Table 4: Clinical evidence tables

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Full citation Al, R. A., Baykal, C., Karacay, O., Geyik, P. O., Altun, S., Dolen, I., Random urine protein-creatinine ratio to predict proteinuria in new-onset mild hypertension in late pregnancy, Obstetrics & Gynecology, 104, 367-71, 2004 **Ref Id** 658834 **Country/ies where the study was carried out** Turkey **Study type** Retrospective cohort study **Aim of the study** to assess diagnostic accuracy of random urine protein:creatinine ratio for prediction of significant proteinuria in patients with new onset mild hypertension in late pregnancy	**Sample size** n=185 **Characteristics** Age, median, years (range): 30 (17-44) Gestation, mean, weeks (SD): 32 (4) BP not reported **Inclusion Criteria** pregnant women with new onset mild hypertension (≥140/90mmHg) in late pregnancy **Exclusion Criteria** severe hypertension (>160/110mmHg measured twice at least 6 hrs apart), elevated liver enzymes, low platelet count syndrome, thrombocytopenia, eclampsia, IUGR,	**Tests** Index test: random urine protein:creatinine ratio (trichloroacetic acid reaction test) Reference standard: ≥ 300mg urinary protein excretion/24 hours	**Methods** 24-hour urine collections were started between 9am-12noon All random samples were collected in the morning before the start of the 24-hour urine collection Urine protein concentration was measured by trichloroacetic acid reaction (coefficient of variation 9%). The urinary creatinine test was performed with the Beckman Synchron LX Delta System (Beckman Instruments, Richmond, CA), which uses the Jaffe rate method.	**Results** AUC: 0.86 (0.80 to 0.93) Cut off 0.19 Sensitivity 85% (70 to 94)Specificity 73% (65 to 80) | | Reference test + | Reference test - | Total | | --- | --- | --- | --- | | Index test + | 33 | 39 | 72 | | Index test - | 6 | 107 | 113 | | Total | 39 | 146 | 185 | *Alternative cut points* Cut off 0.13 Sensitivity 90% (76 to 97)Specificity 65% (57 to 73) | | Reference test + | Reference test - | Total | | --- | --- | --- | --- | | Index test + | 35 | 51 | | | Index test - | 4 | 95 | | | Total | 39 | 146 | 185 | Cut off 0.18 Sensitivity 85% (70 to 94)Specificity 71% (63 to 78)	**Limitations Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Study dates
January 2002 - June 2003

Source of funding
Not reported</td>
<td>chronic hypertension, pre-existing renal disease, co-existing urinary tract infection, inadequate specimen collection</td>
<td></td>
<td></td>
<td>
<table>
<tr><td></td><td>Reference test +</td><td>Reference test -</td><td>Total</td></tr>
<tr><td>Index test +</td><td>33</td><td>42</td><td></td></tr>
<tr><td>Index test -</td><td>6</td><td>104</td><td></td></tr>
<tr><td>Total</td><td>39</td><td>146</td><td>185</td></tr>
</table>
Cut off 0.20 Sensitivity 80% (64 to 91)Specificity 74% (66 to 81)
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<tr><td></td><td>Reference test +</td><td>Reference test -</td><td>Total</td></tr>
<tr><td>Index test +</td><td>31</td><td>38</td><td></td></tr>
<tr><td>Index test -</td><td>8</td><td>108</td><td></td></tr>
<tr><td>Total</td><td>39</td><td>146</td><td>185</td></tr>
</table>
Cut off 0.49 Sensitivity 74% (58 to 87)Specificity 84% (77 to 90)
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<tr><td></td><td>Reference test +</td><td>Reference test -</td><td>Total</td></tr>
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<tr><td>Index test -</td><td>10</td><td>123</td><td></td></tr>
<tr><td>Total</td><td>39</td><td>146</td><td>185</td></tr>
</table>
</td>
<td>exclusions? yes

Could the selection of patients have introduced bias? RISK: LOW
B. CONCERNS REGARDING APPLICABILITY Is there concern that the included patients do not match the review question? CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS

1. Were the index test results interpreted</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? unclear **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the reference standard results interpreted without knowledge of the results of

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					the index test? unc lear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the analysis? No – included

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					n=185/204; 91% (n=221 with new onset mild hypertension; 204 who had 24hr urine analysis) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Amin, S. V., Illipilla, S., Hebbar, S., Rai, L., Kumar, P., Pai, M. V., Quantifying Proteinuria in Hypertensive Disorders of Pregnancy, International Journal of Hypertension, 2014, 941408, 2015 **Ref Id** 812372	**Sample size** n=102 (n=78 with proteinuria≥300mg/24hrs) **Characteristics** age: 27.4 ± 4.3 (20–41) years GA at delivery: 35.3 ± 3.3 (25–39) weeks	**Tests** Index test: random urine protein estimation (PCR) Reference test: 24 hour urine collection	**Methods** 24 hour urine collection: 24-hour urine protein estimation was carried out after admission. Patient was asked to discard the first void early morning sample.	**Results** cut-off values: 0.30, 0.45, 0.60, 0.75, 0.90 to predict proteinuria of >=300mg/day 0.30: Sens 89.7; Spec 54.2; LR+ 1.96; LR- 0.19; [TP 70; FP 11; FN 8; TN 13; back calculated by NGA] **0.45: 82.1; 87.5; 6.56; 0.21; AUC: 0.89 (0.83-0.95) [TP 64; FP 3; FN 14; TN 21; back calculated by NGA]** 0.60: 75.6; 87.5; 6.05; 0.28; [TP 59; FP 3; FN 19; TN 21; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Country/ies where the study was carried out India **Study type** Prospective cohort study **Aim of the study** comparison of diagnostic utility of two tests: urine dipstick method and spot urine protein:creatinine ratio in diagnosis of significant proteinuria in patients with hypertensive disorder of pregnancy **Study dates** July 2009 - June 2011 **Source of funding** Manipal University institutional grant	**Inclusion Criteria** Hypertensive disorders of pregnancy, recruited after GA 20weeks (hypertension: DBP>90, and SBP>110; or increase in SBP by 30 and DBP by 15) **Exclusion Criteria** all cases of chronic renal disease, secondary hypertension due to immunological diseases such as lupus erythematosus, and overt diabetes mellitus. Patients who delivered due to urgent indications for termination of pregnancy (could not complete 24-hour collection)			0.75: 67.9; 100; 33.29; 0.32 [TP 53; FP 0; FN 25; TN 24; back calculated by NGA] 0.90: 61.5; 100; 30.15; 0.38 [TP 48; FP 0; FN 30; TN 24]; back calculated by NGA]	random sample of patients enrolled? unclear 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? unclear

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard likely to correctly classify the target condition ? yes 2. Were the referenc e standard results interpret ed without knowled ge of the results of the index test? unc lear **Could the reference standard, its conduct, or its interpretatio n have introduced bias? RISK:LOW** **B. CONCERNS REGARDIN**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					G APPLICABILITY Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard ? yes 2. Did all patients receive a

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					3. Did patients receive the same reference standard? yes 4. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Bhatti, S., Cordina, M., Penna, L., Sherwood, R., Dew, T., Kametas, N. A., The effect of ethnicity on the performance of protein-	**Sample size** n=476 (all ethnicities) (n=106 with proteinuria≥300mg/24hrs; n=370 with <300)	**Tests** Index test: urine sample for PCR after completion of 24 hour collection Reference test: 24 hour urine collection	**Methods** Each patient provided a urine sample for the calculation of the PCR immediately after the completion of the 24-h urine collection. The urine samples	**Results** n=106 with proteinuria≥300mg/24hrs; n=370 with <300 **PCR cut-off: 30mg/mmol and "optimal" based on ROC curve**	**Limitations Risk of bias assessed using QUADAS-II**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
creatinine ratio in the prediction of significant proteinuria in pregnancies at risk of or with established hypertension: an implementation audit and cost implications, Acta Obstetricia et Gynecologica Scandinavica, 97, 598-607, 2018 **Ref Id** 838660 **Country/ies where the study was carried out** UK **Study type** Prospective cohort study **Aim of the study** assess the performance of PCR to predict proteinuria of ≥300 mg in a 24-h concentration in an antenatal population and comparing its cost-efficiency in black and nonblack populations **Study dates** January 2011 - December 2012	**Characteristics** 204 women of white, 239 women of black and 33 women with other (mixed) ethnicity age: 33.7 SD 5.6 years GA at referral: 35.3 (IQR 30.3-37.7) weeks **Inclusion Criteria** attending an antenatal hypertension clinic during study period: women with an increased risk of hypertensive complications, such as chronic hypertension or a history of hypertension in a previous pregnancy, women with new onset hypertension during their pregnancy **Exclusion Criteria** None reported		for PCR were not early morning samples PCR: Urinary protein quantitation was determined by the pyrogallol red molybdate dye-binding assay with the Advia 2400 analyzer (Siemens Healthcare, Frimley, Surrey) and urinary creatinine was determined by the modified Jaffe's reaction	30 mg/mmol: Sens 64.7 (54.8-73.8); Spec 94.6 (91.8-96.7); **[TP 69; FP 20; FN 37; TN 350; back calculated by NGA]** **"optimal for entire cohort" 20.56 mg/mmol:** 87.6 (79.8-93.2); 83.0 (78.9-86.7); **[TP 93; FP 63; FN 13, TN 307; back calculated by NGA]**	**DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Source of funding No specific funding grant					**B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? unclear

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					2. If a threshold was used, was it pre-specified ? unclear **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 3: REFERENCE STANDARD **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					its interpretation have introduced bias? RISK:LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 5. Was there appropriate interval

