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Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections (Review)

Haas DM, Morgan S, Contreras K, Kimball S

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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	4
BACKGROUND	6
OBJECTIVES	6
METHODS	6
RESULTS	10
Figure 1.	11
Figure 2.	13
Figure 3.	14
Figure 4.	16
DISCUSSION	18
AUTHORS' CONCLUSIONS	18
ACKNOWLEDGEMENTS	19
REFERENCES	20
CHARACTERISTICS OF STUDIES	24
DATA AND ANALYSES	51
Analysis 1.1. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 1: Post-cesarean endometritis	53
Analysis 1.2. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 2: Postoperative fever	54
Analysis 1.3. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 3: Postoperative wound infection	55
Analysis 1.4. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 4: Composite wound complication	55
Analysis 1.5. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 5: Composite wound complication or endometritis	56
Analysis 2.1. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 1: Post-cesarean endometritis	57
Analysis 2.2. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 2: Postoperative fever	58
Analysis 2.3. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 3: Postoperative wound infection	59
Analysis 2.4. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 4: Composite wound complication	60
Analysis 2.5. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 5: Composite wound complication or endometritis	60
Analysis 3.1. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 1: Post-cesarean endometritis	62
Analysis 3.2. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 2: Postoperative fever	63
Analysis 3.3. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 3: Postoperative wound infection	64
Analysis 3.4. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 4: Composite wound complication	65
Analysis 3.5. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 5: Composite wound complication or endometritis	65
APPENDICES	66
WHAT'S NEW	66
HISTORY	67
CONTRIBUTIONS OF AUTHORS	67
DECLARATIONS OF INTEREST	67

SOURCES OF SUPPORT	67
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	67
INDEX TERMS	68

[Intervention Review]

Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections

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ABSTRACT

Background

Cesarean delivery is one of the most common surgical procedures performed by obstetricians. Infectious morbidity after cesarean delivery can have a tremendous impact on the postpartum woman's return to normal function and her ability to care for her baby. Despite the widespread use of prophylactic antibiotics, postoperative infectious morbidity still complicates cesarean deliveries. This is an update of a Cochrane Review first published in 2010 and subsequently updated in 2012, twice in 2014, in 2017 and 2018.

Objectives

To determine if cleansing the vagina with an antiseptic solution before a cesarean delivery decreases the risk of maternal infectious morbidities, including endometritis and wound complications. We also assessed the side effects of vaginal cleansing solutions to determine adverse events associated with the intervention.

Search methods

We searched the Cochrane Pregnancy and Childbirth's Trials Register, [ClinicalTrials.gov](https://www.clinicaltrials.gov), the World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP) (7 July 2019), and reference lists of retrieved studies.

Selection criteria

We included randomized controlled trials (RCTs) and quasi-RCTs assessing the impact of vaginal cleansing immediately before cesarean delivery with any type of antiseptic solution versus a placebo solution/standard of care on post-cesarean infectious morbidity.

Cluster-RCTs were eligible for inclusion, but we did not identify any. We excluded trials that utilized vaginal preparation during labor or that did not use antibiotic surgical prophylaxis. We also excluded any trials using a cross-over design. We included trials published in abstract form only if sufficient information was present in the abstract on methods and outcomes to analyze.

Data collection and analysis

At least three of the review authors independently assessed eligibility of the studies. Two review authors were assigned to extract study characteristics, quality assessments, and data from eligible studies.

Main results

We included 21 trials, reporting results for 7038 women evaluating the effects of vaginal cleansing (17 using povidone-iodine, 3 chlorhexidine, 1 benzalkonium chloride) on post-cesarean infectious morbidity. Trials used vaginal preparations administered by sponge

sticks, douches, or soaked gauze wipes. The control groups were typically no vaginal preparation (17 trials) or the use of a saline vaginal preparation (4 trials). One trial did not report on any outcomes of interest. Trials were performed in 10 different countries (Saudi Arabia, Pakistan, Iran, Thailand, Turkey, USA, Egypt, UK, Kenya and India). The overall risk of bias was low for areas of attrition, reporting, and other bias. About half of the trials had low risk of selection bias, with most of the remainder rated as unclear. Due to lack of blinding, we rated performance bias as high risk in nearly one-third of the trials, low risk in one-third, and unclear in one-third.

Vaginal preparation with antiseptic solution immediately before cesarean delivery probably reduces the incidence of post-cesarean **endometritis** from 7.1% in control groups to 3.1% in vaginal cleansing groups (average risk ratio (aRR) 0.41, 95% confidence interval (CI) 0.29 to 0.58; 20 trials, 6918 women; moderate-certainty evidence). This reduction in endometritis was seen for both iodine-based solutions and chlorhexidine-based solutions. Risks of **postoperative fever** and **postoperative wound infection** are also probably reduced by vaginal antiseptic preparation (fever: aRR 0.64, 0.50 to 0.82; 16 trials, 6163 women; and wound infection: RR 0.62, 95% CI 0.50 to 0.77; 18 trials, 6385 women; both moderate-certainty evidence). Two trials found that there may be a lower risk of a **composite outcome of wound complication or endometritis** in women receiving preoperative vaginal preparation (RR 0.46, 95% CI 0.26 to 0.82; 2 trials, 499 women; low-certainty evidence). No **adverse effects** were reported with either the povidone-iodine or chlorhexidine vaginal cleansing.

Subgroup analysis suggested a greater effect with vaginal preparations for those women in labour versus those not in labour for four out of five outcomes examined (post-cesarean endometritis; postoperative fever; postoperative wound infection; composite wound complication or endometritis). This apparent difference needs to be investigated further in future trials. We did not observe any subgroup differences between women with ruptured membranes and women with intact membranes.

Authors' conclusions

Vaginal preparation with povidone-iodine or chlorhexidine solution compared to saline or not cleansing immediately before cesarean delivery probably reduces the risk of post-cesarean endometritis, postoperative fever, and postoperative wound infection. Subgroup analysis found that these benefits were typically present whether iodine-based or chlorhexidine-based solutions were used and when women were in labor before the cesarean. The suggested benefit in women in labor needs further investigation in future trials.

There was moderate-certainty evidence using GRADE for all reported outcomes, with downgrading decisions based on limitations in study design or imprecision.

As a simple intervention, providers may consider implementing preoperative vaginal cleansing with povidone-iodine or chlorhexidine before performing cesarean deliveries. Future research on this intervention being incorporated into bundles of care plans for women receiving cesarean delivery will be needed.

PLAIN LANGUAGE SUMMARY

Vaginal cleansing with antiseptic solution before cesarean delivery to reduce infections after surgery

We set out to determine from randomized controlled trials if cleansing the vagina with an antiseptic solution before a cesarean delivery safely decreases the risk of maternal infections.

What is the issue?

Cleansing the vagina before the cesarean delivery can reduce the number of bacteria that are naturally present in the vagina. These bacteria in the vagina and cervix can move up into the uterus during the surgical procedure and cause infection in the lining of the uterus and in the surgical wound. Antibiotics are routinely given before the surgery to reduce the risk of infections, but some women still suffer from these complications. Some antibiotics do not always eradicate all bacteria, and antibiotic resistant bacteria may be present. Vaginal preparation may not be included in the care provided to women to reduce infection following surgery. Vaginal cleansing solutions, such as chlorhexidine and povidone-iodine are inexpensive, and have very few side effects.

Why is this important?

Cesarean deliveries are common, with almost one in three babies born by cesarean in some countries such as the USA. It is not uncommon for women having a cesarean delivery to develop an infection of the uterus (endometritis) or a problem with their skin incision. The risk of infection is greater if a woman's waters have broken or she is in labor before the cesarean section. These complications may slow a woman's recovery from the surgery and can affect her ability to take care of her baby. This is a Cochrane Review first published in 2010 and updated in 2012, 2014, and in 2017.

What evidence did we find?

We searched for new evidence on 7 July 2019. In this update, we have included 21 randomized controlled studies, involving a total of 7038 women undergoing cesarean section. The studies took place in 10 countries (Saudi Arabia, Pakistan, Iran, Thailand, Turkey, USA, Egypt, UK, Kenya and India). The control group had no vaginal preparation in 18 studies and in three studies participants used a saline vaginal preparation. We did not include trials that did not give antibiotics before or during the surgery, or where women received vaginal

preparation during labor. Seventeen studies used povidone-iodine for vaginal cleansing, three chlorhexidine, and one benzalkonium chloride.

Cleansing the vagina with antiseptic solution immediately before cesarean delivery probably reduces the incidence of post-cesarean infection of the uterus (20 trials, 6918 women; moderate-certainty evidence). This reduction was seen for both iodine-based solutions and chlorhexidine-based solutions. The risk of postoperative fever (16 trials, 6163 women) and postoperative wound infection (18 trials, 6385 women) are also probably reduced by vaginal cleansing; both moderate-certainty evidence). The risk of having wound complication or infection of the uterus may be lower in women receiving preoperative vaginal cleansing with antiseptic solution (2 trials, 499 women). None of the studies reported any adverse events, such as an allergic reaction to the cleansing solution or irritation.

