answerable with available literature.

† Primary sub-questions that were reliant on numerator-only studies (mainly malpractice claims, incident reports) because of unavailability of stronger study designs were KQ1a and KQ3a. By contrast, numerator-only studies were excluded from consideration for answers to the other primary sub-questions (KQ2a, KQ2b, and KQ3d).

Key Questions

KQ 1: What clinical conditions are associated with the greatest number and highest risk of ED diagnostic errors and associated harms?

a. What diseases or syndromes are associated with the greatest total number and the highest risk of diagnostic errors or misdiagnosis-related harms?
b. Do results vary based on the severity of any resulting misdiagnosis-related harms (e.g., death or permanent disability, as opposed to less serious harms)?
c. What are the most common clinical presenting symptoms or signs associated with diagnostic errors or misdiagnosis-related harms in the ED?
d. Do the most common clinical presenting symptoms or signs associated with diagnostic error or misdiagnosis-related harms vary by disease or syndrome?

KQ 2: Overall and for the clinical conditions of interest, how frequent are ED diagnostic errors and associated harms?

a. On a per-visit or symptom-specific basis, what is the rate of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms?
b. On a per-disease/syndrome basis, what is the rate of diagnostic errors, misdiagnosis-related harms, and serious misdiagnosis-related harms?
c. Approximately how many patients does this equate to nationally in the United States?
d. Are there clear commonalities or differences across clinical conditions in the frequency or risk of ED diagnostic errors or misdiagnosis-related harms?

KQ 3: Overall and for the clinical conditions of interest, what are the major causal factors associated with ED diagnostic errors and associated harms?

a. What are the most frequent causes identified?
b. Do causes identified differ based on severity of harms?
c. Do different causes have differential impact on patient outcomes (i.e., harms)?
d. Overall and for each clinical condition:
    i. Are patient characteristics (e.g., age, gender, race/ethnicity, language, socioeconomic status/income, health literacy) associated with errors/harms?

ii. Are illness characteristics (e.g., symptom type, clinical presentation, mode of arrival) associated with errors/harms?
iii. Are clinician characteristics (e.g., provider type, training background, experience level, prior disciplinary action) associated with errors/harms?
iv. Are facility or health system characteristics (e.g., region, ED patient volumes or discharge fraction, teaching status, access to imaging, access to or type of electronic health record system) associated with errors/harms?
v. Are context-specific systems factors (e.g., at the time of the error—high ED patient volume or severity of illness, night or weekend shift, provider fatigue, change of shift/handoff) associated with errors/harms?

e. Are there significant commonalities or differences among causes of ED diagnostic errors or associated harms across clinical conditions?

Search Strategies

The search strategies are listed in Tables A-2, A-3, and A-4.

Table A-2. PubMed Search Strategy

#	String
1	"diagnosis error"[tiab] OR "diagnosis errors"[tiab] OR "diagnostic error"[tiab] OR "diagnostic errors"[tiab] OR "misdiagnosis"[tiab] OR "misdiagnoses"[tiab] OR "missed diagnosis"[tiab] OR "missed diagnoses"[tiab] OR "wrong diagnosis"[tiab] OR "wrong diagnoses"[tiab] OR "inaccurate diagnosis"[tiab] OR "inaccurate diagnoses"[tiab] OR "delayed diagnosis"[tiab] OR "delayed diagnoses"[tiab] OR "diagnosis delay"[tiab] OR "diagnosis delays"[tiab] OR "diagnostic delay"[tiab] OR "diagnostic delays"[tiab] OR "failure to diagnose"[tiab] OR "diagnostic interval"[tiab] OR "diagnostic intervals"[tiab] OR (Delayed diagnosis[mh]) OR (diagnos*[tiab] AND delay*[tiab])
2	emergency services, hospital[mh] OR emergency treatment[mh] OR emergency department*[tiab] OR emergency service*[tiab] OR emergency physician*[tiab] OR casualty[tiab] OR ambulance*[tiab] OR initial diagnosis[tiab] OR initial contact[tiab] OR warning[tiab] OR urgent care[tiab]) OR emergency room[tiab] OR “accident and emergency”[tiab] OR “accident & emergency”[tiab] OR “Emergency department returns”[tiab] OR “ED returns”[tiab]
3	#1 AND #2
4	Cerebrovascular disorders[mh:noexp] OR Basal ganglia cerebrovascular disease[mh] OR Brain ischemia[mh] OR Carotid artery diseases[mh] OR Intracranial arterial diseases[mh] OR "Intracranial embolism and thrombosis"[mh] OR Intracranial hemorrhages[mh] OR Stroke[mh:noexp] OR Brain infarction[mh] OR Vertebral artery dissection[mh] OR stroke[tiab] OR cerebrovasc*[tiab] OR brain vasc*[tiab] OR cerebral vasc*[tiab] OR CVA[tiab] OR apoplex*[tiab] OR ((brain*[tiab] OR cerebr*[tiab] OR cerebell*[tiab] OR vertebrovasilar[tiab] OR hemispher*[tiab] OR intracran*[tiab] OR intracerebral[tiab] OR infratentorial[tiab] OR supratentorial[tiab] OR MCA[tiab] OR anterior circulation[tiab] OR posterior circulation[tiab] OR basal gangla[tiab]) AND (ischaemi*[tiab] OR ischemi*[tiab] OR infarct*[tiab] OR thrombo*[tiab] OR emboli*[tiab])) OR ((brain*[tiab] OR cerebr*[tiab] OR cerebell*[tiab] OR intracerebral[tiab] OR intracran*[tiab] OR parenchymal[tiab] OR intraventricular[tiab] OR infratentorial[tiab] OR supratentorial[tiab] OR basal gangli*[tiab]) AND (haemorrhage*[tiab] OR hemorrhage*[tiab] OR haematoma*[tiab] OR hematoma*[tiab] OR bleed*[tiab])) OR Myocardial infarction[mh] OR myocardial infarct*[tiab] OR heart infarct*[tiab] OR (coronary[tiab] AND syndrome[tiab]) OR heart attack[tiab] OR Thrombosis[mh:noexp] OR Thromboembolism[mh:noexp] OR Venous thromboembolism[mh:noexp] OR Venous thrombosis[mh] OR thromboprophyla*[tiab] OR thrombus*[tiab] OR thrombotic*[tiab] OR thrombolic*[tiab] OR thromboemboli*[tiab] OR thrombos*[tiab] OR embol*[tiab] OR Pulmonary embolism[mh] OR PE[tiab] OR DVT[tiab] OR VTE[tiab] OR ((vein*[tiab] OR veno*[tiab] OR vent*[tiab]) AND thromb*[tiab]) OR Aortic aneurysm[mh] OR Aneurysm, dissecting[mh:noexp] OR Aneurysm, ruptured[mh] OR ((aort*[tiab] AND (aneurys*[tiab] OR dissect*[tiab] OR ruptur*[tiab] OR tear*[tiab] OR trauma*[tiab] OR split*[tiab])) OR Mesenteric ischemia[mh] OR (ischemi*[tiab] AND mesenteric[tiab]) OR (arterial[tiab] AND thromb*[tiab]) OR Sepsis[mh] OR Septicemia[mh] OR Shock, Septic[mh] OR septicem*[tiab] OR septicaem*[tiab] OR seps*[tiab] OR (sept*[tiab] AND shock*[tiab]) OR Meningitis[mh] OR meningit*[tiab] OR Encephalitis[mh] OR encephalitis[tiab] OR meningoencephalitis[tiab] OR ((brain[tiab] OR cerebral[tiab]) AND (infection*[tiab] OR infectious[tiab] OR inflamm*[tiab] OR swell*[tiab])) OR Epidural Abscess[mh] OR ((spin* OR epidural[tiab]) AND abscess*[tiab]) OR Pneumonia[mh] OR Respiratory tract infections[mh] OR pneumonia*[tiab] OR lung inflammation*[tiab] OR respiratory tract infection*[tiab] OR respiratory infection*[tiab]) OR Endocarditis[mh] OR endocarditis[tiab] OR (endocardium AND (inflamm*[tiab] OR infect*[tiab])) OR Appendicitis[mh] OR appendic*[tiab] OR appendicitis acuta[tiab] OR fracture*[tiab] OR "spermatic cord torsion"[mh] OR ("spermatic"[tiab] AND "cord"[tiab] AND "torsion"[tiab]) OR "spermatic cord torsion"[tiab] OR ("testicular"[tiab] AND "torsion"[tiab]) OR "testicular torsion"[tiab] OR "necrotising enterocolitis"[tiab] OR "enterocolitis, necrotizing"[mh] OR ("enterocolitis"[tiab] AND "necrotizing"[tiab]) OR "necrotizing enterocolitis"[tiab] OR ("necrotizing"[tiab] AND "enterocolitis"[tiab]) OR "pregnancy, ectopic"[mh] OR ("pregnancy"[tiab] AND "ectopic"[tiab]) OR "ectopic pregnancy"[tiab] OR ("ectopic"[tiab] AND "pregnancy"[tiab]) OR "pre eclampsia"[mh] OR "pre eclampsia"[tiab] OR "preeclampsia"[tiab] OR "eclampsia"[mh] OR "eclampsia"[tiab] OR "eclampsias"[tiab]
5	#1 AND #4
6	#3 OR #5
7	Animals[mh] NOT humans[mh]
8	#6 not #7
9	Study protocol[ti] OR trial protocol[ti] OR review protocol[ti] OR editorial[pt] OR letter[pt] OR case reports[pt]
10	#8 NOT #9
11	Filters: **from 2000 - 2021**

Table A-3. Embase Search Strategy

#	String
1	"diagnosis error":ti,ab OR "diagnosis errors":ti,ab OR "diagnostic error":ti,ab OR "diagnostic errors":ti,ab OR "misdiagnosis":ti,ab OR "misdiagnoses":ti,ab OR "missed diagnosis":ti,ab OR "missed diagnoses":ti,ab OR "wrong diagnosis":ti,ab OR "wrong diagnoses":ti,ab OR "inaccurate diagnosis":ti,ab OR "inaccurate diagnoses":ti,ab OR "delayed diagnosis":ti,ab OR "delayed diagnoses":ti,ab OR "diagnosis delay":ti,ab OR "diagnosis delays":ti,ab OR "diagnostic delay":ti,ab OR "diagnostic delays":ti,ab OR "failure to diagnose":ti,ab OR "diagnostic interval":ti,ab OR "diagnostic intervals":ti,ab
2	'hospital emergency service'/de OR 'emergency treatment'/de OR "emergency department*":ti,ab OR "emergency service*":ti,ab OR "emergency physician*":ti,ab OR "emergency room":ti,ab OR "accident and emergency":ti,ab OR "accident & emergency":ti,ab OR "Emergency department returns":ti,ab OR "ED returns":ti,ab
3	#1 AND #2
4	'cerebrovascular disease'/de OR 'basal ganglion hemorrhage'/de OR 'brain ischemia'/de OR 'carotid artery disease'/de OR 'cerebral artery disease'/de OR 'thromboembolism'/de OR 'brain hemorrhage'/de OR 'cerebrovascular accident'/de OR 'brain infarction'/de OR 'artery dissection'/de OR stroke:ti,ab OR cerebrovasc*:ti,ab OR "brain vasc*":ti,ab OR "cerebral vasc*":ti,ab OR CVA:ti,ab OR apoplex*:ti,ab OR ((brain*:ti,ab OR cerebr*:ti,ab OR cerebell*ti,ab OR vertebrovasilar:ti,ab OR hemispher*:ti,ab OR intracran*:ti,ab OR intracerebral:ti,ab OR infratentorial:ti,ab OR supratentorial:ti,ab OR MCA:ti,ab OR "anterior circulation":ti,ab OR "posterior circulation":ti,ab OR "basal gangla":ti,ab) AND (ischaemi*:ti,ab OR ischemi*:ti,ab OR infarct*:ti,ab OR thrombo*:ti,ab OR emboli*:ti,ab)) OR ((brain*:ti,ab OR cerebr*:ti,ab OR cerebell*:ti,ab OR intracerebral:ti,ab OR intracran*:ti,ab OR parenchymal:ti,ab OR intraventricular:ti,ab OR infratentorial:ti,ab OR supratentorial:ti,ab OR "basal gangli*":ti,ab) AND (haemorrhage*:ti,ab OR hemorrhage*:ti,ab OR haematoma*:ti,ab OR hematoma*:ti,ab OR bleed*ti,ab)) OR 'heart infarction'/de OR "myocardial infarct*":ti,ab OR "heart infarct*":ti,ab OR (coronary:ti,ab AND syndrome:ti,ab) OR heart attack:ti,ab OR 'thrombosis'/de OR 'thromboembolism'/de OR 'venous thromboembolism'/de OR 'vein thrombosis'/de OR thromboprophyla*:ti,ab OR thrombus*:ti,ab OR thrombotic*:ti,ab OR thrombolic*:ti,ab OR thromboemboli*:ti,ab OR thrombos*:ti,ab OR embol*:ti,ab OR 'lung embolism'/de OR PE:ti,ab OR DVT:ti,ab OR VTE:ti,ab OR ((vein*:ti,ab OR veno*:ti,ab OR vent*:ti,ab) AND thromb*:ti,ab) OR 'aortic aneurysm'/de OR 'dissecting aneurysm'/de OR 'aneurysm rupture'/de OR (aort*:ti,ab AND (aneurys*:ti,ab OR dissect*:ti,ab OR ruptur*:ti,ab OR tear*:ti,ab OR trauma*:ti,ab OR split:ti,ab)) OR 'mesenteric ischemia'/de OR (ischemi*:ti,ab AND mesenteric:ti,ab) OR (arterial:ti,ab AND thromb*:ti,ab) OR 'sepsis'/de OR 'septicemia'/de OR 'septic shock'/de OR septicem*:ti,ab OR septicaem*:ti,ab OR seps*:ti,ab OR (sept*:ti,ab AND shock*:ti,ab) OR 'meningitis'/de OR meningit*:ti,ab OR 'encephalitis'/de OR encephalitis:ti,ab OR meningoencephalitis:ti,ab OR ((brain:ti,ab OR cerebral:ti,ab AND (infection*:ti,ab OR infectious:ti,ab OR inflamm*:ti,ab OR swell:ti,ab)) OR 'encephalitis'/de OR ((spin* OR epidural:ti,ab) AND abscess*:ti,ab) OR 'pneumonia'/de OR 'respiratory tract infection'/de OR pneumonia*:ti,ab OR "lung inflammation*":ti,ab OR "respiratory tract infection*":ti,ab OR "respiratory infection*":ti,ab) OR 'endocarditis'/de OR endocarditis:ti,ab OR (endocardium:ti,ab AND (inflamm*:ti,ab OR infect*:ti,ab)) OR 'appendicitis'/de OR appendic*:ti,ab OR "appendicitis acuta":ti,ab OR fracture*:ti,ab OR 'testis torsion'/de OR (spermatic:ti,ab AND cord:ti,ab AND torsion:ti,ab) OR "spermatic cord torsion":ti,ab OR (testicular:ti,ab AND torsion:ti,ab) OR "testicular torsion":ti,ab OR "necrotising enterocolitis":ti,ab OR 'necrotizing enterocolitis'/de OR (enterocolitis:ti,ab AND necrotising:ti,ab) OR "necrotizing enterocolitis":ti,ab OR (necrotizing:ti,ab AND enterocolitis:ti,ab) OR 'ectopic pregnancy'/de OR (pregnancy:ti,ab AND ectopic:ti,ab) OR "ectopic pregnancy":ti,ab OR 'preeclampsia'/de OR "pre eclampsia":ti,ab OR preeclampsia:ti,ab OR 'eclampsia'/de OR eclampsia:ti,ab OR eclampsias:ti,ab
5	#1 AND #4
6	#3 OR #5
7	'animal'/de NOT 'human'/de
8	#6 not #7
9	"Study protocol":ti OR "trial protocol":ti OR "review protocol":ti OR editorial:it,pt OR letter:it,pt OR "case reports":it,pt OR ‘conference paper’/de OR conference:it,pt OR (‘review’/de OR ‘review’ OR ‘review’/it)
10	#8 NOT #9
11	#10 AND (2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py)

Table A-4. Cumulative Index to Nursing and Allied Health Literature Search Strategy

#	String
1	(TI "diagnosis errors" OR AB "diagnosis errors") OR (TI "diagnostic error" OR AB “diagnostic error) OR (TI "diagnostic errors" OR AB “diagnostic errors”) OR (TI “diagnostic errors" OR AB “diagnostic errors") OR (TI “misdiagnosis” OR AB “misdiagnosis) OR (TI "misdiagnoses" OR AB “misdiagnoses) OR (TI "missed diagnosis" OR AB “missed diagnosis) OR (TI "missed diagnoses" OR AB “missed diagnoses") OR (TI "wrong diagnosis” OR AB “wrong diagnosis”) OR (TI "wrong diagnoses” OR AB “wrong diagnoses”) OR (TI "inaccurate diagnosis" OR AB “inaccurate diagnosis”) OR (TI "inaccurate diagnoses" OR AB “inaccurate diagnoses”) OR (TI "delayed diagnosis" OR AB “delayed diagnosis) OR (TI "delayed diagnoses" OR AB “delayed diagnoses”) OR (TI "diagnosis delay" OR AB “diagnostic delay”) OR (TI "diagnosis delays" OR AB “diagnostic delays”) OR (TI "diagnostic delay" OR AB “diagnostic delay”) OR (TI "diagnostic delays" OR AB “diagnostic delays”) OR (TI "failure to diagnose" OR AB “failure to diagnose”) OR (TI "diagnostic interval" OR AB “diagnostic interval) OR (TI "diagnostic intervals" OR AB “diagnostic intervals”)
2	(MH "Emergency Service+") OR (MH "Emergency Treatment+") OR (TI “emergency department*” OR AB “emergency department*”) OR (TI “emergency service*” OR AB “emergency service*”) OR (TI “emergency physician*” OR AB “emergency physician”) OR (TI casualty OR AB casualty) OR (TI ambulance* OR AB ambulance*) OR (TI “initial diagnosis” OR AB “initial diagnosis”) OR (TI “initial contact” OR AB “initial contact) OR (TI warning OR AB warning) OR (TI “urgent care” OR AB “urgent care”) OR (TI “emergency room” OR AB “emergency room) OR (TI “accident and emergency” OR AB “accident and emergency”) OR (TI “accident & emergency” OR AB “accident & emergency) OR (TI “Emergency department returns” OR AB “Emergency department returns”) OR (TI “ED returns” OR AB “ED returns”)
3	S1 AND S2

#	String
4	(MM "Cerebrovascular Disorders") OR (MH "Basal Ganglia Cerebrovascular Disease+") OR (MH "Cerebral Ischemia+") OR (MH "Carotid Artery Diseases+") OR (MH "Intracranial Arterial Diseases+") OR (MH "Intracranial Embolism and Thrombosis+") OR (MH "Intracranial Hemorrhage+") OR (MM "Stroke") OR (MH "Hypoxia-Ischemia, Brain+") OR (MM "Vertebral Artery Dissections") OR stroke[tiab] OR (TI cerebrovasc* OR AB cerebrovasc*) OR (TI brain vasc* OR AB brain vasc*) OR (TI cerebral vasc* OR AB cerebral vasc*) OR (TI CVA OR AB CVA) OR (TI apoplex* OR AB apoplex*) OR (TI brain* OR AB brain*) OR (TI cerebr* AB cerebr*) OR (TI cerebell* OR AB cerebell*) OR (TI vertebrovasilar OR AB vertebrovasilar) OR (TI hemispher* OR AB hemispher*) OR (TI intracran* OR AB intracan*) OR (TI intracerebral OR AB intracerbal) OR (TI infratentorial OR AB infratentorial) OR (TI supratentorial OR AB supratentorial) OR (TI MCA OR AB MCA) OR (TI anterior circulation OR AB anterior circulation) OR (TI posterior circulation OR AB posterior circulation) OR (TI basal gangla OR AB basal gangla) AND (TI ischaemi* OR AB ischaemi*) OR (TI ischemi* OR AB ischemi*) OR (TI infarct* OR AB infarct*) OR (TI thrombo* OR AB thrombo*) OR (TI emboli OR AB emboli)) OR (TI brain* OR AB brain*) OR (TI cerebr* OR AB cerebr*) OR (TI cerebell* OR AB cerebell*) OR (TI intracerebral OR AB intracerebral) OR (TI intracran* OR intracran*) OR (TI parenchymal OR AB parenchymal) OR (TI intraventricular OR AB intraventricular) OR (TI infratentorial OR AB infratentorial) OR (TI supratentorial OR AB supratentorial) OR (TI basal gangli* OR AB basal gangli*) AND (TI haemorrhage* OR AB haemorrhage*) OR (TI hemorrhage* OR AB hemorrhage*) OR (TI haematoma* OR AB haematoma*) OR (TI hematoma* OR AB hematoma*) OR (TI bleed* OR AB bleed*))) OR (MH "Myocardial Infarction+") OR (TI myocardial infarct* OR AB myocardial infarct*) OR (TI heart infarct* OR AB heart infarct*) OR (TI coronary OR AB coronary) AND (TI syndrome OR AB syndrome) OR (TI heart attack OR AB heart attack) OR (MM "Thrombosis") OR (MM "Thromboembolism") OR (MM "Venous Thromboembolism") OR (MH "Venous Thrombosis+") OR (TI thromboprophyla* OR AB thromboprophyla*) OR (TI thrombus* OR AB thrombus*) OR (TI thrombotic* OR AB thrombotic*) OR (TI thrombolic* OR AB thrombolic*) OR (TI thromboemboli* OR AB thromboemboli*) OR (TI thrombos* OR AB thrombos*) OR (TI embol* OR embol*) OR (MM "Pulmonary Embolism") OR (TI PE OR AB PE) OR (TI DVT OR AB DVT) OR (TI VTE OR AB VTE) OR ((TI vein* OR AB vein*) OR (TI veno* OR AB veno*) OR (TI vent* OR AB vent*) AND (TI thromb* OR AB thromb*) OR (MH "Aortic Aneurysm+") OR (MM "Aneurysm, Dissecting") OR (MM "Heart Rupture") OR ((TI aort* OR AB aort*) AND (TI aneurys* OR AB aneurys*) OR (TI dissect* OR AB dissect*) OR (TI ruptur* OR AB ruptur*) OR (TI tear* OR AB tear*) OR (TI trauma* OR AB trauma*) OR (TI split* OR AB split*)) OR (MH "Mesenteric Ischemia") OR (TI ischemi* OR AB ischemi*) AND (TI mesenteric OR AB mesenteric) OR (TI arterial OR AB arterial) AND (TI thromb* OR AB thromb*) OR (MH "Sepsis+") OR OR (MH "Shock, Septic+") OR (TI septicem* OR AB septicem*) OR (TI septicaem* OR AB septicaem*) OR (TI seps* OR AB seps*) OR (TI sept* OR sept*) AND (TI shock* OR AB shock*) OR (MH "Meningitis+") OR (TI meningit* OR AB meningit*) OR (MH "Encephalitis+") OR (TI encephalitis OR AB encephalitis) OR (TI meningoencephalitis OR AB meningoencephalitis) OR ((TI brain OR AB brain) OR (TI cerebral OR AB cerebral) AND (TI infection* OR AB infection*) OR ((TI infectious OR AB infectious) OR (TI inflamm* OR AB inflamm*) OR (TI swell* OR AB swell*))) OR (MM "Epidural Abscess") OR ((TI spin* OR AB spin*) OR (TI epidural OR AB epidural) AND (TI abscess* OR AB abscess*) OR (MH "Pneumonia+") OR (MH "Respiratory Tract Infections+") OR (TI pneumonia* OR AB pneumonia*) OR (TI lung inflammation* OR AB lung inflammation*) OR (TI respiratory tract infection* OR AB respiratory tract infection*) OR (TI respiratory infection* OR AB respiratory infection*)) OR (MH "Endocarditis+") OR (TI endocarditis OR AB endocarditis) OR (endocardium AND ((TI inflamm* OR AB inflamm*) OR (TI infect* OR AB infect*))) OR (MM "Appendicitis") OR (TI appendic* OR AB appendic*) OR (TI appendicitis acuta OR AB appendicitis acuta) OR (TI fracture* OR AB fracture*) OR (MM "Spermatic Cord Torsion") OR (TI "spermatic" OR AB “spermatic) AND (TI "cord" OR AB “cord”) AND (TI "torsion" OR AB "torsion") OR (TI "spermatic cord torsion" OR AB "spermatic cord torsion") OR (TI "testicular" OR AB "testicular") OR (TI "testicular torsion" OR AB "testicular torsion") OR (TI "necrotising enterocolitis" OR AB "necrotising enterocolitis") OR (MM "Enterocolitis, Necrotizing") OR (TI "enterocolitis" OR AB "enterocolitis") AND (TI "necrotizing" OR AB "necrotizing") OR (TI "necrotizing enterocolitis" OR AB "necrotizing enterocolitis") OR (TI "necrotizing" OR AB "necrotizing") AND (TI "enterocolitis" OR AB “enterocolitis”) OR (MM "Pregnancy, Ectopic") OR ((TI "pregnancy" OR AB “pregnancy”) AND (TI "ectopic" OR AB "ectopic") OR (TI "ectopic pregnancy" OR AB "ectopic pregnancy") OR ((TI "ectopic" OR AB “ectopic” AND (TI "pregnancy" OR AB "pregnancy") OR " (MH "Pre-Eclampsia+") OR "TI "pre eclampsia" OR AB "pre eclampsia") OR " (MH "Eclampsia+") OR (TI "eclampsia" OR AB “eclampsia”) OR (TI "eclampsias" OR AB "eclampsias")
5	S1 AND S4
6	S3 OR S5
7	(MH "Animals+") NOT (MM "Human")
8	S6 NOT S7
9	TI Study protocol OR TI trial protocol OR TI review protocol OR PT editorial OR PT letter OR PT case reports OR (PT abstract) OR (PT review)
10	S8 NOT S9
11	Filters: **from 2000 - 2021**

Data Synthesis and Analysis

Key diagnostic accuracy and error terms used in the report are defined in the Methods Section (Data Synthesis and Analysis) as follows:

- false negative rate (1-sensitivity) (denominator is disease present)
- false positive rate (1-specificity) (denominator is disease absent)
- false discovery rate (1-positive predictive value) (denominator is diagnosis label present)
- false omission rate (1-negative predictive value) (denominator is diagnosis label absent)
- total diagnostic error rate (1-accuracy for all patients [disease and non-disease])
- overall cohort-based rates of errors and harms per ED visit (e.g., 2 per 10,000 visits)

Figure A-1 illustrates the formulas used to calculate the false negative rate, the false positive rate, the false discovery rate, and the false omission rate.

Figure A-1. Calculations of false negative rate, false positive rate, false discovery rate, and false omission rate

	Disease Present	Disease Absent
Diagnosis Label Present	TP	FP
Diagnosis Label Absent	FN	TN

$$False\ negative\ rate = \frac{FN}{FN+TP} \qquad False\ discovery\ rate = \frac{FP}{FP+TP}$$

$$False\ positive\ rate = \frac{FP}{FP+TN} \qquad False\ omission\ rate = \frac{FN}{FN+TN}$$

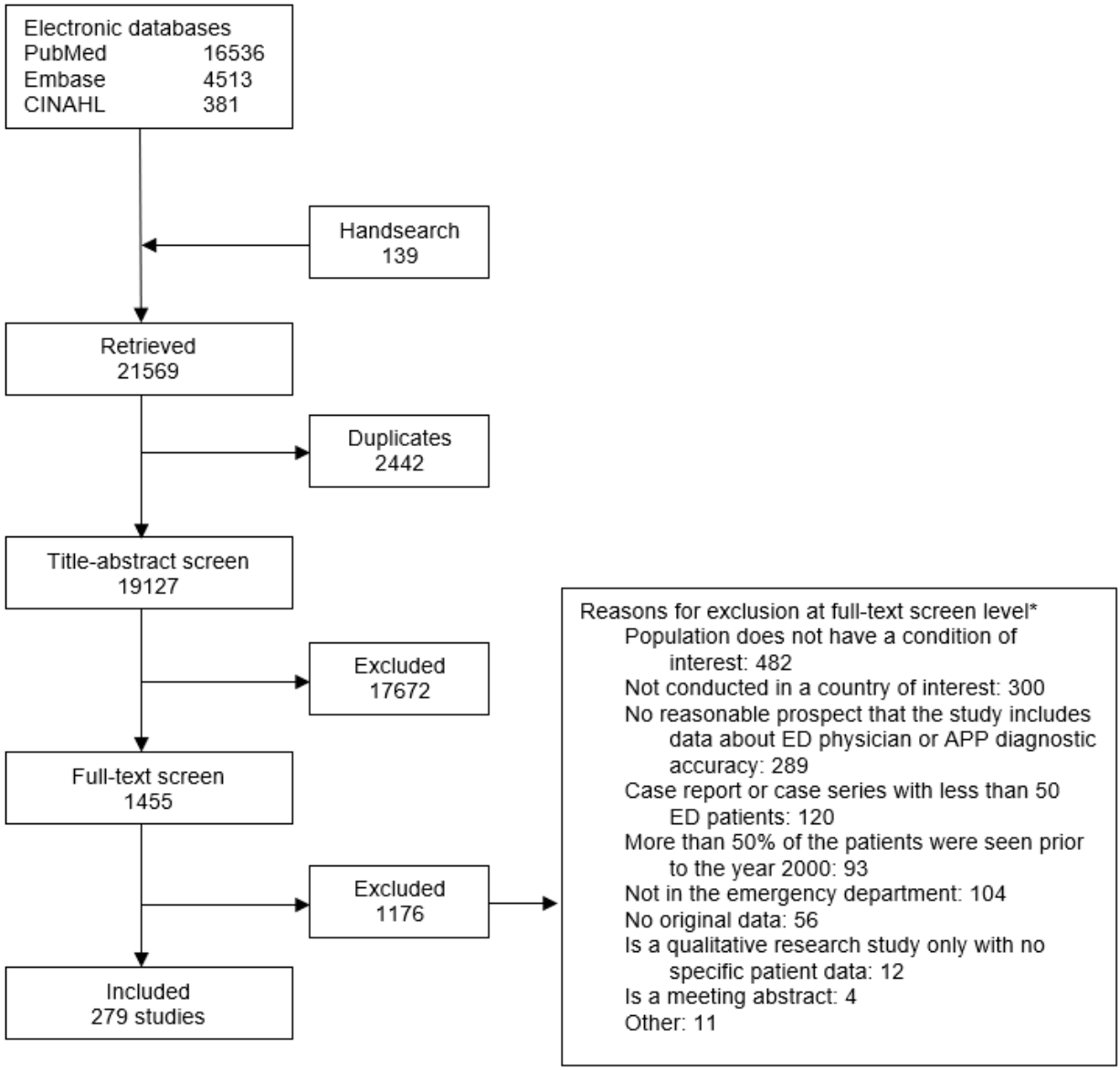
$$Total\ diagnostic\ error\ rate = \frac{FN+FP}{FN+TP+FP+TN}$$

Appendix B. Results

Results of Literature Searches

Figure B-1 show the literature flow for our searches.

Figure B-1. Literature flow diagram



APP = advanced practice provider; CINAHL = Cumulative Index to Nursing and Allied Health Literature; ED = emergency department

* Studies can be excluded for more than one reason.

Results of Grey Literature Searches

Table B-1 displays the results of our review of malpractice claims reports from major medical liability insurance carriers or similar risk management entities.

Table B-1. Summary of the status of malpractice claims reports

Citation	Status
CRICO Strategies. 2011 Annual Benchmarking Report: Malpractice Risks in Emergency Medicine. CRICO Strategies, Cambridge, MA. www.rmfstrategies.com	Obtained data relevant to the emergency department from authors and included data in KQ1.
Diagnostic Error in Acute Care. Pennsylvania Patient Safety Advisory. 2010: 7(3).	Excluded because no original data.
The Doctors Company. Emergency Medicine Closed Claims Study. www.thedoctors.com/patientsafety	Excluded because relevant data was not limited to diagnostic errors.
Hanscom R, Small M, Lambrecht A. Diagnostic Accuracy: Room for Improvement. Coverys. www.coverys.com	Excluded because relevant data was not limited to diagnostic errors in the emergency department.
Troxel DB. Diagnostic Error in Medical Practice by Specialty. The Doctor's Advocate. 2014 Sep:2.	Included in KQ1.

Table B-2. Summary of studies reporting on symptom-specific rates of diagnostic error

Author, Year	Symptom	Country/Region	Population	Diagnostic Error Rate	Harm Rate	Serious Harm Rate
Caterino, 2012[21]	Infection	US	Adults (65+)	18.4% (19/103) rate of over-diagnosis	NA	NA
Chung, 2009[22]	Torso imaging	US	NA	2% (95 of 4768)	0.3% resulted in change in management or recall to ED (16 of 4768)	No serious harm
Crosby, 2013[16]	Minor head trauma, Testicular pain, Abdominal pain	Western Europe	Pediatrics	Head trauma: 0.3% (by surgeon and/or EM provider); Testicular pain: 1.6% surgeon, 0% EM; Abdominal pain: 1% surgeon, 0.3% EM, P-value sig; Combined three conditions 0.9%, surgeon, 0.3% EM	NA	NA
Dubosh, 2015[11]	Atraumatic headache, Atraumatic back pain	US	Adults	NA	NA	0.5% headache; 0.2% back pain
Ferree, 2016[1]	Polytrauma	Western Europe	Adults	12% DDI	4.2% (% of DDI patients that underwent operative intervention for the DDI)	NA
Filippi, 2008[23]	Neuro MRI	US	NA	7.2% (26 of 361)	4.2% (15 of 361)	NA
Freedman, 2017[17]	Constipation	US	Pediatrics	0.28% (784 of 282,225)	NA	NA
Gallagher, 2006[13]	Abdominal pain	US	Adults	14.1% (11/78) pts receiving morphine; 14.6% (11/75) pts not receiving morphine	NA	NA
Kline, 2009[20]	Low-risk chest pain	US	Adults	NA	0.5% missed/delayed ACS in control group, 0% in intervention group (received printout on risk assessment)	NA
Kornblith, 2013[7]	Found down	US	Adults	16.9%	NA	NA
Miller, 2018[12]	Headache	US	Adults + pediatrics	0.17 (10/583)	NA	NA
Moeller, 2008[10]	Any neurological complaint (requiring neurology consult)	Canada	NA	17% between emergency physician and final diagnosis, 19% between ED trainee & final diagnosis,	NA	NA

Author, Year	Symptom	Country/Region	Population	Diagnostic Error Rate	Harm Rate	Serious Harm Rate
Montmany, 2008[5]	Polytrauma	Western Europe	Adults (16+)	40.3% missed injury	17% clinically significant missed injury	NA
Muhm, 2012[3]	Polytrauma	Western Europe	NA	23% missed injuries after primary survey, 12% missed after secondary survey, 4% after 24h	0.20%	NA
Osterwalder, 2020[14]	Abdominal pain	Western Europe	Adults	5.6% (27/480)	1.7% requiring surgery	NA
Pirozzi, 2014[19]	Dyspnea	Western Europe	Adults	5% with POCUS, 50% w/o POCUS (no difference in clinical outcomes/harms between groups)	NA	NA
Postma, 2012[4]	Trauma (flight crash)	Western Europe	NA	NA	12% clinical significant DDI among hospitalized patients (8 of 66 patients)	6% (4 of 66 patients required surgery for the delayed diagnosis)
Ray, 2006[18]	Dyspnea/acute respiratory failure	Western Europe	Adults (65+)	20% (101/514)	NA	NA
Royl, 2011[9]	Dizziness (neurology consulted)	Western Europe	NA	44%	6%: primary diagnosis changed from benign to serious; 5% primary serious diagnosis changed to another serious diagnosis	NA
Saaristo, 2020[15]	Abdominal pain	Western Europe	Adults + pediatrics	3% (303 of 10,609 patients returned to ED w/in 48 hours)	0.7% hospitalized; 0.06% had immediate surgery.	NA
Snoek, 2013[2]	High-energy trauma	Western Europe	Adults	2.7% DDI	NA	NA
Sun, 2007[8]	Syncope/near-syncope	US	Adults	4%	NA	NA
Willner, 2012[6]	Trauma	US	Pediatrics	8% DDI (26 of 324 patients)	0.3% clinically significant DDI (1 patient)	NA

ACS = acute coronary syndrome; DDI = delayed diagnosis of injury; ED = emergency department; EM = emergency medicine; MRI = magenntic resonance imaging; NA = not applicable; POCUS = point-of-care ultrasound; US = United States

Appendix C. List of Excluded Articles

1. Aaronson E, Benzer T, Borczuk P. Seventy-Two-Hour Returns Are Not Useful in Identifying Emergency Department Patients With a Concerning Intra-Abdominal Process. J Emerg Med. 2016 Apr;50(4):560-6. doi: 10.1016/j.jemermed.2015.11.015. PMID: 27016953. **Exclusion**: Is a meeting abstract
2. Abe T, Tokuda Y, Shiraishi A, et al. In-hospital mortality associated with the misdiagnosis or unidentified site of infection at admission. Critical care (London, England). 2019 Jun 6;23(1):202. doi: 10.1186/s13054-019-2475-9. PMID: 31171006. **Exclusion:** Not conducted in a country of interest
3. Aboal J, Ramos R, Loma-Osorio P, et al. Time from electrocardiographic diagnosis of ST-elevation myocardial infarction to guidewire crossing in patients transferred to a hospital for primary angioplasty: factors associated with delay. Emergencias. 2021 Jun;33(3):195-202. PMID: 33978333. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy
4. Abujudeh HH, Boland GW, Kaewlai R, et al. Abdominal and pelvic computed tomography (CT) interpretation: discrepancy rates among experienced radiologists. Eur Radiol. 2010 Aug;20(8):1952-7. doi: 10.1007/s00330-010-1763-1. PMID: 20336300. **Exclusion**: Not in the emergency department
5. Acar A, Oğuz O, Çayönü M, et al. Evaluation of the final diagnosis of elderly patients admitted to the emergency department with a complaint of vertigo. Turk Geriatri Dergisi. 2015;18(3):194-8. **Exclusion:** Not conducted in a country of interest
6. Accident & emergency - Failure to diagnose scaphoid fracture. Clinical Risk. 2002;8(2):84. **Exclusion**: Population does not have a condition of interest
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13. Ahc M. Cardiology-Related Misdiagnoses Frequently Alleged in ED Malpractice Claims. ED Legal Letter. 2021;32(3):1-3. PMID: 148698671. Language: English. Entry Date: 20210217. Revision Date: 20210217. Publication Type: Article. Journal Subset: Biomedical. **Exclusion**: Is a meeting abstract

14. Ahmad NH, Tan TL. Aortic dissection: A life-threatening stroke mimicker. Hong Kong Journal of Emergency Medicine. 2018;25(2):98-101. doi: 10.1177/1024907917745155. **Exclusion:** Not conducted in a country of interest

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95. Baumgartner A, Rauer S, Hottenrott T, et al. Admission diagnoses of patients later diagnosed with autoimmune encephalitis. Journal of neurology. 2019 Jan;266(1):124-32. doi: 10.1007/s00415-018-9105-3. PMID: 30421340. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

96. Beach R, Reading R. The importance of acknowledging clinical uncertainty in the diagnosis of epilepsy and non-epileptic events. Archives of disease in childhood. 2005 Dec;90(12):1219-22. doi: 10.1136/adc.2004.065441. PMID: 16131503. **Exclusion:** Population does not have a condition of interest

97. Beckmann NM, Crawford L. Salter-Harris I fracture of the distal humerus in a neonate: imaging appearance of radiographs, ultrasound, and arthrography. Radiology Case Reports. 2017;12(3):571-6. doi: 10.1016/j.radcr.2017.04.013. **Exclusion:** Population does not have a condition of interest

98. Behrbalk E, Salame K, Regev GJ, et al. Delayed diagnosis of cervical spondylotic myelopathy by primary care physicians. Neurosurgical focus. 2013 Jul;35(1):E1. doi: 10.3171/2013.3.focus1374. PMID: 23815245. **Exclusion:** Population does not have a condition of interest

99. Bellenger NG, Peebles C, Harden S, et al. Troponin-positive chest pain with unobstructed coronary arteries: a role for delayed enhanced cardiovascular magnetic resonance in the diagnosis of non-ST elevation myocardial infarction. The Journal of invasive cardiology. 2006 Dec;18(12):594-98. PMID: 17197709. **Exclusion:** Case report or case series with less than 50 ED patients

100. Bellini T, Rotulo GA, Carlucci M, et al. Complicated appendicitis due to diagnosis delay during lockdown period in Italy. Acta Paediatr. 2021 Jun;110(6):1959-60. doi: 10.1111/apa.15756. PMID: 33438280. **Exclusion**: No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

101. Ben-Haim G, Zabatani A, Orion D, et al. The Pandemic's impacts on patients without Covid-19 on multidisciplinary aspects in emergency medicine care. Intern Emerg Med. 2021 Mar 1:1-8. doi: 10.1007/s11739-021-02680-5. PMID: 33650082. **Exclusion:** Not conducted in a country of interest

102. Bendon CL, Crick A. Occult deep vein thrombosis in lower limb trauma requiring microsurgical reconstruction-A retrospective cohort study. J Plast Reconstr Aesthet Surg. 2021 Apr;74(4):775-84. doi: 10.1016/j.bjps.2020.10.019. PMID: 33342745. **Exclusion**: Not in the emergency department

103. Benedict K, Beer KD, Jackson BR. Histoplasmosis-related Healthcare Use, Diagnosis, and Treatment in a Commercially Insured Population, United States. Clin Infect Dis. 2020 Mar 3;70(6):1003-10. doi: 10.1093/cid/ciz324. PMID: 31037290. **Exclusion**: Population does not have a condition of interest

104. Bengtzen RR, Petering RC. Point-of-Care Ultrasound Diagnosis of Posterior Sternoclavicular Joint Dislocation. Journal of Emergency Medicine. 2017;52(4):513-5. doi: 10.1016/j.jemermed.2016.11.001. **Exclusion:** No original data

105. Bergeron E. Clinical judgment remains of great value in the diagnosis of acute appendicitis. Canadian journal of surgery. 2006 Apr;49(2):96-100. PMID: 16630419. **Exclusion:** More than 50% of the patients were seen prior to the year 2000

106. Berghaus TM, Thilo C, von Scheidt W, et al. The impact of age on the delay in diagnosis in patients with acute pulmonary embolism. Clinical and applied thrombosis/hemostasis. 2011 Nov-Dec;17(6):605-10. doi: 10.1177/1076029611404218. PMID: 21593023. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

107. Berghaus TM, von Scheidt W, Schwaiblmair M. Time between first symptoms and diagnosis in patients with acute pulmonary embolism: are patients with recurrent episodes diagnosed earlier? Clinical research in cardiology. 2011 Feb;100(2):117-9. doi: 10.1007/s00392-010-0217-8. PMID: 20821017. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

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109. Berlot G, Vergolini A, Calderan C, et al. Acute myocardial infarction in non-cardiac critically ill patients: a clinical-pathological study. Monaldi archives for chest disease. 2010 Dec;74(4):164-71. doi: 10.4081/monaldi.2010.257. PMID: 21329270. **Exclusion:** Not in the emergency department

110. Berne JD, Norwood SH, McAuley CE, et al. The high morbidity of blunt cerebrovascular injury in an unscreened population: more evidence of the need for mandatory screening protocols. Journal of the American College of Surgeons. 2001 Mar;192(3):314-21. doi: 10.1016/s1072-7515(01)00772-4. PMID: 11245373. **Exclusion:** More than 50% of the patients were seen prior to the year 2000

111. Berne JD, Reuland KS, Villarreal DH, et al. Sixteen-slice multi-detector computed tomographic angiography improves the accuracy of screening for blunt cerebrovascular injury. The Journal of trauma. 2006 Jun;60(6):1204-9; discussion 9-10. doi: 10.1097/01.ta.0000220435.55791.ce. PMID: 16766962. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

112. Bernstein DN, McCalla DJ, Molinari RW, et al. An Analysis of Patient and Fracture Characteristics and Clinical Outcomes in Patients With Hyperostotic Spine Fractures. Global spine journal. 2019 Nov 12:2192568219887157. doi: 10.1177/2192568219887157. PMID: 32875832. **Exclusion:** Population does not have a condition of interest

113. Bertozzi G, Maglietta F, Baldari B, et al. Mistrial or Misdiagnosis: The Importance of Autopsy and Histopathological Examination in Cases of Sudden Infant Bronchiolitis-Related Death. Frontiers in Pediatrics. 2020;8. doi: 10.3389/fped.2020.00229. **Exclusion**: Case report or case series with less than 50 ED patients

114. Bhakthavatsala Reddy C, Cyriac C, Desle HB. Role of "Ischemia Modified Albumin" (IMA) in acute coronary syndromes. Indian heart journal. 2014 Nov-Dec;66(6):656-62. doi: 10.1016/j.ihj.2014.12.005. PMID: 25634401. **Exclusion:** Not conducted in a country of interest

115. Bhansali A, Bhadada S, Sharma A, et al. Presentation and outcome of rhino-orbital-cerebral mucormycosis in patients with diabetes. Postgraduate medical journal. 2004 Nov;80(949):670-4. doi: 10.1136/pgmj.2003.016030. PMID: 15537854. **Exclusion:** Not conducted in a country of interest

116. Bhise V, Meyer AND, Singh H, et al. Errors in Diagnosis of Spinal Epidural Abscesses in the Era of Electronic Health Records. The American journal of medicine. 2017 Aug;130(8):975-81. doi: 10.1016/j.amjmed.2017.03.009. PMID: 28366427. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

117. Bhui K, Ullrich S, Coid JW. Which pathways to psychiatric care lead to earlier treatment and a shorter duration of first-episode psychosis? BMC psychiatry. 2014 Mar 12;14:72. doi: 10.1186/1471-244x-14-72. PMID: 24620939. **Exclusion:** Population does not have a condition of interest

118. Biagini E, Lofiego C, Ferlito M, et al. Frequency, determinants, and clinical relevance of acute coronary syndrome-like electrocardiographic findings in patients with acute aortic syndrome. The American journal of cardiology. 2007 Sep 15;100(6):1013-9. doi: 10.1016/j.amjcard.2007.04.044. PMID: 17826389. **Exclusion:** More than 50% of the patients were seen prior to the year 2000

119. Bilaszewski Ł, Timler W, Budrewicz K, et al. The Impact of COVID-19 on Admissions and Management of Patients with Atrial Fibrillation Episodes in the Emergency Department. Int J Environ Res Public Health. 2021 Jun 4;18(11). doi: 10.3390/ijerph18116048. PMID: 34199795. **Exclusion**: Not conducted in a country of interest

120. Billard-Pomares T, Herwegh S, Wizla-Derambure N, et al. Application of quantitative PCR to the diagnosis and monitoring of Pseudomonas aeruginosa colonization in 5-18-year-old cystic fibrosis patients. Journal of medical microbiology. 2011 Feb;60(Pt 2):157-61. doi: 10.1099/jmm.0.023838-0. PMID: 20947668. **Exclusion:** Case report or case series with less than 50 ED patients

121. Binkovitz LA, Unsdorfer KM, Thapa P, et al. Pediatric appendiceal ultrasound: accuracy, determinacy and clinical outcomes. Pediatr Radiol. 2015 Dec;45(13):1934-44. doi: 10.1007/s00247-015-3432-7. PMID: 26280637. **Exclusion**: No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

122. Biondi EA, McCulloh R, Staggs VS, et al. Reducing Variability in the Infant Sepsis Evaluation (REVISE): A National Quality Initiative. Pediatrics. 2019 Sep;144(3). doi: 10.1542/peds.2018-2201. PMID: 31434688. **Exclusion:** Not in the emergency department

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124. Birkeland S, Brabrand M, Mikkelsen KL, et al. Changes in compensation claim contents following reorganization of emergency hospital care. Int J Qual Health Care. 2020 Dec 15;32(10):685-93. doi: 10.1093/intqhc/mzaa131. PMID: 33031503. **Exclusion:** Population doesn't have a condition of interest

125. Birkenbeuel J, Vu K, Lehrich BM, et al. Medical Malpractice of Vestibular Schwannoma: A 40-Year Review of the United States Legal Databases. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2019 Mar;40(3):391-7. doi: 10.1097/mao.0000000000002133. PMID: 30742599. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

126. Blanco-Molina A, Rota LL, Di Micco P, et al. Venous thromboembolism during pregnancy, postpartum or during contraceptive use. Thrombosis and haemostasis. 2010 Feb;103(2):306-11. doi: 10.1160/th09-08-0559. PMID: 20126835. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

127. Blankenship JC, Skelding KA, Scott TD, et al. Predictors of reperfusion delay in patients with acute myocardial infarction undergoing primary percutaneous coronary intervention from the HORIZONS-AMI trial. The American journal of cardiology. 2010 Dec 1;106(11):1527-33. doi: 10.1016/j.amjcard.2010.07.033. PMID: 21094350. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

128. Blankstein A, Cohen I, Heiman Z, et al. Ultrasonography as a diagnostic modality and therapeutic adjuvant in the management of soft tissue foreign bodies in the lower extremities. The Israel Medical Association journal : IMAJ. 2001 Jun;3(6):411-3. PMID: 11433632. **Exclusion:** More than 50% of the patients were seen prior to the year 2000

129. Bloos F, Bayer O, Sachse S, et al. Attributable costs of patients with candidemia and potential implications of polymerase chain reaction-based pathogen detection on antifungal therapy in patients with sepsis. J Crit Care. 2013 Feb;28(1):2-8. doi: 10.1016/j.jcrc.2012.07.011. PMID: 22999484. **Exclusion**: No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

130. Blum RA, Tomlinson AR, Jetté N, et al. Assessment of long-term psychosocial outcomes in anti-NMDA receptor encephalitis. Epilepsy & behavior : E&B. 2020 Jul;108:107088. doi: 10.1016/j.yebeh.2020.107088. PMID: 32375094. **Exclusion:** Qualitative research study only with no specific patient data

131. Boccardi L, Verde M. Gender differences in the clinical presentation to the emergency department for chest pain. Italian heart journal : official journal of the Italian Federation of Cardiology. 2003 Jun;4(6):371-3. PMID: 12898800. **Exclusion:** No original data

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133. Bochicchio GV, Lumpkins K, O'Connor J, et al. Blast injury in a civilian trauma setting is associated with a delay in diagnosis of traumatic brain injury. The American surgeon. 2008 Mar;74(3):267-70. PMID: 18376697. **Exclusion:** Population does not have a condition of interest

134. Bodilsen J, Brandt CT, Sharew A, et al. Early versus late diagnosis in community-acquired bacterial meningitis: a retrospective cohort study. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2018 Feb;24(2):166-70. doi: 10.1016/j.cmi.2017.06.021. PMID: 28652113. **Exclusion:** Not in the emergency department

135. Boesebeck F, Freermann S, Kellinghaus C, et al. Misdiagnosis of epileptic and non-epileptic seizures in a neurological intensive care unit. Acta neurologica Scandinavica. 2010 Sep;122(3):189-95. doi: 10.1111/j.1600-0404.2009.01287.x. PMID: 20003086. **Exclusion:** Population does not have a condition of interest

136. Boi L, Savastano S, Beghetto M, et al. Embolization of iatrogenic uterine pseudoaneurysm. Gynecology and Minimally Invasive Therapy. 2017;6(2):85-8. doi: 10.1016/j.gmit.2017.02.004. **Exclusion:** No original data

137. Boivin-Proulx LA, Matteau A, Pacheco C, et al. Effect of Real-Time Physician Oversight of Prehospital STEMI Diagnosis on ECG-Inappropriate and False Positive Catheterization Laboratory Activation. CJC Open. 2021 Apr;3(4):419-26. doi: 10.1016/j.cjco.2020.11.013. PMID: 34027344. **Exclusion**: Not in the emergency department.

