National Institute for Health and Care Excellence

Final

Intrapartum care

[J] Evidence reviews for prophylactic antibiotics for birth with forceps or ventouse

NICE guideline NG235

Evidence reviews underpinning recommendation 1.9.43 and a research recommendation in the NICE guideline

September 2023

Final

These evidence reviews were developed by NICE

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Contents

Prophylactic antibiotics for birth with forceps or ventouse

Review question

What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Introduction

Assisted vaginal births carry a higher risk of infection due to their invasive nature and the increase in vaginal examinations that are required, with evidence showing that there is an increased incidence of postnatal infections in women who have had a vaginal birth with forceps or ventouse. Prophylactic antibiotic use might prevent postnatal infections associated with assisted vaginal birth, however the effectiveness is unclear.

This review aims to find out whether administration of prophylactic antibiotics reduces the risk of infections related to assisted vaginal births with forceps or ventouse, and to determine if there are any negative effects on neonatal outcomes such as breastfeeding, and on the incidence of maternal adverse reactions.

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 labour who are pregnant with a single baby, who go into labour at term (37 to 42 weeks of pregnancy) and who do not have any pre-existing medical conditions or antenatal conditions that predispose to a higher risk birth • Women in labour whose baby has not been identified before labour to be at high risk of adverse outcome • Singleton babies born at term (37 to 42 weeks of pregnancy) with no previously identified problems (for example congenital malformations, genetic anomalies, intrauterine growth restriction, placental problems) • Women having an assisted vaginal birth (forceps or vacuum/suction birth) without evidence of an active infection or other conditions requiring antibiotics
Intervention	Prophylactic antibiotics given immediately before or as soon as possible after an assisted vaginal birth (forceps or vacuum birth)
Comparison	• Placebo • Standard care (no antibiotics)
Outcome	**Critical:** • Endometritis • Infection at perineal/vaginal or episiotomy site (up till 6 weeks) • Sepsis following perineum infection or endometritis **Important:** • Maternal adverse reaction to antibiotics • Long-term neonatal outcomes (asthma, allergies) • Breastfeeding at 6 weeks • Perineal pain at 6 weeks • Antibiotic resistance

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.

Effectiveness evidence

Included studies

One Cochrane systematic review (Liabsuetrakul 2020), which 2 included randomised controlled trials (RCTs) (Heitmann 1989 and Knight 2019) was included in this review.

One RCT (Heitmann 1989) compared prophylactic antibiotics given postnatally to no treatment. One RCT (Knight 2019) compared prophylactic antibiotics given postnatally to placebo.

Studies were from the United Kingdom and the United States.

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
Liabsuetrakul 2020 Cochrane Systematic Review United Kingdom; United States	K=2	Heitmann 1989: N=393 women undergoing forceps or vacuum birth	2g of cefotetan (cephalosporin). Single dose, IV administration Given after cord-clamping.	No treatment	• Endometritis
		Knight 2019: N= 3420 women undergoing forceps or vacuum birth	1g Amoxicillin and 200mg clavulanic acid (co-amoxiclav). Single dose, IV administration. Given as soon as possible after birth (no more than 6 hours).	Placebo: 20ml IV sterile 0.9% saline within the same timeframe.	• Endometritis • Infection at perineal/vaginal episiotomy site • Sepsis following perineum infection or endometritis • Maternal adverse reaction to antibiotics • Breastfeed at 6 weeks • Perineal pain at 6 weeks

IV: intravenous

See the full evidence tables in appendix D. No meta-analysis was conducted (and so there are no forest plots in appendix E).

Summary of the evidence

Prophylactic antibiotics were compared to either no treatment or placebo. All of the evidence used a single dose of antibiotics given intravenously (IV) after birth. All of the evidence included women who had undergone an assisted birth using forceps or vacuum, but the data were not available to analyse the 2 assistance methods separately. The antibiotic used was either cefotetan or co-amoxiclav.

Prophylactic antibiotics, using cefotetan, was compared to no treatment. The evidence showed an important benefit for cefotetan over no treatment for endometritis, with unknown follow-up period. The evidence was rated low quality for some concerns around bias, and some concerns around indirectness of the population.

Prophylactic antibiotics, using co-amoxiclav, was compared to placebo. The evidence showed an important benefit for co-amoxiclav over placebo in terms of infection at

episiotomy or laceration site. The evidence showed no evidence of an important difference between groups for endometritis, systemic sepsis, maternal adverse reactions and perineal pain at 6 weeks. The evidence ranged from very low to moderate quality, with some concerns over indirectness and some concerns over imprecision around the estimate of the effect. Moderate quality evidence showed no important difference between groups for breastfeeding at 6 weeks, with some concerns around indirectness of the population.

No evidence was identified for long term neonatal outcomes, or antibiotic resistance.

See appendix F for full GRADE tables.

Economic evidence

Included studies

One economic study was identified which was relevant to this question (Knight 2019).

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

Excluded studies

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

Summary of included economic evidence

See Table 3 for the economic evidence profile of the included study.

Table 3: Economic evidence profile of a systematic review of economic evaluations of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effect	Cost effectivenss	
Knight 2019 Prophylactic antibiotic after operative birth versus placebo	Potentially serious limitations[1,2]	Directly applicable	Cost analysis alongside a randomised controlled trial	-£52	80 per 1000 fewer suspected or confirmed infections at 6 weeks post birth[3]	Dominance	99% confidence intervals were reported for point estimates of mean difference in costs Sensitivity analysis was undertaken with imputation for missing data

[1] Staffing and consumable costs were not included in the intervention costs.
[2] There were statistically significant differences in the characteristics of the women who returned the postal questionnaire and those who did not.
[3] Taken from the primary outcome of the study but not reported as part of the cost analysis

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Unit costs

Resource	Unit costs	Source
Co-amoxiclav 1000mg/200mg powder for solution for injection vials	£1.06	BNF https://bnf.nice.org.uk/drugs/co-amoxiclav/medicinal-forms/#powder-for-solution-for-injection (accessed 21/06/2022)
20ml sterile water	£0.72	NHS Drugs Tariff (July 2022)
20ml syringe	£0.13	https://www.medisave.co.uk/bd-discarditm-20ml-2-piece-eccentric-tip-syringe-box-of-100.html (accessed 19/07/2022)
Drawing up needle	£0.11	https://www.medisave.co.uk/bd-blunt-fill-safety-draw-up-needle-18-g-red-40-mm-1-45-degr-qty100.html?gclid=Cj0KCQiAjc2QBhDgARIsAMc3SqRwZqK-ke3ULYIprmDFAt_Dc9aR0oMuZrNws704GeECKKs7fGV8K2gaAqUGEALw_wcB (accessed 31/05/2022)
Obstetrician [a]	£52 per hour	PSSRU (2021)
Midwife [b]	£51 per hour	PSSRU (2021)

BNF: British National Formulary; NHS: National Health Service; PSSRU: Personal Social Services Research Unit
a) Obstetrician prescribes antibiotic
b) Midwives check and administer drug

The committee's discussion and interpretation of the evidence

The outcomes that matter most

As the main aim following prophylactic use of antibiotics is a reduction in the risk of infection, the committee chose endometritis, infection at the perineal or vaginal episiotomy site, and sepsis following perineum infection or endometritis, as the critical outcomes for this review. They agreed that all 3 outcomes would provide information regarding the efficacy of prophylactic antibiotics at reducing the risk of local infections following assisted vaginal birth. They also agreed that this would provide information on whether antibiotics reduce the risk of any systematic infections that develop following local perineum infections or endometritis.

The committee also agreed to look at maternal adverse reactions as an important outcome, as it was necessary to consider any of the harms associated with antibiotic use. The committee also chose to include long term neonatal outcomes such as asthma and allergies. They discussed that antibiotics could have an effect on the neonatal immune system, if given immediately before birth, and also after birth if the woman is breastfeeding. They agreed this longer term outcome could provide an insight into the impact of antibiotic use in early neonatal life. The committee also wanted to find out whether prophylactic antibiotics had an impact on a breastfeeding rates at 6 weeks postnatal, as it would be key to inform women if antibiotics have an effect on breastfeeding. Perineal pain at 6 weeks was also an important outcome chosen by the committee as it affects the quality of a woman's life. Antibiotic resistance was another outcome the committee chose as important due to emergence of bacteria with resistance to many different types of antibiotics.

The quality of the evidence

The quality of the evidence for outcomes was assessed with GRADE and was rated as moderate to low. All of the evidence was downgraded for indirectness as there was not enough information regarding non-cephalic presentations in the population. Some of the evidence was also downgraded for risk of bias, with some concerns around concealment of randomisation and not enough information to judge selective reporting. Most of the evidence was also downgraded for imprecision around the estimate of effect.

Benefits and harms

The committee discussed the evidence for prophylactic antibiotics use following vaginal birth with forceps or ventouse, which showed a benefit for prophylactic antibiotics at reducing the rates of endometritis and infected episiotomy/lacerations.

The committee discussed whether there were any adverse outcomes associated with prophylactic antibiotics. They agreed that the evidence suggested there was no difference in maternal adverse reactions or perineal pain at 6 weeks, and that there was evidence showing that there was no difference between groups on breastfeeding at 6 weeks. They agreed that the evidence supported the use of prophylactic antibiotics in terms of endometritis and infection at the episiotomy or laceration site, and did not lead to any harms. Births with forceps or ventouse have a higher chance of needing an episiotomy, so the committee discussed whether the source of infection is due to the instrument used or the episiotomy. Based on their personal experience and expertise, they noted that infections are usually due to the increased number of examinations needed for an assisted birth. Coupled with these factors, the committee agreed that the evidence supported a recommendation for prophylactic antibiotics following a birth with forceps or ventouse.