Further analysis suggested a greater effect for those women in labour versus those not in labour for four out of five outcomes examined (post-cesarean infection of the uterus; postoperative fever; postoperative wound infection; wound complication or infection of the uterus) but this apparent difference needs to be investigated further in future trials. We did not observe any differences between groups of women with ruptured membranes and women with intact membranes.

What does this mean?

Cleansing the vagina with povidone-iodine or chlorhexidine solution (compared to saline or not cleansing) immediately before cesarean delivery probably reduces the risk of infection of the uterus, fever, and infection of the surgical wound. Further analysis found that these benefits were typically present whether iodine-based or chlorhexidine-based solutions were used and when women were in labor before the cesarean.

Vaginal preparation is a simple and well-tolerated way to lower the chances of developing an infection after having a baby by cesarean.

SUMMARY OF FINDINGS

Summary of findings 1. Vaginal preparation with antiseptic solution compared to control (no preparation or saline preparation) for preventing postoperative infections

Vaginal preparation with antiseptic solution compared to control (no preparation or saline preparation) for preventing postoperative infections

Patient or population: pregnant women undergoing cesarean section

Setting: hospital (Egypt, India, Iran, Kenya, Pakistan, Saudi Arabia, Thailand, Turkey, UK, USA)

Intervention: vaginal preparation with antiseptic solution

Comparison: control (no preparation or saline preparation)

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	Nº of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with control (no preparation or saline preparation)	Risk with vaginal preparation with antiseptic solution				
Post-cesarean endometritis	Study population		RR 0.41 (0.29 to 0.58)	6918 (20 RCTs)	⊕⊕⊕⊖ Moderate ^{a,b}	
	72 per 1000	30 per 1000 (21 to 42)				
Postoperative fever	Study population		RR 0.64 (0.50 to 0.82)	6163 (16 RCTs)	⊕⊕⊕⊖ Moderate ^{a,b}	
	120 per 1000	77 per 1000 (60 to 99)				
Postoperative wound infection	Study population		RR 0.62 (0.50 to 0.77)	6385 (18 RCTs)	⊕⊕⊕⊖ Moderate ^b	
	61 per 1000	38 per 1000 (31 to 48)				
Composite wound complication or endometritis	Study population		RR 0.46 (0.26 to 0.82)	499 (2 RCTs)	⊕⊕⊕⊖ Low ^c	
	135 per 1000	62 per 1000 (35 to 111)				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **RCT:** randomized controlled trial; **RR:** risk ratio.

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: we are moderately confident in the effect estimate; the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low certainty: our confidence in the effect estimate is limited; the true effect may be substantially different from the estimate of the effect.

Very low certainty: we have very little confidence in the effect estimate; the true effect is likely to be substantially different from the estimate of effect.

^aThere is some funnel plot asymmetry. Having conducted sensitivity analyses to investigate the contribution of small studies and studies at high risk of bias, we do not believe that the effect estimate has been biased by possible missing results due to non-publication. We did not downgrade.

^bWe downgraded (-1) for serious concerns about limitations in study design due to most of the pooled effect being provided by studies that are at moderate risk of bias.

^cWe downgraded (-1) for serious concerns about limitations in study design due to a substantial proportion of pooled effect provided by studies at moderate risk of bias. We downgraded (-1) for serious concerns about imprecision due to two small studies, with relatively few events.

BACKGROUND

Cesarean section delivery rates are increasing worldwide, with rates in Latin America and North America of 40.5% and 32.3%, respectively (Betran 2016). Cesarean section deliveries are often complicated by infections occurring after surgery (Zuarez-Easton 2017).

Description of the condition

Endometritis, an infection of the uterus in the postpartum period, can complicate the postoperative course of a cesarean delivery 6% to 27% of the time (Guzman 2002; Smaill 2014). This complication, up to 10 times more frequent after a cesarean delivery than after vaginal delivery, can lead to serious complications of bacterial infection in the blood (10% to 20%), peritonitis (general infection in the abdominal cavity), intra-abdominal abscess (cavity filled with infected material), and sepsis (Mackeen 2015; Yokoe 2001). Additionally, cesarean deliveries are frequently complicated by maternal fever and wound complications, including seroma (fluid collection under the skin), hematoma (blood clots under the skin), infection, and separation (Zuarez-Easton 2017). These morbidities could lead to a delay in return to normal function.

Fevers and infections after cesarean deliveries are associated with the length of ruptured membranes, length of labor, and number of vaginal examinations (Disgupta 1988; Yonekura 1985). Post-cesarean endometritis and infectious morbidity are the result often of the presence of bacteria in the vagina and cervix that move higher in the genital tract to infect the uterus (Martens 1991). These bacteria have been shown to be responsible for failure of antibiotic prophylaxis during cesarean deliveries (Watts 1991). Additionally, some antibiotics do not consistently eradicate some bacteria (such as *Enterococcus spp.*), and the vagina has been shown to become colonized with antibiotic resistant bacteria after preoperative surgical antibiotic prophylaxis (Gibbs 1982; Graham 1993; Stiver 1984). Currently, it is standard care to give preoperative antibiotics to women receiving a cesarean delivery (Smaill 2014), but the rate of post-cesarean infections remains a problem.

Description of the intervention

As many pelvic organ infections after surgeries, such as cesarean deliveries, contain organisms from the vagina, cleansing the vagina with antiseptic solutions before surgeries, such as hysterectomies, has been performed for years (ACOG 2018; Haeri 1976; Osborne 1977). As it has been used to reduce infections after hysterectomies, it is logical that after a cesarean delivery, where the uterus remains potentially exposed to the vagina through the cervix, reducing the bacterial content before a cesarean delivery could reduce post-cesarean infections of the uterus. Previous studies have evaluated whether vaginal cleansing before a cesarean delivery with various solutions can reduce the incidence of febrile morbidity (endometritis and wound infections). Povidone-iodine, chlorhexidine, and vaginal metronidazole have been reported with varying results (Pitt 2001; Suarez-Easton 2017). Older data comparing iodine with chlorhexidine before hysterectomy showed lower morbidity in the iodine group, with improved activity against anaerobic pathogens (Duignan 1975; Haeri 1976). Vaginal preparation has not typically been included in evidence-based bundles to reduce post-cesarean infectious morbidity (Carter 2017; Hsu 2016; NICE 2011). Vaginal cleansing solutions, such as chlorhexidine and povidone-iodine, have very few side effects in

general, with low rates of noted allergies or irritation symptoms. Thus, the intervention is now appearing in recommendations about post-cesarean recovery protocols (Caughey 2018).

How the intervention might work

By cleansing the vagina of bacteria before the cesarean delivery occurs, there may be less of a bacterial load in the vagina that might cause infectious morbidity postoperatively. As ascending infection is thought to be a major etiology of postoperative endometritis, this could logically reduce that risk (Martens 1991).

Why it is important to do this review

Rates of cesarean delivery are increasing, particularly in high-income countries (Betran 2016). Postoperative infectious morbidity after cesarean delivery may impact the woman's return to normal function, and potentially her bonding with the newborn, as she is dealing with additional healthcare needs to treat the infection (Zuarez-Easton 2017). It can also cause major medical problems and sequelae and increase healthcare costs (Olsen 2010). Finding an easy, inexpensive method to reduce this risk could have a major public health impact in high-, middle-, and low-income countries.

OBJECTIVES

To determine if cleansing the vagina with an antiseptic solution before a cesarean delivery decreases the risk of maternal morbidities, including endometritis and wound complications. We also assessed the side effects of vaginal cleansing solutions to determine adverse events associated with the intervention.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomized controlled trials (RCTs) and two quasi-RCTs. Cluster-RCTs were eligible for inclusion, but we did not identify any.

Types of participants

Pregnant women who were about to receive a cesarean delivery. This included women receiving elective, laboring, or urgent cesareans.

Types of interventions

Any method of vaginal cleansing (including douches, wipes, sponges, etc.) with any type of antiseptic solution (povidone-iodine, chlorhexidine, etc.) versus a placebo solution/standard care (no vaginal preparation).

We included only studies where vaginal preparation was performed no more than one hour before surgery. This review addressed the use of preoperative vaginal cleansing after the decision to perform a cesarean had been made. This review did not address the use of vaginal preparation during labor. Thus, we excluded trials utilizing vaginal cleansing solutions during labor. We also excluded studies where prophylactic surgical antibiotics were explicitly not used. Surgical prophylaxis with intravenous antibiotics before or during cesarean deliveries has been clearly demonstrated as beneficial in reducing postoperative infectious morbidities (Smaill 2014). Thus, it is the standard of care. Inclusion of trials not utilizing general

surgical antibiotic prophylaxis would not represent the current standard of care and the results would not be translatable into current practice. We did not discriminate trials on the basis of when the antibiotics were administered (before or after infant umbilical cord clamping), as this practice has changed over time ([Mackeen 2014](#)).

