National Institute for Health and Care Excellence

Final

Intrapartum care

[L] Evidence reviews for route of administration of oxytocin in the third stage of labour

NICE guideline NG235

Evidence reviews underpinning recommendation 1.10.12 in the NICE guideline

September 2023

Final

These evidence reviews were developed by NICE

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Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

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Contents

Route of administration of oxytocin in the third stage of labour 6

Review question 6

Introduction 6

Summary of the protocol 6

Methods and process 6

Effectiveness evidence 7

Summary of included studies 7

Summary of the evidence 8

Economic evidence 9

Economic model 9

Unit costs 9

The committee's discussion and interpretation of the evidence 9

Recommendations supported by this evidence review 11

References – included studies 11

Appendices 12

Appendix A Review protocols 12

Review protocol for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 12

Appendix B Literature search strategies 19

Literature search strategies for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 19

Review question search strategies 19

Health economics search strategies 21

Appendix C Effectiveness evidence study selection 25

Study selection for: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 25

Appendix D Evidence tables 26

Evidence tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 26

Appendix E Forest plots 47

Forest plots for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 47

Appendix F GRADE tables 52

GRADE tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 52

Appendix G Economic evidence study selection....56

Study selection for: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 56

Appendix H Economic evidence tables 57

Economic evidence tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?....57

Appendix I Economic model....58

Economic model for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?....58

Appendix J Excluded studies....59

Excluded studies for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?....59

Appendix K Research recommendations – full details....62

Research recommendations for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour? 62

Route of administration of oxytocin in the third stage of labour

Review question

Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Introduction

Women may choose to have active or physiological management of the third stage or labour. Active management includes clamping of the umbilical cord, administration of a medication (uterotonic) to increase contraction of the uterus and controlled cord traction to deliver the placenta. Oxytocin is a commonly used uterotonic administered for active management of the third stage of labour and the current guideline recommends that this is administered by intramuscular injection.

The aim of this review is to find out whether oxytocin is more effective if administered intravenously or intramuscularly, in the active management of the third stage of labour.

Summary of the protocol

See Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women in the third stage of labour who have given birth (spontaneous or assisted vaginal birth) to a single baby, who went into labour at term (37 to 42 weeks of pregnancy)
Intervention	Intravenous administration of oxytocin in the third stage of labour
Comparison	Intramuscular administration of oxytocin in the third stage of labour
Outcome	**Critical** • Maternal admission to intensive therapy unit or high-dependency area • Primary postpartum haemorrhage (PPH) at time of birth and up to 24 hours (PPH > 500 mL) • Severe PPH at time of birth and up to 24 hours (PPH > 1000 mL) **Important** • Need for manual removal of placenta • Need for additional uterotonics during the third stage or within the first 48 hours • Side effects (for example, change in blood pressure, headache, nausea/ vomiting, pain analgesia) during the third stage of labour or within the first 24 hours • Women's experience of labour and birth

PPH: postpartum haemorrhage

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual. Methods specific to this review question are described in the review protocol in appendix A and the methods document (supplementary document 1).

Declarations of interest were recorded according to NICE's conflicts of interest policy.

During guideline development, the BNF notation for oxytocin dose changed to 'units', so this has been reflected in the evidence report. The evidence tables in appendix D reflect the dose notations as defined by the original study.

Effectiveness evidence

Included studies

Two studies were included for this review, 1 randomised controlled trial (RCT) (Biradar 2021) and 1 Cochrane systematic review (Oladapo 2020), which included 7 RCTs (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019, Neri-Mejia 2016, Oguz 2014, Sangkhomkhamhang 2015).

Both studies compared intravenous (IV) administration of 10 units oxytocin to intramuscular (IM) injection of 10 units oxytocin. The route of administration of IV oxytocin varied: 5 included RCTs in the Cochrane systematic review administered an IV oxytocin bolus injection (Adnan 2018, Charles 2019, Neri-Mejia 2016, Oguz 2014, Sangkhomkhamhang 2015) and 3 included RCTs in the Cochrane systematic review administered an IV oxytocin slow infusion (Charles 2019, Dagdeviren 2016, Durocher 2019). One RCT administered a combined IV oxytocin bolus injection and IV oxytocin infusion (Biradar 2021).

The included studies are summarised in Table 2.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review are listed, and reasons for their exclusion are provided in appendix J.

Summary of included studies

Summaries of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes
Biradar 2021 Randomised controlled trial India	N= 320 women with singleton pregnancy who had a vaginal birth at 37-42 weeks Women who received oxytocin in 1st stage of labour not excluded	3 units IV oxytocin bolus injection and 7 units oxytocin IV slow infusion following vaginal birth	10 units IM oxytocin following vaginal birth	• Need for additional uterotonics
Oladapo 2020 Cochrane systematic review Ireland, Egypt, Turkey, Argentina, Mexico, Thailand	K= 7 (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019, Neri-Mejia 2016, Oguz 2014, Sangkhomkhamhang 2015) N= 7817 women with planned vaginal birth	• 10 units IV oxytocin bolus injection following vaginal birth (K= 5) • 10 units IV oxytocin slow infusion following	10 units IM oxytocin following vaginal birth	• Maternal admission to ITU or high-dependency area • Primary PPH • Severe PPH • Need for manual removal of placenta

Study	Population	Intervention	Comparison	Outcomes
	regardless of other aspects of third stage management Women who received oxytocin in 1st stage of labour not excluded	vaginal birth (K= 3)		• Need for additional uterotonics • Side effects

IM: intramuscular; ITU: intensive therapy unit; IV: intravenous; PPH: postpartum haemorrhage

See the full evidence tables in appendix D and the forest plots in appendix E.

Summary of the evidence

The evidence was stratified in a hierarchy by the following pre-specified variables: type of oxytocin IV administration (IV bolus injection and IV slow infusion) and women who had had oxytocin in the first stage of labour versus women who had not. There was insufficient evidence to stratify by body mass index (BMI), mode of birth and risk of postpartum haemorrhage (PPH) and no need to stratify by dosage of oxytocin as all studies administered 10 units oxytocin.

For overall estimates comparing IV oxytocin (administered by either bolus or infusion) to IM oxytocin, there was consistent evidence in favour of IV oxytocin on outcomes. There was low quality evidence of an important benefit in terms of primary PPH, severe PPH and need for additional uterotonics. There was low quality evidence showing a possible important benefit in terms of need for manual removal of placenta. The evidence contributing to the outcomes of maternal admission to intensive therapy unit (ITU) and side effects were from studies administering IV oxytocin by IV bolus injection only.

For oxytocin IV bolus injection compared to oxytocin IM injection, there was moderate quality evidence of a possible important benefit of IV bolus injection in terms of maternal admission to ITU and an important benefit in terms of severe PPH. For the same comparison, there was low quality evidence of an important benefit on a reduction in primary PPH and the need for manual removal of placenta and low quality evidence of no important difference on the need for additional uterotonics or on side effects.

For oxytocin delivered by IV slow infusion compared to oxytocin IM injection, there was moderate quality evidence of no important difference in terms of primary PPH, no evidence of an important difference for need for manual removal of placenta and low quality evidence of no important difference in terms of reducing severe PPH. There was high quality evidence that IV oxytocin delivered by slow infusion had a possible important benefit compared to IM oxytocin in terms of need for additional uterotonics.

For oxytocin delivered by a combined IV bolus injection and IV slow infusion compared to IM oxytocin, there was low quality evidence of no evidence of important difference in terms of need for additional uterotonics. No other outcomes were reported for this stratification.

For women who had oxytocin in the first stage of labour, there was moderate quality evidence that oxytocin IV bolus injection in the third stage of labour had no evidence of an important difference on primary PPH and high quality evidence that it had an important benefit in terms of reducing severe PPH compared to IM injection. For women who did not have oxytocin in the first stage of labour, there was low quality evidence that oxytocin IV bolus injection in the third stage of labour had no important difference on primary PPH and severe PPH compared to IM injection. There was insufficient evidence to stratify any other reported outcomes by women who had received oxytocin in the first stage of labour or not.

There was no evidence for women's experience of labour and birth for any of the comparisons.

See appendix F for full GRADE tables.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation. This was because recommendations were not expected to generate a significant resource impact to the NHS.

Unit costs

Resource	Unit costs	Source
Oxytocin 10 unit per 1 ml for injection	£0.91	BNF accessed 17/02/2023

The committee's discussion and interpretation of the evidence

The outcomes that matter most

The aim of this review was to determine the effectiveness of intravenous administration of oxytocin compared with intramuscular administration in the third stage of labour to prevent excessive bleeding after the birth of the baby. The committee therefore agreed that maternal admission to an ITU or high-dependency area, primary PPH and severe PPH were critical outcomes which would directly capture the effectiveness and safety of the intervention.

The committee agreed that need for manual removal of the placenta was an important outcome which would determine the effectiveness of the mechanism of action of the intervention as oxytocin helps to prevent blood loss after birth of the baby by stimulating the uterus to contract, closing the blood vessels to the placenta and helping the placenta to separate. The committee agreed that the need for additional uterotonics during the third stage or within the first 48 hours should be included as an important outcome as they wanted to know whether IV oxytocin would reduce the need for additional interventions in the third stage compared to IM oxytocin.

The committee included side effects during the third stage or within the first 24 hours as an important outcome as oxytocin administered intravenously as a bolus injection has been associated with hypotension and tachycardia. The committee agreed that women's experience of labour and birth should be included as an important outcome to capture the acceptability of the intervention and any wider impacts on the woman associated with the differential route of administration of oxytocin.

The quality of the evidence

The quality of the evidence ranged from high to low, with most of the evidence being of low quality. Most of the included RCTs were of high quality, but some outcomes were downgraded for risk of bias where evidence came from studies at risk of selective reporting bias or where outcome assessors were not blinded. Evidence was not downgraded in cases where participants or study personnel were not blinded as the outcomes were measured objectively and the intervention was administered once, so the risk of bias due to deviations from the intervention was low. Outcomes were downgraded for imprecision in some cases where 95% confidence intervals (CIs) crossed the minimally important differences, indicating the effect size was small.

Benefits and harms

The committee discussed the evidence and used this alongside their expert opinion and clinical knowledge to make recommendations. Based on overall effect estimates, the committee agreed there was consistent evidence of benefits of IV oxytocin compared to IM oxytocin in the third stage of labour in terms of maternal admission to ITU, primary PPH, severe PPH, need for manual removal of placenta and need for additional uterotonics. The committee considered the outcomes stratified by type of administration and noted that IV bolus injection had important benefits in terms of primary PPH, severe PPH and need for manual removal of placenta compared to IM injection, whereas there was no difference or no evidence of important difference for IV infusion. There was no important difference in terms of side effects, with the data contributing to this outcome only from studies administering IV injection compared to IM injection.

The committee discussed the evidence from two large RCTs comparing IV oxytocin injection to IM oxytocin stratified by women who have had and have not had oxytocin in the first stage of labour. The committee acknowledged that the stratified analysis did not substantially change the effect estimate in terms of primary PPH, however, in terms of severe PPH, the effect estimate was larger in favour of IV injection for women who had had oxytocin compared to the non-stratified effect estimate and conversely there was no important difference found for women who had not had oxytocin in the first stage of labour. Based on this evidence and insufficient data to stratify other critical and important outcomes by women who had and had not had oxytocin in the first stage of labour, the committee agreed that the evidence supported a recommendation for oxytocin to be administered by IV injection in the third stage for women who had had oxytocin in the first stage of labour, but not for women who had not previously received oxytocin.