The committee considered the evidence to guide their recommendations for a specific antibiotic type. They discussed that cefotetan, as used in one of the studies showing a benefit for endometritis, is a second generation cephalosporin not currently used in the UK, and therefore they could not recommend this antibiotic specifically, but agreed that cefuroxime would be an equivalent available in the UK. The committee discussed that the evidence which used co-amoxiclav (a mixture of penicillin and clavulanic acid) was from the UK and would therefore be directly applicable to practice in the UK. They agreed with the reasons stated in the study for co-amoxiclav use, such as the wide spectrum of activity which is important considering contamination with bacteria around the perineum region. However, the committee discussed that co-amoxiclav used antenatally has an increased risk of necrotising enterocolitis to the neonate. They agreed that they would include in the recommendation that co-amoxiclav should be given postnatally to prevent this. The committee also included in their recommendation that the co-amoxiclav should be administered no more than 6 hours after cord clamping, as this was in line with the time of administration used in the study.

The committee also specified that the route of administration for the antibiotics should be IV, based on the evidence which had used this route. They discussed the availability of IV antibiotics across different birth places, and whether limiting to IV would have an impact on access. They agreed that this was unlikely to be an issue as assisted vaginal births only take place in settings where IV antibiotics are available (alongside midwifery units and obstetric units).

The committee recognised that co-amoxiclav may not be appropriate for all women: hospitals may have different antibiotic resistance profiles and some women may be allergic to penicillin, therefore they included that a local alternative could also be used.

The committee discussed that that the evidence only supported IV administration, but IV administration requires 2 trained staff to check and administer the antibiotic, therefore it may be preferable for oral antibiotics to be used. The committee wanted to know whether oral

antibiotics would be effective as prophylaxis for postnatal infections. They agreed a research recommendation was necessary and made one to address this gap in evidence.

Cost effectiveness and resource use

One study (Knight 2019) undertook a within trial cost analysis of prophylactic antibiotic for preventing postnatal infections in birth with forceps or ventouse. It found that overall, when compared to placebo, that antibiotics produced a mean cost saving of £52.60 per woman. This was driven by statistically significant reductions in GP visits, home visits by a midwife or nurse and outpatient hospital visits. An important limitation of this study was that the characteristics of women who returned the postal questionnaire, which captured data on resource use, differed systematically from those women who did not return the questionnaire. However, a sensitivity analysis involving imputation of missing data values reported a very similar mean cost saving £50.90. However, the cost analysis omitted staff costs to administer the antibiotic and all consumables apart from the drug cost. Therefore, the committee acknowledged that the cost saving was probably overstated by the analysis. However, given the “downstream” savings demonstrated by the cost analysis and improvements to health-related quality of life arising from lower infection rates, the committee considered that prophylactic antibiotics were likely to be cost-effective. According to NHS episode hospital statistics there are approximately 70,000 births with forceps or ventouse per annum (https://digital.nhs.uk/data-and-information/publications/statistical/nhs-maternity-statistics/2020-21) and the committee reasoned that given this size of population and “downstream” savings in resource use, from reduced outpatient hospital visits and other contacts with healthcare professionals, that their recommendations were unlikely to have a significant resource impact.

Other factors the committee took into account

The committee discussed one of the specifications of the protocol regarding instrument type. They had hoped to find evidence to determine if the benefits of prophylaxis antibiotic were dependent on the type of instrument used (vacuum, forceps or sequential). In the absence of direct evidence to address this stratified analysis, the committee used a post-hoc analysis from the ANODE study (Knight 2019) that looked at a composite measure of suspected and maternal infections, stratified by type of instrument used. The data for this outcome showed a benefit of prophylaxis antibiotics on forceps use and vacuum extraction. Although this outcome did not specifically meet the criteria of the protocol, as it could include other infections not related to instrumental birth, the committee agreed that it was useful for providing reassurance that in principle there are no differences in the benefits of antibiotics between types of instrument.

Recommendations supported by this evidence review

This evidence review supports recommendation 1.9.43 and a research recommendation.

References – included studies

Effectiveness

Heitmann 1989

Heitmann, J. A. and Benrubi, G. I. (1989) Efficacy of prophylactic antibiotics for the prevention of endomyometritis after forceps delivery. Southern medical journal 82(8): 960-2

Knight 2019

Knight, Marian, Chiocchia, Virginia, Partlett, Christopher et al. (2019) Prophylactic antibiotics in the prevention of infection after operative vaginal delivery (ANODE): a multicentre randomised controlled trial. Lancet (London, England) 393(10189): 2395-2403

Liabsuetrakul 2020

Liabsuetrakul, Tippawan, Choobun, Thanapan, Peeyananjarassri, Krantarat et al. (2020) Antibiotic prophylaxis for operative vaginal delivery. Cochrane Database of Systematic Reviews 2020(3): cd004455

Economic

Knight 2019

Knight M, Chiocchia V, Partlett C, Rivero-Arias O, Hua X, Bowler U, et al. Intravenous co-amoxiclav to prevent infection after operative vaginal delivery: the ANODE RCT. Health Technology Assessment 2019;23(54)

Appendices

Appendix A Review protocols

Review protocol for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Table 4: Review protocol

Field	Content
PROSPERO registration number	CRD42021288216
Review title	Effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth
Review question	What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?
Objective	To assess the effectiveness of prophylactic antibiotics during labour in women undergoing an assisted vaginal birth, for preventing postnatal infections.
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 (IHTA) Searches will be restricted by: • English language only • Human studies only Other searches:

Field	Content
	• 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. Key papers • Cochrane systematic review 2020 DOI: https://doi.org/10.1002/14651858.CD004455.pub5 • ANODE 2019 DOI: https://doi.org/10.1016/S01406736(19)30773-1
Condition or domain being studied	Prophylactic antibiotics for women in labour undergoing an assisted vaginal birth.
Population	• Women in labour who are pregnant with a single baby, who go into labour at term (37 to 42 weeks of pregnancy) and who do not have any pre-existing medical conditions or antenatal conditions that predispose to a higher risk birth • Women in labour whose baby has not been identified before labour to be at high risk of adverse outcome • Singleton babies born at term (37 to 42 weeks of pregnancy) with no previously identified problems (for example congenital malformations, genetic anomalies, intrauterine growth restriction, placental problems) • Women having an assisted vaginal birth (forceps or vacuum/suction birth) without evidence of an active infection or other conditions requiring antibiotics
Intervention	Prophylactic antibiotics given immediately before or as soon as possible after an assisted vaginal birth (forceps or vacuum birth)
Comparator	• Placebo • Standard care (no antibiotics)

Field	Content
Types of study to be included	Include published full-text papers: • Systematic reviews of RCTs • Parallel RCTs (individual, cluster) Conference abstracts will not be included because these do not typically have sufficient information to allow full critical appraisal.
Other exclusion criteria	Population: • Women in labour who are identified before labour to be at high risk, or whose baby is at high risk, of complications or adverse outcomes • Women with non-cephalic presentation • Women in preterm labour • Women with an intrauterine fetal death • Women pregnant with multi-fetal pregnancies Setting: • Countries other than high income countries (as defined by the OECD) *If any study or systematic review includes <1/3 of women with the above characteristics/ who received care in the above setting, it will be considered for inclusion but, if included, the evidence will be downgraded for indirectness.*
Context	This guideline will partly update the following: Intrapartum care for healthy women and babies (CG190)
Primary outcomes (critical outcomes)	• Endometritis • Infection at perineal/vaginal or episiotomy site (up till 6 weeks)

Field	Content
	• Sepsis following perineum infection or endometritis
Secondary outcomes (important outcomes)	• Maternal adverse reaction to antibiotics • Long-term neonatal outcomes (asthma, allergies) • Breastfeeding at 6 weeks • Perineal pain at 6 weeks • Antibiotic resistance
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 trials The quality assessment will be performed by one reviewer and this will be quality assessed by a senior reviewer.

Field	Content
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 differences or standardised mean differences for continuous outcomes. Heterogeneity in the effect estimates of the individual studies will be assessed using the I2 statistic. Alongside visual inspection of the point estimates and confidence intervals, I2 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:
	• Antibiotics provided before versus after birth
	• Antibiotic route of administration
	  ○ Intravenous
	  ○ Oral
	• Single dose versus course of antibiotics
	• Type of antibiotic:

Field	Content
	○ Co-amoxiclav (trade name Augmentin) ○ 'Cef & Met' – A cephalosporin (group of antibiotics +/- Metronidazole ○ Other • Type of instrument: ○ Vacuum ○ Forceps ○ Sequential • Group B Streptococcus test positive Stratifications will be dealt with in a hierarchy (this is, by timing when antibiotics were provided, then by route of administration, then by antibiotic treatment type, then by type of antibiotic, then by type of instrument, then by group B Streptococcus test positive) 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 • Black and Minority Ethnic background 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

Field	Content	
	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	
Country	England	
Anticipated or actual start date	13/12/2021	
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 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 NGA: • Senior Systematic Reviewer • Systematic Reviewer	

Field	Content
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.
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: https://www.nice.org.uk/guidance/cg190
Other registration details	None
URL for published protocol	https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=288216
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	[Give words or phrases that best describe the review.]
Details of existing review of same topic by same authors	Not applicable
Additional information	None
Details of final publication	www.nice.org.uk

CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; GRADE: Grading of Recommendations Assessment, Development and Evaluation; I(HTA): International Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NHS: National

health service; NICE: National Institute for Health and Care Excellence; OECD: Organisation for Economic Co-operation and Development; RCT: randomised controlled trial PRESS: peer review of electronic search strategies; 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: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Database: Medline – OVID interface