Types of outcome measures

Primary outcomes

1. Post-cesarean endometritis: defined as a clinical diagnosis, usually involving fever, uterine fundal tenderness, or purulent lochia requiring antibiotic therapy.

Secondary outcomes

1. Postoperative fever: defined as greater than 38 °C or 100.4 °F.
2. Postoperative wound infection: defined as erythema, tenderness, purulent drainage from the incision site, with or without fever, requiring antibiotic therapy.
3. Postoperative wound seroma or hematoma: defined as collection of serous fluid or blood/clot in the subcutaneous area of the incision.
4. Composite wound complications: defined as the presence of any one of the following: wound infection, seroma, hematoma, separation.
5. Composite wound complications or endometritis.
6. Side effects of vaginal preparation (maternal allergy, irritation). As these solutions are applied gently and not absorbed, there should be no adverse fetal/neonatal events. We did not anticipate or find mention of adverse neonatal events from the vaginal cleansing.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Electronic searches

For this update, we searched Cochrane Pregnancy and Childbirth's Trials Register by contacting their Information Specialist (7 July 2019).

The Register is a database containing over 25,000 reports of controlled trials in the field of pregnancy and childbirth. It represents over 30 years of searching. For full current search methods used to populate Pregnancy and Childbirth's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this [link](#).

Briefly, Cochrane Pregnancy and Childbirth's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);

5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Search results are screened by two people and the full text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth review topic (or topics), and is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set that has been fully accounted for in the relevant review sections ([Included studies](#); [Excluded studies](#); [Studies awaiting classification](#); [Ongoing studies](#)).

In addition, we searched [ClinicalTrials.gov](#) and the WHO International Clinical Trials Registry Platform (ICTRP) for unpublished, planned and ongoing trial reports (7 July 2019) using the search methods detailed in [Appendix 1](#).

Searching other resources

We searched the reference lists of retrieved studies. We attempted to contact trialists for further information (September 2019). We did not apply any language or date restrictions.

Data collection and analysis

For the methods used when assessing the trials identified in the previous version of this review, see [Haas 2018](#).

For this update, we used the following methods for assessing the 14 new reports that were identified as a result of the updated search.

Selection of studies

At least three review authors (DH, SM, KC, SE) independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion.

Data extraction and management

We designed a form to extract data. We extracted trial information and dates, outcomes, sources of trial funding, and trial authors' declarations of interest (if available). For eligible studies, at least two review authors extracted the data using the agreed form. Assignments for data extraction were distributed among the four review authors equitably. We resolved discrepancies through discussion. We entered data into Review Manager software ([Review Manager 2014](#)).

When information regarding any of the above was unclear, we attempted to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Three review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). We resolved any disagreement by discussion.

(1) Random sequence generation (checking for possible selection bias)

We described the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

For each included study we assessed the method as being at:

1. low risk of bias (any truly random process, e.g. random number table; computer random number generator);
2. high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
3. unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

For each included study we described the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as being at:

1. low risk of bias (e.g. telephone or central randomization; consecutively numbered sealed opaque envelopes);
2. high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
3. unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

For each included study we described the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding was unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as being at:

1. low, high or unclear risk of bias for participants;
2. low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

For each included study we described the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as being at:

1. low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

For each included study, and for each outcome or class of outcomes, we described the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included

in the analysis at each stage (compared with the total randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we planned to reinstate missing data in the analyses that we undertook.

We assessed methods as being at:

1. low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
2. high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomization);
3. unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

For each included study we described how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as being at:

1. low risk of bias (where it was clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported);
2. high risk of bias (where not all the study's prespecified outcomes were reported; one or more reported primary outcomes were not prespecified; outcomes of interest were reported incompletely and so could not be used; study failed to include results of a key outcome that would have been expected to have been reported);
3. unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

For each included study we described any important concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgments about whether studies were at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it was likely to have an impact on the findings. In future updates, we will explore the impact of the level of bias through undertaking sensitivity analyses (Sensitivity analysis).

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratios (RRs) with 95% confidence intervals (CIs).

Continuous data

None of our outcomes are continuous in nature. If an outcome is added in the future that contains continuous data, we plan to use the mean difference (MD) if outcomes were measured in the same way between trials. We plan to use the standardized

mean difference (SMD) to combine trials that measured the same outcome, but used different methods.

Unit of analysis issues

Cluster-randomized trials

We did not identify any cluster-randomized trials. If, in future updates we identify cluster-randomized trials, we will include them in the analyses along with individually-randomized trials. We will adjust their sample sizes using the methods described in the *Handbook* (Higgins 2011), using an estimate of the intracluster correlation coefficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomized trials and individually-randomized trials, we plan to synthesize the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomization unit is considered to be unlikely.

We will also acknowledge heterogeneity in the randomization unit and perform a sensitivity analysis to investigate the effects of the randomization unit.

Cross-over trials

Cross-over trials are not relevant for this intervention and are not included.

Other unit of analysis issues

We found one trial that compared three groups. It did not contribute outcome data (Goymen 2017). However, if it had or we encounter three-armed trials in future updates, we would utilize the methods in the *Handbook* to decide the optimal way to include them in the meta-analysis. One trial used a "no wash" and a saline wash control group (Hassan 2016). In our analysis, we combined these as controls, as some other trials used a saline wash for the control group.

Dealing with missing data

For included studies, we noted levels of attrition. We did not encounter large levels of attrition. In future updates, if we do encounter large levels of attrition, we will explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analyses.

For all outcomes, we carried out analyses, as far as possible, on an intention-to-treat (ITT) basis, i.e. we attempted to include all participants randomized to each group in the analyses, and all participants were analyzed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. The denominator for each outcome in each trial was the number randomized minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the τ^2 , I^2 and χ^2 statistics. We regarded heterogeneity as substantial if the I^2 was greater than 30% and either a τ^2 was

greater than zero, or there was a low P value (less than 0.10) in the χ^2 test for heterogeneity.

Assessment of reporting biases

There were 21 included studies. Since there were 10 or more studies in the meta-analysis contributing data to the primary outcome, we investigated reporting biases (such as publication bias) using funnel plots. We assessed for reporting bias by inspecting the funnel plot asymmetry visually. Because potential asymmetry was found visually, we tested to see if the results were different when limiting to small (< 300 participants) or large trial effects or if the results were different when excluding trials at high risk of bias in multiple domains.

Data synthesis

We carried out statistical analysis using the Review Manager software (Review Manager 2014). We used a fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect, i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar. If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if we detected substantial statistical heterogeneity, we used a random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. We treated the random-effects summary as the average range of possible treatment effects, and we discussed the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we did not combine trials.

Where we used random-effects analyses, we presented the results as the average treatment effect with 95% CIs, and the estimates of τ^2 and I^2 .

Subgroup analysis and investigation of heterogeneity

For this update, we carried out the following subgroup analyses.

1. Women in labor versus women not in labor.
2. Women with ruptured membranes versus women with intact membranes.

We used all reported outcomes in the primary analysis in the subgroup analyses.

We assessed subgroup differences by interaction tests available within RevMan 5 (Review Manager 2014). We reported the results of subgroup analyses quoting the χ^2 statistic and P value, and the interaction test I^2 value. Where we identified significant heterogeneity, we used a random-effects analysis to produce the summaries of effect.

We were unable to carry out the following subgroup analyses because this information was not reported in the included studies.

1. Women with chorioamnionitis preoperatively versus women without chorioamnionitis.
2. Women undergoing emergency cesarean versus those undergoing unscheduled cesarean versus those undergoing scheduled cesarean.

3. Women with internal fetal or uterine monitors in place versus those with only external monitors in place before the cesarean.

Sensitivity analysis

We did not perform any sensitivity analyses due to a lack of studies included within the analyses. In future updates, we plan to carry out sensitivity analyses to explore the effect of trial quality assessed by concealment of allocation, high attrition rates (> 20%), or both, and exclude poor quality studies from the analyses, in order to assess whether this makes any difference to the overall result.

Summary of findings and assessment of the certainty of the evidence

For this update, we assessed the certainty of the evidence using the GRADE approach, as outlined in the *GRADE Handbook* in order to assess the certainty of the body of evidence relating to the following outcomes for the main comparisons ([Schünemann 2013](#)).