The committee also discussed the feasibility and acceptability of administering oxytocin by IV injection, as IM injections are quick to administer and do not require an IV access to be sited using a cannula. The committee also discussed that to reduce the possible haemodynamic effects of IV oxytocin it should be administered slowly (over a few minutes), and a slow IV injection would therefore be more time-consuming for the midwife to administer compared to an IM injection. The committee raised concerns that IV administration in midwifery-led settings may be less acceptable as inserting cannulas during third stage of labour may be less commonplace than in obstetric units and it increases the medicalisation of birth which women in these settings may wish to avoid. The committee were also concerned by the need for 2 midwives to be present during the third stage in order to check and administer the slow IV injection while also ensuring that the baby was safe and well, as in their experience this may not be feasible in all settings due to resource constraints. These considerations confirmed the committee's evidence-based recommendation to offer oxytocin by slow IV injection only to women who had had oxytocin during labour and therefore would have existing IV access. The committee noted that, although 2 midwives may still be needed during the third stage to check and administer the IV oxytocin, it would remove the need to insert and check a cannula during the third stage. The committee noted the lack of evidence in terms of women's experience of labour and birth, but agreed that, in their experience, women would prefer to avoid having an intramuscular injection which can be painful, if IV access was already established and another option was as safe and effective.

Cost effectiveness and resource use

The committee noted that there was no difference in the acquisition costs to the NHS of oxytocin whether given by IM or IV injection. The committee recognised that putting in IV access solely for the purposes of administering IV oxytocin would be resource intensive, requiring 2 midwives to be present to insert the access, check it and administer a flush and then the oxytocin. The committee also discussed the related practical difficulties of recommending IV oxytocin for all women with current levels of staffing. Therefore, they

confirmed that the recommendations should restrict the use of IV oxytocin to women who had already received oxytocin in labour and who therefore have IV access is situ.

Recommendations supported by this evidence review

This evidence review supports recommendation 1.10.14.

References – included studies

Effectiveness

Biradar 2021

Biradar, Aruna M., Yaliwal, Rajasri G., Kori, Shreedevi S. et al. (2021) Randomised control trial of 3 iu intravenous oxytocin bolus with 7 iu oxytocin infusion versus 10 iu intramuscular oxytocin in the third stage of labour in the prevention of postpartum hemorrhage. International Journal of Women's Health and Reproduction Sciences 9(3): 171-175Hilton 2016

Oladapo 2020

Oladapo, Olufemi T., Okusanya, Babasola O., Abalos, Edgardo et al. (2020) Intravenous versus intramuscular prophylactic oxytocin for reducing blood loss in the third stage of labour. Cochrane Database of Systematic Reviews 2020(12): cd009332

Appendices

Appendix A Review protocols

Review protocol for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Table 3: Review protocol

Field	Content
PROSPERO registration number	CRD42021269397
Review title	Intravenous administration of oxytocin compared with intramuscular administration in the active management of the third stage of labour
Review question	Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?
Objective	To draft recommendations for the route of administration of oxytocin in the active management in the third stage of labour. Surveillance has identified that, compared to the intramuscular route, intravenous administration of oxytocin (as part of active management) may be associated with significantly lower rates of severe postpartum haemorrhage, the need for blood transfusion and admission to a high dependency unit.
Searches	The following databases will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL) • Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • International Health Technology Assessment database Searches will be restricted by: • No date limitations • English language only

Field	Content
	• Human studies only Other searches: • Inclusion lists of systematic reviews The full search strategies for MEDLINE database will be published in the final review. For each search, the principal database search strategy is quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist.
Condition or domain being studied	Labour and birth
Population	Women in the third stage of labour who have given birth (spontaneous or assisted vaginal birth) to a single baby, who went into labour at term (37 to 42 weeks of pregnancy)
Intervention	Intravenous administration of oxytocin in the third stage of labour
Comparator	Intramuscular administration of oxytocin in the third stage of labour
Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • Parallel RCTs (individual or cluster) If not enough evidence from RCTs is found: • Prospective and retrospective cohort studies • Conference abstracts will not be included because these do not typically have sufficient information to allow full critical appraisal.
Other exclusion criteria	None
Context	This guideline will partly update the following: Intrapartum care for healthy women and babies (CG190)
Primary outcomes (critical outcomes)	• Maternal admission to intensive therapy unit (ITU) or high-dependency area • Primary postpartum haemorrhage (PPH) at time of birth and up to 24 hours (PPH > 500 mL) • Severe primary postpartum haemorrhage (PPH) at time of birth and up to 24 hours (PPH > 1000 mL)

Field	Content
Secondary outcomes (important outcomes)	• Need for manual removal of placenta • Need for additional uterotonics during the third stage or within the first 48 hours • Side effects (for example, change in blood pressure, headache, nausea/ vomiting, pain analgesia) during the third stage of labour or within the first 24 hours • Women's experience of labour and birth
Data extraction (selection and coding)	All references identified by the searches and from other sources will be uploaded into EPPI and de-duplicated. Titles and abstracts of the retrieved citations will be screened to identify studies that potentially meet the inclusion criteria outlined in the review protocol. Dual sifting will be performed on at least 10% of records; 90% agreement is required. Disagreements will be resolved via discussion between the two reviewers, and consultation with senior staff if necessary. Full versions of the selected studies will be obtained for assessment. Studies that fail to meet the inclusion criteria once the full version has been checked will be excluded at this stage. Each study excluded after checking the full version will be listed, along with the reason for its exclusion. A standardised form will be used to extract data from studies. The following data will be extracted: study details (reference, country where study was carried out, type and dates), participant characteristics, inclusion and exclusion criteria, details of the interventions if relevant, setting and follow-up, relevant outcome data and source of funding. One reviewer will extract relevant data into a standardised form, and this will be quality assessed by a senior reviewer.
Risk of bias (quality) assessment	Quality assessment of individual studies will be performed using the following checklists: • ROBIS tool for systematic reviews • Cochrane RoB tool v.2 for RCTs • Cochrane RoB tool v.2 for cluster randomised controlled trials • ROBINS-I tool for non-randomised (clinical) controlled trials and cohort studies The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.
Strategy for data synthesis	Quantitative findings will be formally summarised in the review. Where multiple studies report on the same outcome for the same comparison, meta-analyses will be conducted using Cochrane Review Manager software. A fixed effect meta-analysis will be conducted and data will be presented as risk ratios if possible or odds ratios when required (for example, if only available in this form in included studies) for dichotomous outcomes, and mean

Field	Content
	differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I^2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I^2 values of greater than 50% and 80% will be considered as significant and very significant heterogeneity, respectively. Heterogeneity will be explored as appropriate using sensitivity analyses and pre-specified subgroup analyses. If heterogeneity cannot be explained through subgroup analysis then a random effects model will be used for meta-analysis, or the data will not be pooled. The confidence in the findings across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group: http://www.gradeworkinggroup.org/ **Minimally important differences:** • Validated scales/continuous outcomes: published MIDs where available • All other outcomes & where published MIDs are not available: 0.8 and 1.25 for all relative dichotomous outcomes ; +/- 0.5x control group SD for continuous outcomes
Analysis of subgroups	Evidence will be stratified by: • BMI thresholds on booking: o Underweight range: <18.5 kg/m2 o Healthy weight range: 18.5 to 24.9 kg/m2 o Overweight range: 25 to 29.99 kg/m2 o Obesity range 1: 30 to 34.99 kg/m2 o Obesity range 2: 35 to 39.99 kg/m2 • Dosage of oxytocin (5 IU oxytocin vs 10 IU oxytocin) • Intravenous oxytocin bolus injection vs IV oxytocin slow infusion • Mode of birth (spontaneous vaginal vs instrumental vaginal) • Risk of PPH (high risk vs moderate vs low), as defined by study authors • Women who have had oxytocin in the first stage of labour vs women who have not **Amendment:** The term 'IV oxytocin slow bolus injection' originally described in the analysis of subgroups section in the protocol has been replaced for the term 'IV oxytocin slow infusion' to more accurately describe the route of administration of intravenous.

Field	Content	
	Stratifications will be dealt with in a hierarchy (this is, first by BMI thresholds on booking, then by dosage of oxytocin, then by oxytocin given as bolus or slow bolus injection, then by mode of birth, then by risk of PPH and then by women who have had oxytocin in the first stage of labour versus women who have not) Evidence will be subgrouped by the following only in the event that there is significant heterogeneity in outcomes: • Age of woman (<35 vs >/= 35) • Ethnicity • White • Asian/Asian British • Black/African/Caribbean/Black British • Mixed/Multiple ethnic groups • Other ethnic group • Women with disability vs not • Deprived socioeconomic group vs not Where evidence is stratified or subgrouped the committee will consider on a case by case basis if separate recommendations should be made for distinct groups. Separate recommendations may be made where there is evidence of a differential effect of interventions in distinct groups. If there is a lack of evidence in one group, the committee will consider, based on their experience, whether it is reasonable to extrapolate and assume the interventions will have similar effects in that group compared with others.	
Type and method of review	☒	Intervention
	☐	Diagnostic
	☐	Prognostic
	☐	Qualitative
	☐	Epidemiologic
	☐	Service Delivery
	☐	Other (please specify)
Language	English	

Field	Content
Country	England
Anticipated or actual start date	14/07/2021
Anticipated completion date	22/03/2023
Named contact	5a. Named contact Guideline Development Team National Guideline Alliance (NGA) 5b. Named contact e-mail IPCupdate@nice.org.uk 5c. Organisational affiliation of the review Guideline Development Team NGA, Centre for Guidelines, National Institute for Health and Care Excellence (NICE)
Review team members	From the Guideline Development Team: • Senior Systematic Reviewer • Systematic Reviewer
Funding sources/sponsor	This systematic review is being completed by the Guideline Development Team NGA, Centre for Guidelines, which is part of the National Institute for Health and Care Excellence (NICE).
Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.

Field	Content
Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website.
Other registration details	None
URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=269397
Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE.
Keywords	Oxytocin; route of administration; third stage of labour
Details of existing review of same topic by same authors	Not applicable
Additional information	None
Details of final publication	www.nice.org.uk

BMI: body mass index; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; PPH: postpartum haemorrhage; PRESS: peer review of electronic search strategies; RCT: randomised controlled trial; RoB(IS): risk of bias (in systematic reviews); SD: standard deviation

Appendix B Literature search strategies

Literature search strategies for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Review question search strategies

Database: Medline – OVID interface

Date of last search: 07/12/2022

#	Searches
1	OXYTOCIN/
2	(ocytocin or oxytocin or pitocin or syntocinon).mp.
3	or/1-2
4	exp ADMINISTRATION, INTRAVENOUS/
5	(intravenous* or intra-venous*).ti,ab.
6	IV.ti,ab.
7	or/4-6
8	INJECTIONS, INTRAMUSCULAR/
9	(intramuscular* or intra-muscular*).ti,ab.
10	IM.ti,ab.
11	or/8-10
12	3 and 7 and 11
13	limit 12 to english language
14	LETTER/
15	EDITORIAL/
16	NEWS/
17	exp HISTORICAL ARTICLE/
18	ANECDOTES AS TOPIC/
19	COMMENT/
20	CASE REPORT/
21	(letter or comment*).ti.
22	or/14-21
23	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
24	22 not 23
25	ANIMALS/ not HUMANS/
26	exp ANIMALS, LABORATORY/
27	exp ANIMAL EXPERIMENTATION/
28	exp MODELS, ANIMAL/
29	exp RODENTIA/
30	(rat or rats or mouse or mice).ti.
31	or/24-30
32	13 not 31
33	META-ANALYSIS/
34	META-ANALYSIS AS TOPIC/
35	(meta analy* or metanaly* or metaanaly*).ti,ab.
36	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
37	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
38	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
39	(search* adj4 literature).ab.
40	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
41	cochrane.jw.
42	or/33-41
43	randomized controlled trial.pt.
44	controlled clinical trial.pt.
45	pragmatic clinical trial.pt.
46	randomi#ed.ab.
47	placebo.ab.
48	randomly.ab.
49	CLINICAL TRIALS AS TOPIC/
50	trial.ti.
51	or/43-50