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					between index tests and reference standard? yes 6. Did all patients receive a reference standard? yes 7. Did patients receive the same reference standard? Yes 8. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW**

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>Other information</td></tr>
<tr><td>Full citation

Durnwald, C., Mercer, B., A prospective comparison of total protein/creatinine ratio versus 24-hour urine protein in women with suspected preeclampsia, American Journal of Obstetrics & Gynecology, 189, 848-52, 2003

Ref Id

658885

Country/ies where the study was carried out

USA

Study type

Prospective cohort study

Aim of the study
to assess the value of protein/creatinine ratio in prediction of 24 hour urinary protein in women with suspected pre-eclampsia</td><td>Sample size
n=220

Characteristics
Age, mean, years: 26.1
Gestation, mean, weeks: 36.5
BP not reported

Inclusion Criteria
pregnant women ≥ 24 weeks gestation, undergoing evaluation for suspected pre-eclampsia (including ≥ 1 of the following: hypertension, oedema, new-onset proteinuria on dipstick)

Exclusion Criteria
chronic hypertension, diabetes mellitus, renal disease, pre-existing proteinuria (1+ dipstick on initial office visit)</td><td>Tests
<u>Index test:</u> random urine protein:creatinine ratio (biuret reaction test)
<u>Reference standard:</u> ≥ 300mg urinary protein excretion/24 hours</td><td>Methods
a random urine collection was collected for the calculation of the protein/creatinine ratio before the initiation of the 24-hour urine collection
Proteinuria on 24-hour urine collection was defined as ‘‘significant’’ (>=300 mg) or ‘‘severe’’ (>=5000 mg), and mild proteinuria was defined as 300 to 4999 mg. Urinary protein quantitation was determined by the biuret reaction, and urinary creatinine was determined by the modified Jaffe´ reaction (Roche Laboratories)</td><td>Results
AUC: 0.80
n.b. cut offs are given as mg/g. Approximated to mg/mmol by conversion factor of 0.1, although actual conversion factor 0.113 <u>Cut off ~0.15 (150mg/g)</u>Sensitivity 92.9%Specificity 32.7%
<table><tr><td></td><td>Reference test +</td><td>Reference test -</td><td>Total</td></tr><tr><td>Index test +</td><td>156</td><td>35</td><td>191</td></tr><tr><td>Index test -</td><td>12</td><td>17</td><td>29</td></tr><tr><td>Total</td><td>168</td><td>52</td><td>220</td></tr></table><u>Cut off ~0.2 (200mg/g)</u>
Sensitivity 90.5%Specificity 48.1%
<table><tr><td></td><td>Reference test +</td><td>Reference test -</td><td>Total</td></tr></table></td><td>Limitations Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? unclear
2. Was a case-control design avoided? yes
3. Did the study avoid inappropriate</td></tr>
</table>

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Study dates
January 2001 - June 2002

Source of funding
National Center for Research Resources</td>
<td></td>
<td></td>
<td></td>
<td>
<table>
<tr><td>Index test +</td><td>152</td><td>27</td><td></td></tr>
<tr><td>Index test -</td><td>16</td><td>25</td><td></td></tr>
<tr><td>Total</td><td>168</td><td>52</td><td>220</td></tr>
</table>
<u>Cut off ~0.30 (300mg/g)</u>
Sensitivity 81.0%Specificity 55.8%
<table>
<tr><td></td><td>Reference test +</td><td>Reference test -</td><td>Total</td></tr>
<tr><td>Index test +</td><td>136</td><td>23</td><td></td></tr>
<tr><td>Index test -</td><td>32</td><td>29</td><td></td></tr>
<tr><td>Total</td><td>168</td><td>52</td><td>220</td></tr>
</table>
<u>Cut off ~0.39 (390mg/g)</u>
Sensitivity 72.6%Specificity 73.1%
</td>
<td>exclusions? yes

Could the selection of patients have introduced bias? RISK: LOW

B. CONCERNS REGARDING APPLICABILITY Is there concern that the included patients do not match the review question? CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS

1. Were the index test results interpret</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					ed without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? unclear **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index

	Reference test +	Reference test -	Total
Index test +	122	14	
Index test -	46	38	
Total	168	52	220

Cut off ~0.40 (400mg/g)
Sensitivity 71.4%Specificity 76.9%

	Reference test +	Reference test -	Total
Index test +	120	12	
Index test -	48	40	
Total	168	52	220

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>Cut off ~0.50 (500mg/g)
Sensitivity 63.1%Specificity 82.7%
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<tr><td>Index test -</td><td>62</td><td>43</td><td></td></tr>
<tr><td>Total</td><td>168</td><td>52</td><td>220</td></tr>
</table></td><td>test, its conduct, or interpretation differ from the review question? CONCERN: LOW

<u>DOMAIN 3: REFERENCE STANDARD</u>
A. RISK OF BIAS

1. Is the reference standard likely to correctly classify the target condition? yes
2. Were the reference standard results interpreted without knowledge of the</td></tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					results of the index test? unc lear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 4: FLOW AND TIMING **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Dwyer, B. K., Gorman, M., Carroll, I. R., Druzin, M., Urinalysis vs urine protein - Creatinine ratio to predict significant proteinuria in pregnancy, Journal of Perinatology, 28, 461-467, 2008 **Ref Id** 838685 **Country/ies where the study was carried out** USA **Study type** Prospective cohort study	**Sample size** n=116 (n=60 proteinuria<300mg/24hr ; n=56 proteinuria≥300mg/24hr) **Characteristics** <u>women with proteinuria≥300mg/day</u> age: 30.8 SD 6.5 years SBP: 143.3 SD 16.3 mmHg DBP: 91.5 SD 12.8 mmHg <u>women with proteinuria< 300mg/day</u> age: 30.8 SD 6.2 years SBP: 141.4 SD 13.1 mmHg	**Tests** Index test: spot urine PCR (prior to 24 hr collection if possible) Reference test: 24 hr urine collection	**Methods** Urine PCR were usually obtained immediately before the 24-h urine collection was begun. If that sample was not available at the time of enrolment, a sample was obtained immediately after the 24-h collection. Samples were collected via clean catch unless the membranes had been ruptured, in which case specimens were obtained by catheter Urinary protein and creatinine were measured using Synchron LX Systems (Beckman Coulter Inc., Fullerton, CA, USA), which uses the pyrogallol red/molybdate and Jaffe rate methods	**Results** n=60 proteinuria<300mg/24hr; n=56 proteinuria≥300mg/24hr **AUC=0.89 (0.83-0.95)** <u>cut-offs: ≥0.15 (maximise sensitivity), ≥0.28 (max specificity), ≥0.19 (optimise sens and spec)</u> 0.15: Sens 0.96 (0.87 - 0.99); spec 0.53 (0.40 - 0.66); [TP 54; FP 28; FN 2; TN 32; back calculated by NGA] **0.19: 0.89 (0.78 - 0.96); 0.70 (0.59-0.83); [TP 50; FP 18; FN 6; TN 42; back calculated by NGA]** 0.28: 0.66 (0.52 -0.78); 0.95 (0.86 - 0.99); [TP 37; FP 3; FN 19; TN 57; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Aim of the study To compare the urine protein–creatinine ratio with urinalysis to predict significant proteinuria (≥300 mg per day) **Study dates** September 2002 - March 2004 **Source of funding** supported by the Department of Gynecology and Obstetrics, Stanford University.	DBP: 89.3 SD 11.3 mmHg **Inclusion Criteria** all women being evaluated for pre-eclampsia, regardless of the alerting sign or symptom, suspected severity or comorbid conditions **Exclusion Criteria** urinalysis contained >10 WBCs per h.p.f., if a catheter was not used after membrane rupture or if an outpatient 24-h urine collection was incomplete				control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **DOMAIN 2: INDEX TESTS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					B. CONCERNS REGARDING APPLICABILITY Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the referenc

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					e standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard ? Yes 4. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Eslamian, L., Behnam, F., Tehrani, Z. F., Jamal, A., Marsoosi, V., Random urine protein creatinine ratio as a preadmission test in hypertensive pregnancies with urinary protein creatinine ratio, Acta Medica Iranica, 49, 81-4, 2011 **Ref Id** 658175	**Sample size** n=113 enrolled; n=100 in final analysis (n=46 proteinuria≥300mg/day; n=4 proteinuria≥2000mg/day) **Characteristics** age: 30.6 (19-44) years gestational age: 31 (22-39) weeks SBP: 145 (120-180) mmHg	**Tests** Index test: spot urine PCR Reference test: 24 hr urine collection (proteinuria ≥300mg/day)	**Methods** Random urine sample for assessing PCR was obtained after admission, excluding the 1st voided morning urine. 24h urine collection started from 8 AM on the morning following admission. patients were on moderate bed rest and were recommended to have a left lateral decubitis position when in bed. They were allowed to spend a few hours out of bed.	**Results** n=46 proteinuria≥300mg/day; n=54 proteinuria <300mg/day AUC: 0.926 (95%CI 0.854-0.995) cut off: 0.22mg/mg: sens 0.879; spec 0.926 [TP 40; FP 4; FN 6; TN 50; back calculated by NGA]	**Limitations Risk of bias assessed using QUADAS-II <u>DOMAIN 1: PATIENT SELECTION</u> A. RISK OF BIAS** 1. Was a consecutive or random sample