1. Post-cesarean endometritis: defined as a clinical diagnosis, usually involving fever, uterine fundal tenderness, or purulent lochia requiring antibiotic therapy.
2. Postoperative fever: defined as greater than 38 °C or 100.4 °F.

3. Postoperative wound infection: defined as erythema, tenderness, purulent drainage from the incision site, with or without fever, requiring antibiotic therapy.
4. Composite wound complications or endometritis.

We used the GRADEpro Guideline Development Tool to import data from Review Manager 5 ([GRADEpro GDT 2015](#); [Review Manager 2014](#)), in order to create a 'Summary of findings' table. Using the GRADE approach, we produced a summary of the intervention effect and a measure of certainty for each of the above outcomes. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the certainty of the body of evidence for each outcome. The evidence can be downgraded from 'high certainty' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

RESULTS

Description of studies

Results of the search

See [Figure 1](#).

Figure 1. Study flow diagram.

An updated search in July 2019 retrieved 22 new trial reports to assess and we also reassessed two trials 'awaiting classification' and the six trials listed as 'ongoing' in the previous version of the review. We also assessed and subsequently excluded two additional trial reports (Pitt 2001; Sweeten 1997). After title evaluation, and review of the full-text manuscripts and trial registry reports, we included 10 new trials (14 reports) and excluded seven additional trials (eight reports). Six trials are ongoing (see [Characteristics of ongoing studies](#)). Four trials are awaiting further classification (see [Characteristics of studies awaiting classification](#)).

Included studies

Methods

In this updated review we included 21 studies, reporting results for 7038 women. Nineteen trials were randomized controlled trials (RCTs) and two were quasi-RCTs.

Settings

All trials were either in academic centers or large hospitals. Five trials were performed in the USA (Guzman 2002; Haas 2010; Reid 2001; Rouse 1997; Starr 2005), three in Pakistan (Asad 2017; Kiani 2018; Memon 2011), three in Turkey (Goymen 2017; Olmez 2013; Yildirim 2012), two in Iran (Asghania 2011; Barat 2016), two in Egypt (Hassan 2016; Mohamed 2015), two in Saudi Arabia (Ahmed 2017; Aref 2019), one in Thailand (Charoenviboonphan 2011), one in the UK (Hodgetts 2019), one in Kenya (Mwangi 2013), and one in India (Nandi 2015). The Charoenviboonphan 2011 trial was written in Thai, with the abstract and results tables in English. We were able to secure a translation of the methods of the trial for abstraction.

Trial dates

The trials were reported as being conducted during the following periods.

1. Ahmed 2017 - October 2014 to December 2015
2. Aref 2019 - September 2016 to December 2017
3. Asad 2017 - 1 February 2016 to 31 July 2016
4. Asghania 2011 - May 2007 to April 2008
5. Barat 2016 - 2013 to 2014 (months not stated)
6. Charoenviboonphan 2011 - September 2010 to January 2011
7. Goymen 2017 - July 2014 to August 2014
8. Guzman 2002 - March 2000 to July 2001
9. Haas 2010 - September 2006 to January 2009
10. Hassan 2016 - September 2015 to March 2016
11. Hodgetts 2019 - 13 November 2017 to 3 March 2018
12. Kiani 2018 - September 2014 to January 2015
13. Memon 2011 - February 2010 to July 2010
14. Mohamed 2015 - May 2014 to August 2014
15. Mwangi 2013 - July 2016 to October 2016
16. Nandi 2015 - January 2013 to July 2014
17. Olmez 2013 - September 2009 to July 2010
18. Reid 2001 - May 1996 to September 1998
19. Rouse 1997 - February 1994 to January 1996
20. Starr 2005 - November 1997 to March 2000
21. Yildirim 2012 - January 2011 to August 2011

Participants

Six trials only included women for scheduled or elective cesareans (Ahmed 2017; Aref 2019; Barat 2016; Goymen 2017; Hassan 2016; Mohamed 2015). Two trials only included women who were in labor (Asad 2017; Kiani 2018), and the remainder of the studies included women both in labor and for scheduled cesareans (Asghania 2011; Guzman 2002; Haas 2010; Hodgetts 2019; Memon 2011; Mwangi 2013; Nandi 2015; Olmez 2013; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012). Two trials specifically excluded women with ruptured membranes (Ahmed 2017; Goymen 2017). One of the trials that included only women for elective cesareans excluded women with premature ruptured membranes (Barat 2016). By consensus, we did not believe we could judge if women presenting for elective cesareans might have been in labor. However, we judged that all women presenting for an elective cesarean would have been likely to have had intact membranes to be included. Thus, we counted trials including women for elective cesareans as having women with intact membranes as well. Seven trials specifically excluded women with chorioamnionitis (Asad 2017; Goymen 2017; Kiani 2018; Mwangi 2013; Reid 2001; Rouse 1997; Starr 2005). Three trials excluded women undergoing emergency cesarean deliveries (Aref 2019; Guzman 2002; Reid 2001).

Interventions and comparisons

Three studies compared chlorhexidine cleansing versus no cleansing (Ahmed 2017; Hodgetts 2019; Mohamed 2015). One study compared chlorhexidine solution versus a saline solution (Rouse 1997). One trial used cetrimide, which the authors noted contained chlorhexidine and thus we included with the chlorhexidine subgroup (Mohamed 2015). One report had two intervention groups compared with controls without cleansing - one group received povidone-iodine cleansing and one group received benzalkonium chloride cleansing (Goymen 2017). All other studies compared preoperative vaginal povidone-iodine solution preparation with a control group. In one trial (Guzman 2002), the control group was a saline vaginal wash. Hassan 2016 used two intervention groups, one a saline washing and one a povidone-iodine wash, while the control group had no washing. We combined the saline group and no washing groups as the control group, per the protocol definitions for the review. The other 14 trials compared vaginal cleansing with an iodine-based solution to no vaginal cleansing (Aref 2019; Asad 2017; Asghania 2011; Barat 2016; Charoenviboonphan 2011; Haas 2010; Kiani 2018; Memon 2011; Mwangi 2013; Nandi 2015; Olmez 2013; Reid 2001; Starr 2005; Yildirim 2012).

Outcomes

All but one trial (Goymen 2017), reported on various infectious morbidity outcomes specified in this review (see [Characteristics of included studies](#)).

The Goymen 2017 study did not report on any of the primary or secondary outcomes prespecified for this review. The reported outcomes for that study were associated with postoperative recovery of bowel function and pain scores. Thus, it did not contribute any data to the analyses.

All the studies contributing data reported on the outcome of endometritis, while 16 studies reported on postoperative fever, and 17 reported on wound infection (see [Characteristics of included](#)

studies). Two studies reported any wound complication and a composite of endometritis or any wound complication.

Sources of trial funding

Five trials reported sources of funding. [Haas 2010](#), [Mwangi 2013](#), and [Starr 2005](#) reported internal institutional or hospital funding. [Rouse 1997](#) received federal funding from the United States Department of Health and Human Services. [Hodgetts 2019](#) stated funding from the Birmingham Women's and Children's National Health Service Foundation Trust. One trial specifically listed no sources of support ([Aref 2019](#)). All other reports did not list any sources of funding.

Declarations of interest

Ten trials specified no conflicts of interest from the authors ([Ahmed 2017](#); [Aref 2019](#); [Barat 2016](#); [Goymen 2017](#); [Haas 2010](#); [Hassan 2016](#);

[Hodgetts 2019](#); [Mohamed 2015](#); [Mwangi 2013](#); [Yildirim 2012](#)). The remainder of the trials did not mention declarations of interest.

Excluded studies

We excluded one trial as the journal retracted the publication ([Abdallah 2015](#)). Seven other trials were excluded due to the wrong comparisons or intervention timing ([Pitt 2001](#); [Sweeten 1997](#); [Tewfik 2015](#); [NCT03925155](#); [Dudko 2018](#); [NCT03133312](#); [Lakhi 2016](#)).

Risk of bias in included studies

See 'Risk of bias' tables for the included studies in [Characteristics of included studies](#) and [Figure 2](#); and [Figure 3](#), for summaries of 'Risk of bias' assessments.

Figure 2. Methodological quality graph: review authors' judgements about each methodological quality item presented as percentages across all included studies.

Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias): All outcomes	Blinding of outcome assessment (detection bias): All outcomes	Incomplete outcome data (attrition bias): All outcomes	Selective reporting (reporting bias)	Other bias
Ahmed 2017	+	?	-	+	+	+	+
Aref 2019	?	+	-	?	+	+	+
Asad 2017	?	?	-	?	?	+	+
Asghania 2011	-	-	+	+	+	+	-
Barat 2016	+	?	?	+	+	+	+
Charoenviboonphan 2011	+	?	?	?	+	+	+
Goymen 2017	+	?	-	?	+	+	+
Guzman 2002	?	?	+	+	+	+	+
Haas 2010	+	+	+	+	+	+	?
Hassan 2016	-	?	?	?	+	+	+
Hodgetts 2019	+	+	+	+	+	+	+
Kiani 2018	+	?	?	+	+	+	+
Memon 2011	?	?	?	+	+	+	+
Mohamed 2015	-	?	?	?	+	+	+
Mwangi 2013	+	+	+	+	+	+	+
Nandi 2015	+	?	-	?	+	+	+
Olmez 2013	?	+	?	?	+	+	+
Reid 2001	+	+	?	+	+	-	+
Rouse 1997	+	+	+	+	+	+	+
Starr 2005	+	+	+	+	?	+	+
Yildirim 2012	+	+	-	-	+	+	+

Overall, the quality of these 21 studies was generally moderate, as defined by Higgins 2011.

Allocation

Random sequence generation

Five trials were unclear about the randomization sequence generation (Aref 2019; Asad 2017; Guzman 2002; Memon 2011; Olmez 2013). We judged three studies to be at potentially high risk of bias for random sequence generation. Asghania 2011 was a quasi-randomized trial with alternate allocation, earning a high risk of bias rating. Hassan 2016 used number patient name lists, assigning evens to control group and odds to one of two intervention groups. Mohamed 2015 also used an odd-even alternating randomization. The remaining trials were at a low risk of bias due to random sequence generation (Ahmed 2017; Barat 2016; Charoenviboonphan 2011; Goymen 2017; Haas 2010; Hodgetts 2019; Kiani 2018; Mwangi 2013; Nandi 2015; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012).

Allocation concealment

Eleven of the reports were unclear about allocation concealment (Ahmed 2017; Asad 2017; Barat 2016; Charoenviboonphan 2011; Goymen 2017; Guzman 2002; Hassan 2016; Kiani 2018; Memon 2011; Mohamed 2015; Nandi 2015), mainly due to no mention of that in the publication. One trial had a high risk of bias due to alternating sequence (Asghania 2011). The other trials had low risk of allocation bias (Aref 2019; Haas 2010; Hodgetts 2019; Mwangi 2013; Olmez 2013; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012).

Blinding

Blinding of participants and personnel (performance bias)

Six trials had a high risk of bias regarding blinding of the participants and care providers (Ahmed 2017; Aref 2019; Asad 2017; Goymen 2017; Nandi 2015; Yildirim 2012). As the intervention involved vaginal cleansing or not, it is understandable that in some clinical scenarios, blinding of this step might be difficult. Eight trials were at unclear risk of bias because it was not stated (Barat 2016; Charoenviboonphan 2011; Hassan 2016; Kiani 2018; Memon 2011; Mohamed 2015; Olmez 2013; Reid 2001).

Seven trials specifically noted ways they attempted to blind participants and/or care providers, or noted how it was unlikely for them to know the group assignment (i.e. participant had regional anesthesia and was behind a drape, surgeons were not in the room during surgical preparation) (Asghania 2011; Guzman 2002; Haas 2010; Hodgetts 2019; Mwangi 2013; Rouse 1997; Starr 2005). We assessed these trials as having a low risk of performance bias.

Blinding of outcome assessment (detection bias)

Twelve trials blinded outcomes assessors (Ahmed 2017; Asghania 2011; Barat 2016; Guzman 2002; Haas 2010; Hodgetts 2019; Kiani 2018; Memon 2011; Mwangi 2013; Reid 2001; Rouse 1997; Starr 2005), and we assessed them at low risk of detection bias. One trial stated that the researchers were not blinded and that the assignment was written in the medical records (Yildirim 2012), so outcome assessors were unlikely to be blinded either; we assessed this trial as having a high risk of detection bias. The remaining studies did not state blinding of outcomes assessors and we judged them to have a low risk of detection bias (Aref 2019; Asad 2017;

Charoenviboonphan 2011; Goymen 2017; Hassan 2016; Mohamed 2015; Nandi 2015; Olmez 2013).

Incomplete outcome data

One report did not describe attrition fully as it was a published abstract, earning it an unclear 'Risk of bias' assessment (Asad 2017). We also rated other trial as unclear for attrition bias (Starr 2005); of 400 participants randomized, 92 (23%) were excluded after randomization: 33 due to lost envelopes, six for violations of inclusion criteria, and 53 because their hospital charts could not be located. Of all the women excluded, 54 were in the vaginal cleansing group and 38 were in the control group. Only outcomes for women for whom all data were available were reported. The large number of women excluded also makes this trial subject to an unclear risk of bias, however as there are no outcome data for the excluded participants, the potential impact is unclear (Starr 2005). The remaining 19 studies had a low risk of attrition bias.

Selective reporting

One trial had a large number of participants excluded after randomization who had chorioamnionitis (a known risk factor for postoperative infectious morbidity) because their inclusion "distorted the absolute rates of fever and infectious morbidity" (Reid 2001). That trial states that when the 68 participants with antepartum infection were included, the estimates of effect of vaginal preparation were not meaningfully different. Thus, they planned to exclude those participants from reports of outcomes. As this represented 13.5% of the originally randomized sample, however, there is a risk that this introduced selective reporting bias into the trial. We assessed this trial as having a high risk of reporting bias (Reid 2001). The other 20 trials were at low risk of reporting bias.

Other potential sources of bias

One trial was stopped early at a planned safety analysis due to difficulty recruiting participants (Haas 2010); we assessed this trial at unclear risk of other bias. The Asghania 2011 trial had large differences in the baseline and labor characteristics between the groups, including more examinations, longer labors, more preterm deliveries, longer surgery times, and longer duration of membrane rupture in the cleansing group. We assessed this trial as having a high risk of potential bias. The other 19 trials were at low risk of other sources of bias.

Effects of interventions

See: **Summary of findings 1** Vaginal preparation with antiseptic solution compared to control (no preparation or saline preparation) for preventing postoperative infections

Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation) (comparison 1)

Primary outcome: post-cesarean endometritis

Vaginal cleansing with povidone-iodine solution reduced the risk of post-cesarean endometritis from 7.2% in control groups to 3.1% in vaginal cleansing groups (average risk ratio (aRR) 0.41, 95% confidence interval (CI) 0.29 to 0.58; 20 trials, 6918 women; moderate-certainty evidence). We used a random-effects meta-analysis for this outcome because of high heterogeneity ($I^2 = 44\%$ and $\text{Tau}^2 = 0.22$; Analysis 1.1). The substantial

heterogeneity indicates that treatment effects vary between studies, so we investigated the factors affecting treatment effects by the prespecified subgroup analyses (see below). As all of the trials did not include all subgroups, it is unclear if the subgroup analyses were able to account for all of the heterogeneity. However, we considered that the trials were similar enough clinically that the average treatment effect would be clinically meaningful. Stratifying these findings by solution yielded similar results for iodine-based solution and chlorhexidine-based solution (aRR 0.41, 95% CI 0.28 to 0.60; 16 trials, 6197 women for iodine; aRR 0.38, 95% CI 0.28 to 0.89; 4 trials, 721 women for chlorhexidine; [Analysis 1.1](#)).

Assessment of reporting (publication) biases for the primary outcome

Since our primary outcome analysis included more than 10 studies, we investigated reporting bias. We prepared a funnel plot ([Figure](#)

4), and this shows signs of visual asymmetry. To determine if this potential publication bias influenced the results, we then carried out a number of tests as to whether this made a difference to the results. In these analyses, we restricted the analysis to the larger trials (> 300 total participants), only small trials, and trials deemed of lower risk of bias by having no domains judged as high risk of bias. Limiting the results by trial size or quality did not change the overall findings of benefit for the primary outcome. Thus, we do not believe that selective reporting (publication) biased these findings. It is possible that some of the funnel plot asymmetry is present due to the wide variation in apparent population risk among the trials. The rates of endometritis in the control groups varies greatly. These different baseline population risk differences may have contributed to the asymmetry.

Figure 4. Funnel plot of comparison: 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation), outcome: 1.1 Post-cesarean endometritis.

Secondary outcomes

Vaginal cleansing also led to a clear reduction in the outcomes of **postoperative fever** (aRR 0.64, 95% CI 0.50 to 0.82; 16 trials, 6163 women; moderate-certainty evidence; [Analysis 1.2](#)) and **postoperative wound infection** (RR 0.62, 95% CI 0.50 to 0.77; 18 trials, 6385 women; moderate-certainty evidence; [Analysis](#)

1.3). There was more uncertainty around the estimate of vaginal cleansing's impact on **composite wound complications** (RR 0.63, 95% CI 0.37 to 1.07; 2 trials, 729 women; moderate-certainty evidence; [Analysis 1.4](#)). However, based mainly on the results for endometritis, vaginal cleansing may lead to a reduction in the **composite wound complication or endometritis** outcome

(RR 0.46, 95% CI 0.26 to 0.82; 2 trials, 499 women; low-certainty evidence; [Analysis 1.5](#)). The improved outcomes for women receiving vaginal cleansing were noted for subgroups receiving both iodine-based solutions and chlorhexidine-based solutions for postoperative fever and postoperative wound infection ([Analysis 1.2](#); [Analysis 1.3](#)). We did not note any **side effects of vaginal preparation** in the four trials commenting on possible adverse events from the vaginal preparation solution ([Ahmed 2017](#); [Goymen 2017](#); [Haas 2010](#); [Rouse 1997](#)). None of the other trials mentioned any adverse events, but did not specifically discuss the topic.