Date of last search: 07/12/2022

#	Searches
1	(assist* adj3 (birth* or born or deliver*)).ti,ab.
2	(operat* adj3 vagina* adj3 (birth* or born or deliver*)).ti,ab.
3	exp EXTRACTION, OBSTETRICAL/
4	((extract* or vacuum*) adj3 (birth* or born or deliver* or obstetric*)).ti,ab.
5	(vacuum* adj3 extract*).ti,ab.
6	ventouse?.ti,ab.
7	OBSTETRICAL FORCEPS/
8	(forcep? adj5 (birth* or born or deliver* or obstetric*)).ti,ab.
9	or/1-8
10	ANTIBIOTIC PROPHYLAXIS/
11	((antibiotic* or anti-biotic*) adj3 prophyla*).ti,ab.
12	exp ANTI-BACTERIAL AGENTS/
13	(Acetic Acid or Alamethicin or Amdinocillin or Amikacin or Amoxicillin or Amoxicillin Potassium Clavulanate or Amphotericin B or Ampicillin or Anisomycin or Antimycin A or Aurodox or Azithromycin or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Brefeldin A or Butirosin Sulfate or Calcimycin or Candicidin or Capreomycin or Carbenicillin or Carfecillin or Cefaclor or Cefadroxil or Cefamandole or Cefatrizine or Cefazolin or Cefdinir or Cefepime or Cefixime or Cefmenoxime or Cefmetazole or Cefonicid or Cefoperazone or Cefotaxime or Cefotetan or Cefotiam or Cefoxitin or Cefsulodin or Ceftazidime or Ceftibuten or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephacetrile or Cephalexin or Cephaloglycin or Cephaloridine or Cephalosporin? or Cephalothin or Cephamycin? or Cephapirin or Cephradine or Chloramphenicol or Chlortetracycline or Cilastatin Imipenem or Ciprofloxacin or Citrinin or Clarithromycin or Clavulanic Acid? or Clindamycin or Cloxacillin or Colistin or Cyclacillin or Dactinomycin or Daptomycin or Demeclocycline or Dibekacin or Dicloxacillin or Dihydrostreptomycin Sulfate or Diketopiperazine? or Distamycin? or Doripenem or Doxycycline or Echinomycin or Edeine or Enoxacin or Enrofloxacin or Enviomycin or Ertapenem or Erythromycin or Fidaxomicin or Filipin or Floxacillin or Fluoroquinolone? or Fosfomycin or Framycetin or Fusidic Acid or Gatifloxacin or Gemifloxacin or Gentamicin? or Gramicidin or Hygromycin B or Imipenem or Josamycin or Kanamycin or Kitasamycin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lucensomycin or Lymecycline or Mafenide or Mepartricin or Meropenem or Methacycline or Methicillin or Metronidazole or Mezlocillin or Mikamycin or Minocycline or Miocamycin or Moxalactam or Moxifloxacin or Mupirocin or Mycobacillin or Nafcillin or Nalidixic Acid or Natamycin or Nebramycin or Neomycin or Netilmicin or Netropsin or Nigericin or Nisin or Nitrofurantoin or Norfloxacin or Novobiocin or Nystatin or Ofloxacin or Oleandomycin or Oligomycin? or Oxacillin or Oxolinic Acid or Oxytetracycline or Paromomycin or Pefloxacin or Penicillanic Acid or Penicillic Acid or Penicillin? or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Ribostamycin or Rifabutin or Rifamycin? or Rifaximin or Ristocetin or Rolitetracycline or Roxarsone or Roxithromycin or Rutamycin or Sirolimus or Sisomicin or Spectinomycin or Spiramycin or Streptogramin? or Streptomycin or Streptovaricin or Sulbactam or Sulbenicillin or Sulfacetamide or Sulfadiazine or Sulfamerazine or Sulfamethoxypyridazine or Sulfanilamide or Talampicillin or Tazobactam or Teicoplanin or Tetracycline or Thiamphenicol or Thienamycin? or Thiostrepton or Ticarcillin or Tigecycline or Tinidazole or Tobramycin or Trimethoprim Sulfamethoxazole or Troleandomycin or Tunicamycin or Tylosin or Tyrocidine or Tyrothricin or Valinomycin or Vancomycin or Vernamycin B or Viomycin or Virginiamycin).mp.
14	or/10-13
15	9 and 14
16	limit 15 to english language
17	LETTER/
18	EDITORIAL/
19	NEWS/
20	exp HISTORICAL ARTICLE/
21	ANECDOTES AS TOPIC/
22	COMMENT/
23	CASE REPORT/
24	(letter or comment*).ti.
25	or/17-24
26	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
27	25 not 26
28	ANIMALS/ not HUMANS/
29	exp ANIMALS, LABORATORY/
30	exp ANIMAL EXPERIMENTATION/

#	Searches
31	exp MODELS, ANIMAL/
32	exp RODENTIA/
33	(rat or rats or mouse or mice).ti.
34	or/27-33
35	16 not 34
36	META-ANALYSIS/
37	META-ANALYSIS AS TOPIC/
38	(meta analy* or metanaly* or metaanaly*).ti,ab.
39	((systematic* or evidence*) adj2 (review* or overview*)).ti,ab.
40	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
41	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
42	(search* adj4 literature).ab.
43	(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.
44	cochrane.jw.
45	or/36-44
46	randomized controlled trial.pt.
47	controlled clinical trial.pt.
48	pragmatic clinical trial.pt.
49	randomi#ed.ab.
50	placebo.ab.
51	randomly.ab.
52	CLINICAL TRIALS AS TOPIC/
53	trial.ti.
54	or/46-53
55	35 and 45
56	35 and 54
57	or/55-56

Database: Embase – OVID interface

Date of last search: 07/12/2022

#	Searches
1	(assist* adj3 (birth* or born or deliver*)).ti,ab.
2	(operat* adj3 vagina* adj3 (birth* or born or deliver*)).ti,ab.
3	VACUUM EXTRACTION/
4	OBSTETRIC VACUUM DELIVERY KIT/
5	((extract* or vacuum*) adj3 (birth* or born or deliver* or obstetric*)).ti,ab.
6	(vacuum* adj3 extract*).ti,ab.
7	ventouse?.ti,ab.
8	FORCEPS DELIVERY/
9	exp OBSTETRIC FORCEPS/
10	(forcep? adj5 (birth* or born or deliver* or obstetric*)).ti,ab.
11	or/1-10
12	ANTIBIOTIC PROPHYLAXIS/
13	((antibiotic* or anti-biotic*) adj3 prophyla*).ti,ab.
14	exp ANTIINFECTIVE AGENT/
15	(Acetic Acid or Alamethicin or Amdinocillin or Amikacin or Amoxicillin or Amoxicillin Potassium Clavulanate or Amphotericin B or Ampicillin or Anisomycin or Antimycin A or Aurodox or Azithromycin or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Brefeldin A or Butirosin Sulfate or Calcimycin or Candicidin or Capreomycin or Carbenicillin or Carfecillin or Cefaclor or Cefadroxil or Cefamandole or Cefatrizine or Cefazolin or Cefdinir or Cefepime or Cefixime or Cefmenoxime or Cefmetazole or Cefonicid or Cefoperazone or Cefotaxime or Cefotetan or Cefotiam or Cefoxitin or Cefsulodin or Ceftazidime or Ceftibuten or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephacetrile or Cephalexin or Cephaloglycin or Cephaloridine or Cephalosporin? or Cephalothin or Cephamycin? or Cephapirin or Cephradine or Chloramphenicol or Chlortetracycline or Cilastatin Imipenem or Ciprofloxacin or Citrinin or Clarithromycin or Clavulanic Acid? or Clindamycin or Cloxacillin or Colistin or Cyclacillin or Dactinomycin or Daptomycin or Demeclocycline or Dibekacin or Dicloxacillin or Dihydrostreptomycin Sulfate or Diketopiperazine? or Distamycin? or Doripenem or Doxycycline or Echinomycin or Edeine or Enoxacin or Enrofloxacin or Enviomycin or Ertapenem or Erythromycin or Fidaxomicin or Filipin or Floxacillin or Fluoroquinolone? or Fosfomycin or Framycetin or Fusidic Acid or Gatifloxacin or Gemifloxacin or Gentamicin? or Gramicidin or Hygromycin B or Imipenem or Josamycin or Kanamycin or Kitasamycin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lucensomycin or Lymecycline or Mafenide or Mepartricin or Meropenem or Methacycline or Methicillin or Metronidazole or Mezlocillin or Mikamycin or Minocycline or Miocamycin or Moxalactam or Moxifloxacin or Mupirocin or Mycobacillin or Nafcillin or Nalidixic Acid or Natamycin or Nebramycin or Neomycin or Netilmicin or Netropsin or Nigericin or Nisin or Nitrofurantoin or Norfloxacin or Novobiocin or Nystatin or Ofloxacin or Oleandomycin or Oligomycin? or Oxacillin or Oxolinic Acid or Oxytetracycline or Paromomycin or Pefloxacin or Penicillanic Acid or Penicillic Acid or Penicillin? or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Ribostamycin or Rifabutin or Rifamycin? or Rifaximin or Ristocetin or

#	Searches
	Rolitetracycline or Roxarsone or Roxithromycin or Rutamycin or Sirolimus or Sisomicin or Spectinomycin or Spiramycin or Streptogramin? or Streptomycin or Streptovaricin or Sulbactam or Sulbenicillin or Sulfacetamide or Sulfadiazine or Sulfamerazine or Sulfamethoxypyridazine or Sulfanilamide or Talampicillin or Tazobactam or Teicoplanin or Tetracycline or Thiamphenicol or Thienamycin? or Thiostrepton or Ticarcillin or Tigecycline or Tinidazole or Tobramycin or Trimethoprim Sulfamethoxazole or Troleandomycin or Tunicamycin or Tylosin or Tyrocidine or Tyrothricin or Valinomycin or Vancomycin or Vernamycin B or Viomycin or Virginiamycin).mp.
16	or/12-15
17	11 and 16
18	limit 17 to english language
19	letter.pt. or LETTER/
20	note.pt.
21	editorial.pt.
22	CASE REPORT/ or CASE STUDY/
23	(letter or comment*).ti.
24	or/19-23
25	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
26	24 not 25
27	ANIMAL/ not HUMAN/
28	NONHUMAN/
29	exp ANIMAL EXPERIMENT/
30	exp EXPERIMENTAL ANIMAL/
31	ANIMAL MODEL/
32	exp RODENT/
33	(rat or rats or mouse or mice).ti.
34	or/26-33
35	18 not 34
36	SYSTEMATIC REVIEW/
37	META-ANALYSIS/
38	(meta analy* or metanaly* or metaanaly*).ti,ab.
39	((systematic or evidence) adj2 (review* or overview*)).ti,ab.
40	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
41	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
42	(search* adj4 literature).ab.
43	(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.
44	((pool* or combined) adj2 (data or trials or studies or results)).ab.
45	cochrane.jw.
46	or/36-45
47	random*.ti,ab.
48	factorial*.ti,ab.
49	(crossover* or cross over*).ti,ab.
50	((doubl* or singl*) adj blind*).ti,ab.
51	(assign* or allocat* or volunteer* or placebo*).ti,ab.
52	CROSSOVER PROCEDURE/
53	SINGLE BLIND PROCEDURE/
54	RANDOMIZED CONTROLLED TRIAL/
55	DOUBLE BLIND PROCEDURE/
56	or/47-55
57	35 and 46
58	35 and 56
59	or/57-58