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Country/ies where the study was carried out Iran **Study type** Case-series **Aim of the study** to determine whether random urine PCR can be used to rule out significant proteinaria (≥300mg/dl) and to use it as a pre admission test in suspected cases of PE **Study dates** October 2007 - January 2009 **Source of funding** Not reported	DBP: 91.9 (90-110) mmHg **Inclusion Criteria** All pregnant women with new onset hypertension ≥140/90 mmHg after GA of 20 weeks **Exclusion Criteria** • Women suspected of having urinary tract infection • Chronic hypertension before pregnancy or in the first half of pregnancy • Pre-existing renal disease with proteinuria • Women with diabetic nephropathy		Urine protein and creatinine were measured by Biosystems (Barcelona, Spain).		of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretatio**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					n of the index test have introduced bias? RISK: UNCLEAR **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					classify the target condition ? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard ? yes 3. Did patients receive the same reference standard ? Yes 4. Were all patients included in the analysis? No – n=100/113; 88% (113 enrolled, excluded due to inadequate 24 hour collection) **Could the patient flow have introduced bias? RISK: LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Other information
Full citation Kucukgoz Gulec, U., Sucu, M., Ozgunen, F. T., Buyukkurt, S., Guzel, A. B., Paydas, S., Spot Urine Protein-to-Creatinine Ratio to Predict the Magnitude of 24-Hour Total Proteinuria in Preeclampsia of Varying Severity, Journal of Obstetrics & Gynaecology Canada: JOGC, 21, 21, 2017 **Ref Id** 658938 **Country/ies where the study was carried out** Turkey **Study type** Prospective cohort study **Aim of the study** assess the diagnostic accuracy of spot urine PCR for ascertaining the magnitude of proteinuria in women with PE of varying severity	**Sample size** n=276 enrolled; n=205 in final analysis (n=41/205 proteinuria<300mg/24hrs; n=164/205 proteinuria≥300mg/24hrs) **Characteristics** age: 30.1 SD 7.4 years; median 30.0 (range 16-50) GA: 33.7 SD 4.6 weeks; median 34 (range 20-41) **Inclusion Criteria** pregnant women being evaluated for PE **Exclusion Criteria** concurrent diseases: • urinary tract infection, • chronic hypertension,	**Tests** Index test: spot clean catch urine PCR (immediately after 24 hr urine collection) reference test: 24 hour urine collection (proteinuria≥300mg/24hr)	**Methods** Evaluation of PCR did not change treatment/management. Urinary protein and creatinine were measured by the Pyrogallol Red and picrate methods, respectively (Beckman Coulter DXC 800, Beckman Coulter, Krefeld, Germany).	**Results** n=164/205 proteinuria≥300mg/24hrs <u>PCR cut-off:</u> 0.53mg/mg: sensitivity 81.2%; specificity 93.2%; AUC 0.91; [TP 133; FP 3; FN 31; TN 38; back calculated by NGA] 0.28mg/mg: sensitivity 82%; specificity 71%; AUC 0.78; [TP 134; FP 12; FN 30; TN 29; back calculated by NGA]	**Limitations Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates May 2011 - March 2013 **Source of funding** Not reported	• diabetes mellitus • pre-existing renal disease • systemic diseases such as systemic lupus erythematosus				exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpret

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					ed without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the reference standard results interpreted without knowledge of the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the analysis? No – included

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					n=205/276; 74% (excluded because 24-hour urine was not collected and/or PCR was not measured) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Kyle, P. M., Fielder, J. N., Pullar, B., Horwood, L. J., Moore, M. P., Comparison of methods to identify significant proteinuria in pregnancy in the outpatient setting, BJOG: An International Journal of Obstetrics and Gynaecology, 115, 523-527, 2008	**Sample size** n=188 recruited; n=150 in final analysis (at testing, n=13 had proteinuria≥300mg/24hr) **Characteristics** *median (range)*	**Tests** Index test: spot urine PCR, and spot urine ACR Reference test: 24 hr urine collection (after spot tests)	**Methods** Spot urine tests before 24 hr urine collection. First morning void discarded. Participants were encouraged to complete the 24-hour specimen as soon as possible and were given up to 3 days to do so. Mid-stream urine sample was separated into three aliquots for testing including (1) PCR, (2)	**Results** n=13/150 had proteinuria≥300mg/day **<u>ACR cut-offs: ≥8.0; ≥3.5, ≥2.0 mg/mmol</u>** AUC: 0.991 (95%CI 0.974 - 1.000) ≥2.0: sens 100 (75.3-100); spec 67.9 (59.4-75.6); LR+ 3.1 (2.4-4.0); LR- 0.0 (-); [TP 13; FP 44; FN 0; TN 93]; back calculated by NGA] ≥3.5: sens 100 (75.3-100); spec 87.6 (80.9-92.6); LR+ 8.1 (5.2-	**Limitations** **Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Ref Id 838719 **Country/ies where the study was carried out** New Zealand **Study type** Prospective cohort study **Aim of the study** examine the efficacy of the ACR (DCA 2000) in the detection of significant proteinuria when performed in outpatient antenatal clinics compared with the automated dipstick, PCR, and the 24-hour urine protein **Study dates** Not reported **Source of funding** University of Otago Grant 2005, Canterbury District Health Board Research Grant 2005, and Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG)	GA at testing:34.0 (20.1–39.7) weeks SBP: 120 (90–172) mmHg DBP: 75.5 (50–110) mmHg **Inclusion Criteria** Women greater than 20 weeks of gestation (single or multiple gestation) attending the high-risk obstetric medical antenatal clinic **Exclusion Criteria** positive urine culture for urinary tract infection, underlying proteinuric renal disease, diabetes with an abnormal ACR in the first trimester		ACR (DCA 2000), and (3) culture and sensitivity: A spot sample for a PCR was sent to Canterbury Health Laboratories (Abbott Ci8200 Analysers; Chicago, IL, USA). This test quantifies the amount of proteinuria and standardises it against the creatinine concentration. These results take up to 2–4 hours to obtain. A spot sample for an ACR was performed in the antenatal clinic using the DCA 2000 (Bayer Healthcare LLC). The DCA 2000 is a point of care system used to estimate the ACR from a small (40 ml) sample of urine.	12.6); LR- 0.0 (-); [TP 13; FP 17; FN 0; TN 120; back calculated by NGA] **≥8.0: sens 100 (75.3-100); spec 96.4 (91.7-98.8); LR+ 27.4 (11.6-64.8); LR- 0.00 (-) [TP 13; FP 5; FN 0; TN 132; back calculated by NGA]** **<u>PCR ≥30.0mg/mmol</u>** AUC: 0.988 (95%CI 0.971 - 1.000) **≥30.0:** sens 92.3 (64.0-99.8); spec 97.1 (92.7-99.2); LR+ 31.6 (11.9-84.1); LR- 0.1 (0.01-0.52); [TP 12; FP 4; FN 1; TN 133; back calculated by NGA]	1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABIL**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Trainee Scholarship awarded to JNF 2005					**ITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? unclear 2. If a threshold was used, was it pre-

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					B. CONCERNS REGARDING APPLICABILITY Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard ? yes 2. Did all patients receive a reference standard ? yes 3. Did patients receive the same reference standard ? Yes 4. Were all patients included in the analysis? No – included n=150/188; 80% (35 excluded for incomplete 24 hour urine, 3 for having UTI)

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the patient flow have introduced bias? RISK: LOW **Other information**
Full citation Lamontagne, A., Cote, A. M., Rey, E., The urinary protein-to-creatinine ratio in Canadian women at risk of preeclampsia: does the time of day of testing matter?, Journal of Obstetrics & Gynaecology Canada: JOGC, 36, 303-8, 2014 **Ref Id** 658283 **Country/ies where the study was carried out** Canada **Study type** Prospective cohort study **Aim of the study** determine the performance of a protein-to-creatinine ratio threshold of 30mg/mmol	**Sample size** n=119 samples; n=91 in final analysis (n=43 with proteiuria≥300mg/day) **Characteristics** age: 31.8 SD 5.8 years GA at testing: 32.3 SD 3.7 weeks **Inclusion Criteria** older than 18 years, in their second or third trimester of pregnancy, ambulatory, and had an indication for a 24-hour urine collection as part of investigation for pre-eclampsia **Exclusion Criteria**	**Tests** Index test: urine PCR provided at any moment during the day Reference test: 24 hour urine collection (proteinuria ≥300mg/24hrs)	**Methods** Urinalysis, urine culture, and a PCR calculation were performed on the same urine sample provided at any moment during the day. The 24-hour urine collection began immediately afterwards to evaluate 24-hour excretion of protein and creatinine. The physician providing management was blinded to the protein-to-creatinine ratio result. Protein concentration in the urine was determined by a colorimetric method using pyrogallol red-molybdate. Urinary and plasma creatinine concentrations were measured with the Jaffé method. All analyses were performed by the Beckman Coulter multianalyzer with the Synchron LX system (Beckman Coulter Canada LLP, Mississauga, ON). The protein-to-creatinine ratio was	**Results** proteinuria≥300mg/day: n=43/91 PCR cut-off: 30mg/mmol All samples (n=91) **AUC: 0.99 (95%CI 0.97 to 1.0); Sens 81% (67 to 92); Spec 98% (89 to 100); LR+ 39 (6 to 273); LR- 0.19 (0.1 to 0.4); [TP 35; FP 1; FN 8; TN 47; back calculated by NGA]** First morning sample (n=30; no detail on number with +ve ref standard therefore cannot back calculate) AUC: 0.94 (0.86 to 1.0); Sens 58 (28 to 85); Spec 93 (66 to 100); LR+ 8 (1.2 to 57.3); LR- 0.45 (0.2 to 0.9) All samples except first morning void (n=61; no detail on number with +ve ref standard therefore cannot back calculate) AUC: 1.0 (0.99 to 1.0); Sens 90% (74 to 98); Spec 100% (90 to 100); LR+ not calc; LR- 0.1 (0.03 to 0.3)	**Limitations Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
in pregnant women investigated for hypertension according to the time of day of the sample **Study dates** November 2005 - November 2006 **Source of funding** Not reported	serum creatinine level > 150 µmol/L, history of renal transplant, pre-existing microalbuminuria or proteinuria, macroscopic hematuria, known urinary tract infection, and incomplete urine collections, defined by a urinary creatinine < 10 mmol/kg of pre-pregnancy weight		expressed in mg/mmol (mg/mmol = mg/mg × 0.113).		3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **DOMAIN 2: INDEX TESTS** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Were the index test results interpreted without knowledge of the results of the reference standard? yes 2. If a threshold was used, was it pre-specified? yes **Could the conduct or interpretation of the index test have introduced bias?** **RISK: LOW** **B. CONCERNS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					REGARDING APPLICABILITY Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					results interpreted without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question?