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139. Bolorunduro OB, Haider AH, Oyetunji TA, et al. Disparities in trauma care: are fewer diagnostic tests conducted for uninsured patients with pelvic fracture? American journal of surgery. 2013 Apr;205(4):365-70. doi: 10.1016/j.amjsurg.2012.10.026. PMID: 23375757. **Exclusion:** Population does not have a condition of interest

140. Bolvardi E, Alizadeh B, Foroughian M, et al. Quebec Decision Rule in Determining the Need for Radiography in Reduction of Shoulder Dislocation; a Diagnostic Accuracy Study. Archives of academic emergency medicine. 2019;7(1):e21. PMID: 31432031. **Exclusion:** Population does not have a condition of interest

141. Boman E, Duvaland E, Gaarde K, et al. Implementation of advanced practice nursing for minor orthopedic injuries in the emergency care context: A non-inferiority study. Int J Nurs Stud. 2021 Jun;118:103910. doi: 10.1016/j.ijnurstu.2021.103910. PMID: 33773309. **Exclusion**: Not in the emergency department

142. Bonadio W, Peloquin P, Brazg J, et al. Appendicitis in preschool aged children: Regression analysis of factors associated with perforation outcome. Journal of pediatric surgery. 2015 Sep;50(9):1569-73. doi: 10.1016/j.jpedsurg.2015.02.050. PMID: 25783356. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

143. Bonilla L, Gálvez C, Medrano L, et al. [Impact of COVID-19 on the presentation and course of acute appendicitis in paediatrics]. An Pediatr (Engl Ed). 2021 Apr;94(4):245-51. doi: 10.1016/j.anpedi.2020.12.003. PMID: 33431331. **Exclusion**: No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

144. Boon G, Ende-Verhaar YM, Bavalia R, et al. Non-invasive early exclusion of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism: the InShape II study. Thorax. 2021 Oct;76(10):1002-9. doi: 10.1136/thoraxjnl-2020-216324. PMID: 33758073. **Exclusion**: Population does not have a condition of interest

145. Boraiah S, Gardner MJ, Helfet DL, et al. High association of posterior malleolus fractures with spiral distal tibial fractures. Clinical orthopaedics and related research. 2008 Jul;466(7):1692-8. doi: 10.1007/s11999-008-0224-5. PMID: 18347885. **Exclusion:** Population does not have a condition of interest

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147. Borner U, Anschuetz L, Kaiser N, et al. Blunt nasal trauma in children: a frequent diagnostic challenge. European archives of oto-rhino-laryngology : official journal of the European Federation of Oto-Rhino-Laryngological Societies (EUFOS) : affiliated with the German Society for Oto-Rhino-Laryngology - Head and Neck Surgery. 2019 Jan;276(1):85-91. doi: 10.1007/s00405-018-5183-1. PMID: 30382396. **Exclusion:** Population does not have a condition of interest

148. Bos EME, Posner KL, Domino KB, et al. Haematoma, abscess or meningitis after neuraxial anaesthesia in the USA and the Netherlands: A closed claims analysis. European journal of anaesthesiology. 2020 Sep;37(9):743-51. doi: 10.1097/eja.0000000000001260. PMID: 32769504. **Exclusion:** Not in the emergency department

149. Bosanko NC, Chauhan A, Brookes M, et al. Presentations of pyogenic liver abscess in one UK centre over a 15-year period. The journal of the Royal College of Physicians of Edinburgh. 2011 Mar;41(1):13-7. doi: 10.4997/jrcpe.2011.104. PMID: 21365060. **Exclusion:** Population does not have a condition of interest

150. Bosch X, Capdevila A, Grafia I, et al. The impact of Covid-19 on patients with suspected cancer: An analysis of ED presentation and referrals to a quick diagnosis unit. Am J Emerg Med. 2021 Apr 2;48:1-11. doi: 10.1016/j.ajem.2021.03.087. PMID: 33836386. **Exclusion**: Population does not have a condition of interest

151. Bostan H, Sencar ME, Calapkulu M, et al. Two Important Issues in Subacute Thyroiditis Management: Delayed Diagnosis and Inappropriate Use of Antibiotics. Eur Thyroid J. 2021 Jul;10(4):323-9. doi: 10.1159/000513745. PMID: 34395304. **Exclusion:** Population does not have a condition of interest

152. Bourdon H, Herbaut A, Trinh L, et al. An algorithm in ophthalmic emergencies to evaluate the necessity of physical consultation during COVID-19 lockdown in Paris: Experience of the first 100 patients. J Fr Ophtalmol. 2021 Mar;44(3):307-12. doi: 10.1016/j.jfo.2020.12.002. PMID: 33612327. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

153. Bourcier JE, Gallard E, Redonnet JP, et al. Diagnostic performance of abdominal point of care ultrasound performed by an emergency physician in acute right iliac fossa pain. Critical ultrasound journal. 2018;10(1). doi: 10.1186/s13089-018-0112-5. **Exclusion:** Not conducted in a country of interest

154. Bouvier-Colle MH, Saucedo M, Deneux-Tharaux C. [The confidential enquiries into maternal deaths, 1996-2006 in France: what consequences for the obstetrical care?]. Journal de gynecologie, obstetrique et biologie de la reproduction. 2011 Apr;40(2):87-102. doi: 10.1016/j.jgyn.2010.12.007. PMID: 21315522. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

155. Braun EM, Tomazic PV, Ropposch T, et al. Misdiagnosis of acute peripheral vestibulopathy in central nervous ischemic infarction. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2011 Dec;32(9):1518-21. doi: 10.1097/MAO.0b013e318238ff9a. PMID: 22072269. **Exclusion:** Not in the emergency department

156. Braun EM, Tomazic PV, Ropposch T, et al. Misdiagnosis of acute peripheral vestibulopathy in central nervous ischemic infarction. Otol Neurotol. 2011 Dec;32(9):1518-21. doi: 10.1097/MAO.0b013e318238ff9a. PMID: 22072269. **Exclusion**: Not in the emergency department

157. Braun KP, Kappelle LJ, Kirkham FJ, et al. Diagnostic pitfalls in paediatric ischaemic stroke. Developmental medicine and child neurology. 2006 Dec;48(12):985-90. doi: 10.1017/s0012162206002167. PMID: 17109788. **Exclusion:** Case report or case series with less than 50 ED patients

158. Bressan S, Gomez B, Mintegi S, et al. Diagnostic performance of the lab-score in predicting severe and invasive bacterial infections in well-appearing young febrile infants. The Pediatric infectious disease journal. 2012 Dec;31(12):1239-44. doi: 10.1097/INF.0b013e318266a9aa. PMID: 22760529. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

159. Brito M, Laranjo A, Sabino J, et al. Digestive Oncology in the COVID-19 Pandemic Era. GE Port J Gastroenterol. 2021 Mar 22;579:1-8. doi: 10.1159/000514784. PMID: 34192128. **Exclusion**: Not in the emergency department

160. Broder JS, Hollingsworth CL, Miller CM, et al. Prospective double-blinded study of abdominal-pelvic computed tomography guided by the region of tenderness: estimation of detection of acute pathology and radiation exposure reduction. Annals of emergency medicine. 2010 Aug;56(2):126-34. doi: 10.1016/j.annemergmed.2009.11.023. PMID: 20074835. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

161. Brook OR, Kane RA, Tyagi G, et al. Lessons learned from quality assurance: errors in the diagnosis of acute cholecystitis on ultrasound and CT. AJR American journal of roentgenology. 2011 Mar;196(3):597-604. doi: 10.2214/ajr.10.5170. PMID: 21343502. **Exclusion:** Population does not have a condition of interest

162. Brouwers HB, Falcone GJ, McNamara KA, et al. CTA spot sign predicts hematoma expansion in patients with delayed presentation after intracerebral hemorrhage. Neurocritical care. 2012 Dec;17(3):421-8. doi: 10.1007/s12028-012-9765-2. PMID: 22878870. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

163. Brown BL, Fidell A, Ingolia G, et al. Infectious causes and outcomes in patients presenting with cerebral spinal fluid pleocytosis. Journal of neurovirology. 2019 Aug;25(4):448-56. doi: 10.1007/s13365-019-00739-w. PMID: 30850974. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

164. Brown T, Ghelani-Allen A, Yeung D, et al. Comparative effectiveness of physician diagnosis and guideline definitions in identifying sepsis patients in the emergency department. Journal of critical care. 2015 Feb;30(1):71-7. doi: 10.1016/j.jcrc.2014.08.009. PMID: 25241088. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

165. Brown-Forestiere R, Furiato A, Foresteire NP, et al. Acute Appendicitis: Clinical Clues and Conundrums Related to the Greatest Misses. Cureus. 2020 May 11;12(5):e8051. doi: 10.7759/cureus.8051. PMID: 32537270. **Exclusion:** Case report or case series with less than 50 ED patients

166. Brunser AM, Mazzon E, Muñoz P, et al. [Determinants of door to needle time for intravenous thrombolysis in acute ischemic stroke]. Rev Med Chil. 2020 Aug;148(8):1090-5. doi: 10.4067/s0034-98872020000801090. PMID: 33399775. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

167. Brunton NE, Wysokinski WE, Hodge DO, et al. Delayed anticoagulation in venous thromboembolism: Reasons and associated outcomes. Res Pract Thromb Haemost. 2021 May;5(4):e12500. doi: 10.1002/rth2.12500. PMID: 34027287. **Exclusion**: Not in the emergency department

168. Bruoha S, Yosefy C, Gallego-Colon E, et al. Impact in total ischemic time and ST-segment elevation myocardial infarction admissions during COVID-19. Am J Emerg Med. 2021 Jul;45:7-10. doi: 10.1016/j.ajem.2021.02.020. PMID: 33640628. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

169. Brugioni L, de Niederhausern F, Romagnoli E, et al. The predictive value of fruit juice in the esophagus-pleural fistula. Italian Journal of Medicine. 2020;14(3):176-8. doi: 10.4081/ITJM.2020.1285. **Exclusion:** Population does not have a condition of interest

170. Brush JE, Jr., Krumholz HM, Greene EJ, et al. Sex Differences in Symptom Phenotypes Among Patients With Acute Myocardial Infarction. Circulation Cardiovascular quality and outcomes. 2020 Feb;13(2):e005948. doi: 10.1161/circoutcomes.119.005948. PMID: 32063049. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

171. Bryce Y, Emmanuel A, Jr., Agrusa C, et al. Acute limb ischemia in a cancer patient has high morbidity, high mortality, and atypical presentation: a tertiary cancer center's retrospective study. BMC Cancer. 2021 Aug 13;21(1):916. doi: 10.1186/s12885-021-08659-x. PMID: 34388968. **Exclusion**: Case report or case series with less than 50 ED patients

172. Bublak R. Algorithm against misdiagnoses in aortic dissection: Rare cause of chest pain. MMW-Fortschritte der Medizin. 2020;162(6):19. doi: 10.1007/s15006-020-0321-2. **Exclusion:** No original data (e.g., review, simulation study, editorial)

173. Buchan JC, Saihan Z, Reynolds AG. Nurse triage, diagnosis and treatment of eye casualty patients: a study of quality and utility. Accident and emergency nursing. 2003 Oct;11(4):226-8. doi: 10.1016/s0965-2302(03)00039-0. PMID: 14521969. **Exclusion:** Population does not have a condition of interest

174. Buell JF, Gross T, Alloway RR, et al. Central nervous system tumors in donors: misdiagnosis carries a high morbidity and mortality. Transplantation proceedings. 2005 Mar;37(2):583-4. doi: 10.1016/j.transproceed.2004.12.125. PMID: 15848464. **Exclusion:** Not in the emergency department

175. Bulbul Y, Ayik S, Oztuna F, et al. The relationship between socio-demographic characteristics of patients and diagnostic delay in acute pulmonary thromboembolism. Upsala journal of medical sciences. 2011 Mar;116(1):72-6. doi: 10.3109/03009734.2010.530701. PMID: 21070094. **Exclusion:** Not conducted in a country of interest

176. Bulbul Y, Ozsu S, Kosucu P, et al. Time delay between onset of symptoms and diagnosis in pulmonary thromboembolism. Respiration; international review of thoracic diseases. 2009;78(1):36-41. doi: 10.1159/000167409. PMID: 18957839. **Exclusion:** Not conducted in a country of interest

177. Bullard MJ, Chan T, Brayman C, et al. Revisions to the Canadian Emergency Department Triage and Acuity Scale (CTAS) Guidelines. Cjem. 2014 Nov;16(6):485-9. PMID: 25358280. Bullard 19058. **Exclusion**: No original data (e.g., review, simulation study, editorial)

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1112. Tu PH, Liu ZH, Yang TC, et al. Delayed diagnosis of traumatic cervical subluxation in patients with mandibular fractures: a 5-year retrospective study. The Journal of trauma. 2010 Nov;69(5):E62-5. doi: 10.1097/TA.0b013e3181d7807d. PMID: 20526213. **Exclusion:** Not conducted in a country of interest

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1114. Tung-Chen Y, Martí de Gracia M, Díez-Tascón A, et al. Correlation between Chest Computed Tomography and Lung Ultrasonography in Patients with Coronavirus Disease 2019 (COVID-19). Ultrasound in medicine & biology. 2020 Nov;46(11):2918-26. doi: 10.1016/j.ultrasmedbio.2020.07.003. PMID: 32771222. **Exclusion:** Population does not have a condition of interest

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1123. Vaienti E, Pogliacomi F. Delayed diagnosis of isolated coracoid process fractures: results of 9 cases treated conservatively. Acta bio-medica : Atenei Parmensis. 2012 Aug;83(2):138-46. PMID: 23393922. **Exclusion:** Population does not have a condition of interest

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1128. Van Der Linden MC, Van Loon M, Feenstra NSF, et al. Assessing bottlenecks in Emergency Department flow of patients with abdominal pain. International emergency nursing. 2018 Sep;40:1-5. doi: 10.1016/j.ienj.2018.03.006. PMID: 29636284. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

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1220. Yigit B, Citgez B, Tanal M, et al. Comparison of the management of emergency and oncological surgeries during the COVID-19 pandemic with the previous experience. A single-center retrospective study. Ann Ital Chir. 2021;92:323-9. PMID: 33200752. **Exclusion:** No reasonable prospect that the study includes data about ED physician or APP diagnostic accuracy

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1230. Yu DW, Jung YJ, Choi BY, et al. Subarachnoid hemorrhage with negative baseline digital subtraction angiography: is repeat digital subtraction angiography necessary? Journal of cerebrovascular and endovascular neurosurgery. 2012 Sep;14(3):210-5. doi: 10.7461/jcen.2012.14.3.210. PMID: 23210049. **Exclusion:** Not conducted in a country of interest

1231. Yu F, Xie G, Zheng S, et al. Assessment of the Diagnostic Ability of Four Detection Methods Using Three Sample Types of COVID-19 Patients. Front Cell Infect Microbiol. 2021;11:685640. doi: 10.3389/fcimb.2021.685640. PMID: 34164346. **Exclusion:** Not conducted in a country of interest

1232. Yu RF, San Jose MC, Manzanilla BM, et al. Sources and reasons for delays in the care of acute stroke patients. Journal of the neurological sciences. 2002 Jul 15;199(1-2):49-54. doi: 10.1016/s0022-510x(02)00103-x. PMID: 12084442. **Exclusion:** Not conducted in a country of interest

1233. Zahavi A, Luckman J, Yassur I, et al. Severe cranial neuropathies caused by falls from heights in children. Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie. 2016 Apr;254(4):765-72. doi: 10.1007/s00417-015-3199-4. PMID: 26553199. **Exclusion:** Population does not have a condition of interest

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1238. Zhong H, Bi Y. Pediatric Trauma-Induced Testicular Torsion: A Surgical Emergency. Urol Int. 2021;105(3-4):221-4. doi: 10.1159/000511747. PMID: 33378756. **Exclusion**: Not conducted in a country of interest

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1242. Zingg T, Agri F, Bourgeat M, et al. Avoiding delayed diagnosis of significant blunt bowel and mesenteric injuries: Can a scoring tool make the difference? A 7-year retrospective cohort study. Injury. 2018 Jan;49(1):33-41. doi: 10.1016/j.injury.2017.09.004. PMID: 28899564. **Exclusion:** Population does not have a condition of interest

1243. Zou J, Lu MH, Guan Z, et al. Diagnosis and treatment of 163 patients with ectopic pregnancy in exceptional site. Medical Journal of Chinese People's Liberation Army. 2013;38(5):404-8. **Exclusion**: Not conducted in a country of interest

Appendix D. Evidence Tables

Table D-1. Characteristics of studies that evaluated diagnostic errors in the emergency department

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Aaronson, 2016[204]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: GI ICD-9 Dates: 2013 to 2014	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Other: Subsequently, all patients with one return to the ED during the study period were identified. Patients with two or more visits were not included, because we believe that high utilizers represent a distinct population with unique reasons for return Total N: 10012 Age: Mean, 43.3 Male, n (%): 4683 (46.8) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Aaronson, 2018[177]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Unclear or NR Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Numerator and denominator Named data source: Dates: 2012 to 2015	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 413,167 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Nurses, PAs Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2005 to 2015	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: Outcome severity (e.g., only death): resulted in an ICU admission Total N: 254 Age: Male, n (%): 19 for deviation115 no deviation Race, n (%): White, 22 for deviation, 141 no deviation	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Agrawal, 2019[157]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2012 to 2015	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients with a catheterization lab alert Total N: 361 Age: Mean, 60 Male, n (%): 221 (61) Race, n (%): Black/African American, 270 (75)	Care delivered entirely within ED: Unclear or NR Consultants involved: Interventional cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Patients were classified as true STEMI alert or as false STEMI alerts after reviewing their peak troponin values, angiography reports, and clinical record. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Aneiros, 2019[146]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2000 to 2013	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 1736 Age: Range, 0 to 15 Male, n (%): 1088 (63%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Arch, 2016[205]	Patient type: general and neurology ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2013 to 2014	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 465 Age: Mean, 72 Male, n (%): 212 (46%) Race, n (%): White, 329 (71)	Care delivered entirely within ED: ED only Consultants involved: neurology Non-physicians involved: Unclear or NR Non-EM physicians involved: neurology Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed Opportunity (Singh 2014) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Atzema, 2011[52]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 82 Annual ED volume: Multiple Ownership: Multiple	Country: Canada Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Enhanced Feedback for Effective Cardiac Treatment study Dates: 2004 to 2005	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients who were admitted to an acute care hospital with a most responsible diagnosis of acute MI. Total N: 6605 Age: Male, n (%): 4100 (62) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Multiple definitions Conceptual harms definition: Unclear or NR Harms severity: None Causal taxonomy used: None
Augustin, 2011[54]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2000 to 2005	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Other: underwent appendectomy Total N: 380 Age: Mean, 34 Range, 6 to 79 Male, n (%): 231 (61%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Surgical Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Avelino-Silva, 2020[117]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: National Hospital Ambulatory Medical Survey Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Secondary analysis on National Hospital Ambulatory Medical Survey Comparison group: None Look back or look forward analysis: Data source: National Hospital Ambulatory Medical Survey Numerator: Numerator and denominator Named data source: NHAMSC Dates: 2005 to 2010	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: Other: admitted from EDs to hospitals Total N: Age: Mean, 79 Male, n (%): (42) Race, n (%): (12) (84)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: We defined "substantial diagnostic discrepancy" as present when the admission and discharge diagnoses were classified as distantly related (category 3) or unrelated (category 4), or absent in other situations. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Bartiaux, 2017[181]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Unclear or NR Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Questionnaire Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Questionnaire Numerator: Numerator and denominator Named data source: Dates: 2009 to 2009	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Interhospital transfer for which the patient does not stay in the ED Total N: 332 Age: Range, 15->75 Male, n (%): 196 (59) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Conceptual harms definition: Harms severity: Causal taxonomy used:

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Bastakoti, 2021	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Other Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2019 to 2019	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 418 Age: Mean, 64.1 Male, n (%): 201 (48%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Bayne, 2017[184]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Case-control Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Previous study Numerator: Numerator and denominator Named data source: Dates: 2005 to 2015	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: Other: We excluded cases of suspected intermittent torsion and patients under 2 years of age (to omit neonatal torsion and the inability to reliably communicate symptoms)Presentations were considered acute (Total N: 218 Age: Mean, 12.9 for acute, 12.6 for delayed Male, n (%): 218 (100) Race, n (%): (9 for acute, 7 for delayed) (70 for acute, 69 for delayed)	Care delivered entirely within ED: ED only Consultants involved: Urologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Beaver, 2005[107]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Multiple EDs transferred patients to one referral hospital Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: South Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2002 to 2003	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients with thoracic aortic dissection transferred to hospital Total N: 100 Age: Mean, 63 Range, 11 to 87 Male, n (%): 63 (63%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: radiologists Non-physicians involved: nurses Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: discrepancy between transferring and actual diagnosis Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Bhattacharya, 2013	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator Named data source: Dates: 2000 to 2009	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Multiple: excluded: patients who did not follow up in outpatient, patients whose stroke was due to substance abuse, patients who had no fixed address Total N: 77 Age: Mean, 37.9 Range, 16-49 Male, n (%): 33 (43%) Race, n (%): (58.4%) (37.7%)	Care delivered entirely within ED: ED only Consultants involved: primary stroke center Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Excluded	Conceptual Dx error definition: misdiagnosis meant that an acute stroke was not considered in the differential upon initial evaluation inthe emergency room Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Bourdon, 2020[123]	Patient type: Eye and Ear ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: a primary and secondary ophthalmic emergency office Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2020 to 2020	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: None: Total N: 500 Age: NR Male, n (%): 303 (61%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: ophthalmologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Branstetter, 2007	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 1999 to 2004	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Other: radiograph Total N: 65780 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: radiology Consultants involved: radiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Breen, 2017[179]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Unclear or NR	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: CRICO Dates: 2010 to 2014	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: Other: We excluded claims relating to obstetrics. Total N: 71 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Breidthardt, 2019	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 6 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR Named data source: Dates: 2009 to 2012	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Symptom (e.g., dizziness): addressing urgent vs. nonurgent abdominal pain Total N: 1038 Age: NR Male, n (%): 531 (51) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Unclear or NR Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Broadley, 2003	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2000 to 2002	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 284 Age: Mean, 72 Range, 20-100 Male, n (%): 138 (56%) Race, n (%): NR	Care delivered entirely within ED: Stroke Unit Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Calder, 2010[58]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 2 Annual ED volume: >=80,000 Ownership: Public	Country: Canada Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2004 to 2004	Disease specificity: Not restricted by diseases Diseases studied: Other Other inclusion criteria: Multiple: Cognitive impairment due to an organic brain process or major psychiatric illness and no available substitute decision maker; critically ill or in too much distress to be capable of informed consent; unable to complete a telephone interview in English or French (or their substitute decision maker was unable); dis- charged home and did not have a telephone or other- wise unavailable for follow-up 2 weeks later (as deter- mined at enrolment). Total N: 503 Age: Median, 57 Range, 18-98 Male, n (%): 249 (50%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: Multiple definitions Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Calder, 2021	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 6 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: prospective data by electronic health record databases Dates: 2013 to 2018	Disease specificity: Multiple diseases Diseases studied: Arrythmias Other inclusion criteria: Multiple: We included discharged ED patients who met the following criteria: (1) discharged from the ED with a primary diagnosis of acute heart failure, recent-onset atrial fibrillation, or syncope; (2) assigned a Canadian Triage and Acuity Scale (CTAS; a validated Total N: 4741 Age: Mean, 70.2 Male, n (%): 2428 (51%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: We adapted our adverse event determination method from the Harvard Medical Practices study. 1) Dx error: not acting on documented signs, symptoms, laboratory tests, or imaging or not ordering an indicated diagnostic test; for example, missing pneu Harms severity: A single reviewer (L.A.C.) determined severity for all adverse events, using a priori–created classification systems in accordance with previous adverse event studies. 10,15 We classified adverse event severity from a patient perspective as asymptomatic lab Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Calic, 2016[195]	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2011 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 115 Age: Mean, 66 Male, n (%): 59 (51) Race, n (%): NR	Care delivered entirely within ED: neurology Consultants involved: neurology Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (broken out)	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Carlton, 2015[69]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Public	Country: UK Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2012 to 2013	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Symptom (e.g., dizziness): primary complaint of chest pain and for whom the treating physician in the ED determined that delayed (6 hours post attendance) troponin testing as required for the assessment of an ACS Total N: 912 Age: Mean, 58.0 Male, n (%): 546 (59.9) Race, n (%): White, 869 (95.3)	Care delivered entirely within ED: ED only Consultants involved: cardiology Non-physicians involved: Unclear or NR Non-EM physicians involved: acute general internist Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Catapano, 2017[176]	Patient type: orthopaedic care Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 20,000 to 39,999 Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2016 to 2016	Disease specificity: Not restricted by diseases Diseases studied: Other Other inclusion criteria: Other: in absence of attending radiologist Total N: 23,455 Age: Mean, 36.7 Male, n (%): 184 (1%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: radiologist Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Excluded	Conceptual Dx error definition: A radiology resident with five years' experience in musculoskeletal radiology reviewed the discrepancy register and divided the cases as follows: (i) false negatives related to missed fractures, including cases wrongly interpreted as negative, those with Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Caterino, 2012[21]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Private, not for profit	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2006 to 2009	Disease specificity: Multiple diseases Diseases studied: MULTI-INFECTION Other inclusion criteria: None: incarcerated, non-English speaking, seen within prior 7 days for same condition, previously enrolled in the study, evaluated by the trauma team, lacked ability to give consent when no proxy was available Total N: 103 Age: Range, 55 subjects 65-74, 34 subsubjects 75-84, 14 subjects >= 85 Male, n (%): 49 (47.6) Race, n (%): White, 83 (80)	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: Graber 2005

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Chan, 2019[150]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2012 to 2017	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: Symptom (e.g., dizziness): Patients with greater than 48 h of pain were excluded from this analysis as these patients would have either chronic scrotal pain or perceived to have low testicular salvage potential, which may result in bias toward a disproportionately higher orchiectomy rate. Total N: 46 Age: NR Male, n (%): 46 (100) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Nurses Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Chan, 2020[125]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2015 to 2017	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Other: Patients with a positive pulmonary embolism on computed tomography pulmonary angiogram, high-probability ventilation perfusion scan, or intermediate-probability VQ scan with positive DVT on duplex ultrasound Total N: 302 Age: Range, 38.1% =85 Male, n (%): 100 (33%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Diagnosis more than 7 days after symptom onset Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Chang, 2019[169]	Patient type: General ED Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Mixed Named data source: Dates: 2013 to 2015	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Unclear or NR: Total N: 208 Age: Mean, 29 Male, n (%): 110 (53%) Race, n (%): NR	Care delivered entirely within ED: ED and Surgery Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: Unclear or NR Harms severity: Unclear or NR Causal taxonomy used: Unclear or NR
Chen, 2016[197]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2012 to 2013	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Other: Appendectomy Total N: 249 Age: Mean, 35.1 Male, n (%): 113 (45.4) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Cheong, 2014[34]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm) Named data source: Discharge Abstract Database (DAD) Dates: 2004 to 2010	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 41,405 Age: Range, 0-17 Male, n (%): 24429 (59) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Choinski, 2021	Patient type: Unclear Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Multiple	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: Westlaw Dates: 1987 to 2019	Disease specificity: Multiple diseases Diseases studied: AAD Other inclusion criteria: None: Total N: 346 Age: Mean, 56 Range, 3-84 Male, n (%): 256 (74) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Chompoopong, 2017[182]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2001 to 2009	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: 82 (3.4%) patients were admitted due to their comorbidities, which were likely not a result of a stroke and were also excluded Total N: 2303 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Christenson, 2004	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2000 to 2001	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Symptom (e.g., dizziness): chest pain Total N: 1819 Age: Mean, 58.2 Male, n (%): 1051 (57.8%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (broken out)	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Chu, 2015[73]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: California State Inpatient Database and State ED Database Dates: 2005 to 2011	Disease specificity: Single disease Diseases studied: Endocarditis Other inclusion criteria: Symptom (e.g., dizziness): with a first recorded diagnosis of ischemic stroke or TIA. Total N: 38485 Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Chung, 2009[22]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: West Urban/rural: Unclear or NR	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2005 to 2007	Disease specificity: Multiple Diseases Diseases studied: Other Other inclusion criteria: : excluded patients with incomplete records Total N: 112 Age: Range, '102 adults and 10 children' Male, n (%): 72 (64%) Race, n (%): NR	Care delivered entirely within ED: Other location (specify) Consultants involved: Radiologists only, did not study EM providers Non-physicians involved: Emergency physicians only Non-EM physicians involved: only studied radiologists, not EM providers Trainees involved: Included trainees How left without treatment was handled:	Conceptual Dx error definition: discrepancy between resident and attending radiologist reading of trauma CT torso Conceptual harms definition: Changed in management as a result of discrepancy Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Cifra, 2020[130]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: the Agency for Healthcare Research and Quality's HCUP Dates: 2010 to 2011	Disease specificity: Single disease Diseases studied: Sepsis Other inclusion criteria: None: Total N: 1945 Age: Mean, 8.2 Male, n (%): 1035 (52.9) Race, n (%): White, 651 (35.2) Black/African American, 330 (17.9)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: the Symptom-Disease Pair Analysis of Dx error (SPADE) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Comolli, 2020[129]	Patient type: Ear, nose, and throat ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2013 to 2013	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Symptom (e.g., dizziness): Patients with vertigo Total N: 286 Age: Mean, 49 Male, n (%): 129 (45.1) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Internal medicine, surgery, shock room, neurology Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Conti, 2003[112]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Unclear or NR Numerator: Numerator and denominator Named data source: NA Dates: 1999 to 2001	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: Symptom (e.g., dizziness): Patients presenting with chest pain and normal/non-diagnostic ECG Total N: 306 Age: Mean, 59.7 Male, n (%): 200 (65) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Serum cardiac injury markers as compared to scan strategy in diagnosing CAD in ED patients with chest pain and non-diagnostic ECG Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Copson, 2020[209]	Patient type: Other ED (specify) Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: Unclear or NR to Unclear or NR	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 26 for specialist obstetric and 19 for general hospital Age: Mean, 31 for specialist obstetric and 29 for general hospital Male, n (%): 0 (0) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Included consultants (specify) Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Corral Gudino, 2003[111]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2001 to 2002	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Multiple: with a definite diagnosis of PE(probability of suffering from the disease higher than 80%) Total N: 58 Age: Mean, 71.5 (70, 76) Male, n (%): 25 (43%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Crosby, 2013[16]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Seen by surgeon or seen by ED physician Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2005 to 2008	Disease specificity: Multiple diseases Diseases studied: Other Other inclusion criteria: Multiple: Exclusion criteria include patients who left without being seen, patients seen by pediatricians for surgical complaints prior to systems changes, polytrauma, major head injury, isolated spine injury, patients sent from triage directly to an ambulatory clinic for low-acuity complaints, incomplete data on chart review and inappropriate coding Total N: 2415 Age: Range, 1 month -18 year Male, n (%): 1311 (54) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Surgeons Non-physicians involved: Included other ED clinicians (specify) Non-EM physicians involved: Surgeon Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: misdiagnosis /return ED visit w/in 72 hours for same condition Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Czolgosz, 2019[142]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Private, not for profit	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2012 to 2014	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: Transfer > 12 hours after admission, direct admission from other facility (no ED care), Non-medical (surgical) admissions, Direct admissions to pICU from ED (no medical floor), duplicate patient records, NICU admissions Total N: 164 Age: Median, 30 months Range, 0 to 19 Male, n (%): 86 (52.4%) Race, n (%): NR	Care delivered entirely within ED: ED to PICU Consultants involved: PICU Non-physicians involved: pediatricians and Nurse practitioners Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Daverio, 2016[201]	Patient type: pediatric Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2003 to 2012	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): receiving imaging study Total N: 90 Age: Median, 7.4 Male, n (%): 34 (38%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: neurology Non-physicians involved: Unclear or NR Non-EM physicians involved: neurology, anesthesiology Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Degheim, 2019[149]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2015 to 2016	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: All STEMI catheterization laboratory activations Total N: 375 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: cardiac catheterization lab Consultants involved: Cardiologist Non-physicians involved: EMTs Non-EM physicians involved: cardiologists Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Cardiac catheterization lab (activated by EMT or ED physician) cancelled by interventional cardiologist Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
DeVon, 2020	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 5 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Unclear or NR Comparison group: None Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator Named data source: Dates: 2011 to 2014	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: None: Total N: 975 Age: Mean, 60 Male, n (%): 609 (62.5) Race, n (%): White, 674 (69.1)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Drapkin, 2020[173]	Patient type: Psychiatric ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Intermountain Electronic Data Warehouse Dates: 2009 to 2014	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 1678 Age: Mean, 9.9 Range, 1 to 17 Male, n (%): 923 (55) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Emergency clinicians only Non-physicians involved: Nurses, patient care technicians Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: We defined cases of missed appendicitis as a patient who presented to the pediatric ED within the 7 days preceding their diagnosis of acute appendicitis when the initial visit could plausibly be related to the ultimate diagnosis of appendicitis. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Dubosh, 2015[11]	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Multiple	Country: US Region, if US: Other Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator Named data source: State ED Databases and State Inpatient Databases Dates: 2006 to 2012	Disease specificity: Multiple diseases Diseases studied: Other Other inclusion criteria: Multiple: We excluded patients with trauma, those who left the hospital against medical advice, those who were transferred to another acute care facility, those who died at the index ED visit, and out-of-state residents. Total N: 2,101,081 Age: Mean, 57 Median, 57 Male, n (%): 1008519 (48) Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: ED revisit with serious neurological condition or in-hospital death within 30 days of treat-and-release ED visit for non-specific headache or back pain Harms severity: Unclear or NR Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Dubosh, 2019[154]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: State ED Databases and State Inpatient Databases Dates: 2006 to 2012	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: Using the ED visit data from the 6 states, included: ED patients (18 years) discharged (i.e., treat and release) to home or a nonacute facility with a primary discharge diagnosis of nonspecific headache or back pain (ICD codes)excluded: patients with trauma, those who left the hospital against medical advice, those who were transferred to another acute care facility, those who died at the index ED visit, and out-of-state residents. Similar to previous research on revisits and readmissions, additional ED discharges for headache or back pain within a 30-day period from the index ED visit were not considered, whereas subsequent ED visits occurring after 30 days were counted as an index ED visit if they met the inclusion criteria. Total N: Headache , Back pain: 2101081, 1381614 (Table E1) Age: Median, 39,44 Male, n (%): 527051, 592288 (25.2, 43.1) Race, n (%): White, 1015261,724213 (48.3,52.4) Black/African American, 391544,247768 (18.6,17.9)	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: MisDx-Related Harms (DNT, 2009) Harms severity: None Causal taxonomy used: Kachalia 2007

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Dupond-Athénor, 2021	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 9 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 1997 to 2017	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: None: Total N: 60 Age: Median, 2.2 Male, n (%): 60 (100) Race, n (%): NR	Care delivered entirely within ED: surgery Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
England, 2006[100]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 1999 to 2004	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 311 Age: Range, 1 to 15 Male, n (%): 183 (59%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Faiz, 2014[30]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Unclear or NR Named data source: NA Dates: 2009 to 2010	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Excluded patients with intracerebral hemorrhage, TIA, in-hospital strokes, and stroke mimics. Total N: 290 Age: Median, 75 Male, n (%): 153 (52.8) Race, n (%): NR	Care delivered entirely within ED: Stroke unit Consultants involved: Neurologists Non-physicians involved: Nurse Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Time from admission to being evaluated by a nurse, to being examined by a doctor, to initiation of computed tomography scan Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Fasen, 2020[131]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2019 to 2019	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients with a clinical diagnosis of acute ischemic stroke who underwent CTA to evaluate LVO of the proximal anterior circulation; excluded patients with suspected posterior circulation symptoms or occlusion Total N: 520 Age: Mean, 72 Range, 19 to 100 Male, n (%): 255 (49) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: neuroradiologists, non-neuroradiologists, or senior radiology residents Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed LVO at initial interpretation Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Fernholm, 2019[145]	Patient type: NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: nationwide patient-reported harm database Dates: 2011 to 2016	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Ferree, 2016[1]	Patient type: General ED Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Other (specify) Look back or look forward analysis: Data source: Other (specify) Numerator: Numerator and denominator Named data source: Dutch National Trauma Database (DNTD), electronic health record Dates: 2007 to 2012	Disease specificity: Multiple diseases Diseases studied: Other Other inclusion criteria: Mechanism (e.g.,, multi-trauma): inclusion: age=>16 years,, ISS=>16, body regions involved=>2, exclusion: dead on arrival, transferred <24h Total N: 172 Age: Mean, 44 Male, n (%): 118 (69%) Race, n (%):	Care delivered entirely within ED: Other location (specify) Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: %requiring surgical intervention Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Filippi, 2008[23]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: Northeast Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: First-year resident interpretation vs upper-level residents, residents vs attending radiologists Look back or look forward analysis: Unsure Data source: Multiple Numerator: Numerator and denominator Named data source: Dates: 2006 to 2007	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: None: Total N: Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiology Non-physicians involved: Emergency physicians only Non-EM physicians involved: Included physicians with other training (specify) Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: a major discrepancy/error was 'one that could potentially adversely affect outcome, change management, or incur disability or mortality' Harms severity: None Causal taxonomy used: None
Fordyce, 2003	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Unsure Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2001 to 2001	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 1935 Age: NR Male, n (%): (47.6%) Race, n (%): White, 989 (51.1) Black/African American, 271 (14.0)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: nurses Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Freedman, 2014[37]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2008 to 2010	Disease specificity: Multiple Diseases Diseases studied: Other Other inclusion criteria: None: Patients who developed constipation during their hospitalization were excluded. Total N: 3685 Age: Mean, 6.6 Male, n (%): 1842 (50) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: Misdiagnosis was defined as an alternative diagnosis assigned within 7 days, meeting all the following criteria: (1) resulted in hospitalization or outpatient procedure; (2) required a surgical or radiologic intervention(eg, air enema, bone marrow Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Freedman, 2017[17]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 23 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Abdominal radiograph vs Non abdominal radiograph performed Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2004 to 2015	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: Multiple: Visit represented revisit within 7 days (n = 4984)Transferred (n = 2274)Significant misdiagnosis code assigned at index visit (n = 1367) Unable to track for 7 days pre/post visit (n = 906) Total N: 282 225 Age: Median, Abdominal radiograph performed7 (3, 11); Abdominal radiograph not performed 3 (0, 7) Male, n (%): (Abdominal radiographs performed 48.2 abdominal radiographs not performed 46.8) Race, n (%): (44.6 for abdominal radiograph performed, 30.4 for abdominal radiograph not performed) (24.0 for abdominal radiograph performed, (32.4) for abdominal radiograph not performed)	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Gaither, 2016[202]	Patient type: General ED Patient age: Both adults and children Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Case series Comparison group: Hospital vs different health system Look back or look forward analysis: Unsure Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: e LexisNexis Academic legal search database Dates: 1985 to 2015	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: Other: Cases that were for worker's compensation, disability, or against another person or institution other than a hospital were excluded from the analysis Total N: 53 Age: Mean, 15.4 Range, 2 to 47 Male, n (%): 53 (100) Race, n (%): NR	Care delivered entirely within ED: Other location (specify) Consultants involved: Urologist Non-physicians involved: Nurse Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Gallagher, 2006[13]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Randomized controlled trial Comparison group: Concurrent control Look back or look forward analysis: Not a cohort study Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2002 to 2004	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Symptom (e.g., dizziness): inclusion: atraumatic abdominal pain Total N: 160 Age: Mean, 45.5 Male, n (%): 55 (34%) Race, n (%): Black/African American, 42 (26)	Care delivered entirely within ED: Unclear or NR Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Clinically important Dx error was defined as any disagreement between the initial provisional and final diagnosis that might reasonably be expected to have an adverse impact on the patient's health status. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Garfield, 2004[108]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2002 to 2003	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 124 Age: Male, n (%): 75 (60) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Surgery Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Gargano, 2009[83]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 15 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Midwest Urban/rural: Multiple settings	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Michigan Acute Stroke Care Overview and Treatment Surveillance System Dates: 2002 to 2002	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Acute stroke or transient ischemic attack admissions Total N: Age: Male, n (%): 881 (48.5) Race, n (%): White, 1414 (73.6) Black/African American, 340 (17.7)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: door-to-doctor and door-to-imaging times Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Gaughan, 2009[82]	Patient type: General ED Patient age: Unclear or NR Teaching status: Non-academic/Non-teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: UK Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2000 to 2006	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients undergoing surgery for emergency acute aortic aneurysm Total N: 98 Age: Median, 74 Range, 57 to 88 Male, n (%): 76 (77.6) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Misdiagnosis, time from presentation to diagnosis Conceptual harms definition: 30-day mortality Harms severity: None Causal taxonomy used: None
Gergenti, 2019[153]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: Unclear or NR Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2013 to 2014	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 174 Age: Mean, 42.9 Range, 0-88 Male, n (%): 58 (33) Race, n (%): White, 153 (88) Black/African American, 10 (6)	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Geyer, 2013[214]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2003 to 2005	Disease specificity: Single disease Diseases studied: OTHER MULTIPLE Other inclusion criteria: Other: A total of 206 patients were excluded because they did not have a WBCT(n=69) or documentation was incomplete (n =137) Total N: 336 Age: Mean, 42 Male, n (%): 259 (77.1) Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Ghobadi, 2021	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 14 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2014 to 2016	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Process (e.g., left without treatment): >50 yo and had d-dimer test Total N: 10534 Age: Mean, 64.9 Male, n (%): 3887 (36.9) Race, n (%): White, 6605 (62.7) Black/African American, 1580 (15)	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Gleason, 2020[115]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 3 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: Other Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2019 to 2019	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Symptom (e.g., dizziness): People aged 18 and older who were seen at the ED within the past seven days with one or more common chief complaints (chest pain, upper back pain, abdominal pain, shortness of breath/cough, dizziness, and headache) and one or more chronic conditions (hypertension, diabetes, history of stroke, arthritis, cancer, heart disease,osteoporosis, depression, and/or chronic obstructive lung disease) were eligible to join the study. Total N: 59 Age: Mean, 49.88 Range, 21-83 Male, n (%): (36%) Race, n (%): White, 31 (53%) Black/African American, 24 (41%)	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Gold, 2020[119]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator only (error/harm) Named data source: IBM MarketScan Research Databases Dates: 2011 to 2015	Disease specificity: Single disease Diseases studied: Pneumonia Other inclusion criteria: Other: We also excluded patients with insurance plans that did not contribute prescription drug data to MarketScan (n = 886), for a final cohort of 3983 patients. Total N: 3938 Age: Median, 60 for +, 45 for - Male, n (%): 1910 (48.5) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Gouin, 2006[103]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Public	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Unsure Data source: Other (specify) Numerator: Numerator and denominator Named data source: Dates: 2001 to 2002	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Outside films as well as ultrasonograms, magnetic resonance imaging, computed tomography, and bone scan studies were excluded. Total N: Age: Mean, 6 Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: Included physicians with other training (specify) Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Discrepancy between emergency physician and radiologist read of plain films Conceptual harms definition: Discrepancy in radiology report leading to a change in patient management Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Goulet, 2015[70]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 4 Annual ED volume: 60,000 to 79,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2007 to 2011	Disease specificity: Not restricted by disease Diseases studied: OTHER MULTIPLE Other inclusion criteria: Unclear or NR: Total N: 1279 Age: Mean, 79 Male, n (%): 652 (51) Race, n (%): NR	Care delivered entirely within ED: ED to hospital Consultants involved: Included consultants (specify) Non-physicians involved: Included other ED clinicians (specify) Non-EM physicians involved: Included physicians with other training (specify) Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed Opportunity (Singh 2014) Conceptual harms definition: MisDx-Related Harms (DNT, 2009) Harms severity: Death within 72 hours of hospital admission Causal taxonomy used: Unclear or NR
Goyal, 2020[116]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 7 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Pediatric Emergency Care Applied Research Network (PECARN) Registry Numerator: Numerator and denominator Named data source: Pediatric Emergency Care Applied Research Network (PECARN) Registry Dates: 2014 to 2018	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 7,417 Age: Male, n (%): 4458 (60.1) Race, n (%): White, 4057 (54.7)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Graff, 2006[99]	Patient type: General ED Patient age: Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Historical comparisons Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Connecticut Medicare Part A Dates: 1992 to 2001	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients with a principal diagnosis of acute MI Total N: 7888 Age: Mean, 79.3 Male, n (%): 3707 (47) Race, n (%): White, 7391 (93.7)	Care delivered entirely within ED: Unclear or NR Consultants involved: cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Admission diagnosis differed from final diagnosis Conceptual harms definition: Mortality Harms severity: None Causal taxonomy used: None
Graff, 2014[29]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: NA Dates: 1997 to 2007	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: None: Total N: 295758 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: ACS cases with 1) ED evaluation within the previous 21 days not resulting in admission; 2) chief complaint for the first ED visit consistent with ACS, that is, either chest pain or chest pain equivalent (shortness of breath, palpitation, syncope, unexpla Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Grewal, 2015	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2006 to 2011	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): received CT imaging Total N: 17164 Age: Mean, 63 Male, n (%): (38%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Groot, 2016[71]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2011 to 2012	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: patients with suspected STEMI undergoing invasive coronary angiography Total N: 827 Age: NR Male, n (%): 601 (73%) Race, n (%): NR	Care delivered entirely within ED: catheterization laboratory Consultants involved: Unclear or NR Non-physicians involved: EMS nurse Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: false-positive STEMI activation (patients referred for emergency invasive coronary angiography with suspected STEMI with no visible culprit stenosis on invasive coronary angiography) Conceptual harms definition: 30-day and 1-year all cause mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Grosmaitre, 2013[36]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single health system, multiple EDs Number of EDs involved: 4 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2004 to 2008	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Admitted with a main diagnosis of STEMI Total N: 255 Age: Mean, 84.6 Male, n (%): 95 (27.3) Race, n (%): NR	Care delivered entirely within ED: cardiology department Consultants involved: Unclear or NR Non-physicians involved: triage nurse Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: waiting time (time from registration at reception desk to the time of first medical contact) and time for diagnosis and decision making (time between the first medical observation and that of the note in which therapeutic strategy chosen was described for Conceptual harms definition: 1-month mortality Harms severity: None Causal taxonomy used: None
Guillan, 2012[43]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2004 to 2011	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients treated with IV-tPA Total N: 606 Age: Mean, 72 Male, n (%): 292 (48.2) Race, n (%): NR	Care delivered entirely within ED: Stroke unit Consultants involved: Neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: neurologists Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Diagnosis of a stroke mimic was established when clinical or paraclinical (i.e., radiological) evidence of an alternative diagnosis to stroke was ascertained. Conceptual harms definition: Complications of IV-tPA Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Gurley, 2018[211]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Case series Comparison group: None Look back or look forward analysis: Not a cohort study Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: CRICO Comparative Benchmarking System Dates: 2009 to 2012	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 845 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: NAIC Scale (9-Tier) Causal taxonomy used: Kachalia 2007
Hallas, 2006[102]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Rural	Study design: Case-control Comparison group: A control group consisting of 100 patients was randomly selected from all patients who were correctly diagnosed with a fracture on their first visit to the ED during the two year period. Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2002 to 2004	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: None: Total N: 161 Age: Mean, 44 Male, n (%): 77 (48) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologist and surgery Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Guly HR: Dx errors in an accident and ED. Emerg Med J 2001, 18:263-269 Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Hansen, 2007[94]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2000 to 2004	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients with definite AAS, confirmed by imaging, operative findings, or postmortem examination Total N: 66 Age: Mean, 62 Range, 19 to 87 Male, n (%): 50 (76) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: incorrect initial misdiagnosis Conceptual harms definition: major bleeding or in-hospital mortality Harms severity: None Causal taxonomy used: None
Hansen, 2016[198]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Multiple	Country: Australia Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Unclear or NR Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: EMER Dates: 2012 to 2015	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Non-specific com- plaint about nursing management and was excluded Total N: 150 Age: NR Male, n (%): 76 (51) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: nurse Non-EM physicians involved: Radiology, General Surgery Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Harbison, 2003[113]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2000 to 2000	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients referred to stroke service Total N: 487 Age: Mean, 72 Range, 22 to 98 Male, n (%): 234 (48) Race, n (%): NR	Care delivered entirely within ED: transferred to stroke service Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Accuracy of stroke diagnosis Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Harris, 2011[49]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 24 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Multiple Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm) Named data source: International Registry of Acute Aortic Dissection Dates: 1996 to 2007	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: acute onset type A IV-tPA Total N: 894 Age: Median, 62 Male, n (%): 600 (67.1) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: time from the initial ED presentation to diagnosis Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Hautz, 2019[148]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2015 to 2016	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: All patients of 18 years or older hospitalized from the emergency room (ER) to any internal medicine (IM) ward were included in the study and followed up until hospital discharge or death. Patients were excluded if admitted to IM for palliative care or for social reasons or if they presented with an acute traumatic injury and were admitted to IM for reasons of age, comorbidities, or surgical ward crowding Total N: 755 Age: Mean, 65.14 Male, n (%): 433 (57.3) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: MisDx-Related Harms (DNT, 2009) Harms severity: None Causal taxonomy used: Kachalia 2007
Heckmann, 2004[110]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Unclear or NR Numerator: Numerator and denominator Named data source: Dates: 2002 to 2003	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients suspected of stroke Total N: 462 Age: Mean, 64.2 Range, 17 to 94 Male, n (%): 265 (57%) Race, n (%): NR	Care delivered entirely within ED: stroke unit Consultants involved: neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Admitted to stroke unit, but did not have a stroke Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Heitmann, 2016[194]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: <20,000 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: 3 cohorts Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2014 to 2014	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 1440 Age: Mean, 60 Male, n (%): 749 (52) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Hendriks, 2015[63]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Ambidirectional Cohort Study Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator only (error/harm) Named data source: Dates: 2007 to 2012	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 1102 Age: Mean, 25 Range, 2 to 94 Male, n (%): 572 (52%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: surgery Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: diagnostic test accuracy (false positive) Conceptual harms definition: Unclear or NR Harms severity: Unclear or NR Causal taxonomy used: Unclear or NR

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Hillinger, 2017[199]	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 9 Annual ED volume: Unclear or NR Ownership: Multiple	Country: Multiple Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator only (error/harm) Named data source: Dates: 2006 to 2013	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Symptom (e.g., dizziness): Total N: 2795 Age: Median, 62 Male, n (%): 1901 (68) Race, n (%): NR	Care delivered entirely within ED: cardiology Consultants involved: Emergency clinicians only Non-physicians involved: Unclear or NR Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: Early diagnostic uncertainty in the ED was quantified by assessing clinical judgment of the treating ED physician. Clinical judgment was quantified by a visual analogue scale (VAS) for ACS probability ranging from 0to 100 %. The treating ED physician Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Hochberg, 2011[47]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Randomized controlled trial Comparison group: Concurrent control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2007 to 2009	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): Included all head CTA examinations ordered after hours by ED physicians; excluded if resident indicated that the preliminary interpretation was aided by the "back-up" neuroradiology attending physician or fellow on call Total N: 83 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: radiology resident Non-physicians involved: Unclear or NR Non-EM physicians involved: radiology resident Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Agreement between resident preliminary CTA interpretation and final DSA results Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Hoekstra, 2009[78]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 12 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Controlled trial Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Optimal Cardiovascular Diagnostic Evaluation Enabling Faster Treatment of MI Dates: 2006 to 2008	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Symptom (e.g., dizziness): Patients presenting to the ED with chest pain and moderate to high risk for adverse clinical outcomes Total N: 1830 Age: Male, n (%): Race, n (%): NR	Care delivered entirely within ED: Catheterization laboratory Consultants involved: cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: STEMI detected with 80-lead ECG and not detected with 12-lead ECG Conceptual harms definition: all-cause mortality, recurrent MI, percutaneous coronary intervention, coronary artery bypass grafting surgery, and rehospitalization for coronary complications at 30 days Harms severity: None Causal taxonomy used: None
Holland, 2015[72]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: one transfer center serves 2 hospitals; unclear how referring hospitals are related Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2012 to 2013	Disease specificity: Multiple diseases Diseases studied: Other Other inclusion criteria: Other: All patient transfer requests to the adult neurosurgical service Total N: 1323 Age: Male, n (%): 650 (49.1) Race, n (%):	Care delivered entirely within ED: transferred to neurosurgical service Consultants involved: neurosurgeons Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: diagnostic concordance Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Huang, 2019[156]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Unclear or NR Named data source: Dates: 2008 to 2017	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: Other: Neonatal torsion patients were excluded from this study. Two patients, both of whom were successfully salvaged, did not receive any ultrasound examinations before surgical intervention and were excluded from the analysis. Total N: 133 Age: Range, 0-20 Male, n (%): 133 (100) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Humphries, 2018	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2008 to 2013	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: : Consecutive British Columbians (≥20 years)who presented to the ED of these two hospitals andwere assessed for a chief complaint of ischemic chestpain between May 1, 2008, and March 30, 2013, wereincluded. Subjects were excluded if the chest pain wasunlikely to be ischemic in nature Total N: 7272 Age: NR Male, n (%): 4339 (60%) Race, n (%): NR	Care delivered entirely within ED: follows after admission Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Husabø, 2020[133]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 24 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2015 to 2017	Disease specificity: Single disease Diseases studied: Sepsis Other inclusion criteria: None: Total N: 1559 Age: Mean, 67.0 Median, 71 Male, n (%): 800 (51.3) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm) Named data source: National Reporting and Learning System Dates: 2013 to 2015	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: 2288 Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Society to Improve Diagnosis in Medicine Conceptual harms definition: None Harms severity: World Health Organization International Classification for Patient Safety Causal taxonomy used: Carson-Stevens 2015