We did not find any evidence of differences between subgroups according to the subgroup differences test we performed.

Subgroup analysis: women in labor versus women not in labor (comparison 2)

Five trials stratified data for women in labor versus not in labor ([Haas 2010](#); [Memon 2011](#); [Mwangi 2013](#); [Reid 2001](#); [Yildirim 2012](#)), while two trials only included women in labor ([Asad 2017](#); [Kiani 2018](#)). One trial included 14 women receiving irrigation before elective cesareans not in labor and only reported on the endometritis outcome for the group ([Rouse 1997](#)). Two trials reported on the outcomes of post-cesarean endometritis and composite wound complication ([Haas 2010](#); [Reid 2001](#)). Four studies reported on stratified outcomes for post-cesarean endometritis, postoperative fever, and postoperative wound infection ([Asad 2017](#); [Kiani 2018](#); [Mwangi 2013](#); [Yildirim 2012](#)). One trial only reported stratified results for composite infectious morbidity ([Memon 2011](#)).

Primary outcome: post-cesarean endometritis

There was a reduction in rates of post-cesarean endometritis for women undergoing a cesarean after being in labor who received vaginal preparation from 9.3% in the control group to 3.4% in the vaginal preparation group (aRR 0.35, 95% CI 0.19 to 0.67; 6 trials, 1634 women; [Analysis 2.1](#)). There was no clear difference in rates of post-cesarean endometritis for women who were not in labor (7.8% in control group versus 3.7% in vaginal preparation group (aRR 0.86, 95% CI 0.33 to 2.21; 5 trials, 1043 women; [Analysis 2.1](#)). However, there were no clear differences between these two subgroups, as indicated by the subgroup interaction test (test for subgroup differences: $\text{Chi}^2 = 2.37$, $\text{df} = 1$ ($P = 0.12$), $I^2 = 57.8\%$).

Secondary outcomes

Women in labor reported a reduction in rates of **postoperative fever** (RR 0.61, 95% CI 0.42 to 0.87; 5 trials, 1415 women; [Analysis 2.2](#)), **postoperative wound infection** (RR 0.52, 95% CI 0.30 to 0.90; 5 trials, 1415 women; [Analysis 2.3](#)), and the **composite wound complication or endometritis** outcome (RR 0.34, 95% CI 0.13 to 0.87; 2 trials, 164 women; [Analysis 2.5](#)). The small number of women in these groups limits this conclusion. There were no clear differences in rates of **composite wound complications** for women receiving vaginal preparation (RR 0.77, 95% CI 0.36 to 1.61; 2 trials, 314 women; [Analysis 2.4](#)).

The subgroup analyses, specifically for women who were not in labor before the cesarean delivery, failed to demonstrate any clear differences in any secondary outcomes: **postoperative fever** (RR 0.93, 95% CI 0.60 to 1.43; 3 trials, 818 women; [Analysis 2.2](#)); **postoperative wound infection** (RR 0.67, 95% CI 0.35 to 1.31; 3

trials, 818 women; [Analysis 2.3](#)); **composite wound complication** (RR 0.54, 95% CI 0.25 to 1.16; 2 trials, 415 women; [Analysis 2.4](#)); **composite wound complication or endometritis** (RR 0.60, 95% CI 0.29 to 1.26; 2 trials, 335 women; [Analysis 2.5](#)).

We did not find any evidence of differences between subgroups according to the subgroup differences test we performed.

Subgroup analysis: women with ruptured membranes versus women with intact membranes (comparison 3)

Five trials stratified data for women with ruptured membranes versus women without ruptured membranes ([Guzman 2002](#); [Haas 2010](#); [Memon 2011](#); [Mwangi 2013](#); [Yildirim 2012](#)). Five trials excluded women with premature ruptured membranes in women only undergoing elective cesarean ([Ahmed 2017](#); [Aref 2019](#); [Barat 2016](#); [Kiani 2018](#); [Mohamed 2015](#)). These trials only contributed data to the intact membranes subgroup. Two trials reported on the outcomes of post-cesarean endometritis and postoperative fever ([Guzman 2002](#); [Haas 2010](#)). Most other studies reported on stratified outcomes for post-cesarean endometritis, postoperative fever, and postoperative wound infection ([Ahmed 2017](#); [Aref 2019](#); [Barat 2016](#); [Haas 2010](#); [Kiani 2018](#); [Mohamed 2015](#); [Mwangi 2013](#); [Yildirim 2012](#)). One trial only reported stratified results for composite wound complications or endometritis ([Memon 2011](#)).

Primary outcome postpartum endometritis

For women with ruptured membranes, there was a reduction in the rates of post-cesarean endometritis for women receiving vaginal preparation preoperatively (3.4% in the vaginal cleansing group versus 13.7% in the control group; RR 0.23, 95% CI 0.12 to 0.45; 5 trials, 552 women; [Analysis 3.1](#)). There was also a reduction in the rate of post-cesarean endometritis for women with intact membranes who received vaginal cleansing before cesarean delivery (rate of 4.1% in the vaginal cleansing group versus 8.7% in the control group; RR 0.48, 95% CI 0.34 to 0.68; 8 trials, 2082 women) and the subgroup interaction test indicated that there may be a suggestion of a difference between these two subgroups (test for subgroup differences: $\text{Chi}^2 = 3.59$, $\text{df} = 1$ ($P = 0.06$), $I^2 = 72.2\%$).

Secondary outcomes

There was a reduction in **postoperative fever** for women with ruptured membranes receiving vaginal preparation (aRR 0.42, 95% CI 0.22 to 0.80; 4 trials, 480 women; [Analysis 3.2](#)), but not for other secondary outcomes: **postoperative wound infection** (aRR 0.54, 95% CI 0.19 to 1.50; 5 trials, 552 women; [Analysis 3.3](#)); **composite wound complication** (RR 0.53, 95% CI 0.15 to 1.89; 1 trial, 76 women; [Analysis 3.4](#)); **composite wound complication or endometritis** (RR 0.39, 95% CI 0.13 to 1.13; 2 trials, 134 women; [Analysis 3.5](#)).

For women with intact membranes, there was also a reduction in **postoperative fever** for women receiving vaginal preparation (aRR 0.70, 95% CI 0.49 to 0.99; 7 trials, 1994 women; [Analysis 3.2](#)). All of the other reported secondary outcomes for women without ruptured membranes were not clearly different between the vaginal preparation and control groups: **postoperative wound infection** (aRR 0.73, 95% CI 0.50 to 1.07; 8 trials, 2082 women; [Analysis 3.3](#)); **composite wound complication** (RR 0.73, 95% CI 0.25 to 2.10; 1 trial, 224 women; [Analysis 3.4](#)); **composite wound complication or endometritis** (RR 0.52, 95% CI 0.26 to 1.04; 2 trials, 336 women; [Analysis 3.5](#)).

We did not find any evidence of differences between subgroups according to the subgroup differences test we performed.

Other planned subgroup analyses: women with chorioamnionitis preoperatively versus women without chorioamnionitis; women undergoing emergency cesarean versus those undergoing unscheduled cesarean versus those undergoing scheduled cesarean; women with internal fetal or uterine monitors in place versus those with only external monitors in place before the cesarean

Neither of the two trials that specifically included women diagnosed with chorioamnionitis stratified their data based on the presence or absence of chorioamnionitis. Neither of the two trials that did not exclude women undergoing emergency cesarean stratified their data based on emergency cesarean versus unscheduled versus scheduled cesarean. In addition, while three trials reported on the presence of internal monitoring (Haas 2010; Starr 2005; Yildirim 2012), none of them stratified their outcome data based on this variable. Thus we did not perform these three subgroup analyses.

DISCUSSION

Summary of main results

Vaginal cleansing with either povidone-iodine or chlorhexidine solutions before cesarean delivery can reduce the incidence of post-cesarean endometritis, postoperative fever, and postoperative wound infections. A clear reduction in the rate of endometritis from 7.2% to 3.4% was seen. The heterogeneity in the results for these outcomes may be explainable by the study design and patient populations. The Guzman 2002, Hassan 2016, and Rouse 1997 studies used a placebo vaginal saline or water wash. This may have led to a lower baseline incidence of postoperative morbidity. Haas 2010 and many of the trials added in this update contained a majority of women or only women who were obtaining planned repeat cesarean deliveries, a group known to be at lower risk for postoperative infectious morbidities. Additionally, vaginal preparation before cesarean delivery reduced the rate of a composite outcome of the presence of wound complication or endometritis. These results are summarized in Summary of findings 1.