#	Searches
52	COHORT STUDIES/
53	FOLLOW-UP STUDIES/
54	LONGITUDINAL STUDIES/
55	PROSPECTIVE STUDIES/
56	RETROSPECTIVE STUDIES/
57	((cohort* or follow-up or follow?up or longitudinal* or prospective* or retrospective*) adj1 (stud* or research or analys*)).tw.
58	(incidence? adj (stud* or research or analys*)).tw.
59	(longitudinal* adj1 (survey* or evaluat*)).tw.
60	(prospective* adj method*).tw.
61	(retrospective* adj design*).tw.
62	or/52-61
63	32 and 42
64	32 and 51
65	32 and 62
66	or/63-65

Database: Embase – OVID interface

Date of last search: 07/12/2022

#	Searches
1	OXYTOCIN/
2	(ocytocin or oxytocin or pitocin or syntocinon).mp.
3	or/1-2
4	INTRAVENOUS DRUG ADMINISTRATION/
5	(intravenous* or intra-venous*).ti,ab.
6	IV.ti,ab.
7	or/4-6
8	INTRAMUSCULAR DRUG ADMINISTRATION/
9	(intramuscular* or intra-muscular*).ti,ab.
10	IM.ti,ab.
11	or/8-10
12	3 and 7 and 11
13	limit 12 to english language
14	letter.pt. or LETTER/
15	note.pt.
16	editorial.pt.
17	CASE REPORT/ or CASE STUDY/
18	(letter or comment*).ti.
19	or/14-18
20	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
21	19 not 20
22	ANIMAL/ not HUMAN/
23	NONHUMAN/
24	exp ANIMAL EXPERIMENT/
25	exp EXPERIMENTAL ANIMAL/
26	ANIMAL MODEL/
27	exp RODENT/
28	(rat or rats or mouse or mice).ti.
29	or/21-28
30	13 not 29
31	SYSTEMATIC REVIEW/
32	META-ANALYSIS/
33	(meta analy* or metanaly* or metaanaly*).ti,ab.
34	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
35	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
36	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
37	(search* adj4 literature).ab.
38	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
39	((pool* or combined) adj2 (data or trials or studies or results)).ab.
40	cochrane.jw.
41	or/31-40
42	random*.ti,ab.
43	factorial*.ti,ab.
44	(crossover* or cross over*).ti,ab.

#	Searches
45	((doubl* or singl*) adj blind*).ti,ab.
46	(assign* or allocat* or volunteer* or placebo*).ti,ab.
47	CROSSOVER PROCEDURE/
48	SINGLE BLIND PROCEDURE/
49	RANDOMIZED CONTROLLED TRIAL/
50	DOUBLE BLIND PROCEDURE/
51	or/42-50
52	COHORT ANALYSIS/
53	FOLLOW UP/
54	LONGITUDINAL STUDY/
55	PROSPECTIVE STUDY/
56	RETROSPECTIVE STUDIES/
57	((cohort* or follow-up or follow?up or longitudinal* or prospective* or retrospective*) adj1 (stud* or research or analys*)).tw.
58	(incidence? adj (stud* or research or analys*)).tw.
59	(longitudinal* adj1 (survey* or evaluat*)).tw.
60	(prospective* adj method*).tw.
61	(retrospective* adj design*).tw.
62	or/52-61
63	30 and 41
64	30 and 51
65	30 and 62
66	or/63-65

Databases: Cochrane Central Register of Controlled Trials; Cochrane Database of Systematic Reviews – Wiley interface

Date of last search: 07/12/2022

#	Searches
#1	MeSH descriptor: [Oxytocin] this term only
#2	(ocytocin or oxytocin or pitocin or syntocinon):ti,ab
#3	#1 or #2
#4	MeSH descriptor: [Administration, Intravenous] explode all trees
#5	(intravenous* or intra-venous*):ti,ab
#6	IV:ti,ab
#7	#4 or #5 or #6
#8	MeSH descriptor: [Injections, Intramuscular] this term only
#9	(intramuscular* or intra-muscular*):ti,ab
#10	IM:ti,ab
#11	#8 or #9 or #10
#12	#3 and #7 and #11

Database: International Health Technology Assessment

Date of last search: 07/12/2022

#	Searches
	MeSH Search: OXYTOCIN
	OR All: ocytocin or oxytocin or pitocin or syntocinon

Health economics search strategies

Database: Medline – OVID interface

Date of last search: 07/12/2022

#	Searches
1	OXYTOCIN/
2	(ocytocin or oxytocin or pitocin or syntocinon).mp.
3	or/1-2
4	exp ADMINISTRATION, INTRAVENOUS/
5	(intravenous* or intra-venous*).ti,ab.
6	IV.ti,ab.
7	or/4-6
8	INJECTIONS, INTRAMUSCULAR/
9	(intramuscular* or intra-muscular*).ti,ab.
10	IM.ti,ab.
11	or/8-10
12	3 and 7 and 11
13	limit 12 to english language
14	LETTER/
15	EDITORIAL/
16	NEWS/
17	exp HISTORICAL ARTICLE/
18	ANECDOTES AS TOPIC/
19	COMMENT/
20	CASE REPORT/
21	(letter or comment*).ti.
22	or/14-21
23	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
24	22 not 23
25	ANIMALS/ not HUMANS/
26	exp ANIMALS, LABORATORY/
27	exp ANIMAL EXPERIMENTATION/
28	exp MODELS, ANIMAL/
29	exp RODENTIA/
30	(rat or rats or mouse or mice).ti.
31	or/24-30
32	13 not 31
33	ECONOMICS/
34	VALUE OF LIFE/
35	exp "COSTS AND COST ANALYSIS"/
36	exp ECONOMICS, HOSPITAL/
37	exp ECONOMICS, MEDICAL/
38	exp RESOURCE ALLOCATION/
39	ECONOMICS, NURSING/
40	ECONOMICS, PHARMACEUTICAL/
41	exp "FEES AND CHARGES"/
42	exp BUDGETS/
43	budget*.ti,ab.
44	cost*.ti,ab.
45	(economic* or pharmaco?economic*).ti,ab.
46	(price* or pricing*).ti,ab.
47	(financ* or fee or fees or expenditure* or saving*).ti,ab.
48	(value adj2 (money or monetary)).ti,ab.
49	resourc* allocat*.ti,ab.
50	(fund or funds or funding* or funded).ti,ab.
51	(ration or rations or rationing* or rationed).ti,ab.
52	ec.fs.
53	or/33-52
54	32 and 53

Database: Embase – OVID interface

Date of last search: 07/12/2022

#	Searches
1	OXYTOCIN/
2	(ocytocin or oxytocin or pitocin or syntocinon).mp.
3	or/1-2
4	INTRAVENOUS DRUG ADMINISTRATION/
5	(intravenous* or intra-venous*).ti,ab.

#	Searches
6	IV.ti,ab.
7	or/4-6
8	INTRAMUSCULAR DRUG ADMINISTRATION/
9	(intramuscular* or intra-muscular*).ti,ab.
10	IM.ti,ab.
11	or/8-10
12	3 and 7 and 11
13	limit 12 to english language
14	letter.pt. or LETTER/
15	note.pt.
16	editorial.pt.
17	CASE REPORT/ or CASE STUDY/
18	(letter or comment*).ti.
19	or/14-18
20	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
21	19 not 20
22	ANIMAL/ not HUMAN/
23	NONHUMAN/
24	exp ANIMAL EXPERIMENT/
25	exp EXPERIMENTAL ANIMAL/
26	ANIMAL MODEL/
27	exp RODENT/
28	(rat or rats or mouse or mice).ti.
29	or/21-28
30	13 not 29
31	HEALTH ECONOMICS/
32	exp ECONOMIC EVALUATION/
33	exp HEALTH CARE COST/
34	exp FEE/
35	BUDGET/
36	FUNDING/
37	RESOURCE ALLOCATION/
38	budget*.ti,ab.
39	cost*.ti,ab.
40	(economic* or pharmaco?economic*).ti,ab.
41	(price* or pricing*).ti,ab.
42	(financ* or fee or fees or expenditure* or saving*).ti,ab.
43	(value adj2 (money or monetary)).ti,ab.
44	resourc* allocat*.ti,ab.
45	(fund or funds or funding* or funded).ti,ab.
46	(ration or rations or rationing* or rationed).ti,ab.
47	or/31-46
48	30 and 47

Database: Cochrane Central Register of Controlled Trials – Wiley interface

Date of last search: 07/12/2022

#	Searches
#1	MeSH descriptor: [Oxytocin] this term only
#2	(ocytocin or oxytocin or pitocin or syntocinon):ti,ab
#3	#1 or #2
#4	MeSH descriptor: [Administration, Intravenous] explode all trees
#5	(intravenous* or intra-venous*):ti,ab
#6	IV:ti,ab
#7	#4 or #5 or #6
#8	MeSH descriptor: [Injections, Intramuscular] this term only
#9	(intramuscular* or intra-muscular*):ti,ab
#10	IM:ti,ab
#11	#8 or #9 or #10
#12	#3 and #7 and #11
#13	MeSH descriptor: [Economics] this term only
#14	MeSH descriptor: [Value of Life] this term only
#15	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#16	MeSH descriptor: [Economics, Hospital] explode all trees
#17	MeSH descriptor: [Economics, Medical] explode all trees

#	Searches
#18	MeSH descriptor: [Resource Allocation] explode all trees
#19	MeSH descriptor: [Economics, Nursing] this term only
#20	MeSH descriptor: [Economics, Pharmaceutical] this term only
#21	MeSH descriptor: [Fees and Charges] explode all trees
#22	MeSH descriptor: [Budgets] explode all trees
#23	budget*:ti,ab
#24	cost*:ti,ab
#25	(economic* or pharmaco?economic*):ti,ab
#26	(price* or pricing*):ti,ab
#27	(financ* or fee or fees or expenditure* or saving*):ti,ab
#28	(value near/2 (money or monetary)):ti,ab
#29	resourc* allocat*:ti,ab
#30	(fund or funds or funding* or funded):ti,ab
#31	(ration or rations or rationing* or rationed):ti,ab
#32	#13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31
#33	#12 and #32