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Jaffe, 2020	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2016 to 2018	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Multiple: Age <18 (n=6)• LKW >8hrs• 4.5 hours < LKW < 8 hours and NIHSS≤ 6 (n = 187) Total N: 495 Age: Median, 73 Male, n (%): 248 (50) Race, n (%): White, 358 (72.3) Black/African American, 39 (7.9)	Care delivered entirely within ED: Unclear or NR Consultants involved: neurology, radiology Non-physicians involved: pharmacist, CT technologist Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Jiménez Castro, 2007[93]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2003 to 2005	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: None: Patients who presented with symptoms of acute pulmonary embolism and had pulmonary embolism confirmed by objective testing Total N: 397 Age: Mean, 69 Male, n (%): 177 (45) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: Mortality during the first 3-months after diagnosis and treatment Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kamal, 2017[187]	Patient type: neurology Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 1422 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator Named data source: Get With The Guideline Stroke data base Dates: 2012 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Multiple: Total N: 55296 Age: Mean, 71,72,71 Male, n (%): 27825 (50%) Race, n (%): (70.30, 72.93, 68.46) (14.65, 13.99, 16.54)	Care delivered entirely within ED: ED only Consultants involved: neurologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Kargl, 2019[158]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2014 to 2015	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: None: Total N: 2316 Age: Range, 1-17 Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: Pediatric surgeons Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kerber, 2006	Patient type: General ED Patient age: Adults only Teaching status: Non-academic/Non-teaching Hospital setting: Multi-center study Number of EDs involved: 7 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2000 to 2003	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): dizziness, vertigo, or imbalance (isolated or combined with other symptoms) Total N: 1666 Age: NR Male, n (%): 603 (36%) Race, n (%): White, 566 (34%)	Care delivered entirely within ED: ED only Consultants involved: sometimes neurologists (rarely) Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Kerber, 2014	Patient type: General ED Patient age: Adults only Teaching status: Non-academic/Non-teaching Hospital setting: Multi-center study Number of EDs involved: 6 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: South Urban/rural: Multiple settings	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2011 to 2012	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): dizziness symptoms Total N: 1245 Age: Median, 61.8 Male, n (%): (39%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kerkman, 2020[124]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single health system, multiple EDs Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: data set Numerator: Numerator and denominator Named data source: NA Dates: 2015 to 2016	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients with an ACS identified as STEMI Total N: 787 Age: Mean, 61(men)-68(women) Male, n (%): 558 (71) Race, n (%): NR	Care delivered entirely within ED: EMS Consultants involved: Cardiologist Non-physicians involved: Nurse, ambulance staff Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: System delay time (time from ambulance dispatch until reaching the patient and recording the first ECG, from STEMI diagnosis to arrival at the pPCI center, from pPCI center to arterial access and from arterial access to balloon inflation in the culprit ar Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Kim, 2007[90]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2000 to 2006	Disease specificity: Single disease Diseases studied: Pneumonia Other inclusion criteria: None: Total N: 109 Age: Mean, 5 Range, 0.3 to 19 Male, n (%): 58 (53%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kline, 2007[92]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2002 to 2005	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Other: All chest computed tomographic angiography orders performed in the hospital (both inpatient and ED patients); included patients with a CTA interpretation as positive for a filling defect consistent with acute PE, and a systolic blood pressure consistently greater than 100 mm Hg; excluded patients with a comorbidity with a predicted 6-month mortality > 50%, treatment of any thrombosis during the same hospitalization; >24 hours elapsed since start of heparin therapy; overread of a initial positive CTA interpretation as negative for PE and no further imaging Total N: 207 Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: ED + n medical, surgical, and obstetric wards, and all adult intensive care units. Consultants involved: radiologists, cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delayed diagnosis (pulmonary embolism was diagnosed by CTA ordered up to 48 hours after the patient left the ED) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kline, 2009[20]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Private, not for profit	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Randomized controlled trial Comparison group: Concurrent control Look back or look forward analysis: Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2005 to 2007	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Other: Cocaine use or elopement from care Total N: 369 Age: Mean, 46 Male, n (%): (Control 39, Intervention 36) Race, n (%): (Control 44, Intervention 45) Black/African American, Control 57, Intervention 55	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Triage nurse Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Ko, 2018	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 179 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Mutliple Numerator: Numerator and denominator Named data source: Health Information National Ambulatory Care Reporting System Database, Canadian Institute for Health Information-Discharge Abstract Database, Ontario Health Insurance Physician Claims Database, Ontario Drug Benefit Database, and the Ontario Registered Pe Dates: 2008 to 2014	Disease specificity: Not restricted by diseases Diseases studied: MI Other inclusion criteria: Symptom (e.g., dizziness): included: chest pain (as intake symptom or discharge diagnosis)We excluded patients who had scheduled visits to EDs,transferred in from other acute care hospitals, or had anassessment in pediatric, psychiatric, and very small EDs (<30chest pain cases per year). We also excluded patients whowere not Ontario residents, had invalid Ontario healthcarenumbers, or invalid dates of assessment because of the inability to examine their outcomes Total N: 498291 Age: Mean, 59 Male, n (%): (46.7%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: MisDx-Related Harms (DNT, 2009) Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kondis, 2017[186]	Patient type: pediatric ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2006 to 2011	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: Multiple: Inclusion criteria included age 0 to 6 months, discharge diagnosis including “fracture,” “broken” (or break), or “trauma” or any child abuse diagnosis or chief complaint of “fussy” or “crying” as documented in the electronic medical record by the triage nurse Total N: 18 Age: Male, n (%): (66%) Race, n (%): White, 6 (33) Black/African American, 12 (66)	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Nurses Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Kornblith, 2013[7]	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator Named data source: Dates: 2007 to 2011	Disease specificity: Multiple Diseases Diseases studied: Other Other inclusion criteria: Other: patients younger than 18 years and incarcerated patients were excluded Total N: 201 Age: Mean, 53.8 Male, n (%): 138 (68.7) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: triage nurse Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: Delayed diagnosis Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Kuruvilla, 2011[60]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Young Stroke Registry Dates: 2001 to 2006	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients with a confirmed diagnosis of ischemic stroke who were seen at the outpatient stroke clinic of a university medical center Total N: 57 Age: Mean, 38.1 Male, n (%): 23 (40.4) Race, n (%): White, 40 (70) Black/African American, 16 (28)	Care delivered entirely within ED: Unclear or NR Consultants involved: vascular neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Patients were given a non-stroke diagnosis and either admitted to the hospital or discharged from the ED Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Ladner, 2015	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2011 to 2014	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: stroke alert Total N: 124 Age: Mean, 11.2 Male, n (%): 63 (51%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Pediatric EM, Critical Care Medicine, Neurology, and Radiology Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Lastunen, 2021	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2014 to 2015	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Multiple: CT not performed n = 1009 Complicated appendicitis on CT n = 199 Normal CT scan n = 11 Other pathology seen on CT (no appendicitis) n = 6 No contrast used in CT n = 38 Normal appendix on histopathological examination n = 7 Other pathology on histop Total N: 837 Age: NR Male, n (%): 402 (48) Race, n (%): NR	Care delivered entirely within ED: surgery Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Le, 2007	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Unclear or NR	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2004 to 2005	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Process (e.g., left without treatment): had head CT imaging done in the ED Total N: 3886 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: radiology Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Leeuwenburgh, 2014[25]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 6 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2010 to 2010	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 230 Age: Mean, 35 Range, 24 to 49 Male, n (%): 92 (40%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled:	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Lehtimäki, 2015	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator Named data source: hospital registries Dates: 2009 to 2013	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Multiple: Patients with chronic mesenteric ischemia (n = 25), Acute mesenteric ischemia secondary to iatrogenic injury (n = 3), aortic surgery or aortic dissection (n = 6), or tumor infiltration of the mesenteric arteries (n = 2) were excluded. Furthermore, five acute mesenteric ischemia patients without CT examination prior to treatment were excluded. Total N: 95 patients with 97 acute mesenteric ischemia events Age: Mean, 76 Male, n (%): 45 (47) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: radiologist Non-physicians involved: Emergency physicians only Non-EM physicians involved: Body imaging specialist, Angiologist, Other subspecialist Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Lever, 2013[44]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2008 to 2009	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients in whom stroke was diagnosed with MRI within first 24-48 hours of admission; also included patients with atypical symptoms who progressed to typical symptoms. Excluded with TIA or hemorrhagic stroke or in-hospital strokes, patients who were transferred, or diagnosed with stroke prior to ED arrival Total N: 189 Age: Mean, 70.4 Median, 73 Range, 20 to 99 Male, n (%): 95 (50.3) Race, n (%): White, 117 (61.9) Black/African American, 51 (27.0)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed ischemic stroke Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Liberman, 2018[168]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: HCUP Dates: 2005 to 2013	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: All hospitalized adult patients with a first-recorded discharge diagnosis of cerebral venous thrombosis Total N: 5966 Age: Mean, 44.2 Male, n (%): 1690 (28%) Race, n (%): White, 3229 (54%) Black/African American, 945 (16%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Probable misdiagnosis of cerebral venous thrombosis (an ED visit for headache or seizure in the 14 days before CVT hospitalization that did not result in an admission or transfer to another hospital) Conceptual harms definition: rates of intracerebral hemorrhage, in-hospital death, and unfavorable discharge disposition Harms severity: modified Rankin Scale Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Liberman, 2019[144]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 3 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2005 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients who were discharged with a first-recorded diagnosis of cerebral venous thrombosis Total N: 53 Age: Mean, 47.8 Male, n (%): 21 (40%) Race, n (%): Black/African American, 21 (44.7)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: Missed Opportunity (Singh 2014) Conceptual harms definition: Intracerebral hemorrhage, in-hospital death, discharge disposition, and modified Rankin Scale Harms severity: None Causal taxonomy used: Safer Dx (Singh)

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Liberman, 2019[155]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2014 to 2015	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: The cohort was subsequently filtered to only include those who had diagnostic images commonly read by emergency physicians and radiology trainees: all plain radiographs, computed tomography studies (CTs) of the brain or abdomen-pelvis, and ultrasounds of the abdomen, pylorus, and pelvis were included. We excluded all other imaging not commonly interpreted by emergency physicians, such as magnetic resonance imaging (MRI) and fluoroscopy. ED point-of-care ultrasounds were similarly excluded. Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: Radiology Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: Unclear or NR Harms severity: Unclear or NR Causal taxonomy used: Unclear or NR

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Liberman, 2020[114]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 4 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator Named data source: NA Dates: 2013 to 2018	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): ED patients with a discharge diagnosis of headache; excluded patients who were admitted to a hospital from an index ED visit; Hospitalizations for transient ischemic attack (TIA) or cervicocranial dissection without evidence of cerebral infarction or intracranial hemorrhage were not included as the outcome of interest. Total N: 28,121 Age: Mean, 43 Male, n (%): 7935 (28.2) Race, n (%): White, 2131 (8%) Black/African American, 9667 (34%)	Care delivered entirely within ED: ED only Consultants involved: Neurology Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Hospitalizations for new cerebrovascular event (ischemic stroke, intracranial hemorrhage, venous infarction, or intracerebral hemorrhage) within 1 year after index ED visit where patient was discharged for headache Conceptual harms definition: Mortality Harms severity: None Causal taxonomy used: None
Liberman, 2020[127]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Florida Agency for Health Care Administration and New York Statewide Planning and Research Cooperative System Dates: 2005 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): Patients with an index hospitalization for cervicocephalic artery dissection Total N: 7090 Age: Mean, 52.7 Male, n (%): 3909 (55.1) Race, n (%): White, 4799 (68%) Black/African American, 819 (12%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Probable ED misdiagnosis is having had an ED treat-and-release visit for signs and symptoms related to dissection in the 14 days before dissection hospitalization Conceptual harms definition: Stroke and death Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Liberman, 2020[139]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: Controlled Risk Insurance Company (CRICO) Strategies Comparative Benchmarking System (CBS) Dates: 2006 to 2016	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Cases with a final diagnosis of stroke Total N: 235 Dx error claimants (demographics not presented separately for ED claims) Age: Range, 18-45 (25.1%); >= 45 (70.2%); unknown (4.7%) Male, n (%): 118 (50.2) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: None Harms severity: NAIC Scale (9-Tier) Causal taxonomy used: CRICO Taxonomy
Liberman, 2020[210]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 4 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: EPIC Dates: 2013 to 2018	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): Total N: 186 Age: Mean, 64 Male, n (%): 45 (37) Race, n (%): White, 12 (11) Black/African American, 38 (41)	Care delivered entirely within ED: ED only Consultants involved: neurologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Lindsey, 2018[161]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Data source: Radiographs Numerator: Numerator and denominator Named data source: Dates: 2000 to 2016	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: None: Total N: 135,409 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologists, orthopedic surgeons Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Littman, 2021	Patient type: pediatric Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2015 to 2020	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: None: Total N: 78 Age: Mean, 12.86 Male, n (%): 78 (100) Race, n (%): White, 28 (35.9) Black/African American, 38 (48.7)	Care delivered entirely within ED: surgery Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Lowe, 2021	Patient type: pediatric Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Unclear or NR Named data source: Dates: Unclear or NR to Unclear or NR	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 170 Age: Mean, 8 Male, n (%): 100 (58%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: surgery Non-physicians involved: NP Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Lucas, 2021	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2019 to 2020	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Process (e.g., left without treatment): upgraded within 48 hours to ICU Total N: 100 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: non-critical care unit Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Madsen, 2016[200]	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 16 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Midwest Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator Named data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Dates: 2010 to 2010	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 2027 Age: Mean, 69.5,69.4 Male, n (%): 906 (45) Race, n (%): Black/African American, 436 (22)	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: Missed ED diagnoses were physician-verified strokes that did not receive a diagnosis indicative of stroke in the ED Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Mahajan, 2020[132]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Clinformatics Data Mart (Optum Insights) Dates: 2010 to 2017	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 95315 for adults and 21363 for children Age: Mean, 43.9 for adults and 12 for children Male, n (%): 47276 for adults and 12265 for children (49.6 for adults and 57.4 for children) Race, n (%): White, 53199 for adults and 12281 for children (55.8 for adults and 57.5 for children) Black/African American, 5929 for adults and 991 for children (6.2 for adults and 4.6 for children)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: We defined a potentially missed diagnosis of appendicitis as an initial (or index) ED visit at which a patient presented with any single undifferentiated symptom or combination of undifferentiated symptoms associated with appendicitis for which the patient Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Mahajan, 2020[134]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 3 Annual ED volume: Unclear or NR Ownership: Public	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: HDP or No HDP Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2011 to 2012	Disease specificity: Single disease Diseases studied: Preeclampsia/eclampsia Other inclusion criteria: Other: All postpartum women who presented to three tertiary care EDs within 42 days of delivering a live or stillborn infant in Calgary, Alberta, Canada over the study period were eligible. Total N: 119 Age: Median, 31 for HDP, 29.5 for No HDP Range, 19–46 for HDP, 18–37 for no HDP Male, n (%): 0 (0) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Internal medicine, OBGYN, Neurology, cardiology Non-physicians involved: Unclear or NR Non-EM physicians involved: Internal medicine, OBGYN, Neurology, cardiology Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Mansella, 2020[121]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2011 to 2013	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Other: Patients who received any cardiology workup (at least an ECG) or any pulmonary workup (at least a chest X-ray) Total N: 226 Age: Median, 68.5 Male, n (%): 124 (54.9) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiology Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Early (PE confirmed during early workup in the ED) vs. delayed (PE confirmed by imaging or autopsy during delayed workup) diagnosis Conceptual harms definition: In-hospital mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
March, 2014[27]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Australia Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2009 to 2013	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Other: The time to operation >48 hours Total N: 81 Age: NR Male, n (%): 29 (36%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Mark, 2017[178]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single health system, multiple EDs Number of EDs involved: Unclear or NR Annual ED volume: >=80,000 Ownership: Private, not for profit	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator Named data source: Dates: 2007 to 2013	Disease specificity: Single disease Diseases studied: BIG THREE Other inclusion criteria: Multiple: Excluded: Non-traumatic, no SAH presentation at ED, pregnant, no health plan membership, prior SAH Total N: 450 Age: Mean, 59 Male, n (%): 112 (25) Race, n (%): White, 220 (49) Black/African American, 58 (13)	Care delivered entirely within ED: Outpatient, inpatient, telephone Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: modified Rankin Scale (mRS) Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Martin, 2011[48]	Patient type: Multiple EDs Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single health system, multiple EDs Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Swiss Neuropediatric Stroke Registry Dates: 2000 to 2006	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Diagnosed with acute ischemic stroke Total N: 91 Age: Median, 5.3 Male, n (%): 61 (67) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delay in diagnosis > 6 hours Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Matera, 2020	Patient type: pediatric Patient age: Children only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 15 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2019 to 2020	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 62476 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Mattijssen-Horstink, 2020[126]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 20,000 to 39,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Hospital complication list and EHRs Numerator: Numerator and denominator Named data source: Dates: 2012 to 2017	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: Symptom (e.g., dizziness): Wounds excluded Total N: 26246 Age: Male, n (%): Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Guly HR. Dx errors in an accident and ED.Emerg Med J. 2001;18(4):263–9 Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Mattsson, 2018[172]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 20,000 to 39,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2012 to 2013	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: Multiple: Of these patients, we included all those for whom radiological studies had been ordered. Patients consulting directly with specialist clinics (orthopaedics, neurosurgery, hand surgery, plastic surgery, nephrology and urology) for non-urgent reasons were excluded since the procedures of how and when radiological findings are reported to the requesting physicians differ strongly depending on requesting departments Total N: 1522 Age: Median, 53.74 Male, n (%): 868 (57) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
McGann Donlan, 2009[80]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2005 to Unclear or NR	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 137 Age: Mean, 36.3 Male, n (%): 72 (53%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
McLaren, 2021	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: retrospective chart review' Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator only (error/harm) Named data source: Dates: 2020 to 2021	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: During the baseline, prepandemic period, 2 patients were excluded due to incomplete data. 148 were excluded because their STEMI code did not come from the ED. During the pandemic period, 5 patients were excluded due to incomplete data, and 155 were excl Total N: 151 Age: Median, 63.5 Male, n (%): 85 (56%) Race, n (%): NR	Care delivered entirely within ED: cath lab Consultants involved: emergency physicians can 'request a STAT cardiology consult for equivocal cases' Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Unclear or NR	Study design: Case series Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2011 to 2013	Disease specificity: Multiple Diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: Symptom (e.g., dizziness): abdominal pain Total N: 100 Age: Mean, 41.4 Non-errors, 43.7 Errors Male, n (%): Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: surgical specialties Non-physicians involved: physician assistants and nurse practitioners Non-EM physicians involved: Unclear Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed Opportunity (Singh 2014) Conceptual harms definition: Unclear or NR Harms severity: Singh (8-Tier) Causal taxonomy used: Safer Dx (Singh)
Metcalfe, 2016[207]	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 9 Annual ED volume: Unclear or NR Ownership: Public	Country: UK Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2011 to 2012	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: None: Total N: 85 Age: Median, 76 Range, 69-97 Male, n (%): 70 (82.4) Race, n (%): NR	Care delivered entirely within ED: vascular center Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: cases that were not initially recognized as ruptured Abdominal Aortic Aneurysm by the first clinician performing a full assessment. Conceptual harms definition: perioperative mortality, in-hospital mortality, 30and 60-day mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Metts, 2017[192]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: UK Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2011 to 2013	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 130 Age: Mean, 65.9 Male, n (%): 61 (47%) Race, n (%): White, 69 (93.2) Black/African American, 4 (5.4)	Care delivered entirely within ED: neurology Consultants involved: Emergency clinicians only Non-physicians involved: neurology Non-EM physicians involved: neurology Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Michelson, 2019[137]	Patient type: General ED Patient age: Children only Teaching status: Non-academic/Non-teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: PHIS and BCH EHRs Dates: 2008 to 2018	Disease specificity: Multiple diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: Other: We excluded cases from the manual record review if they did not have sufficient information in the medical record to make an outcome determination (for instance, because of incomplete or missing documentation). Total N: 158 Age: Mean, 8.7 Male, n (%): 91 (58%) Race, n (%): White, 67 (42%) Black/African American, 12 (8%)	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed Opportunity (Singh 2014) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Michelson, 2021	Patient type: General ED Patient age: Both adults and children Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 5 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: case control Comparison group: Concurrent control Look back or look forward analysis: Not a cohort study Data source: Pediatric Health Information System database. Numerator: Numerator only (error/harm) Named data source: Pediatric Health Information System database Dates: 2010 to 2019	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Multiple: Cases were drawn from a cohort of patients treated for appendicitis who visited 1 of 5 US pediatric EDs from January 1, 2010, to December 31, 2019, identified in the Pediatric Health Information System database. Control patients were children with a timel Total N: 748 Age: Mean, 10.2 Male, n (%): 392 (52.4) Race, n (%): White, 427 (57.1) Black/African American, 44 (5.9)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: Delayed diagnosis was defined by reviewer determination that appendicitis was probably or near-definitely present but not diagnosed during the index encounter Harms severity: None Causal taxonomy used: None
Miedema, 2011[51]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 31 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Multiple settings	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2003 to 2009	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: STEMI or new left bundle-branch block in patients with chest pain of 24 hours' duration Total N: 2015 Age: Mean, Delay < 120 mins 61.3 Delay >120 mins 64.0 Male, n (%): (Delay < 120 mins 73.9 Delay >120 mins 70.6) Race, n (%):	Care delivered entirely within ED: PCI center at referral hospital Consultants involved: cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delays resulting from non-diagnostic ECG, diagnostic dilemma, or ED delay: "A delay resulting from nondiagnostic ECG was documented if the patient's initial ECG was nondiagnostic, with a subsequent ECG revealing a STEMI. A delay resulting Conceptual harms definition: In-hospital, 30-day, and 1-year mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Miller, 2018[12]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Private, not for profit	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2012 to 2014	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: Multiple: Patients of all ages presenting to the ED complaining of headache who had been sampled for the initial QI effort were eligible for inclusion. Exclusion criteria included patients who arrived after inter-hospital transfer, patients admitted during their index visit, and those with a history of ventriculoperitoneal shunt. Total N: 582 Age: Median, 34 Male, n (%): 215 (36.9) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Mirete, 2005[212]	Patient type: General ED Patient age: Adults only Teaching status: Non-academic/Non-teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2004 to 2004	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 528 Age: Mean, 73 Male, n (%): 313 (59.3) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Mitchell, 2006	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 3 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Multiple settings	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2003 to 2004	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Other: exclude: cocaine use Total N: 1087 Age: NR Male, n (%): 627 (58%) Race, n (%): White, 495 (46%) Black/African American, 516 (47%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Moeller, 2008[10]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2005 to 2006	Disease specificity: Multiple diseases Diseases studied: NA Other inclusion criteria: None: Total N: 493 Age: Male, n (%): Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Neurologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Mohamed, 2013[42]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Young Stroke registry Dates: Unclear or NR to Unclear or NR	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): Patients who presented to an ED after onset of acute neurologic symptoms. Excluded patients with ongoing substance abuse and those without a permanent address. Total N: 93 Age: Mean, 38.1 Male, n (%): 39 (41.9) Race, n (%): White, 50 (53.8) Black/African American, 41 (44.1)	Care delivered entirely within ED: Unclear or NR Consultants involved: Neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: 'whether the patient's diagnosis was initially missed at the presenting hospital. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Montmany, 2008[5]	Patient type: General ED Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2006 to 2007	Disease specificity: Multiple diseases Diseases studied: Other inclusion criteria: : exclusion: patients younger than 16 years Total N: 122 Age: Mean, 44 Range, 16-99 Male, n (%): 93 (76%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: radiology, surgeon Non-physicians involved: Unclear or NR Non-EM physicians involved: radiologists, surgeons Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: Unclear or NR Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Montmany, 2017[175]	Patient type: General ED Patient age: Both adults and children Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Multiple	Country: Multiple Region, if US: Northeast Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Trauma database Numerator: Numerator and denominator Named data source: Dates: 2002 to 2016	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: The study analyzes only the patients registered in the database who were deceased, excluding those under the age of16 (treated by pediatric medical teams at both centers)and those who had died before arrival at the hospital (due to lack of data that would impede the analysis of their quality of care).The inclusion criteria for our study are polytrauma patients who were deceased and had been treated at the American trauma center or the critical care unit at the Spanish referral hospital. At both hospitals, we have included patients who died before being admitted to the corresponding hospitalization areas Total N: 1524 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: trauma surgery Non-physicians involved: Nurse Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Moonen, 2017[188]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2015 to 2015	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: Multiple: Inclusion criteria: all patients of all ages after ambulatory ED admission, attending a subsequent outpatient follow up clinic and with a different diagnosis in comparison to ED diagnosis. Exclusion criteria: non-trauma patients, intra-cranial and thoraco-abdominal trauma of internal organs, patients admitted to hospital, loss to follow up, all knee trauma with planned advanced imaging techniques Total N: 56 Age: Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologist Non-physicians involved: Emergency physicians only Non-EM physicians involved: (surgery, anesthesiology, emergency and internal medicine Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Morgan, 2021	Patient type: Level II trauma center Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Unclear or NR	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Not a cohort study Data source: radiographs Numerator: Numerator and denominator Named data source: Dates: 2015 to 2016	Disease specificity: Multiple diseases Diseases studied: Other Other inclusion criteria: None: Total N: 121 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Morgenstern, 2004	Patient type: General ED Patient age: Adults only Teaching status: Non-academic/Non-teaching Hospital setting: Multi-center study Number of EDs involved: 7 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2000 to 2002	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Multiple: Cases with a missing ED diagnosis (n _ 93),with a missing ED or medical record (n _ 20), or seen atan out-of-area ED (n _ 10) were excluded. An additional12 cases (7 Asian Pacific Islander and 5 unknown race/ethnicity) were excluded based on race/ethnicity becausethe sample sizes were too small to analyze, leaving 2,059eligible cases. Patients were excluded from theanalysis if they were not seen in the ED (n _ 339), had anin-hospital stroke (n _ 91), or had left against medicaladvice before evaluation was complete (n _ 10). Total N: 2059 Age: Range, 45-75+ Male, n (%): 875 (42.5%) Race, n (%): White, 891 (43.3%) Black/African American, 119 (5.8%)	Care delivered entirely within ED: ED only Consultants involved: neurologists in 160 cases Non-physicians involved: Unclear or NR Non-EM physicians involved: There are 41 physicians who practice in ED in this community. Of these, 19 are board certified in EM, 14 in family practice, 5 in internal medicine, 2 in general surgery, and 1 is not board certified. Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Mounts, 2011[57]	Patient type: General ED Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Private, for profit	Country: US Region, if US: South Urban/rural: Unclear or NR	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Discrepancy folder Dates: 2006 to 2009	Disease specificity: Multiple Diseases Diseases studied: Fractures Other inclusion criteria: Other: Total N: Age: Mean, 9.5 Range, 3 months to 20 years Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologist Non-physicians involved: Emergency physicians only Non-EM physicians involved: Pediatricians Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: discordant interpretation ED extremity x-rays between pediatric ED providers and radiologists Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Mouthon-Reignier, 2016[190]	Patient type: neurology Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2014 to 2014	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: all patients admitted in the intensive SU for potential thrombolysis Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: neurology stroke unit Consultants involved: neurologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Moy, 2015[24]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 797 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator Named data source: HCUP State Inpatient Databases and State ED Databases Dates: 2007 to 2007	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: patients with an index admission of acute MI Total N: 111973 Age: NR Male, n (%): 67256 (60%) Race, n (%): White, 86038 (77%) Black/African American, 9275 (8%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: APSF/Graber 2005 Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Muhm, 2012[3]	Patient type: General ED Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: group A consisted of patients without delays in diagnosis, and group B with delays in diagnosis Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2008 to 2009	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 111 Age: Mean, 43 Range, 11-85 Male, n (%): 80 (72) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: Radiologists Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: 'diagnostic efficacy" page 8 Conceptual harms definition: None Harms severity: Hoyt et al., missed diagnosis categorized 'missed' diagnosis as 'justified/acceptable' or unjustified Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Musunuru, 2007[91]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2002 to 2004	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 411 Age: Mean, 34.7 Male, n (%): 230 (56%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Surgeons Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Naiditch, 2013[39]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2007 to 2010	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 816 Age: NR Male, n (%): 476 (58%) Race, n (%): White, 186 (23%) Black/African American, 55 (7%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Nevo, 2017[189]	Patient type: pediatric ED in children's hospital Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Other Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: f patients who underwent orchiectomy and those who underwent orchiopexy Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Dates: 2008 to 2014	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: None: Total N: 100 Age: Median, 11 Male, n (%): 100 (100) Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Radiologist Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Newman-Toker, 2014[33]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 1016 Annual ED volume: Unclear or NR Ownership: Multiple	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: HCUP Dates: 2008 to 2009	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Stroke admissions via the ED Total N: 26052 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: APSF/Graber 2005 Conceptual harms definition: Hospitalization for stroke Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Normahani, 2017[196]	Patient type: General ED Patient age: Adults only Teaching status: Non-academic/Non-teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: UK Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Unclear or NR Named data source: Dates: 2003 to 2014	Disease specificity: Single disease Diseases studied: Arterial thromboembolism Other inclusion criteria: None: Total N: 67 Age: Median, 68.4 Male, n (%): 41 (61%) Race, n (%): NR	Care delivered entirely within ED: vascular surgery Consultants involved: vascular surgeon Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Included (no subgroup analysis)	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: Unclear or NR Harms severity: Unclear or NR Causal taxonomy used: Unclear or NR
Nuñez, 2006[101]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Case-control Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2004 to 2004	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: Exclusion criteria were age Total N: 500 Age: Mean, 45 Male, n (%): 245 (49) Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Nurse Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Discordance between 1st and final diagnosis in ED records for cases of dx error, or the primary health care medical records for controls Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Ohle, 2019[151]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2002 to 2014	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients who presented to an ED or a regional cardiac referral center with acute onset of non-traumatic abdominal/back/chest/flank pain and a new diagnosis of acute aortic dissection Total N: 194 Age: Mean, 65 Male, n (%): 129 (66.7) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: A missed case of AAD was defined by failure to diagnose within the ED, treatment for an alternative diagnosis (i.e., anticoagulation for a pulmonary embolism) within the ED, or re-presentation within 14 days of the initial visit with a new diagnosis of AA Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Ois, 2019[138]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: SAH-Basicmar Dates: 2007 to 2017	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients admitted to hospital with a diagnosis of spontaneous (nontraumatic) aneurysmal and nonaneurysmal SAH Total N: 400 Age: Mean, 56.02 Range, 17 to 97 Male, n (%): 155 (38.8) Race, n (%): NR	Care delivered entirely within ED: tertiary stroke center Consultants involved: neurologist, neurointensivist, neurovascular interventionists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Failure to correctly identify a subsequently documented SAH in the first physician evaluation Conceptual harms definition: modified Rankin Scale score of 3 to 6 Harms severity: Modified Rankin Scale Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: N: Annual ED volume: 60,000 to 79,999 Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Case series Comparison group: None Look back or look forward analysis: Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm) Named data source: Dates: 2009 to 2013	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: 214 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: advanced practice professionals Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: None Harms severity: Schiff (4-Tier) Causal taxonomy used: Graber 2005
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2015 to 2016	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: 697 Age: Mean, 51.6 Male, n (%): 342 (49.1) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: The accuracy of provisional diagnoses was assessed by comparing the absolute agreement between the provisional diagnosis in the ED (ED) and the final diagnosis given by the ophthalmology resident. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Osterwalder, 2020[14]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2013 to 2015	Disease specificity: Multiple diseases Diseases studied: NA Other inclusion criteria: Multiple: Pediatric and obstetric patients presenting to facilities nearby were not included. Patients undergoing life-saving interventions and patients who were unconscious, intoxicated, or could not be interviewed due to mental issues were not included. Multiple presentation was not excluded Total N: 3960 Age: Median, 47 for abdominal pain, 51 for no abdominal pain Male, n (%): (47.3 % abdominal pain, 52.3% no abdominal pain) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Nurses Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Pacheco, 2021	Patient type: General ED Patient age: Adults only Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2007 to 2015	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: None: Total N: 179 Age: NR Male, n (%): 132 (74%) Race, n (%): NR	Care delivered entirely within ED: ambulance Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Palomeras Soler, 2015[32]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Data source: Unclear or NR Numerator: Numerator and denominator Named data source: NA Dates: 2007 to 2012	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Unclear or NR: Total N: 411 Age: Mean, 71.5 Male, n (%): 231 (56%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delay between arrival at the Emergency Service and the neurologist's assessment was less than 24 hours in 82% of cases and less than 48 hours in 93.9% Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Pare, 2016[62]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 3 Annual ED volume: Multiple Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2013 to 2015	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Treated at one of the affiliated EDs within 1 months preceding diagnosis for a visit attributed to AAD or during the same hospital visit Total N: 31 Age: Median, FOCUS 16 Non-FOCUS 13 Male, n (%): 18 (58%) Race, n (%): Black/African American, Non-white 1	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Multiple definitions Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Parikh, 2008[89]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: NA Dates: 2000 to 2006	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Symptom (e.g., dizziness): Two cohorts: (1) Patients eligible for primary percutaneous coronary intervention and (2) excluded patients with atypical symptoms and/or presentations of STEMI that resulted in inherent delay in diagnosis and treatment Total N: 184 Age: Mean, 55 Male, n (%): 137 (74) Race, n (%): White, 62 (34) Black/African American, 45 (24)	Care delivered entirely within ED: cardiac catheterization laboratory Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: door-to-balloon time (cumulative time from ED presentation to first balloon inflation and concomitant reestablishment of antegrade blood flow in the infarct-related artery Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Pehle, 2006[98]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 1998 to 2002	Disease specificity: Multiple diseases Diseases studied: Fractures Other inclusion criteria: Other: Patients who, within the shock space supply phase died, excluded from the analysis, there the early diagnosis not completed could be and due to the lowgen autopsy rate not confirmed and complete final diagnoses are present. Total N: 1,187 Age: Median, 40 Male, n (%): 71 (6%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Peng, 2015[26]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Data source: Prospective data collection Numerator: Numerator only (error/harm) Named data source: Dates: 2007 to 2009	Disease specificity: Multiple Diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Perry, 2020[208]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator only (error/harm) Named data source: Dates: 2016 to 2019	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: Harms severity: Causal taxonomy used:

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Petinaux, 2011	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 1996 to 2005	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Other: This study was a retrospective review of all plain radiographs ordered Total N: 5308 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Pihlasviita, 2018[164]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Helsinki Ultra-acute Stroke Biomarker Study Dates: 2013 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients who required primary stroke-code transport to hospital Total N: 1015 Age: Mean, 69 Male, n (%): 568 (56) Race, n (%): NR	Care delivered entirely within ED: CT suite Consultants involved: stroke neurologist or stroke-trained neurology resident Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: The initial diagnosis was incorrect, unclear, or missing Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Piper, 2008[88]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2006 to 2006	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Other: underwent urgent appendectomy Total N: 134 Age: Mean, 37 Male, n (%): 67 (50%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Pirozzi, 2014[19]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Randomized controlled trial Comparison group: Concurrent control Look back or look forward analysis: Both Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2012 to 2012	Disease specificity: Multiple Diseases Diseases studied: Other Other inclusion criteria: Multiple: We included 180 patients admitted to the ED (after pre-hospital care for some of them) because of complaining dyspnea, defined as either the sudden onset of shortness of breath without history of chronic symptoms or as increase in the severity of the chronic shortness of breath. Exclusion criteria were age Total N: 168 Age: Mean, 74 Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Podolnick, 2017[183]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: Other (specify) Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator Named data source: EPIC Dates: 2010 to 2015	Disease specificity: Single disease Diseases studied: NA Other inclusion criteria: Multiple: We excluded patients who were transferred less than 12 hours after presentation, patients who died less than 12 hours after presentation, and consultations for contusions, abrasions, sprains not requiring intervention, and superficial lacerations. Total N: 1009 Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Anesthesiologist on-call, Radiology technologist, respiratory care practitioners Non-physicians involved: nurses Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: The rate of missed injury or delayed diagnosis of injury (a DDI) was defined as an injury not detected or suspected on the primary and secondary survey and diagnosed after 12 hours of hospitalization. Conceptual harms definition: A clinically significant injury was defined as an injury that prolonged hospitalization, changed management, or required surgical intervention. Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Postma, 2012[4]	Patient type: General ED Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 13 Annual ED volume: Multiple Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Hospitalized with DDI vs Hospitalized without DDI Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator Named data source: Dates: 2009 to 2009	Disease specificity: Multiple diseases Diseases studied: Other Other inclusion criteria: Unclear or NR: inclusion: patients admitted from the ED after airplane crash Total N: Age: Mean, 38 Range, 11 months to 76 years Male, n (%): (66) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: Clinically significant injury: 'an injury if unnoticed, would possibly lead to a delayed or poor healing, and could have consequences for a patient's recovery and daily activities. This definition is not based on severity as a treat to life, but more as Harms severity: Clinically significant injury: 'an injury if unnoticed, would possibly lead to a delayed or poor healing, and could have consequences for a patient's recovery and daily activities. This definition is not based on severity as a treat to life, but more as Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Prabhakaran, 2008[86]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: NA Dates: Unclear or NR to Unclear or NR	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): Patients with transient focal neurologic episodes lasting less than 24 hours and in whom the initial admitting diagnosis was transient ischemic attack Total N: 100 Age: Mean, 60.9 Male, n (%): 40 (40%) Race, n (%): White, 43 (43) Black/African American, 49 (49)	Care delivered entirely within ED: Stroke Service Consultants involved: Neurology residents Non-physicians involved: Unclear or NR Non-EM physicians involved: Neurology residents Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Diagnosis of TIA was definite if an appropriate acute ischemic lesion was seen on brain imaging and probable if there was agreement by two stroke neurologists. The remaining TNA were classified according to etiology if found or unclassifiable if none was Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Rapezzi, 2008[85]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Multiple	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: NA Dates: 1996 to 2006	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients who received a final diagnosis of spontaneous acute aortic aneurysm Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: in hospital diagnostic time < 12 hours (75th percentile) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Raposo, 2018[159]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: NA Dates: 2012 to 2013	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients referred to our TIA clinic Total N: 354 Age: Mean, 61.2 Male, n (%): 178 (50%) Race, n (%): NR	Care delivered entirely within ED: local stroke team Consultants involved: stroke team Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delay from symptom onset to admission to the TIA clinic Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Ravichandiran, 2010[76]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Recognized cases vs Missed cases Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 1993 to 2007	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: Multiple: The study sample included only cases for which the first physician visit was primarily for an isolated fracture. Cases were excluded when the child's clinical presentation was predominantly consistent with some other type of trauma, medical records were inaccessible, only metaphyseal corner chip fractures (usually asymptomatic) were present, or the cause of the fracture was indeterminate or accidental Total N: 258 Age: Mean, 8.28 for recognized cases, 9.24 for missed cases Male, n (%): (44.4 for recognized cases, 60.8 for missed cases) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: HSC SCAN consists of specialty pediatricians, psychologists, social workers, and nurse practitioners. Non-EM physicians involved: EM trained physicians only Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Ray, 2006[18]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Other (specify) Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2001 to 2002	Disease specificity: Multiple Diseases Diseases studied: Other Other inclusion criteria: Other: Age at least 65 years; acute dyspnea of less than two weeks' duration, a subjective criterion defined by the patient (the dyspnea was present if the patient answered one of the following questions in the affirmative: Are you breathless? Do you feel short of breath? Do you experience air hunger? Do you feel increased effort of breathing?); and one of the following objective criteria of ARF: a respiratory rate at least 25 minute-1, an arterial partial pressure of oxygen (PaO2) of 70 mmHg or less, a peripheral oxygen saturation (SpO2) of 92% or less while breathing room air, and an arterial partial pressure of CO2 (PaCO2) of 45 mmHg or more with an arterial pH of 7.35 or less. Total N: 514 Age: Mean, 80+/-9 Male, n (%): 253 (49%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Richoz, 2015	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2003 to 2011	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 2200 Age: Mean, 72.6 Male, n (%): 1233 (56.2%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Rizos, 2009[79]	Patient type: specialized neurological ER Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2005 to 2007	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Multiple: There were 2 cohorts: (a) all patients with a discharge diagnosis of 'stroke' and (b) patients with an admission diagnosis of stroke Total N: 13,635 p Age: Mean, 70 Male, n (%): (52.2) Race, n (%):	Care delivered entirely within ED: access to a stroke and neurointensive care unit Consultants involved: neurology specialist Non-physicians involved: Unclear or NR Non-EM physicians involved: neurology Trainees involved: Fully-trained emergency clinicians only How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: If the admission diagnosis did not match the discharge diagnosis Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Rønning, 2005[106]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Unclear or NR Numerator: Numerator and denominator Named data source: NA Dates: 2004 to 2004	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients admitted to the stroke unit for suspected stroke Total N: 354 Age: Mean, 70 Range, 21 to 96 Male, n (%): 171 (48%) Race, n (%): NR	Care delivered entirely within ED: stroke unit Consultants involved: neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Suspected stroke, but did not have stroke Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Rose, 2008[87]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 46 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: South Urban/rural: Multiple settings	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: North Carolina Collaborative Stroke Registry Dates: 2005 to 2008	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients with a presumptive stroke-related admission diagnosis (ischemic stroke, hemorrhagic stroke, transient ischemic attack [TIA], stroke not specified). Total N: Age: Mean, 6984 Median, 46 Male, n (%): Race, n (%): White, 10779 (71) Black/African American, 3969 (26)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: CT delay (hours) was calculated as the time from hospital arrival (ER triage) until initial brain-imaging. We also dichotomized delay time by the NINDS guideline of receipt of a CT scan within 25 minutes of hospital arrival. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Rosenkrantz, 2016[203]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Departmental database Dates: 2009 to 2015	Disease specificity: Multiple Diseases Diseases studied: NA Other inclusion criteria: : Total N: Age: Male, n (%): Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Rosenman, 2020	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2012 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Multiple: Patients aged 60–89 years who were discharged to homefrom the ED within 24 hours, without an InternationalStatistical Classification of Diseases and Related Health Problems, 9th or 10th Revision (ICD-9/10) diagnosis of TIA orstroke or other cerebral/precerebral artery occlusion(433.xx, 434.xx, 435.xx, or 436.xx, I63.xx or G45.xx), wereincluded Total N: 36301 Age: NR Male, n (%): 14945 (41%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Rostanski, 2016[191]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2011 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): included patients that received thrombolysis Total N: 350 Age: Mean, 67.9 Male, n (%): 132 (37.7) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: neurologist Non-physicians involved: Unclear or NR Non-EM physicians involved: neurologist Trainees involved: Included trainees How left without treatment was handled: Included (broken out)	Conceptual Dx error definition: Patients who present with stroke symptoms and are treated with IV tPA but are later found to have a diagnosis other than AIS upon further workup, i.e.. stroke mimics. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Royl, 2011[9]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2005 to 2006	Disease specificity: Not restricted by diseases Diseases studied: Other Other inclusion criteria: None: Total N: 475 Age: Median, 53 Male, n (%): 190 (40) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Neurologists only Non-physicians involved: Included other ED clinicians (specify) Non-EM physicians involved: Included physicians with other training (specify) Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Russell, 2013[40]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Other Urban/rural: Urban / metropolitan	Study design: Ambidirectional cohort study Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator only (error/harm) Named data source: Dates: 2008 to 2011	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 166 Age: Mean, 10.2 Male, n (%): 104 (63%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Surgeon Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Saaristo, 2020[15]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2015 to 2016	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: None: Total N: 10,609 Age: Mean, 38 yr Median, 32 yr Male, n (%): (40%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Included consultants (specify) Non-physicians involved: Emergency physicians only Non-EM physicians involved: surgeons Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: Short-term (48 hr) return to ED Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sadighi, 2019[147]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 3 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: Unclear or NR to Unclear or NR	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients who were hospitalized with the admission diagnosis of transient ischemic attack or were referred with the referral diagnosis of transient ischemic attack Total N: 254 Age: Mean, 68.7 Male, n (%): 104 (40.9) Race, n (%): White, 243 (95.7)	Care delivered entirely within ED: Unclear or NR Consultants involved: general neurologist within 24 hours Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Admission diagnosis was consistent with the final diagnosis Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Saleh Velez, 2021	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: Multiple (but not all) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2012 to 2019	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: None: Total N: 37 Age: Mean, 60.8 Male, n (%): 23 (62.1) Race, n (%): White, 6 (16.2) Black/African American, 30 (81.1)	Care delivered entirely within ED: inpatient Consultants involved: neurology Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sanders, 2017[174]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 2 Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Rural	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: Unclear or NR to Unclear or NR	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: patients with signs and symptoms of acute MI as main complaint; excluded patients arriving by ambulance Total N: 283 Age: Mean, 61 Range, 26 to 95 Male, n (%): 136 (48.1) Race, n (%): White, 190 (67.1) Black/African American, 88 (31.1)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: emergency nurses Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delay (more than 10 minutes from arrival until triage and ECG) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Santos, 2009[77]	Patient type: General ED Patient age: Both adults and children Teaching status: Non-academic/Non-teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Numerator and denominator Named data source: Dates: 2007 to 2007	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Unclear or NR: Total N: 100 Age: Mean, 22.6 Range, 2-81 Male, n (%): 61 (61) Race, n (%): NR	Care delivered entirely within ED: Surgery Consultants involved: Surgical Resident Non-physicians involved: Unclear or NR Non-EM physicians involved: Surgery Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Conceptual harms definition: Harms severity: Causal taxonomy used:

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sarraj, 2015[41]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Unclear or NR Named data source: UT Houston Stroke Registry database Dates: 2008 to 2010	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: AIS patients who were treated with IV t-PA within 4.5 hour window. Excluded patients who had ischemic infarctions evident in both anterior and posterior circulation territories, patients without evidence of new infarct on MRI diffusion-weighted images or follow-up CT imaging, or patients with incomplete time data. Total N: 252 Age: Mean, 67, 65 Male, n (%): 113 (44.8) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Vascular neurologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Time from door to doctor, to evaluation by neurologist, to computed tomography scan, to needle Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Scheuermeyer, 2012[46]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: NA Dates: 2006 to 2006	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Symptom (e.g., dizziness): patients with chest pain and no clear noncardiac cause Total N: 1116 Age: Mean, 54.7 Male, n (%): 668 (60) Race, n (%): NR	Care delivered entirely within ED: also Cardiology referral Consultants involved: cardiologist Non-physicians involved: triage nurse Non-EM physicians involved: cardiologists Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: a patient who was discharged from the ED with a non-ACS diagnosis, without specific follow-up, who subsequently proved to have an ACS diagnosis or an adverse event within 30 days Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Schnapp, 2018[163]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Public	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2013 to 2014	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: Cases were excluded if the patient was under 18 or over the age of 89, the second visit was planned during the first visit (e.g. wound check follow-up), the patient was admitted on the first visit or if the patient was discharged on both visits. Total N: 271 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: APSF/Graber 2005 Conceptual harms definition: Dx AEs (Schiff, 2009; Zwaaan, 2010) Harms severity: None Causal taxonomy used: None
Schrock, 2012[53]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: >=80,000 Ownership: Public	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2004 to 2007	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: All subjects aged 18+ years who received an ED diagnosis of transient ischemic attack. Total N: 429 Age: Mean, 60, 57 Male, n (%): 161 (38%) Race, n (%): White, 229 (53%) Black/African American, 156 (36%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: neurologists Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: ED diagnosis disagrees with neurologist diagnosis Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Schull, 2006[97]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 171 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Discharge Abstract Database and the National Ambulatory Care Reporting System Dates: 2002 to 2003	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients admitted to hospital through an ED with a diagnosis of acute MI Total N: 19663 Age: Mean, 68.3 Male, n (%): 12388 (63) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed acute MI (the ED discharge diagnosis was chest pain, angina, shortness of breath, congestive heart failure, abdominal pain, heartburn, esophagitis, or gastritis, syncope/malaise) Conceptual harms definition: 30-day and 1-year mortality Harms severity: None Causal taxonomy used: None
Scott, 2018[171]	Patient type: General ED Patient age: Children only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 5 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2014 to 2015	Disease specificity: Single disease Diseases studied: Sepsis Other inclusion criteria: None: Total N: 996 for tertiary sites and 98 for community sites Age: Mean, 5.8 for tertiary sites and 4.4 for community sites Male, n (%): 580 for tertiary sites and 53 for community sites (58.2 for tertiary sites and 54.1 for community sites) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Pharmacist Non-physicians involved: Nurses, respiratory technicians Non-EM physicians involved: Pediatricians Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Identified and missed patients were identified and included in the registry in 2 ways. 1. Missed patients with sepsis in whom the sepsis pathway was not initiated clinically were identified through standardized chart review conducted by 5 clinicians mont Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sederholm Lawesson, 2018[167]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 5 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: electronic health records and patient interviews Numerator: Numerator and denominator Named data source: SymTime Dates: 2012 to 2014	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients with a confirmed STEMI diagnosis Total N: 449 Age: Mean, 64.5-69.8 Male, n (%): 340 (76%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Time from first medical contact to diagnostic ECG (first medical contact could be primary healthcare center, Swedish Healthcare Direct, EMS or ED) Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Seetahal, 2011[56]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: >=80,000 Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator only (error/harm) Named data source: National Inpatient Sample Dates: 1998 to 2007	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Other: with appendectomy Total N: 475651 Age: Median, 42 Male, n (%): 15832 (3%) Race, n (%): White, 30748 (6%) Black/African American, 4061 (1%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Settelmeier, 2020[118]	Patient type: Chest pain unit Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Registry Comparison group: None Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: CPU registry Dates: 2008 to 2014	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Other: Only patients consenting to be contacted for follow-up (FU) were included in the present analysis Total N: 5,259 (Age: Mean, 70.5 years [f] vs. 65.6 years [m] Male, n (%): (62.2) Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Sevdalis, 2010[59]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Registry Comparison group: None Look back or look forward analysis: Unsure Data source: Electronic database of adverse events in NHS Numerator: Numerator only (error/harm) Named data source: NRLS Dates: 2003 to 2005	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Seward, 2003[213]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Multi-center study Number of EDs involved: 3 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2000 to Unclear or NR	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Other: Deaths within 7 days of admission (excluded if died within an hour of arrival) Total N: 200 Age: Median, 79 Male, n (%): 77 (38%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Sharif, 2018[166]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2011 to 2015	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: Other: Point-of-care ultrasound Total N: 90 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sharp, 2020[120]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single health system, multiple EDs Number of EDs involved: 14 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2009 to 2017	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients with an acute MI discharge Total N: 44473 (LBA) 325,088 (LFA) Age: Mean, 68.0 (LBA), 48.9 (LFA) Male, n (%): 28137 (LBA), 139126 (LFA) (63.3% (LBA), 42.8% (LFA)) Race, n (%): White, 23,542 (LBA), 125,132 (LFA) (52.9% (LBA), 38.5% (LBA)) Black/African American, 5,111 (LBA), 43.447 (LFA) (11.5% (LBA), 13.4% (LFA))	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: IOM/NAM 2015 Conceptual harms definition: MisDx-Related Harms (DNT, 2009) Harms severity: None Causal taxonomy used: IOM/NAM 2015
Shokoohi, 2020	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 2 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2018 to 2020	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Process (e.g., left without treatment): Patients who expired in the ED, eloped, left against medical advice,or were transferred to an outside hospital were also excluded asthe irregularity and often incompleteness of their ED courses waspredicted to reflect inaccurate time measurements. Simi Total N: 161122 Age: Mean, 56 Male, n (%): 74310 (46%) Race, n (%): White, 105601 (65.2) Black/African American, 21561 (13.4)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: nurses Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Smidfelt, 2017[180]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 11 Annual ED volume: Unclear or NR Ownership: Multiple	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Swedvasc Dates: 2008 to 2014	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Process (e.g., left without treatment): only patients treated for the disease Total N: 261 Age: Mean, 75 Male, n (%): 201 (77.0) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Emergency physicians only Non-EM physicians involved: internal medicine, surgery (general and orthopedic), urology Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Smidfelt, 2020[122]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 11 Annual ED volume: Multiple Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Swedish Cause of Death Registry and Swedish National Registry for Vascular Surgery Dates: 2010 to 2015	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients who were treated with open repair or EVAR for ruptured abdominal aortic aneurysm Total N: 455 Age: Mean, 79.1-79.5 Male, n (%): 322 (71%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: radiologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Patients who did not meet any of these criteria: 1) aortic aneurysm or rupture was mentioned ad the preliminary or differential diagnosis by the first physician to assess patient in ED, 2) the patient was referred from the ED for an acute CT scan of the a Conceptual harms definition: In-hospital mortality or 30-day mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Smith, 2012[50]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Suburban / micropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2002 to 2005	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Symptom (e.g., dizziness): Included patients with symptoms compatible with acute pulmonary embolism (i.e., chest pain, dyspnea, hypoxia, pre-syncope, or syncope), diagnosis was made with computed tomography at institution; excluded asymptomatic patients and patients diagnosed before arrival Total N: 400 Age: Median, 68 Male, n (%): 195 (48.8) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Early diagnosis was defined as having the confirmatory CT < 12 hours from ED arrival and delayed diagnosis was defined as a CT > 12 hours from arrival Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Snoek, 2013[2]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Other (specify) Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2009 to 2010	Disease specificity: Single disease Diseases studied: OTHER MULTIPLE Other inclusion criteria: Other: Excluded the patients who were not admitted for observation and who could not be examined at tertiary trauma survey Total N: 13 (delayed diagnosis patients) Age: Mean, 48 Male, n (%): 10 (77) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Trauma surgery(attending), "surgery resident “Neurology, pediatrics, anesthesiology (provider and assistant), radiology(resident and assistants), surgery resident Non-physicians involved: ED Nurses Non-EM physicians involved: Neurology, pediatrics, anesthesiology, radiology, trauma surgeon, surgical resident Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: Injury not diagnosed by 1st and 2nd trauma survey Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Somers, 2021	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Other (specify) Comparison group: Pre/post comparison Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2019 to 2020	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 130 Age: Range, 16-82 Male, n (%): 62 (48%) Race, n (%): NR	Care delivered entirely within ED: surgery Consultants involved: radiology, surgery Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Soundappan, 2004[109]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Australia Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Comparison with and without missed injuries by tertiary survey Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2002 to 2003	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Outcome severity (e.g., only death): inclusion: Trauma patients with an ISS of 9 or above were included the study. Total N: 76 Age: Mean, 8.4 years Range, 1 month -15 years Male, n (%): 50 (66%) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: trauma team at the hospital included the surgical fellow or registrar, emergency fellow or registrar, anesthetic registrar, intensive care registrar, ED nurses, and radiographer. Non-physicians involved: Nurses, radiographer Non-EM physicians involved: trauma team at the hospital included the surgical fellow or registrar, emergency fellow or registrar, anesthetic registrar, intensive care registrar, ED nurses, and radiographer. Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sporer, 2013[45]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: None Look back or look forward analysis: Data source: Prospective data collection Numerator: Numerator only (error/harm) Named data source: Dates: 2008 to 2009	Disease specificity: Not restricted by disease Diseases studied: Other Other inclusion criteria: Symptom (e.g., dizziness): Initial Glasgow Coma Scale (GCS) score of #14 Total N: 112 Age: Mean, 52.4 Male, n (%): 77 (69) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: Unclear Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Staab, 2020	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Multi-center study Number of EDs involved: 3 Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Unclear or NR	Study design: case control Comparison group: Concurrent control Look back or look forward analysis: Not a cohort study Data source: Data from a QI project Numerator: Numerator and denominator Named data source: Dates: 2015 to 2016	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 223 Age: Range, 6-14 Male, n (%): 132 (59%) Race, n (%): NR	Care delivered entirely within ED: Other location (specify) Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Suda, 2021	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2016 to 2019	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Other: inclusion: all trauma patients patients 2016-2019, exclusion: patients were excluded if they were discharged from the ED (outpatient management) and/or if there was insufficient data on the patient Total N: 3124 Age: Mean, 44 Range, 0-99 Male, n (%): 2090 (67) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: They used missed injuries definition: 'American College of Surgeons defines “missed injury” as an injury-related diagnosis discovered after the initial workup is completed and the admission diagnosis is determined' Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Sun, 2007[8]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2005 to 2006	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Multiple: Exclusion criteria included loss of consciousness related to a witnessed seizure, loss of consciousness after head trauma, ongoing confusion (including baseline cognitive impairment or dementia), intoxication, age younger than 18, inability to speak English or Spanish, do-not-resuscitate (DNR) or do-not-intubate (DNI) status, and lack of follow-up contact information. Total N: 463 Age: Range, 18 to 96 Male, n (%): 204 (44) Race, n (%): White, 357 (77)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Nurses Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Sundberg, 2018[165]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2010 to 2015	Disease specificity: Multiple diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: None: Total N: 55,233 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Teichman, 2021	Patient type: level 1 trauma Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Northeast Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2015 to 2019	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: None: Total N: 5645 Age: Median, 55 Male, n (%): 3615 (64) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Tien, 2021	Patient type: Level 1 trauma center Patient age: Both adults and children Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: South Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: patient charts Dates: 2016 to 2019	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Mechanism (e.g.,, multi-trauma): patients had to have had a blunt cerebrovascular injury Total N: 40 Age: Mean, 44.1 Male, n (%): 32 (80) Race, n (%): White, 19 (48) Black/African American, 20 (50)	Care delivered entirely within ED: Unclear or NR Consultants involved: Emergency clinicians only Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Torres-Macho, 2013[38]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 3 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2008 to 2011	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Other: Patients admitted to hospital with a diagnosis of acute symptomatic pulmonary embolism confirmed by chest computed tomography Total N: 436 Age: Mean, 67.4 Male, n (%): 212 (48.6) Race, n (%): NR	Care delivered entirely within ED: hospital Ward Consultants involved: radiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: radiologist Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delayed diagnosis (pulmonary embolism was diagnosed by chest CT that was ordered while the patient was still at the ED vs. pulmonary embolism that was diagnosed by chest CT ordered during hospitalization after the patient had left the ED Conceptual harms definition: Mortality during hospitalization Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Tsivgoulis, 2011[55]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Stroke registry data Numerator: Numerator and denominator Named data source: Barrow Neurological Institute stroke database Dates: 2003 to 2008	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Acute ischemic stroke admissions treated with 0.9 mg/kg dose of intravenous tPA within 3 hours of stroke onset Total N: 483 Age: Mean, 67 Male, n (%): 270 (56) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: stroke mimic Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Tudela, 2005[105]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 20,000 to 39,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2001 to 2003	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: discharged from the emergency medical area (excluding going the areas of traumatology, surgery, pediatrics and gynecology) Total N: 669 Age: Mean, 66.1 Male, n (%): 416 (62%) Race, n (%): NR	Care delivered entirely within ED: multiple Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Tzovaras, 2007[96]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Randomized controlled trial Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2002 to 2005	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 78 Age: NR Male, n (%): 78 (100) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Uchino, 2010	Patient type: General ED Patient age: Adults only Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 39 Annual ED volume: Unclear or NR Ownership: Multiple	Country: US Region, if US: Multiple (but not all) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2002 to 2005	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Process (e.g., left without treatment): received IV- tPA treatment (included) Total N: 254 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Vaghani, 2021	Patient type: VA Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 130 Annual ED volume: Multiple Ownership: Public	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2016 to 2017	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): ER visit with dizziness or headache Total N: 217 Age: Mean, 68.1 Male, n (%): 209 (96.3) Race, n (%): White, 140 (64.5) Black/African American, 66 (30.4)	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: NP, PA Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Vagnarelli, 2016[206]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Unclear or NR Named data source: Dates: to	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: must have the diagnosis of Acute Aortic syndrome and a troponin was drawn to be included Total N: Age: Mean, 66.7 Male, n (%): (66.8) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled:	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: Unclear or NR Harms severity: Unclear or NR Causal taxonomy used: Unclear or NR