Interestingly, the benefits of vaginal preparation were seen with both iodine-based and chlorhexidine-based solutions for both post-cesarean endometritis and postoperative fever. The effects of the intervention seemed bigger in some subgroups although the interaction tests for subgroup differences were not statistically significant. The subgroup analyses demonstrated that the reduction in postoperative endometritis is most pronounced for women with ruptured membranes and those women who undergo a cesarean delivery after already being in labor. These subgroup analyses should be interpreted with caution, however, as the number of participants and events is relatively low. Ruptured membranes and being in labor are known risk factors for post-cesarean infectious morbidity. The use of vaginal preparation in women in labor or with ruptured membranes thus makes particular sense.

Overall completeness and applicability of evidence

While there is heterogeneity in study design, the evidence is relatively complete, consistent, and highly applicable

to clinical care. Currently, there are six ongoing trials (NCT02495753; NCT02693483; NCT03093194; NCT03397615; NCT03423147; PACTR201709002597110).

Certainty of the evidence

The risk of bias of the 21 included trials is reasonably low to moderate, with only a few areas being identified as potential sources of high risk of bias (Figure 2; Figure 3). The most common area found to have high risk of bias was in the area of blinding. This is because the control groups in most trials did not receive vaginal cleansing and often the participant and providers may have known who received the vaginal preparation as it would be obvious to anyone standing in the operating room. There were also some areas at unclear risk of bias, often in allocation concealment due to lack of commenting on that factor in the trial report. The agreement of the trial data in general, and the large number of participants represented, lend validity to the results of the meta-analysis. The clinical heterogeneity was essentially eliminated in the subgroup analyses, the results of which were consistent with the overall group results.

The certainty of the evidence using GRADE was moderate for post-cesarean endometritis, postoperative fever and postoperative wound infection with downgrading decisions based on limitations in study design (risk of bias). The certainty of the evidence was low for the composite outcome of wound complication or endometritis, with downgrading decisions based on both limitations in study design (risk of bias) and imprecision (Summary of findings 1).

Potential biases in the review process

There is always potential that the review process was biased. However, the updated trial search yielded several additional studies. The study evaluation and data extraction were performed by four review authors, with almost no discrepancies that needed to be resolved by consensus. Thus, there is a minimal risk of bias in the review process. The studies were carried out in a wide variety of low-, middle-, and high-income countries.

Agreements and disagreements with other studies or reviews

We added 10 new trials to this update, giving a total of 21 included studies. The addition of the new trials strengthens the conclusions of the earlier versions of this review (Haas 2010a; Haas 2013; Haas 2014a; Haas 2014b; Haas 2018). The additional evidence changes the conclusions by also showing that vaginal preparation lowers the rates of both postoperative fever and postoperative wound infection. The findings of lower risk of post-cesarean endometritis is consistent with a recently published meta-analysis (Caissutti 2017). We plan to include data from ongoing trials in future updates of this review. Uniformity in the reporting of the data outcomes and the subgroup data stratification would have also aided this review.

AUTHORS' CONCLUSIONS

Implications for practice

Vaginal preparation with povidone-iodine or chlorhexidine solution immediately before cesarean delivery reduces the risk of post-cesarean endometritis, postoperative fever, and postoperative wound infection. We did not note any adverse events in any of the trials. The subgroup analysis, with the intention of

being observational for hypothesis generation, also indicated that many of these outcomes may be reduced for women in labor and for women who had both ruptured and unruptured membranes. As a simple, generally inexpensive intervention (povidone-iodine swabs cost USD 4 in our hospital), providers may consider implementing preoperative vaginal cleansing with povidone-iodine or chlorhexidine before performing cesarean deliveries. Information on whether other methods of vaginal preparation reduce postoperative infectious morbidity is lacking.

Implications for research

As practice changes and providers begin to routinely implement preoperative vaginal cleansing before cesarean deliveries, postoperative infectious morbidities can be tracked and compared with the same outcomes before the practice change. Epidemiological- or population-based research into the impact of bundles of care surrounding reducing post-cesarean endometritis and other infectious morbidity can help determine the impact of multiple interventions in this area. In addition, factor analyses can help discover the most important components of preoperative bundles. Consistency in defining postoperative infectious morbidity will aid in data synthesis, as will consistency in adverse event reporting. A core outcome set for infectious morbidity after cesarean has been published and is registered on the COMET website (www.comet-initiative.org/studies; [Briscoe 2019](#)). For this update, we did not include maternal mortality or neonatal morbidity, two of the outcomes in the proposed core outcome set. We plan to include them in the next update.

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The 'Summary of findings' table in this update was prepared by Myfanwy Williams, PhD using GradePro software ([GRADEpro GDT 2015](#)).

As part of the prepublication editorial process, this review has been commented on by four peers (an editor and three referees who are external to the editorial team) and the Group's Statistical Adviser. The authors are grateful to the following peer reviewers for their time and comments: Dr Charles Anawo Ameh, Centre for Maternal and Newborn Health, International Public Health, Liverpool School of Tropical Medicine, UK; Robert S Kerr, Department of Obstetrics and Gynaecology, St Michael's Hospital, Bristol, UK; Carolina C Ribeiro-do-Valle, MD, MSc, Department of Obstetrics and Gynecology, School of Medical Sciences, University of Campinas, Campinas, Brazil.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Ahmed 2017

Study characteristics	
Methods	RCT
Participants	<p>218 women randomized (109 in each group)</p> <p>Inclusion: pregnant women scheduled for term elective cesarean section - indications were prior cesarean, abnormal presentation, maternal request, prior cystocele repair or prior perineal tear</p> <p>Exclusion: emergency cesarean, premature ruptured membranes, placenta previa, immunocompromized status</p> <p>Setting: Saudi Arabia</p>
Interventions	<p>Intervention: chlorhexidine 0.25% antiseptic wipes in vagina (3 lots of 10 cm x 10 cm pieces used from apex to introitus including fornices for approximately 1 minute total time)</p> <p>Control: no vaginal cleansing</p> <p>Intention-to-treat analysis</p>
Outcomes	<p>Outcomes</p> <ol style="list-style-type: none"> Infectious morbidities <ol style="list-style-type: none"> Endometritis - fever with tenderness and offensive lochia Febrile morbidity - fever of 38 °C or more without infectious clinical findings Wound infection - erythema or wound edge separation with purulent discharge requiring antibiotics and wound care Side effects
Notes	<p>All outcomes are summed for overall results. Apparently no one with endometritis also had a wound infection. These are not necessarily mutually exclusive. October 2014 to end of December 2015.</p> <p>October 2014 to December 2015</p> <p>Funding source: not stated</p> <p>Authors' declarations of interest: no conflicts of interest</p>

Ahmed 2017 (Continued)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomization method used
Allocation concealment (selection bias)	Unclear risk	No other information was provided beside the use of sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	High risk	Vaginal scrub was performed while the surgeon was in the room.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Clinical care team was blinded to either arm.
Incomplete outcome data (attrition bias) All outcomes	Low risk	7 in intervention and 11 in control arm lost to follow-up. Otherwise, complete outcome data
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	None

Aref 2019

Study characteristics

Methods	RCT
Participants	<p>226 women randomized (113 in each group)</p> <p>Inclusion: singleton term pregnancy, scheduled elective cesarean section</p> <p>Exclusion: emergency cesarean section, PROM, positive bacterial vaginosis and/or GBS within 2 weeks prior to cesarean section, women with autoimmune disease or immunosuppression (chronic steroid use, diabetes)</p> <p>Setting: single institution, Saudi Arabia</p>
Interventions	<p>Intervention: povidone-iodine 10% solution on gauze vaginal wash for 1 minute</p> <p>Control: no vaginal wash</p> <p>Intention-to-treat: not stated</p>
Outcomes	<ol style="list-style-type: none"> 1. Endometritis 2. Febrile morbidity 3. Fever 4. Wound infection
Notes	September 2016 to December 2017

Aref 2019 (Continued)

Funding source: stated the authors received no financial support

Authors' declaration of interest: no conflict of interest or financial support

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "simple randomization method" Comment: but not stated how sequence was generated
Allocation concealment (selection bias)	Low risk	2 sealed envelopes, women chose the envelope themselves, thus likely low risk of bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Scrub nurse did vaginal cleansing while surgeons did the abdominal scrub. No mention of participant blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Number of withdrawals: 7 study, 12 control (8.4%)
Selective reporting (reporting bias)	Low risk	All expected outcomes reported on
Other bias	Low risk	No other sources of bias identified