Database: International Health Technology Assessment

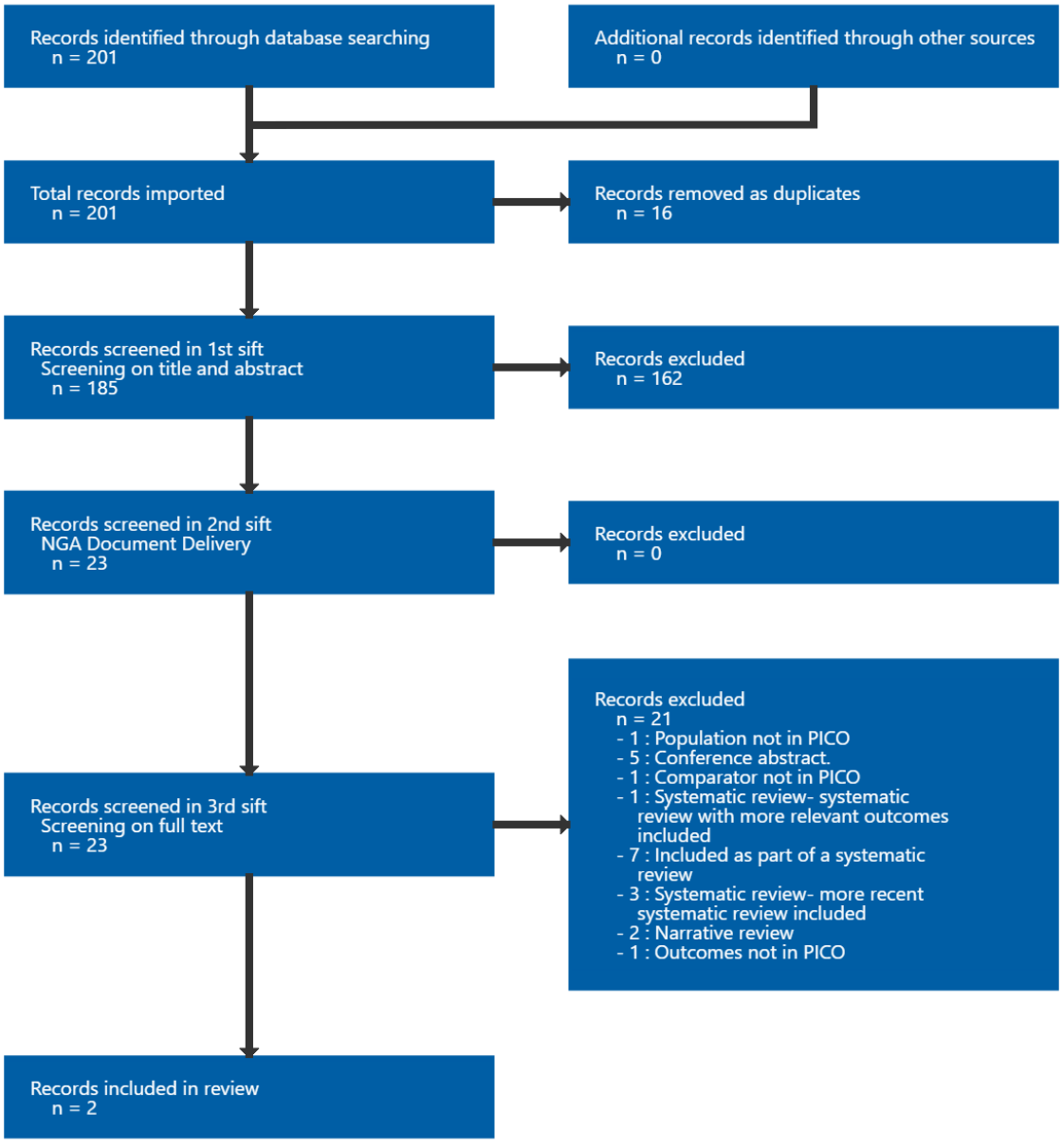
Date of last search: 07/12/2022

#	Searches
	MeSH Search: OXYTOCIN
	OR All: ocytocin or oxytocin or pitocin or syntocinon

Appendix C Effectiveness evidence study selection

Study selection for: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Figure 1: Study selection flow chart



Note: for this review, de-duplication was done outside of EPPI in EndNote for practical reasons, therefore the study selection flowchart foes not accurately reflect the records removed as duplicates.

Appendix D Evidence tables

Evidence tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Biradar, 2021

Bibliographic Reference	Biradar, Aruna M.; Yaliwal, Rajasri G.; Kori, Shreedevi S.; Mathapati, Sangamesh S.; Shiragur, Shobha S.; Mudanur, Subhashchandra R.; Randomised control trial of 3 iu intravenous oxytocin bolus with 7 iu oxytocin infusion versus 10 iu intramuscular oxytocin in the third stage of labour in the prevention of postpartum hemorrhage; International Journal of Women's Health and Reproduction Sciences; 2021; vol. 9 (no. 3); 171-175

Study details

Country/ies where study was carried out	India
Study type	Randomised controlled trial (RCT)
Study dates	25th February - 25th May 2020
Inclusion criteria	women with singleton pregnancy gestational age 37-42 weeks vaginal delivery
Exclusion criteria	history of uterine surgery (c-section, myomectomy) severe diseases: anemia; coagulopathies; associated cardiac, hepatic and renal diseases known conditions predisposing to atonic PPH: hydramnios; multiple gestations; severe pre-clampsia; eclampsia women undergoing vacuum delivery via forceps cervical lacerations

Patient characteristics	No differences at baseline Proportion of women receiving oxytocin in 1st stage of labour not reported
Intervention(s)/control	Group 1 (n= 160): received 3 IU IV oxytocin bolus and 7 IU oxytocin IV infusion Group 2 (n= 160): received 10 IU IM oxytocin
Duration of follow-up	60 min
Sources of funding	n/a
Sample size	N= 320 women randomised Group 1: n= 160 (included in analysis) Group 2: n= 160 (included in analysis)
Other information	

Outcomes

Outcome	**Group 1 , , N = 160**	**Group 2, , N = 160**
Additional Uterotonics (n (%)) No of events	n = 0	n = 3

Critical appraisal

Section	**Question**	**Answer**
Domain 1: Bias arising from the randomisation process	Risk of bias judgement for the randomisation process	Some concerns *(Allocation was random. No information on allocation*

Section	Question	Answer
		concealment, but no differences in baseline characteristics to suggest a concern.)
Domain 2a: Risk of bias due to deviations from the intended interventions (effect of assignment to intervention)	Risk of bias for deviations from the intended interventions (effect of assignment to intervention)	Low *(Carers administering intervention and participants not blinded, but no evidence that assignment to intervention affected implementation. No evidence that ITT protocol not followed.)*
Domain 2b: Risk of bias due to deviations from the intended interventions (effect of adhering to intervention)	Risk of bias judgement for deviations from the intended interventions (effect of adhering to intervention)	Low *(Carers administering intervention and participants not blinded, but low risk of bias due to non-adherence as intervention administered once.)*
Domain 3. Bias due to missing outcome data	Risk-of-bias judgement for missing outcome data	Low *(No evidence of missing outcome data)*
Domain 4. Bias in measurement of the outcome	Risk-of-bias judgement for measurement of the outcome	Low *(Low risk of bias for the objective outcome 'need for additional uterotonics' (assumed to be determined by blood loss).)*
Domain 5. Bias in selection of the reported result	Risk-of-bias judgement for selection of the reported result	Some concerns *(A pre-specified protocol was not available to determine selective reporting bias)*
Overall bias and Directness	Risk of bias judgement	Some concerns
Overall bias and Directness	Overall Directness	Directly applicable
Overall bias and Directness	Risk of bias variation across outcomes	Not applicable

Oladapo, 2020

Bibliographic Reference	Oladapo, Olufemi T.; Okusanya, Babasola O.; Abalos, Edgardo; Gallos, Ioannis D.; Papadopoulou, Argyro; Intravenous versus intramuscular prophylactic oxytocin for reducing blood loss in the third stage of labour; Cochrane Database of Systematic Reviews; 2020; vol. 2020 (no. 12); cd009332

Study details

Country/ies where study was carried out	Ireland, Egypt, Turkey, Argentina, Mexico, Thailand,
Study type	Cochrane systematic review of randomised controlled trials (RCT)
Study dates	Adnan 2018 January 2016 - December 2017 Charles 2019 April 2014 - September 2015 Dagdeviren 2016 February 2014 - March 2015 Durocher 2019 December 2016 - September 2017 Neri-Mejia 2016 August 2015 - December 2015 Oguz 2014 January 2010 - October 2010 Sangkhomkhamhang 2015 February 2012 - June 2012

Inclusion criteria	Women with planned vaginal birth regardless of other aspects of third stage management Study specific inclusion criteria: Adnan 2018 • 18+ years • Singleton term pregnancy (>37 weeks) • Aiming for a vaginal birth Charles 2019 • No pre-delivery oxytocin (for induction or augmentation of labour) • Live vaginal birth • Dagdeviren 2016 • 18-45 years • Singleton term pregnancy (37-42 weeks) • Cephalic presentation, • Normal blood pressure (< 140/90 mmHg) • Intending to have vaginal birth Durocher 2019 • Active labour with a live fetus • Vaginal delivery Neri-Mejia 2016 • Singleton term pregnancy • Cephalic presentation • No evident cephalopelvic disproportion • Spontaneous labour • Induced onset of labour • Vaginal delivery

	• Provided written informed consent • Haemoglobin measured during labour Oguz 2014 • Singleton pregnancy > 37 weeks • cephalic presentation • In active phase of labour • Normal vaginal birth Sangkhomkhamhang 2015 • Singleton pregnancy • Attending hospital for a vaginal birth
Exclusion criteria	Not specified Study specific exclusion criteria: Adnan 2018 • Women at an increased risk of PPH • Women whose caregiver had pre-decided to administer an additional oxytocin infusion • Women with a history of atonic PPH, fibroids and coagulopathy • Women receiving anticoagulant treatment • Women with thrombocytopenia. • Women with pre-existing cardiovascular disease, • Women who did not understand English Charles 2019 • Women who received pre-delivery oxytocin • Women who had a caesarean section • Women who could not provide written informed consent Dagdeviren 2016

	• Grand multiparity (not clearly defined, parity ranged from 1-6 in women recruited) • Hb < 7 g/dL • Prolonged 1st stage of labour • Induction (oxytocin for ≥12hours), • Previous caesarean birth or uterine surgery • Uterine myoma or serious obstetric or other comorbidity • Previous PPH • History of coagulopathies and anticoagulant treatment around the time of delivery • Haemorrhage during current pregnancy, • History of placental abruption, macrosomia or polyhydramnios. Durocher 2019 • Women who had a caesarean delivery • Women who could not provide informed consent. Neri-Mejia 2016 • Not clearly specified Oguz 2014 • Fetal death • Multiple pregnancy • Coagulation disorder • Placental pathology • Liver disease • Thrombocytopenia • Hypertension or taking anticoagulants • Caesarean or operative birth • Deep vaginal tear • Chorioamnionitis • HELLP syndrome • Disseminated intravascular coagulation before delivery

	Sangkhomkhamhang 2015 • Women with obstetric complications or medical problems. • Women with a history of curettage, manual removal of the placenta, cardiovascular instability or oxytocin hypersensitivity

Patient characteristics	Adnan 2018
	no differences at baseline
	Charles 2019
	• Episiotomy, n (%)
	  ○ IV infusion group: 930 (44.1)
	  ○ IV bolus injection group: 312 (44.5)
	  ○ IM injection group: 826 39.3
	  ▪ P-value =0.002
	Dagdeviren 2016
	no differences at baseline
	• Augmentation with oxytocin, n (%)
	  ○ IV infusion group: 28 (21.9)
	  ○ IM injection group: 18 (14.1)
	  ▪ P-value= 0.104
	Durocher 2019
	• Labour induced with uterotonics, n (%):
	  ○ IV infusion group: 16 (6.7)
	  ○ IM injection group: 25 (10.4)
	• Labour augmented with uterotonics, n (%)
	  ○ IV infusion group: 40 (16.7)
	  ○ IM injection group: 27 (11.2)
	Neri-Mejia 2016

	no differences at baseline
	
	Oguz 2014
	
	• Augmentation of labour, n (%)
	  ○ IV bolus injection group: 140 (46.7)
	  ○ IM injection group: 107 (35.7)
	