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: 31 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Case series Comparison group: None Look back or look forward analysis: Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: Dates: 2001 to 2002	Disease specificity: Not restricted by diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: Other: We selected diagnosis-related settled and closed claim files. Total N: 50 Age: Mean, 44 Male, n (%): 28 (57) Race, n (%):	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Vanbrabant, 2009[75]	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2006 to 2007	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Other: Inclusion (only patients managed by General Internal Medicine service--patients brought in for a medical problem that were not referred to a specific department (cardiology, GI, hepatology). Major trauma, burn, obstetric and pediatric patients were not included Total N: 4860 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Patients return to the ED within 72 hours of a discharge with an new or additional diagnosis. Conceptual harms definition: Return to ED within 72 hours of discharge. Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Vargas-Blasco, 2021	Patient type: Unclear Patient age: Both adults and children Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Multiple	Country: Other Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: The Professional Liability Service of the Council of Medical Associations of Catalonia Medical Practice Liability database and the Confide insurance brokerage firm MPL database. Dates: 2000 to 2018	Disease specificity: Single disease Diseases studied: Testicular torsion Other inclusion criteria: None: Total N: 80 Age: Mean, 16 Range, 0 to 43 Male, n (%): 80 (100) Race, n (%): NR	Care delivered entirely within ED: Primary care, tertiary care hospital, basic hospital Consultants involved: Family Physician, 'family physician + other professional', pediatrician, general or pediatric surgeon, resident physician, urology resident + urologist + 'general surgeon', urologist Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Vasconcelos-Castro, 2020[140]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2017 to 2018	Disease specificity: Single disease Diseases studied: Other Other inclusion criteria: Other: Four patients were excluded owing toundescended testis and neonatal presentation. Seven patients were excluded owing to lack of information about the precise location of painonset Total N: 73 Age: Median, 15.3 Male, n (%): 73 (100) Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Venkat, 2018[162]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: Australia Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Case-control Comparison group: Matched control group Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2014 to 2016	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients presenting to the hospital ED and admitted to the ward with a final discharge diagnosis of stroke (excluding TIA); also included patients with an alternative non-TIA/stroke ED diagnosis; excluded patients with a non-ischemic or primary hemorrhagic stroke Total N: 312 Age: Median, 77 Male, n (%): 178 (57%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: neurology service Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed stroke diagnosis (patients with an alternative non-TIA/stroke ED diagnosis) Conceptual harms definition: discharge modified Rankin Scale and in-hospital mortality Harms severity: modified Rankin Scale Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Verelst, 2014	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 40,000 to 59,999 Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2010 to 2011	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: All patients >= 16 years who returned to the ED due to a related condition within 72 h after ED or hospital discharge wereincluded. Total N: 784 Age: Mean, 47 Male, n (%): 413 (47%) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: departments of Internal Medicine, Pediatrics, Neurology, Surgery, and Psychiatry. Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Vermeulen, 2007[95]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 147 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Canada Region, if US: All US Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Discharge Abstract Database and National Ambulatory Care Reporting System Dates: 2002 to 2005	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients admitted to any hospital though an ED with a diagnosis of nontraumatic subarachnoid hemorrhage Total N: 1507 Age: Mean, 57.9 Male, n (%): 580 (38%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Missed SAH was defined as the presence of an alternative ED main discharge diagnosis, including migraine/headache, neck pain, hypertension, sinusitis, stroke/transient ischemic attack, meningitis, syncope and collapse, or giant cell arteritis Conceptual harms definition: 30-day and 1-year mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Vinz, 2015[64]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Unclear or NR Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator and denominator Named data source: Dates: 2000 to 2012	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: None: Total N: 271 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Vioque, 2014[35]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Registry Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Pennsylvania Trauma Outcomes Study, Dates: 2002 to 2010	Disease specificity: Not restricted by diseases Diseases studied: Other Other inclusion criteria: None: Total N: 106 Age: Mean, 23.2 Male, n (%): 81 (76.4) Race, n (%): NR	Care delivered entirely within ED: Other location (specify) Consultants involved: trauma surgery, anesthesia, Non-physicians involved: nurse, paramedic, respiratory technician Non-EM physicians involved: trauma surgery, radiology, anesthesia Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Unclear or NR Conceptual harms definition: (Trauma PI Conference) Mackenzie et al Harms severity: Injury severity scale ISS and Trauma Score- ISS TRISS Causal taxonomy used: Joint Commission (5 interacting root nodes: impact, type, domain, cause, and prevention)

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Warrick, 2014[31]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Case series Comparison group: Unclear or NR Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2010 to 2011	Disease specificity: Multiple Diseases Diseases studied: Unclear or NR Other inclusion criteria: : Surgical cases, elective day cases with known diagnoses and cases where an initial or discharge diagnosis was not recorded were excluded from the study. Surgical cases were excluded, as in the UK healthcare system, these cases are often referred directly to a surgical center by the primary care physician. Total N: 703 Age: NR Male, n (%): Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Included physicians with other training (specify) Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: APSF/Graber 2005 Conceptual harms definition: Unclear or NR Harms severity: Unclear or NR Causal taxonomy used: Unclear or NR
Waxman, 2018[170]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Medicare standard analytic files Dates: 2007 to 2014	Disease specificity: Multiple diseases Diseases studied: MULTI-VASCULAR Other inclusion criteria: Process (e.g., left without treatment): All fee-for-service Medicare patients newly diagnosed as having ruptured abdominal aortic aneurysm, acute MI, stroke, aortic dissection, or subarachnoid hemorrhage Total N: 1561940 Age: Mean, 77.9 Male, n (%): 716792 (46%) Race, n (%): White, 1278212 (82%) Black/African American, 165287 (11%)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Number of excess ED discharges Conceptual harms definition: Mortality Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Weinberg, 2010[74]	Patient type: General ED Patient age: Both adults and children Teaching status: Academic/Teaching Hospital setting: Single health system, multiple EDs Number of EDs involved: 2 Annual ED volume: Unclear or NR Ownership: Private, not for profit	Country: US Region, if US: Northeast Urban/rural: Urban / metropolitan	Study design: Prospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: Dates: 2007 to 2008	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: Multiple: Inclusion criteria consisted of the following: (1) patients Total N: 212 Age: Median, 13 Male, n (%): Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: Sonologists, radiologists Non-physicians involved: Emergency physicians only Non-EM physicians involved: Sonologists, radiologists Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: MisDx-Related Harms (DNT, 2009) Harms severity: None Causal taxonomy used: None
Wemeijer, 2021	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2010 to 2019	Disease specificity: Not restricted by diseases Diseases studied: NA Other inclusion criteria: Multiple: multi trauma, had an exploring thoracotomy Total N: 51 Age: Mean, 59 Male, n (%): 38 (75%) Race, n (%): NR	Care delivered entirely within ED: surgery Consultants involved: radiology, surgery Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Whiteley, 2011	Patient type: General ED Patient age: Adults only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Public	Country: UK Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Not a cohort study Data source: Unclear or NR Numerator: Numerator and denominator Named data source: NR Dates: 2007 to 2009	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Symptom (e.g., dizziness): We defined suspected acute stroke in those patients: (1) whose symptoms began less than 24 h before admission, (2) who were still symptomatic at the time of assessment and (4) in whom a general practitioner, a paramedic or a member of the ED staff had made a diagnosis of 'suspected stroke.' Total N: 356 Age: Mean, 72 Male, n (%): 173 (49) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: neurologists and neuroradiologists Non-physicians involved: nurse Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Williams, 2009[81]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Comparison of Patients With and Without a DDI Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 1997 to 2006	Disease specificity: Multiple diseases Diseases studied: OTHER MULTIPLE Other inclusion criteria: Process (e.g., left without treatment): Patients who were directly admitted from another hospital or died in the ED were excluded Total N: 1100- 44 with DDI Age: Range, 0-14 Male, n (%): Race, n (%):	Care delivered entirely within ED: ED only Consultants involved: Emergency clinicians only Non-physicians involved: Emergency physicians only Non-EM physicians involved: EM trained physicians only Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delayed diagnosis of injury (DDI)-DDI as any injury that was not identified until after astable patient arrived at his or her hospital room. In patients immediately transported to the operating suite upon arrival, DDI was defined as an injury not identified Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Williams, 2019[152]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 37 Annual ED volume: Multiple Ownership: Multiple	Country: Australia Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2011 to 2016	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: Patients presenting to the hospital with STEMI and failed to receive timely reperfusion therapy Total N: 1392 Age: Mean, 63.9 -66.3 Male, n (%): 1020 (73%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Cardiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Patients who presented with a STEMI and who were not identified, had treatment commenced, or it was clear on review that STEMI was not considered within a four-hour period were defined as missed acute MI Conceptual harms definition: Inpatient mortality Harms severity: None Causal taxonomy used: None
Willms, 2021	Patient type: General ED Patient age: Both adults and children Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 41 Annual ED volume: Multiple Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Pre/post comparison Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2019 to 2020	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 1915 Age: NR Male, n (%): 978 (51%) Race, n (%): NR	Care delivered entirely within ED: surgery Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Willner, 2012[6]	Patient type: General ED Patient age: Children only Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: 60,000 to 79,999 Ownership: Private, for profit	Country: US Region, if US: West Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator Named data source: EHRs Dates: 2005 to 2008	Disease specificity: Not restricted by diseases Diseases studied: Other Other inclusion criteria: Other: excluded trauma patients initially treated at other institutions and transferred directly to an inpatient unit Total N: 324 Age: Median, 7.5 Male, n (%): 193 (59.6) Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: trauma tea: pediatric EM attending, pediatric surgery attending or fellow, ED residents, surgical residents, pediatric ICU and pediatric ED nurses, radiologists, orthopedics Non-physicians involved: ED nurses, pediatric ICU nurses Non-EM physicians involved: Radiologist, orthopedics, surgery Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Delayed diagnosis of injury: a previously unsuspected injury attributable to trauma greater than 12 hours after presentation Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Wilson, 2014[28]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: 4576 Annual ED volume: Multiple Ownership: Multiple	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Cross-sectional Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator Named data source: Inpatient and Outpatient Standard Analytic Files Dates: 2004 to 2005	Disease specificity: Single disease Diseases studied: MI Other inclusion criteria: Other: diagnosed with acute MI who presented to the ED for initial care; included patients who were admitted to the hospital, discharged to home or a skilled nursing facility, or transferred to another facility for further care Total N: 371638 Age: Median, 80 Male, n (%): 177650 (48) Race, n (%): White, 326129 (88) Black/African American, 29292 (8)	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Excluded	Conceptual Dx error definition: missed acute MI diagnosis (ED discharge home with a condition suggestive of cardiac ischemia with subsequent hospital admission within 7 days with acute MI. Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Wilson, 2020[141]	Patient type: Unclear or NR Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Multi-center study Number of EDs involved: Unclear or NR Annual ED volume: Multiple Ownership: Unclear or NR	Country: US Region, if US: All US Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm) Named data source: Westlaw database Dates: 1987 to 2018	Disease specificity: Single disease Diseases studied: VTE Other inclusion criteria: Other: Jury verdicts involving pulmonary embolism or deep vein thrombosis; included cases involving surgical management, medical management, interventional management, and anesthesia Total N: 277 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Reason the physician was being help liable Conceptual harms definition: The complication endured by the patient for which the defendant was being held liable Harms severity: None Causal taxonomy used: None
Winkler, 2009[84]	Patient type: Stroke Unit Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Suburban / micropolitan	Study design: Registry Comparison group: Concurrent control Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator Named data source: NA Dates: 1998 to 2007	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Patients treated with intravenous thrombolysis Total N: 250 Age: Mean, 67.8 Male, n (%): 147 (59) Race, n (%): NR	Care delivered entirely within ED: intensive care unit Consultants involved: neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: neurologists Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Stroke mimic (final diagnosis other than stroke) Conceptual harms definition: Rankin scale, death, occurrence of orolingual angioedema, and intracranial hemorrhage Harms severity: Rankin scale Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Wireklint Sundström, 2015[68]	Patient type: General ED Patient age: Unclear or NR Teaching status: Mixed EDs included Hospital setting: Single health system, multiple EDs Number of EDs involved: 9 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Multiple settings	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Unclear or NR Named data source: NA Dates: 2010 to 2011	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Admitted to hospital with final diagnosis of stroke (intracerebral hemorrhage, unspecific brain hemorrhage, cerebral infarction, and stroke not classified as infarction or hemorrhage). Excluded patients with in-hospital stroke, subarachnoid hemorrhage, and extracranial hemorrhage. Total N: 1376 Age: Median, 79 Male, n (%): 702 (51) Race, n (%):	Care delivered entirely within ED: Stroke unit Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Time from arrival in hospital to radiological evaluation, arrival in ward, and thrombolysis or thrombectomia Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Yeboah, 2019[160]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2012 to 2015	Disease specificity: Single disease Diseases studied: Stroke Other inclusion criteria: Other: Trauma as reason for presentation to the ED; excluded patients with intracranial hemorrhage Total N: 11 Age: Median, 49 Male, n (%): 8 (73%) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Diagnosed with stroke on initial presentation to the ED Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
Yi, 2017[185]	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: US Region, if US: Midwest Urban/rural: Urban / metropolitan	Study design: Comparison group: Unclear or NR Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR Named data source: Dates: 2015 to 2016	Disease specificity: Single disease Diseases studied: BIG THREE Other inclusion criteria: Unclear or NR: Total N: 192 Age: Mean, 67.3 Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: ED only Consultants involved: stroke neurologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
York, 2005[104]	Patient type: General ED Patient age: Children only Teaching status: Unclear or NR Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Canada Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm) Named data source: Dates: 2002 to 2004	Disease specificity: Single disease Diseases studied: Appendicitis Other inclusion criteria: None: Total N: 197 Age: Mean, 10.5 Range, 2-17 Male, n (%): 122 (62) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: radiologists Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None

Author, Year	Characteristics of ED	Location	Study Design Characteristics	Patient Characteristics	Study Details	Diagnostic Error Definition/Taxonomy
York, 2020	Patient type: General ED Patient age: Unclear or NR Teaching status: Academic/Teaching Hospital setting: Single hospital ED Number of EDs involved: 1 Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: UK Region, if US: NA (non-US) Urban/rural: Urban / metropolitan	Study design: Retrospective cohort Comparison group: None Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: Dates: 2011 to 2014	Disease specificity: Single disease Diseases studied: Fractures Other inclusion criteria: None: Total N: 2947 Age: NR Male, n (%): NR Race, n (%): NR	Care delivered entirely within ED: radiology Consultants involved: Emergency clinicians only Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Included trainees How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: None Conceptual harms definition: None Harms severity: None Causal taxonomy used: None
Zaschke, 2020[128]	Patient type: General ED Patient age: Unclear or NR Teaching status: Unclear or NR Hospital setting: Transferred from another regional hospital Number of EDs involved: Unclear or NR Annual ED volume: Unclear or NR Ownership: Unclear or NR	Country: Western Europe Region, if US: NA (non-US) Urban/rural: Unclear or NR	Study design: Retrospective cohort Comparison group: Concurrent control Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator Named data source: NA Dates: 2012 to 2016	Disease specificity: Single disease Diseases studied: AAD Other inclusion criteria: Other: Patients with non-iatrogenic type A aortic dissection Total N: 350 Age: Mean, 63.2 Male, n (%): 222 (63.4) Race, n (%): NR	Care delivered entirely within ED: Unclear or NR Consultants involved: Unclear or NR Non-physicians involved: Unclear or NR Non-EM physicians involved: Unclear or NR Trainees involved: Unclear or NR How left without treatment was handled: Unclear or NR	Conceptual Dx error definition: Initial misdiagnosis vs. aortic dissection included as sole or differential diagnosis in initial workup Conceptual harms definition: 30-day mortality Harms severity: None Causal taxonomy used: None

AAD: Aortic aneurysm and dissection; ACS: Acute coronary Syndrome; APSF: Anesthesia Patient Safety Foundation; CI: Confidence Interval; Dx: Diagnostic Error; ED: Emergency Department; EM: Emergency Medicine; HCUP: Healthcare Cost and Utilization Project; HDP: Hypertensive disorders of pregnancy; IOM: Institutes of Medicine; ISS: Injury Severity Score; IV-tPA: Intravenous tissue plasminogen activator; NA: Not Applicable; NAM: National Academies of Medicine; NR: Not reported; pICU: Pediatric Intensive Care Unit; STEMI: ST-elevated myocardial infarction; UK: United Kingdom; US: United States; VTE: Venous thromboembolism; MI: Myocardial infarction

Table D-2. Results of studies that reported on the distribution of diseases with diagnostic errors in the emergency department

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Neurologic	NR	NR	9	NR	NR	NR
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Infectious	NR	NR	7	NR	NR	NR
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Cardiac	NR	NR	4	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Abdominal	NR	NR	3	NR	NR	NR
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Withdrawal/intoxication	NR	NR	1	NR	NR	NR
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	1,106,606	511	31	NR	NR	NR
Aaronson, 2020[136]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Other	NR	NR	7	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Avelino-Silva, 2020[117]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Secondary analysis on National Hospital Ambulatory Medical Survey Data source: National Hospital Ambulatory Medical Survey Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	5,767	NR	588	NR	NR	NR
Bourdon, 2020[123]	Patient type: Eye and Ear ED Patient age: Multiple Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	500	NR	32	NR	NR	NR
Breen, 2017[179]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Registry Data source: Malpractice claims Numerator: Numerator only (error/harm)	Fractures	N/A	NR	12	NR	NR	NR
Breen, 2017[179]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Registry Data source: Malpractice claims Numerator: Numerator only (error/harm)	Congenital/development anomalities	N/A		8	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Breen, 2017[179]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Registry Data source: Malpractice claims Numerator: Numerator only (error/harm)	Cancer (leukemia, lymphoma, bone, CNS, other)	N/A	NR	7	NR	NR	NR
Breen, 2017[179]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Registry Data source: Malpractice claims Numerator: Numerator only (error/harm)	Other (GI, GU, respiratory, MSK deformity)	N/A	NR	13	NR	NR	NR
Breen, 2017[179]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Registry Data source: Malpractice claims Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	n/A	NR	50	NR	NR	NR
Calder, 2021	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Canada	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator and denominator	Arrythmias	1911	NR	13	NR	NR	NR
Calder, 2021	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Canada	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator and denominator	Acute Heart Failure	867	NR	10	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Calder, 2021	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Canada	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	4741	NR	34	NR	NR	NR
Calder, 2021	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Canada	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator and denominator	Syncope	1912	NR	11	NR	NR	NR
Catapano, 2017[176]	Patient type: orthopaedic care Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	13561	NR	337	NR	NR	NR
Catapano, 2017[176]	Patient type: orthopaedic care Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Fractures	NR	NR	337	147	NR	NR
Fernholm, 2019[145]	Patient type: NR Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Malpractice claims Numerator: Numerator only (error/harm)	Fractures	NR	NR	138	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Fernholm, 2019[145]	Patient type: NR Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Malpractice claims Numerator: Numerator only (error/harm)	Ruptured tendons	NR	NR	107	NR	NR	NR
Fernholm, 2019[145]	Patient type: NR Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Malpractice claims Numerator: Numerator only (error/harm)	Appendicitis	NR	NR	24	NR	NR	NR
Fernholm, 2019[145]	Patient type: NR Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Malpractice claims Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	N/A	N/A	578	NR	NR	45
Fernholm, 2019[145]	Patient type: NR Patient age: Not age restricted Country: Western Europe	Study design: Retrospective cohort Data source: Malpractice claims Numerator: Numerator only (error/harm)	infection	NR	NR	58	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	N/A	N/A	20	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	Appendicitis	NR	NR	7	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	intussusception	NR	NR	2	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	bowel obstruction	NR	NR	2	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	ovarian torsion	NR	NR	1	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	thalamic brain tumor	NR	NR	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	acute lymphoblastic leukemia	NR	NR	1	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	perianal abscess	NR	NR	1	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	cardiomyopathy	NR	NR	1	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	bladder rhabdomyosarcoma	NR	NR	1	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	pancreatitis	NR	NR	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	perforated Hartman's pouch	NR	NR	1	NR	NR	NR
Freedman, 2014[37]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	ileal volvulus	NR	NR	1	NR	NR	NR
Gleason, 2020[115]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	53	NR	6	NR	NR	NR
Goulet, 2015[70]	Patient type: General ED Patient age: Unclear or NR Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	484	47	18	18	18	18

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Fractures	NR	NR	1007	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Other/Diagnosis not specified	NR	NR	679	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	MI	NR	NR	161	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Stroke	NR	NR	97	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Intracranial Bleed	NR	NR	140	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Acute Abdomen	NR	NR	77	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Arterial thromboembolism	NR	NR	34	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Ectopic pregnancy	NR	NR	31	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Appendicitis	NR	NR	17	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Ischemic Limb	NR	NR	15	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	VTE	NR	NR	11	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Meningitis	NR	NR	11	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	Pneumonia	NR	NR	8	NR	NR	NR
Hussain, 2019[135]	Patient type: NR Patient age: Unclear or NR Country: UK	Study design: Cross-sectional Data source: National Reporting and Learning System (NRLS) Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	N/A	N/A	2288	NR	128	NR
Liberman, 2020[210]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Stroke	186	NR	93	NR	NR	NR
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	acute gallbladder pathology	NR	NR	10	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	urinary system infections	NR	NR	5	NR	NR	NR
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	diverticulitis	NR	NR	2	NR	NR	NR
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	small bowel obstruction	NR	NR	2	NR	NR	NR
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Appendicitis	NR	NR	2	NR	NR	NR
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	cancer	NR	NR	2	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	ectopic pregnancy	NR	NR	2	NR	NR	NR
Medford-Davis, 2016[66]	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	621	100	35	NR	NR	NR
Mirete, 2005[212]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Cross-sectional Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	528	NR	104	NR	NR	6
Montmany, 2008[5]	Patient type: General ED Patient age: Multiple Country: Western Europe	Study design: Prospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Missed Injuries in Polytrauma Patients, Clinically Relevant	75	NR	29	NR	NR	5

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pregnancy	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pulmonary oedema	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Spinal cord compression	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Strangulated abdominal hernia	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Symptomatic anemia	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Urethral injury	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Urinary retention	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Worsening brain metastasis	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Stroke	N/A	N/A	10	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Arrythmias	N/A	N/A	7	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Arterial thromboembolism	N/A	N/A	5	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Sepsis	N/A	N/A	20	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Meningitis	N/A	N/A	3	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pneumonia	N/A	N/A	5	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Appendicitis	N/A	N/A	4	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Fractures	N/A	N/A	18	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	N/A	N/A	209	172	34	
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Acute coronary syndrome	N/A	N/A	19	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Vascular injury	N/A	N/A	18	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Non-septic shock	N/A	N/A	6	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Hypoglycemia	N/A	N/A	6	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Electrolyte derangement	N/A	N/A	5	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pericardial effusion	N/A	N/A	5	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Abscess	N/A	N/A	4	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Bowel injury	N/A	N/A	4	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Gastrointestinal bleeding	N/A	N/A	4	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Coagulopathy	N/A	N/A	3	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Haemoperitoneum	N/A	N/A	3	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Intestinal malrotation	N/A	N/A	3	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Peritonitis	N/A	N/A	3	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Rh-negative status	N/A	N/A	3	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Small bowel obstruction	N/A	N/A	3	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Cerebral oedema	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Cholecystitis	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Diabetic ketoacidosis	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Epidural hematoma	N/A	N/A	2	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Hypoxia	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Intraocular foreign body	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Subdural hematoma	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Testicular injury	N/A	N/A	2	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Urinary tract infection/pyelonephritis	N/A	N/A	2	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Acute closure glaucoma	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Angioedema	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Autonomic dysreflexia	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Cancer	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Cardiac injury	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Central vertigo	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Complex migraine	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Cranial nerve palsy	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Hirschsprung enterocolitis	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Hyperglycemia	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Hypokalemic periodic paralysis	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Infected kidney stone	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Intra-abdominal bleeding	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Intracranial shunt malfunction	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Laryngeal mass	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Nephrotic syndrome	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Demyelinating disease	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Neutropenia	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Ovarian torsion	N/A	N/A	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pericarditis	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pleural effusion	N/A	N/A	1	NR	NR	NR
Okafor, 2016[65]	Patient type: General ED Patient age: Unclear or NR Country: US	Study design: Case series Data source: Voluntary Medical Error Reporting System Numerator: Numerator only (error/harm)	Pulmonary contusion	N/A	N/A	1	NR	NR	NR
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Anterior segment	NR	254	76	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Posterior segment	NR	191	81	NR	NR	NR
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Orbit & ocular adnexa	NR	66	13	NR	NR	NR
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Neurologic	NR	60	25	NR	NR	NR
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Uveitis	NR	40	3	NR	NR	NR
Oliver, 2019[143]	Patient type: Eye and Ear ED Patient age: Unclear or NR Country: Canada	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Glaucoma	NR	25	7	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Functional impairment	NR	NR	30	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Urinary tract infection	NR	NR	26	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Electrolyte disorders	NR	NR	19	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Depression/anxiety	NR	NR	17	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Heart failure	NR	NR	14	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Dementia	NR	NR	13	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Malignant neoplasie	NR	NR	14	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Dehydration	NR	NR	8	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Renal failure	NR	NR	20	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Orthostasis	NR	NR	10	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Intoxication	NR	NR	16	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Pneumonia	NR	NR	12	NR	NR	NR
Peng, 2015[26]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	N/A	N/A	199	NR	NR	NR
Perry, 2020[208]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Multiple Numerator: Numerator only (error/harm)	Appendicitis	NR	NR	19	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Perry, 2020[208]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Multiple Numerator: Numerator only (error/harm)	Fractures	NR	NR	10	NR	NR	NR
Perry, 2020[208]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Multiple Numerator: Numerator only (error/harm)	nonaccidental trauma	NR	NR	6	NR	NR	NR
Perry, 2020[208]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Multiple Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	NR	105	105	NR	NR	NR
Petinaux, 2011	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Evaluation of bone xray	82557	NR	NR	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Petinaux, 2011	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Abdomen x-ray evaluation	5987	NR	NR	NR	NR	NR
Petinaux, 2011	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	chest xray evaluation	63149	NR	NR	NR	NR	NR
Petinaux, 2011	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Evaluation of bone xray	82557	NR	NR	NR	NR	NR
Petinaux, 2011	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Abdomen x-ray evaluation	5987	NR	NR	NR	NR	NR
Petinaux, 2011	Patient type: General ED Patient age: Not age restricted Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	chest xray evaluation	63149	NR	NR	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Seward, 2003[213]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: UK	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	200	NR	39	NR	NR	NR
Seward, 2003[213]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: UK	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	190	NR	30	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Other	NR	NR	1	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Isolated alcohol intoxication	NR	NR	7	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Seizure/post-ictal	NR	NR	1	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Stroke	NR	NR	3	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Isolated other drug intoxication	NR	NR	6	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Traumatic brain injury	NR	NR	3	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Other metabolic derangement	NR	NR	6	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Sepsis	NR	NR	2	NR	NR	NR
Sporer, 2013[45]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: US	Study design: Prospective cohort Data source: Prospective data collection Numerator: Numerator only (error/harm)	Combination alcohol/other drug intoxication	NR	NR	10	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Appendicitis	1135	85	7	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Pancreatitis	310	85	16	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Septic shock	225	116	6	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Kawasaki disease	194	66	17	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Septic arthritis	162	39	12	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Ovarian torsion	58	7	3	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	VTE	22	13	2	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Stroke	20	16	2	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Hemolytic uremic syndrome	18	4	2	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Arterial thromboembolism	7	1	0	NR	NR	NR
Sundberg, 2018[165]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: US	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	2151	432	67	NR	NR	NR
Tudela, 2005[105]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	NR	NR	NR	NR	NR	NR	NR
Tudela, 2005[105]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	669	669	42	18	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Missed fractures	NR	NR	16	NR	NR	NR
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Delayed diagnoses of fractures	NR	NR	12	NR	NR	NR
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Missed luxations	NR	NR	5	NR	NR	NR
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Delayed diagnoses of luxations	NR	NR	1	NR	NR	NR
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Missed tendon lesions	NR	NR	5	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Missed other diagnoses	NR	NR	8	NR	NR	NR
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	Other	NR	NR	3	NR	NR	NR
van Noord, 2010[61]	Patient type: Unclear or NR Patient age: Unclear or NR Country: Western Europe	Study design: Case series Data source: Malpractice claims Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	N/A	N/A	50	NR	NR	NR
Vanbrabant, 2009[75]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Appendicitis	4860	NR	2	NR	NR	NR
Vanbrabant, 2009[75]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	ACS	4860	NR	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Vanbrabant, 2009[75]	Patient type: General ED Patient age: Adults (i.e., >=18 years) Country: Western Europe	Study design: Retrospective cohort Data source: Electronic health record data Numerator: Numerator and denominator	Pneumonia	4860	NR	1	NR	NR	NR
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	TOTAL ACROSS ALL DISEASES (REPORTED IN STUDY)	NR	NR	19	NR	NR	NR
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Neurology/psychiatry	NR	NR	7	NR	NR	NR
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Cardiology	NR	NR	2	NR	NR	NR
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Respiratory	NR	NR	1	NR	NR	NR

Author, Year	ED Characteristics	Study Design Characteristics	Condition	N (Source Population)	N (Trigger Positive)	N (Diagnostic Errors)	N (Misdiagnosis-Related Harms)	N (Serious Misdiagnosis-Related Harms)	N (Misdiagnosis-Related Deaths)
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Gastroenterology	NR	NR	2	NR	NR	NR
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Musculoskeletal	NR	NR	1	NR	NR	NR
Warrick, 2014[31]	Patient type: General ED Patient age: Children (i.e., <18 years) Country: UK	Study design: Case series Data source: Electronic health record data Numerator: Numerator only (error/harm)	Infection/ immunology	NR	NR	6	NR	NR	NR

ACS: Acute coronary syndrome; CI: Confidence Interval; DecrRisk: Decreased Risk; ED: Emergency Department; IncrRisk: Increased Risk; RLQ: Right lower quadrant; SES: Socioeconomic status

Table D-3. Results of studies that reported on the rates of diagnostic errors in the emergency department

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Aaronson, 2016[204]	Accuracy across all diseases if more than one category	NA	1006	NR	NR	20	127	NR	NR	NR	86.39	NR	NR	NR	NR
Aaronson, 2016[204]	Patients >72 hours returns	NA	1006	NR	NR	124	735	NR	NR	NR	85.56	NR	NR	NR	NR
Aaronson, 2018[177]	Accuracy across all diseases if more than one category	NA	413,167	NR	413177	60	NR	NR	NR	NR	NR	NR	NR	NR	NR
Agrawal, 2019[157]	MI	STEMI	361	82	279	NR	NR	NR	NR	77.29	NR	NR	NR	NR	NR
Arch, 2016[205]	Stroke	Stroke - Ischemic stroke	465	NR	362	103	NR	77.8	NR	NR	NR	NR	NR	NR	NR
Bartiaux, 2017[181]	Accuracy across all diseases if more than one category	NA	332	NR	NR	20	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bastakoti, 2021	Accuracy across all diseases if more than one category	NA	418	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	76.1	21.8
Bayne, 2017[184]	Testicular torsion	Undetermined	216	NR	NR	12	NR	NR	NR	NR	NR	NR	NR	NR	NR
Beaver, 2005[107]	AAD	Undetermined	100	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	76	24
Beaver, 2005[107]	AAD	Aortic aneurysm	100	7	NR	7	NR	NR	NR	NR	NR	NR	NR	NR	NR
Beaver, 2005[107]	AAD	Aortic dissection	100	14	NR	6	NR	NR	NR	NR	NR	NR	NR	NR	NR
Bhattacharya, 2013	Stroke	NA	77	NR	66	11	NR	85.7	NR	NR	NR	NR	NR	NR	NR
Branstetter, 2007	Diagnosis based on radiograph	NA	65780	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2.2%

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Breen, 2017[179]	Accuracy across all diseases if more than one category	NA	71	NR	NR	50	NR	NR	NR	NR	NR	NR	NR	NR	NR
Breen, 2017[179]	Fractures	NA (all fractures)	71	NR	NR	12	NR	NR	NR	NR	NR	NR	NR	NR	NR
Broadley, 2003	Stroke	NA	284	39	245	NR	NR	NR	NR	86.27	NR	NR	NR	NR	NR
Calder, 2010[58]	Accuracy across all diseases if more than one category	NA	418	NR	493	10	NR	98	NR	NR	NR	NR	NR	NR	NR
Calic, 2016[195]	Stroke	Stroke - Ischemic stroke	NR	0	76	39	0	66.1	NR	100	0	NR	NR	NR	NR
Carlton, 2015[69]	MI	Undetermined	912	336	58	56	462	50.9	57.89	14.72	89.19	NR	NR	NR	NR
Catapano, 2017[176]	Fractures	NA (all fractures)	13561	44	NR	293	NR	NR	NR	NR	NR	NR	NR	97.5	2.5
Caterino, 2012[21]	Acute Urinary Tract Infection	NA	275	4	14	10	75	58	95	78	88	11.52	0.44	NR	NR
Caterino, 2012[21]	Osteomyelitis	NA	275	2	1	2	98	33	98	33	98	16.67	0.68	NR	NR
Caterino, 2012[21]	Sepsis	Acute Bloodstream Infection/Bacteremia	275	16	6	9	69	40	78	24	88	1.85	0.76	NR	NR
Caterino, 2012[21]	Acute Pulmonary Infection (Pnuemonia/ Emypema)	NA	275	17	38	4	44	90	72	69	92	3.24	0.13	NR	NR
Caterino, 2012[21]	Acute Skin and Soft Tissue Infection	NA	275	3	11	3	86	79	96	79	97	23.31	0.22	NR	NR
Caterino, 2012[21]	Acute GI Infection (Including appendicitis)	NA	275	3	4	4	92	50	97	57	96	15.83	0.52	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Caterino, 2012[21]	Acute Central Nervous System Infection (Including Meningtis, Epidural Abscess)	NA	275	0	1	0	102	100	100	1	1	NR	0	NR	NR
Chan, 2019[150]	Testicular torsion	Absent or diminished flow	46	1	41	3	1	93.02	50	95.24	40	NR	NR	NR	NR
Chan, 2019[150]	Testicular torsion	Absence of arterial waveform	46	NR	26	18	NR	58.33	NR	100	0	NR	NR	NR	NR
Chan, 2019[150]	Testicular torsion	Heterogeneous echotexture	46	1	15	29	1	35.48	66.67	91.67	9.09	NR	NR	NR	NR
Chan, 2019[150]	Testicular torsion	Absence of doppler flow	46	1	29	15	1	65.12	75	96.55	16.67	NR	NR	NR	NR
Chan, 2020[125]	VTE	VTE - Pulmonary embolism	123	NR	230	72	NR	76.2	NR	NR	NR	NR	NR	NR	NR
Chompoopong, 2017[182]	Stroke	Stroke - Ischemic stroke	90000	NR	1384	919	NR	60.1	NR	NR	NR	NR	NR	NR	NR
Christenson, 2004	Acute coronary syndrome	NA	1819	373	377	21	1048	94.7	73.8	50.3	98.0	3.61	0.07	NR	NR
Chung, 2009[22]	Radiologist resident misread of torso CT relative to attending radiologists (gold standard)	NA	4768	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2%
Comolli, 2020[129]	Stroke	Ischemic stroke or TIA	286	NR	NR	9	NR	NR	NR	NR	NR	NR	NR	NR	NR
Conti, 2003[112]	MI	Perfusion defects	306	60	45	3	198	93.8	76.74	42.86	98.51	NR	NR	NR	NR
Conti, 2003[112]	MI	Wall motion abnormalities	306	42	45	4	216	91.8	83.72	51.72	98.18	NR	NR	NR	NR
Corral Gudino, 2003[111]	pulmonary embolism	NA	58	NR	43	15	NR	74.1	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Crosby, 2013[16]	Accuracy across all diseases if more than one category	NA	2415	NR	2402	13	NR	99.5	NR	NR	NR	NR	NR	NR	NR
Czolgosz, 2019[142]	Accuracy across all diseases if more than one category	NA	164	NR	160	4	NR	97.6	NR	NR	NR	NR	NR	NR	NR
Degheim, 2019[149]	MI	STEMI	347	37	328	2	8	99.4	17.78	89.86	80	NR	NR	NR	NR
Dubosh, 2015[11]	Serious neurologic disorder or in-hospital death with misdiagnosis of headache	NA	143000000	NR	NR	10374	2090707	NR	NR	NR	99.5	NR	NR	NR	NR
Dubosh, 2015[11]	Serious neurologic disorder or in-hospital death with misdiagnosis of back pain	NA	143000000	NR	NR	2,850	1378764	NR	NR	NR	99.8	NR	NR	NR	NR
Dubosh, 2019[154]	Neurologic events with headache diagnosis	NA	3482695	NR	NR	10374	NR	NR	NR	NR	NR	NR	NR	NR	NR
Dubosh, 2019[154]	Neurologic events with back pain diagnosis	NA	3482695	NR	NR	2850	NR	NR	NR	NR	NR	NR	NR	NR	NR
Fasen, 2020[131]	Stroke	Large vessel occlusion in acute anterior circulation ischemic stroke	520	NR	67	17	NR	79.8	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Ferree, 2016[1]	Delayed identification of physical injuries (including fractures, ligament/tendon injuries, external wounds, burns, bowel perforation, hemothorax)	NA	1416	NR	NR	170	NR	NR	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Hand	1416	NR	33	39	NR	46	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Foot	1416	NR	38	23	NR	62	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Tibia	1416	NR	42	11	NR	79	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Fibula	1416	NR	18	4	NR	82	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Ankle	1416	NR	40	7	NR	85	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Humerus	1416	NR	75	13	NR	85	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Radius	1416	NR	98	11	NR	90	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Knee	1416	NR	24	2	NR	92	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Ulna	1416	NR	88	8	NR	92	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Clavicle	1416	NR	184	12	NR	94	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Scapula	1416	NR	122	5	NR	96	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Femur	1416	NR	131	3	NR	98	NR	NR	NR	NR	NR	NR	NR
Ferree, 2016[1]	Fractures	Cruris	1416	NR	84	2	NR	98	NR	NR	NR	NR	NR	NR	NR
Filippi, 2008[23]	Accuracy across all diseases if more than one category	NA	361	3	170	23	165	88	98.2	98.3	87.8	NR	NR	NR	NR
Freedman, 2017[17]	Abdominal radiograph not performed	NA	282225	NR	NR	30581	NR	NR	NR	NR	NR	NR	NR	NR	NR
Freedman, 2017[17]	Abdominal radiograph performed	NA	282225	NR	NR	21333	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gallagher, 2006[13]	Acute Abdominal Pain	NA	153	NR	NR	NR	NR	0.97	0.3	NR	NR	NR	NR	NR	NR
Gallagher, 2006[13]	Acute Abdominal Pain	NA	153	NR	NR	NR	NR	0.98	0.46	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Garfield, 2004[108]	Appendicitis	Undetermined	124	2	40	NR	NR	NR	NR	95	NR	NR	NR	NR	NR
Garfield, 2004[108]	Appendicitis	Undetermined	124	4	63	NR	NR	NR	NR	94	NR	NR	NR	NR	NR
Garfield, 2004[108]	Appendicitis	Undetermined	124	1	7	NR	NR	NR	NR	87.5	NR	NR	NR	NR	NR
Garfield, 2004[108]	Appendicitis	Undetermined	124	1	7	NR	NR	NR	NR	87.5	NR	NR	NR	NR	NR
Garfield, 2004[108]	Appendicitis	Undetermined	124	8	116	NR	NR	NR	NR	93.5	NR	NR	NR	NR	NR
Gaughan, 2009[82]	AAD	AAD - Abdominal aortic aneurysm	98	NR	54	44	NR	55.1	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Accuracy across all diseases if more than one category	NA	172907	NR	NR	174	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	NA (all fractures)	172907	NR	NR	19	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Face	172907	NR	NR	4	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Leg	172907	NR	NR	3	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Hand	172907	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Foot	172907	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Rib	172907	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Pelvis	172907	NR	NR		NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Scapula	172907	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Gergenti, 2019[153]	Fractures	Vertebrae	172907	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Geyer, 2013[214]	Fractures	NA (all fractures)	375	NR	336	39	NR	89.6	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Ghobadi, 2021	VTE	NA	10534	NR	NR	6	NR	95.2	68.6	2.4	99.9	NR	NR	NR	NR
Gleason, 2020[115]	Accuracy across all diseases if more than one category	NA	59	NR	47	6	NR	88.7	NR	NR	NR	NR	NR	NR	NR
Gouin, 2006[103]	Posttime period PCAS	NA	3074	NR	NR	NR	NR	96.4	98.9	97.7	98.3	NR	NR	NR	NR
Gouin, 2006[103]	Pretime period PCAS	NA	3074	NR	NR	NR	NR	98.1	96.6	99.2	99.2	NR	NR	NR	NR
Goulet, 2015[70]	Accuracy across all diseases if more than one category	NA	555	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Graff, 2006[99]	MI	Undetermined	7888	NR	5861	2027	NR	74.3	NR	NR	NR	NR	NR	NR	NR
Graff, 2014[29]	MI	Undetermined	295758	NR	6291	181	NR	97.2	NR	NR	NR	NR	NR	NR	NR
Grewal, 2015	Stroke	Undetermined	8596	NR	NR	25	8571	NR	NR	NR	99.71	NR	NR	NR	NR
Groot, 2016[71]	MI	STEMI	827	68	759	NR	NR	NR	NR	91.78	NR	NR	NR	NR	NR
Grosmaitre, 2013[36]	MI	Undetermined	255	NR	189	66	NR	74.1	NR	NR	NR	NR	NR	NR	NR
Grosmaitre, 2013[36]	MI	Undetermined	255	NR	149	106	NR	58.4	NR	NR	NR	NR	NR	NR	NR
Guillan, 2012[43]	Stroke	Undetermined	621	15	606	NR	NR	NR	NR	97.58	NR	NR	NR	NR	NR
Hallas, 2006[102]	Fractures	NA (all fractures)	1323	21	NR	40	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hallas, 2006[102]	Fractures	Ankle	1323	NR	NR	11	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hallas, 2006[102]	Fractures	Lower arm	1323	NR	NR	9	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hallas, 2006[102]	Fractures	Hand	1323	NR	NR	4	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hallas, 2006[102]	Fractures	Hip	1323	NR	NR	4	NR	NR	NR	NR	NR	NR	NR	NR	NR
Hansen, 2007[94]	AAD	Undetermined	66	NR	40	26	NR	60.6	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Hansen, 2016[198]	Accuracy across all diseases if more than one category	NA	151	NR	NR	48	NR	NR	NR	NR	NR	NR	NR	NR	NR
Harbison, 2003[113]	Stroke	Undetermined	93	27	66	NR	NR	NR	NR	70.97	NR	NR	NR	NR	NR
Hautz, 2019[148]	Accuracy across all diseases if more than one category	NA	755	NR	NR	68	NR	NR	NR	NR	NR	NR	NR	87.8%	12.2%
Heckmann, 2004[110]	Stroke	Undetermined	138	29	109	NR	NR	NR	NR	78.99	NR	NR	NR	NR	NR
Heitmann, 2016[194]	Accuracy across all diseases if more than one category	NA	162	NR	151	13	NR	92.1	NR	NR	NR	NR	NR	NR	NR
Hochberg, 2011[47]	Stroke	Stroke - Subarachnoid hemorrhage	83	1	46	7	29	.87	.97	.98	.81	NR	NR	NR	NR
Hoekstra, 2009[78]	MI	STEMI	1830	NR	91	25	1714	78.4	NR	NR	98.56	NR	NR	NR	NR
Holland, 2015[72]	Stroke	Stroke - Intracerebral hemorrhage	984	22	291	NR	NR	NR	NR	92.97	NR	NR	NR	NR	NR
Holland, 2015[72]	Stroke	Stroke - Subarachnoid hemorrhage	984	37	270	NR	NR	NR	NR	87.95	NR	NR	NR	NR	NR
Jiménez Castro, 2007[93]	VTE	VTE - Pulmonary embolism	397	NR	325	72	NR	81.9	NR	NR	NR	NR	NR	NR	NR
Jiménez Castro, 2007[93]	VTE	VTE - Pulmonary embolism	397	NR	NR	9	NR	NR	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	NA (all fractures)	2,316	63	NR	62	NR	NR	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Elbow	2,316	NR	146	20	NR	88	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Wrist	2,316	NR	277	25	NR	91.7	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Fingers	2,316	NR	727	35	NR	95.4	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Metacarpus	2,316	NR	136	6	NR	95.8	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Kargl, 2019[158]	Fractures	Toes	2,316	NR	220	8	NR	96.5	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Knee	2,316	NR	192	4	NR	98	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Midfoot	2,316	NR	310	6	NR	98.1	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Ankle	2,316	NR	322	6	NR	98.2	NR	NR	NR	NR	NR	NR	NR
Kargl, 2019[158]	Fractures	Skull	2,316	NR	1884	4	NR	99.8	NR	NR	NR	NR	NR	NR	NR
Kerber, 2006	Stroke	of those who had ref dx of stroke, these had an index dx of stroke (regardless of symptom)	1666	NR	30	16	NR	65.2	NR	NR	NR	NR	NR	NR	NR
Kerber, 2006{Kerber, 2006 #18946}	Stroke	of those presenting with isolated dizziness, the following were diagnosed with stroke	1666	10	5	NR	NR	NR	NR	33.33	NR	NR	NR	NR	NR
Kerber, 2014	Stroke	NA	1245	NR	NR	15	1230	NR	NR	NR	98.8	NR	NR	NR	NR
Kim, 2007[90]	Pneumonia	Round pneumonia	112	3	109	NR	NR	NR	NR	97.32	NR	NR	NR	NR	NR
Kline, 2007[92]	VTE	VTE - Pulmonary embolism	161	NR	141	20	NR	87.6	NR	NR	NR	NR	NR	NR	NR
Kline, 2009[20]	ACS	NA	400	NR	184	1	NR	99.5	NR	NR	NR	NR	NR	NR	NR
Kline, 2009[20]	ACS	NA	400	0	184	NR	NR	NR	NR	100	NR	NR	NR	NR	NR
Ko, 2018	MI	or unstable angina (death or hospitalization)	498291	NR	NR	3488	494803	NR	NR	NR	NR	NR	NR	NR	NR
Kondis, 2017[186]	Fractures	NA (all fractures)	2284	0.00716846	0.05734767	NR	0.93548387	NR	100	NR	NR	NR	NR	NR	NR
Kornblith, 2013[7]	Accuracy across all diseases if more than one category	NA	201	NR	31	10	NR	75.6	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Kornblith, 2013[7]	Accuracy across all diseases if more than one category	NA	201	NR	136	24	NR	85	NR	NR	NR	NR	NR	NR	NR
Kuruvilla, 2011[60]	Stroke	Stroke - Ischemic stroke	57	NR	49	8	NR	86	NR	NR	NR	NR	NR	NR	NR
Ladner, 2015	Stroke	Undetermined	124	92	32	NR	NR	NR	NR	25.81	NR	NR	NR	NR	NR
Le, 2007	Accuracy across all diseases if more than one category	NA	3886	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	2.7%
Leeuwenburgh, 2014[25]	Appendicitis	NA	6	10	125	3	102	97.7	91.07	92.59	97.14	NR	NR	NR	NR
Leeuwenburgh, 2014[25]	Appendicitis	NA	6	25	78	9	118	89.7	82.52	75.73	92.91	NR	NR	NR	NR
Leeuwenburgh, 2014[25]	Appendicitis	NA	6	7	15	16	192	48.4	96.48	68.18	92.31	NR	NR	NR	NR
Leeuwenburgh, 2014[25]	Appendicitis	NA	6	7	113	4	99	96.6	93.4	94.17	96.12	NR	NR	NR	NR
Leeuwenburgh, 2014[25]	Appendicitis	NA	6	19	71	117	16	37.8	45.71	78.89	12.03	NR	NR	NR	NR
Leeuwenburgh, 2014[25]	Appendicitis	NA	6	13	17	13	180	56.7	93.26	56.67	93.26	NR	NR	NR	NR
Leeuwenburgh, 2014[25]	Appendicitis	Total suspected cases	6	10	118	NR	NR	NR	NR	92.19	NR	NR	NR	NR	NR
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	76	12
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	62	16
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	85	15
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	100	0

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	93	7
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	94	6
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	92	8
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	74	26
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	97	3
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	81	19
Lehtimäki, 2015	acute mesenteric ischemia	NA	97	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	86	14
Lever, 2013[44]	Stroke	Undetermined	189	NR	160	29	NR	84.7	NR	NR	NR	NR	NR	NR	NR
Liberman, 2018[168]	Stroke	cerebral venous thrombosis	5966	NR	5750	216	NR	96.4	NR	NR	NR	NR	NR	NR	NR
Liberman, 2018[168]	Stroke	cerebral venous thrombosis	5966	NR	126	8	NR	94	NR	NR	NR	NR	NR	NR	NR
Liberman, 2019[144]	Stroke	cerebral venous thrombosis	53	NR	42	11	NR	79.2	NR	NR	NR	NR	NR	NR	NR
Liberman, 2019[144]	Stroke	Cerebral Venous Thrombosis	53	NR	52	1	NR	98.1	NR	NR	NR	NR	NR	NR	NR
Liberman, 2019[155]	Accuracy across all diseases if more than one category	NA	8310	NR	8103	NR	NR	NR	NR	NR	NR	NR	NR	97.5%	2.5%