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

Date of last search: 07/12/2022

#	Searches
#1	(assist* near/3 (birth* or born or deliver*)):ti,ab
#2	(operat* near/3 vagina* near/3 (birth* or born or deliver*)):ti,ab
#3	MeSH descriptor: [Extraction, Obstetrical] explode all trees
#4	((extract* or vacuum*) near/3 (birth* or born or deliver* or obstetric*)):ti,ab
#5	(vacuum* near/3 extract*):ti,ab
#6	ventouse*:ti,ab
#7	MeSH descriptor: [Obstetrical Forceps] this term only
#8	(forcep* near/5 (birth* or born or deliver* or obstetric*)):ti,ab
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8

#	Searches
#10	MeSH descriptor: [Antibiotic Prophylaxis] this term only
#11	((antibiotic* or anti-biotic*) near/3 prophyla*):ti,ab
#12	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#13	("Acetic Acid" or Alamethicin or Amdinocillin or Amikacin or Amoxicillin or "Amoxicillin Potassium Clavulanate" or "Amphotericin B" or Ampicillin or Anisomycin or "Antimycin A" or Aurodox or Azithromycin or Azlocillin or Aztreonam or Bacitracin or Bacteriocin* or Bambermycin* or "Bongkrekic Acid" or "Brefeldin A" or "Butirosin Sulfate" or Calcimycin or Candicidin or Capreomycin or Carbenicillin or Carfecillin or Cefaclor or Cefadroxil or Cefamandole or Cefatrizine or Cefazolin or Cefdinir or Cefepime or Cefixime or Cefmenoxime or Cefmetazole or Cefonicid or Cefoperazone or Cefotaxime or Cefotetan or Cefotiam or Cefoxitin or Cefsulodin or Ceftazidime or Ceftibuten or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephacetrile or Cephalexin or Cephaloglycin or Cephaloridine or Cephalosporin* or Cephalothin or Cephamycin* or Cephapirin or Cephradine or Chloramphenicol or Chlortetracycline or "Cilastatin Imipenem" or Ciprofloxacin or Citrinin or Clarithromycin or "Clavulanic Acid*" or Clindamycin or Cloxacillin or Colistin or Cyclacillin or Dactinomycin or Daptomycin or Demeclocycline or Dibekacin or Dicloxacillin or "Dihydrostreptomycin Sulfate" or Diketopiperazine* or Distamycin* or Doripenem or Doxycycline or Echinomycin or Edeine or Enoxacin or Enrofloxacin or Enviomycin or Ertapenem or Erythromycin or Fidaxomicin or Filipin or Floxacillin or Fluoroquinolone* or Fosfomycin or Framycetin or "Fusidic Acid" or Gatifloxacin or Gemifloxacin or Gentamicin* or Gramicidin or "Hygromycin B" or Imipenem or Josamycin or Kanamycin or Kitasamycin or Lactam* or Lasalocid or Leucomycin* or Levofloxacin or Lincomycin or Lincosamide* or Linezolid or Lucensomycin or Lymecycline or Mafenide or Mepartricin or Meropenem or Methacycline or Methicillin or Metronidazole or Mezlocillin or Mikamycin or Minocycline or Miocamycin or Moxalactam or Moxifloxacin or Mupirocin or Mycobacillin or Nafcillin or "Nalidixic Acid" or Natamycin or Nebramycin or Neomycin or Netilmicin or Netropsin or Nigericin or Nisin or Nitrofurantoin or Norfloxacin or Novobiocin or Nystatin or Ofloxacin or Oleandomycin or Oligomycin* or Oxacillin or "Oxolinic Acid" or Oxytetracycline or Paromomycin or Pefloxacin or "Penicillanic Acid" or "Penicillic Acid" or Penicillin* or "Pipemidic Acid" or Piperacillin or Pivampicillin or "Polymyxin B" or Polymyxin* or Pristinamycin or Prodigiosin or Ribostamycin or Rifabutin or Rifamycin* or Rifaximin or Ristocetin or Rolitetracycline or Roxarsone or Roxithromycin or Rutamycin or Sirolimus or Sisomicin or Spectinomycin or Spiramycin or Streptogramin* or Streptomycin or Streptovaricin or Sulbactam or Sulbenicillin or Sulfacetamide or Sulfadiazine or Sulfamerazine or Sulfamethoxypyridazine or Sulfanilamide or Talampicillin or Tazobactam or Teicoplanin or Tetracycline or Thiamphenicol or Thienamycin* or Thiostrepton or Ticarcillin or Tigecycline or Tinidazole or Tobramycin or "Trimethoprim Sulfamethoxazole" or Troleandomycin or Tunicamycin or Tylosin or Tyrocidine or Tyrothricin or Valinomycin or Vancomycin or "Vernamycin B" or Viomycin or Virginiamycin):ti,ab
#14	#10 or #11 or #12 or #13
#15	#9 and #14

Database: International Health Technology Assessment

Date of last search: 07/12/2022

#	Searches
	All: ("assisted birth" or "assisted births" or "assisted delivery" or "assisted deliveries" or "operative vaginal birth" or "operative vaginal births" or "operative vaginal delivery" or "operative vaginal deliveries" or "extraction birth" or "extraction births" or "extraction delivery" or "extraction deliveries" or "vacuum birth" or "vacuum births" or "vacuum delivery" or "vacuum deliveries" or "obstetric extraction" or "obstetric extractions" or "obstetrical extraction" or "obstetrical extractions" or "vacuum extraction" or "vacuum extractions" or ventouse or ventouses or forcep or forceps)

Health Economics Search Strategies

Database: Medline – OVID interface

Date of last search: 07/12/2022

#	Searches
1	(assist* adj3 (birth* or born or deliver*)).ti,ab.
2	(operat* adj3 vagina* adj3 (birth* or born or deliver*)).ti,ab.
3	exp EXTRACTION, OBSTETRICAL/
4	((extract* or vacuum*) adj3 (birth* or born or deliver* or obstetric*)).ti,ab.
5	(vacuum* adj3 extract*).ti,ab.
6	ventouse?.ti,ab.
7	OBSTETRICAL FORCEPS/
8	(forcep? adj5 (birth* or born or deliver* or obstetric*)).ti,ab.
9	or/1-8

#	Searches
10	ANTIBIOTIC PROPHYLAXIS/
11	((antibiotic* or anti-biotic*) adj3 prophyla*).ti,ab.
12	exp ANTI-BACTERIAL AGENTS/
13	(Acetic Acid or Alamethicin or Amdinocillin or Amikacin or Amoxicillin or Amoxicillin Potassium Clavulanate or Amphotericin B or Ampicillin or Anisomycin or Antimycin A or Aurodox or Azithromycin or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Brefeldin A or Butirosin Sulfate or Calcimycin or Candicidin or Capreomycin or Carbenicillin or Carfecillin or Cefaclor or Cefadroxil or Cefamandole or Cefatrizine or Cefazolin or Cefdinir or Cefepime or Cefixime or Cefmenoxime or Cefmetazole or Cefonicid or Cefoperazone or Cefotaxime or Cefotetan or Cefotiam or Cefoxitin or Cefsulodin or Ceftazidime or Ceftibuten or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephacetrile or Cephalexin or Cephaloglycin or Cephaloridine or Cephalosporin? or Cephalothin or Cephamycin? or Cephapirin or Cephradine or Chloramphenicol or Chlortetracycline or Cilastatin Imipenem or Ciprofloxacin or Citrinin or Clarithromycin or Clavulanic Acid? or Clindamycin or Cloxacillin or Colistin or Cyclacillin or Dactinomycin or Daptomycin or Demeclocycline or Dibekacin or Dicloxacillin or Dihydrostreptomycin Sulfate or Diketopiperazine? or Distamycin? or Doripenem or Doxycycline or Echinomycin or Edeine or Enoxacin or Enrofloxacin or Enviomycin or Ertapenem or Erythromycin or Fidaxomicin or Filipin or Floxacillin or Fluoroquinolone? or Fosfomycin or Framycetin or Fusidic Acid or Gatifloxacin or Gemifloxacin or Gentamicin? or Gramicidin or Hygromycin B or Imipenem or Josamycin or Kanamycin or Kitasamycin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lucensomycin or Lymecycline or Mafenide or Mepartricin or Meropenem or Methacycline or Methicillin or Metronidazole or Mezlocillin or Mikamycin or Minocycline or Miocamycin or Moxalactam or Moxifloxacin or Mupirocin or Mycobacillin or Nafcillin or Nalidixic Acid or Natamycin or Nebramycin or Neomycin or Netilmicin or Netropsin or Nigericin or Nisin or Nitrofurantoin or Norfloxacin or Novobiocin or Nystatin or Ofloxacin or Oleandomycin or Oligomycin? or Oxacillin or Oxolinic Acid or Oxytetracycline or Paromomycin or Pefloxacin or Penicillanic Acid or Penicillic Acid or Penicillin? or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Ribostamycin or Rifabutin or Rifamycin? or Rifaximin or Ristocetin or Rolitetracycline or Roxarsone or Roxithromycin or Rutamycin or Sirolimus or Sisomicin or Spectinomycin or Spiramycin or Streptogramin? or Streptomycin or Streptovaricin or Sulbactam or Sulbenicillin or Sulfacetamide or Sulfadiazine or Sulfamerazine or Sulfamethoxypyridazine or Sulfanilamide or Talampicillin or Tazobactam or Teicoplanin or Tetracycline or Thiamphenicol or Thienamycin? or Thiostrepton or Ticarcillin or Tigecycline or Tinidazole or Tobramycin or Trimethoprim Sulfamethoxazole or Troleandomycin or Tunicamycin or Tylosin or Tyrocidine or Tyrothricin or Valinomycin or Vancomycin or Vernamycin B or Viomycin or Virginiamycin).mp.
14	or/10-13
15	9 and 14
16	limit 15 to english language
17	LETTER/
18	EDITORIAL/
19	NEWS/
20	exp HISTORICAL ARTICLE/
21	ANECDOTES AS TOPIC/
22	COMMENT/
23	CASE REPORT/
24	(letter or comment*).ti.
25	or/17-24
26	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
27	25 not 26
28	ANIMALS/ not HUMANS/
29	exp ANIMALS, LABORATORY/
30	exp ANIMAL EXPERIMENTATION/
31	exp MODELS, ANIMAL/
32	exp RODENTIA/
33	(rat or rats or mouse or mice).ti.
34	or/27-33
35	16 not 34
36	ECONOMICS/
37	VALUE OF LIFE/
38	exp "COSTS AND COST ANALYSIS"/
39	exp ECONOMICS, HOSPITAL/
40	exp ECONOMICS, MEDICAL/
41	exp RESOURCE ALLOCATION/
42	ECONOMICS, NURSING/
43	ECONOMICS, PHARMACEUTICAL/
44	exp "FEES AND CHARGES"/
45	exp BUDGETS/
46	budget*.ti,ab.
47	cost*.ti,ab.
48	(economic* or pharmaco?economic*).ti,ab.
49	(price* or pricing*).ti,ab.
50	(financ* or fee or fees or expenditure* or saving*).ti,ab.
51	(value adj2 (money or monetary)).ti,ab.
52	resourc* allocat*.ti,ab.
53	(fund or funds or funding* or funded).ti,ab.