	Sangkhomkhamhang 2015
	
	no differences at baseline
	
	• Proportion of women receiving oxytocin in 1st stage of labour not reported

Intervention(s)/control	Adnan 2018 Intervention: IV oxytocin 10 IU in 1 mL over 1 minute and 1 mL 0.9% normal saline as placebo intramuscularly immediately after the delivery of the baby Control: IM oxytocin 10 IU in 1 mL and 1 mL 0.9% normal saline as placebo intravenously over 1 minute immediately after the delivery of the baby Charles 2019 Intervention group 1: IV oxytocin 10 IU in 500 mL saline through gravity-driven infusion with the roller clamp fully open after the delivery of the baby Intervention group 2: IV oxytocin 10 IU oxytocin over 1 minute after the delivery of the baby Control: IM oxytocin 10 IU after the delivery of the baby Dagdeviren 2016 Intervention: IV oxytocin 10 IU in 1000 mL saline at a rate of 1 mL/minute after delivery of the anterior shoulder Control: IM oxytocin 10 IU after delivery of the anterior shoulder Durocher 2019

	Intervention: IV oxytocin 10 IU in 500 mL saline solution at a rate of 12 mL/minute and 1 ampoule intramuscularly immediately after delivery of the baby Control: IM oxytocin 10 IU and 1 ampoule in 500 mL saline solution as placebo intravenously at a rate of 12 mL/minute immediately after the delivery of the baby Neri-Mejia 2016 Intervention group 1: IV oxytocin 10 IU over 1 minute after the delivery of the anterior shoulder Intervention group 2: IV oxytocin 20 IU in 1000 mL 5% glucose solution at a rate of 150 mL/hour after the delivery of the placenta (group not eligible for inclusion in this review) Control group: IM oxytocin 10 IU after the delivery of the anterior shoulder. Oguz 2014 Intervention group 1: 10 IU IV oxytocin at 1 mL/minute, this was given after delivery of the baby and cord clamping, Intervention group 2: 10 IU IV oxytocin at 1 mL/minute, this was given at the point of delivery of the anterior shoulder. Control group 1: 10 IU IM oxytocin, this was given after delivery of the baby and cord clamping Control group 2: 10 IU IM oxytocin, this was given at the point of delivery of the anterior shoulder. Sangkhomkhamhang 2015 Intervention: IV 10 IU of oxytocin in 10 mL normal saline administered over 2 minute after delivery of the anterior shoulder Control: IM 10 IU of oxytocin after delivery of the anterior shoulder
Duration of follow-up	N/A
Sources of funding	Adnan 2018 Trinity College, University of Dublin

	Coombe Women and Infants University Hospital Charles 2019 The Bill & Melinda Gates Foundation Dagdeviren 2016 Source of funding not reported Durocher 2019 The Bill & Melinda Gates Foundation Neri-Mejia 2016 Source of funding not reported Oguz 2014 Source of funding not reported Sangkhomkhamhang 2015 Source of funding not reported
Sample size	Adnan 2018 N= 1075 randomised IV bolus oxytocin n= 517 IM oxytocin n= 518 Charles 2019 N= 4913 randomised IV infusion oxytocin 10 IU in 500 mL saline n= 2108 IV bolus oxytocin 10 IU oxytocin over 1 minute n= 701

	IM oxytocin n= 2104 Dagdeviren 2016 N= 256 randomised IV oxytocin n=128 IM oxytocin n=128 Durocher 2019 N= 480 randomised IV infusion oxytocin n= 239 IM oxytocin n= 241 Neri-Mejia 2016 N= 66 randomised (23 excluded from the review) IV bolus oxytocin n= 23 IM oxytocin n= 22 Oguz 2014 N= 600 randomised IV bolus oxytocin after the delivery of the baby n= 150 IV bolus oxytocin at the point of delivery of the anterior shoulder n=150 IM oxytocin after the delivery of the baby n= 150 IM oxytocin at the point of delivery of the anterior shoulder n=150 Sangkhomkhamhang 2015 N= 450 randomised

	IV bolus oxytocin n= 225 IM oxytocin n=225
Other information	Setting: Adnan 2018 University affiliated maternity unit Charles 2019 1 teaching hospital and 1 university hospital Dagdeviren 2016 Teaching hospital Durocher 2019 Tertiary- level hospital Neri-Mejia 2016 Regional Hospital Oguz 2014 Teaching hospital Sangkhomkhamhang 2015 Hospital

Outcomes

Adnan 2018

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 517	Intramuscular oxytocin during third stage of labour, , N = 518	Intravenous oxytocin infusion during third stage of labour, , N =
Side effects after oxytocin Nausea, vomiting, hypotension, tachycardia, headaches, shivering No of events	n = 21	n = 27	*N/A*
Primary PPH (≥ 500 mL) No of events	n = 97	n = 120	*N/A*
Severe PPH (≥ 1000 mL) No of events	n = 24	n = 42	*N/A*
Need for additional uterotonics No of events	n = 128	n = 140	*N/A*
Admission to a high dependency unit No of events	n = 9	n = 19	*N/A*

Charles 2019

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 701	Intramuscular oxytocin during third stage of labour, , N = 2104	Intravenous oxytocin infusion during third stage of labour, , N = 2108
Primary PPH No of events	n = 5	n = 21	n = 11

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 701	Intramuscular oxytocin during third stage of labour, , N = 2104	Intravenous oxytocin infusion during third stage of labour, , N = 2108
Severe PPH No of events	n = 1	n = 9	n = 4
Need for manual placenta removal No of events	n = 9	n = 60	n = 50
Need for additional uterotonics No of events	n = 7	n = 23	n = 13

Dagdeviren 2016

Outcome	Intravenous oxytocin bolus during third stage of labour, , N =	Intramuscular oxytocin during third stage of labour, , N = 128	Intravenous oxytocin infusion during third stage of labour, , N = 128
Primary PPH No of events	*N/A*	n = 15	n = 15
Severe PPH No of events	*N/A*	n = 0	n = 4
Need for manual removal of placenta No of events	*N/A*	n = 2	n = 2

Outcome	Intravenous oxytocin bolus during third stage of labour, , N =	Intramuscular oxytocin during third stage of labour, , N = 128	Intravenous oxytocin infusion during third stage of labour, , N = 128
Need for additional uterotonics No of events	*N/A*	n = 3	n = 12

Durocher 2019

Outcome	Intravenous oxytocin bolus during third stage of labour, , N =	Intramuscular oxytocin during third stage of labour, , N = 241	Intravenous oxytocin infusion during third stage of labour, , N = 239
Primary PPH Primary PPH No of events	*N/A*	n = 57	n = 49
Severe PPH Severe PPH No of events	*N/A*	n = 18	n = 14
Need for manual removal of placenta No of events	*N/A*	n = 3	n = 0
Need for additional utertonics No of events	*N/A*	n = 30	n = 13

Orguz Orhan 2014

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 300	Intramuscular oxytocin during third stage of labour, , N = 300	Intravenous oxytocin infusion during third stage of labour, , N =
Primary PPH (≥ 500 mL) Reported blood loss > 600 mL No of events	n = 12	n = 18	*N/A*
Need for additional uterotonics No of events	n = 6	n = 9	*N/A*
Retained placenta or manual removal of placenta No of events	n = 2	n = 2	*N/A*

Neri-Meija 2016

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 21	Intramuscular oxytocin during third stage of labour, , N = 22	Intravenous oxytocin infusion during third stage of labour, , N =
Need for additional uterotonics No of events	n = 0	n = 2	*N/A*
Retained placenta or manual removal of placenta No of events	n = 0	n = 0	*N/A*
Side effects Hypotension	n = 1	n = 0	*N/A*

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 21	Intramuscular oxytocin during third stage of labour, , N = 22	Intravenous oxytocin infusion during third stage of labour, , N =
No of events			

Sangkomkamhang 2015

Outcome	Intravenous oxytocin bolus during third stage of labour, , N = 225	Intramuscular oxytocin during third stage of labour, , N = 225	Intravenous oxytocin infusion during third stage of labour, , N =
PPH ≥ 500 mL PPH not clearly defined by authors (measured up to 24 hours postpartum) No of events	n = 5	n = 11	*N/A*

Critical Appraisal

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
Oladapo 2020	Total score: 13/16
Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool	
Adnan 2018	Random sequence generation: low Allocation concealment: low Incomplete outcome data: low Selective reporting: low Other bias: low Blinding of participants and personnel: low

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
	Blinding of outcome assessment: low
Charles 2019	Random sequence generation: low Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: low Other bias: some concerns Blinding of participants and personnel: high Blinding of outcome assessment: some concerns
Dagdeviren 2016	Random sequence generation: low Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: low Other bias: low Blinding of participants and personnel: high Blinding of outcome assessment: high
Durocher 2019	Random sequence generation: low Allocation concealment: low Incomplete outcome data: low Selective reporting: low

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
	Other bias: low Blinding of participants and personnel: low Blinding of outcome assessment: low
Neri- Mejia 2016	Random sequence generation: some concerns Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: some concerns Other bias: low Blinding of participants and personnel: some concerns Blinding of outcome assessment: some concerns
Oguz 2014	Random sequence generation: low Allocation concealment: some concerns Incomplete outcome data: low Selective reporting: high Other bias: some concerns Blinding of participants and personnel: high Blinding of outcome assessment: some concerns
Sangkhomkhamhang 2015	Random sequence generation: some concerns Allocation concealment: some concerns

Quality of the Cochrane Systematic review assessed using AMSTAR checklist	
	Incomplete outcome data: low Selective reporting: low Other bias: low Blinding of participants and personnel: high Blinding of outcome assessment: high

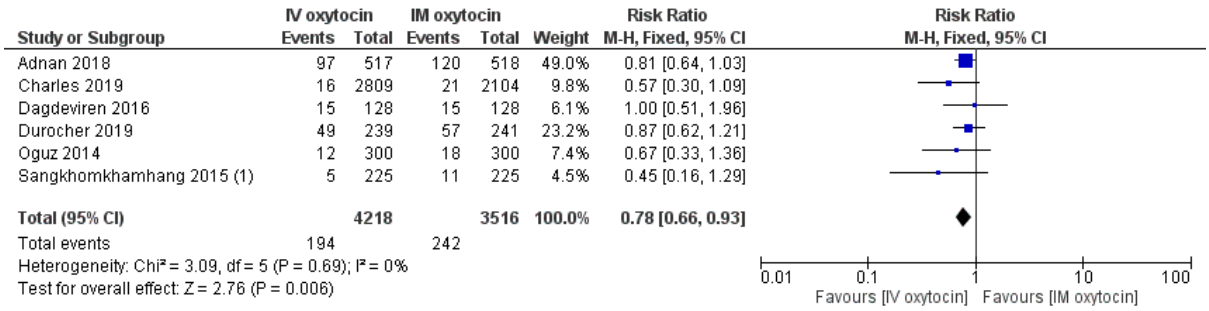
Appendix E Forest plots

Forest plots for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here; the quality assessment for such outcomes is provided in the GRADE profiles in appendix F.