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Liberman, 2020[114]	Stroke	Stroke - Ischemic stroke	28,121	NR	NR	90	28,030	NR	NR	NR	99.68	NR	NR	NR	NR
Liberman, 2020[114]	Stroke	Any cerebrovascular event	28,121	NR	NR	111	28010	NR	NR	NR	99.61	NR	NR	NR	NR
Liberman, 2020[127]	Stroke	cervicocephalic artery dissection	7090	NR	6872	218	NR	96.9	NR	NR	NR	NR	NR	NR	NR
Lindsey, 2018[161]	Fractures	Aided	135,409	NR	NR	NR	NR	91.5	93.9	NR	NR	NR	NR	NR	NR
Lindsey, 2018[161]	Fractures	Unaided	135,409	NR	NR	NR	NR	81.8	87.5	NR	NR	NR	NR	NR	NR
Madsen, 2016[200]	Stroke	Stroke - Ischemic stroke	2027	0	1744	283	NR	86	NR	100	NR	NR	NR	NR	NR
Mahajan, 2020[134]	Preeclampsia/eclampsia	HDP	111	NR	28	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mansella, 2020[121]	VTE	VTE - Pulmonary embolism	2058	NR	NR	19	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mansella, 2020[121]	VTE	VTE - Pulmonary embolism	2058	NR	182	44	1832	80.5	NR	NR	97.65	NR	NR	NR	NR
Mark, 2017[178]	aneurysmal subarachnoid hemorrhage	NA		NR	404	46	NR	89.8	NR	NR	NR	NR	NR	NR	10
Martin, 2011[48]	Stroke	Undetermined	91	NR	32	59	NR	35.2	NR	NR	NR	NR	NR	NR	NR
Mattijssen-Horstink, 2020[126]	Fractures	NA (all fractures)	26246	NR	25957	289	NR	98.9	NR	NR	NR	NR	NR	NR	NR
Mattsson, 2018[172]	Fractures	Hand	1522	NR	NR	12	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mattsson, 2018[172]	Fractures	Thorax	1522	NR	NR	74	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mattsson, 2018[172]	Fractures	Pelvis	1522	NR	NR	14	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mattsson, 2018[172]	Fractures	Knee	1522	NR	NR	56	NR	NR	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Mattsson, 2018[172]	Fractures	Ankle	1522	NR	NR	10	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mattsson, 2018[172]	Fractures	NA	1522	NR	NR	381	NR	NR	NR	NR	NR	NR	NR	NR	NR
Metcalfe, 2016[207]	AAD	AAD - Abdominal aortic aneurysm	85	NR	64	21	NR	75.3	NR	NR	NR	NR	NR	75.29	24.7
Michelson, 2019[137]	Sepsis	Undetermined	5457	2	5	13	59	27.8	96.72	71.4	81.94	NR	NR	NR	NR
Michelson, 2019[137]	Sepsis	Undetermined	5457	4	7	11	57	38.9	93.44	63.6	83.82	NR	NR	NR	NR
Michelson, 2019[137]	Sepsis	Undetermined	5457	10	7	11	51	38.9	83.61	41.2	82.26	NR	NR	NR	NR
Michelson, 2019[137]	Appendicitis	Undetermined	5457	1	25	33	20	43.1	95.24	96.2	37.74	NR	NR	NR	NR
Michelson, 2019[137]	Appendicitis	Undetermined	5457	2	39	19	19	67.2	90.48	95.1	50	NR	NR	NR	NR
Michelson, 2019[137]	Appendicitis	Undetermined	5457	3	44	14	18	75.9	85.71	93.6	56.25	NR	NR	NR	NR
Miedema, 2011[51]	MI	Undetermined	2028	NR	1378	650	NR	67.9	NR	NR	NR	NR	NR	NR	NR
Miedema, 2011[51]	MI	Undetermined	2028	NR	2004	24	NR	98.8	NR	NR	NR	NR	NR	NR	NR
Miedema, 2011[51]	MI	Undetermined	2028	NR	1980	48	NR	97.6	NR	NR	NR	NR	NR	NR	NR
Miller, 2018[12]	Accuracy across all diseases if more than one category	NA	582	NR	NR	10	NR	NR	NR	NR	NR	NR	NR	NR	NR
Mirete, 2005[212]	Accuracy across all diseases if more than one category	NA	528	0	424	104	0	80.3	NR	100	0	NR	NR	80.3	19.7
Mitchell, 2006	Acute coronary syndrome	NA	1114	772	49	2	291	96.1	26.1	5.97	99.32	NR	NR	NR	NR
Mitchell, 2006	acute coronary syndrome	NA	1114	760	50	1	303	98.0	27.4	6.17	99.67	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Mitchell, 2006	acute coronary syndrome	NA	1114	1007	51	0	56	100	6.1	4.82	100	NR	NR	NR	NR
Moeller, 2008[10]	Disagreement in diagnosis between ED attending/trainees and neurology consult	NA	493	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	36
Mohamed, 2013[42]	Stroke	Undetermined	93	NR	60	13	NR	82.2	NR	NR	NR	NR	NR	NR	NR
Montmany, 2008[5]	Missed Injuries in Polytrauma Patients, Clinically Significant	NA	122	NR	NR	21	NR	NR	NR	NR	NR	NR	NR	NR	NR
Montmany, 2008[5]	Missed injury	NA	NR	NR	101	21	NR	82.8	NR	NR	NR	NR	NR	NR	NR
Montmany, 2017[175]	Spain Trauma center	NA	1521	NR	NR	6	NR	NR	NR	NR	NR	NR	NR	NR	NR
Montmany, 2017[175]	US trauma center	NA	1521	NR	NR	28	NR	NR	NR	NR	NR	NR	NR	NR	NR
Moonen, 2017[188]	Accuracy across all diseases if more than one category	NA	56	NR	NR	6	NR	NR	NR	NR	NR	NR	NR	NR	NR
Moonen, 2017[188]	Fractures	Humerus	56	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Moonen, 2017[188]	Fractures	Foot	56	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Moonen, 2017[188]	Fractures	Pelvis	56	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Moonen, 2017[188]	Fractures	Spine	56	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Moonen, 2017[188]	Fractures	Thorax	56	NR	NR	1	NR	NR	NR	NR	NR	NR	NR	NR	NR
Morgan, 2021	Accuracy of radiographic readings of all severe trauma patients	NA	752	NR	NR	14	738	NR	NR	NR	98.14	NR	NR	98.1	1.9

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Morgenstern, 2004	Stroke	NA	13015	201	1647	153	58	91.5	22.39	89.1	27.49	NR	NR	NR	NR
Mouthon-Reignier, 2016[190]	Stroke	Stroke - Ischemic stroke	81	24	57	0	0	100	0	70.37	NR	NR	NR	NR	NR
Moy, 2015[24]	MI	Undetermined	111973	NR	110980	993	NR	NR	NR	NR	NR	NR	NR	NR	NR
Muhm, 2012[3]	Accuracy across all diseases if more than one category	NA	111	NR	462	56	NR	89	NR	NR	NR	NR	NR	NR	NR
Muhm, 2012[3]	Accuracy across all diseases if more than one category	NA	111	NR	86	25	NR	77.5	NR	NR	NR	NR	NR	NR	NR
Nevo, 2017[189]	Testicular torsion	Torsion of the spermatic cord	134	NR	59	13	NR	81.9	NR	NR	NR	NR	NR	NR	NR
Newman-Toker, 2014[33]	Stroke	Undetermined	187188	NR	26005	2243	NR	92.1	NR	NR	NR	NR	NR	NR	NR
Newman-Toker, 2014[33]	Stroke	Undetermined	187188	NR		11	NR		NR	NR	NR	NR	NR	NR	NR
Nuñez, 2006[101]	Unscheduled returns	NA	500	NR	230	20	NR	92	NR	NR	NR	NR	NR	NR	NR
Nuñez, 2006[101]	Non-returns	NA	500	NR	246	4	NR	98.4	NR	NR	NR	NR	NR	NR	NR
Ohle, 2019[151]	AAD	Acute aortic dissection	194	NR	160	34	NR	82.5	NR	NR	NR	NR	NR	NR	NR
Ois, 2019[138]	Stroke	Stroke - Subarachnoid hemorrhage	400	NR	296	104	NR	74	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Appendicitis	Undetermined	480	NR	1	1	NR	50	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Cholelithiasis	NA	480	NR	6	2	NR	75	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Gastroenteritis	NA	480	NR	2	5	NR	28.6	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Urinary retention	NA	480	NR	4	0	NR	100	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Osterwalder, 2020[14]	Constipation	NA	480	NR	1	1	NR	50	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Disorders of ovary	NA	480	NR	1	1	NR	50	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Diverticulitis	NA	480	NR	2	0	NR	100	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Endometriosis	NA	480	NR	2	0	NR	100	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Food intolerance	NA	480	NR	0	2	NR	0	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Malignant diseases	NA	480	NR	0	2	NR	0	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Pyelonephritis	NA	480	NR	2	0	NR	100	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Urolithiasis	NA	480	NR	1	1	NR	50	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Others	NA	480	NR	13	10	NR	56.5	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	NSAP	NA	480	NR	2	1	NR	66.7	NR	NR	NR	NR	NR	NR	NR
Osterwalder, 2020[14]	Abdominal pain	NA	480	NR	453	27	NR	94.4	NR	NR	NR	NR	NR	NR	NR
Palomeras Soler, 2015[32]	Stroke	Stroke - Transient ischemic attack	411	NR	337	74	NR	82	NR	NR	NR	NR	NR	NR	NR
Palomeras Soler, 2015[32]	Stroke	Stroke - Transient ischemic attack	411	NR	386	25	NR	93.9	NR	NR	NR	NR	NR	NR	NR
Pare, 2016[62]	AAD	Undetermined	32	NR	16	0	NR	100	NR	NR	NR	NR	NR	NR	NR
Pare, 2016[62]	AAD	Undetermined	32	NR	9	7	NR	56.2	NR	NR	NR	NR	NR	NR	NR
Pehle, 2006[98]	Fractures	NA (all fractures)	1187	NR	NR	58	NR	NR	NR	NR	NR	NR	NR	NR	NR
Pihlasviita, 2018[164]	Stroke	Undetermined	1015	150	865	NR	NR	NR	NR	85.22	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	AHF (After POC-US) (G2)	NA	168	NR	NR	NR	NR	100	98.4	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Pirozzi, 2014[19]	Pneumonia	After POC-US (G1+G2)	168	NR	NR	NR	NR	92	98	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	AHF (Standard protocol (G2))	NA	168	NR	NR	NR	NR	78.2	67.7	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Acute heart failure (After POC-US (G1+G2)	NA	168	NR	NR	NR	NR	100	99	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Pneumonia	After POC-US G2	168	NR	NR	NR	NR	93.3	98.5	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Arterial thromboembolism	VTE - Pulmonary embolism	168	NR	NR	NR	NR	89	100	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Pneumonia	Standard protocol (G2 prior to POC-US)	168	NR	NR	NR	NR	14.2	97.1	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Arterial thromboembolism	VTE - Pulmonary embolism	168	NR	NR	NR	NR	0	98.8	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Arterial thromboembolism	VTE - Pulmonary embolism	168	NR	NR	NR	NR	83.3	100	NR	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Undifferentiated Dyspnea	NA	168	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	0.95	NR
Podolnick, 2017[183]	Fractures	NA (all fractures)	196	NR	178	18	NR	90.8	NR	NR	NR	NR	NR	NR	NR
Postma, 2012[4]	Delayed diagnosis of injury after plane crash	NA	66	NR	58	8	NR	88	NR	NR	NR	NR	NR	NR	NR
Prabhakaran, 2008[86]	Stroke	Stroke - Transient ischemic attack	100	60	40	NR	NR	NR	NR	40	NR	NR	NR	NR	NR
Rapezzi, 2008[85]	AAD	Undetermined	161	NR	121	40	NR	75.2	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Rapezzi, 2008[85]	AAD	AAD - Stanford Group A dissection (Debakey type I and II)	161	NR	86	29	NR	74.8	NR	NR	NR	NR	NR	NR	NR
Raposo, 2018[159]	Stroke	Stroke - Transient ischemic attack	169	NR	128	41	NR	75.7	NR	NR	NR	NR	NR	NR	NR
Ravichandiran, 2010[76]	Fractures	NA (all fractures)	258	NR	204	54	NR	79.1	NR	NR	NR	NR	NR	NR	NR
Ray, 2006[18]	CPE, cardiogenic pulmonary edema	NA	514	NR	NR	NR	NR	.71	.80	.74	.78	NR	NR	NR	NR
Ray, 2006[18]	Pneumonia	Community-acquired pneumonia	514	NR	NR	NR	NR	.86	.76	.66	.91	NR	NR	NR	NR
Ray, 2006[18]	Acute exacerbation of CRD chronic respiratory disease	NA	514	NR	NR	NR	NR	.71	.83	NR	NR	.66	.86	NR	NR
Ray, 2006[18]	Pulmonary embolism	NA	514	NR	NR	NR	NR	.75	.78	.43	.93	NR	NR	NR	NR
Ray, 2006[18]	Asthma	NA	514	NR	NR	NR	NR	.67	.97	.42	.99	NR	NR	NR	NR
Richoz, 2015	Stroke	NA		NR	2153	47	NR	97.9				NR	NR	NR	NR
Rizos, 2009[79]	Stroke	Undetermined	1735	86	121	11	213	91.7	71.24	58.45	95.09	NR	NR	NR	NR
Rizos, 2009[79]	Stroke	Undetermined	1735	104	105	3	175	97.2	62.72	50.24	98.31	NR	NR	NR	NR
Rizos, 2009[79]	Stroke	Undetermined	1735	104	140	5	150	96.6	59.06	57.38	96.77	NR	NR	NR	NR
Rønning, 2005[106]	Stroke	Undetermined	354	88	266	NR	NR	NR	NR	75.14	NR	NR	NR	NR	NR
Rose, 2008[87]	Stroke	Undetermined	15117	NR	1738	13379	NR	11.5	NR	NR	NR	NR	NR	NR	NR
Rosenkrantz, 2016[203]	Accuracy across all diseases if more than one category	NA	3940	NR	NR	785	NR	NR	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Rosenman, 2020	Stroke	Undetermined	35622	NR	NR	40	35582	NR	NR	NR	NR	NR	NR	NR	NR
Rostanski, 2016[191]	Stroke	Stroke - Ischemic stroke	350	48	302	0	0	100	0	86.29	NR	NR	NR	86.3	13.7
Royl, 2011[9]	Dizziness	NA	475	NR	69	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Saaristo, 2020[15]	Non-specific abdominal pain (revisit to ED w/in 48 hours of discharge)	NA	173,630	NR	210	78	NR	72.9	NR	NR	NR	NR	NR	NR	NR
Sadighi, 2019[147]	Stroke	Stroke - Transient ischemic attack	254	190	64	NR	NR	NR	NR	25.2	NR	NR	NR	NR	NR
Santos, 2009[77]	Appendicitis	Undetermined	100	4	66	NR	NR	NR	NR	94.3	NR	NR	NR	NR	NR
Santos, 2009[77]	Appendicitis	Undetermined	100	3	37	NR	NR	NR	NR	92.5	NR	NR	NR	NR	NR
Santos, 2009[77]	Appendicitis	Undetermined	100	1	29	NR	NR	NR	NR	96.6	NR	NR	NR	NR	NR
Scheuermeyer, 2012[46]	MI	Undetermined	1116	NR	120	0	NR	100	NR	NR	NR	NR	NR	NR	NR
Schnapp, 2018[163]	Accuracy across all diseases if more than one category	NA	271	NR	219	52	NR	80.8	NR	NR	NR	NR	NR	NR	NR
Schrock, 2012[53]	Stroke	Stroke - Transient ischemic attack	429	156	273	NR	NR	NR	NR	63.64	NR	NR	NR	64	36
Schull, 2006[97]	MI	Undetermined	19663	NR	19244	419	NR	97.9	NR	NR	NR	NR	NR	NR	NR
Sederholm Lawesson, 2018[167]	MI	STEMI	437	NR	350	87	NR	80.1	NR	NR	NR	NR	NR	NR	NR
Sederholm Lawesson, 2018[167]	MI	STEMI	437	NR	299	142	NR	67.8	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Sevdalis, 2010[59]	Accuracy across all diseases if more than one category	NA	136	NR	NR	208	NR	NR	NR	NR	NR	NR	NR	NR	NR
Sharif, 2018[166]	Appendicitis	NA	90	6	18	8	58	0.692	0.906	7.4	0.3	NR	NR	NR	NR
Sharp, 2020[120]	MI	Undetermined	44473	NR	43899	574	NR	NR	NR	NR	NR	NR	NR	NR	NR
Sharp, 2020[120]	MI	Undetermined	44473	NR	NR	508	324580	NR	NR	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	AAD	AAD - Abdominal aortic aneurysm	NR	NR	175	86	NR	67	NR	NR	NR	NR	NR	NR	33
Smidfelt, 2020[122]	AAD	AAD - Abdominal aortic aneurysm	455	NR	278	177	NR	61.1	NR	NR	NR	NR	NR	NR	NR
Smith, 2012[50]	VTE	VTE - Pulmonary embolism	400	NR	327	73	NR	81.8	NR	NR	NR	NR	NR	NR	NR
Snoek, 2013[2]	Delayed diagnostic injuries (includiding fractures, myocardial contusion, pneumothorax, intercrebral bleeding, renal contusion)	NA	475	NR	462	13	NR	97.3	NR	NR	NR	NR	NR	NR	NR
Somers, 2021	Appendicitis	NA	130	18	51	NR	NR	NR	NR	73.91	NR	NR	NR	NR	NR
Somers, 2021	Appendicitis	NA	130	1	39	NR	NR	NR	NR	97.5	NR	NR	NR	NR	NR
Soundappan, 2004[109]	Fractures	Spine	76	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Soundappan, 2004[109]	Accuracy across all diseases if more than one category	NA	76	NR	65	12	NR	84.4	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Soundappan, 2004[109]	Fractures	Head and face	76	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Soundappan, 2004[109]	Fractures	Upper limb	76	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Soundappan, 2004[109]	Fractures	Lower limb	76	NR	NR	2	NR	NR	NR	NR	NR	NR	NR	NR	NR
Suda, 2021	Hollow organ injuries from emergency trauma	NA	2694	NR	NR	7	2687	NR	NR	NR	99.7	NR	NR	99.7	0.3
Sun, 2007[8]	Diagnostic delay after treat-and-release ED visit for syncope/near syncope	NA	NR	NR	445	18	NR	96.1	NR	NR	NR	NR	NR	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	98.2	8.8	4.2	99.2	1.1	0.2	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	98.2	8.8	4.2	99.2	1.1	0.2	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	96.3	19.0	4.6	99.2	1.2	0.2	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	93.6	26.0	4.9	99.0	1.3	0.2	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	89.5	37.0	5.4	98.9	1.4	0.3	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	83.6	49.6	6.3	98.7	1.7	0.3	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	73.1	62.4	7.3	98.3	1.9	0.4	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	62.6	70.4	7.9	97.9	2.1	0.5	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	56.2	77.9	9.3	97.8	2.5	0.6	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	45.7	84.8	10.8	97.5	3.0	0.6	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	39.7	89.4	13.2	97.4	3.8	0.7	NR	NR
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	29.7	93.0	14.5	97.0	4.2	0.8	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Teichman, 2021	VTE	NA	5645	NR	NR	NR	NR	98.6	0.9	3.9	94.2	1.0	1.5	NR	NR
Torres-Macho, 2013[38]	VTE	VTE - Pulmonary embolism	436	NR	290	146	NR	66.5	NR	NR	NR	NR	NR	NR	NR
Tsivgoulis, 2011[55]	Stroke	Stroke - Ischemic stroke	539	56	483	NR	NR	NR	NR	89.61	NR	NR	NR	NR	NR
Tudela, 2005[105]	Accuracy across all diseases if more than one category	NA	669	0	627	42	0	93.7	NR	100	0	NR	NR	NR	NR
Uchino, 2010	Stroke	Undetermined	254	9	245	NR	NR	NR	NR	96.46	NR	NR	NR	NR	NR
Vaghani, 2021	Stroke	NA	217	NR	NR	124	93	NR	NR	31.2	42.86	NR	NR	87.3	NR
Vanbrabant, 2009[75]	Accuracy across all diseases if more than one category	NA	141	NR	121	20	NR	85.8	85.8	NR	NR	NR	NR	NR	NR
Venkat, 2018[162]	Stroke	Undetermined	1514	485	779	NR	NR	NR	NR	61.63	NR	NR	NR	NR	NR
Venkat, 2018[162]	Stroke	Undetermined	1514	NR	1358	156	NR	89.7	NR	NR	NR	NR	NR	NR	NR
Verelst, 2014	Accuracy across all diseases if more than one category	NA	44574	100	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Vermeulen, 2007[95]	Stroke	Stroke - Subarachnoid hemorrhage	1507	NR	1426	81	NR	94.6	NR	NR	NR	NR	NR	NR	NR
Vinz, 2015[64]	Accuracy across all diseases if more than one category	NA	271	95	176	NR	NR	NR	NR	64.94	NR	NR	NR	NR	NR
Vioque, 2014[35]	Preventable/Possibly Preventable Trauma Death	NA	11100	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Waxman, 2018[170]	AAD	Ruptured abdominal aortic aneurysm	1561940	NR	17352	611	NR	96.6	NR	NR	NR	NR	NR	NR	NR
Waxman, 2018[170]	MI	Undetermined	1561940	NR	297965	7015	NR	NR	NR	NR	NR	NR	NR	NR	NR
Waxman, 2018[170]	AAD	Aortic dissection	1561940	NR	18790	885	NR	95.5	NR	NR	NR	NR	NR	NR	NR
Waxman, 2018[170]	Stroke	Stroke - Subarachnoid hemorrhage	1561940	NR	36355	1319	NR	NR	NR	NR	NR	NR	NR	NR	NR
Waxman, 2018[170]	Stroke	Undetermined	1561940	NR	1133200	48448	NR	NR	NR	NR	NR	NR	NR	NR	NR
Weinberg, 2010[74]	Fractures	Mandible	348	NR	NR	NR	NR	67	100	NR	NR	NR	.33	NR	NR
Weinberg, 2010[74]	Fractures	Clavicle	348	NR	NR	NR	NR	89	83	NR	NR	5.3	.13	NR	NR
Weinberg, 2010[74]	Fractures	Proximal humerus	348	NR	NR	NR	NR	100	100	NR	NR	NR	0	NR	NR
Weinberg, 2010[74]	Fractures	Ulna	348	NR	NR	NR	NR	50	95	NR	NR	11	.52	NR	NR
Weinberg, 2010[74]	Fractures	Metacarpal	348	NR	NR	NR	NR	80	85	NR	NR	5.4	.23	NR	NR
Weinberg, 2010[74]	Fractures	Phalange	348	NR	NR	NR	NR	50	97	14.5	.51	NR	NR	NR	NR
Weinberg, 2010[74]	Fractures	Patella	348	NR	NR	NR	NR	NR	100	NR	NR	NR	NR	NR	NR
Weinberg, 2010[74]	Fractures	Tibia	348	NR	NR	NR	NR	83	93	NR	NR	11.7	.18	NR	NR
Weinberg, 2010[74]	Fractures	Fibula	348	NR	NR	NR	NR	67	97	NR	NR	22.7	.34	NR	NR
Weinberg, 2010[74]	Fractures	Metacarsal	348	NR	NR	NR	NR	100	93	14	0	NR	NR	NR	NR
Weinberg, 2010[74]	Fractures	Elbow	348	NR	NR	NR	NR	80	87	NR	NR	6	.23	NR	NR
Weinberg, 2010[74]	Fractures	Skull	348	NR	NR	NR	NR	100	100	NR	NR	NR	0	NR	NR
Wemeijer, 2021	injury	NA	51	NR	NR	8	43	NR	NR	NR	84.31	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Whiteley, 2011	Stroke	Acute cerebrovascular disease including Ischaemic stroke (80% of cases), Transient ischaemic attack (15% of cases), Intracerebral haemorrhage, and Subarachnoid haemorrhage	356	62	203	43	48	83	44	76.6	52.75	NR	NR	NR	NR
Whiteley, 2011	Stroke	Acute cerebrovascular disease including Ischaemic stroke (80% of cases), Transient ischaemic attack (15% of cases), Intracerebral haemorrhage, and Subarachnoid haemorrhage	356	67	199	47	43	81	39	74.81	47.78	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Whiteley, 2011	Stroke	Acute cerebrovascular disease including Ischaemic stroke (80% of cases), Transient ischaemic attack (15% of cases), Intracerebral haemorrhage, and Subarachnoid haemorrhage	356	45	187	58	65	76	59	80.6	52.85	NR	NR	NR	NR
Williams, 2009[81]	Fractures	NA (all fractures)	1100	NR	1056	44	NR	96	NR	NR	NR	NR	NR	NR	NR
Williams, 2019[152]	MI	STEMI	1392	NR	1368	24	NR	98.3	NR	NR	NR	NR	NR	NR	NR
Williams, 2019[152]	MI	STEMI	1392	NR	1292	100	NR	92.8	NR	NR	NR	NR	NR	NR	NR
Willner, 2012[6]	Delayed Diagnosis of Injury After Pediatric Trauma	NA	324	NR	298	26	NR	92	NR	NR	NR	NR	NR	NR	NR
Wilson, 2014[28]	MI	Undetermined	371638	NR	366864	4774	NR	NR	NR	NR	NR	NR	NR	NR	NR
Winkler, 2009[84]	Stroke	Stroke - Ischemic stroke	250	7	243		NR	NR	NR	97.2	NR	NR	NR	NR	NR
Yeboah, 2019[160]	Stroke	Undetermined	11	NR	0	11	NR	0	NR	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Stroke	Undetermined	NR	71	88	NR	NR	NR	NR	55.35	NR	NR	NR	NR	NR
York, 2020	Fractures	NA	2947	20	1582	61	1284	96.3	98.47	98.75	95.46	NR	NR	NR	NR

Author, Year	Condition	Subtype	Total ED N	FP	TP	FN	TN	Sens (Calc)	Spec (Calc)	PPV (Calc)	NPV (Calc)	PLR	NLR	% Conc	% Disc
Zaschke, 2020[128]	AAD	AAD - Stanford Group A dissection (Debakey type I and II)	350	NR	76	274	NR	21.7	NR	NR	NR	NR	NR	NR	NR

AAD: aortic aneurysm and dissection; aOR: adjusted odds ratio; CI: confidence interval; Conc: concordant; DecrRisk: decreased risk; Disc: discordant; Dx Error: diagnostic error; ED: emergency department; FN: false negatives; FP: false positives; IncrRisk: increased risk; ISS: Injury Severity Score; NA: not applicable; NLR: negative likelihood ratio; NPV: negative predictive value; NR: not reported; OR: odds ratio; PLR: positive likelihood ratio; PPV: positive predictive value; Sens: sensitivity; SP: specificity; STEMI: ST-elevated myocardial infarction; TN: true negatives; TP: true positives; VTE: venous thromboembolism

Table D-4. Results of studies that reported on causes of diagnostic errors in the emergency department

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Aaronson, 2016[204]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	Mixed (specify)	However sex, insurance status, pain scale at presentation, ED occupancy, and admission to ED observation did not make them more or less likely to return within 72 hours Male, n (%) <72 hours n=147 70 (47.6) >72 hours n=857 408 (47.6) p-value: 1	1022	NOT STAGE SPECIFIC	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Aaronson, 2016[204]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	Mixed (specify)	However sex, insurance status, pain scale at presentation, ED occupancy, and admission to ED observation did not make them more or less likely to return within 72 hours Private insurance, n (%) <72 hours n=147 78 (53.1) >72 hours n=857 402 (46.9) p-	1022	NOT STAGE SPECIFIC	Other (specify)	Either/Both
Aaronson, 2016[204]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	DecrRisk - Significant	<72 hours n=147 Mean age: 40.8 >72 hours n=857 Mean age: 47.5 p:0.005 Patients who returned within 72 hours were more likely to be younger (mean age, 40.8 vs 47.5; p = 0.005)	1022	NOT STAGE SPECIFIC	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Agrawal, 2019[157]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	% African American among true STEMI vs. false STEMI, 73% vs. 82%	361	NOT STAGE SPECIFIC	MI	Dx Error
Agrawal, 2019[157]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Smoking	No effect - wide CI	% smoking among true STEMI vs. false STEMI, 42% vs. 48%, p = 0.38	361	NOT STAGE SPECIFIC	MI	Dx Error
Agrawal, 2019[157]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Body mass index	No effect - wide CI	Median BMI among true STEMI vs. false STEMI, 28 vs. 28, p = 0.43	361	NOT STAGE SPECIFIC	MI	Dx Error
Agrawal, 2019[157]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male among true STEMI vs. false STEMI, 60% vs. 67%, p = 0.25	361	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Agrawal, 2019[157]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	DecrRisk - Significant	aOR for chest pain vs other, 0.54 (95% CI, 0.32 to 0.93)	82	NOT STAGE SPECIFIC	MI	Dx Error
Agrawal, 2019[157]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Median age among true STEMI vs. false STEMI, 60 vs. 57, p = 0.32	361	NOT STAGE SPECIFIC	MI	Dx Error
Aneiros, 2019[146]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Aneiros, 2019[146]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	DecrRisk - Significant	One hundred and thirty children (8.9% of 1453) in the group C (6-15 years) and 45 children (15.9% of 283) in the group D (0-5 years) had previously been examined without a correct diagnosis (p=0.0003).	1736	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	smoking, illicit drug use, heavy alcohol use	No effect - wide CI	NR	465	NOT STAGE SPECIFIC	Stroke	Dx Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Code in ED	DecrRisk - Significant	8% vs 46% in missed vs not missed stroke (p<0.001)	465	ED Dx Process	Stroke	Dx Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	White 67% vs 72% (0.341) in missed vs not missed stroke	465	NOT STAGE SPECIFIC	Stroke	Dx Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	posterior stroke	IncrRisk - Significant	Posterior vs anterior stroke misdiagnosis rate: 37% vs 16% (P<0.001)	465	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	Female 48% vs 56% (p 0.114) in missed vs not missed stroke	465	NOT STAGE SPECIFIC	Stroke	Dx Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	nausea/vomiting (odds ratio [OR], 4.02; 95% ACS [CI], 1.60–10.1), dizziness (OR, 1.99; 95% CI, 1.03–3.84)	465	ED Dx Process	Stroke	Dx Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mfean 71.5 vs 72.6 in missed vs not missed stroke; p 0.543	465	NOT STAGE SPECIFIC	Stroke	Dx Error
Arch, 2016[205]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Atzema, 2011[52]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	Median door-to-ECG time (min) for high priority vs. low priority patients, 14.0 vs. 28.0, p < 0.001	6605	ED Dx Process	MI	Dx Error
Augustin, 2011[54]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	No effect - wide CI	Male N=218 Mean=9.2 Female N=137 Mean=10.7 P=0.16	380	Patient interval	Appendicitis	Dx Error
Augustin, 2011[54]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	DecrRisk - Significant	RLQ tenderness 7.6 (6; 0.7–39) vs 12.2 (6.8; 0.4–127)	NR	NR	Appendicitis	NR
Augustin, 2011[54]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Augustin, 2011[54]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Race	NR	NR	NR	NR	NR	NR
Augustin, 2011[54]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Multiple	IncrRisk - not sig	Heart rate <100 n=231 Mean=9 ≥100 n=96 Mean=12 P=0.22 Temperature (°F) >101.5 n=21 Mean=7.8 (6.6; 1–26) ≤101.5 n=308 Mean=9.3 (6.5; 0.7–64) P=0.65 RLQ tenderness No n=167 Mean=12.2 Yes n=182 Mean=7.6 P=0.01 Classic presentation No n=228 M	380	Patient interval	NR	NR
Augustin, 2011[54]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	No effect - wide CI	≤15 N=71 Mean=8.5 15–45 N=180 Mean=9.9 45–55 N=52 Mean=9 >60 N=52 Mean=8.9 P=0.68	380	Patient interval	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	concordant: 63.7 discordant: 65.2 p=0.402	418	NOT STAGE SPECIFIC	Other (specify) : all disease	Dx Error
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	mortality	IncrRisk - Significant	mortality OR:3.64 (1.03-12.9) p=0.045 concordance vs. discordance	418	NOT STAGE SPECIFIC	Other (specify) : all disease	MisDx Harm
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	concordant: 49.4% male discordant: 44.0% male p=0.405	418	NOT STAGE SPECIFIC	Other (specify) : all disease	Dx Error
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	ICU up-triage OR 5.51 (2.4-12.5) p<0.001 concordance vs. discordance	418	NOT STAGE SPECIFIC	Other (specify) : all disease	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	concordant: 63.7 discordant: 65.2 p=0.402	418	NOT STAGE SPECIFIC	Other (specify) : all disease	Dx Error
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	mortality	IncrRisk - Significant	mortality OR:3.64 (1.03-12.9) p=0.045 concordance vs. discordance	418	NOT STAGE SPECIFIC	Other (specify) : all disease	MisDx Harm
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	concordant: 49.4% male discordant: 44.0% male p=0.405	418	NOT STAGE SPECIFIC	Other (specify) : all disease	Dx Error
Bastakoti, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	ICU up-triage OR 5.51 (2.4-12.5) p<0.001 concordance vs. discordance	418	NOT STAGE SPECIFIC	Other (specify) : all disease	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Bayne, 2017[184]	Study design: Case-control Look back or look forward analysis: Look back method (disease denominator) Data source: Previous study Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Isolated scrotal pain was more common in those correctly diagnosed in the acute setting than those initially misdiagnosed (71.1% vs 41.6%; P = .051). Nausea and vomiting were reported by a smaller proportion of misdiagnosed patients than those presenting	218	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Bayne, 2017[184]	Study design: Case-control Look back or look forward analysis: Look back method (disease denominator) Data source: Previous study Numerator: Numerator and denominator	Age	IncrRisk - Significant	Misdiagnosed patients were younger and weighed less than those correctly diagnosed in the acute setting (9.9 vs 12.9 years; P = .006; 42.6 vs 59.2 kg; P = .01).	12	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Beaver, 2005[107]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	Reported but not quantified	NR	100	NOT STAGE SPECIFIC	AAD	Dx Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Age	IncrRisk - Significant	Age (lower age is more likely to be misdiagnosed) p = 0.15 (univariate); p = 0.047 (multivariate)	77	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	DecrRisk of misdiagnosis via ambulance; p = 0.18 (univariate); p = 0.06 (multivariate)	77	NOT STAGE SPECIFIC	Stroke	Dx Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Access to consultation	No effect - wide CI	presentation to a PSC p = 0.44	77	NOT STAGE SPECIFIC	Stroke	Dx Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Race	No effect - wide CI	p - 0.51	77	NOT STAGE SPECIFIC	Stroke	Dx Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Sex	No effect - wide CI	p = 0.51	77	NOT STAGE SPECIFIC	Stroke	Dx Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Symptom type	Reported but not quantified	Symptom and Frequency of patients for those with misdiagnosis Gait difficulty 4 Severe headache 3 Speech difficulty 1 Visual problems 1 Arm weakness 1 Facial numbness 1	11	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Bhattacharya, 2013	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Mutliple Numerator: Numerator and denominator	Tests ordered	DecrRisk - Significant	MRI within 48 hrs was associated with lower rates of misdx (p=0.036 - univariate) (p=0.023 - multivariate)	77	NOT STAGE SPECIFIC	Stroke	Dx Error
Branstetter, 2007	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	No effect - narrow CI	Within radiologists reading CT, junior staff performed slightly better than residents, and residents performed slightly better than senior staff. Reading CR, junior staff and residents performed similarly, and senior staff performed slightly better. No	65780	NOT STAGE SPECIFIC	Other (specify) : radiograph	Dx Error
Branstetter, 2007	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - not sig	In both CT and CR, clinicians performed significantly worse than radiologists, with error rates two to three times as high as residents.'	65780	NOT STAGE SPECIFIC	Other (specify) : radiograph	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Branstetter, 2007	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	No effect - narrow CI	Within radiologists reading CT, junior staff performed slightly better than residents, and residents performed slightly better than senior staff. Reading CR, junior staff and residents performed similarly, and senior staff performed slightly better. No	65780	NOT STAGE SPECIFIC	Other (specify) : radiograph	Dx Error
Branstetter, 2007	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - not sig	In both CT and CR, clinicians performed significantly worse than radiologists, with error rates two to three times as high as residents.'	65780	NOT STAGE SPECIFIC	Other (specify) : radiograph	Dx Error
Breidthardt, 2019	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Tests ordered	DecrRisk - Significant	those who received a interleukin-6 blood test were significantly more likely to be correctly diagnosed with urgent abdominal pain (23.3 vs 4.4 in urgent vs unurgent pain, p <0.001)	1038	NOT STAGE SPECIFIC	Other (specify) : urgent abdominal pain	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Breidthardt, 2019	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Tests ordered	DecrRisk - not sig	those who received a interleukin-6 blood test were significantly more likely to be correctly diagnosed with urgent abdominal pain	1038	NOT STAGE SPECIFIC	Other (specify) : urgent abdominal pain	Dx Error
Broadley, 2003	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	IncrRisk - not sig	Age > 59 OR: 1.51 (0.70â€“3.25)	245	NOT STAGE SPECIFIC	Stroke	Dx Error
Broadley, 2003	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	DecrRisk - not sig	Female OR: 0.93 (0.52â€“1.67)	245	NOT STAGE SPECIFIC	Stroke	Dx Error
Broadley, 2003	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	IncrRisk - not sig	More severe strokes (modified barthel index <50) 1.62 (0.84â€“3.14), large lesions on CT or MRI) (1.69 (0.87â€“3.26)) or who were unconscious on arrival (OR: 1.49; 0.54 - 4.05); primary hemorrhage 1.51 (0.67â€“3.37), dysphasia 1.05 (0.54â€“2.06)	245	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Calic, 2016[195]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	IncrRisk - Significant	OR 2.3, 95% CI 1.01–5.5, p = 0.046	NR	NOT STAGE SPECIFIC	Stroke	NR
Calic, 2016[195]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Mode of arrival	DecrRisk - not sig	NR	NR	Pre-hospital interval	Stroke	Dx Error
Calic, 2016[195]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Atypical presentation	IncrRisk - Significant	(OR 3.5, 95% CI 1.5–8.0, p = 0.003)	225	NOT STAGE SPECIFIC	Stroke	NR
Carlton, 2015[69]	Study design: Prospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	Reported but not quantified	NR	912	NOT STAGE SPECIFIC	MI	Dx Error
Carlton, 2015[69]	Study design: Prospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	Reported but not quantified	Specificity ranged from 51.3% to 57.%; sensitivity ranged from 39.3% to 53.1%	912	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Chan, 2020[125]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	NR	NR	NR	NR	NR	NR
Chan, 2020[125]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Delayed vs. not delayed, % without dyspnea 38.9% vs. 26.1%; % with cardiopulmonary disease, 52.8% vs. 23.5%; with altered mental status, 8.3% vs. 2.2%	302	NOT STAGE SPECIFIC	VTE	Dx Error
Chan, 2020[125]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	% with delayed diagnosis among < 65, 65-84, and >=85, 50% vs. 80.8% vs. 92.9%, p = 0.038	302	NOT STAGE SPECIFIC	VTE	Dx Error
Chang, 2019[169]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Mixed	Sex	Reported but not quantified	The rate of negative appendicectomy was 16.3% (16/98) in females and 7.3% (8/110) in males.	208	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Chang, 2019[169]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Mixed	Tests ordered	Mixed (specify)	Comparing test results between negative and positive appendicectomy patients WCC X2=4.304 P=0.038 Neutrophils X2=7.070 P=0.008 CRP X2=4.053 P=0.044 Bilirubin X2=10.860 P=0.001 GGT X2=0.025 P=0.873 ALP X2=2.259 P=0.133 ALT X2=0.051 P=0.822	208	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Chang, 2019[169]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Mixed	Age	NR	NR	NR	NR	NR	NR
Chen, 2016[197]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	Reported but not quantified	Of the male patients who had appendectomy (113), 90.3% had true appendicitis while 9.7% had a normal appendix. In comparison, of the female patients who had an appendectomy (136), only 61% had appendicitis and 39% had a normal appendix.	249	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Chen, 2016[197]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	NR	NR	NR	NR	NR	NR
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Geographic region	IncrRisk - Significant	western Canada (OR 1.21, p < 0.02)	NR	NR	NR	NR
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Type of treating hospital	IncrRisk - Significant	Non-children's OR=1.42 95%CI: 1.13–1.79 P=0.003 Children's (reference)	NR	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Domicile	No effect - wide CI	Rural OR=1.02 95%CI: 0.90–1.16 P=0.72 Urban (reference)	41405	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Race	NR	NR	NR	NR	NR	NR
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Geographic region	Mixed (specify)	Ontario OR=0.91 95%CI: 0.77–1.09 P=0.30 West OR=1.21 95%CI1.02–1.44 P=0.03 Territories OR=1.51 95%CI0.93–2.46 P=0.10 Maritime reference	41405	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	SES/Income	Mixed (specify)	SES Lowest OR=0.81 95%CI: 0.70–0.94 P=.06 2nd lowest OR=0.95 95%CI: 0.82–1.09 P=0.23 Middle OR=0.91 95%CI: 0.79–1.04 P=0.78 2nd highest OR=0.82 95%CI: 0.71–0.94 P=0.06 Highest (reference)	41405	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Sex	DecrRisk - Significant	Male OR=0.43 95%CI: 0.39–0.48 P=0.0001	41405	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Ethnicity	NR	NR	NR	NR	NR	NR
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Age	Mixed (specify)	0–5 years old OR=1.51 95%CI: 1.2–1.84 P=0.0001 6–11 years old OR=0.79 95%CI: 0.71–0.87 P=0.0001 12–17 years old (reference)	41405	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Language	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Cheong, 2014[34]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Discharge Abstract Database (DAD) Numerator: Numerator only (error/harm)	Health literacy	NR	NR	NR	NR	NR	NR
Choinski, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	AAD	Dx Error
Choinski, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Tests ordered	NR	NR	NR	NR	NR	NR
Choinski, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	AAD	Dx Error
Choinski, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Tests ordered	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Chompoopong, 2017[182]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Reported but not quantified	NR	NR	NR	NR	NR
Chompoopong, 2017[182]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncRisk - Significant	NR	NR	NR	NR	NR
Chompoopong, 2017[182]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	Reported but not quantified	41.6% of FN with non-neurologic diagnoses	273	ED Dx Process	Stroke	Dx Error
Chompoopong, 2017[182]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Chung, 2009[22]	Study design: Cross-sectional Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Provider type/role	Reported but not quantified	Discrepancy rate between resident and attending radiologist: 2% (95 of 4768) Discrepancy rate between 2 attending radiologists (15%) (17 of 112)	NR	NR	Other (specify) : discrepancy in read of CT torso between radiology resident and attending	Either/Both
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	No effect - narrow CI	1.11 (0.79 1.56) 0.53	1922	NR	NR	NR
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Children's hospital	IncrRisk - not sig	Yes OR=1.22 (0.73 2.05)	1922	NOT STAGE SPECIFIC	Sepsis	Dx Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Has a pediatric ED/Has a pICU	IncrRisk - not sig	Yes OR=1.20 (0.72 2.00) Yes OR=0.85 (0.42 1.76)	NR	NOT STAGE SPECIFIC	Sepsis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ownership/business model	Mixed (specify)	Private, nonprofit OR=1.39 (0.81 2.38) Private, for-profit OR=0.81 (0.24 2.79)	1922	NOT STAGE SPECIFIC	Sepsis	Dx Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Geographic region	IncrRisk - Significant	California OR=2.26 (1.34 3.82) Florida OR=3.33 (1.95 5.70) Massachusetts OR=2.87 (1.35 6.09)	1922	NR	Sepsis	Dx Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Teaching status	DecrRisk - not sig	Yes OR=0.81 (0.41 1.58)	1922	NOT STAGE SPECIFIC	Sepsis	Dx Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	ED volume/annual visits	No effect - narrow CI	OR=1.00 (1.00 1.00)	1622	NOT STAGE SPECIFIC	Sepsis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Access to EHR/EHR type	DecrRisk - not sig	Yes OR=0.91 (0.62 1.35)	1922	NOT STAGE SPECIFIC	Sepsis	Dx Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	No effect - narrow CI	NR	NR	NR	NR	NR
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	No effect - narrow CI	OR 1.00 (0.98, 1.03) 0.84	1922	NR	NR	NR
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	No effect - narrow CI	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Cifra, 2020[130]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	No effect - narrow CI	NR	NR	NR	NR	NR
Copson, 2020[209]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Specialist vs. General	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	Appendicitis	Unclear or NR
Corral Gudino, 2003[111]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	Not compared statistically between groups: Male 60% vs 37%, NS	NR	NR	VTE	NR
Corral Gudino, 2003[111]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Risk factor	Mixed (specify)	DecRisk-significant: Surgery 0% vs 20.9%, p 0.05 DecRisk-NS: Immobilization, Fracture, cancer, hypertension, smoking, previous stroke IncRisk-NS: Previous PE	NR	NR	VTE	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Corral Gudino, 2003[111]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	IncRisk-Significant: Dyspnea 100% vs 79.1% p0.05 DecRisk-NS chest pain, pleuritic pain, non-pleuritic pain, hemoptysis, IncRisk-NS: cough, discomfort	58	NOT STAGE SPECIFIC	VTE	Dx Error
Corral Gudino, 2003[111]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	TVP on Doppler less frequent in the misdiagnosed group but not significantly (Dec risk-NS); Higher number of segments affected on V/Q scan in misdiagnosed group (IncRisk-S): unclear whether tests were ordered at initial evaluation	58	NOT STAGE SPECIFIC	VTE	Dx Error
Corral Gudino, 2003[111]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	PE not suspected initially vs PE suspected initially: mean age 76 vs 70 , p 0.05	58	NOT STAGE SPECIFIC	VTE	Dx Error
Crosby, 2013[16]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Provider type/role	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Crosby, 2013[16]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - Significant	Surgeons had a total of nine patients with misdiagnoses or complicated 72 h returns during the study period compared with four patients who were treated by emergency physicians (p¼0.052). There is an overall trend towards fewer missed diagnoses by emerge	2415	ED Dx Process	Other (specify) : triage diagnosis of head trauma, abdominal pain, testicular torsion	Either/Both
Crosby, 2013[16]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	Reported but not quantified	NR	2415	ED Dx Process	Other (specify) : triage diagnosis of head trauma, testicular pain, abdominal pain	Either/Both
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	No effect - wide CI	Childhood arterial ischemic stroke/TIA: conscious state, focal symptoms, and signs on arrival were not associated with the type of first imaging or time to diagnostic MRI	90	Stroke	NR	NR
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Off hours	No effect - wide CI	NR	NR	NR	NR	NR
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Triage intake severity	Reported but not quantified	NR	NR	NR	NR	NR
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	No effect - wide CI	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Atypical presentation	NR	NR	NR	NR	NR	NR
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Mode of arrival	Reported but not quantified	NR	NR	NR	NR	NR
Daverio, 2016[201]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	ED illness severity	No effect - wide CI	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	Time ratio: 1.93 p-value<0.001	432	Pre-hospital interval	Other (specify) : Acute coronary syndrome	Unclear or NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Health literacy	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Health insurance	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Symptom (lightheaded)	DecrRisk - Significant	time ratio: 0.67 p-value: 0.022	432	Pre-hospital interval	Other (specify) : acute coronary syndrome	Unclear or NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Unusual fatigue	IncrRisk - Significant	time ratio: 1.71 p-value: 0.002	432	Pre-hospital interval	Other (specify) : acute coronary syndrome	Unclear or NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Mode of arrival (transfer from another facility as compared to EMS)	DecrRisk - not sig	p=0.349	NR	Pre-hospital interval	Other (specify) : Acute coronary syndrome	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Race	No effect - wide CI	p=0.661 for black or African American with white as reference. p=0.585 for Hispanic with white as reference. p=0.106 for other with white as reference	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	SES/Income	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Symptom type	DecrRisk - Significant	time ratio: 0.65 p-value: 0.013	432	Pre-hospital interval	Other (specify) : Acute coronary syndrome	Unclear or NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	Time ratio: 1.93 p-value<0.001	432	Pre-hospital interval	Other (specify) : Acute coronary syndrome	Unclear or NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Health literacy	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Health insurance	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Symptom (lightheaded)	DecrRisk - Significant	time ratio: 0.67 p-value: 0.022	432	Pre-hospital interval	Other (specify) : acute coronary syndrome	Unclear or NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Unusual fatigue	IncrRisk - Significant	time ratio: 1.71 p-value: 0.002	432	Pre-hospital interval	Other (specify) : acute coronary syndrome	Unclear or NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Mode of arrival (transfer from another facility as compared to EMS)	DecrRisk - not sig	p=0.349	NR	Pre-hospital interval	Other (specify) : Acute coronary syndrome	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Race	No effect - wide CI	p=0.661 for black or African American with white as reference. p=0.585 for Hispanic with white as reference. p=0.106 for other with white as reference	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	SES/Income	Reported but not quantified	NR	NR	NR	NR	NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Symptom type	DecrRisk - Significant	time ratio: 0.65 p-value: 0.013	432	Pre-hospital interval	Other (specify) : Acute coronary syndrome	Unclear or NR
DeVon, 2020	Study design: Unclear or NR Look back or look forward analysis: Both Data source: Think Symptoms Study Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR
Drapkin, 2020[173]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	WBC count	DecrRisk - not sig	14.4 vs 12.3 * 10**3/µL P = 0.115	1678	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Drapkin, 2020[173]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	triage chief complaints nonspecific	IncrRisk - Significant	OR, 2.46; 95% CI, 1.1–5.6	1678	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Drapkin, 2020[173]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Drapkin, 2020[173]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NR	NR	NR
Drapkin, 2020[173]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	Reported but not quantified	NR	NR	NR	NR	NR
Drapkin, 2020[173]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Atypical presentation	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Race	Reported but not quantified	Frequency of serious neurologic event and in hospital death within 30 days after ED discharge with diagnosis of headache and back pain, overall In hospital death or serious neurologic events within 30 days after ED discharge for Headache, No. (%) Non-His	NR	NOT STAGE SPECIFIC	Other (specify) : Serious neurological disorder or in-hospital death	Either/Both
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Ethnicity	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Health insurance	Reported but not quantified	Frequency of serious neurologic event and in hospital death within 30 days after ED discharge with diagnosis of headache and back pain, overall In hospital death or serious neurologic events within 30 days after ED discharge for Headache, No. (%) Medicare	NR	NOT STAGE SPECIFIC	Other (specify) : Serious neurological disorder or in-hospital death	Either/Both
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Age	Reported but not quantified	Frequency of serious neurologic event and in hospital death within 30 days after ED discharge with diagnosis of headache and back pain, Sample Size: Headache: 10,374 Sample Size: Backache: 2,850 In hospital death or serious neurologic events within 30	NR	Unclear or NR	Other (specify) : Serious neurological disorder or in-hospital death	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	SES/Income	Reported but not quantified	Frequency of serious neurologic event and In hospital death within 30 days after ED discharge with diagnosis of headache and back pain, overall In hospital death or serious neurologic events within 30 days after ED discharge, No for Headache. (%)	NR	NOT STAGE SPECIFIC	Other (specify) : Serious neurological disorder or in-hospital death	Either/Both
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Sex	Reported but not quantified	Frequency of serious neurologic event and In hospital death within 30 days after ED discharge with diagnosis of headache and back pain, overall Sample Size: Headache: 10,374 Sample Size: Backache: 2,850 In hospital death or serious neurologic events	NR	NOT STAGE SPECIFIC	Other (specify) : Serious neurological disorder or in-hospital death	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Number of Comorbiditie s	Reported but not quantified	Frequency of serious neurologic event and In hospital death within 30 days after ED discharge with diagnosis of headache and back pain, overall In hospital death or serious neurologic events within 30 days after ED discharge for Headache, No. (%) 0 5440	NR	NR	NR	NR
Dubosh, 2015[11]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Time of Year (Quarter)	Reported but not quantified	Frequency of serious neurologic event and In hospital death within 30 days after ED discharge with diagnosis of headache and back pain, overall In hospital death or serious neurologic events within 30 days after ED discharge for Headache, No. (%) Jan-Mar	NR	NR	Other (specify) : Serious neurologica l disorder or in-hospital death	Either/Bot h