#	Searches
54	(ration or rations or rationing* or rationed).ti,ab.
55	ec.fs.
56	or/36-55
57	35 and 56

Database: Embase – OVID interface

Date of last search: 07/12/2022

#	Searches
1	(assist* adj3 (birth* or born or deliver*)).ti,ab.
2	(operat* adj3 vagina* adj3 (birth* or born or deliver*)).ti,ab.
3	VACUUM EXTRACTION/
4	OBSTETRIC VACUUM DELIVERY KIT/
5	((extract* or vacuum*) adj3 (birth* or born or deliver* or obstetric*)).ti,ab.
6	(vacuum* adj3 extract*).ti,ab.
7	ventouse?.ti,ab.
8	FORCEPS DELIVERY/
9	exp OBSTETRIC FORCEPS/
10	(forcep? adj5 (birth* or born or deliver* or obstetric*)).ti,ab.
11	or/1-10
12	ANTIBIOTIC PROPHYLAXIS/
13	((antibiotic* or anti-biotic*) adj3 prophyla*).ti,ab.
14	exp ANTIINFECTIVE AGENT/
15	(Acetic Acid or Alamethicin or Amdinocillin or Amikacin or Amoxicillin or Amoxicillin Potassium Clavulanate or Amphotericin B or Ampicillin or Anisomycin or Antimycin A or Aurodox or Azithromycin or Azlocillin or Aztreonam or Bacitracin or Bacteriocin? or Bambermycin? or Bongkrekic Acid or Brefeldin A or Butirosin Sulfate or Calcimycin or Candicidin or Capreomycin or Carbenicillin or Carfecillin or Cefaclor or Cefadroxil or Cefamandole or Cefatrizine or Cefazolin or Cefdinir or Cefepime or Cefixime or Cefmenoxime or Cefmetazole or Cefonicid or Cefoperazone or Cefotaxime or Cefotetan or Cefotiam or Cefoxitin or Cefsulodin or Ceftazidime or Ceftibuten or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephacetrile or Cephalexin or Cephaloglycin or Cephaloridine or Cephalosporin? or Cephalothin or Cephamycin? or Cephapirin or Cephradine or Chloramphenicol or Chlortetracycline or Cilastatin Imipenem or Ciprofloxacin or Citrinin or Clarithromycin or Clavulanic Acid? or Clindamycin or Cloxacillin or Colistin or Cyclacillin or Dactinomycin or Daptomycin or Demeclocycline or Dibekacin or Dicloxacillin or Dihydrostreptomycin Sulfate or Diketopiperazine? or Distamycin? or Doripenem or Doxycycline or Echinomycin or Edeine or Enoxacin or Enrofloxacin or Enviomycin or Ertapenem or Erythromycin or Fidaxomicin or Filipin or Floxacillin or Fluoroquinolone? or Fosfomycin or Framycetin or Fusidic Acid or Gatifloxacin or Gemifloxacin or Gentamicin? or Gramicidin or Hygromycin B or Imipenem or Josamycin or Kanamycin or Kitasamycin or Lactam? or Lasalocid or Leucomycin? or Levofloxacin or Lincomycin or Lincosamide? or Linezolid or Lucensomycin or Lymecycline or Mafenide or Mepartricin or Meropenem or Methacycline or Methicillin or Metronidazole or Mezlocillin or Mikamycin or Minocycline or Miocamycin or Moxalactam or Moxifloxacin or Mupirocin or Mycobacillin or Nafcillin or Nalidixic Acid or Natamycin or Nebramycin or Neomycin or Netilmicin or Netropsin or Nigericin or Nisin or Nitrofurantoin or Norfloxacin or Novobiocin or Nystatin or Ofloxacin or Oleandomycin or Oligomycin? or Oxacillin or Oxolinic Acid or Oxytetracycline or Paromomycin or Pefloxacin or Penicillanic Acid or Penicillic Acid or Penicillin? or Pipemidic Acid or Piperacillin or Pivampicillin or Polymyxin B or Polymyxin? or Pristinamycin or Prodigiosin or Ribostamycin or Rifabutin or Rifamycin? or Rifaximin or Ristocetin or Rolitetracycline or Roxarsone or Roxithromycin or Rutamycin or Sirolimus or Sisomicin or Spectinomycin or Spiramycin or Streptogramin? or Streptomycin or Streptovaricin or Sulbactam or Sulbenicillin or Sulfacetamide or Sulfadiazine or Sulfamerazine or Sulfamethoxypyridazine or Sulfanilamide or Talampicillin or Tazobactam or Teicoplanin or Tetracycline or Thiamphenicol or Thienamycin? or Thiostrepton or Ticarcillin or Tigecycline or Tinidazole or Tobramycin or Trimethoprim Sulfamethoxazole or Troleandomycin or Tunicamycin or Tylosin or Tyrocidine or Tyrothricin or Valinomycin or Vancomycin or Vernamycin B or Viomycin or Virginiamycin).mp.
16	or/12-15
17	11 and 16
18	limit 17 to english language
19	letter.pt. or LETTER/
20	note.pt.
21	editorial.pt.
22	CASE REPORT/ or CASE STUDY/
23	(letter or comment*).ti.
24	or/19-23
25	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
26	24 not 25
27	ANIMAL/ not HUMAN/
28	NONHUMAN/
29	exp ANIMAL EXPERIMENT/
30	exp EXPERIMENTAL ANIMAL/
31	ANIMAL MODEL/
32	exp RODENT/
33	(rat or rats or mouse or mice).ti.

#	Searches
34	or/26-33
35	18 not 34
36	HEALTH ECONOMICS/
37	exp ECONOMIC EVALUATION/
38	exp HEALTH CARE COST/
39	exp FEE/
40	BUDGET/
41	FUNDING/
42	RESOURCE ALLOCATION/
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	or/36-51
53	35 and 52