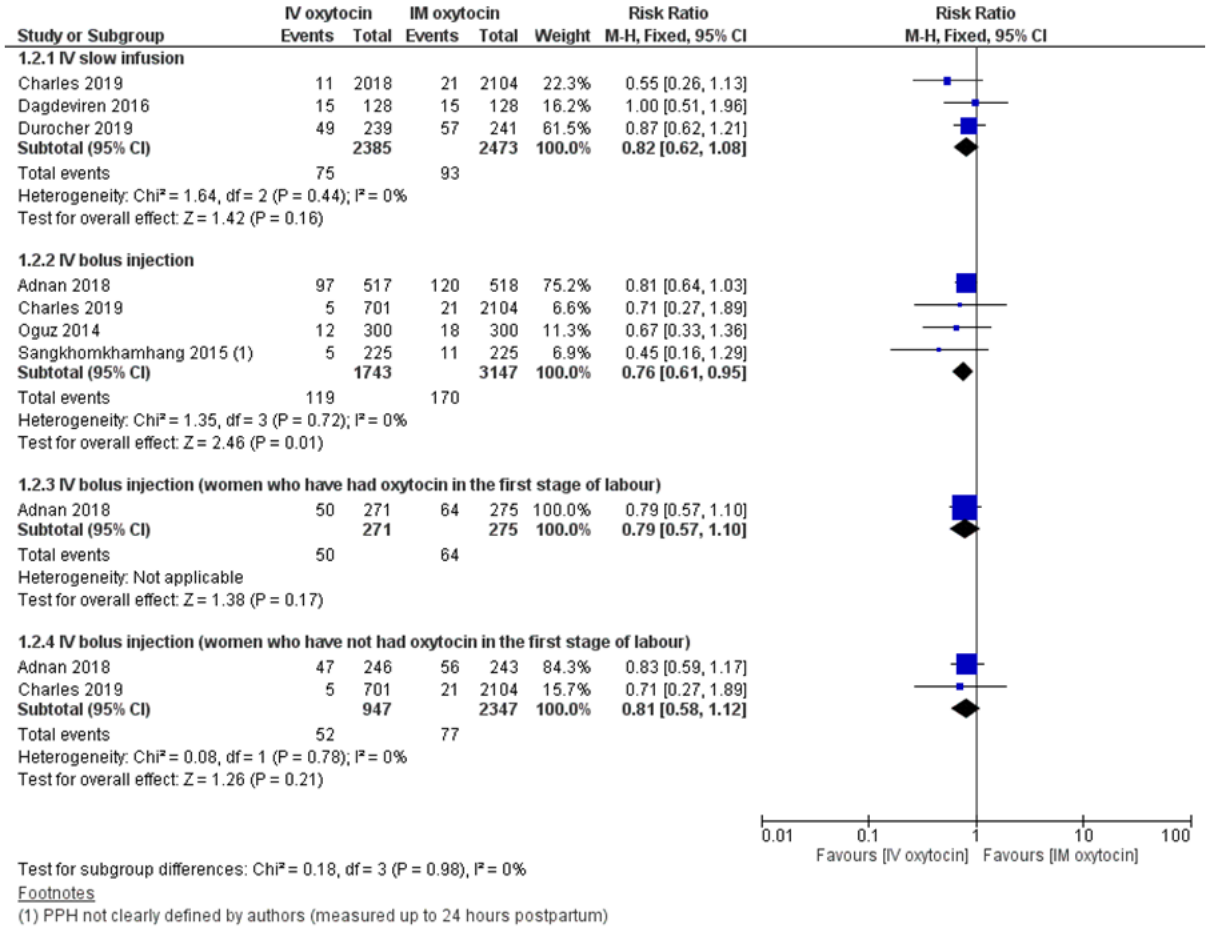
Comparison 1: IV oxytocin vs IM oxytocin

Figure 2: Primary PPH (blood loss ≥ 500 mL) – overall estimate



Footnotes
(1) PPH not clearly defined by authors (measured up to 24 hours postpartum)

Figure 3: Primary PPH (blood loss ≥ 500 mL) - by type of IV administration and women who have had oxytocin in the first stage or not



Test for subgroup differences: Chi² = 0.18, df = 3 (P = 0.98), I² = 0%

Footnotes

(1) PPH not clearly defined by authors (measured up to 24 hours postpartum)

Figure 4: Severe PPH (blood loss ≥ 1000 mL) - overall estimate

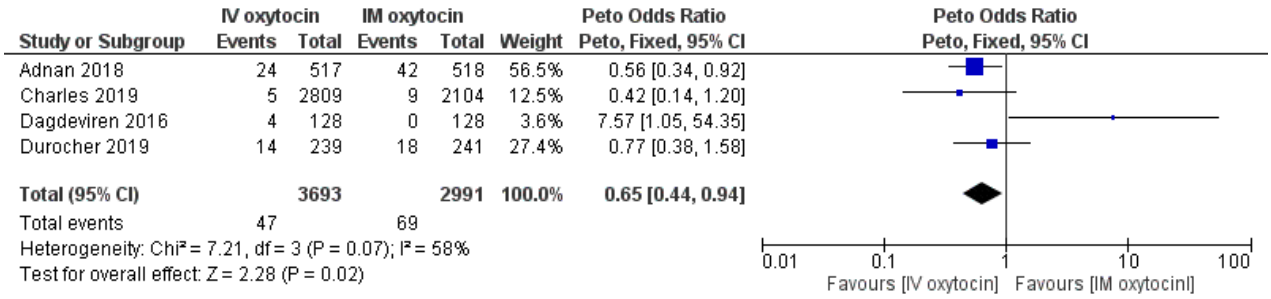


Figure 5: Severe PPH (blood loss ≥ 1000 mL) - by type of IV administration and women who have had oxytocin in the first stage or not

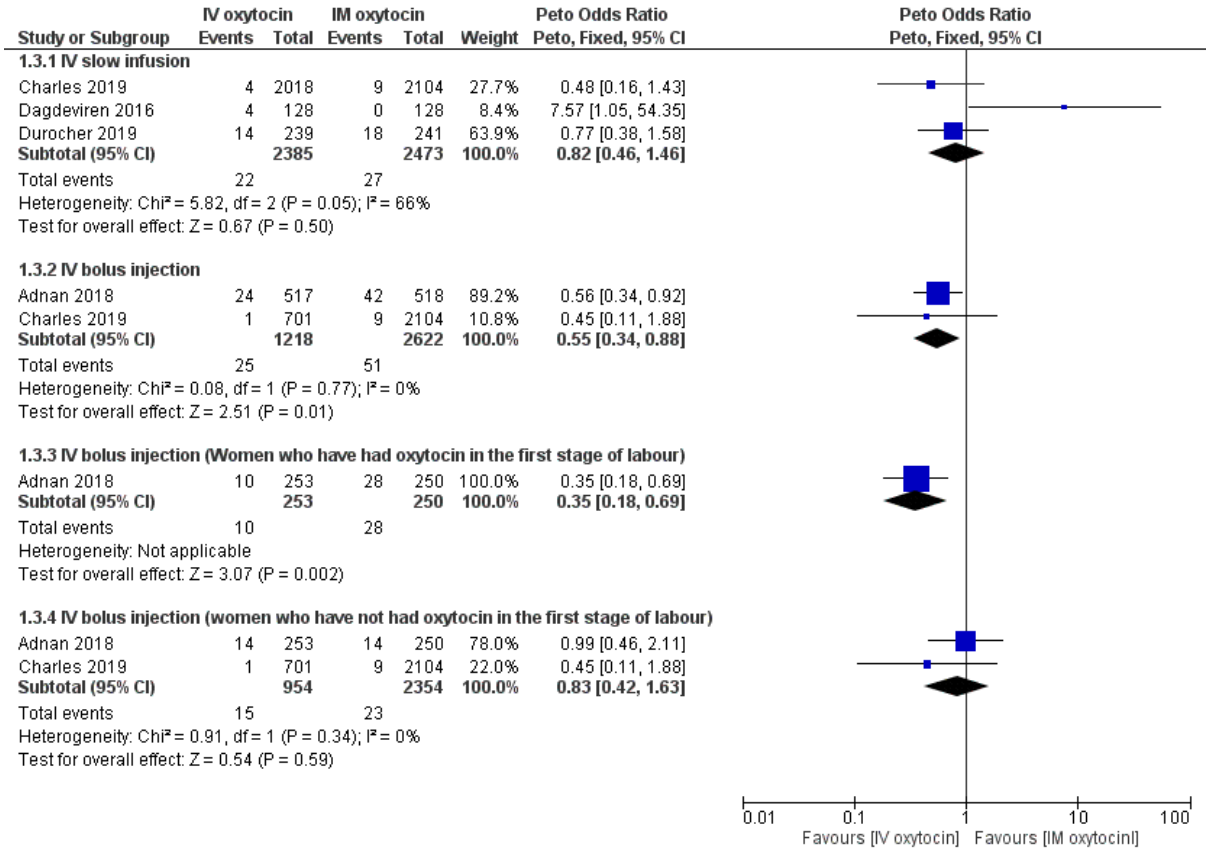


Figure 6: Need for manual removal of placenta – overall estimate

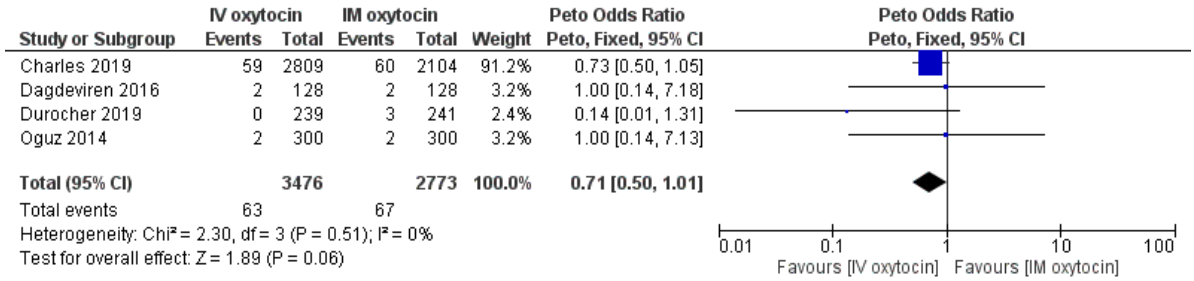


Figure 7: Need for manual removal of placenta - by type of IV administration and women who have had oxytocin in the first stage or not

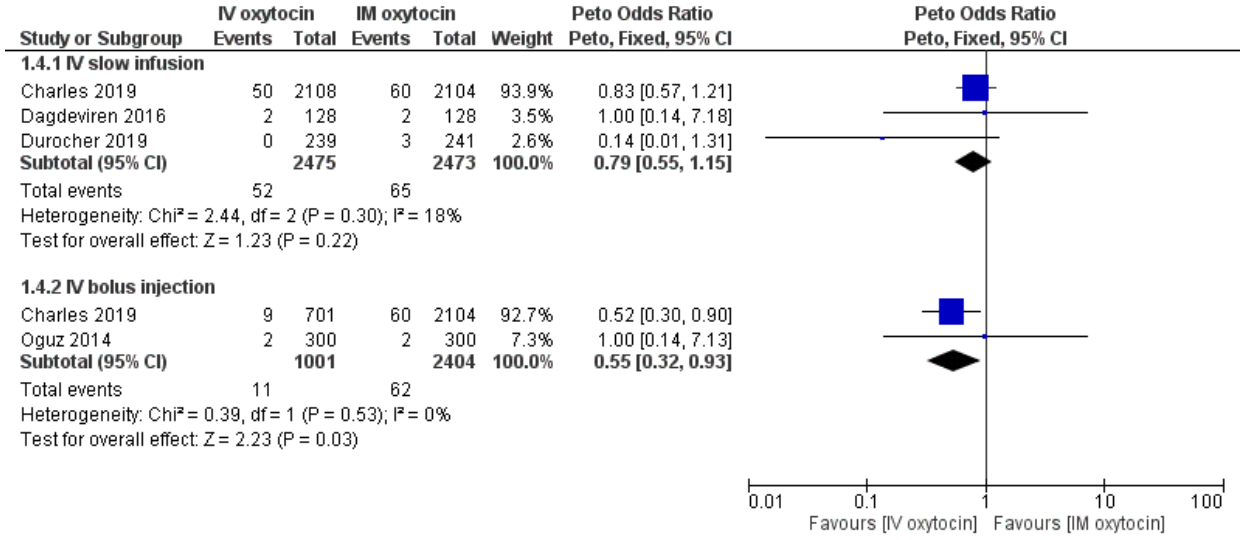


Figure 8: Need for additional uterotonics during the third stage or within the first 48 hours – overall estimate