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2019[154]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	SES/Income	No effect - wide CI	In hospital Death or Serious Neurologic Events Within 7 Days After ED Discharge, Risk(%) Median household income state quartile for patient zip code 1 st Q(lowest quartile) : 0.3%, 0.1% 2ndQ: 0.3%, 0.1% 3rd Q: 0.3%, 0.1% 4th Q (highest quartile) 0.3%,	2,101,081	NOT STAGE SPECIFIC	Other (specify) : Headache and Backpain	Either/Both
Dubosh, 2019[154]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	DecrRisk - Significant	In hospital Death or Serious Neurologic Events Within 30 Days After ED Discharge, aOR (95% CI) for headache and back pain, respectively: Non-Hispanic white : ref Non-Hispanic black 0.92 (0.87-0.98), 0.65 (0.57-0.74) Hispanic 0.76 (0.72-0.81), 0.70 (0.63-0	2,101,081	NOT STAGE SPECIFIC	Other (specify) : Headache and Backpain	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2019[154]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	DecrRisk - Significant	In hospital Death or Serious Neurologic Events Within 30 Days After ED Discharge, aOR (95% CI) for headache and back pain, respectively: Men: ref Women: 0.88 (0.84-0.92), 0.61 (0.56-0.66)	2,101,081	NOT STAGE SPECIFIC	Other (specify) : Headache and Backpain	Either/Both
Dubosh, 2019[154]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Symptom type	DecrRisk - Significant	In hospital Death or Serious Neurologic Events Within 30 Days After ED Discharge, aOR (95% CI) for headache: Type of headache at the index visit migraine: ref non-migraine: 0.53 (0.50-0.56)	NR	ED Dx Process	Other (specify) : Headache and Backpain	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dubosh, 2019[154]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	Mixed (specify)	In hospital Death or Serious Neurologic Events Within 30 Days After ED Discharge, aOR (95% CI) for headache and back pain, respectively: Medicare ref Medicaid: 0.99 (0.92-1.08), 0.96 (0.83-1.11) Private: 0.95 (0.89-1.02), 0.78 (0.69-0.88) Self-pay:0.71	2,101,081	NOT STAGE SPECIFIC	Other (specify) : Headache and Backpain	Either/Both
Dubosh, 2019[154]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	IncrRisk - Significant	In hospital Death or Serious Neurologic Events Within 30 Days After ED Discharge, aOR (95% CI) for headache and back pain, respectively: Age 18-39 (ref) Age 40-64: 1.88 (1.79-1.98), 2.66 (2.35-3.01) Age 65-84: 3.19 (2.93-3.48), 5.93 (5.05-6.95) Age >8	2,101,081	NOT STAGE SPECIFIC	Other (specify) : Headache and Backpain	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	p=.76	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	fever p=0.31 vomiting p=0.51 local inflammation p<0.01 (more in delay) pain location p=0.56 UT side right p=0.57 UT side left p=0.23 UT side bilateral p=0.47 Type of UT p=0.13	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	preoperative CDU p=0.39 correct dx on CDU p=0.05	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - Significant	no surgical consult p=0.02	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	p=.76	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	fever p=0.31 vomiting p=0.51 local inflammation p<0.01 (more in delay) pain location p=0.56 UT side right p=0.57 UT side left p=0.23 UT side bilateral p=0.47 Type of UT p=0.13	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	preoperative CDU p=0.39 correct dx on CDU p=0.05	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error
Dupond-Athénor, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - Significant	no surgical consult p=0.02	60	NOT STAGE SPECIFIC	Testicular torsion	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
England, 2006[100]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Use of antibiotics	No effect - wide CI	In-hospital delay Group 1 received antibiotics n=45 median=0 range=(0–2) Group 2 did not receive antibiotics n=266 median=0 range=(0–7) P=0.7	311	Patient interval	Appendicitis	Dx Error
England, 2006[100]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NR	NR	NR
England, 2006[100]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR
England, 2006[100]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Atypical presentation	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Faiz, 2014[30]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Unclear or NR	Pre-hospital delay <=3.5 hours vs. >3.5 hours	IncrRisk - Significant	Median in-hospital time intervals comparing prehospital delay <=3.5 hr to > 3.5 hr: Evaluation by a nurse 8 vs. 15; Examination by a doctor 20 vs. 80; Initiation of a CT scan 51 vs. 138	290	Pre-hospital interval	Stroke	Dx Error
Fasen, 2020[131]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - Significant	aOR for non-neuroradiologists vs. neuroradiologists, 5.62 (95% CI, 1.06 to 29.85)	60	NOT STAGE SPECIFIC	Stroke	Dx Error
Fasen, 2020[131]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Location of LVO	IncrRisk - Significant	aOR for M2 segment vs. distal internal carotid artery and/or M1 segment, 5.69 (95% CI, 1.44 to 22.57)	82	NOT STAGE SPECIFIC	Stroke	Dx Error
Fasen, 2020[131]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	No effect - wide CI	unadjusted OR for reporting of lateralizing symptoms/signs or suspected location of stroke on the request form for CTA, 0.91	84	ED Dx Process	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Fasen, 2020[131]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	No effect - wide CI	unadjusted OR, 1.89 (95% CI, 0.63 to 5.70)	84	NOT STAGE SPECIFIC	Stroke	Dx Error
Fasen, 2020[131]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	No effect - wide CI	Range in aOR for senior residents vs. neuroradiologists and vs. non-neuroradiologists, 0.29 to 1.63	51	NOT STAGE SPECIFIC	Stroke	Dx Error
Ferree, 2016[1]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Other (specify) Numerator: Numerator and denominator	Level of consciousness, GCS=<8	No effect – wide CI	Patients with delayed diagnosed injuries N=172; Level of consciousness GCS=<8 (N, %): 43 (25); Patients without delayed diagnosed injuries N=1244; Level of consciousness GCS=<8 (N, %): 388 (31); p-value: 0.099	1416	Multiple stages	Fractures, Other (specify) : ligament/tendon injuries, external wounds, burns, bowel perforation, hemothorax	Either/Both
Ferree, 2016[1]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Other (specify) Numerator: Numerator and denominator	Sex	Reported but not quantified	Patients with delayed diagnosed injuries N=172; Male gender (N, %): 118 (69); Patients without delayed diagnosed injuries N=1244; Male gender (N, %): 864 (69); p-value: 0.821	1416	NOT STAGE SPECIFIC	Fractures, Other (specify) : ligament/tendon injuries, external wounds, burns, bowel perforation, hemothorax	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Ferree, 2016[1]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Other (specify) Numerator: Numerator and denominator	Mode of arrival	Mixed (specify)	Patients with delayed diagnosed injuries N=172; Direct transport to OR (N, %): 25 (15); Patients without delayed diagnosed injuries N=1244; Direct transport to OR (N, %): 170 (14); p-value: 0.756; Patients with delayed diagnosed injuries N=172; Transport	1416	Multiple stages	Fractures, Other (specify) : ligament/tendon injuries, external wounds, burns, bowel perforation, hemothorax	Either/Both
Ferree, 2016[1]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Other (specify) Numerator: Numerator and denominator	Age	Reported but not quantified	Patients with delayed diagnosed injuries N=172; Age overall (years; IQR): 44 (33–61); Patients without delayed diagnosed injuries N=1244; Age overall (years; IQR): 48 (28–67); p-value: 0.211	1416	NOT STAGE SPECIFIC	Fractures, Other (specify) : ligament/tendon injuries, external wounds, burns, bowel perforation, hemothorax	Either/Both
Filippi, 2008[23]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Multiple Numerator: Numerator and denominator	Provider type/role	Reported but not quantified	MRI discrepancy reading between radiology residents and attending radiologists: 26 of 361 cases (7.2%); 15 of 261 were major discrepancies	361	ED Dx Process	Other (specify) : MRI reading discrepancy between radiology residents and attendings	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Filippi, 2008[23]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Multiple Numerator: Numerator and denominator	Clinical experience	IncrRisk - Significant	Year of Training 1 Total No. of Discrepancies 14 (10.9) Year of Training 2 Total No. of Discrepancies 5 (4.7) Year of Training 3 Total No. of Discrepancies 7(6.0) Year of Training 4 Total No. of Discrepancies 0 Note.—Data are number of examination	26	NOT STAGE SPECIFIC	Other (specify) : MRI reading discrepancy between radiology residents and attendings	Either/Both
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Antiemetic administered	IncrRisk - not sig	Unadjusted ORs and 95% ACSs of the risk of a 3-day clinically-important related revisit with an alternate diagnosis Antiemetic administered OR 3.13 (2.60,3.61)	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - Significant	Race or ethnic group, n (%) Abdominal radiograph performed (N = 185 439) Non-Hispanic white 82 797 (44.6) Non-Hispanic black 44 559 (24.0) Hispanic. 40 028 (21.6) Asian 2966 (1.6) Other 15 089 (8.1) Abdominal radiograph not performed (N = 96 786) No	NR	NOT STAGE SPECIFIC	NR	Either/Both
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Analgesic administered	IncrRisk - Significant	Unadjusted ORs and 95% ACSs of the risk of a 3-day clinically-important related revisit with an alternate diagnosis Non-narcotic analgesic administered OR 2.38 (2.00,2.83) Narcotic analgesic administered OR 5.58 (4.41, 7.07)	28225	NR	Other(Specify) : Pediatric constipation	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - Significant	Male, n (%) Abdominal radiograph performed (N = 185 439) 89 324 (48.2) Abdominal radiograph not performed (N = 96 786) 45 331 (46.8) p-value <.001 unadjusted OR of the risk of a 3 day clinically important related revisit with an alternative di	NR	NOT STAGE SPECIFIC	Other (specify) : Constipation	Either/Both
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	Unadjusted ORs of 3 days clinically important related revisit with an alternative diagnosis, Abdominal / pelvic radiograph performed OR 1.98 (1.66, 2,35) Abdominal/pelvic ultrasound performed OR 1.22 (0.94, 1.59) CRP/ESR performed OR 1.86 (1.47,	282225	NOT STAGE SPECIFIC	Other(Specify) : Pediatric constipation	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Only for 3 day revisit with clinically important related revisit with an alternative diagnosis Age < 1 OR 0.40 (0.30, 0.54)	NR	NOT STAGE SPECIFIC	Other (specify) : Constipation	Either/Both
Freedman, 2017[17]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	DecrRisk - Significant	Payer, n (%) Abdominal radiograph performed (N = 185 439) Government 101 075 (55.2) Private 60 135 (32.8) Other 22 030 (12.0) Abdominal radiograph not performed (N = 96 786) Government 64 456 (67.3) Private 21 451 (22.4) Other9826 (10.3) p-value <.00	NR	NOT STAGE SPECIFIC	NR	Either/Both
Gaither, 2016[202]	Study design: Case series Look back or look forward analysis: Unsure Data source: Malpractice claims Numerator: Numerator only (error/harm)	Symptom type	DecrRisk - not sig	Abdominal pain initial symptoms 0.44 (0.13-1.44) p: 0.17	53	ED Dx Process	Testicular torsion	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Gaither, 2016[202]	Study design: Case series Look back or look forward analysis: Unsure Data source: Malpractice claims Numerator: Numerator only (error/harm)	Tests ordered	DecrRisk - not sig	US on first presentation 0.99 (0.33-2.95) p: 0.99 CT on first presentation 0.5 (0.08-3.00) p: 0.45	NR	ED Dx Process	Testicular torsion	Either/Both
Gaither, 2016[202]	Study design: Case series Look back or look forward analysis: Unsure Data source: Malpractice claims Numerator: Numerator only (error/harm)	Age	DecrRisk - not sig	Univariate OR (95% CI for OR) 0.99 (0.91-1.09) p .90	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Gallagher, 2006[13]	Study design: Randomized controlled trial Look back or look forward analysis: Not a cohort study Data source: Prospective data collection Numerator: Numerator and denominator	received intravenous morphine for abdominal pain	No effect - wide CI	Clinically important diagnostic accuracy was 86% in the morphine group (67/78 provisional diagnoses correctly predicted the final diagnoses) versus 85% in the placebo group (64/75 provisional diagnoses correctly predicted the final diagnoses)	153	NOT STAGE SPECIFIC	Other (specify) : Acute Abdominal Pain	Either/Both
Garfield, 2004[108]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests Ordered	Reported but not quantified	Negative Laparotomy Rate No imaging 5% (0, 12) Abdominal CT only 6% (0, 12) Abdominal sonogram only 12% (0, 42) CT and sonogram 15.8 12% (0, 42)	124	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Garfield, 2004[108]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Reported but not quantified	Preoperative ED LOS Hours No imaging 6.6 (5.5-7.8) Abdominal CT only 15.8 (14.2-17.4) Abdominal sonogram only 10.0 (7.4-12.6) CT and sonogram 15.8 (13.0-18.6)	124	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Race	Mixed (specify)	Range in adjusted time ratio for door-to-doctor time, 0.89 to 0.99; range in adjusted time ratio for door-to-image time, 0.87 to 1.23 (ref = white race)	1992	NOT STAGE SPECIFIC	Stroke	Dx Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Range in aTR for door-to-doctor time, 0.61 to 1.23; range in aTR for door-to-image times, 0.85 to 1.33	1992	NOT STAGE SPECIFIC	Stroke	Dx Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	IncrRisk - Significant	Adjusted time ratio for door-to-doctor time and door-to-image time, 1.11 and 1.15 (ref = males)	1992	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Onset to arrival interval	DecrRisk - Significant	Range in aTR for door-to-doctor times, 0.67 to 0.79 (ref = symptoms >= 6 hours or unknown); range in aTR for door-to-image times, 0.63 to .80	1992	NOT STAGE SPECIFIC	Stroke	Dx Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Nursing home resident	IncrRisk - Significant	aTR for door-to-image time for nursing home resident vs. not, 1.31	1992	NOT STAGE SPECIFIC	Stroke	Dx Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - narrow CI	Range in adjusted time ratio for door-to-doctor times, 0.99 to 1.02; range in time ratios for door-to-image times, 0.93 to 1.02 (ref >=80 years old)	1992	NOT STAGE SPECIFIC	Stroke	Dx Error
Gargano, 2009[83]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Mode of arrival	DecrRisk - Significant	aTR comparing arrived by emergency medical services vs. not for door-to-doctor time, 0.65 and door-to-image time, 0.76	1992	NOT STAGE SPECIFIC	Stroke	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Gaughan, 2009[82]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	% misdiagnosed among patients who were stable vs. in shock, 58.9% vs. 26.2%, p = 0.002; Patients who were hemodynamically stable at presentation had a significantly longer delay to diagnosis than those who were in shock (p,0.0001)	98	NOT STAGE SPECIFIC	AAD	MisDx Harm
Geyer, 2013[214]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mean ISS	Reported but not quantified	The mean ISS was 25.8 (+ 17.0 SD)	NR	NR	Other (specify) : trauma	NR
Gold, 2020[119]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NR	NR	NR
Gold, 2020[119]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator only (error/harm)	Tests ordered	NR	NR	3938	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Gouin, 2006[103]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Other (specify) Numerator: Numerator and denominator	Access to EHR/EHR type	IncrRisk - not sig	Diagnostic accuracy pre-PCAS: 98.5 (87.5 , 100) Diagnostic accuracy post-PCAS: 98.1 (94.5, 100) P-value: 0.39	3074	ED Dx Process	Other (specify) : Peds Emergency physician accuracy of x-rays relative to radiologists	Either/Both
Goulet, 2015[70]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	Failure to order appropriate diagnostic tests in 18 of 47 (38%) deaths w/in 72 hours of admission.	47	ED Dx Process	NR	Either/Both
Goulet, 2015[70]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	Reported but not quantified	NR	47	NOT STAGE SPECIFIC	NR	Either/Both
Goyal, 2020[116]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Pediatric Emergency Care Applied Research Network (PECARN) Registry Numerator: Numerator and denominator	Race	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Goyal, 2020[116]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Pediatric Emergency Care Applied Research Network (PECARN) Registry Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR
Goyal, 2020[116]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Pediatric Emergency Care Applied Research Network (PECARN) Registry Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Goyal, 2020[116]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Pediatric Emergency Care Applied Research Network (PECARN) Registry Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NH-white Referent NH-Black 1.81 (1.09–2.98) Hispanic 1.14 (0.73–1.79) Other 0.92 (0.48–1.78)	7298	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Graff, 2006[99]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	IncrRisk - Significant	% female for ACS vs. not ACS, 51.1% vs. 57.7%	7888	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Graff, 2006[99]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	No effect - narrow CI	% non-white for ACS vs. not ACS, 6.1% vs. 6.7%	7888	NOT STAGE SPECIFIC	MI	Dx Error
Graff, 2006[99]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	IncrRisk - Significant	% aged >=85 for ACS vs. not ACS, 24.6% vs. 36.3%	7888	NOT STAGE SPECIFIC	MI	Dx Error
Graff, 2014[29]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	ACS testing threshold (percent of chest pain cases seen by that physician who were evaluated with hospitalization or observation)	DecrRisk - Significant	r = 0.45, p < 0.001	6472	Learning from error	MI	Dx Error
Graff, 2014[29]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Feedback of return visit	DecrRisk - Significant	Missed ACS rate decreased from 1.5% in 1997 to 0.3% in 2007	6472	Learning from error	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Groot, 2016[71]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Troponin levels at baseline and peak troponin	DecrRisk - Significant	median hs-troponin baseline: 0 vs 59 ng/l; p<0.001, peak hs-troponin: 32 vs 2601 ng/l; p<0.001 in false activation vs. STEMI groups	827	NOT STAGE SPECIFIC	MI	Dx Error
Groot, 2016[71]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	aOR, 0.598	827	NOT STAGE SPECIFIC	MI	Dx Error
Groot, 2016[71]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	DecrRisk - Significant	aOR, 0.963	827	NOT STAGE SPECIFIC	MI	Dx Error
Groot, 2016[71]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	Interhospital transfer, 26% of false-positive activation, 16% STEMI	827	Pre-hospital interval	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Grosmaitre, 2013[36]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	IncrRisk - Significant	Waiting time > 1 hour: 11.4% with chest pain and 36% with atypical presentation; decision-making > 1 hour, 23.8% with chest pain, 54% with atypical presentation	255	NOT STAGE SPECIFIC	MI	Dx Error
Guillan, 2012[43]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	% female for stroke vs. stroke mimics, 51.8% vs. 66.6%	621	NOT STAGE SPECIFIC	Stroke	Dx Error
Guillan, 2012[43]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	DecrRisk - Significant	% with clinical symptoms ranged from 1.3 to 64.3% in stroke patients and 0 to 80% in stroke mimics.	621	NOT STAGE SPECIFIC	Stroke	Dx Error
Guillan, 2012[43]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	NIHSS score at 0 hours was 13 for ischemic stroke and 8 for stroke mimics.	621	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Guillan, 2012[43]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Mean age for stroke vs. stroke mimics, 72 vs. 53.7	621	NOT STAGE SPECIFIC	Stroke	Dx Error
Gurley, 2018[211]	Study design: Case series Look back or look forward analysis: Not a cohort study Data source: Malpractice claims Numerator: Numerator only (error/harm)	Clinical experience	Mixed (specify)	May be some increased effect for cardiac cases: Cardiac related 21 (18.6) 71 (10.0) <0.005* but otherwise no significant effect	NR	NR	NR	NR
Hallas, 2006[102]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	Mixed (specify)	Age years (s. d.) False Positive 31 (20.6) False negative 45.1 (27.7) Sum Dx errors 40.2 (26.2) Control group 44.7 (27.3) P NS No difference between a fracture location in misdiagnosed cases vs control	NR	NOT STAGE SPECIFIC	Fractures	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Hallas, 2006[102]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Mixed (specify)	Male: Female False Positive 8:13 False negative 19:21 Sum Dx errors 427:34 Control group 50:50 P NS No difference between a fracture location in misdiagnosed cases vs control	NR	NOT STAGE SPECIFIC	Fractures	Either/Both
Hallas, 2006[102]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	No effect - wide CI	Seen only by an intern False Positive 14 False negative 23 Sum Dx errors 37 Control group 86 P NS Intern + a resident 4 14 18 10 <0.05 False Positive 4 False negative 14 Sum Dx errors 18 Control group 10 P <.05 No difference between a fracture location in misdiagnosed cases vs control	NR	NOT STAGE SPECIFIC	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Hansen, 2007[94]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	aOR for age, 1.06 p = 0.02	66	NOT STAGE SPECIFIC	AAD	Dx Error
Hansen, 2007[94]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	No effect - wide CI	Number of diagnostic tests among misdiagnosed vs. correctly diagnosed, 1.7 vs. 1.9 p = NS	66	NOT STAGE SPECIFIC	AAD	Dx Error
Hansen, 2007[94]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	aOR for anterior chest pain, 7.12 p = 0.002	66	NOT STAGE SPECIFIC	AAD	Dx Error
Hansen, 2007[94]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	NR	NR	NR	NR	NR	NR
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Race	No effect - wide CI	Median time to diagnosis for white race vs. non-white race, 4.23 vs. 3.58 h; p = 0.619	894	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Tests ordered	Mixed (specify)	The initial diagnostic test and its results had incremental impact on the time to diagnosis (Table 3). Patients with an ECG suggestive of myocardial ischemia required more time to establish the diagnosis of aortic dissection. Abnormalities on the chest x-	894	NOT STAGE SPECIFIC	AAD	Dx Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Sex	IncrRisk - Significant	Delay time ratio for females, 1.73; p = 0.001	894	NOT STAGE SPECIFIC	AAD	Dx Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Symptom type	Mixed (specify)	Delay in time ratio, 0.61 p = 0.001 for posterior chest pain; 0.53 p = 0.001 for worst pain ever; 5.11 p < 0.001 for febrile; 0.43 p = 0.002 for abrupt onset of pain; 2.45 p < 0.001 for admission SBP >=105 mmHg	894	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Tests ordered	Mixed (specify)	Median time to diagnosis by first imaging test: CT vs. other, 3.93 vs. 5.00 p = 0.005; TEE/TTE vs. other, 4.62 vs. 4.00 p = 0.14; MRI vs. not 96.00 vs. 4.07 p = 0.012; Aortogram vs. not 16.50 vs. 4.00 p = 0.014	894	NOT STAGE SPECIFIC	AAD	Dx Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Triage intake severity	NR	NR	NR	NR	NR	NR
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Mode of arrival	IncrRisk - Significant	Delay time ratio for transferred from another hospital, 3.34, p < 0.001	894	NOT STAGE SPECIFIC	AAD	Dx Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Atypical presentation	IncrRisk - Significant	Median time to Dx for mild pain (yes: 17 vs No: 3.78; p=0.008), febrile (32.5 vs 4.1; p= 0.001), No pain vs any pain (24 vs 4.01; p<0.001)	894	NOT STAGE SPECIFIC	AAD	Dx Error
Harris, 2011[49]	Study design: Retrospective cohort Look back or look forward analysis: Data source: AAD database Numerator: Numerator only (error/harm)	Age	No effect - narrow CI	Median time to diagnosis for age >=70 years vs. < 70 years, 5.04 vs. 4.02; p = 0.051	894	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Hautz, 2019[148]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Triage intake severity	IncrRisk - not sig	Triage category (n [%]) See immediately Without diagnostic discrepancy n = 662 (87.68%) 36 (5.44%) With diagnostic discrepancy n = 93 (12.32%) 7 (7.53%) 0.281 Effect Size* Kendall's τ Estimate 0.04 CI −0.03 – 0.11	755	NOT STAGE SPECIFIC	NR	Either/Both
Hautz, 2019[148]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	IncrRisk - not sig	Age (years; mean [SD]) Without diagnostic discrepancy n = 662 (87.68%) 64.84 (18.68) With diagnostic discrepancy n = 93 (12.32%) 67.21 (16.17) p: 0.199 Effect Size* Type Cohen's d Estimate 0.13 95% CI§ −0.10 – 0.35	755	NOT STAGE SPECIFIC	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Hillinger, 2017[199]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator only (error/harm)	Sex	No effect - narrow CI	A significant difference in early diagnostic uncertainty was observed between younger women and younger men. Women aged 54 years or younger had an AUC of 0.96 (95 % CI 0.93–0.99) compared to an AUC of 0.87 in younger men (95 % CI 0.84–0.91, p\0.001,	NR	ED Dx Process	MI	NR
Hillinger, 2017[199]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator only (error/harm)	Age	Reported but not quantified	NR	NR	NR	NR	NR
Hochberg, 2011[47]	Study design: Randomized controlled trial Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	No effect - wide CI	Sensitivity for 2nd year vs. 3rd year residents, 93% vs. 81%	83	Unclear or NR	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Hochberg, 2011[47]	Study design: Randomized controlled trial Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Size of aneurysm	DecrRisk - Significant	(1) Sensitivity for aneurysms >=3 mm vs. <3 mm, 73% vs. 29% (2) Sensitivity for aneurysms in anterior communicating artery vs. middle cerebral artery vs. internal carotid artery vs. posterior circulation vs. posterior communicating artery, 95% vs. 76% vs.	84	ED Dx Process	Stroke	Dx Error
Hoekstra, 2009[78]	Study design: Controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Smoker	No effect - wide CI	% smoker for 12-lead STEMI, 80-lead STEMI, and 12-lead non-STEMI, 31, 32, 31	236	NOT STAGE SPECIFIC	MI	Dx Error
Hoekstra, 2009[78]	Study design: Controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age for 12-lead STEMI, 80-lead STEMI, and 12-lead non-STEMI, 63.8, 66.4, and 63.6	236	NOT STAGE SPECIFIC	MI	Dx Error
Hoekstra, 2009[78]	Study design: Controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male for12-lead STEMI, 80-lead STEMI, and 12-lead non-STEMI, 60, 68, and 70	236	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Huang, 2019[156]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Unclear or NR	Tests ordered	Mixed (specify)	Repeat ultrasound Orchiectomy (n = 60) 38% (23) Salvaged (n = 73) 18% (13) p-value 0.008 Single ultrasound Orchiectomy (n = 60) 62% (37) Salvaged (n = 73) 82% (60) p-value 0.008	NR	NR	Testicular Torsion	NR
Huang, 2019[156]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Unclear or NR	Mode of arrival	IncrRisk - not sig	Transferred from outside institution Orchiectomy (total n (transfer +primary)= 60) 58% (35) Salvaged (total n (transfer +primary) = 73) 45% (33) p-value 0.132	133	Pre-hospital interval	Testicular Torsion	Either/Both
Humphries, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Humphries, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - Significant	among patients triaged as chest pain with cardiac features and with peak cTnI levels > 99th percentile, females were significantly less likely to be diagnosed with MI (46.4% vs 57.5% p=0.007)	7272	NOT STAGE SPECIFIC	MI	Dx Error
Humphries, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	NR	NR	NR	NR	NR	NR
Humphries, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - Significant	among patients triaged as chest pain with cardiac features and with peak cTnI levels > 99th percentile, females were significantly less likely to be diagnosed with MI p=0.007	7272	NOT STAGE SPECIFIC	MI	Dx Error
Humphries, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	among patients triaged as chest pain with cardiac features and with peak cTnI levels > 99th percentile, females were significantly less likely to be diagnosed with MI p=0.007	7272	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Race	NR	NR	NR	NR	NR	NR
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Examination by physician not in accordance with priority	IncrRisk - Significant	38.0 (16.1 to 59.8)	1307	NOT STAGE SPECIFIC	Sepsis	Dx Error
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Not triaged within 15 minutes	IncrRisk - Significant	25.8 (3.8 to 47.8)	1307	NOT STAGE SPECIFIC	Sepsis	Dx Error
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Lactate not measured within 1 hour	IncrRisk - Significant	71.4 (56.0 to 86.8)	1307	NOT STAGE SPECIFIC	Sepsis	Dx Error
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Inadequate observation regimen	IncrRisk - Significant	23.9 (10.5 to 37.3)	1307	NOT STAGE SPECIFIC	Sepsis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NR	NR	NR
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	IncrRisk - Significant	Lactate not measured within 1 hour unadjusted 81.6 (65.9 to 97.2) model 1 86.2 (71.5 to 100.8) model 2 71.4 (56.0 to 86.8)	1559	NR	Sepsis	NR
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Triage intake severity	IncrRisk - Significant	Not triaged within 15 minutes unadjusted 54.4 (32.9 to 75.9) model 1 54.7 (33.2 to 76.2) model 2 25.8 (3.8 to 47.8)	NR	NR	Sepsis	NR
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Atypical presentation	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Ethnicity	NR	NR	NR	NR	NR	NR
Husabø, 2020[133]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	Reported but not quantified	NR	NR	NR	NR	NR
Jaffe, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	ED crowding	No effect - wide CI	[looks at how the following changes in relation to crowding] median door-to-imaging time: p = 0.5 median door-to-imaging time among patients receiving alteplase: p = 0.74 median door-to-needle time p=0.41 median door to groin puncture time p=0.54 doo	495	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Jaffe, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	ED crowding	No effect - wide CI	[looks at how the following changes in relation to crowding] median door-to-imaging time: p = 0.5 median door-to-imaging time among patients receiving alteplase: p = 0.74 median door-to-needle time p=0.41 median door to groin puncture time p=0.54 doo	495	NOT STAGE SPECIFIC	Stroke	Dx Error
Kamal, 2017[187]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator	lab/vitals at admission	IncrRisk - Significant	Median Glucose 120 vs 118, median SBP 158 vs 154; p <0.0001 in delayed vs =< 60 min DTN	55296	ED Dx Process	Stroke	Dx Error
Kamal, 2017[187]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator	Race	IncrRisk - Significant	Black : 16.54% vs 14.65% in delayed vs =< 60 min DTN p <0.0001	55296	NOT STAGE SPECIFIC	Stroke	Dx Error
Kamal, 2017[187]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator	Sex	IncrRisk - Significant	female 52.13% vs 47.68%, p<0.0001, in delayed vs =< 60 min DTN	55296	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Kamal, 2017[187]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	NIHSS score 10(6-10) vs 9 (5-16) p <0.0001	55296	ED Dx Process	Stroke	Dx Error
Kamal, 2017[187]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator	Health insurance	Mixed (specify)	self pay/no 6.55 % vs 6.53%; medicare 37.20% vs 37.44%; medicaid 10.77% vs 9.77%; private/VA/other 44.8% vs 45.6%, in in delayed vs =< 60 min DTN; p 0.0007	55296	NOT STAGE SPECIFIC	Stroke	Dx Error
Kamal, 2017[187]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Multiple Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	Private 20.95% vs 22.24%; EMS 78.51% vs 85.54% in delayed vs =< 60 min DTN p< 0.0001	55296	Pre-hospital interval	Stroke	Dx Error
Kargl, 2019[158]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	IncrRisk - not sig	The highest error rate was found in elbow trauma: in 12% of the cases radiography was misinterpreted initially (Table 1). Elbow injuries counted for a high rate of misses: in 14 of 20 errors fracture (12 supracondylar fractures, one lateral condyle fractures	125	NOT STAGE SPECIFIC	Fractures	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Kerkman, 2020[124]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: data set Numerator: Numerator and denominator	Sex	No effect - wide CI	Median system delay time for women vs. men, 97 vs. 93	787	NOT STAGE SPECIFIC	MI	Dx Error
Kerkman, 2020[124]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: data set Numerator: Numerator and denominator	Age	NR	NR	NR	NR	NR	NR
Kline, 2007[92]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Those with altered mental status at diagnosis were more likely to have a delayed diagnosis (8% vs. 30%, p = 0..009). Those who were immobile were less likely to have a delayed diagnosis (21% vs. 5%). Other symptoms were similar between groups.	161	NOT STAGE SPECIFIC	VTE	Dx Error
Kline, 2007[92]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Smoker	No effect - wide CI	% smoker among those with an ED diagnosis vs. a delayed diagnosis, 60% vs. 65%	161	NOT STAGE SPECIFIC	VTE	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Kline, 2007[92]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	% white among those with an ED diagnosis vs. a delayed diagnosis, 57% vs. 45%	161	NOT STAGE SPECIFIC	VTE	Dx Error
Kline, 2007[92]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male among those with an ED diagnosis vs. a delayed diagnosis, 59% vs. 60%	161	NOT STAGE SPECIFIC	VTE	Dx Error
Kline, 2007[92]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Mean age among those with an ED diagnosis vs. a delayed diagnosis, 51 vs. 61 p < 0.001	161	NOT STAGE SPECIFIC	VTE	Dx Error
Ko, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Mutliple Numerator: Numerator and denominator	ED volume/annual visits	DecrRisk - Significant	The higher the volume of annual chest pain patients per ED, the lower the rate of death or hospitalization (up until ~1400 patients/year, rates plateaued for higher volumes) Death, MI, or unstable angina, % 30 days after discharge Low: 1% Low Mediu	498291	NOT STAGE SPECIFIC	MI	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Ko, 2018	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Mutliple Numerator: Numerator and denominator	ED volume/annual visits	DecrRisk - Significant	The larger the hospital, the lower the rate of death or hospitalization post-negative result. Death, MI, or unstable angina, % 30 days after discharge Low: 1% Low Medium: 0.8% Medium: 0.8% High: 0.8% p<0.001 Hospitalization for MI or unstable	498291	NOT STAGE SPECIFIC	MI	MisDx Harm
Kondis, 2017[186]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - not sig	Thirty-nine percent were evaluated by a pediatric emergency medicine–trained physician during their initial fussy visit, whereas 78% were evaluated by pediatric emergency medicine trained physician during their subsequent visit	279	ED Dx Process	Fractures	Either/Both
Kondis, 2017[186]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	Fifteen (83%) of 18 infants were 3 months or younger at the time of the fussy visit	18	NOT STAGE SPECIFIC	Fractures	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Kuruvilla, 2011[60]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male among misdiagnosed vs. correctly diagnosed, 50% vs. 38.7%	57	NOT STAGE SPECIFIC	Stroke	Dx Error
Kuruvilla, 2011[60]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Smoking	No effect - wide CI	% active smoker among misdiagnosed vs. correctly diagnosed, 0% vs. 22.4%, p = 0.33; % past smoker among misdiagnosed vs. correctly diagnosed, 0% vs. 24.5%, p = 0.18	57	NOT STAGE SPECIFIC	Stroke	Dx Error
Kuruvilla, 2011[60]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	% Black race among misdiagnosed vs. correctly diagnosed, 25% vs. 28.6%; p = 0.73	57	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Kuruvilla, 2011[60]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	The rate of misdiagnosis was 5% among those with anterior circulation (n = 41) and 38% among those with posterior circulation (n = 16); p = 0.006. The rate of misdiagnosis was 11% among those with migraine (n=9) and 15% among those without migraine (n =	57	NOT STAGE SPECIFIC	Stroke	Dx Error
Kuruvilla, 2011[60]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age for misdiagnosed vs. correctly diagnosed, 34.3 vs. 38.7; p = 0.18; 33% of those under age 35 were misdiagnosed vs. 9% of those over age 35; p = 0.052	57	NOT STAGE SPECIFIC	Stroke	Dx Error
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	p=0.504	124	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	p=0.40	124	NOT STAGE SPECIFIC	Stroke	Dx Error
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	p=0.13	124	NOT STAGE SPECIFIC	Stroke	Dx Error
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	p=0.504	124	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	p=0.40	124	NOT STAGE SPECIFIC	Stroke	Dx Error
Ladner, 2015	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	p=0.13	124	NOT STAGE SPECIFIC	Stroke	Dx Error
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	complicated vs uncomplicated: Age mean 55vs 44(p<0.001) Age 45+ OR 2.40 (1.69, 3.40)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	transfer	DecrRisk - not sig	Transfer from another hospital for surgery: OR 0.842(0.547,1.299)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	Male 0.95 (0.69, 1.32)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	complicated vs uncomplicated: WBC count : mean 55 vs 44 (p<0.0001) WBC count >13_109/l: OR:1.40 (1.01, 1.94) CRP (mg/l)*: mean 78 vs 35 (p<0.001) CRP >50 mg/l OR: 2.76 (1.96, 3.87) CRP >100 mg/L OR: 3.88 (2.72, 5.55) Body temperature : mean 37.5 vs	837	ED Dx Process	Appendicitis	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Atema score 9 vs 4 (p<0.001) Atema score >6 ,5.68 (3.98, 8.09)	837	ED Dx Process	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Age AUROC 0.655 (0.610, 0.700) Age 45+ OR 2.40 (1.69, 3.40)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	Mixed (specify)	WBC count (109/l)*: AUROC: 0.559 (0.512, 0.607) WBC count >13_109/l: OR:1.40 (1.01, 1.94) CRP (mg/l)*: AUROC: 0.696 (0.653, 0.739) CRP >50 mg/l OR: 2.76 (1.96, 3.87) CRP >100 mg/L OR: 3.88 (2.72, 5.55) Body temperature (_C)* AUROC: 0.687 (0.643, 0.73	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	delays	Mixed (specify)	Pre-CT delay (h)*: AUROC: 0.632 (0.586, 0.678) Preoperative delay (h)*: AUROC: 0.446 (0.400, 0.493) Total delay (h)*: AUROC: 0.620 (0.574, 0.667) Pre-CT delay over 48 h: OR: 2.46 (1.75, 3.46) Antibiotics started before entering theatre: OR: 3.11 (2.06	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	transfer	No effect - wide CI	Transfer from another hospital for surgery: AUROC: 0.843 (0.547, 1.299)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	Male 0.95 (0.69, 1.32)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	Laparoscopic surgery: OR: 0.65 (0.44, 0.96) Appendicolith on CT: OR: 3.06 (2.18, 4.28) Periappendiceal fluid on CT: OR: 3.15 (1.92, 5.18) Extraluminal air on CT: OR: 4.28 (1.29, 14.17) Any risk factorâ€¡ on CT: OR: 3.67 (2.62, 5.15) No risk factorâ€¡	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lastunen, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Atema score AUROC 0.775 (0.736, 0.814) Atema score >6 5.68 (3.98, 8.09)	837	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Lehtimäki, 2015	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	First reader aware of AMI suspicion in CT referral	DecrRisk - Significant	When a suspicion of AMI was expressed in the CT referral, the ï¬rst readerâ€™s CT report was more frequently correct (97%, 29/30) than when the suspicion was not expressed (81%, 54/67, p = 0.04).	97	NOT STAGE SPECIFIC	Other (specify) : acute mesenteric ischemia	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lehtimäki, 2015	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Training background	DecrRisk - Significant	The rate of correct initial CT reports was signiï¬□cantly higher for residents, body imaging specialists and angiologists than for the other subspecialists (p<0.01) (93%, 94%, 92% vs. 74%).	97	NOT STAGE SPECIFIC	Other (specify) : acute mesenteric ischemia	Dx Error
Lever, 2013[44]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	IncrRisk - Significant	OR, 43.4	189	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2018[168]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	No effect - narrow CI	Among no misdiagnosis vs. probable misdiagnosis, % white 55.3% vs. 55.4%; % black 16% vs. 22.8%; % other 10.1% vs. 7.4%	5966	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2018[168]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	No effect - narrow CI	% female among no misdiagnosis vs. probable misdiagnosis, 71.5% vs. 76.4%	5966	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Liberman, 2018[168]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	No effect - narrow CI	Among no misdiagnosis vs. probable misdiagnosis, % Medicare 19.7% vs. 8.8%; % Medicaid 23.1% vs. 25.5%; % private 47.0% vs. 54.6%; % self-pay/other 10.2% vs. 11.1%	5966	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2018[168]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	DecrRisk - Significant	Mean age among no misdiagnosis vs. probable misdiagnosis, 44.4 vs. 38.5	5966	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2018[168]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	No effect - narrow CI	Among no misdiagnosis vs. probable misdiagnosis, % Hispanic, 18.6% vs. 14.4%	5966	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% female among no Dx error vs. Dx error, 54.8% vs. 81.8%, p = 0.17	53	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	% Black race among no Dx error vs. Dx error, 44.4% vs. 45.5%, p = 1.0; % other race, 36.1% vs. 45.5%, p = 0.73	53	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	SES/Income	No effect - wide CI	Mean SES score among no Dx error vs. Dx error, -2.8 vs. -3.0, p = 0.43	53	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	No effect - wide CI	Radiologic features for no Dx error vs. Dx error: cortical thrombosis, 16.7% vs. 9.1%; deep vein thrombosis, 9.5% vs. 9.1%; dural sinus thrombosis, 73.8% vs. 81.8%; ICH 35.7% vs. 36.4%	53	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	No effect - wide CI	Neurology consultation obtained among no Dx error vs. Dx error, 95.2% vs. 81.8%, p = 0.19	53	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Language	No effect - wide CI	% non-English preferred language among no Dx error vs. Dx error, 12.8% vs. 0%, p = 0.57	53	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2019[144]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age for no Dx error vs. Dx error, 49.3 vs. 42.2, p = 0.13	53	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2020[114]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	RR 1.9 (95% CI, 1.1 to 3.1)	20,592	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Liberman, 2020[127]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	IncrRisk - Significant	% female among no misdiagnosis vs. probable misdiagnosis, 44.3% vs. 61.9%, aOR, 1.76 (95% CI, 1.33 to 2.34)	7090	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Liberman, 2020[127]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	No effect - wide CI	aOR, 0.86 (95% CI, 0.54 TO 1.37) for black race	7090	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2020[127]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	DecrRisk - Significant	Mean age among no misdiagnosis vs. probable misdiagnosis, 53.0 vs. 43.3, $p < 0.001$; aOR, 0.97 (95% CI, 0.96 to 0.98)	7090	NOT STAGE SPECIFIC	Stroke	Dx Error
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	SES/Income	No effect - wide CI	NR	NR	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - wide CI	NR	NR	NR	Stroke	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	NR	NR	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	DecrRisk - not sig	Neurologic consult and neuroimaging at index visit for headache was more frequent in patient with subsequent TIA	186	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	NR	NR	NR	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Language	No effect - wide CI	NR	NR	NR	Stroke	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	NR	NR	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	NR	NR	NR	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health literacy	NR	NR	NR	NR	Stroke	NR
Liberman, 2020[210]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	No effect - wide CI	NR	NR	NR	Stroke	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lindsey, 2018[161]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Radiographs Numerator: Numerator and denominator	Provider type/role	DecrRisk - Significant	The sensitivity and specificity of the emergency medicine MDs were significantly improved with the assistance of the deep learning model (one-sided, two-sample Wilcoxon signed rank test for sensitivity: P < 10−4, d = 1.17; specificity: P < 10−5, d = 1.24)	NR	NR	NR	NR
Lowe, 2021	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Unclear or NR	Ventilator	IncrRisk - Significant	Ventilator: if the child needed a ventilator that was associated with longer time to dx 59% vs. 21%; p < 0.01	170	ED Dx Process	Other (specify) : injury	Dx Error
Lowe, 2021	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Unclear or NR	Symptom type	IncrRisk - Significant	Number of injuries: The more injuries a child had, the longer it took for dx score of 10 (no delay) vs 17 (delay)	170	ED Dx Process	Other (specify) : injury	Dx Error
Lowe, 2021	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Unclear or NR	Ventilator	IncrRisk - Significant	if the child needed a ventilator that was associated with longer time to dx 59% vs. 21%; p < 0.01	170	ED Dx Process	Other (specify) : injury	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Lowe, 2021	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Unclear or NR	Symptom type	IncrRisk - Significant	The more injuries a child had, the longer it took for dx score of 10 (no delay) vs 17 (delay)	170	ED Dx Process	Other (specify) : injury	Dx Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Race	No effect - wide CI	black 22.6% vs 21.3%, 0.63, in missed vs diagnosed stroke	2027	NOT STAGE SPECIFIC	Stroke	Dx Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Sex	No effect - wide CI	female 56.5% vs 55.1%, p 0.65, in missed vs diagnosed stroke	2027	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Those presenting with focal weakness were 62% less likely to have missed ED AIS diagnoses (95% CI = 0.31 to 0.48). The only symptom that was associated with an increase in the likelihood of missed ED diagnosis of AIS was decreased LOC; those with a decrease	2027	ED Dx Process	Stroke	Dx Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Tests ordered	DecrRisk - Significant	Brain imaging completed in ED 83.8% vs 97.4%, p<0.0001 in missed vs diagnosed stroke	2027	ED Dx Process	Stroke	Dx Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Age	DecrRisk - not sig	aOR = 0.99, 95% CI = 0.98 to 1.0 for each 1-year increase	2027	ED Dx Process	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Atypical presentation	IncrRisk - Significant	symptoms other than focal weakness, focal numbness, LOC, speech, headache, vision, dizziness/vertigo: 60.1% vs 51.4%, p0.007, in missed vs diagnosed stroke	2027	ED Dx Process	Stroke	Dx Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	by EMS: 67% vs 53.9%, p <0.0001, in missed vs diagnosed stroke	2027	Pre-hospital interval	Stroke	Dx Error
Madsen, 2016[200]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: The Greater Cincinnati /Northern Kentucky Stroke Study (GCNKSS) Numerator: Numerator and denominator	ED crowding	No effect - wide CI	arrival during peak hours: 63.5% vs 64.5%, p 0.77, in missed vs diagnosed stroke	2027	ED Dx Process	Stroke	Dx Error
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	Reported but not quantified					