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					4. Were all patients included in the analysis? No – included n=91/119; 76% (exclusions because of labour (n = 6), incomplete 24-hour collection (n = 2), renal insufficiency (n = 1), urinary tract infection (n = 1), previous collection in the study (n = 6), and laboratory problems (form

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					error, n = 12)) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Leanos-Miranda, A., Marquez-Acosta, J., Romero-Arauz, F., Cardenas-Mondragon, G. M., Rivera-Leanos, R., Isordia-Salas, I., Ulloa-Aguirre, A., Protein:creatinine ratio in random urine samples is a reliable marker of increased 24-hour protein excretion in hospitalized women with hypertensive disorders of pregnancy, Clinical Chemistry, 53, 1623-8, 2007 **Ref Id** 658946 **Country/ies where the study was carried out** Mexico	**Sample size** n=1198 enrolled; n=927 in final analysis (proteinuria≥300mg/day n=282) **Characteristics** age: 28.6 (6.2) years (range 14–45 years) GA: 33 weeks (range 21–40 weeks) **Inclusion Criteria** GA≥20 weeks had new onset of hypertension with or without suspicion of pre-eclampsia or chronic hypertension (before 20 weeks of gestation) with suspected	**Tests** Index test: random urine sample for PCR (before or after start of 24 hr collection; not first voided sample) Reference test: 24 hour urine collection	**Methods** Urine protein was measured by the Bradford method (Bio-Rad Protein Assay Kit, Bio-Rad Laboratories) using BSA (Bio-Rad) as a calibrator. Assay manually as described by the manufacturer. Urine creatinine was measured by the modified kinetic Jaffe reaction in a 96-well plate with a filter at 490 nm.	**Results** proteinuria≥300mg/day n=282/927 PCR cut-off: 30mg/mmol AUC 0.998 (95%CI 0.993-1.0); Sens 98.2% (95.9-99.4); spec 98.8% (97.6-99.5); LR+ 79.2 (39.8-157.7); LR- 0.02 (0.008-0.043); FP 8; FN 5; [TP 277; TN 637; back calculated by NGA] proteinuria≥2g/day PCR cut off: 1.45 AUC 0.998 (0.993-1.0); sens 100% (95.6-100); spec 97% (95.7-98.1); LR+ 33.8	**Limitations Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study type Prospective cohort study **Aim of the study** assess whether measurement of urine PCR in a single urine specimen in clinical practice provides a reliable estimate of significant proteinuria (≥300mg/24hrs) in women with hypertensive disorders of pregnancy **Study dates** Not reported **Source of funding** Grant funding/support: This study was supported by Grant FP-2005/1/I/119 (to A.L.-M.) from the Fondo para el Fomento de la Investigacion-IMSS, Mexico	superimposed pre-eclampsia. hospitalized pregnant women (GA≥20 weeks) where a hypertensive disorder of pregnancy was ruled out were also included in the study **Exclusion Criteria** Not reported				avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? unclear **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					B. CONCERNS REGARDING APPLICABILITY Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					reference standard? Yes 4. Were all patients included in the analysis? No – included N=927/1198; 77% (271 excluded for inadequate 24 hour urine collection) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation	**Sample size**	**Tests**	**Methods**	**Results**	**Limitations**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Mohseni, S. M., Moez, N., Naghizadeh, M. M., Abbasi, M., Khodashenas, Z., Correlation of random urinary protein to creatinine ratio in 24-hour urine samples of pregnant women with preeclampsia, Journal of Family & Reproductive Health, 7, 95-101, 2013 **Ref Id** 658966 **Country/ies where the study was carried out** Iran **Study type** Prospective cohort study **Aim of the study** determine the value of random urinary protein to creatinine ratio (UPCR) for diagnosis of proteinuria in pregnant women with PE **Study dates** May 2006 - May 2008 **Source of funding**	n=66 (proteinuria≥300mg n=49) **Characteristics** age: 24.45 SD 7.6 years (range 14-46) GA: 28.18 SD 2.75 weeks (24-35) **Inclusion Criteria** GA≥24 weeks, diagnosed with increase in blood pressure after 20th week of pregnancy to≥140/90mm Hg, and subjected to a 24-hour urine protein assay **Exclusion Criteria** chronic hypertension, diabetic mellitus, kidney disease and urinary infection	Index test: samples at 10am and 4pm (first voided sample discarded) Reference test: 24 hr urine collection (proteinuria≥300mg/24hrs)	Urine creatinine was assayed using Jaffe reaction and picric acid reagent.(Roche, Germany). Proteinuria in the 24-hour urine collection was assayed using the turbidimetric test along with the Trichloro - acetic acid reagent. All reagents were prepared by the Roche, Germany Company.	proteinuria≥300mg n=49/66 <u>PCR cut offs at 10am:</u> AUC 0.890 SE 0.055 0.299: TN 13; FN 2; FP 6; TP 46 0.349: 14; 3; 5; 45 0.399: 14; 4; 5; 44 0.449: 16; 6; 3; 42 0.499: 16; 6; 3; 42 0.549: 16; 8; 3; 40 **0.595mg: sens 91.67%; spec 94.74% [TP 45; FP 1; FN 4; TN 16; back calculated by NGA]** 0.599: 16; 8; 3; 40 <u>PCR cut offs at 4pm:</u> AUC 0.932 SE 0.049 0.399: TN 15; FN 2; FP 4; TP 46 0.449: 16; 2; 3; 46 **0.470mg: sens 87.5%; spec 84.21% [TP 43; FP 3; FN 6; TN 14; back calculated by NGA]** 0.499: 16; 3; 3; 45 0.549: 17; 4; 2; 44 0.599: 18; 4; 1; 44 0.649: 18; 5; 1; 43 0.699: 18; 8; 1; 40 0.749: 18; 12; 1; 36 0.799: 18; 13; 1; 35	**Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Not reported					**introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the referenc

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					e standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question?

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Was there appropriate interval between index tests and reference standard ? yes 2. Did all patients receive a reference standard ? yes 3. Did patients receive the same reference standard ? Yes 4. Were all patients included in the analysis? yes **Could the patient flow**

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<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>have introduced bias? RISK: LOW

Other information</td></tr>
<tr><td>Full citation

Nisar, N., Akhtar, N., Dars, S., Diagnostic accuracy of spot urine protein-creatinine ratio in women with pre-eclapmsia, Medical Forum Monthly, 28, 6-10, 2017

Ref Id

838736

Country/ies where the study was carried out

India

Study type

Descriptive

Aim of the study
to determine the diagnostic accuracy of spot urine PCR in women with PE compared with 24-hour urine protein excretion

Study dates</td><td>Sample size
n=404 (n=246 PE according to 24hr collection; n=358 PE according to PCR)

Characteristics
age: 27.08 SD 5.84 years (range 16-40)
GA at testing: 36.26 SD 4.59 weeks
SBP: 161.68 SD 19.59 mmHg
DBP: 104.70 SD 12.65 mmHg

Inclusion Criteria
GA≥20 weeks, SBP≥140mmHg, or DBP≥90mmHg

Exclusion Criteria
women with ruptured membranes, and who delivered during urine</td><td>Tests
Index test: spot mid-stream urine sample (taken before 24 hr collection; PCR cut off set at 0.2)
Reference test: 24 hour urine collection: 8am to 8am</td><td>Methods
Spot urine sample prior to 24 hr collection.
Total protein concentration was measured by biuret colorimeter assay and creatinine level measured by modified Jaffe test.
If PE was confirmed, women were treated.</td><td>Results
n=246/404 PE (≥300mg/24hr) according to 24hr collection
PCR cut off 0.2: Sensitivity 0.975; Specificity 0.253
<table><tr><td></td><td>24hr +ve</td><td>24hr -ve</td><td>total</td></tr><tr><td>PCR +ve</td><td>240</td><td>118</td><td>358</td></tr><tr><td>PCR -ve</td><td>6</td><td>40</td><td>46</td></tr><tr><td>total</td><td>246</td><td>158</td><td>404</td></tr></table></td><td>Limitations Risk of bias assessed using QUADAS-II
<u>DOMAIN 1: PATIENT SELECTION</u>
A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? yes
2. Was a case-control design avoided? yes
3. Did the study avoid</td></tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
20 February 2015 - 19 February 2016 **Source of funding** Not reported	collection, women with urinary tract infection and associated medical disorders (renal disease, diabetes mellitus), women who had bedrest longer than 24 hours at presentation				inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **DOMAIN 2: INDEX TESTS** **A. RISK OF BIAS** 1. Were the index test