Database: Cochrane Central Register of Controlled Trials – Wiley interface

Date of last search: 07/12/2022

#	Searches
#1	(assist* near/3 (birth* or born or deliver*)):ti,ab
#2	(operat* near/3 vagina* near/3 (birth* or born or deliver*)):ti,ab
#3	MeSH descriptor: [Extraction, Obstetrical] explode all trees
#4	((extract* or vacuum*) near/3 (birth* or born or deliver* or obstetric*)):ti,ab
#5	(vacuum* near/3 extract*):ti,ab
#6	ventouse*:ti,ab
#7	MeSH descriptor: [Obstetrical Forceps] this term only
#8	(forcep* near/5 (birth* or born or deliver* or obstetric*)):ti,ab
#9	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8
#10	MeSH descriptor: [Antibiotic Prophylaxis] this term only
#11	((antibiotic* or anti-biotic*) near/3 prophyla*):ti,ab
#12	MeSH descriptor: [Anti-Bacterial Agents] explode all trees
#13	("Acetic Acid" or Alamethicin or Amdinocillin or Amikacin or Amoxicillin or "Amoxicillin Potassium Clavulanate" or "Amphotericin B" or Ampicillin or Anisomycin or "Antimycin A" or Aurodox or Azithromycin or Azlocillin or Aztreonam or Bacitracin or Bacteriocin* or Bambermycin* or "Bongkrekic Acid" or "Brefeldin A" or "Butirosin Sulfate" or Calcimycin or Candicidin or Capreomycin or Carbenicillin or Carfecillin or Cefaclor or Cefadroxil or Cefamandole or Cefatrizine or Cefazolin or Cefdinir or Cefepime or Cefixime or Cefmenoxime or Cefmetazole or Cefonicid or Cefoperazone or Cefotaxime or Cefotetan or Cefotiam or Cefoxitin or Cefsulodin or Ceftazidime or Ceftibuten or Ceftizoxime or Ceftriaxone or Cefuroxime or Cephacetrile or Cephalexin or Cephaloglycin or Cephaloridine or Cephalosporin* or Cephalothin or Cephamycin* or Cephapirin or Cephradine or Chloramphenicol or Chlortetracycline or "Cilastatin Imipenem" or Ciprofloxacin or Citrinin or Clarithromycin or "Clavulanic Acid*" or Clindamycin or Cloxacillin or Colistin or Cyclacillin or Dactinomycin or Daptomycin or Demeclocycline or Dibekacin or Dicloxacillin or "Dihydrostreptomycin Sulfate" or Diketopiperazine* or Distamycin* or Doripenem or Doxycycline or Echinomycin or Edeine or Enoxacin or Enrofloxacin or Enviomycin or Ertapenem or Erythromycin or Fidaxomicin or Filipin or Floxacillin or Fluoroquinolone* or Fosfomycin or Framycetin or "Fusidic Acid" or Gatifloxacin or Gemifloxacin or Gentamicin* or Gramicidin or "Hygromycin B" or Imipenem or Josamycin or Kanamycin or Kitasamycin or Lactam* or Lasalocid or Leucomycin* or Levofloxacin or Lincomycin or Lincosamide* or Linezolid or Lucensomycin or Lymecycline or Mafenide or Mepartricin or Meropenem or Methacycline or Methicillin or Metronidazole or Mezlocillin or Mikamycin or Minocycline or Miocamycin or Moxalactam or Moxifloxacin or Mupirocin or Mycobacillin or Nafcillin or "Nalidixic Acid" or Natamycin or Nebramycin or Neomycin or Netilmicin or Netropsin or Nigericin or Nisin or Nitrofurantoin or Norfloxacin or Novobiocin or Nystatin or Ofloxacin or Oleandomycin or Oligomycin* or Oxacillin or "Oxolinic Acid" or Oxytetracycline or Paromomycin or Pefloxacin or "Penicillanic Acid" or "Penicillic Acid" or Penicillin* or "Pipemidic Acid" or Piperacillin or Pivampicillin or "Polymyxin B" or Polymyxin* or Pristinamycin or Prodigiosin or Ribostamycin or Rifabutin or Rifamycin* or Rifaximin or Ristocetin or Rolitetracycline or Roxarsone or Roxithromycin or Rutamycin or Sirolimus or Sisomicin or Spectinomycin or Spiramycin or Streptogramin* or Streptomycin or Streptovaricin or Sulbactam or Sulbenicillin or Sulfacetamide or Sulfadiazine or Sulfamerazine or Sulfamethoxypyridazine or Sulfanilamide or Talampicillin or Tazobactam or Teicoplanin or Tetracycline or Thiamphenicol or Thienamycin* or Thiostrepton or Ticarcillin or Tigecycline or Tinidazole or Tobramycin or "Trimethoprim Sulfamethoxazole" or Troleandomycin or Tunicamycin or Tylosin or Tyrocidine or Tyrothricin or Valinomycin or Vancomycin or "Vernamycin B" or Viomycin or Virginiamycin):ti,ab
#14	#10 or #11 or #12 or #13
#15	#9 and #14
#16	MeSH descriptor: [Economics] this term only

#	Searches
#17	MeSH descriptor: [Value of Life] this term only
#18	MeSH descriptor: [Costs and Cost Analysis] explode all trees
#19	MeSH descriptor: [Economics, Hospital] explode all trees
#20	MeSH descriptor: [Economics, Medical] explode all trees
#21	MeSH descriptor: [Resource Allocation] explode all trees
#22	MeSH descriptor: [Economics, Nursing] this term only
#23	MeSH descriptor: [Economics, Pharmaceutical] this term only
#24	MeSH descriptor: [Fees and Charges] explode all trees
#25	MeSH descriptor: [Budgets] explode all trees
#26	budget*:ti,ab
#27	cost*:ti,ab
#28	(economic* or pharmaco?economic*):ti,ab
#29	(price* or pricing*):ti,ab
#30	(financ* or fee or fees or expenditure* or saving*):ti,ab
#31	(value near/2 (money or monetary)):ti,ab
#32	resourc* allocat*:ti,ab
#33	(fund or funds or funding* or funded):ti,ab
#34	(ration or rations or rationing* or rationed):ti,ab
#35	#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 or #32 or #33 or #34
#36	#15 and #35

Database: International Health Technology Assessment

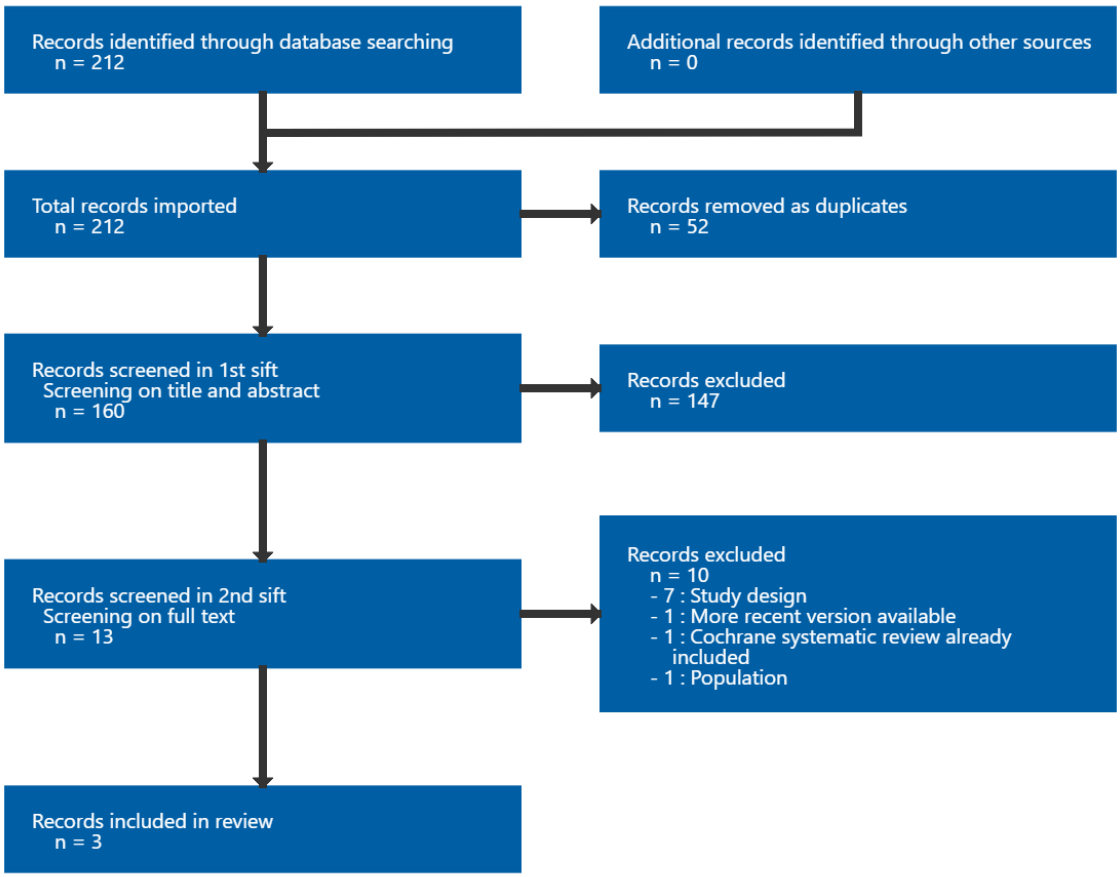
Date of last search: 07/12/2022

#	Searches
	All: ("assisted birth" or "assisted births" or "assisted delivery" or "assisted deliveries" or "operative vaginal birth" or "operative vaginal births" or "operative vaginal delivery" or "operative vaginal deliveries" or "extraction birth" or "extraction births" or "extraction delivery" or "extraction deliveries" or "vacuum birth" or "vacuum births" or "vacuum delivery" or "vacuum deliveries" or "obstetric extraction" or "obstetric extractions" or "obstetrical extraction" or "obstetrical extractions" or "vacuum extraction" or "vacuum extractions" or ventouse or ventouses or forcep or forceps)

Appendix C Effectiveness evidence study selection

Study selection for: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Figure 1: Study selection flow chart



Appendix D Evidence tables

Evidence tables for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Liabsuetrakul, 2020

Bibliographic Reference	Liabsuetrakul, Tippawan; Choobun, Thanapan; Peeyananjarassri, Krantarat; Islam, Q. Monir; Antibiotic prophylaxis for operative vaginal delivery; Cochrane Database of Systematic Reviews; 2020; vol. 2020 (no. 3); cd004455

Study details

Country/ies where study was carried out	Heitmann 1989 United States Knight 2019 United Kingdom
Study type	Cochrane Systematic Review of Randomised Controlled Trials
Study dates	Heitmann 1989 September 1986 to February 1989 Knight 2019 13 March 2016 to 13 June 2018
Inclusion criteria	Heitmann 1989 not specified. *Knight 2019 • 16 years or older • able to give informed consent • had undergone operative vaginal birth at 36 weeks or more gestation

	• women who had antibiotics antenatally or intrapartum (such as for prolonged rupture of membranes) were not excluded.
Exclusion criteria	Heitmann 1989 • Chorioamnionitis or other infections • allergic to penicillin or cephalosporins. Knight 2019 • Any clinical indication for antibiotic administration after delivery (such as, confirmed antenatal or intrapartum infection, third or fourth degree perineal tears) • known allergy to penicillin or any of the components of amoxicillin and clavulanic acid • history of anaphylaxis to another beta-lactam agent.
Patient characteristics	*Heitmann 1989 **Maternal age - mean (SD)** Intervention: 21.38 (4.98), Comparator: 20.73 (4.48) **Parity - mean (SD)** Intervention: 0.46 (0.92), Comparator: 0.47 (0.79) **Actual mode of birth** Forceps: Intervention: 43.2%, Comparator: 41.3% Vacuum: Intervention: 56.8%, Comparator: 58.7% *No information on whether presentation was non-cephalic. No significant differences between groups.