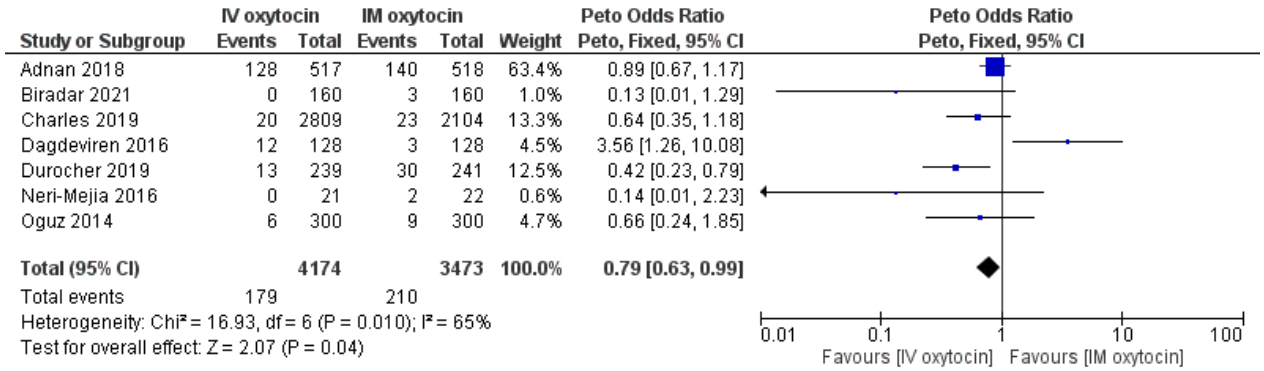


Figure 9: Need for additional uterotonics during the third stage or within the first 48 hours - by type of IV administration and women who have had oxytocin in the first stage or not

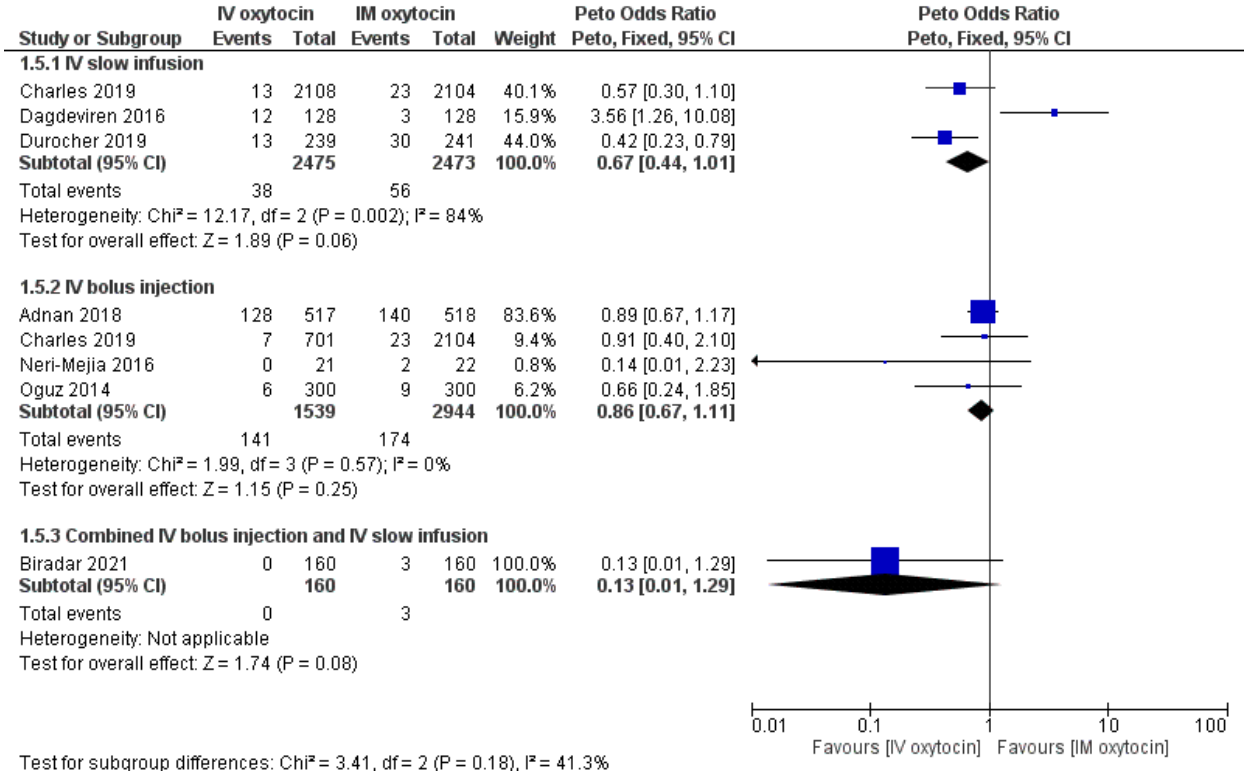
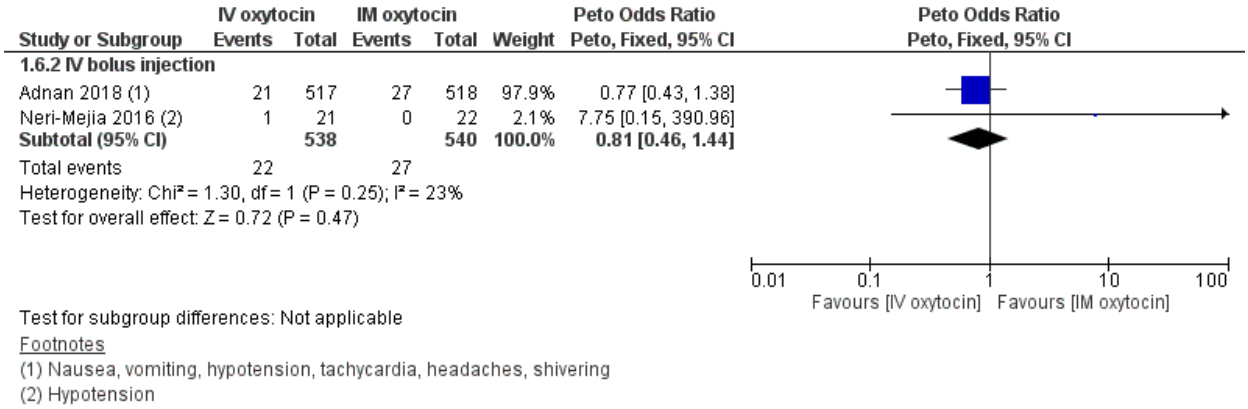


Figure 10: Side effects - by type of IV administration and women who have had oxytocin in the first stage or not



Footnotes

(1) Nausea, vomiting, hypotension, tachycardia, headaches, shivering

(2) Hypotension

Appendix F GRADE tables

GRADE tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Table 4: Evidence profile for comparison 1: IV oxytocin vs IM oxytocin

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**IV oxytocin**	**IM oxytocin**	**Relative (95% CI)**	**Absolute**		
Maternal admission to intensive therapy unit (ITU) or high-dependency area - IV bolus injection												
1 (Adnan 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	9/517 (1.7%)	19/518 (3.7%)	RR 0.47 (0.22 to 1.04)	19 fewer per 1000 (from 29 fewer to 1 more)	MODERATE	CRITICAL
Primary PPH (blood loss ≥ 500 mL)- overall estimate												
6 (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019, Oguz 2014, Sangkhomkhamhang 2015)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	198/4218 (4.6%)	242/3516 (6.9%)	RR 0.78 (0.66 to 0.93)	15 fewer per 1000 (from 5 fewer to 23 fewer)	LOW	CRITICAL
Primary PPH (blood loss ≥ 500 mL) - IV slow infusion												
3 (Charles 2019, Dagdeviren 2016, Durocher 2019)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	75/2385 (3.1%)	93/2473 (3.8%)	RR 0.82 (0.62 to 1.08)	7 fewer per 1000 (from 14 fewer to 3 more)	MODERATE	CRITICAL
Primary PPH (blood loss ≥ 500 mL) - IV bolus injection												
4 (Adnan 2018, Charles 2019, Oguz 2014, Sangkhomkhamhang 2015)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	119/1743 (6.8%)	170/3147 (14.3%)	RR 0.76 (0.61 to 0.95)	13 fewer per 1000 (from 3 fewer to 21 fewer)	LOW	CRITICAL
Primary PPH (blood loss ≥ 500 mL) - IV bolus injection (women who have had oxytocin in the first stage of labour)												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**IV oxytocin**	**IM oxytocin**	**Relative (95% CI)**	**Absolute**		
1 (Adnan 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	50/ 271 (18.5%)	64/ 275 (23.3%)	RR 0.79 (0.57 to 1.1)	49 fewer per 1000 (from 100 fewer to 23 more)	MODERATE	CRITICAL
Primary PPH (blood loss ≥ 500 mL) - IV bolus injection (women who have not had oxytocin in the first stage of labour)												
2 (Adnan 2018, Charles 2019)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	52/947 (5.5%)	77/2347 (3.3%)	RR 0.81 (0.58 to 1.12)	6 fewer per 1000 (from 14 fewer to 4 more)	LOW	CRITICAL
Severe PPH (blood loss ≥ 1000 mL)- overall estimate												
4 (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019)	observational studies	no serious risk of bias	serious[3]	no serious indirectness	serious[1]	none	47/3693 (1.3%)	69/2991 (2.3%)	POR 0.65 (0.44 to 0.94)	8 fewer per 1000 (from 1 fewer to 13 fewer)	LOW	CRITICAL
Severe PPH (blood loss ≥ 1000 mL) - IV slow infusion												
3 (Charles 2019, Dagdeviren 2016, Durocher 2019)	randomised trials	no serious risk of bias	serious[3]	no serious indirectness	very serious[4]	none	22/2385 (0.92%)	27/2473 (1.1%)	POR 0.82 (0.46 to 1.46)	2 fewer per 1000 (from 6 fewer to 5 more)	LOW	CRITICAL
Severe PPH (≥ 1000 mL) - IV bolus injection												
2 (Adnan 2018, Charles 2019)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	24/517 (4.6%)	42/518 (8.1%)	POR 0.55 (0.34 to 0.88)	36 fewer per 1000 (from 6 fewer to 54 fewer)	MODERATE	CRITICAL
Severe PPH (blood loss ≥ 1000 mL) - IV bolus injection (women who have had oxytocin in the first stage of labour)												
1 (Adnan 2018)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	10/253 (4%)	28/250 (11.2%)	POR 0.35 (0.18 to 0.69)	73 fewer per 1000 (from 35 fewer to 92 fewer)	HIGH	CRITICAL
Severe PPH (blood loss ≥ 1000 mL) - IV bolus injection (women who have not had oxytocin in the first stage of labour)												
2 (Adnan 2018, Charles 2019)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	15/954 (1.6%)	23/2354 (1%)	POR 0.83 (0.42 to 1.63)	2 fewer per 1000 (from 6 fewer to 6 more)	LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	IV oxytocin	IM oxytocin	Relative (95% CI)	Absolute		
Need for manual removal of placenta- overall estimate												
4 (Charles 2019, Dagdeviren 2016, Durocher 2019, Oguz 2014)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	63/3476 (1.8%)	67/4877 (2.4%)	POR 0.71 (0.50 to 1.01)	7 fewer per 1000 (from 12 fewer to 0 more)	LOW	IMPORTANT
Need for manual removal of placenta - IV slow infusion												
3 (Charles 2019, Dagdeviren 2016, Durocher 2019)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious[1]	none	52/2475 (2.1%)	65/2473 (2.6%)	POR 0.79 (0.55 to 1.15)	6 fewer per 1000 (from 12 fewer to 4 more)	MODERATE	IMPORTANT
Need for manual removal of placenta - IV bolus injection												
2 (Charles 2019, Oguz 2014)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	11/1001 (1.1%)	62/2404 (2.6%)	POR 0.55 (0.32 to 0.93)	12 fewer per 1000 (from 2 fewer to 18 fewer)	LOW	IMPORTANT
Need for additional uterotonics during the third stage or within the first 48 hours- overall estimate												
6 (Adnan 2018, Charles 2019, Dagdeviren 2016, Durocher 2019, Neri-Mejia 2016, Oguz 2014)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	179/4174 (4.3%)	230/3463 (6.6%)	POR 0.79 (0.63 to 0.99)	14 fewer per 1000 (from 1 fewer to 25 fewer)	LOW	IMPORTANT
Need for additional uterotonics during the third stage or within the first 48 hours - IV slow infusion												
3 (Charles 2019, Dagdeviren 2016, Durocher 2019)	randomised trials	no serious risk of bias	serious[3]	no serious indirectness	serious[1]	none	38/2475 (1.5%)	56/2473 (2.3%)	POR 0.67 (0.44 to 1.01)	7 fewer per 1000 (from 13 fewer to 0 MORE)	HIGH	IMPORTANT
Need for additional uterotonics during the third stage or within the first 48 hours - IV bolus injection												
4 (Adnan 2018, Charles 2019, Neri-Mejia 2016, Oguz 2014)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	serious[1]	none	141/1539 (9.2%)	174/2944 (5.9%)	POR 0.86 (0.67 to 1.11)	8 fewer per 1000 (from 20 fewer to 7 more)	LOW	IMPORTANT
Need for additional uterotonics during the third stage or within the first 48 hours - Combined IV bolus injection and IV slow infusion												

