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)

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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	

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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