	*Knight 2019 **Maternal age - mean (SD)** Intervention: 30.3 (5.37), Comparator: 30.2 (5.49) **Gestational age - median (IQR)** Intervention: 40 (39 to 41), Comparator: 40 (39 to 41) **(36 to <38:** Intervention: 136 (8%), Comparator: 123 (7%)) **BMI at booking - median (IQR)** Intervention: 25 (22 to 28), Comparator: 25 (22 to 29) **Twin pregnancy - number (%)** Intervention: 11 (1%), Comparator: 9 (1%) **Actual mode of birth - number (%)** Spontaneous vaginal: Intervention: 7 (<1%), Comparator: 3 (<1%) Forceps: Intervention: 1086 (63%), Comparator: 1148 (67%) Vacuum extraction: Intervention: 633 (37%), Comparator: 563 (33%) *Study specifies women were not excluded based on the station of the fetal head at the time of instrument application, nor specific mention of exclusion of non-cephalic presentation. Characteristics between groups similar.

Intervention(s)/control	Heitmann 1989 Intervention: 2g of cefotetan given IV after cord clamping Control: No treatment Knight 2019 Intervention: A single dose of IV amoxicillin (1g) and clavulanic acid (200mg), as soon as possible after giving birth, and no more than 6 hours. Control: Placebo. 20ml of IV sterile 0.9% saline within the same timeframe. *Antibiotics were given after birth in both studies *Route of administration was IV for both studies *Single dose for both studies *Type of antibiotic: Heitmann 1989: cephalosporin Knight 2019: co-amoxiclav *Both studies had instrumental and forceps delivery, but data not analysed separately. *No information on Group B Streptococcus test, although other infections or antibiotics for other infections excluded from populations.
Sources of funding	Heitmann 1989 Not specified Knight 2019 Not industry funded
Sample size	Heitmann 1989 N=393 women undergoing forceps or vacuum birth Intervention, n=192 Control, n=201 Knight 2019

	N=3420 women undergoing forceps or vacuum birth Intervention, n=1715 Control, n=1705

Outcomes

Heitmann 1989

Outcome	Prophylactic antibiotics, , N = 192	Control, , N = 201
Endometritis No of events	n = 0	n = 7

Knight 2019 (ANODE)

Outcome	Prophylactic antibiotics, , N = 1715	Control, , N = 1705
Endometritis No of events	n = 15	n = 23
Infected episiotomy/laceration Superficial or deep perineal wound; organ or space infection; No of events	n = 111	n = 222
Systemic sepsis (*) according to modified SIRS criteria for pregnancy No of events	n = 6	n = 10
Maternal adverse reactions No of events	n = 2	n = 1
Breastfeeding at 6 weeks No of events	n = 662	n = 657

Outcome	Prophylactic antibiotics, , N = 1715	Control, , N = 1705
Perineal pain at 6 weeks post-delivery No of events	n = 592	n = 707

Critical appraisal - NGA Critical appraisal - ROBIS checklist

Section	Question	Answer
Study eligibility criteria	Concerns regarding specification of study eligibility criteria	Low
Identification and selection of studies	Concerns regarding methods used to identify and/or select studies	Low
Data collection and study appraisal	Concerns regarding methods used to collect data and appraise studies	Low *(Some study characteristics were not extracted relevant to the protocol, but low risk of bias as the main ones were for the Cochrane review)*
Synthesis and findings	Concerns regarding the synthesis and findings	Low *(Sensitivity analysis was not carried out as only 2 studies were included, however the authors addressed this.)*
Overall study ratings	Overall risk of bias	Low
Overall study ratings	Applicability as a source of data	Fully applicable

Limitations for each of the included studies assessed with the Cochrane Risk of Bias Tool v1, based on the Cochrane review assessments

Study	Answer
Heitmann 1989	Random sequence generation (selection bias): Low risk Allocation concealment (selection bias): Some concerns Blinding of participants and personnel (performance bias): Some concerns Blinding of outcome assessment (detection bias): Some concerns Incomplete outcome data (attrition bias): Low risk Selective reporting (reporting bias): Some concerns Other bias: Low risk
Knight 2019	Random sequence generation (selection bias): Low risk Allocation concealment (selection bias): Low risk Blinding of participants and personnel (performance bias): Low risk Blinding of outcome assessment (detection bias): Low risk Incomplete outcome data (attrition bias): Low risk Selective reporting (reporting bias): Low risk Other bias: Low risk

IQR: interquartile range; IV: intravenous; SD: standard deviation; SIRS: systemic inflammatory response syndrome

Appendix E Forest plots

Forest plots for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

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.

Appendix F GRADE tables

GRADE tables for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Table 5: Comparison 1: Prophylactic antibiotics (cephalosporin) versus no treatment

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic antibiotics	No treatment	Relative (95% CI)	Absolute		
Endometritis												
1 (Heitmann 1989)	randomised trials	serious[1]	no serious inconsistency	serious[2]	no serious imprecision	none	0/192 (0%)	7/201 (3.5%)	Peto OR 0.14 (0.03 to 0.61)	30 fewer per 1000 (from 14 fewer to 34 fewer)	LOW	CRITICAL

CI: confidence interval; OR: odds ratio
1 Serious risk of bias in the evidence contributing to the outcomes as per RoB 2
2 Population downgraded for indirectness due to no information on non-cephalic presentations

Table 6: Comparison 2: Prophylactic antibiotics (co-amoxiclav) versus placebo

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic antibiotics	Placebo	Relative (95% CI)	Absolute		
Endometritis												
1 (Knight 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	serious[2]	none	15/1715 (0.87%)	23/1705 (1.3%)	RR 0.65 (0.34 to 1.24)	5 fewer per 1000 (from 9 fewer to 3 more)	LOW	CRITICAL
Infected episiotomy/laceration												

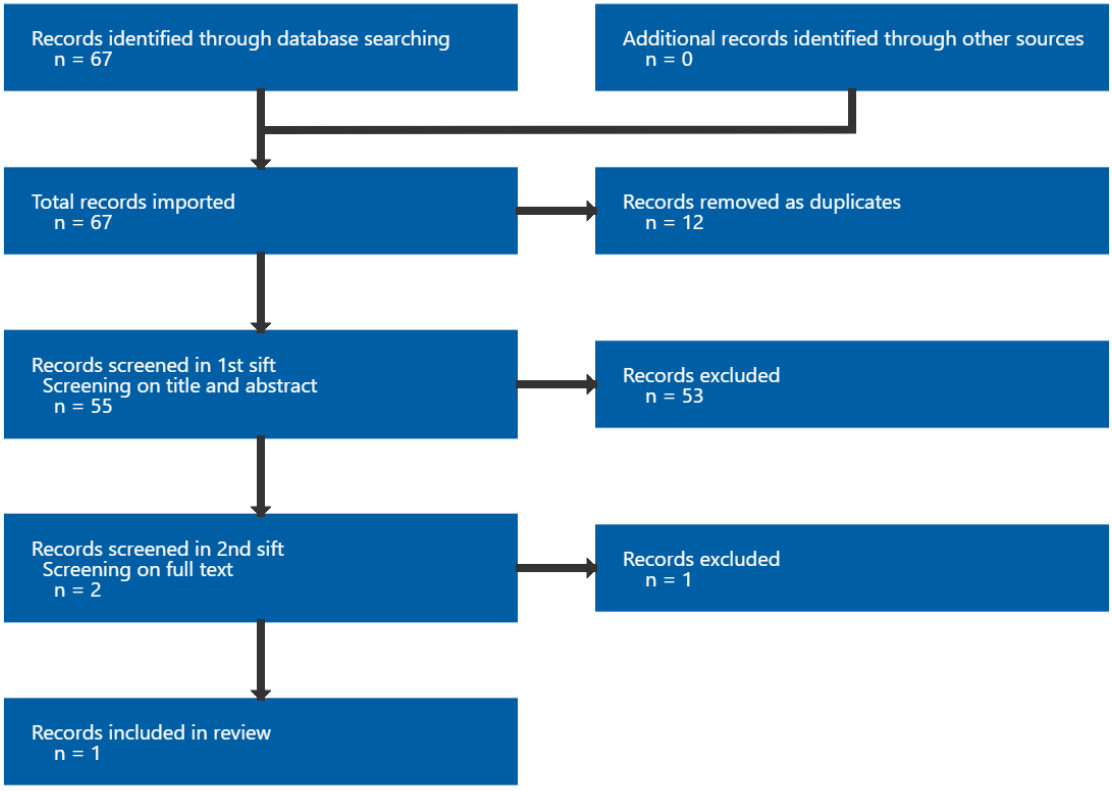
Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Prophylactic antibiotics	Placebo	Relative (95% CI)	Absolute		
1 (Knight 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	111/1715 (6.5%)	222/1705 (13%)	RR 0.5 (0.4 to 0.62)	65 fewer per 1000 (from 49 fewer to 78 fewer)	MODERATE	CRITICAL
Systemic sepsis												
1 (Knight 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[3]	none	6/1715 (0.35%)	10/1705 (0.59%)	RR 0.6 (0.22 to 1.64)	2 fewer per 1000 (from 5 fewer to 4 more)	VERY LOW	CRITICAL
Maternal adverse reactions												
1 (Knight 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	very serious[3]	none	2/1296 (0.15%)	1/1297 (0.08%)	RR 2 (0.18 to 22.05)	1 more per 1000 (from 1 fewer to 16 more)	VERY LOW	IMPORTANT
Breastfeeding at 6 weeks												
1 (Knight 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	662/1296 (51.1%)	657/1297 (50.7%)	RR 1.01 (0.93 to 1.09)	5 more per 1000 (from 35 fewer to 46 more)	MODERATE	IMPORTANT
Perineal pain at 6 weeks												
1 (Knight 2019)	randomised trials	no serious risk of bias	no serious inconsistency	serious[1]	no serious imprecision	none	592/1296 (45.7%)	707/1297 (54.5%)	RR 0.84 (0.78 to 0.91)	87 fewer per 1000 (from 49 fewer to 120 fewer)	MODERATE	IMPORTANT