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Adults Total, No.100833 Abdominal pain only 0.65 (0.62-0.69) Abdominal pain and constipation 1.51 (1.31-1.75) Abdominal pain and nausea and/or vomiting 0.90 (0.84-0.97) Abdominal pain, nausea and/or vomiting, and fever 0.78 (0.64-0.95) Abdominal pain	116678	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	Reported but not quantified	NR	NR	NR	NR	NR
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Atypical presentation	NR	NR	NR	NR	NR	NR
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
Mahajan, 2020[132]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Mahajan, 2020[134]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Main symptom at presentation Median, Range Headache True case (HDP)36, 55.4% (43.0–67.1) True control (No HDP) 12, 26.1% (15.3–40.9) p-value 0.002 Visual disturbances True case (HDP) 17, 26.2% (16.8–38.4) True control (No HDP) 4, 8.7% (3.2–21.4)	NR	NOT STAGE SPECIFIC	Other(Specify) : HDP	Either/Both
Mansella, 2020[121]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - narrow CI	% male among patients with early workup vs. delayed workup, 54.4% vs. 56.8%	226	NOT STAGE SPECIFIC	VTE	Dx Error
Mansella, 2020[121]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Among patients with early workup vs. delayed workup, % with dyspnea, 59.9% vs. 45.5% p 0.117; % with chest pain, 49.5% vs. 18.2% p<0.001; % with nonspecific complaints, 8.8% vs. 29.5% p<0.001	266	NOT STAGE SPECIFIC	VTE	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Mansella, 2020[121]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	Among patients with early workup vs. delayed workup, % diagnosed with D-dimer testing, 70.9% vs. 6.8%; % diagnosed with echocardiography, 32.4% vs. 52.3%; % diagnosed with chest CT, 88.5% vs. 54.5% ; all p-values significant	226	NOT STAGE SPECIFIC	VTE	Dx Error
Mansella, 2020[121]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Median age of patients with early workup vs. delayed workup, 67 vs. 77.5	226	NOT STAGE SPECIFIC	VTE	Dx Error
March, 2014[27]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Mode of arrival	NR	NR	NR	NR	NR	NR
March, 2014[27]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Triage intake severity	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
March, 2014[27]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Mixed (specify)	A negative triple test (WCC, CRP level and preoperative diagnostic imaging, all three tests negative/equivocal) was a strong indicator of a negative appendicitis (p=0.0158, NPV: 0.91, 95% CI: 0.59–0.99).	NR	ED Dx Process	Appendicitis	NR
March, 2014[27]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Diagnostic Imaging	Mixed (specify)	A positive triple test (combination of a positive imaging result, elevated CRP and a raised WCC) was a strong predictor of appendicitis (p=0.0213, PPV: 1.00, 95% CI: 0.40–1.00).	81	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Martin, 2011[48]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	No effect - wide CI	p > 0.05	91	Multiple stages	Stroke	Dx Error
Martin, 2011[48]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	No effect - wide CI	p = 0.311	91	Multiple stages	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Martin, 2011[48]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	No effect - wide CI	p = 0.512	91	Multiple stages	Stroke	Dx Error
Martin, 2011[48]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	p = 0.205	91	Multiple stages	Stroke	Dx Error
Martin, 2011[48]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	No effect - wide CI	p = 0.079 (pediatric): first contact w medical center	91	Multiple stages	Stroke	Dx Error
Martin, 2011[48]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	p = 0.551	91	Multiple stages	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Matera, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Yellow triage code: increased from 2019 to 2020 p<0.001 10.4% -> 12.6% in high incidence areas 10.9% -> 16.4% in low incidence areas	62476	NOT STAGE SPECIFIC	Other (specify) : all diseases	Dx Error
Matera, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Yellow triage code: increased from 2019 to 2020 p<0.001 10.4% -> 12.6% in high incidence areas 10.9% -> 16.4% in low incidence areas	62476	NOT STAGE SPECIFIC	Other (specify) : all diseases	Dx Error
Mattijssen-Horstink, 2020[126]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Hospital complication list and EHRs Numerator: Numerator and denominator	Age	Mixed (specify)	0 to 14 years 77 (26.6%) 15 to 64 years 145 (50.2%) 65 years and older 67 (23.2%) OR or RR NR	289	NOT STAGE SPECIFIC	Fractures	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Mattsson, 2018[172]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	Women Total number of patients, n 654 Overall discrepancies, n (%) 135 (20.6) Clinically significant discrepancies, n (%) 36 (5.5) 0.911 P value (significant discrepancies) 0.911	1522	NOT STAGE SPECIFIC	Fractures	Either/Both
Mattsson, 2018[172]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	65 and older Total number of patients, n 543 Overall discrepancies, n (%) 176 (32.4) Clinically significant discrepancies, n (%) 45 (8.3) P value (significant discrepancies) 0.002	1522	NOT STAGE SPECIFIC	Fractures	Either/Both
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Race	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	SES/Income	NR	NR	NR	NR	NR	NR
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	NR	NR	NR	NR	NR	NR
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Language	NR	NR	NR	NR	NR	NR
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	IncrRisk - Significant	The median time from triage arrival to CT order was 138 minutes in females vs 95 minutes in males for a difference of 43 minutes (95% CI, 15-60; P = .0012). The median time from initial physician evaluation to CT order was 45 minutes in females and 28 mi	137	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Ethnicity	NR	NR	NR	NR	NR	NR
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Health literacy	NR	NR	NR	NR	NR	NR
McGann Donlan, 2009[80]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Health insurance	NR	NR	NR	NR	NR	NR
Metcalfe, 2016[207]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	DecrRisk - Significant	Association with correct diagnosis: palpable AAA (OR 3.3, 95% CI 1.1–9.4, P= 0.029) and collapse (OR 3.2, 95% CI 1.0–10.0, P= 0.042)	85	ED Dx Process	AAD	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Michelson, 2021	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Pediatric Health Information System database. Numerator: Numerator only (error/harm)	Age	No effect - wide CI	reference group : age<5y. 5-9y: Model 1 aOR=0.54 (0.24-1.20); Model 2 aOR=0.63 (0.24-1.65). 10-14y: Model 1 aOR=0.48 (0.20-1.15); Model 2 aOR=0.68 (0.23-2.00). >14y: Model 1 aOR=0.72 (0.33-1.58); Model 2 aOR=0.70 (0.27-1.84).	748	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Michelson, 2021	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Pediatric Health Information System database. Numerator: Numerator only (error/harm)	Care received	Mixed (specify)	Use of nonsteroidal anti-inflammatory drug: Model 2 aOR=3.78 (2.10-6.80). Use of Opioid: Model 2 aOR=0.26 (0.14-0.49). Use of Ondansetron: Model 2 aOR=1.99 (1.10-3.61)	748	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Michelson, 2021	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Pediatric Health Information System database. Numerator: Numerator only (error/harm)	Sex	No effect - wide CI	Male vs Female: Model 1 aOR=0.93 (0.61-1.43); Model 2 aOR=0.82 (0.49-1.38).	748	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Michelson, 2021	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Pediatric Health Information System database. Numerator: Numerator only (error/harm)	Symptom type	Mixed (specify)	Complex chronic condition: Model 1 aOR=2.34 (1.05-5.23) . Model 2 aOR= 2.23 (0.89-5.60). Abdominal pain duration, 24-47h vs. <24 Or unknown: Model 1 aOR=1.28 (0.77-2.14) . Model 2 aOR= 1.56 (0.81-2.99). Abdominal pain duration, 48-96h vs. <24 Or unknown	748	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Michelson, 2021	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Pediatric Health Information System database. Numerator: Numerator only (error/harm)	Tests ordered	DecrRisk - Significant	Use of CT scan: Model 2 aOR=0.10 (0.05-0.22). Use of Ultrasonography: Model 2 aOR=0.13 (0.08-0.24).	748	NOT STAGE SPECIFIC	Appendicitis	MisDx Harm
Miedema, 2011[51]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - narrow CI	% male with delay <=120 min vs. delay >120 min, 73.9% vs. 70.6%, p = 0.12	2015	NOT STAGE SPECIFIC	MI	Dx Error
Miedema, 2011[51]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Mean age with delay <=120 min vs. delay >120 min, 61.3 vs. 64.0, p < 0.001	2015	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Miller, 2018[12]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - not sig	Missed Diagnosis 10 (1.7) CT at index Yes 3 (1.6) No 7 (70.0) P value 0.893 Epoch Pre-intervention 3 (1.7) Post education 5 (2.3) Post- data review 1 (0.5) P value 0.337	582	ED Dx Process	Other(Specify) : Headache	Dx Error
Mirete, 2005[212]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	Sex Male Woman Group C (N104) Male 73 (70.2%) Female 31 (29.8%) Group A+B (n=424) Male 238 (56.2%) Female 186 (43.8%) p = 0.06; OR = 1.52 95% CI, 0.98-2.38	NR	NR	NR	Dx Error
Mirete, 2005[212]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	NR	NR	NOT STAGE SPECIFIC	NR	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Mirete, 2005[212]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	No effect - wide CI	NR	NR	NR	NR	Dx Error
Mohamed, 2013[42]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	NR	93	NOT STAGE SPECIFIC	Stroke	Dx Error
Mohamed, 2013[42]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Teaching status	DecrRisk - not sig	Rates of misdiagnosis among hospitals without vs. with a residency program: emergency medicine, 16.2% vs. 12.5%; neurology, 18% vs. 6.3%	93	NOT STAGE SPECIFIC	Stroke	Dx Error
Montmany, 2008[5]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Mean ISS among those with no unnoticed injuries vs. with unnoticed injuries, 18.3 vs. 22.4; p = 0.01	122	NOT STAGE SPECIFIC	Other (specify) : missed injury in polytrauma patients	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Montmany, 2008[5]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Prehospital intubation; hospital intubation	No effect - narrow CI	Prehospital intubation among those with no unnoticed injuries vs. with unnoticed injuries, 15.8% vs. 36.4%, p = 0.024 Hospital intubation among those with no unnoticed injuries vs. with unnoticed injuries, 25% vs. 51.5%, p = 0.009	122	NOT STAGE SPECIFIC	Other (specify) : missed injury in polytrauma patients	Either/Both
Montmany, 2017[175]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Trauma database Numerator: Numerator and denominator	Provider type/role	Mixed (specify)	Domain error Physician 142 errors at the US trauma center (106 deaths) 86% (122 errors) 51 errors at the Spanish referral hospital (21 deaths) 96% (49 errors) p: .06 Physician and nurse 142 errors at the US trauma center (106 deaths) 8% (12 errors) 51	106	ED Dx Process	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Moonen, 2017[188]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	There was a significant statistical difference in age (44 vs. 34, p < 0.005) presentation of our population in comparison to overall minor trauma patients.	NR	NOT STAGE SPECIFIC	Fractures	Either/Both
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	false neg: 60+ OR: 0.82 (0.56-1.23) false pos: 60+ OR: 1.34 (0.90-2.00)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Access to consultation	DecrRisk - not sig	FN (yes) 0.46 (0.2, 1.07) FP 0.59 (0.3, 1.14)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	IncrRisk - not sig	FN: has insurance OR 0.96 (0.6,1.93) FP: has insurance OR 1.47 (0.67,3.23)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	hospital location	DecrRisk - not sig	seven hospitals in analysis. #1 used as ref category FN (CI), FP (CI) 2 1.49 (0.62, 3.62) 0.71 (0.26, 1.95) 3 0.89 (0.48, 1.65) 0.83 (0.47, 1.45) 4 0.72 (0.31, 1.71) 0.69 (0.32, 1.49) 5 0.65 (0.35, 1.22) 0.56 (0.31, 0.98) 6 0.81 (0.47, 1.40) 0.82 (0	NR	NOT STAGE SPECIFIC	Stroke	Dx Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	NIH Stroke Scale	DecrRisk - not sig	FN Moderate 0.54 (0.26, 1.13) Severe 0.98 (0.56,1.71)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	History of Stroke	IncrRisk - Significant	FN (yes) 0.93 (0.66, 1.31) FP 1.66 (1.24, 2.22)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - not sig	FN: Mexican American OR 1.36 (0.96,1.94) African American OR 1.59 (0.8,3.14) FP: MA OR 0.93 (0.69,1.26) AA OR 1.24 (0.68, 2.26)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	FN: Female OR: 1.25 (0.89,1.75) FP: Female OR: 1.15 (0.86,1.55)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error
Morgenstern, 2004	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	DecrRisk - not sig	[reference category not given...] FN: sensory 0.82 (0.57,1.19) motor 0.55 (0.39, 0.78) visual 0.78 (0.46,1.34) language 0.71 (0.49,1.04) FP: sensory 0.43 (0.29,0.63) motor 0.39 (0.29, 0.53) visual 0.74 (0.46, 1.2) language 0.96 (0.7,1.32)	2059	NOT STAGE SPECIFIC	Stroke	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Month of visit	DecrRisk - Significant	OR (ref July-December), 0.693 ($p<0.0001$)	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Health insurance	Mixed (specify)	Range in OR for expected primary payer (reference = private), 0.801 to 1.124	111973	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Inpatient occupancy rate	DecrRisk - Significant	Range in OR for occupancy rate (ref = low), 0.576 to 0.625	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Off hours	No effect - narrow CI	OR (ref = weekend), 0.994	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Ethnicity	No effect - narrow CI	OR, 1.193	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	ED crowding	Mixed (specify)	Range in OR for ED crowding on day of visit (ref = low), 0.781 (p=0.0085) for high to 0.910 (p=0.2590) for medium	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Average discharge fraction	DecrRisk - Significant	Range in OR for percent admitted from ED (ref = low), 0.150 to 0.497	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Access to testing	DecrRisk - Significant	Range in OR for availability of cardiac catheterization lab (ref = not available), 0.186 to 0.777	111973	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Age	DecrRisk - Significant	OR range 0.492 to 0.700 (ref 18-44 years)	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Population density	Mixed (specify)	Range in OR (ref = large metropolitan area), 0.856 to 1.968	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	ED volume/annual visits	No effect - narrow CI	Range in OR (ref = low), 0.951 to 1.080	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Ownership/business model	No effect - narrow CI	Range in OR (ref = private, not-for-profit), 0.944 to 0.990	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Teaching status	DecrRisk - Significant	OR (ref = non-teaching), 0.603; p = 0.0002	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Sex	No effect - narrow CI	OR, 0.988 (ref female)	111973	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	SES/Income	No effect - narrow CI	Range in OR for median household income by ZIP code (ref = highest), 0.906 to 1.067	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Geographic region	Mixed (specify)	Range in OR (ref = Northeast), 0.664 to 2.169	111973	NOT STAGE SPECIFIC	MI	Dx Error
Moy, 2015[24]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: HCUP databases Numerator: Numerator and denominator	Race	IncrRisk - Significant	OR range, 1.314 to 1.452 (ref White)	111973	NOT STAGE SPECIFIC	MI	Dx Error
Muhm, 2012[3]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	Reported but not quantified	Group A w/o diagnostic delay: mean age 44 Group B w/diagnostic delay: mean age 42	111	NR	Other (specify) : delayed diagnosis after primary/secondary trauma survey	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Muhm, 2012[3]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	Mixed (specify)	Admission to the emergency room Time interval Weekday 08.01–16.00 Group A (without delay in diagnosis) n (%)25 (29) Group B (with delay in diagnosis) n (%)5 (20) Weekday 16:01-8:00 Group A (without delay in diagnosis) n (%)36 (42) Group B (with delay	111	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosis after primary/secondary trauma survey	Dx Error
Muhm, 2012[3]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	Whole Body CTs Performed Group A w/o diagnostic delay: 64% Group B w/diagnostic delay: 92% P-Value: NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Muhm, 2012[3]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	Mixed (specify)	Mean ISS after Primary Survey: Group A w/o diagnostic delay: 17.0 Group B w/diagnostic delay: 26.9 P-Value <0.0001 Mean ISS after Secondary Survey: Group A w/o diagnostic delay: 17.0 Group B w/diagnostic delay: 29.2 P-Value <0.0001 NACA: 'Scores h	111		Other (specify) : delayed diagnosis after primary/secondary trauma survey	Dx Error
Muhm, 2012[3]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Reported but not quantified	Group A w/o diagnostic delay: 71% male Group B w/diagnostic delay: 76% male	111	NR	Other (specify) : delayed diagnosis after primary/secondary trauma survey	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Musunuru, 2007[91]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	No effect - wide CI	The negative appendectomy rate for patients diagnosed with appendicitis on CT was 8% (19:227). For all patients who underwent appendectomy without preoperative imaging, the negative appendectomy rate was 14% (22:155), which was not significantly different	411	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	DecrRisk - not sig	(<6.9 years) Referent (6.9–9.6 years) OR=0.60 (0.28–1.32) (9.7–12.6 years) OR=0.49 (0.22–1.13)	816	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Primary language	No effect - wide CI	Obese	816	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	NR	NR	NR	NR	NR
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Language	IncrRisk - not sig	English Referent Spanish OR=1.38 (0.63–3.02)	NR	NR	NR	NR
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - not sig	White Referent African American OR=3.05 (0.38–24.67)	816	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	IncrRisk - not sig	Private Referent Medicaid OR=1.42 (0.52–3.87)	816	NOT STAGE SPECIFIC	Appendicitis	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Naiditch, 2013[39]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	IncrRisk - not sig	Hispanic OR=3.20 (0.64–16.03)	NR	NR	NR	NR
Nevo, 2017[189]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	clinic visit prior	IncrRisk - Significant	increased delay (48% p=0.008) if patient went to clinic before coming to the ed and also increased missed diagnosis. (50%, p= 0.02)	NR	NR	NR	NR
Nevo, 2017[189]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Median duration of pain (IQR) Median age (IQR) Correct Diagnosis 5 (2-12) Missed Diagnosis 60 (30-72) Delayed Presentation 48 (15-69)	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Nevo, 2017[189]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	Mixed (specify)	Median age (IQR) Correct Diagnosis 13 (10-15) Missed Diagnosis 12 (3-14) Delayed Presentation 11 (2-13)	NR	NOT STAGE SPECIFIC	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Nevo, 2017[189]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Off hours	Mixed (specify)	Time ultrasound was performed Morning Correct Diagnosis 21 (58%) Missed Diagnosis 6 (60%) Delayed Presentation 12 (52%) Evening Correct Diagnosis 8 (21%) Missed Diagnosis 3 (30%) Delayed Presentation 8 (35%) Night Correct Diagnosis 8 (21%) Mi	NR	ED Dx Process	Testicular torsion	Either/Both
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	ED visit not complete	IncrRisk - Significant	OR, 2.94	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ownership/business model	Mixed (specify)	Range in OR, 0.80 to 0.99	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - Significant	Range in OR, 1.18 to 1.29	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Geographic region	DecrRisk - not sig	Range in OR, 0.84 to 0.97	187,188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	DecrRisk - Significant	OR 0.75	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	ED volume/annual visits	Mixed (specify)	Range in OR, 1.11 to 1.57	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	DecrRisk - Significant	Range in OR, 0.19 to 0.43	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	SES/Income	IncrRisk - not sig	Range in OR, 1.05 to 1.06	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Teaching status	IncrRisk - Significant	OR, 1.45	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	Mixed (specify)	Range in OR, 0.63 to 1.01	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	ED crowding	No effect - wide CI	Range in OR, 0.98 to 1.08	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Current discharge fraction	IncrRisk - Significant	Range in OR, 1.40 to 6.34	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Average discharge fraction	IncrRisk - Significant	Range in OR, 1.24 to 1.55	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Inpatient occupancy rate	No effect - wide CI	Range in OR, 1.00 to 1.11	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	IncrRisk - Significant	OR, 1.11	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Population density	Mixed (specify)	Range in OR, 0.77 to 1.23	187,188	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Newman-Toker, 2014[33]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	IncrRisk - Significant	OR 1.30	187188	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Ohle, 2019[151]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male among diagnosed vs. missed, 65.6 vs. 64.7, p =.19	194	NOT STAGE SPECIFIC	AAD	Dx Error
Ohle, 2019[151]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age of diagnosed vs. missed, 65.2 vs. 65.6, p = 0.2	194	NOT STAGE SPECIFIC	AAD	Dx Error
Ois, 2019[138]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male of misdiagnosis vs. no misdiagnosis, 38.8% vs. 33.7%, p = 2.15	400	NOT STAGE SPECIFIC	Stroke	Dx Error
Ois, 2019[138]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Current smoking	No effect - wide CI	% current smoking among misdiagnosis vs. no misdiagnosis, 39.4% vs. 33.1%, p = 0.245	400	NOT STAGE SPECIFIC	Stroke	Dx Error
Ois, 2019[138]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	For both the Hunt and Hess scale and the Fisher scale, higher scores were associated with fewer misdiagnoses p < 0.001	400	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Ois, 2019[138]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age of misdiagnosis vs. no misdiagnosis, 54.68 vs. 56.52, p = 0.282	400	NOT STAGE SPECIFIC	Stroke	Dx Error
Oliver, 2019[143]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Reported but not quantified	Diagnostic agreement by category, %: anterior segment, 70.2%; posterior segment, 57.6%; orbit & ocular adnexa, 80.3%; neurologic, 57.7%; uveitis, 92%; glaucoma, 73.7%	697	NOT STAGE SPECIFIC	Other (specify) : ophthalmology consults	Dx Error
Osterwalder, 2020[14]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Hospitalization at index visit	DecrRisk - Significant	0 of 170 hospitalized vs 27 of 310 discharged with outpatient treatment were misdiagnosed at index visit.	480	NOT STAGE SPECIFIC	Other (specify) : abdominal pain	Dx Error
Pacheco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	door to device over 90 minutes (younger than 75 vs. 75+): p<0.01 first medical contact to device over 90 minutes (younger than 75 vs. 75+): p<0.01	179	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Pacheco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - Significant	door to device over 90 minutes (male vs. female (female is more at risk)): p<0.01 first medical contact to device over 90 minutes (male vs. female (female is more at risk)): p=0.02	170	NOT STAGE SPECIFIC	MI	Dx Error
Pacheco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	door to device over 90 minutes (younger than 75 vs. 75+): p<0.01 first medical contact to device over 90 minutes (younger than 75 vs. 75+): p<0.01	179	NOT STAGE SPECIFIC	MI	Dx Error
Pacheco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - Significant	door to device over 90 minutes (male vs. female (female is more at risk)): p<0.01 first medical contact to device over 90 minutes (male vs. female (female is more at risk)): p=0.02	170	NOT STAGE SPECIFIC	MI	Dx Error
Pare, 2016[62]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	1) median time to diagnosis, 80 minutes for FOCUS group, 226 minutes for non-FOCUS group 2) Missed dissection 0% in FOCUS group, 43.8% in non-FOCUS group	32	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Off hours	IncrRisk - Significant	Median door-to-balloon time for nighttime vs. daytime presentation, 132 vs. 112 p < 0.05, and for weekend vs. weekday presentation, 133 vs. 122 p < 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - wide CI	Median door-to-balloon time for age >=65 to age < 65 years, 132 vs. 122, p > 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Health insurance	No effect - wide CI	Median door-to-balloon time for uninsured vs. not, 131 vs. 123 p > 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Language	IncrRisk - Significant	Median door-to-balloon time for English-speaking vs. not, 134 vs. 118, p < 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Mode of arrival	No effect - wide CI	Median door-to-balloon time for arrived by ambulance vs. not, 119 vs. 130 p > 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Median door-to-balloon time for left ventricular ejection fraction < 0.05 vs. not, 142 vs. 123 p > 0.05; and for cardiogenic shock vs. not, 183 vs. 128 p < 005	184	NOT STAGE SPECIFIC	MI	Dx Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	No effect - wide CI	Median door-to-balloon time for male sex vs. female sex, 122 vs. 130, p > 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Tobacco use	No effect - wide CI	Median door-to-balloon time for those with vs. without a family history of coronary artery disease, 122 vs. 126 p > 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Parikh, 2008[89]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Cocaine positive on admission	No effect - wide CI	Median door-to-balloon time for cocaine positive vs. negative on admission, 139 vs. 124 p > 0.05	184	NOT STAGE SPECIFIC	MI	Dx Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Smoking	No effect - narrow CI	Among correct diagnosis vs. misdiagnosis, % current smoking, 24.0% vs. 18.0% p = 0.105; % previous smoking, 44% vs. 42% p = 0.641	1015	NOT STAGE SPECIFIC	Stroke	Dx Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Alcohol use	Mixed (specify)	Among correct diagnosis vs. misdiagnosis, % heavy alcohol use, 13.3% vs. 17.3% p = 0.187; % acute alcohol use, 6.2% vs. 10.7% p = 0.048	1015	NOT STAGE SPECIFIC	Stroke	Dx Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - narrow CI	% male among correct diagnosis vs. misdiagnosis, 56.6% vs. 52.0%, p = 0.290	1015	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	Among correct diagnosis vs. misdiagnosis, % with facial paresis, 47.9% vs. 30.7%; % with unilateral weakness 68.3% vs. 50.7%; speech disturbance 76.3% vs. 64.0%	1015	NOT STAGE SPECIFIC	Stroke	Dx Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	NIHSS score on admission (ref 0-8), aOR for 9-15, 0.35 (95% CI, 0.16 to 0.76); aOR for >15, 0.30 (95% CI 0.09 to 1.05); Also, % with GCS score on admission < 15 were higher among correct diagnosis than misdiagnosis.	1015	NOT STAGE SPECIFIC	Stroke	Dx Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	No effect - narrow CI	Admission doctor resident among correct diagnosis vs. misdiagnosis, 42.1% vs. 46.7% p = 0.295	1015	NOT STAGE SPECIFIC	Stroke	Dx Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	No effect - narrow CI	% office hours among correct diagnosis vs. misdiagnosis, 34.6% vs. 38.0% p = 0.416	1015	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Pihlasviita, 2018[164]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	Age	DecrRisk - Significant	aOR for misdiagnosis (ref <60 y): 60-80 y, 0.57 (95% CI, 0.38 to 0.87); >80 y, 0.55 (95% CI, 0.31 to 0.95)	1015	NOT STAGE SPECIFIC	Stroke	Dx Error
Piper, 2008[88]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Perforation	No effect - wide CI	The time interval from presentation in the emergency room to surgery did not differ significantly for patients with or without perforation or for patients who had preoperative imaging versus those who did not.	134	Patient interval	Appendicitis	Dx Error
Piper, 2008[88]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR
Pirozzi, 2014[19]	Study design: Randomized controlled trial Look back or look forward analysis: Both Data source: Prospective data collection Numerator: Numerator and denominator	Tests ordered	DecrRisk - Significant	Frequency of incorrect initial diagnosis POC-US used: 5% (4 out of 88) POC-US not used: 50% (40 out of 80) (Fisher's test p < 0.0001).	168	ED Dx Process	Other (specify) : undifferentiated dyspnea	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Podolnick, 2017[183]	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - not sig	White No DDI (N = 178), N (%) 97 (54.5) DDI (N = 18), (N = 196), N (%)11 (61.1) Total (N = 196), N (%)108 (55.1) 0.9163 African-American No DDI (N = 178), 49 (27.5) DDI (N = 18), N (%) 6 (33.3) Total (N = 196), N (%) 55 (28.1) Asian/Pacific Islander No	NR	NOT STAGE SPECIFIC	NR	NR
Podolnick, 2017[183]	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	No DDI Age, months N 178 Mean 121.12 SD 55.35 Median 127 Range1–225 DDI Age, months N 18 Mean 132.22 SD 62.27 Median 159 Range 30–199 P 0.3952	178	NOT STAGE SPECIFIC	NR	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Postma, 2012[4]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Symptom type	Reported but not quantified	No. of injuries Mean no. of injuries (range, median) in hospitalized patients (N=66, 8 with DDI, 58 w/o DDI) Hospitalized Pt with DDI: 5.6 (1–12, 5) Hospitalized Pt without DDI: 2.2 (0–11, 1.5) % of patients with >5 injuries Hospitalized Pt with DDI:	126	NOT STAGE SPECIFIC	Other (specify) : Delayed diagnosis of injury after a plane crash	Either/Both
Postma, 2012[4]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Other (specify) Numerator: Numerator and denominator	Triage intake severity	Reported but not quantified	Mean ISS (range, median); N=66, 8 with DDI, 58 w/o DDI Hospitalized Pt with DDI: 19.5(4-57; 11) Hospitalized Pt without DDI: 8.6(1-34, 5) # with Head injury (AIC=>2) Hospitalized Pt with DDI: 3 (of 8) Hospitalized Pt without DDI: 13 (of 58)	NR	NR	Other (specify) : Delayed diagnosis of injury after a plane crash	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Race	No effect - wide CI	% white for TIA vs. NI-TNA, 52.5% vs. 36.7%, p = 0.150	100	NOT STAGE SPECIFIC	Stroke	Dx Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom onset	IncrRisk - Significant	gradual symptom onset aOR, 6.7, p = 0.002	100	NOT STAGE SPECIFIC	Stroke	Dx Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	No effect - wide CI	% male for TIA vs. NI-TNA, 52.5% vs. 31.7%, p = 0.06	100	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Increased/significant: Nonspecific symptoms (: aOR 4.2, p 0.008 *nonspecific symptoms included non-rotary lightheadedness, pain such as throat tightness or chest pain, gastrointestinal symptoms, or 'ill feeling', or vague cognitive symptoms No effect- wi	NR	NR	Stroke	Dx Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	% in TIA vs NI-TNA: Nonsignificant difference for magnetic resonance imaging, Significant difference for neurovascular imaging (inc), echocardiography(inc), and electroencephalography(dec)	100	NOT STAGE SPECIFIC	Stroke	Dx Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Triage intake severity	No effect - wide CI	ABCD2 > 3 for TIA vs. NI-TNA, 55% vs. 55%, p = 1.0	100	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom duration, time from symptom onset to ED arrival	No effect - wide CI	NR	100	NOT STAGE SPECIFIC	Stroke	Dx Error
Prabhakaran, 2008[86]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age for TIA vs. NI-TNA, 63.0 vs. 59.5, p = 0.298	100	NOT STAGE SPECIFIC	Stroke	Dx Error
Rapezzi, 2008[85]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Range in OR, 0.078 to 3.96	161	NOT STAGE SPECIFIC	AAD	Dx Error
Rapezzi, 2008[85]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Atypical presentation	No effect - wide CI	OR for >=1 'characteristic' finding vs. not, 1.24 (95% CI, 0.48 to 3.18)	161	NOT STAGE SPECIFIC	AAD	Dx Error
Rapezzi, 2008[85]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	IncrRisk - Significant	OR for age <70 years vs. >=70 years, 2.34 (95% CI, 1.03 to 5.36)	161	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rapezzi, 2008[85]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	No effect - wide CI	OR for males vs. females, 1.83 (95% CI, 0.80 to 4.20)	161	NOT STAGE SPECIFIC	AAD	Dx Error
Raposo, 2018[159]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	No effect - wide CI	% female among evaluation initiated with 12 h vs. beyond 12 h, 47.3% vs. 52.9%, p = 0.29	354	NOT STAGE SPECIFIC	Stroke	Dx Error
Raposo, 2018[159]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age among evaluation initiated with 12 h vs. beyond 12 h, 60.1 vs. 62.5, p = 0.28	354	NOT STAGE SPECIFIC	Stroke	Dx Error
Raposo, 2018[159]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Tests ordered	No effect - wide CI	% with MRI performed among evaluation initiated with 12 h vs. beyond 12 h, 79.1% vs. 77.1%, p = 0.65; % with cervical & intracranial vessel imaging, 87.6% vs. 85.0%, p = 0.48	354	NOT STAGE SPECIFIC	Stroke	Dx Error
Raposo, 2018[159]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	% with ABCD>=4 among evaluation initiated with 12 h vs. beyond 12 h, 43.3% vs. 31.4%	354	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Raposo, 2018[159]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Mode of arrival	DecrRisk - Significant	Among evaluation initiated with 12 h vs. beyond 12 h, % referred from office-based physician, 36.3% vs. 72.2%; % referred from emergency medical services, 63.7% vs. 26.8%, p < 0.0001	354	NOT STAGE SPECIFIC	Stroke	Dx Error
Ravichandiran, 2010[76]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - Significant	Male vs female gender OR: 2.00 95% CI: 1.03–3.80	258	NOT STAGE SPECIFIC	Fractures	Either/Both
Ravichandiran, 2010[76]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Setting	IncrRisk - not sig	Setting Primary care office vs pediatric ED OR: 5.20 95% CI 1.77–15.39 General ED vs pediatric ED OR:7.20 95% CI: 3.00–17.30	NR	NOT STAGE SPECIFIC	Fractures	Either/Both
Ravichandiran, 2010[76]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Extremity versus axial skeleton fracture	IncrRisk - Significant	Extremity vs axial skeleton fracture OR :2.30 95% CI: 1.10–4.77	258	NOT STAGE SPECIFIC	Fractures	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Richoz, 2015	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - narrow CI	younger people 0.97 (0.97-0.99)	2200	NOT STAGE SPECIFIC	Stroke	Dx Error
Richoz, 2015	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Atypical presentation	DecrRisk - Significant	Eye deviation (0.17 - 0.04,0.71) Paresis (0.5 - 0.27,0.91) Sensory deficit (0.52 - 0.28,0.97) bilateral stroke (3.19 - 1.6, 6.37) delay stroke onset to ED arrival (0.99 - 0.95,1.04)	2200	NOT STAGE SPECIFIC	Stroke	Dx Error
Richoz, 2015	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	TOAST mechanism	DecrRisk - not sig	atherosclerotic 0.45 (0.14-1.47) cardiac 1.85 (1.02-3.34) lacunar 0.42 (0.13-1.35)	2200	NOT STAGE SPECIFIC	Stroke	Dx Error
Richoz, 2015	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	DecrRisk - not sig	Male 0.66 (0.36-1.21)	2200	NOT STAGE SPECIFIC	Stroke	Dx Error
Richoz, 2015	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Triage intake severity	No effect - narrow CI	NIH Stroke Scale low 0.97 (0.93 - 1.02) Prestroke Rankin Scale low 1.09 (0.83 - 1.44)	2200	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rønning, 2005[106]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Unclear or NR Numerator: Numerator and denominator	Sex	IncrRisk - not sig	Among those who did not have stroke, 47/88 (53%) were women	88	NOT STAGE SPECIFIC	Stroke	Dx Error
Rønning, 2005[106]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Unclear or NR Numerator: Numerator and denominator	Mode of arrival	No effect - wide CI	% that did not have stroke among those admitted via the Emergency Medical Communication Center (AMK) vs. referred by doctor or ED, 24% vs. 25%	354	NOT STAGE SPECIFIC	Stroke	Dx Error
Rønning, 2005[106]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Unclear or NR Numerator: Numerator and denominator	Age	IncrRisk - not sig	Average age among those with stroke vs. without stroke, 71.5 vs. 65.5 years	354	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	IncrRisk - Significant	B coefficients (positive numbers indicate longer delay times) for female vs. male, 0.06, $p < 0.001$	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Health insurance	No effect - narrow CI	Median CT delay in hours for Medicare patients, patients with no insurance, and patients with other insurance, 1.2, 1.1, 1.2	15117	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Mode of arrival	DecrRisk - Significant	B coefficients (positive numbers indicate longer delay times) for EMS arrival vs. other mode, -0.36, p < 0.0001	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - narrow CI	Median CT delay in hours for patients aged 18-44, 45-64, 65-74, and 75+, 1.2, 1.2, 1.2, and 1.2	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Race	Mixed (specify)	B coefficients (positive numbers indicate longer delay times) for Black vs. White, 0.09, p < 0.0001 and for Other vs. White, -0.01, p > 0.05	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Teaching status	Mixed (specify)	B coefficients (positive numbers indicate longer delay times) for JCPSC teaching, JCPSC nonteaching, not JCPSC teaching (ref = not JCPSC not teaching), 0.12 p < 0.0001, -0.02 p > 0.05, 0.21 p < 0.001	15117	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	No effect - narrow CI	Median delay in CT imaging in hours for ambulation at admission vs. not, 1.2 vs. 1.2	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Off hours	Mixed (specify)	B coefficients (positive numbers indicate longer delay times) for time of day of arrival: evening vs. daytime -0.09 p > 0.05; late night vs. daytime, -0.18 p < 0.0001; weekend vs. weekday -0.07 p < 0.0001	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Arrival at hospital within 2 hours of symptom onset	IncrRisk - Significant	% Receiving a CT scan within 25 minutes of hospital arrival among patients arriving at hospital within 2 hours of symptom onset vs. >2 hours of symptom onset vs. unknown symptom onset time, 23.6%, 8.8% vs. 6.7%	15117	NOT STAGE SPECIFIC	Stroke	Dx Error
Rose, 2008[87]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Presumptive diagnosis at arrival	Mixed (specify)	B coefficients (positive numbers indicate longer delay times) for IS, HS, and TIA (ref = stroke not specified), -0.01 p > 0.05, -0.13 p < 0.0001, and 0.21 p < 0.0001	15117	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	OR 1.04 (1.02,1.06)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	IncrRisk - not sig	Hispanic reference Not hispanic OR 2.01 (0.96,4.21) Other OR 1.62 (0.64,4.11)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	IncrRisk - not sig	self pay (reference) medicaid OR 2.78 (0.96 - 8.09) private OR 2.12 (0.75,5.98) medicare OR 2.14 (0.78-5.92) other OR 2.43 (0.6,9.96)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	hospital 1 vs. hospital 2	No effect - wide CI	Index hospital 1 (reference: Hospital 2) 0.98 (0.72, 1.34)	NR	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Previous hospitalizations	IncrRisk - not sig	Number of ED visits in the preceding year 1.06 (0.99, 1.14) Number of hospitalizations in the preceding year 1.08 (0.97, 1.21)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - Significant	white (ref) black OR 1.8 (1.29, 2.52) other OR 1.19(0.8,1.77)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	male (ref: female) OR: 1.31 (1, 1.71)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	Group 1: No CT, no symptoms reference Group 2: No CT, symptoms OR: 0.61 (0.22,1.67) Group 3: CT, no symptoms OR: 1.56 (1.16, 2.09) Group 4: CT, symptoms OR: 3.3 (1.61, 6.76)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	Group 1: No CT, no symptoms reference Group 2: No CT, symptoms OR: 0.61 (0.22,1.67) Group 3: CT, no symptoms OR: 1.56 (1.16, 2.09) Group 4: CT, symptoms OR: 3.3 (1.61, 6.76)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	OR 1.04 (1.02,1.06)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	IncrRisk - not sig	Hispanic reference Not hispanic OR 2.01 (0.96,4.21) Other OR 1.62 (0.64,4.11)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	IncrRisk - not sig	self pay (reference) medicaid OR 2.78 (0.96 - 8.09) private OR 2.12 (0.75,5.98) medicare OR 2.14 (0.78-5.92) other OR 2.43 (0.6,9.96)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	hospital 1 vs. hospital 2	No effect - wide CI	Index hospital 1 (reference: Hospital 2) 0.98 (0.72, 1.34)	NR	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Previous hospitalizations	IncrRisk - not sig	Number of ED visits in the preceding year 1.06 (0.99, 1.14) Number of hospitalizations in the preceding year 1.08 (0.97, 1.21)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	IncrRisk - Significant	white (ref) black OR 1.8 (1.29, 2.52) other OR 1.19(0.8,1.77)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	male (ref: female) OR: 1.31 (1, 1.71)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	Group 1: No CT, no symptoms reference Group 2: No CT, symptoms OR: 0.61 (0.22,1.67) Group 3: CT, no symptoms OR: 1.56 (1.16, 2.09) Group 4: CT, symptoms OR: 3.3 (1.61, 6.76)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Rosenman, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	IncrRisk - Significant	Group 1: No CT, no symptoms reference Group 2: No CT, symptoms OR: 0.61 (0.22,1.67) Group 3: CT, no symptoms OR: 1.56 (1.16, 2.09) Group 4: CT, symptoms OR: 3.3 (1.61, 6.76)	35622	NOT STAGE SPECIFIC	Stroke	MisDx Harm
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age of nurse	No effect - wide CI	OR 0 .95 p > 0.05 for delay of electrocardiogram	283	NOT STAGE SPECIFIC	MI	Dx Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Years of ED experience for nurse	No effect - wide CI	OR = 0.77 p > 0.05 for delay of electrocardiogram	283	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	Mixed (specify)	For Caucasian vs. non-Caucasian, B = 0.24 p < 0.05 for length of delay in triage; OR = 2.12 p > 0.05 for delay of electrocardiogram	283	NOT STAGE SPECIFIC	MI	Dx Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Mixed (specify)	B = 0.25 p < 0.05 for length of delay in triage; OR = 1.42 p > 0.05 for delay of electrocardiogram	283	NOT STAGE SPECIFIC	MI	Dx Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	X2(1) = 7.56 p = 0.006; more delay in No chest pain	283	NOT STAGE SPECIFIC	MI	Dx Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	No effect - wide CI	B for triage level 2 vs. triage level 3, 0.09, p > 0.05	283	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	B = -0.00, p > 0.05 for length of delay in triage; OR = 0.98 p > 0.05 for delay of electrocardiogram	283	NOT STAGE SPECIFIC	MI	Dx Error
Sanders, 2017[174]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	IncrRisk - Significant	Years of experience for nurse, B = 0.03 p < 0.001 for length of delay in triage; OR = 1.10 p = 0.038 for delay of electrocardiogram	238	NOT STAGE SPECIFIC	MI	Dx Error
Sarraj, 2015[41]	Study design: Cross-sectional Look back or look forward analysis: Data source: Electronic health record data Numerator: Unclear or NR	Symptom type	Mixed (specify)	NR	252	NOT STAGE SPECIFIC	Stroke	Dx Error
Sarraj, 2015[41]	Study design: Cross-sectional Look back or look forward analysis: Data source: Electronic health record data Numerator: Unclear or NR	Mode of arrival	Reported but not quantified	NR	252	NOT STAGE SPECIFIC	Stroke	Dx Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	Reported but not quantified	Concordant diagnosis group vs. discordant diagnosis group: % white 53% vs. 55%; % black 38% vs. 34%	429	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Reported but not quantified	38% and 37% of the concordant and discordant diagnosis groups were male.	429	NOT STAGE SPECIFIC	Stroke	Dx Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	OR, 0.53	429	NOT STAGE SPECIFIC	Stroke	Dx Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	IncrRisk - not sig	OR, 1.20	436	NOT STAGE SPECIFIC	Stroke	Dx Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	Concordant diagnosis group vs. discordant diagnosis group: % Hispanic 6% vs. 10%	429	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	Reported but not quantified	Median age is 60 in the concordant diagnosis group and 57 in the discordant diagnosis group.	429	NOT STAGE SPECIFIC	Stroke	Dx Error
Schrock, 2012[53]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Atypical presentation	Mixed (specify)	Range in OR, 0.54 to 3.19	429	NOT STAGE SPECIFIC	Stroke	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	DecrRisk - Significant	Range in aOR for age groups (ref = age 20-49), 0.53 to 0.75	19,663	NOT STAGE SPECIFIC	MI	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	Among those with AMI not missed vs. missed, % with resuscitation/emergent triage acuity is 57.1% vs. 31.7% and % with less urgent/nonurgent triage acuity is 4.3% vs. 13.9%	19663	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Off hours	Mixed (specify)	aOR for weekday vs. weekend, 1.26 (95% CI 1.01 to 1.58); range in aOR evening and night vs. daytime, 0.76 to 1.01 p > 0.05	19663	NOT STAGE SPECIFIC	MI	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	SES/Income	No effect - narrow CI	Range in aOR by income quintile (ref = highest income quintile), 0.95 to 1.31	19663	NOT STAGE SPECIFIC	MI	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Teaching status	No effect - wide CI	aOR, 0.91	19663	NOT STAGE SPECIFIC	MI	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Symptom type	Mixed (specify)	aOR for diabetes and congestive heart failure is 0.37 and 0.67. Shock, cancer, stroke, pulmonary edema, acute renal failure, chronic renal failure, and dysrhythmia were not significant, range in aOR, 0.84 to 1.43	19663	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	No effect - narrow CI	aOR (female = reference), 1.08	19663	NOT STAGE SPECIFIC	MI	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	ED AMI volume	Mixed (specify)	Very low and low ED AMI volume had an IncrRisk of missed AMI, range in aOR (ref = very high), 1.57 to 1.96; there was no statistically significant difference for medium and high, range in aOR, 1.20 to 1.33		NOT STAGE SPECIFIC	MI	Dx Error
Schull, 2006[97]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Visits to the same ED in previous year, per visit	No effect - narrow CI	aOR, 105	19663	NOT STAGE SPECIFIC	MI	Dx Error
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Community vs. tertiary sites	IncrRisk - Significant	Among patients in the sepsis-ICU group, the relative risk of missed diagnosis in community sites was 4.30 (2.15-8.60) compared with the tertiary site. In patients in the sepsis-VV group, the relative risk of a missed diagnosis in community sites was 14.0	NR	NOT STAGE SPECIFIC	Sepsis	Dx Error
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Triage intake severity	Reported but not quantified	NR	NR	NR	NR	NR
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	Reported but not quantified	NR	NR	NR	NR	NR
Scott, 2018[171]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Atypical presentation	Reported but not quantified	NR	1094	NR	NR	NR
Sederholm Lawesson, 2018[167]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: electronic health records and patient interviews Numerator: Numerator and denominator	Sex	No effect - wide CI	Median (IQR) time from first medical contact to diagnostic ECG among men vs. women, 25 (15-49) vs. 33 (15-61) p = 0.09	449	NOT STAGE SPECIFIC	MI	Dx Error
Sederholm Lawesson, 2018[167]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: electronic health records and patient interviews Numerator: Numerator and denominator	Age	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Settelmeier, 2020[118]	Study design: Registry Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator only (error/harm)	Sex	Mixed (specify)	OR 95% CI Age >75, % 1.70 (1.58–1.83) Smoking 0.51 (0.47–0.55) AHT 1.07 (0.99–1.16) Diabetes mellitus 0.85 (0.78–0.92) Hyperlipidemia 0.75 (0.70–0.81) BMI n.a CKD 0.72 (0.63–0.82) COPD 0.92 (0.77–1.11) OR, odds ratio; CI, ACS; RF, risk	NR	NR	MI	NR
Settelmeier, 2020[118]	Study design: Registry Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator only (error/harm)	Age	IncrRisk - Significant	Age >75 years OR: 1.70 (1.58–1.83) 95% CI Females vs males	NR	NR	MI	NR
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	SES/Income	Mixed (specify)	% median income < $45k among not missed vs. missed AMI in the look-back analysis, 24.4% vs. 27.7%; % median income < $45k among no AMI vs. missed AMI in the look-forward analysis, 26.9% vs. 27.6%	NR	NOT STAGE SPECIFIC	MI	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Education	Mixed (specify)	% with at least some college among not missed vs. missed AMI in the look-back analysis,18.6% vs. 17.5%; % with at least some college among no AMI vs. missed AMI in the look-forward analysis, 19.0% vs. 17.7%	NR	NOT STAGE SPECIFIC	MI	Either/Both
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Married or partnered	Mixed (specify)	% married or partnered among not missed vs. missed AMI in the look-back analysis, 57% vs. 53.7%; % married or partnered among no AMI vs. missed AMI in the look-forward analysis, 47.5% vs. 55.5%	NR	NOT STAGE SPECIFIC	MI	Either/Both
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Race	Mixed (specify)	% Black among not missed vs. missed AMI in the look-back analysis, 11.5% vs. 14.5%, OR 1.3, 95% CI, 1.1 to 1.6, p=0.0077 vs. whites; % black among no AMI vs. missed AMI in the look-forward analysis, 13.4% vs. 12.6%	NR	NOT STAGE SPECIFIC	MI	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Smoking	IncrRisk - Significant	% active smoking among not missed vs. missed AMI in the look-back analysis, 12.1% vs. 11.5%; % active smoking among no AMI vs. missed AMI in the look-forward analysis, 8.3% vs. 12.4%	NR	NOT STAGE SPECIFIC	MI	Either/Both
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Mixed (specify)	% female among not missed vs. missed AMI in the look-back analysis, 36.6% vs. 43.4%, OR 1.3, 95% CI, 1.2 to 1.5, p<0.001; % female among no AMI vs. missed AMI in the look-forward analysis, 57.2% vs. 40.6%	NR	NOT STAGE SPECIFIC	MI	Either/Both
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Mean age of not missed vs. missed AMI in the look-back analysis, 67.9 vs. 68.9; Mean age of no AMI vs. missed AMI in the look-forward analysis, 48.9 vs. 68.7, one-year increase associated with OR 1.0 95% CI, 1.0 to 1.0, p<0.0001	NR	NOT STAGE SPECIFIC	MI	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	Mixed (specify)	% Hispanic among not missed vs. missed AMI in the look-back analysis, 24.5% vs. 24.7%; % Hispanic no AMI vs. missed AMI in the look-forward analysis, 37.0% vs. 25.4% (possibly significant vs. whites)	NR	NOT STAGE SPECIFIC	MI	Either/Both
Sharp, 2020[120]	Study design: Retrospective cohort Look back or look forward analysis: Both Data source: Electronic health record data Numerator: Numerator and denominator	Language	No effect - narrow CI	% needs an interpreter among not missed vs. missed AMI in the look-back analysis, 7.5% vs. 7.5%; % needs an interpreter among no AMI vs. missed AMI in the look-forward analysis, 7.5% vs. 7.5%	NR	NOT STAGE SPECIFIC	MI	Either/Both
Shokoohi, 2020	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	difficult intravenous access	IncrRisk - Significant	If DIVA: +50 min for pain medication adminstration +36 min for intravenous fluid administration +29 min for laboratory results +57 min for intravenous contrast administration +87 min for discharge orders	108256	NOT STAGE SPECIFIC	Other (specify) : all	MisDx Harm

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Shokoohi, 2020	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator and denominator	difficult intravenous access	IncrRisk - Significant	If DIVA: +50 min for pain medication adminstration +36 min for intravenous fluid administration +29 min for laboratory results +57 min for intravenous contrast administration +87 min for discharge orders	108256	NOT STAGE SPECIFIC	Other (specify) : all	MisDx Harm
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Provider type/role	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	SES/Income	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	14.7% misdiagnosis with SBP < 90mmHg; 40.8% misdiagnosed with SBP > 90 mmHg	261	Unclear or NR	AAD	Dx Error
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	43.3% of women misdiagnosed vs 29.9% of men	261	ED Dx Process	AAD	Dx Error
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - Significant	56.6% misdiagnosed by an internist; 25.7% by surgeon	261	ED Dx Process	AAD	Dx Error
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Language	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health insurance	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Disciplinary action	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Health literacy	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Provider fatigue	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Clinical experience	NR	NR	NR	NR	NR	NR
Smidfelt, 2017[180]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Ethnicity	NR	NR	NR	NR	NR	NR
Smidfelt, 2020[122]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% female among misdiagnosis vs. correct diagnosis, 30.5% vs. 28.4%	455	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Smidfelt, 2020[122]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	DecrRisk - Significant	% whose rAAA diagnosis was verified with a CT scan among misdiagnosis vs. correct diagnosis, 67.2% vs. 82.4% p < 0.0001	455	ED Dx Process	AAD	Dx Error
Smidfelt, 2020[122]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	Mean serum creatinine (mmol) at admission among misdiagnosis vs. correct diagnosis, 123 vs. 133, p = 0.03; % with first recorded systolic blood pressure <=90 mmHg, 22.8% vs. 37.7%, p < 0.0001	455	NOT STAGE SPECIFIC	AAD	Dx Error
Smidfelt, 2020[122]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age of misdiagnosis vs. correct diagnosis, 79.5 vs. 79.1, p = 0.66	455	NOT STAGE SPECIFIC	AAD	Dx Error
Smith, 2012[50]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	OR for male vs. female, 0.96 (95% CI, 0.58 to 1.60)	400	NOT STAGE SPECIFIC	VTE	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Smith, 2012[50]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	OR for age > 65 years vs. age <=65 years, 1.38 (95% CI, 1.09 to 1.75) from multivariate analysis	400	NOT STAGE SPECIFIC	VTE	Dx Error
Snoek, 2013[2]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Revised Trauma Score (RTS) OR 0.68 (0.55-0.84), P-value <0.001		NOT STAGE SPECIFIC	Other (specify) : delayed diagnosed injury of trauma patient (including fracture, myocardial contusion, pneumothorax, intracerebral bleed, renal contusion)	Either/Both
Snoek, 2013[2]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Number of injuries	IncrRisk - Significant	Number of injuries OR for delayed dx pts 1.63 (CI 1.31-2.02), p-value <0.001		NOT STAGE SPECIFIC	Other (specify) : delayed diagnosed injury of trauma patient (including fracture, myocardial contusion, pneumothorax, intracerebral bleed, renal contusion)	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Snoek, 2013[2]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	GCS, ISS, ISS/10	Mixed (specify)	GCS OR (for delayed diagnosis pts): 0.78 (0.69-0.88),P-values <0.001 ISS OR (for delayed diagnosis pts): 1.11 (1.07-1.15),P-values <0.001 ISS/10 OR (for delayed diagnosis pts): 2.82 (1.94-4.08),P-values <0.001	NR	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosed injury of trauma patient (including fracture, myocardial contusion, pneumothorax, intracerebral bleed, renal contusion)	Either/Both
Snoek, 2013[2]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	IncrRisk - not sig	No difference by %Male: delayed diagnosis 76.9%, non-delayed diagnosis 60.4%, p =0.228 p-value	475	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosed injury of trauma patient (including fracture, myocardial contusion, pneumothorax, intracerebral bleed, renal contusion)	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Snoek, 2013[2]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - not sig	Diagnostic Delay Mean Age 47.7 (CI 20), Non-Diagnostic Delay: 40.8 (17.9), P-value: 0.202	475	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosed injury of trauma patient (including fracture, myocardial contusion, pneumothorax, intracerebral bleed, renal contusion)	Either/Both
Snoek, 2013[2]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	IncrRisk - Significant	Mobile Medical Team OR for delayed dx pt 6.82 (CI 1.36-34.18), p-value 0.020	475	Pre-hospital interval	Other (specify) : delayed diagnosed injury of trauma patient (including fracture, myocardial contusion, pneumothorax, intracerebral bleed, renal contusion)	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Soundappan, 2004[109]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Reported but not quantified	Sex (male(Missed Injuries, n=12 (%) 8 (66) Patients without Missed Injuries, n =64 (%) 42 (65)	76	NOT STAGE SPECIFIC	Other (specify) : Missed injuries in pediatric trauma patients after primary and secondary survey	Either/Both
Soundappan, 2004[109]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Reported but not quantified	Of 12 patients that had missed injuries, it was presumed that 'head injury' was a contributing factor for delayed diagnosis	NR	NR	Other (specify) : Missed injuries in pediatric trauma patients after primary and secondary survey	Either/Both
Soundappan, 2004[109]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	Reported but not quantified	Mean ISS (n=12) of patients with missed injuries: 15 Mean ISS (n=64) of patients w/o missed injuries: 14	NR	NR	Other (specify) : Missed injuries in pediatric trauma patients after primary and secondary survey	Either/Both
Soundappan, 2004[109]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Language	Reported but not quantified	1 of 12 patients that experienced a diagnostic delay was related to a language barrier	NR	NR	Other (specify) : Missed injuries in pediatric trauma patients after primary and secondary survey	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Soundappan, 2004[109]	Study design: Prospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	Reported but not quantified	Age (mean) Missed Injuries, n 12 (%) 8.6 Patients without Missed Injuries, n 64 (%) 8.4	76	NOT STAGE SPECIFIC	Other (specify) : Missed injuries in pediatric trauma patients after primary and secondary survey	Either/Both
Staab, 2020	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Data from a QI project Numerator: Numerator and denominator	Age	No effect - wide CI	NR	NR	NR	NR	NR
Staab, 2020	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Data from a QI project Numerator: Numerator and denominator	White blood cell count >10 ^3 10^3 /Î¼L	DecrRisk - Significant	p=0.01	192	ED Dx Process	Appendicitis	Either/Both
Staab, 2020	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Data from a QI project Numerator: Numerator and denominator	Reporting less RLQ pain	IncrRisk - Significant	p<0.001	181	ED Dx Process	Appendicitis	Either/Both
Staab, 2020	Study design: case control Look back or look forward analysis: Not a cohort study Data source: Data from a QI project Numerator: Numerator and denominator	Sex	No effect - wide CI	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sun, 2007[8]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	IncrRisk - not sig	Male AOR: 1.8 95% ACS: 0.9-3.3	477	NOT STAGE SPECIFIC	Other (specify) : Serious event after syncope discharge from ED	Either/Both
Sun, 2007[8]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Race	DecrRisk - not sig	Nonwhite AOR 0.7 95% ACS: 0.3–1.4	477	NOT STAGE SPECIFIC	Other (specify) : Serious event after syncope discharge from ED	Either/Both
Sun, 2007[8]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Ethnicity	DecrRisk - not sig	Hispanic AOR 0.8 95% ACS: 0.3–2.6	477	NOT STAGE SPECIFIC	Other (specify) : Serious event after syncope discharge from ED	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Sun, 2007[8]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	Mixed (specify)	Table 3. Multivariate Logistic Regression Model for 14-Day Serious Events Age 40–59 : OR 2.7 CI 0.9–8.4 60–79 : OR 3.8 CI 1.3–12.0 *SIGNIFICANT > 80: OR 3.8 CI 1.2–12.0 *SIGNFICANT AOR 95% ACS Reference group: 1	477	NOT STAGE SPECIFIC	Other (specify) : Serious event after syncope discharge from ED	Either/Both
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health literacy	NR	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	NR	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Language	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Patients who had blunt cerebrovascular injury	Reported but not quantified		40	ED Dx Process	Stroke	Unclear or NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	Reported but not quantified	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	SES/Income	NR	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	Reported but not quantified	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health literacy	NR	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Language	NR	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Patients who had blunt cerebrovascular injury	Reported but not quantified	NR	40	ED Dx Process	Stroke	Unclear or NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	Reported but not quantified	NR	NR	NR	NR	NR
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	SES/Income	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tien, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Torres-Macho, 2013[38]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Electrocardiogram	Mixed (specify)	Rnge in OR, 2.5 to 4.3 for group 2 and range in OR, 2.3 to 5 for group 3: dyspnea dec risk(S), less nonspecific and less severe symptoms like cough, or fever, pleuritic Chest pain, hemoptysis, pulmonary infiltrate on CXR: incRisk significant	436	NOT STAGE SPECIFIC	VTE	Dx Error
Torres-Macho, 2013[38]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Chest x-ray	Mixed (specify)	% with pulmonary infiltrate, 11% among those diagnosed in the ED, 24.4% among those diagnosed in the hospital, 34% among those diagnosed on readmission.	436	NOT STAGE SPECIFIC	VTE	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Torres-Macho, 2013[38]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male, 51.4% among those diagnosed in the ED, 49.4% among those diagnosed in the hospital, 38.4% among those diagnosed on readmission	436	NOT STAGE SPECIFIC	VTE	Dx Error
Torres-Macho, 2013[38]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	Mixed (specify)	NR	436	NOT STAGE SPECIFIC	VTE	Dx Error
Torres-Macho, 2013[38]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	raRnge in OR, 2.5 to 4.3 for group 2 and range in OR, 2.3 to 5 for group 3: dyspnea dec risk(S), less specific and less severe symptoms like cough, or fever, pleuritic Chest pain, hemoptysis, pulmonary infiltrate on CXR: IncrRisk-significant	436	ED Dx Process	VTE	Dx Error
Torres-Macho, 2013[38]	Study design: Retrospective cohort Look back or look forward analysis: Data source: Electronic health record data Numerator: Numerator and denominator	Age	Mixed (specify)	Mean age, 67.3 in group 1 (those diagnosed in the ED), 71.5 in group 2 (those diagnosed in the hospital), 61.4 in group 3 (those diagnosed on readmission)	436	NOT STAGE SPECIFIC	VTE	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tsivgoulis, 2011[55]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Stroke registry data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male for stroke mimics vs. confirmed AIS, 45% vs. 56%; p = 0.096	539	NOT STAGE SPECIFIC	Stroke	Dx Error
Tsivgoulis, 2011[55]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Stroke registry data Numerator: Numerator and denominator	Age	IncrRisk - Significant	Mean age for stroke mimics vs. confirmed AIS, 56 vs. 67; p > 0.001	539	NOT STAGE SPECIFIC	Stroke	Dx Error
Tsivgoulis, 2011[55]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Stroke registry data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Median admission NIHSS score in points for stroke mimics vs. confirmed AIS, 6 vs. 8; p < 0.001	539	NOT STAGE SPECIFIC	Stroke	Dx Error
Tsivgoulis, 2011[55]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Stroke registry data Numerator: Numerator and denominator	Current smoking	No effect - wide CI	% current smoking for stroke mimics vs. confirmed AIS, 32% vs. 33%; p = 0.858	539	NOT STAGE SPECIFIC	Stroke	Dx Error
Tudela, 2005[105]	Study design: Retrospective cohort Look back or look forward analysis: Unsure Data source: Electronic health record data Numerator: Numerator only (error/harm)	Symptom type	IncrRisk - Significant	Dx error in ED: consult for fever	42	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tzovaras, 2007[96]	Study design: Randomized controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	open or the laparoscopic appendectomy	Reported but not quantified	In the group of 38 male patients who were treated laparoscopically, the conversion rate was much higher, 18.5%, and the incidence of wrong diagnosis was only 5.2%. Overall, the incidence of wrong diagnosis in men was 3.8%.	78	NOT STAGE SPECIFIC	Appendicitis	Dx Error
Tzovaras, 2007[96]	Study design: Randomized controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	NR	NR
Tzovaras, 2007[96]	Study design: Randomized controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Tzovaras, 2007[96]	Study design: Randomized controlled trial Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	NR	NR
Uchino, 2010	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	IncrRisk - Significant	IncrRisk with increased age, p <0.001	254	NOT STAGE SPECIFIC	Stroke	Dx Error
Uchino, 2010	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	place where treatment was started	DecrRisk - not sig	it is less likely that the person was a TP if they started treatment at comm. hospital rather than uni. hospital p=0.039	NR	NOT STAGE SPECIFIC	Stroke	Dx Error
Uchino, 2010	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	time until treatment	IncrRisk - not sig	time to tpa treatment, median, min p=0.36	254	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Vaghani, 2021	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	documentation	IncrRisk - Significant	poor documentation led to higher risk p<0.001	217	NOT STAGE SPECIFIC	Stroke	Dx Error
Vaghani, 2021	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Provider type/role	No effect - wide CI	p=0.975	217	NOT STAGE SPECIFIC	Stroke	Dx Error
Vaghani, 2021	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	documentation	IncrRisk - Significant	poor documentation led to higher risk p<0.001	217	NOT STAGE SPECIFIC	Stroke	Dx Error
Vaghani, 2021	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Provider type/role	No effect - wide CI	p=0.975	217	NOT STAGE SPECIFIC	Stroke	Dx Error
Vagnarelli, 2016[206]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Unclear or NR	Tests ordered	IncrRisk - Significant	Troponin positivity (vs. negative Tn +Tn unavailable) 1.87 (1.07–3.26) 0.026	398	ED Dx Process	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Vagnarelli, 2016[206]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Unclear or NR	Symptom type	IncrRisk - Significant	Dyspnea 2.65 (1.48–4.74) Pulse deficit 0.51 (0.28–0.95) Back pain 0.48 (0.31–0.77) 0.002 Pleural effusion 2.01 (1.28–3.43) 0.003 Pericardial effusion 1.72 (1.07–2.77) 0.02	398	NOT STAGE SPECIFIC	AAD	Dx Error
Vagnarelli, 2016[206]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Unclear or NR	Triage intake severity	NR	NR	NR	NR	NR	NR
Vagnarelli, 2016[206]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Unclear or NR	Mode of arrival	NR	NR	NR	NR	NR	NR
Vagnarelli, 2016[206]	Study design: Registry Look back or look forward analysis: Look back method (disease denominator) Data source: Unclear or NR Numerator: Unclear or NR	Atypical presentation	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Vanbrabant, 2009[75]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Observed relative risk of return visit Initial symptom Diarrhea Observed relative risk of return 4.07 95% CI 1.94-8.16 Initial symptom Abdominal pain Observed relative risk of return 1.72 95% CI 1.20-2.43 Initial symptom Fever Observed relative risk		NOT STAGE SPECIFIC	Other (specify) : Return to ED w/in 72 of discharge	Either/Both
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Disciplinary action	NR	NR	NR	NR	NR	NR
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Clinical experience	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Provider fatigue	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Training background	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Disciplinary action	NR	NR	NR	NR	NR	NR
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Clinical experience	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Provider fatigue	NR	NR	NR	NR	NR	NR
Vargas-Blasco, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator only (error/harm)	Training background	Reported but not quantified	NR	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Vasconcelos-Castro, 2020[140]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Pain duration in hours	Reported but not quantified	Median, IQR Total N=73 5 3.0, 15.0 Abdominal pain n=16 22% 48 16.5, 72 Testicular pain (n = 57, 78%) 5 2, 6 Abdominal vs testicular pain (P value) <.001	NR	NOT STAGE SPECIFIC	Testicular torsion	Either/Both
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Language	NR	NR	NR	NR	NR	NR
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Current smoking history	No effect - wide CI	% current smokers among misdiagnosis and control, 17% vs. 24%, p = 0.092	312	NOT STAGE SPECIFIC	Stroke	Dx Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Sex	Reported but not quantified	NR	NR	NR	Stroke	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Among misdiagnosis vs. control, % with altered mental status, 41% vs. 26% p = 0.004; % with LOC reduced, 42% vs. 30% p = 0.025; % with dizziness, 25% vs. 5% p < 0.0001; % with hemiparesis, 23% vs. 70% p < 0.0001; % with syncope/collapse, 17% vs. 4% p = 0.	312	NOT STAGE SPECIFIC	Stroke	Dx Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	Among misdiagnosis vs. control, % who underwent MRI, 72% vs. 69%; median time to MRI, 66 h vs. 47 h	312	NOT STAGE SPECIFIC	Stroke	Dx Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	misdiagnosis vs control: % with ED triage resuscitation/emergency category 33% vs. 58% p < 0.0001; %	312	NOT STAGE SPECIFIC	Stroke	Dx Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Training background	IncrRisk - not sig	% admitted under neurology service among misdiagnosis vs. control, 65% vs. 89% p < 0.0001	312	NOT STAGE SPECIFIC	Stroke	Dx Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Age	Reported but not quantified	NR	NR	NR	Stroke	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Venkat, 2018[162]	Study design: Case-control Look back or look forward analysis: Not a cohort study Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	No effect - wide CI	% with ambulance transport to hospital among misdiagnosis vs. control, 83% vs. 78% p = 0.36	312	NOT STAGE SPECIFIC	Stroke	Dx Error
Vermeulen, 2007[95]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	SES/Income	No effect - narrow CI	Range in aOR by income quintiles (ref = highest income quintile), 0.71 to 0.96	1507	NOT STAGE SPECIFIC	Stroke	Dx Error
Vermeulen, 2007[95]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	No effect - narrow CI	% male among those with SAH not missed vs. missed SAH, 38.5% vs. 38.3% p > 0.05; aOR, 0.92	1507	NOT STAGE SPECIFIC	Stroke	Dx Error
Vermeulen, 2007[95]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Teaching status	IncrRisk - Significant	aOR, 2.12 (95% CI, 1.02 to 4.44)	1507	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Vermeulen, 2007[95]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Triage intake severity	DecrRisk - Significant	aOR for triaged low acuity vs. medium acuity, 2.65 and aOR for triaged high acuity vs. medium acuity, 0.18	1507	NOT STAGE SPECIFIC	Stroke	Dx Error
Vermeulen, 2007[95]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	IncrRisk - Significant	Mean age among those with SAH not missed vs. missed SAH, 58.1 vs. 54.0, $p < 0.05$	1507	NOT STAGE SPECIFIC	Stroke	Dx Error
Vermeulen, 2007[95]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Off hours	No effect - narrow CI	Range in aOR for evening and night shift (ref = day shift), 0.69 to 1.18 $p > 0.05$ for both, aOR for weekday vs. weeknight, 0.65	1507	NOT STAGE SPECIFIC	Stroke	Dx Error
Vinz, 2015[64]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Malpractice claims Numerator: Numerator and denominator	Tests ordered	Reported but not quantified	% Omitted or incomplete Medical history and physical examination 36 Failure to perform further diagnostics including imaging 28	195	NOT STAGE SPECIFIC	NR	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Waxman, 2018[170]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	Mixed (specify)	Dec/sig: Asian/pacific for MI (aOR 0.67), stroke (0.68), AD (0.65), SAH (0.52) Hispanic for MI (0.91), stroke (0,90) Inc/sig: Black for ruptured AAA (1.35), MI (1.18), stroke (1.09) other/unknown for stroke (1.07)	1561940	NOT STAGE SPECIFIC	Stroke, MI, AAD	Dx Error
Waxman, 2018[170]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Baseline ED use	IncrRisk - not sig	Range in aOR for number of ED discharges 365-46 d before index event, 1.24 to 1.40, $p < 0.05$ for all conditions	1561940	NOT STAGE SPECIFIC	Stroke, MI, AAD	Dx Error
Waxman, 2018[170]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	IncrRisk - Significant	female aOR for ruptured AAA, 1.25; for AMI, 1.14; for stroke, 1.12; for aortic dissection, 1.19; for subarachnoid hemorrhage, 1.00; $p < 0.05$ for all except subarachnoid hemorrhage	1561940	NOT STAGE SPECIFIC	Stroke, MI, AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Waxman, 2018[170]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	Mixed (specify)	Range in aOR for age <65, 70-74, 75-79, 80-84, >84 (ref 65-69), 0.67 to 1.27 for ruptured abdominal aortic aneurysm, p < 0.05 for older age groups; 0.94 to 1.40 for acute MI, p NS for all; 0.89 to 1.38 for stroke, p < 0.05 for older age groups; 0.89 to 1.	1561940	NOT STAGE SPECIFIC	Stroke, MI ,AAD	Dx Error
Waxman, 2018[170]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Health insurance	IncrRisk - Significant	Range in aOR for dually eligible Medicare and Medicaid, 1.23 to 1.40, p < 0.05 for all conditions	1561940	NOT STAGE SPECIFIC	Stroke, MI, AAD	Dx Error
Waxman, 2018[170]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	Mixed (specify)	Range in aOR for Hispanic, 0.90 to 1.16	1561940	NOT STAGE SPECIFIC	Stroke, MI, AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Weinberg, 2010[74]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	Mixed (specify)	Age >18 N 234 Fx rate (%) 25 Sensitivity 78 Specificity 93 LR+ 9.6 (6.2–14.9) LR- 0.30 (0.21–0.42) Age <18 N 114 Fx rate (%) 22 Sensitivity 60 Specificity 92 LR+ 7.6 (3.5–16.6) LR- 0.43 (0.27–0.70)	348	NOT STAGE SPECIFIC	NR	Either/Both
Weinberg, 2010[74]	Study design: Prospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Training background	Mixed (specify)	Sonologist with 25 US exams N 127 Fx rate (%) 26 Sensitivity 61 Specificity 89 LR+ 5.7 LR- N 221 Fx rate (%)23 Sensitivity 80 Specificity 94 LR+ 13.7 (7.4–25.3) LR-0.21 (0.12–0.36)	NR	NOT STAGE SPECIFIC	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Whiteley, 2011	Study design: Cross-sectional Look back or look forward analysis: Not a cohort study Data source: Unclear or NR Numerator: Numerator and denominator	Provider type/role	No effect - wide CI	Diagnosis based on Recognition of Stroke in the Emergency Room Scale: Sensitivity: Doctor (85%, 95%CI: 76%-93%) vs. Nurse (82%, 76%-87%). Speciï¬□city: Doctor (44%, 95%CI: 27%-60%) vs. Nurse (44%, 32%-55%). ManteleHaenszel chi2 tests p-value: 0.78. Diagn	356	NOT STAGE SPECIFIC	Stroke	Dx Error
Williams, 2009[81]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Mode of arrival	Mixed (specify)	Hospital transfer Relative Risk 0.77 p: not significant Air transportation Relative Risk 1.49 p<0.05	1100	Pre-hospital interval	Fractures	Either/Both
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Prior smoking	DecrRisk - Significant	% prior smoking among treated STEMI vs. MAMI patients, 53.6% vs. 42%, p = 0.039	1392	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Race	No effect - narrow CI	% indigenous among treated STEMI vs. MAMI patients, 3.6% vs. 4%	1392	NOT STAGE SPECIFIC	MI	Dx Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom onset to presentation	No effect - narrow CI	Mean symptom onset to presentation among treated STEMI vs. MAMI patients, 150.5 vs. 155.6 minutes, p = 0.903	1392	NOT STAGE SPECIFIC	MI	Dx Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - narrow CI	% male among treated STEMI vs. MAMI patients, 73.5% vs. 70%, p = 0.465	1392	NOT STAGE SPECIFIC	MI	Dx Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	% anterior infarction among treated STEMI vs. MAMI patients, 41% vs. 67%, p = 0.000	1392	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Population density	IncrRisk - Significant	% am MAMI patients presenting to small rural hospitals, 45%; metropolitan hospital without cardiac catheterization laboratory, 27%; rural referral hospital, 16%; tertiary hospital 11%	100	NOT STAGE SPECIFIC	MI	Dx Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - narrow CI	Mean age of treated STEMI vs. MAMI patients, 63.9 vs. 66.3, p = 0.302	1392	NOT STAGE SPECIFIC	MI	Dx Error
Williams, 2019[152]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	No effect - narrow CI	Among treated STEMI vs. MAMI patients, % presenting to hospital between 7am to 3pm, 54.7% vs. 62% p = 0.190; 3pm to 11pm, 29.2% vs. 21% p = 0.115; 11pm to 7am, 15.8% vs. 17% p = 0.767	1392	NOT STAGE SPECIFIC	MI	Dx Error
Willms, 2021	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	Alvardo score p=0.028 (2019 vs. 2020 during COVID)	1915	NOT STAGE SPECIFIC	Appendicitis	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Willner, 2012[6]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Clinical experience	Reported but not quantified	many of the pelvic DDIs were due to radiology residents missing subtle, nondisplaced torus fractures of the pubic rami what were later noted by an attending physician'		ED Dx Process	Other (specify) : 'many of the pelvic DDIs were due to radiology residents missing subtle, nondisplaced torus fractures of the pubic rami what were later noted by an attending physician'	Either/Both
Willner, 2012[6]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Age	Mixed (specify)	Age (y) All patients (N = 324) 7.5 Patients with DDI (n = 26) 11 Patients without DDI (n = 298) 7 DDI vs no DDI, P value .1	324	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosis of injury in pediatric trauma patient	Either/Both
Willner, 2012[6]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Triage intake severity	IncrRisk - Significant	ISS Score, Median Patients w/DDI (n=26): 12.5 Patients w/o DDI(n-298): 5 p-value: <.001	324	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosis of injury in pediatric trauma patient	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Willner, 2012[6]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Tests ordered	Mixed (specify)	Median Total # of CT Scans: DDI: 4 (IQR 3-4) No DDI: 3 (IRQ 1-4) P=.03 Median Total # Radiologic Studies: DDI: 6.5 (IQR 6-8) No DDI: 6 (IQR 4-8) P=.09	NR	NR	Other (specify) : delayed diagnosis of injury in pediatric trauma patient	NR
Willner, 2012[6]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Symptom type	Mixed (specify)	Blunt mechanism, n (%) All patients (N = 324) 296 (91.4) Patients with DDI (n = 26) 25 (96.2) Patients without DDI (n = 298) 271 (90.9) DDI vs no DDI, P value .71	324	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosis of injury in pediatric trauma patient	Either/Both
Willner, 2012[6]	Study design: Retrospective cohort Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Multiple Numerator: Numerator and denominator	Sex	Mixed (specify)	Patients with DDI (n = 26) 20 (76.9) Patients without DDI (n = 298) 173(58.1) DDI vs no DDI, P value .06	324	NOT STAGE SPECIFIC	Other (specify) : delayed diagnosis of injury in pediatric trauma patient	Either/Both