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? yes **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the reference standard results interpreted without

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 4: FLOW AND TIMING **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Park, Jung-Hwa, Chung, Dawn, Cho, Hee-Young, Kim, Young-Han, Son, Ga-Hyun, Park, Yong-Won, Kwon, Ja-Young, Random urine protein/creatinine ratio readily predicts proteinuria in preeclampsia, Obstetrics & gynecology science, 56, 8-14, 2013 **Ref Id** 813552 **Country/ies where the study was carried out** South Korea **Study type**	**Sample size** n=140 evaluated; n=79/140 assigned to PCR or 24 hr collection; n=33/79 excluded; n=46 where both 24 hr and spot urine collection were available (proteinuria<300mg/24hrs n=2/46; proteinuria 300mg-5000mg/24hrs n=38/46; proteinuria≥5g/24hrs n=6/46) **Characteristics** age: 33.2 SD 4.8 years (range 19-43) GA at delivery: 33.3 SD 3.4 weeks (range 27-40)	**Tests** Index test: random urine PCR using a catheter (before 24 hour collection started) Reference test: 24 hour urine collection (proteinuria≥300mg/24hrs)	**Methods** Urine collected via catheterization for the random urine PCR and the urinary dipstick test. Then, a 24-hour urine was collected via a clean catch. Random urine PCR was determined by a Hitachi 7180 Autoanalyzer (Hitachi, Tokyo, Japan)	**Results** **proteinuria<300mg/24hrs n=2/46; proteinuria≥300mg/24hrs n=44/46** AUC 0.958 (95%CI 0.903-1.0): optimal cutoff 0.63 Sensitivity 87.1%; Specificity 100%; [TP 38; FP 0; FN 6; TN 2; back calculated by NGA] **proteinuria≥5g/24hrs n=6/46: optimal cut-off 4.68** AUC 0.921 (1.074-2.002 [as reported in study]); sensitivity 100%; specificity 85%; [TP 6; FP 6; FN 0; TN 34; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Retrospective cohort study **Aim of the study** assess the diagnostic accuracy of random urine PCR for prediction of significant proteinuria in PE as an alternative to the time-consuming 24-hour urine protein collection **Study dates** January 2006 - June 2011 **Source of funding** National Research Foundation of Korea Grant funded by the Korean Government (2010-0010727)	SBP at admission: 157.8 SD 20.7 mmHg (range 108.0-200.0) DBP at admission: 97/5 SD 9.5 mmHg (range 74.0-120.0) **Inclusion Criteria** Women with symptoms of PE and more than one clinical finding: hypertension, edema accompanied by rapid weight gain with or without headache, and new-onset proteinuria on a urinary dipstick test **Exclusion Criteria** Concurrent preexisting renal disease such as immunoglobulin (Ig) A nephropathy				control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					<u>DOMAIN 2: INDEX TESTS</u> **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					bias? RISK: UNCLEAR **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					condition ? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					defined by the reference standard does not match the review question? CONCERN: UNCLEAR - confusion over data presented **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard ? yes 3. Did patients receive the same reference standard ? Yes 4. Were all patients included in the analysis? No - included n=46/140 ; 33% (n=140 evaluated for PE; n=79/140 assessed using PCR or 24 hr collection ; n=33/79 excluded for incomplete 24hr urine – labour started)

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the patient flow have introduced bias? RISK: LOW **Other information**
Full citation Rizk, D. E. E., Agarwal, M. M., Pathan, J. Y., Obineche, E. N., Predicting proteinuria in hypertensive pregnancies with urinary protein-creatinine or calcium-creatinine ratio, Journal of Perinatology, 27, 272-277, 2007 **Ref Id** 776570 **Country/ies where the study was carried out** United Arab Emirates **Study type** Prospective cohort study **Aim of the study**	**Sample size** n=95 recruited; n=83 in final analysis (n=51 proteinuria≥300mg/24hrs) **Characteristics** age: 29.4 SD 6.6 years (range 16-45) GA at sampling: 32.1 SD 1.6 weeks (range 22-38) SBP at sampling: 153.3 SD 12.9 mmHg (range 130-170) DBP at sampling: 97.2 SD 8.2 mmHg (range 90-110) **Inclusion Criteria** Attended study hospital for management of	**Tests** Index test: spot clean-catch and midstream voided urine sample for PCR (not first morning void) immediately before 24hr collection started Reference test: 24 hr urine collection (8am on morning after admission to 8am following day)	**Methods** None of the spot samples was first-voided morning urine. Spot urine test immediately before 24hr collection. Urinary protein, creatinine and calcium concentrations were measured by a standard technique using the Beckman Synchron (Beckman-Coulter Instruments, Brea, CA, USA). Individual results of spot urinary assays were not made available to the obstetricians responsible for patient care, or the lab technicians and study investigators.	**Results** n=51/83 proteinuria≥300mg/24hrs; n=4/83 proteinuria>5g/24hrs **AUC=0.82 (95%CI 0.72- 0.91)** PCR cut-offs: 0.19, 0.36, 0.55, 0.86, 1.4 **>0.19: n=51; Sens 80.4%; Spec 68.8%; LR+ 2.57; LR- 3.51; [TP 41; FP 10; FN 10; TN 22; back calculated by NGA]** >0.36: n=42; 68.6%; 78.1%; 3.14; 2.49; [TP 35; FP 7; FN 16; TN 25; back calculated by NGA] >0.55: n=31; 52.9%; 87.5%; 4.24; 1.86; [TP 27; FP 4; FN 24; TN 28; back calculated by NGA] >0.86: n=24; 43.1%; 93.8%; 6.90; 1.65; [TP 22; FP 2; FN 29; TN 30; back calculated by NGA] >1.4: n=19; 35.3%; 96.9%; 11.29; 1.50; [TP 18; FP 1; FN 33; TN31; back calculated by NGA]	**Limitations Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Evaluate the value of random urinary PCR and calcium-creatinine (CaCr) ratios to predict 24-h proteinuria in hypertensive pregnancies **Study dates** 1 Novemeber 2005 - 28 February 2006 **Source of funding** Not reported	hypertension in study period **Exclusion Criteria** Women with intrauterine fetal death, coexisting or recurrent urinary tract infection and current diuretic therapy within 7 days of the hospital visit and immuno-compromised patients. Women who have been placed on long-term bed rest at home or strict bed rest in another hospital for more than 36 h before admission				avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **DOMAIN 2: INDEX TESTS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Were the index test results interpreted without knowledge of the results of the reference standard ? yes 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias?** **RISK: LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					B. CONCERNS REGARDING APPLICABILITY Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the referenc

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					e standard results interpreted without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard ? Yes 4. Were all patients included in the analysis? No – included n=83/95; 87% (exclusions: n=7 for inadequate 24 hour urine sample; 5 women refused to participate) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation	**Sample size**	**Tests**	**Methods**	**Results**	**Limitations**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Rodriguez-Thompson, D., Lieberman, E. S., Use of a random urinary protein-to-creatinine ratio for the diagnosis of significant proteinuria during pregnancy, American Journal of Obstetrics & Gynecology, 185, 808-11, 2001 **Ref Id** 659003 **Country/ies where the study was carried out** USA **Study type** Retrospective cohort study **Aim of the study** evaluate whether a random urinary PCR is a clinically useful predictor of significant proteinuria (300mg/24 hour) **Study dates** Not reported **Source of funding** Not reported	n=138 (n=69 proteinuria ≥300mg/24hrs) **Characteristics** median age: 30 years (range 16-49) **Inclusion Criteria** Had both random PCR and 24 hour urine collection **Exclusion Criteria** Patients with pre-existing intrinsic renal disease	Index test: random urinary PCR (before 24 hr collection, and not first morning void) Reference test: 24 hr urine collection (proteinuria≥300mg/24hrs)	Medical records searched for completion of both 24 hour urine collection and random urinary PCR. All random samples collected before 24 hour collection, not first voided. Urinary protein concentration was determined with the use of the Dimension (Dade Behning, Inc, Nework, Del) clinical chemistry system UCFP method, which uses the pyrogallol red-molybdate method; urinary creatinine test was performed with the use of the Dimension (Dade Behning) clinical chemistry system CREA method, which uses a modified Jaffe reaction. Results could be accessed by the clinicians, but no clinical decision was based on the random urine PCR during the study period	n=69/138 proteinuria ≥300mg/24hrs AUC 0.9143 (95%CI 0.87-0.96) PCR cut-offs: 0.14: sens 1.00; spec 0.51; [TP 69; FP 34; FN 0; TN 35; back calculated by NGA] 0.15: 0.99; 0.51; [TP 68; FP 34; FN 1; TN 35; back calculated by NGA] 0.16: 0.99; 0.62; [TP 68; FP 26; FN 1; TN 43; back calculated by NGA] 0.17: 0.94; 0.64; [TP 65; FP 25; FN 4; TN 44; back calculated by NGA] 0.18: 0.90; 0.65; [TP 62; FP 24; FN 7; TN 45; back calculated by NGA] **0.19: sens 90%; spec 70%; FN 7; FP 21; [TP 62; TN 48; calculated by NGA]** 0.20: 0.88; 0.72; [TP 61; FP 19; FN 8; TN 50; back calculated by NGA] 0.21: 0.88; 0.75; [TP 61; FP 17; FN 8; TN 52; back calculated by NGA]	**Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					introduced bias? RISK: LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the referenc

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					e standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question?