CI: confidence interval; RR: risk ratio
1 Population downgraded for indirectness due to no information on non-cephalic presentations
2 95% CI crosses 1 MID
3 95% CI crosses 2 MIDs

Appendix G Economic evidence study selection

Study selection for: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Figure 2: Study selection flow chart



Appendix H Economic evidence tables

Economic evidence tables for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Table 7: Economic evidence tables for prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
Author and year: Knight 2019 **Country:** UK **Type of economic analysis:** Cost analysis **Source of funding:** Health Technology Assessment programme of the National Institute for Health Research	**Intervention:** Women following an operative vaginal birth received a single dose of intravenous co-amoxiclav (1 g of amoxicillin/200 mg of clavulanic acid) **Comparator:** Women following an operative vaginal birth received or a placebo (sterile saline)	**Population characteristics:** Women aged 16 years and over who had an operative vaginal birth at ≥ 36+0 weeks' gestation **Modelling approach/alongside an RCT:** Economic data collected alongside an RCT Source of baseline data: Trial control (placebo) **Source of effectiveness data:** N/A **Source of cost data:**	**Mean cost per participant:** Intervention: £102.50 (SD: £652.40) Control: £155.10 (SD: £497.40) Difference: -£52.60 (99% CI: -£115.10 to £9.90	**ICERs:** N/A **Probability of being cost effective:** No PSA undertaken. **Subgroup analysis:** None **Sensitivity analysis:** Sensitivity analysis was undertaken with imputation for missing data mean difference in the total cost was –£50.90 (99% CI–£114.70 to £12.90; p = 0.040)	**Perspective:** NHS **Currency:** GBP **Cost year:** 2017/18 **Time horizon:** Period following operative birth to 6 weeks after birth **Discounting:** N/A **Applicability:** Directly applicable **Limitations:**

Study country and type	Intervention and comparator	Study population, design and data sources	Costs and outcomes (descriptions and values)	Results	Comments
		Resource use data was collected from a telephone interview and postal questionnaire undertaken at 6 weeks after birth. **Source of unit cost data:** BNF 2017; Unit Costs of Health and Social Care 2017; NHS Reference Costs 2017/18			Potentially serious limitations **Other comments:** Staffing and consumable costs were not included in the costs of the intervention. Uncertainty around point estimate of mean difference in cost estimated using a 99% CI. The RCT reported a significant benefit of prophylactic antibiotic in terms of reduced rates of confirmed or suspected infection at 6 weeks after birth: Relative risk 0.58, 95% CI 0.49 to 0.69)

BNF: British National Formulary; CI: confidence interval; GBP: Great British Pounds; ICER: Incremental cost-effectiveness ratio; NHS: National Health Service; RCT: randomised controlled trial; SD: standard deviation; UK: United Kingdom;

Appendix I Economic model

Economic model for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

No economic analysis was conducted for this review question.

Appendix J Excluded studies

Excluded studies for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

Excluded effectiveness studies

Study	Reason
(2019) LB 3: Prophylactic antibiotics for the prevention of infection following operative vaginal delivery: the ANODE trial. American Journal of Obstetrics and Gynecology 220(1supplement): 685	- Study design Abstract only. Full published results included
Berhan, Yifru; Kirba, Sisay; Gebre, Achamyelesh (2020) Still No Substantial Evidence to Use Prophylactic Antibiotic at Operative Vaginal Delivery: Systematic Review and Meta-Analysis. Obstetrics and gynecology international 2020: 1582653	- Cochrane systematic review already included References checked and no additional studies included that were not included in the Cochrane systematic review included in this review
Buppasiri, P., Lumbiganon, P., Thinkhamrop, J. et al. (2005) Antibiotic prophylaxis for fourth-degree perineal tear during vaginal birth. The Cochrane database of systematic reviews: cd005125	- More recent version available Assessed under Buppasiri 2014
Buppasiri, Pranom, Lumbiganon, Pisake, Thinkhamrop, Jadsada et al. (2014) Antibiotic prophylaxis for third- and fourth-degree perineal tear during vaginal birth. Cochrane Database of Systematic Reviews 2014(10): cd005125	- Population References checked, one included study does not meet the population as 65% of women had a spontaneous vaginal birth (only 35% had a forceps or vacuum assisted vaginal birth).
Knight, Marian (2020) Antibiotic prophylaxis after operative vaginal birth: the ANODE randomized controlled trial. Obstetrics, Gynaecology and Reproductive Medicine 30(10): 326-327	- Study design Summary of a randomised trial already included (ANODE trial)
Knight, Marian, Chiocchia, Virginia, Partlett, Christopher et al. (2019) Intravenous co-amoxiclav to prevent infection after operative vaginal delivery: the ANODE RCT. Health technology assessment (Winchester, England) 23(54): 1-54	- Study design Health Technology Assessment for the ANODE trial which has been included under Cochrane Systematic Review (Liabsuetrakul 2020). Checked for secondary subgroup analysis, but nothing matching the protocol
Knight, Marian, Chiocchia, Virginia, Partlett, Christopher et al. (2019) Prophylactic Antibiotics in the Prevention of Infection After Operative Vaginal Delivery (ANODE): A Multicenter Randomized Controlled Trial. Obstetrical and Gynecological Survey 74(11): 635-637	- Study design Editorial comment
Mohamed-Ahmed, Olaa; Hinshaw, Kim; Knight, Marian (2019) Operative vaginal delivery and post-partum infection. Best practice & research. Clinical obstetrics & gynaecology 56: 93-106	- Study design Not a systematic review or randomised controlled trial. References checked and one relevant study has already been included under a Cochrane review
van Schalkwyk, Julie, Money, Deborah M., Ogilvie, Gina et al. (2010) Antibiotic Prophylaxis in Obstetric Procedures. Journal of Obstetrics and Gynaecology Canada 32(9): 878-884	- Study design Not a systematic review or randomised controlled trial, however references checked. Cochrane systematic review identified, but a

Study	Reason
	more recent one has been included in this review
van Schalkwyk, Julie and Van Eyk, Nancy (2017) No. 247-Antibiotic Prophylaxis in Obstetric Procedures. Journal of Obstetrics and Gynaecology Canada 39(9): e293-e299	- Study design Not a systematic review or randomised controlled trial, however references checked. Cochrane systematic review identified, but a more recent one has been included in this review

Excluded economic studies

Study	Reason
Owens, Sarah, Thayer, Sydney, Hersh, Alyssa R. et al. (2020) 118: Antibiotics at time of operative vaginal delivery: a cost-effectiveness analysis. American Journal of Obstetrics and Gynecology 222(1supplement): 92	- Conference abstract

Appendix K Research recommendations – full details

Research recommendations for review question: What is the effectiveness of prophylactic antibiotics for preventing postnatal infections in assisted vaginal birth?

K.1.1 Research recommendation

What is the effectiveness of prophylactic intravenous (IV) versus oral antibiotics for preventing postnatal infections in assisted vaginal birth?

K.1.2 Why this is important

The administration of antibiotics following assisted vaginal birth has been shown to be safe and effective to reduce endometritis and infection at the site of episiotomy/laceration. The largest trial conducted to date (ANODE; Knight 2019) showed that women who received a single dose of IV co-amoxiclav had a reduction in infections compared to those who received placebo. However, administration of intravenous antibiotics requires an IV line to be in place and requires 2 trained staff to check and administer, and use of oral antibiotics may be less invasive and less expensive. The effectiveness of prophylactic intravenous (IV) compared to oral antibiotics for preventing postnatal infections in assisted vaginal birth has not yet been assessed. Investigating the most appropriate route of administration is important as this could have implications in safety and costs.

K.1.3 Rationale for research recommendation

Table 8: Research recommendation rationale

Importance to 'patients' or the population	Increased options for the administration of prophylactic antibiotics following assisted vaginal birth will mean that women can be given an effective treatment option using the least intrusive method.
Relevance to NICE guidance	Due to limited evidence the committee were only able to recommend the use of prophylactic IV antibiotics. Future research will help to determine whether oral antibiotics could be recommended to reduce the risk of infection following assisted vaginal birth.
Relevance to the NHS	The committee have made recommendations on antibiotic treatment based primarily on the largest trial conducted to date. An increased understanding of whether there is a particular administration route that would most benefit women will help the committee make more specific recommendations in future updates of this guideline
National priorities	Medium
Current evidence base	Minimal long-term data
Equality considerations	All women having an assisted vaginal birth should have equal treatment.

K.1.4 Modified PICO table

Table 9: Research recommendation modified PICO table

Population	• Women in labour who are pregnant with a single baby, who go into labour at term (37 to 42 weeks of pregnancy) and who do not have any pre-existing medical conditions or antenatal conditions that predispose to a higher risk birth • Women in labour whose baby has not been identified before labour to be at high risk of adverse outcome • Singleton babies born at term (37 to 42 weeks of pregnancy) with no previously identified problems (for example congenital malformations, genetic anomalies, intrauterine growth restriction, placental problems) • Women having an assisted vaginal birth (forceps or vacuum/suction birth) without evidence of an active infection or other conditions requiring antibiotics
Intervention	Prophylactic oral antibiotics given immediately before or as soon as possible after an assisted vaginal birth (forceps or vacuum birth)
Comparator	Prophylactic intravenous antibiotics given immediately before or as soon as possible after an assisted vaginal birth (forceps or vacuum birth)
Outcome	• Endometritis • Infection at perineal/vaginal or episiotomy site (up till 6 weeks) • Sepsis following perineum infection or endometritis • Maternal adverse reaction to antibiotics • Long-term neonatal outcomes (asthma, allergies) • Breastfeeding at 6 weeks • Perineal pain at 6 weeks • Antibiotic resistance
Study design	Parallel randomised controlled trial
Timeframe	6 weeks follow-up
Additional information	None