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Hospital size (small, medium, or large; based on the HCUP definitions that consider number of beds, location, and teaching status	DecrRisk - Significant	Range in aOR, 0.46 to 0.5	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Geographic region	Mixed (specify)	range in aOR 0.35 to 1.24	371638	NR	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	percentage of emergency physicians who are US trained	No effect - narrow CI	aOR 0.92 (p > 0.01)	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	percentage of emergency physicians who are male	No effect - narrow CI	aOR 0.98 (p > 0.01)	371638	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	ED's average chest pain acuity (percentage of all chest pain patients diagnosed with AMI within 1 week of ED visit)	DecrRisk - Significant	aOR, 0.23; 99% CI, 0.19 to 0.27	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Volume of chest pain patients seen	DecrRisk - Significant	aOR = 0.65, 99% CI = 0.51 to 0.82	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Technology score (hospitals' overall technology level using a Saidin indes	DecrRisk - Significant	Range in aOR based on increased level of technology score, 0.51 to 0.7	NR	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Training background	DecrRisk - Significant	aOR, 0.60; 99% CI, 0.50 to 0.73	371638	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Race	Mixed (specify)	aOR for African American = 1.26, p < 0.01; range in aOR for race, Asian, and Native American, 0.91 to 1.44 (p > 0.01)	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	SES/Income	No effect - narrow CI	aOR 0.97	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Sex	No effect - narrow CI	aOR 0.83	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Teaching status	DecrRisk - Significant	aOR = 0.74, 99% CI = 0.58 to 0.94	371638	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Access to testing	DecrRisk - not sig	aOR, 0.87 (p>0.01)	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ownership/business model	Mixed (specify)	aOR for private hospital 0.92 (p>0.01); aOR for public hospital 1.33, 99% CI = 1.08 to 1.61 (reference = nonprofit)	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Age	Mixed (specify)	Range in aOR for women, 0.33 to 0.87 (p < 0.01 for older women); range in aOR for men, 1.05 to 1.46 (p > 0.01 for most age categories)	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Population density	IncrRisk - Significant	Range in aOR (ref = urban), 1.47 to 2.61	371638	NOT STAGE SPECIFIC	MI	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Ethnicity	No effect - narrow CI	aOR 1.18	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Clinical experience	No effect - narrow CI	aOR 0.93 (p>0.01)	371638	NOT STAGE SPECIFIC	MI	Dx Error
Wilson, 2014[28]	Study design: Cross-sectional Look back or look forward analysis: Look back method (disease denominator) Data source: Billing/administrative coded diagnoses Numerator: Numerator and denominator	Off hours	No effect - narrow CI	Range in aOR for individual days of week (ref = Sunday), 0.93 to 1.03	371638	NOT STAGE SPECIFIC	MI	Dx Error
Winkler, 2009[84]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Symptom type	IncrRisk - Significant	% with global aphasia without hemiparesis for stroke vs. mimics, 3.3% vs. 42.9%, p = 0.002	250	NOT STAGE SPECIFIC	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Winkler, 2009[84]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Sex	No effect - wide CI	% male for those with stroke vs. stroke mimics, 58.8% vs. 57.1%, p = 0.68	250	NOT STAGE SPECIFIC	Stroke	Dx Error
Winkler, 2009[84]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Triage intake severity	DecrRisk - not sig	Mean NIHSS score for stroke vs. mimics, 13.67 vs. 9.9, p = 0.06	250	NOT STAGE SPECIFIC	Stroke	Dx Error
Winkler, 2009[84]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Smoking	DecrRisk - not sig	% current smoking among stroke vs. mimics, 21.4% vs. 0%	250	NOT STAGE SPECIFIC	Stroke	Dx Error
Winkler, 2009[84]	Study design: Registry Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Prospective data collection Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age for those with stroke vs. stroke mimics, 67.9 vs. 68.1; p = 0.96	250	NOT STAGE SPECIFIC	Stroke	Dx Error
Wireklint Sundström, 2015[68]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Unclear or NR	Teaching status	Mixed (specify)	Differences in the median times between university and county hospitals ranged from 1< minute to almost 1 hour.	1376	ED Dx Process	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Geographic region	Reported but not quantified	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	ED volume/annual visits	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Arrival within 5 hours	DecrRisk - Significant	46% no tx	136	Patient interval	Stroke	Dx Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Ownership/business model	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Delivery/payment method	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Race	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	ED visit not complete	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	SES/Income	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Sex	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	ED staffing	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Symptom type	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Teaching status	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Access to testing	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Tests ordered	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Triage intake severity	DecrRisk - Significant	NIHSS<10 - 88% no tx, NIHSS>20 - 52% tx	192	Unclear or NR	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Inpatient occupancy rate	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Current discharge fraction	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Health insurance	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Language	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Mode of arrival	IncrRisk - Significant	69% no tx	67	Unclear or NR	Stroke	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Atypical presentation	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	ED crowding	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Age	No effect - wide CI	mean age for tx (TP) is 67.8 and mean age for no tx (FP) is 66.8	192	NOT STAGE SPECIFIC	Stroke	Dx Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Population density	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Average discharge fraction	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Health literacy	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Access to consultation	No effect - wide CI	56% with no tx	94	ED Dx Process	Stroke	Dx Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Off hours	DecrRisk - not sig	48% no tx	69	ED Dx Process	Stroke	Dx Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Handoffs	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Ethnicity	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	Access to Electronic Health Record/Electronic Health Record type	NR	NR	NR	NR	NR	NR
Yi, 2017[185]	Study design: Look back or look forward analysis: Look forward method (symptom/presentation denominator) Data source: Electronic health record data Numerator: Unclear or NR	ED illness severity	NR	NR	NR	NR	NR	NR
York, 2005[104]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Tests ordered	Reported but not quantified	The negative appendectomy rates were 10.4% (n = 11) and 4.4% (n = 4) for groups A (Imaging) and B (no Imaging), respectively. Group A patients had an average delay until surgery of 6.7 hours greater than their nonimaged counterparts.	197	NOT STAGE SPECIFIC	Appendicitis	Dx Error
York, 2005[104]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Triage intake severity	NR	NR	NR	NR	NR	NR

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
York, 2005[104]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator only (error/harm)	Mode of arrival	NR	NR	NR	NR	NR	NR
York, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	IncrRisk - not sig	between midnight and seven, IncrRisk of misdx but not significant	2947	NOT STAGE SPECIFIC	Fractures	Dx Error
York, 2020	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Off hours	IncrRisk - not sig	between midnight and seven, IncrRisk of misdx but not significant	2947	NOT STAGE SPECIFIC	Fractures	Dx Error
Zaschke, 2020[128]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Drug abuse, nicotine/alcohol	No effect - wide CI	% nicotine abuse among initial misdiagnosed vs. correct diagnosed, 32.7% vs. 21.6%, p = 0.067; % alcohol abuse initial misdiagnosed vs. correct diagnosed, 4.6% vs. 3.9%, p = 0.835	350	NOT STAGE SPECIFIC	AAD	Dx Error

Author, Year	Study Design Characteristics	Factor	Effect	Magnitude	SS	Stage	Conditions	Error
Zaschke, 2020[128]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Sex	No effect - wide CI	% male among initial misdiagnosed vs. correct diagnosed, 63.9% vs. 61.8%	350	NOT STAGE SPECIFIC	AAD	Dx Error
Zaschke, 2020[128]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Symptom type	Mixed (specify)	aOR for angina pectoris, 0.31; for pain, lumbar region, 4.38; for sweating, 1.86; for any paresis, 1.85; for pain scapulae, 2.03	350	NOT STAGE SPECIFIC	AAD	Dx Error
Zaschke, 2020[128]	Study design: Retrospective cohort Look back or look forward analysis: Look back method (disease denominator) Data source: Electronic health record data Numerator: Numerator and denominator	Age	No effect - wide CI	Mean age of initial misdiagnosed vs. correct diagnosed, 62.7 vs. 65.1; p = 0.162	350	NOT STAGE SPECIFIC	AAD	Dx Error

AAD: Aortic aneurysm and dissection; aOR: Adjusted odds ratio; CI: Confidence Interval; DecrRisk: Decreased Risk; Dx Error: Diagnostic Error; ED: Emergency Department; IncrRisk: Increased Risk; ISS: Injury Severity Score; NA: Not applicable; OR: Odds Ratio; STEMI: ST-elevated myocardial infarction; VTE: Venous thromboembolism

Table D-5. Risk of bias of studies that evaluated diagnostic errors in the emergency department

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Aaronson, 2016[204]	Low	Low	Low	High	Low	Low	Low
Aaronson, 2018[177]	High	Low	Low	Low	Low	Low	Low
Agrawal, 2019[157]	Low	Low	Low	Low	Low	Low	Low
Aneiros, 2019[146]	Low	Low	Low	Low	Low	Low	Low
Atzema, 2011[52]	Low	Low	Low	Low	Low	Low	Low
Augustin, 2011[54]	Low	Low	Low	Low	Low	Low	Low
Bastakoti, 2021	Low	Low	High	Low	Low	Low	Unclear
Beaver, 2005[107]	Low	Low	Low	Low	Low	Low	Low
Bhattacharya, 2013	High	Low	Low	High	High	Low	Low
Branstetter, 2007	Low	Low	High	Low	Low	Low	High
Breen, 2017[179]	High	Low	Low	Low	Low	Low	Low
Breidthardt, 2019	Low	Low	High	Low	Low	Low	Low
Broadley, 2003	Low	Low	Low	High	Low	Low	Low
Calder, 2010[58]	Low	Low	Low	Unclear	Low	Unclear	Low
Calder, 2021	Low	Low	Unclear	High	Low	Low	Unclear
Carlton, 2015[69]	Unclear	Low	Low	Low	Low	Low	Low
Catapano, 2017[176]	Low	Low	High	Low	Low	Low	High
Caterino, 2012[21]	Low	Low	Low	Unclear	Low	Low	Low
Chan, 2019[150]	Low	Low	Low	Low	Low	Low	Low
Chan, 2020[125]	Low	Low	Low	Low	Low	Low	Low
Chang, 2019[169]	Low	Low	Low	Low	Low	Low	Low
Chen, 2016[197]	Low	Low	Low	Low	Low	Low	Low
Cheong, 2014[34]	Low	Low	Low	Low	Low	Low	Low
Choinski, 2021	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Chompoopong, 2017[182]	Low	Low	Low	Low	Low	Low	Low
Christenson, 2004	Low	Low	High	Low	Low	Low	Low
Chu, 2015[73]	Low	Low	Low	Low	Low	Low	Low
Chung, 2009[22]	Unclear	Low	Low	Low	Low	Low	Low
Cifra, 2020[130]	Low	Low	High	Low	Low	Low	High
Conti, 2003[112]	Low	Low	Low	Low	Low	Low	Low
Copson, 2020[209]	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Corral Gudino, 2003[111]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Crosby, 2013[16]	Low	Low	Low	Low	Low	Low	Low

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Degheim, 2019[149]	Low	Low	High	High	Low	Low	High
DeVon, 2020	High	Low	Low	Low	Low	Low	Low
Drapkin, 2020[173]	Low	Low	Low	Low	Low	Low	Low
Dubosh, 2015[11]	Low	Low	Low	Low	Low	Low	Low
Dubosh, 2019[154]	High	Low	Low	Low	Low	Low	Low
Dupond-Athénor, 2021	Low	Low	Low	Low	Low	Low	High
England, 2006[100]	Low	Low	Low	Low	Low	Low	Low
Faiz, 2014[30]	Low	Low	Unclear	High	Low	Low	Low
Fasen, 2020[131]	Low	Low	Low	Low	Low	Low	Low
Fernholm, 2019[145]	High	Unclear	Unclear	Unclear	High	Unclear	Unclear
Ferree, 2016[1]	Low	Low	Low	Low	Low	Low	Low
Filippi, 2008[23]	Low	Low	Low	Low	Low	Low	Low
Fordyce, 2003	Low	High	Low	Unclear	Low	Low	Low
Freedman, 2014[37]	Low	Unclear	Unclear	Low	Low	Low	Unclear
Gallagher, 2006[13]	Unclear	Low	Low	Low	Low	Low	Low
Garfield, 2004[108]	Low	Low	Low	Low	Low	Low	Low
Gargano, 2009[83]	Low	Low	Low	Low	Low	Low	Low
Gaughan, 2009[82]	Low	Low	Unclear	Low	Low	Low	Unclear
Gergenti, 2019[153]	Low	Unclear	Unclear	Unclear	Low	Low	Low
Ghobadi, 2021	Low	Unclear	Low	Low	Low	Low	Low
Gold, 2020[119]	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Gouin, 2006[103]	Low	High	High	High	Low	Low	Low
Goulet, 2015[70]	Low	Low	Low	Low	Low	Low	Unclear
Goyal, 2020[116]	Low	Low	Low	Low	Low	Low	Low
Graff, 2006[99]	Low	Unclear	Low	Low	Low	Low	Low
Graff, 2014[29]	Low	Low	Low	Low	Low	Low	Low
Grewal, 2015	Low	Low	Low	High	Low	Low	Low
Groot, 2016[71]	Low	Low	Low	Low	Low	Low	Low
Grosmaitre, 2013[36]	Low	Low	Low	Low	Low	Low	Low
Guillan, 2012[43]	Low	Low	Low	Low	Low	Low	Low
Gurley, 2018[211]	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Hallas, 2006[102]	Low	Low	High	Low	Low	Low	Low
Hansen, 2007[94]	Low	Low	Low	Low	Low	Low	Low
Harbison, 2003[113]	Low	Low	Unclear	Low	Low	Low	Low

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Harris, 2011[49]	Low	Low	Low	Low	Low	Low	Low
Hautz, 2019[148]	Low	Low	High	Low	Low	Low	Low
Heckmann, 2004[110]	Low	Low	Low	Low	Low	Low	Low
Hendriks, 2015[63]	Low	Low	Low	Low	Low	Low	Low
Hochberg, 2011[47]	Low	Low	Low	Low	Low	Low	Low
Hoekstra, 2009[78]	Low	Low	High	Low	Low	Low	High
Holland, 2015[72]	Low	Low	Unclear	Low	Low	Low	Low
Huang, 2019[156]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Humphries, 2018	Low	High	High	Low	Low	High	Low
Husabø, 2020[133]	Low	Low	Unclear	Low	Low	Low	Unclear
Hussain, 2019[135]	High	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Jaffe, 2020	Low	Low	Low	Low	Low	Low	High
Jiménez Castro, 2007[93]	Low	Low	Low	Low	Low	Low	Low
Kargl, 2019[158]	Low	Low	Low	Low	Low	Low	Low
Kerber, 2006	Low	Low	High	Low	Low	Low	Low
Kerber, 2014	Low	Low	High	Low	Low	Low	Low
Kerkman, 2020[124]	Low	Low	Low	Low	Low	Low	Low
Kim, 2007[90]	Low	Low	Low	Low	Low	Low	Low
Kline, 2007[92]	High	Low	Low	Low	Low	Low	Low
Kline, 2009[20]	Low	Low	Low	Low	Low	Low	Low
Ko, 2018	Low	Low	Low	Low	Low	Low	Low
Kornblith, 2013[7]	Low	Low	Low	Low	Low	Low	Low
Kuruvilla, 2011[60]	Low	Low	Low	Low	Low	Low	Low
Ladner, 2015	Low	Low	Low	Low	Low	High	Low
Lastunen, 2021	Low	Low	Low	Low	Low	Low	Low
Le, 2007	Low	Low	Low	Low	Low	Low	Low
Leeuwenburgh, 2014[25]	Low	Low	Low	Low	Low	Low	Low
Lehtimäki, 2015	Low	Low	Low	High	Low	Low	Low
Lever, 2013[44]	Low	Low	Low	Low	Low	Low	Low
Liberman, 2018[168]	Low	Low	Low	Low	Low	Low	Low
Liberman, 2019[144]	Low	Low	Low	Low	Low	Low	Low
Liberman, 2020[114]	Low	Low	Low	High	Low	Low	Low
Liberman, 2020[127]	Low	Low	Low	Low	Low	Low	Low
Lindsey, 2018[161]	Low	Low	Low	Low	Low	Low	Low

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Littman, 2021	Low	Low	Unclear	Low	Low	Low	High
Lowe, 2021	Low	Low	Low	Low	Low	Low	Low
Lucas, 2021	Low	Low	Low	Low	Low	Low	Low
Mahajan, 2020[132]	Low	Low	Low	Low	Low	Low	Low
Mahajan, 2020[134]	Low	Unclear	Low	Low	Low	Low	Low
Mansella, 2020[121]	Low	Low	Low	Low	Low	Low	Low
March, 2014[27]	High	Low	Low	Low	High	Low	Low
Martin, 2011[48]	Unclear	Low	High	Low	Low	Low	Low
Matera, 2020	Low	Low	High	Low	Low	Low	High
Mattijssen-Horstink, 2020[126]	Low	Low	High	Low	Low	Low	Low
Mattsson, 2018[172]	Low	Low	Low	Low	Low	Low	Low
McGann Donlan, 2009[80]	Low	Low	Low	Low	Low	Low	Low
McLaren, 2021	Unclear	Low	Low	Low	Unclear	High	Low
Medford-Davis, 2016[66]	High	Unclear	Unclear	Unclear	High	Unclear	Unclear
Michelson, 2019[137]	Low	Low	Low	Low	Low	Low	Low
Michelson, 2021	High	High	High	High	High	High	High
Miedema, 2011[51]	Low	Low	Low	Low	Low	Low	Low
Miller, 2018[12]	Low	Low	Low	Low	Low	Low	Low
Mitchell, 2006	Low	Low	Low	Low	Low	Low	Low
Moeller, 2008[10]	Low	Low	Unclear	Low	Low	Low	Low
Mohamed, 2013[42]	Low	Low	Unclear	Low	Low	Low	Unclear
Montmany, 2008[5]	Low	Low	Low	Low	Low	Low	Low
Montmany, 2017[175]	Low	Low	High	Low	Low	Low	Low
Morgan, 2021	Low	Low	Low	Low	Low	Low	Low
Morgenstern, 2004	High	Low	High	Low	Low	Low	Low
Moy, 2015[24]	Low	Low	Low	Low	Low	Low	Low
Muhm, 2012[3]	Low	Low	Low	Low	Low	Low	Low
Musunuru, 2007[91]	Low	Low	Low	Low	Low	Low	Low
Naiditch, 2013[39]	Low	Low	Low	Low	Low	Low	Low
Newman-Toker, 2014[33]	Low	Low	Low	Low	Low	Low	Low
Nuñez, 2006[101]	High	Low	High	High	Low	Low	Low
Ohle, 2019[151]	Low	Low	Low	Low	Low	Low	Low

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Ois, 2019[138]	Low	Low	High	Low	Low	Low	Low
Okafor, 2016[65]	High	Unclear	Unclear	Unclear	High	Unclear	Unclear
Oliver, 2019[143]	Low	Low	High	Low	Low	Low	High
Osterwalder, 2020[14]	Low	Low	Low	Low	Low	Low	Low
Pacheco, 2021	Low	Low	Low	Low	Low	Low	High
Palomeras Soler, 2015[32]	High	Low	High	High	High	Low	High
Pare, 2016[62]	Unclear	Low	Low	Low	Low	Low	Low
Parikh, 2008[89]	Low	Low	Low	Low	Low	Low	Low
Pehle, 2006[98]	Low	Low	Low	Low	Low	Low	Low
Peng, 2015[26]	Low	Low	Low	Low	Low	Low	Low
Petinaux, 2011	Low	High	Low	Low	Low	Low	High
Pihlasviita, 2018[164]	Low	Low	Low	Low	Low	Low	Low
Piper, 2008[88]	Low	Low	Low	Low	Low	Low	Low
Pirozzi, 2014[19]	Low	Low	Low	Low	Low	Low	Low
Postma, 2012[4]	Low	Low	Low	Unclear	Low	Low	Unclear
Prabhakaran, 2008[86]	Low	Low	Low	Low	Low	Low	Low
Rapezzi, 2008[85]	Low	Low	Low	Low	Low	Low	Low
Raposo, 2018[159]	Low	Low	Low	Low	Low	High	Low
Ravichandiran, 2010[76]	Unclear	Low	High	Low	Low	High	Low
Ray, 2006[18]	Low	Low	Low	Low	Low	Low	Low
Richoz, 2015	Low	Low	High	Low	Low	Low	Low
Rønning, 2005[106]	Low	Low	Low	Low	Low	Low	Low
Rose, 2008[87]	Low	Low	Unclear	Low	Low	Low	Unclear
Rosenman, 2020	Low	Low	Low	High	Low	Low	Low
Royl, 2011[9]	High	Low	Low	Unclear	High	Low	Unclear
Russell, 2013[40]	Low	Low	Low	Low	Low	Low	Low
Saaristo, 2020[15]	Low	Low	High	Low	Low	Low	Low
Sadighi, 2019[147]	Low	Low	Low	Low	Low	Low	Low
Saleh Velez, 2021	Low	Low	Low	Low	Low	High	High
Sanders, 2017[174]	High	Low	Low	Low	High	Low	Low
Santos, 2009[77]	Unclear	Low	High	High	Low	Low	Low
Sarraj, 2015[41]	Low	Low	Low	Low	Low	Low	Low
Scheuermeyer, 2012[46]	Low	Low	Low	Low	Low	Low	Low

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Schrock, 2012[53]	Low	Low	Low	Low	Low	Low	Low
Schull, 2006[97]	Low	Low	Low	Low	Low	Low	Low
Scott, 2018[171]	Low	Low	Low	Low	Low	Low	Low
Sederholm Lawesson, 2018[167]	Low	Low	Low	Low	Low	Low	Low
Seetahal, 2011[56]	Low	Low	Low	Low	Low	Low	Low
Settelmeier, 2020[118]	Low	Low	High	Low	Low	Low	Low
Sharif, 2018[166]	Low	Low	Low	Low	Low	Low	Low
Sharp, 2020[120]	Low	Low	Low	Low	Low	Low	Low
Shokoohi, 2020	Low	Low	Low	Low	Low	Low	Low
Smidfelt, 2017[180]	High	Low	Low	Low	High	Low	Low
Smidfelt, 2020[122]	Low	Low	Low	Low	Low	Low	Low
Smith, 2012[50]	High	Low	Low	Low	High	Low	Low
Snoek, 2013[2]	Low	Low	Low	Low	Low	Low	Low
Somers, 2021	High	Low	Low	Low	Low	High	High
Soundappan, 2004[109]	Low	Low	High	Low	Low	Low	Low
Sporer, 2013[45]	Unclear	Low	Low	Low	Unclear	Low	Low
Staab, 2020	Low	Low	Low	Unclear	Low	Low	Low
Suda, 2021	Low	Low	Low	Low	Low	Low	Low
Sun, 2007[8]	Low	Low	Low	Low	Low	Low	Low
Sundberg, 2018[165]	Low	Low	Low	Low	Low	Low	Low
Teichman, 2021	Low	Low	Low	Unclear	Low	Low	High
Tien, 2021	Unclear	Low	High	Low	Low	Low	Low
Torres-Macho, 2013[38]	Low	Low	Low	Low	Low	Low	Low
Tsivgoulis, 2011[55]	Low	Low	Low	Low	Low	Low	Low
Tudela, 2005[105]	Unclear	Unclear	Unclear	Unclear	Low	Low	Low
Tzovaras, 2007[96]	Low	Low	Low	Low	Low	Low	Low
Uchino, 2010	Low	Low	Low	Low	Low	Low	Low
Vaghani, 2021	Low	Low	Low	Low	Low	Low	Low
van Noord, 2010[61]	Low	Unclear	Unclear	Unclear	Low	Unclear	Unclear
Vanbrabant, 2009[75]	Low	Low	Low	Low	Low	Low	Low
Vargas-Blasco, 2021	Low	Low	Low	Low	Low	High	Low
Vasconcelos-Castro, 2020[140]	Low	Unclear	Unclear	Low	Low	Low	Low

Author, Year	Risk of Bias in Patient Selection	Risk of Bias in Index Test	Risk of Bias in Reference Standard	Risk of Bias in Flow and Timing	Applicability of Patient Selection	Applicability of Index Test	Applicability of Reference Standard
Venkat, 2018[162]	High	Low	Low	Low	Low	Low	Low
Verelst, 2014	High	Low	Low	High	Low	Low	Low
Vermeulen, 2007[95]	Low	Low	Unclear	Unclear	Low	Low	Unclear
Vinz, 2015[64]	Low	High	High	Low	Low	Low	Low
Waxman, 2018[170]	Low	Low	Low	Low	Low	Low	Low
Weinberg, 2010[74]	Unclear	Low	Low	Low	Unclear	Low	Low
Wemeijer, 2021	Low	Low	Low	Low	Low	Low	Low
Whiteley, 2011	Low	High	Low	High	Low	Low	Low
Williams, 2009[81]	Low	Low	Low	Low	Low	Low	Unclear
Williams, 2019[152]	Low	Low	High	High	Low	Low	Low
Willms, 2021	Low	Low	Low	Low	Low	Low	High
Willner, 2012[6]	Low	Low	Low	High	Low	Low	Low
Wilson, 2014[28]	Low	Low	Unclear	Low	Low	Low	Low
Winkler, 2009[84]	Low	Low	Low	Low	Low	High	Low
Wireklint Sundström, 2015[68]	Low	Low	Unclear	Low	Low	Low	Low
Yeboah, 2019[160]	Low	Low	Unclear	Low	Low	Low	Unclear
York, 2005[104]	Low	Low	Low	Low	Low	Low	Low
York, 2020	Low	Low	Unclear	Low	Low	Low	Low
Zaschke, 2020[128]	Low	Low	Low	Low	Low	Low	Low

Table D-6. Strength of evidence of studies that evaluate the overall diagnostic error rates, misdiagnosis-related harms, and mortality from diagnostic errors in the emergency department

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Overall diagnostic errors	1 Prospective cohort[58, 148] of ED admissions (755) 1 Prospective cohort with matched controls of ED discharges[101] (500)	Low*	Direct	Consistent	Precise	Undetected	Moderate*	Weighted mean DE rate was 5.6%. As expected, DE rates were lowest for discharges that did not return within 72hrs (4%), higher for those admitted (12.3%), and highest for those discharged who did return within 72hrs (20%).
Misdiagnosis-related harms	1 Prospective cohort [58, 148] 4 Retrospective cohort[75, 177, 194, 215] (436,861)	Low* (prospective) High* (retrospective)	Direct	Consistent†	Precise	Undetected	Moderate*	The prospectively-determined diagnostic adverse event rate (misdiagnosis-related harms) was 2.0% (95% CI 1.0-3.6). Retrospectively determined rates were roughly two orders of magnitude lower (weighted mean 0.02%).
Mortality from diagnostic errors	2 Prospective cohorts [58, 148] (1258) 3 Retrospective cohorts[75, 177, 215] (436,173)	Low* (prospective) High* (retrospective)	Direct	Consistent†	Imprecise	Undetected	Moderate*‡	The prospectively-determined misdiagnosis-related mortality was 0.20 to 0.25%. Retrospectively determined rates were more than 200-fold lower (weighted mean 0.0009%).

CI = confidence interval; DE = diagnostic error; ED = emergency department

* The prospective studies on which the main study results rest for the overall diagnostic error/harm rates (Key Question 2a) had low concerns related to design and risk of bias. Despite different study populations, they had similar diagnostic error definitions. Retrospective studies provided evidence of harms and mortality, but there was strong evidence that these systematically under-ascertained the outcome events of interest, so they were not included as part of the final estimates related to error/harm rates (nor did they count against the overall strength of evidence for estimates derived from the prospective studies). Because there were just three prospective studies (and therefore imperfect generalizability, despite overall consistency and coherence of the results), we rated the evidence supporting these estimates as moderate, rather than high.

† Inconsistency in misdiagnosis-related harm results was principally between the well-designed, prospective studies with systematic follow-up and the four retrospective cohort studies that relied on outcome triggers for ascertainment. Systematic under-ascertainment in retrospective studies was most clearly demonstrated based on two separate studies (one prospective, the other retrospective using triggers) by the same investigators at the same EDs – there was an 18-fold greater diagnostic adverse event rate and 27-fold greater misdiagnosis-related mortality rate when using the prospective design. Differences within the four retrospective studies were readily attributed to outcome windows for ascertainment. Although these retrospective results varied substantially with respect to diagnostic adverse event rates (from 0.01 percent at a large tertiary care ED in the US to 1.6 percent at a small regional ED in Denmark), they were nevertheless fairly comparable, given their design differences (time window for assessment, academic vs. non-academic

setting). Results were ordinal, as expected based on limiting the determination of outcome events (i.e., the shorter the window for determination of outcomes, the lower the rate, and vice versa); the same was true for mortality, but with less precision.

‡ Although the misdiagnosis-related mortality estimates from the Calder, 2010 study were imprecise (with a fairly wide confidence interval around the point estimate of 0.2%, 95% CI 0.005-1.1), results from the other strong, prospective study (Hautz, 2019), which included 33 deaths, were very consistent. We can account for the fact that Hautz, 2019 focused only on admitted patients (who are likely to be at substantially higher risk of death), by constructing a weighted average based on the proportion of ED cases admitted. If misdiagnosis-related deaths only occurred among admitted ED patients (not those discharged), the overall misdiagnosis-related mortality rate based on Hautz would be 0.07 percent. If the death rate among those discharged were the same as in Calder, 2010 (0.2%, 95% CI 0.005-1.1), the overall rate would be 0.25 percent, with a plausible lower bound of 0.08 percent and upper bound of 1.0 percent. The estimate is further corroborated by the fraction of short-term ED deaths, which suggests that a rate of 0.20-0.25% corresponds to 6.7-8.3 percent of post-ED deaths (3.0% 30-day death rate overall) being caused by diagnostic error, which matches fairly closely estimates from autopsy-based studies among hospitalized patients (see KQ2 text for additional details).

Table D-7. Strength of evidence of studies that evaluate the false negative rates for each condition in the emergency department

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Stroke	19 Retrospective cohorts[42, 44, 60, 95, 114, 127, 138, 144, 160, 162, 164, 168, 182, 190, 195, 200, 205, 216, 217] (53,417)	Medium*	Direct	Consistent	Precise	Undetected	High	Among patients with stroke, 17% (95% CI 11% to 23%) are initially misdiagnosed in the ED, but false negative rates tend to vary substantially based on presenting symptoms and, to a lesser extent, stroke subtype.
Pediatric stroke	1 Retrospective cohort[48] (91)	High†	Direct	NA (single study)	Imprecise	Undetected	Insufficient	The available evidence is insufficient to draw a conclusion about false negative rates.
MI	4 Retrospective cohorts[97, 99, 120, 170] (375,588) 2 Cross-sectional studies[24, 28] (483,611)	Medium	Direct	Consistent	Precise	Undetected	High	Among patients with MI, 1.6% (95% CI 1% to 2%) are initially misdiagnosed in the ED.
AAD	11 Retrospective cohorts[49, 62, 82, 85, 94, 107, 122, 128, 151, 180, 207] (2735‡)	Medium§	Direct	Consistent#	Precise	Undetected	Moderate	Among patients with AAD, 28% (95% CI 22% to 34%) are initially misdiagnosed in the ED.
Venous thrombo-embolism	1 Prospective cohort[93] (397) 2 Retrospective cohorts[121, 125] (2360)	Medium¶	Direct	Consistent	Precise	Undetected	Moderate	Among patients with VTE, 20% (95% CI, 17% to 24%) are initially misdiagnosed in the ED.
Meningitis and encephalitis	1 Retrospective cohort[218] (521)	Medium**	Direct	NA (single study)	Precise	Undetected	Low	Among patients with meningitis/encephalitis, 22% (95% CI, 18% to 26%) are initially misdiagnosed in the ED.
Sepsis	4 Retrospective cohorts[137, 171, 218, 219] (3479)	Medium	Direct	Inconsistent††	Precise	Undetected	Moderate	Among patients with sepsis, 19% (95% CI, 11% to 27%) are initially misdiagnosed in the ED.

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Arterial thrombo-embolism	1 Retrospective cohort[220] (72)	Medium¶	Direct	NA (single study)	Imprecise	Undetected	Low	Among patients with arterial thromboembolism (mesenteric ischemia), 15% (95% CI, 7.9% to 26%) are initially misdiagnosed in the ED.
Spinal and intracranial abscess	0 studies‡‡	NA	NA	NA	NA	NA	No studies‡‡	NA‡‡
Pneumonia	1 Prospective cohort[18] (180)	Medium	Direct	NA (single study)	Precise	Undetected	Low	Among patients with pneumonia, 14% (95% CI 10% to 20%) are initially misdiagnosed in the ED.
Appendicitis	2 Retrospective cohorts[39, 137] (874§§)	Medium	Direct	Consistent	Precise	Undetected	Moderate	Among patients with appendicitis, between 2.5% and 4.8% are initially misdiagnosed in the ED.§§
Fractures	3 Prospective cohorts[109, 158, 214] (2767) 9 Retrospective cohorts[1, 76, 81, 102, 126, 153, 172, 176, 188] (133,657) 1 Cross-sectional study [183] (196)	Medium§§	Direct	Consistent§§	Precise	Undetected	Moderate	Among patients with fractures, 1.0% (95% CI 0.9% to 1.2%) are initially misdiagnosed in the ED, but rates range from 0.02 to 40 percent depending on study population and design.
Testicular torsion	2 Retrospective cohorts[150, 184] (262)	Medium	Direct	NA##	Precise	Undetected	Low	Among patients with testicular torsion, 5.3% (95% CI, 2.7% to 9.3%) are initially misdiagnosed in the ED.

CI = confidence interval; ED = emergency department; NA = not applicable

* Observational studies with some concerns for study limitations, such as referral bias,[60] unclear definition of diagnostic errors,[42, 195] sampling error,[164] and ascertainment bias.[127]

† Observational study with no standard definition for diagnostic error, unclear study timepoints, and inferred diagnostic error.

‡ Two studies likely had overlapping study populations so the overall number is participants is less than what is reported here.[122, 180]

§ Retrospective studies with an unclear or low risk of bias conducted a look back analysis to determine the rate of false negative diagnoses.

One study, which used a different definition of diagnostic error, reported a false negative rate that was higher than the other studies.[128]

¶ Cohort studies had a low risk of bias.

** Retrospective, look-back analysis

†† Wide range of diagnostic sensitivity (41% to 97%).

‡‡ Two studies excluded on technical grounds, but with relevant, high-quality data reported. One detailed study of missed spinal abscess cases drawn from a large national clinical data repository through the Veterans Administration (Bhise et al., 2017) was captured but excluded from the review at the full text stage solely because the proportion of cases seen in the ED (as opposed to ambulatory clinic settings) could not be verified (it was otherwise eligible for the review); the study reported a spinal abscess miss rate of 56 percent

(n=66 of 119). A second study (Davis et al., 2004) was excluded based on study dates because the proportion of cases included after the year 2000 was not known and results with more recent cases were not segregated (it was otherwise eligible for the review); the study reported a spinal abscess diagnostic delay rate of 75 percent (n=47 of 63), including 68 percent (n=43 of 63) with multiple ED visits. Taken together, the spinal abscess false negative rate based on these two studies is estimated to be 62% (n=113 of 182, 95% CI 55-69).

§§ One additional retrospective cohort study reported that among 3,685 patients who were diagnosed with constipation in the ED, seven were later diagnosed with appendicitis.[37] These were observational studies, some with a high risk of bias. Studies of patients with fractures differed substantially in the study populations assessed and in definitions. For two large studies of ED misdiagnosis for all-comers with fracture, the error rate was 1.0 percent (n=329 of 31,836, 95% CI 0.9-1.2), but rates ranged from 0.02 to 40 percent.

Studies reported results differently, making it difficult to determine consistency. Bayne et al., 2017 enabled an estimate of ED false negative rate (n=11 of 208 total cases, all in the "delayed presentation" subgroup [n=94]). Chan et al., 2019 focused on testing delays and radiographic errors.

Table D-8. Strength of evidence of studies that evaluate the false omission rates for each condition in the emergency department

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Stroke	1 Retrospective cohort[154] (2,101,081)	Medium	Direct	NA (single study)	Precise	Undetected	High	Among patients who are discharged from the ED with a diagnosis of headache, the false omission rate of stroke is 0.2%.
MI	1 Retrospective cohort[120] (324,580)	Medium	Direct	NA (single study)	Precise	Undetected	High	Among patients who are discharged from the ED with a diagnosis of chest pain or dyspnea, the false omission rate of MI is 0.2% (95% CI, 0.1 to 0.2%).
AAD	0 studies	NA	NA	NA	NA	NA	No studies	NA
VTE	0 studies	NA	NA	NA	NA	NA	No studies	NA
Meningitis and encephalitis	0 studies	NA	NA	NA	NA	NA	No studies	NA
Sepsis	0 studies	NA	NA	NA	NA	NA	No studies	NA
Arterial thrombo-embolism	0 studies	NA	NA	NA	NA	NA	No studies	NA
Spinal and intracranial abscess	1 Retrospective cohort[154] (1,381,614)	Medium	Direct	NA (single study)	Precise	Undetected	High	Among patients who are discharged from the ED with a diagnosis of benign back pain, the false omission rate of spinal abscess is 0.1%
Pneumonia	1 Prospective cohort[18] (278)	Medium	Direct	NA (single study)	Precise	Undetected	Low	Among elderly patients admitted for acute respiratory failure, the false omission of pneumonia is 9% (95% CI, 7% to 13%).
Appendicitis	0 studies	NA	NA	NA	NA	NA	No studies	NA
Fractures	0 studies	NA	NA	NA	NA	NA	No studies	NA
Testicular torsion	0 studies	NA	NA	NA	NA	NA	No studies	NA

CI: confidence interval; ED: emergency department; NA: not applicable; VTE: Venous Thromboembolism

Table D-9. Strength of evidence of studies that evaluate the false positive rates for each condition in the emergency department

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Pneumonia	1 Prospective cohort[18] (333)	Medium	Direct	NA (single study)	Precise	Undetected	Low	Among patients without pneumonia, 24% (95% CI 20% to 29%) are initially misdiagnosed as having pneumonia in the ED.

CI = confidence interval; ED = emergency department; NA = not applicable

Table D-10. Strength of evidence of studies that evaluate the false discovery rates for each condition in the emergency department

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Stroke	2 Prospective cohorts[32, 221] (695) 14 Retrospective studies[43, 53, 55, 72, 84, 86, 106, 110, 113, 147, 159, 191, 216, 222] (8,048)	Medium*	Direct	Consistent†	Precise	Undetected	High	Among patients who are diagnosed with stroke, the false discovery rate is 14% (95% CI, 8% to 19%). Among patients with a presumptive diagnosis of TIA, the false discovery rate is 49% (95% CI, 33% to 65%).
MI	3 Retrospective cohorts[71, 149, 157] (1563)	Medium	Direct	Inconsistent	Precise	Undetected	Low	Among patients who are referred for immediate cardiac catheterization, 14% will not have a MI.
AAD	1 study[107] (100)	High	Direct	NA (single study)	Imprecise	Undetected	Low	Among patients who are suspected of having an aortic aneurysm or dissection, 7% did not have this condition in the final diagnosis.
Venous thrombo-embolism	0 studies	NA	NA	NA	NA	NA	No studies	NA
Meningitis and encephalitis	0 studies	NA	NA	NA	NA	NA	No studies	NA
Sepsis	0 studies	NA	NA	NA	NA	NA	No studies	NA
Arterial thrombo-embolism	0 studies	NA	NA	NA	NA	NA	No studies	NA
Spinal and intracranial abscess	0 studies	NA	NA	NA	NA	NA	No studies	NA
Pneumonia	1 Prospective cohort[18] (236)	Medium	Direct	NA (single study)	Precise	Undetected	Low	Among patients initially diagnosed as pneumonia in the emergency department, 34% (95% CI 29% to 41%) are incorrect.

Condition	Number of Studies (Participants)	Study Limitations	Directness	Consistency	Precision	Reporting Bias	Strength of Evidence	Summary
Appendicitis	2 Prospective cohorts[25, 77] (330) 3 Retrospective cohorts[108, 137, 166] (3,917)	Medium	Direct	Consistent	Precise	Undetected	Moderate	While the sensitivity of appendicitis diagnosis in ED is very high, the false positive rate is relatively high. The studies included a combination of prospective and retrospective cohorts. However, case selection due to inclusion criteria for certain studies limited their generalizability.
Fractures	1 Prospective cohort[158] (125) 2 Retrospective cohorts[102, 176] (398)	Medium	Direct	Inconsistent	Imprecise	Undetected	Insufficient	We are unable to draw a conclusion.
Testicular torsion	1 Retrospective cohort[150] (46)	Medium	Direct	NA (Single study)	Imprecise	Undetected	Insufficient	We are unable to draw a conclusion.

* Observational studies, some with concerns of selection bias[147, 159] or lack of generalizability due to the use of specific local protocols.[32]
† Results are consistent within subtypes of stroke.

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