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear - clinicians had

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					access to the results, but were not used for clinical decisions (if checked) **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					4. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Saudan, P. J., Brown, M. A., Farrell, T., Shaw, L., Improved methods of assessing proteinuria in hypertensive pregnancy, British Journal of Obstetrics & Gynaecology, 104, 1159-64, 1997 **Ref Id** 659007 **Country/ies where the study was carried out** Australia **Study type**	**Sample size** n=103 enrolled; n=100 in final analysis (14% had proteinuria≥300mg/24hrs and PCR>380mg/mmol) **Characteristics** Not reported **Inclusion Criteria** Pregnant women admitted to hospital or pregnancy day assessment unit for	**Tests** Index test: spot midstream urine sample usually (not always) obtained in the morning (before 24 hr collection started) Reference test: 24 hour urine collection (proteinuria≥300mg/24hrs)	**Methods** Urine protein was measured by a benzethoniwn chloride turbidometric method and urine creatinine by the Jaffe method, both using an Hitachi 911 autoanalyser (Boehringer Manheim)	**Results** n=14/100 proteinuria≥300mg/24hrs PCR cut-off: 20: sens 100%; spec 69%; [TP 14; FP27; FN 0; TN 59; back calculated by NGA] 25: 95%; 84%; [TP 13; FP 14; FN 1; TN 72; back calculated by NGA] "optimal" 30mg/mmol: 93%; 92%; [TP 13; FP 7; FN 1; TN 79; back calculated by NGA] 35: 83%; 95%; [TP 12; FP 4; FN 2; TN 82; back calculated by NGA] 40: 81%; 97%; [TP 11; FP 3; FN 3; TN 83; back calculated by NGA] 45: 72%; 100%; [TP 10, FP 0; FN 4; TN 86; back calculated by NGA]	**Limitations Risk of bias assessed using QUADAS-II DOMAIN 1: PATIENT SELECTION A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Prospective cohort study **Aim of the study** determine whether use of an automated urinalysis device will improve the accuracy of detecting proteinuria, and whether spot urine protein to creatinine ratio will provide accurate quantitation of proteinuria in hypertensive pregnant women **Study dates** "a six month interval" **Source of funding** Division of Medicine and Southpath Pathology services, St George Hospital. Lead author was a recipient of the fonds de perfectionnement from the University Hospital, Geneva, Switzerland	management of their hypertensive disorders **Exclusion Criteria** Not reported				2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 2: INDEX TESTS **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					bias? RISK: UNCLEAR **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					condition ? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					receive the same reference standard? Yes 4. Were all patients included in the analysis? No – included n=100/103; 97% (only those with both 24 hour urine and PCR analysis) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Stout, M. J., Scifres, C. M., Stamilio, D. M., Diagnostic	**Sample size** n=356 (proteinuria≥300mg/day n=144)	**Tests** Index test: urine PCR sample prior to 24 hour collection	**Methods** Laboratory methodology used end-point assay colorimetric	**Results** proteinuria≥300mg/day n=144/356 AUC: 0.82 PCR cut-offs	**Limitations Risk of bias assessed**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
utility of urine protein-to-creatinine ratio for identifying proteinuria in pregnancy, Journal of Maternal-Fetal & Neonatal Medicine, 26, 66-70, 2013 **Ref Id** 658483 **Country/ies where the study was carried out** USA **Study type** Retrospective cohort study **Aim of the study** evaluate urine PCR alone and with uric acid and clinical factors to predict or exclude significant proteinuria (>300mg/day) in PE evaluations **Study dates** 2005 - 2007 **Source of funding** Not reported	**Characteristics** <u>women with proteinuria≥300mg/day</u> age: 27.5 SD 6.7 years (range 26.4-28.6) GA at study: 31.3 SD 3.8 weeks (range 30.7-31.9) SBP at first visit: 120.9 SD 18.4 mmHg (115.2-126.7) SBP (mean at study time): 147.5 SD 13.0 mmHg (145.3-149.6) DBP at first visit: 71.3 SD 16.5 mmHg (66.2-76.5) DBP (mean at study time): 89.4 SD 10.9 mmHg (87.6-91.2) **Inclusion Criteria** all patients (GA≥20weeks) with signs or symptoms concerning for the diagnosis of PE who were seen in the obstetrical triage unit and underwent blood pressure monitoring and laboratory evaluation	Reference test: 24 hour urine collection	(benzenethonium chloride) technique for 24hr urine protein and random urine protein and enzymatic creatinase for random urine creatinine.	**>0.08: sens 97%; spec 15%; LR+ 1.14; LR- 0.23; [TP140; FP 180; FN 4; TN 32; back calculated by NGA]** >0.12: 90%; 39%; 1.48; 0.25; [TP 130; FP 129; FN14; TN 83; back calculated by NGA] **>0.19: 78%; 70%; 2.60; 0.31; [TP 112; FP 64; FN 32; TN 148; back calculated by NGA]** >0.40: 50%; 92%; 7.08; 0.53; [TP 72; FP 17; FN 72; TN 195; back calculated by NGA] >0.45: 47%; 96%; 11.0; 0.56; [TP 68; FP 8; FN 76; TN 204; back calculated by NGA] **>1.19: 31%; >99%; 33.1; 0.70; [TP 45; FP 2; FN 99; TN 210; back calculated by NGA]**	**using QUADAS-II <u>DOMAIN 1: PATIENT SELECTION</u> A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
	Exclusion Criteria Proteinuria≥300mg/24hr before 20 weeks GA				**bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					standard ? unclear 2. If a threshold was used, was it pre-specified ? unclear **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question?

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **DOMAIN 4: FLOW AND TIMING** **A. RISK OF BIAS**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					1. Was there appropriate interval between index tests and reference standard ? yes 2. Did all patients receive a reference standard ? yes 3. Did patients receive the same reference standard ? Yes 4. Were all patients included in the analysis? yes **Could the patient flow**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					have introduced bias? RISK: LOW **Other information**
Full citation Tun, C., Quinones, J. N., Kurt, A., Smulian, J. C., Rochon, M., Comparison of 12-hour urine protein and protein:creatinine ratio with 24-hour urine protein for the diagnosis of preeclampsia, American Journal of Obstetrics & Gynecology, 207, 233.e1-8, 2012 **Ref Id** 658513 **Country/ies where the study was carried out** USA **Study type** Prospective cohort study **Aim of the study** evaluate the performance of the 12-hour urine protein >165 mg and PCR >0.15 for the prediction of 24 hour	**Sample size** n=102 enrolled; n=90 in final analysis (n=28 proteinuria≥300mg/24hrs) **Characteristics** women with proteinuria median age: 30 years (range 19-38) median GA: 32.8 weeks (range 24.0-35.4) median SBP on admission: 140 mmHg (117-158) median DBP on admission: 82 mmHg (64-112) **Inclusion Criteria** aged 18-55 years and GA>20 weeks admitted to the study antepartum unit who were undergoing a 24-hour urine collection for the	**Tests** Index test: urine PCR sample (initial urine specimen at time of presentation) - *if this was missed, it was taken from 24 hr collection itself, or immediately after 24hr collection* Reference test: 24 hr urine collection started on admission	**Methods** Only 24 hr urine collection was used for clinical management, spot PCR result unavailable to clinicians (blinded). Pre-specified PCR >0.15 to predict proteinuria≥300mg/24hrs for PE.	**Results** proteinuria≥300mg/24hrs n=28/90 pre-defined cut-off PCR 0.15 TN 30/62; TP 24/28; sens 89% (81-94); spec 49% (39-59); [FP 32; FN 4; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
urine protein of ≥300 mg in patients with suspected PE **Study dates** 1 July 2010 - 31 December 2011 **Source of funding** Lehigh Valley Health Network Department of Obstetrics and Gynecology Research Fund	diagnosis and/or management of PE **Exclusion Criteria** • known pre-pregnancy renal disease (defined as baseline 24hour urine protein≥300 mg) • clinical indication for delivery at the time of admission, • outside the maternal or gestational age parameters a • did not speak English • did not give informed consent for any reason • had been enrolled previously in the study				inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					results interpreted without knowledge of the results of the reference standard? yes 2. If a threshold was used, was it pre-specified? yes: 0.15 **Could the conduct or interpretation of the index test have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABIL**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					ITY Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the reference standard results interpreted

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					without knowledge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 4: FLOW AND TIMING **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					analysis? No – included n=90/102; 88% (excluded n=11 for birth during 24hr collection; n=1 lab error) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Valdes, E., Sepulveda-Martinez, A., Tong, A., Castro, M., Castro, D., Assessment of Protein: Creatinine Ratio versus 24-Hour Urine Protein in the Diagnosis of Preeclampsia, Gynecologic and Obstetric Investigation, 81, 78-83, 2016 **Ref Id**	**Sample size** n=72 in final analysis (proteinuria<300mg/day n=23/72; proteinuria>5g/day n=8/72) **Characteristics** age: 30.5 SD 5.95 years SBP: 151.6 SD 15.38 mmHg	**Tests** Index test: urine sample (15–20ml) collected for quantification of proteinuria and creatinuria concentrations Reference test: 24 hour urine collection (proteinuria>300mg/24hrs)	**Methods** Urine sample collected and stored at –20°C until end of study period (blinded to outcome)	**Results** proteinuria≥300mg/24hrs n=49/72 AUC: 0.8802 (95%CI 0.80230 - 0.95813) PCR cut-off: "optimal" at 0.36 sens 73%; spec 91% [TP 36; FP 2; FN 13; TN 21; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecut

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
838773 **Country/ies where the study was carried out** Chile **Study type** Prospective cohort study **Aim of the study** assess the effectiveness of the PCR in the differential diagnosis of pregnancy hypertensive disorder **Study dates** January 2012 - December 2012 **Source of funding** Oficina de Apoyo a la Investigación Clínica (OAIC) of Hospital Clínico Universidad de Chile (project No. 494/11; internal competition in free topics)	DBP: 94.3 SD 11.26 mmHg **Inclusion Criteria** Every woman admitted at the study hospital in study period with a diagnosis of pregnancy hypertensive disorder **Exclusion Criteria** • twin pregnancies • fetal birth defects (with antenatal diagnosis or diagnosed during the neonatal period) • chronic nephropathies • maternal age under 18 • gestational age <20 weeks • incomplete demographic and perinatal data				ive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? unclear 2. If a threshold was used, was it pre-specified? no

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the referenc

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					e standard likely to correctly classify the target condition ? yes 2. Were the referenc e standard results interpret ed without knowled ge of the results of the index test? yes **Could the reference standard, its conduct, or its interpretatio n have introduced bias? RISK: LOW** **B. CONCERNS REGARDIN**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					G APPLICABILITY Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard ? yes 2. Did all patients receive a

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					2. Is the reference standard likely to correctly classify the target condition? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Waugh, J., Hooper, R., Lamb, E., Robson, S., Shennan, A., Milne, F., Price, C., Thangaratinam, S., Berdunov, V., Bingham, J., Spot protein-creatinine ratio	**Sample size** n=1823 recruited; n=959 had all test data available (PE in n=475/959; severe PE in n=417/475)	**Tests** Index test: routine spot urine sample (recruitment sample): PCR and ACR (collected at recruitment, before 24 hr collection started)	**Methods** pre-specified thresholds of PCR≥30mg/mmol and ACR≥2mg/mmol. Proteinuria was defined as ≥300mg of protein from a 24 hour urine collection using the central laboratory's BZC assay.	**Results** **proteinuria≥300mg/24hrs n=475/959** ACR cut-off - *only data from **central laboratory ACR testing** of recruitment sample and central lab BZC assay of 24 hour urine (≥300mg/l) supplied*	**Limitations** **Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION**

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>and spot albumin-creatinine ratio in the assessment of pre-eclampsia: A diagnostic accuracy study with decision-analytic model-based economic evaluation and acceptability analysis, Health Technology Assessment, 21, 1-90, 2017

Ref Id

838777

Country/ies where the study was carried out

UK

Study type

Prospective cohort study

Aim of the study
evaluate the accuracy of quantitative assessments of spot PCR and spot ACR at different thresholds
in predicting severe PE compared with 24-hour urine protein measurement in pregnant women
with hypertension and suspected proteinuria

Study dates</td>
<td>Characteristics
median age: 30 years (IQR 26-34)
median GA: 37 weeks (IQR 36-39; range 23-43)
median SBP at recruitment: 145 mmHg (IQR 140-152)
median DBP at recruitment: 94 mmHg (IQR 90-100)

Inclusion Criteria
pregnant women aged ≥16 years, GA >20 weeks with new hypertension (systolic BP of ≥140 mmHg and/or diastolic BP of ≥90 mmHg) and a trace or more proteinuria on an automated dipstick urinalysis

Exclusion Criteria

• pre-existing renal disease (proteinuria before GA 20 weeks)</td>
<td>Reference test: 24 hour urine collection (proteinuria≥300mg/24hrs)</td>
<td>The start of 24-hour urine collection could be up to 24 hours after the random/recruitment sample test. A small amount of urine (five 1-ml aliquots) was taken from each
participant’s random/recruitment sample, frozen and stored at –80°C for secondary analysis. The remainder of
the random/recruitment sample was sent to the local laboratory for quantitative assessments of PCR.
Urine samples were sent from each participating site to a central laboratory for analysis using standardised methods. All data were entered into a clinical data management software package supplied by MedSciNet (Stockholm, Sweden)with web-based entry from each of the 36 clinical sites as well as the central lab:

• 24hr urine sample at central lab (BZC assay)
• ACR at central lab
• PCR at local laboratory
• PCR at central lab (BZC assay)
• PCR at central lab (PGR assay)</td>
<td>2mg/mmol (pre-specified): sens 99% (98 to 100); spec 23% (20 to 27; LR+ 1.29 (1.23 to 1.35); LR- 0.03 (0.00 to 0.07)
AUC: 0.92 (95%CI 0.91 to 0.94)
<table>
<tr><th></th><th>Ref +ve</th><th>Ref -ve</th><th>total</th></tr>
<tr><td>ACR≥2</td><td>471</td><td>359</td><td>830</td></tr>
<tr><td>ACR<2</td><td>4</td><td>125</td><td>129</td></tr>
<tr><td>total</td><td>475</td><td>484</td><td>959</td></tr>
</table>
PCR cut-off 30mg/mmol (pre-specified):
<u>data from local laboratory PCR testing of recruitment urine sample and central lab BZC assay of 24 hour urine (≥300mg/l)</u>
Sensitivity 93% (95%CI 90 to 95); Specificity 62% (95%CI 58 to 67); LR+ 2.47 (95%CI 2.18 to 2.76); LR- 0.11 (95%CI 0.08 to 0.15)
AUC: 0.90 (95%CI 0.88 to 0.92)
<table>
<tr><th></th><th>Ref +ve</th><th>Ref -ve</th><th>total</th></tr>
<tr><td>PCR≥30</td><td>441</td><td>182</td><td>623</td></tr>
<tr><td>PCR<30</td><td>34</td><td>302</td><td>336</td></tr>
<tr><td>total</td><td>475</td><td>484</td><td>959</td></tr>
</table>
</td>
<td>A. RISK OF BIAS

1. Was a consecutive or random sample of patients enrolled? yes
2. Was a case-control design avoided? yes
3. Did the study avoid inappropriate exclusions? yes

Could the selection of patients have introduced bias? RISK: LOW

B. CONCERNS REGARDIN</td>
</tr>
</table>

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>33 months up to 30 November 2015

Source of funding
National Institute Health Research (NIHR) Health Technology Assessment (HTA) programme as project number 10/65/02</td>
<td>• pre-gestational diabetes
• chronic hypertension</td>
<td></td>
<td></td>
<td><u>data from central laboratory PCR testing (BZC assay) of recruitment urine sample and central lab BZC assay of 24 hour urine (≥300mg/l)</u>
Sens 93% (90 to 95); spec 68% (63 to 72); LR+2.88 (2.50 to 3.26); LR- 0.11 (0.07 to 0.14)
AUC: 0.91 (95%CI 0.90 to 0.93)
<table>
<tr><td></td><td>Ref +ve</td><td>Ref - ve</td><td>total</td></tr>
<tr><td>PCR≥30</td><td>441</td><td>156</td><td>597</td></tr>
<tr><td>PCR<30</td><td>34</td><td>328</td><td>362</td></tr>
<tr><td>total</td><td>475</td><td>484</td><td>959</td></tr>
</table>
<u>data from central laboratory PCR testing (PGR assay) of recruitment urine sample and central lab BZC assay of 24 hour urine (≥300mg/l)</u>
Sens 95% (92 to 97); spec 56% (51 to 60); LR+ 2.14 (1.93 to 2.35); LR- 0.09 (0.00 to 0.07)
AUC: 0.91 (95%CI 0.89 to 0.93)
<table>
<tr><td></td><td>Ref +ve</td><td>Ref - ve</td><td>total</td></tr>
<tr><td>PCR≥30</td><td>451</td><td>184</td><td>635</td></tr>
<tr><td>PCR<30</td><td>24</td><td>300</td><td>324</td></tr>
</table>
</td>
<td>G APPLICABILITY Is there concern that the included patients do not match the review question? CONCERN: LOW

<u>DOMAIN 2: INDEX TESTS</u>
A. RISK OF BIAS

1. Were the index test results interpreted without knowledge of the results of the reference standard? yes
2. If a threshold was used,</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
				total 475 484 959	was it pre-specified ? yes, but also tested for other thresholds **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR – different results for different testing sites/assays for PCR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the reference standard results interpreted without knowledge of the results of

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					the index test? yes **Could the reference standard, its conduct, or its interpretation have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the analysis? No – included

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					n=959/1823; 53% (165 refused consent; 212+476+10 missing lab test results; 1 missing perinatal outcome) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Waugh, J. J. S., Bell, S. C., Kilby, M. D., Blackwell, C. N., Seed, P., Shennan, A. H., Halligan, A. W. F., Optimal bedside urinalysis for the detection of proteinuria in hypertensive pregnancy: A study of diagnostic accuracy, BJOG: An International Journal of Obstetrics and	**Sample size** n=171 enrolled (n=77/171 proteinuria≥ 300mg/24hr; n=17/77 proteinuria≥ 1g/24hrs; n=6/17 proteinuria≥ 4g/24hrs) **Characteristics** age: 29 years (range 19-40)	**Tests** Index test: DCA2000 from random urine sample for ACR (early morning/first void sample - final sample of 24 hr collection) Reference test: 24 hour urine collection (proteinuria≥300mg/24hr); the first void was discarded and the sample started with the	**Methods** DCA 2000 (Bayer) is a 'point of care system' for the estimation of microalbumin/creatinine ratio (ACR) utilising a cartridge system and a 40µL sample of urine. 24-hour urine samples were analysed in the Chemical Pathology Department of the Leicester Royal Infirmary by benzethonium chloride assay (BCA).	**Results** **n=77/171 proteinuria≥300mg/24hr** Quantitative microalbumin (DCA 2000) **AUC: 0.82 (95%CI 0.88 to 0.97)** "optimal" cut-off: 2.0mg/mmol: Sens 94% (95%CI 85 to 98); spec 94% (95%CI 85 to 98); LR+ 14.6 (6.74 to 31.8); LR- 0.069 (0.030 to 0.16); [TP 72; FP 6; FN 5; TN 88; back calculated by NGA]	**Limitations Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecut

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Gynaecology, 112, 412-417, 2005 **Ref Id** 838779 **Country/ies where the study was carried out** UK **Study type** Prospective cohort study **Aim of the study** compare semi-quantitative visual and automated methods of urine testing with fully quantitative point of care urinalysis (ACR) for the detection of significant proteinuria (300mg/24hrs) in pregnancy complicated by hypertension **Study dates** October 2000 - June 2001 **Source of funding** No funding reported. Authors acknowledge Bayer for supplying the urinanalysers and dipsticks	**Inclusion Criteria** GA>20weeks referred to day assessment unit for new hypertension (first time in pregnancy) **Exclusion Criteria** pre- existing hypertension	second urine specimen, final specimen was first void the following day	For dipstick tests (unclear if blinded for DCA test): The early morning/first void urine sample was first tested visually by two trained observers who were blinded to each other's results as well as to the results from the reference standard		ive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard ? unclear - mentions blinding for dipstick analysis, not DCA 2000 analysis

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 3: REFERENCE STANDARD **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					its interpretation have introduced bias? RISK: LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Other information
Full citation Wheeler, Thomas L., 2nd, Blackhurst, Dawn W., Dellinger, Eric H., Ramsey, Patrick S., Usage of spot urine protein to creatinine ratios in the evaluation of preeclampsia, American Journal of Obstetrics and Gynecology, 196, 465.e1-4, 2007 **Ref Id** 838781 **Country/ies where the study was carried out** USA **Study type** Prospective cohort study **Aim of the study** compare spot urine PCRs with 24 hour urine collections for protein in women being evaluated for PE **Study dates** December 2000 - July 2002	**Sample size** n=154 recruited; n=126 in final analysis **Characteristics** age: 26.6 SD 5.8 years GA: 34.0 SD 3.3 weeks **Inclusion Criteria** Met inpatient admission criteria for the evaluation of PE: • new-onset persistent hypertension: SBP>140mmHg or DBP>90mmHg after 20wks GA (previously normotensive) • worsening hypertension: increase in BP from baseline taken before 2wks GA • proteinuria included patients with renal disease, chronic	**Tests** Index test: urine sample for PCR (beginning of 24hr urine collection. No first morning voids) Reference test: 24 hour urine collection (proteinuria≥300mg/24hrs)	**Methods** Urinary protein was determined by the Biuret method. Urinary creatinine was determined by the 2-point rate method, aliquots were analyzed by a Johnson & Johnson Vitros 250 (Johnson & Johnson Clinical Diagnostics Inc, Rochester, NY)	**Results** n=68/126 with proteinuria≥300mg/24hrs; n=9/68 missed (false neg rate) "optimal" cut-off (from AUC of 0.86): 0.21 Sens 86.8%; spec 77.6%; [TP 59; FP 13; FN 9; TN 45; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **DOMAIN 1: PATIENT SELECTION** **A. RISK OF BIAS** 1. Was a consecutive or random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Source of funding Not reported	hypertension, and diabetes, in whom preexisting proteinuria could exist **Exclusion Criteria** Women who had bacteriuria on microscopy or were on more than 24 hours bed rest				exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do not match the review question? CONCERN: LOW **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpret

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					ed without knowledge of the results of the reference standard ? unclear 2. If a threshold was used, was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **<u>DOMAIN 3: REFERENCE STANDARD</u>** **A. RISK OF BIAS** 1. Is the reference standard likely to correctly classify the target condition ? yes 2. Were the reference standard results interpreted without knowled

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					ge of the results of the index test? unc lear **Could the reference standard, its conduct, or its interpretatio n have introduced bias? RISK: LOW** **B. CONCERNS REGARDIN G APPLICABIL ITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					DOMAIN 4: FLOW AND TIMING **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and reference standard? yes 2. Did all patients receive a reference standard? yes 3. Did patients receive the same reference standard? Yes 4. Were all patients included in the

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					analysis? No – included n=126/154; 82% (n=28 went into labour during 24 hour collection) **Could the patient flow have introduced bias? RISK: LOW** **Other information**
Full citation Wilkinson,C., Lappin,D., Vellinga,A., Heneghan,H.M., O'Hara,R., Monaghan,J., Spot urinary protein analysis for excluding significant proteinuria in pregnancy, Journal of Obstetrics and Gynaecology, 33, 24-27, 2013 **Ref Id** 273183	**Sample size** n=132 24hr urine collections/analyses (performed on 89 women) **Characteristics** No information for maternal age, BP, or GA	**Tests** Index tests: First and last void urine samples were analysed for PCR (PCR1, PCR2) and ACR (ACR1, ACR2) then added back into 24 hr collection Reference test: 24 hour urine collection	**Methods** PCR and ACR were calculated on 132 first and last void urine samples during 24hr collection (and added to collection) Roche Cobas 6000 (Roche Diagnostics GmbH, D68298, Mannheim) performed the protein, albumin and creatinine assays. Protein analysis was performed using the turbidimetric method. Albuminuria was	**Results** n=76/132 had proteinuria<300mg/24hrs (n=56 proteinuria≥300mg/24hrs) <u>PCR cut-offs: 30, 25, 20, 15, 10 mg/mmol</u> 30: Sensitivity 83.9% (95%CI 72.2-91.3); specificity 97.4% (95%CI 90.0-99.3); FN 9/83; [TP 47; FP 2; FN 9; TN 74; back calculated by NGA] 25: 86.2 (75.1-92.8); 91.9 (83.4-96.2); 8/74; [TP 48; FP 6; FN 8; TN 70; back calculated by NGA]	**Limitations** **Risk of bias assessed using QUADAS-II** **<u>DOMAIN 1: PATIENT SELECTION</u>** **A. RISK OF BIAS** 1. Was a consecutive or

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Country/ies where the study was carried out Ireland **Study type** Prospective cohort study **Aim of the study** compare the accuracy of urinary PCR and ACR in defining optimal cut-off points to rule-out significant proteinuria (≥300 mg/24hrs) in pregnancy **Study dates** July 2009 - May 2010 **Source of funding** Not reported	**Inclusion Criteria** GA>20weeks admitted for suspected PE **Exclusion Criteria** No exclusion criteria were applied		quantified using the immunoturbidimetric assay.	20: 96.4 (87.9-99.0); 84.2 (74.4-90.7); 2/66; [TP 54; FP 12; FN 2; TN 64; back calculated by NGA] 15: 98.2 (90.6-99.7); 65.8 (54.6-75.5); 1/51; [TP 55; FP 26; FN 1; TN 50; back calculated by NGA] 10: FN 0/20 [TP 56; FP 56; FN 0; TN 20; back calculated by NGA] <u>ACR cut-offs: 3.5, 3.0, 2.5, 2.0, 1.5, 1.0 mg/mmol</u> 3.5: sensitivity 91.1% (95%CI 80.7-96.1); specificity 80.3% (95%CI 70.0-87.7); FN 5/66; [TP 51; FP 15; FN 5; TN 61; back calculated by NGA] 3.0: 91.1 (80.7-96.1); 78.9 (68.5-86.6); 5/65; [TP 51; FP 16; FN 5; TN 60; back calculated by NGA] 2.5: 96.4 (87.9-99.0); 77.6 (67.1-85.5); 2/61; [TP 54; FP 17; FN 2; TN 59; back calculated by NGA] 2.0: 96.4 (87.9-99.0); 72.4 (61.4-81.2); 2/57; [TP 54; FP 21; FN 2; TN 55; back calculated by NGA] 1.5: 96.4 (87.9-99.0); 65.8 (54.6-75.5); 2/52; [TP 54; FP 26; FN 2; TN 50; back calculated by NGA] 1.0: 98.2 (90.6-99.7); 48.7 (37.8-59.7); 1/38; [TP 55; FP 39; FN 1; TN 37; back calculated by NGA]	random sample of patients enrolled? yes 2. Was a case-control design avoided? yes 3. Did the study avoid inappropriate exclusions? yes **Could the selection of patients have introduced bias? RISK: LOW** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the included patients do

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					not match the review question? CONCERN: LOW - note that 89 women provided the 132 samples used for analysis **<u>DOMAIN 2: INDEX TESTS</u>** **A. RISK OF BIAS** 1. Were the index test results interpreted without knowledge of the results of the reference standard? unclear 2. If a threshold was used,

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					was it pre-specified ? no **Could the conduct or interpretation of the index test have introduced bias? RISK: UNCLEAR** **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the index test, its conduct, or interpretation differ from the review question? CONCERN: LOW **DOMAIN 3: REFERENCE STANDARD**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. RISK OF BIAS 1. Is the reference standard likely to correctly classify the target condition? yes 2. Were the reference standard results interpreted without knowledge of the results of the index test? unclear **Could the reference standard, its conduct, or its interpretation have introduced**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					bias? RISK: LOW **B. CONCERNS REGARDING APPLICABILITY** Is there concern that the target condition as defined by the reference standard does not match the review question? CONCERN: LOW **<u>DOMAIN 4: FLOW AND TIMING</u>** **A. RISK OF BIAS** 1. Was there appropriate interval between index tests and referenc

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					e standard ? yes 2. Did all patients receive a referenc e standard ? yes 3. Did patients receive the same referenc e standard ? Yes 4. Were all patients included in the analysis? yes **Could the patient flow have introduced bias? RISK: LOW** **Other information**