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**IV oxytocin**	**IM oxytocin**	**Relative (95% CI)**	**Absolute**		
1 (Biradar 2021)	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	very serious[4]	none	0/160 (0%)	3/160 (1.9%)	POR 0.13 (0.01 to 1.29)	16 fewer per 1000 (from 19 fewer to 5 more)	LOW	IMPORTANT
Side effects - IV bolus injection												
2 (Adnan 2018, Neri-Mejia 2016)	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[4]	none	22/538 (4.1%)	27/540 (5%)	POR 0.81 (0.46 to 1.44)	9 fewer per 1000 (from 27 fewer to 22 more)	LOW	IMPORTANT

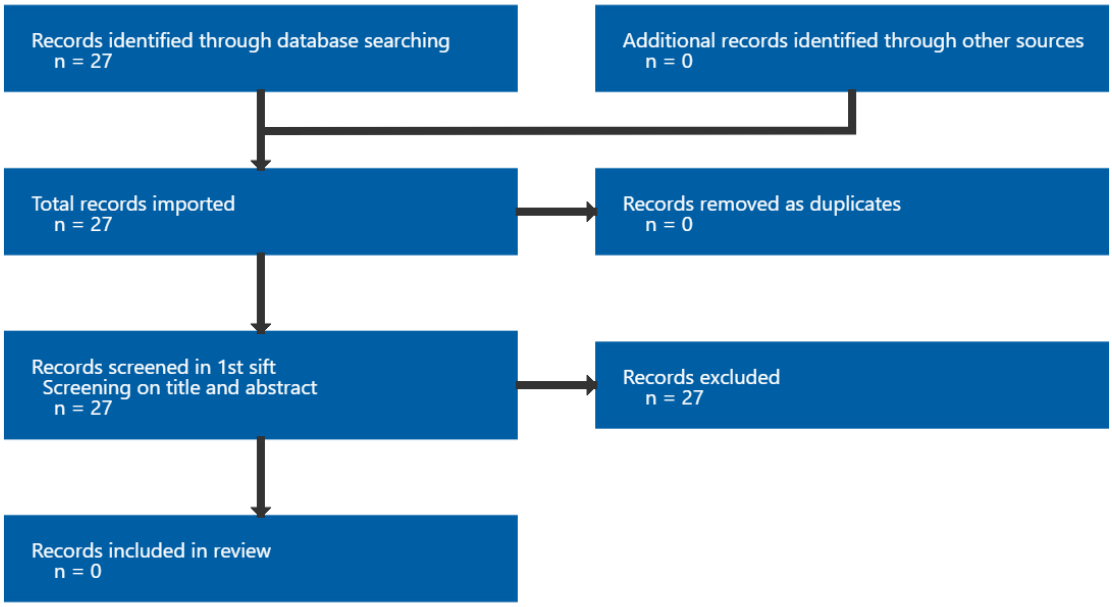
IM: intramuscular; ITU: intensive therapy unit; IV: intravenous; mL: millimetres; POR: peto odds ratio; PPH: postpartum haemorrhage
1 95% CI crosses 1 MID
2 Serious concerns of risk of bias in the evidence contributing to the outcomes as per RoB 2.0
3 Serious heterogeneity
4 95% CI crosses 2 MIDs

Appendix G Economic evidence study selection

Study selection for: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

No economic evidence was identified which was applicable to this review question.

Figure 11: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

No evidence was identified which was applicable to this review question.

Appendix I Economic model

Economic model for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

Excluded effectiveness studies

Table 5: Excluded studies and reasons for their exclusion

Study	Reason
Adnan, Nita, Conlan-Trant, Rebecca, McCormick, Ciara et al. (2018) Intramuscular versus intravenous oxytocin to prevent postpartum haemorrhage at vaginal delivery: randomised controlled trial. BMJ (Clinical research ed.) 362: k3546	- Included as part of a systematic review
Akinaga, Chieko, Uchizaki, Sakiko, Kurita, Tadayoshi et al. (2016) Randomized double-blind comparison of the effects of intramyometrial and intravenous oxytocin during elective cesarean section. The journal of obstetrics and gynaecology research 42(4): 404-9	- Population not in PICO Population is women who have had elective caesarean birth
Ashwal, E., Hiersch, L., Wertheimer, A. et al. (2016) The effect of post-partum oxytocin regimen on hemoglobin decline-a randomized controlled trial. American journal of obstetrics and gynecology 214(1): S197-S198	- Conference abstract
Blum, J., Durocher, J., Trussell, J. et al. (2011) How effective are the components of active management of the third stage of labor?. Contraception 84(3): 336	- Conference abstract
Carroli, G., Durocher, J., Dzuba, I. et al. (2018) Does route matter? intravenous versus intramuscular oxytocin for prevention of postpartum hemorrhage. International journal of gynaecology and obstetrics 143: 236	- Conference abstract.
Charles, Dyanna, Anger, Holly, Dabash, Rasha et al. (2019) Intramuscular injection, intravenous infusion, and intravenous bolus of oxytocin in the third stage of labor for prevention of postpartum hemorrhage: a three-arm randomized control trial. BMC pregnancy and childbirth 19(1): 38	- Included as part of a systematic review
Dagdeviren, Hediye, Cengiz, Huseyin, Heydarova, Ulkar et al. (2016) Intramuscular versus intravenous prophylactic oxytocin for postpartum hemorrhage after vaginal delivery: a randomized controlled study. Archives of gynecology and obstetrics 294(5): 911-916	- Included as part of a systematic review
Durocher, J., Blum, J., Sheldon, W. R. et al. (2012) Does the effect of oxytocin prophylaxis on post-partum blood loss depend on route of administration?. International journal of gynaecology and obstetrics 119: S332	- Conference abstract
Durocher, Jill, Dzuba, Ilana G., Carroli, Guillermo et al. (2019) Does route matter?	- Included as part of a systematic review

Study	Reason
Impact of route of oxytocin administration on postpartum bleeding: A double-blind, randomized controlled trial. PloS one 14(10): e0222981	
Ebada, Mahmoud Ahmed; Elmatboly, Abdelmagid M.; Baligh, Galal (2020) Intravenous Oxytocin versus Intramuscular Oxytocin for the Management of Postpartum Hemorrhage: A Systematic Review and Meta-Analysis. Current drug research reviews 12(2): 150-157	- Systematic review- more recent systematic review included
Leduc, Dean, Senikas, Vyta, Lalonde, Andre B. et al. (2009) Active management of the third stage of labour: prevention and treatment of postpartum hemorrhage. Journal of obstetrics and gynaecology Canada : JOGC = Journal d'obstetrique et gynecologie du Canada : JOGC 31(10): 980-993	- Narrative review
Neri-Mejía, M. and Pedraza-Avilés, A. G. (2016) Active management of the third stage of labor: three schemes of oxytocin: randomised clinical trial. Ginecologia y obstetricia de Mexico 84(5): 306-313	- Included as part of a systematic review
Oguz Orhan, E., Dilbaz, B., Aksakal, S. E. et al. (2014) Prospective randomized trial of oxytocin administration for active management of the third stage of labor. International journal of gynaecology and obstetrics 127(2): 175-179	- Included as part of a systematic review
Oladapo, Olufemi T.; Okusanya, Babasola O.; Abalos, Edgardo (2018) Intramuscular versus intravenous prophylactic oxytocin for the third stage of labour. The Cochrane database of systematic reviews 9: cd009332	- Systematic review- more recent systematic review included
Paikhomba Singh, K.; Kameshore, N.; Kamei, H. (2015) Prophylactic intramuscular injection of oxytocin vs intravenous infusion of oxytocin to minimise blood loss at caesarean section. International Journal of Gynecology and Obstetrics 131(suppl5): e290	- Conference abstract
Sangkomkamhang, U. and Kruangpatee, A. (2015) A randomised controlled trial of intravenous versus intramuscular oxytocin in the prevention of postpartum hemorrhage during the third stage of labor. Journal of health science 24(2): 354-359	- Included as part of a systematic review
Westhoff, Gina; Cotter, Amanda M.; Tolosa, Jorge E. (2013) Prophylactic oxytocin for the third stage of labour to prevent postpartum haemorrhage. The Cochrane database of systematic reviews: cd001808	- Comparator not in PICO Systematic review comparing oxytocin to no uterotonics or other uterotonics
Wu, Yu, Wang, Huan, Wu, Qi-Yan et al. (2020) A meta-analysis of the effects of intramuscular and intravenous injection of oxytocin on the third stage of labor. Archives of gynecology and obstetrics 301(3): 643-653	- Systematic review- systematic review with more relevant outcomes included
Zhou, Yuan-Hong, Xie, Yan, Luo, You-Zhen et al. (2020) Intramuscular versus intravenous oxytocin for the third stage of labor after vaginal	- Systematic review- more recent systematic review included

Study	Reason
delivery to prevent postpartum hemorrhage: a meta-analysis of randomized controlled trials. European journal of obstetrics, gynecology, and reproductive biology 250: 265-271	

Excluded economic studies

No economic evidence was identified for this review.

Appendix K Research recommendations – full details

Research recommendations for review question: Is intravenous administration of oxytocin more effective than intramuscular administration in the active management of the third stage of labour?

No research recommendations were made for this review question.