Asad 2017

Study characteristics

Methods	RCT
Participants	434 women randomized (217 in each group) Inclusion: women undergoing emergency cesarean with labor duration > 6 hours regardless of membrane rupture Exclusion: diabetes, anemia, obstructed labor, any febrile condition Setting: Islamabad, Pakistan
Interventions	Intervention: vaginal cleansing with povidone-iodine Control: no vaginal cleansing
Outcomes	1. Fever 2. Wound infection 3. Endometritis
Notes	1 February 2016 to 31 July 2016

Asad 2017 (Continued)

Funding source: not stated

Author declarations of interest: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Population randomized, but not clearly stated how it was accomplished
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	Participants were not blinded.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not described
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not described
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	None

Asghania 2011
Study characteristics

Methods	Double-blind quasi-RCT
Participants	<p>585 women randomized (294 vaginal preparation, 291 control)</p> <p>Inclusion: women undergoing non-emergent or laboring cesarean delivery</p> <p>Exclusion: iodine sensitivity, chorioamnionitis, gestational herpes, abnormal vaginal discharge, emergency cesarean (due to fetal distress, placenta previa)</p> <p>Setting: Iran</p>
Interventions	<p>Intervention: 2 lots of 4 x 4 gauze sponges soaked in 10% povidone-iodine solutions rotated 360 degrees for 30 seconds from vault to introitus</p> <p>Control: no vaginal cleansing</p> <p>Intention-to-treat analysis</p>
Outcomes	<ol style="list-style-type: none"> 1. Febrile morbidity 2. Endometritis 3. Wound infection

Asghania 2011 (Continued)

Notes

May 2007 to April 2008

Funding source: not stated

Author declarations of interest: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quasi-randomized, alternating sequence
Allocation concealment (selection bias)	High risk	Quasi-randomized, alternating sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants: unclear but stated "double-blind"
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors blinded - all data reviewed by 1 physician without knowledge of patient assignment
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete outcome data. 10 withdrawals from intervention group, 7 from control group
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	High risk	Large differences in baseline characteristics - more examinations, longer labor, more preterm, longer surgery, longer duration of PROM in vaginal cleansing group

Barat 2016

Study characteristics

Methods	RCT
Participants	400 women randomized (200 in each group) Inclusion: term singleton pregnancy undergoing elective cesarean delivery Exclusion: allergy to povidone-iodine, antepartum hemorrhage, and premature rupture of membrane. Also those suffering from diabetes and those on antibiotics or under cortisone treatment were excluded from the study. Setting: single university setting in Babol, Iran
Interventions	Intervention: povidone-iodine 10% vaginal preparation Control: no vaginal preparation Intention-to-treat: not stated

Barat 2016 (Continued)

Outcomes	1. Postoperative fever 2. Postpartum endometritis 3. Early wound complications	
Notes	2013 to 2014 (months not specified) Funding source: not stated Authors' conflict of interest: no conflict of interest	
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number table
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Data collected by one of the "researchers, blinded to the allocation"
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition noted
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	No other sources of bias identified

Charoenviboonphan 2011

Study characteristics	
Methods	RCT
Participants	600 women randomized (299 analyzed in vaginal cleansing, 300 in control group) Inclusion: women undergoing cesarean, > 17 years old without previous history of allergy to iodine, fever before delivery, and vaginal bleeding Exclusion: unknown Setting: Nakhon Pathom Hospital, Thailand Calculated sample size to account for 20% incomplete data was 600 women
Interventions	Intervention: 1% povidone-iodine vaginal painting before cesarean

Charoenviboonphan 2011 (Continued)

Control: no vaginal painting

Intention-to-treat: unknown

Outcomes	1. Composite of febrile morbidity 2. Endometritis 3. Wound infection 4. Length of hospital stay
Notes	Only abstract and data tables in English. Unable to get translated from original. September 2010 to January 2011 Funding source: unknown Authors' declaration of interest: unknown (no translation of those areas of manuscript) From translated methods section

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "random allocation software was used." Comment: This is likely the equivalent to a computer generated list
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only 1 woman lost to follow up
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	No other sources of bias identified

Goymen 2017

Study characteristics

Methods	RCT
Participants	120 women randomized (41 in povidone-iodine group, 39 in benzalkonium group, 40 in control group)

Goymen 2017 (Continued)

Inclusion: pregnant women undergoing elective cesarean delivery, no active infection, completion of week 37 of gestation

Exclusion: preterm labor, PROM, emergency cesarean, body temperature above 38 °C, severe anemia, allergic reaction to agents

Setting: Sanko University, Turkey

Interventions	<p>Intervention group 1: povidone-iodine vaginal cleansing for 30 seconds</p> <p>Intervention group 2: benzalkonium chloride vaginal cleansing for 30 seconds</p> <p>Control: no vaginal cleansing</p> <p>Intention-to-treat analysis</p>
Outcomes	<ol style="list-style-type: none"> 1. Postoperative pain evaluation 2. Time to flatulence and defecation 3. Hb, WBC, Plt, CRP in 24 hours
Notes	<p>July 2014 to August 2014</p> <p>Funding source: not stated</p> <p>Author declarations of interest: no conflicts of interest</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Simple randomization method
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Operating physician applied cleansing agents
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	Complete outcome data, all women were in hospital, so none lost to follow-up
Selective reporting (reporting bias)	Low risk	No evidence of selective outcome reporting
Other bias	Low risk	None

Guzman 2002

Study characteristics

Guzman 2002 (Continued)

Methods	RCT
Participants	160 randomized (80 in each group) Inclusion: 160 women undergoing cesarean delivery Exclusion: medical contraindications to vaginal preparation - emergency cesarean, allergy, placenta previa Setting: University Medical Center in TX, USA
Interventions	Intervention: povidone-iodine vaginal wash (concentration not specified) Control: saline vaginal wash
Outcomes	1. Endometritis (temperature > 100.4 °F at least twice > 24 hours after surgery or of 101 °F any time after surgery, with abdominal/uterine tenderness) 2. Cellulitis (advancing erythema around the incision)
Notes	March 2000 to July 2001 Funding source: not stated Authors' declarations of interest: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not specified, simply states "randomized into one of two arms"
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Cleansing done by nurse while providers outside and thus providers were blinded to the intervention
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessors blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No incomplete outcome data
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Low risk	No evidence of other bias

Haas 2010
Study characteristics

Haas 2010 (Continued)

Methods	RCT
Participants	<p>300 women randomized (155 in vaginal preparation group, 145 in control group)</p> <p>Inclusion: all women undergoing cesarean delivery, age ≥ 18 years</p> <p>Exclusion: emergency cesarean delivery, allergy to iodine</p> <p>Setting: academic medical center in Indiana, USA</p>
Interventions	<p>Intervention: preoperative vaginal cleansing with 1% povidone-iodine scrubs. 3 sponge sticks soaked in 1% povidone-iodine in a prepackaged sterile pouch. The vaginal scrub encompassed the vaginal apex to the introitus with attention to the anterior, posterior, and lateral walls including all fornices</p> <p>Control: no preoperative vaginal cleansing</p> <p>Intention-to-treat analysis</p>
Outcomes	<ol style="list-style-type: none"> 1. Post-cesarean endometritis (uterine tenderness plus postoperative fever requiring antibiotics) 2. Postoperative fever ($> 38^{\circ}\text{C}$ > 24 hours after surgery) 3. Wound infection requiring antibiotics 4. Wound separation, seroma, hematoma, or need for debridement 5. Composite infectious morbidity outcome: either endometritis, fever, sepsis, hospital readmission, wound infection, or wound complication
Notes	<p>The trial was stopped early due to difficulty recruiting.</p> <p>September 2006 to January 2009</p> <p>Funding source: internally funded</p> <p>Author declarations of interest: no conflicts of interest</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number table, replacement randomization
Allocation concealment (selection bias)	Low risk	Sequentially-numbered opaque security envelopes
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Not specifically blinded, but after anesthesia care providers did not necessarily know group
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessor blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Appeared to be complete data on all participants
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting

Haas 2010 (Continued)

Other bias	Unclear risk	Trial stopped early at safety analysis due to difficulty recruiting and effect seen.
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Hassan 2016
Study characteristics

Methods	RCT
Participants	<p>150 women randomized (50 in each of the three groups)</p> <p>Inclusion: women aged 20 to 40 years, primipara, singleton undergoing an elective cesarean, healthy and free of any medical, infectious, obstetrical and gynecological diseases</p> <p>Exclusion: povidone-iodine sensitivity, emergency cesarean</p> <p>Setting: single center at Mansoura University Hospital, Egypt</p>
Interventions	<p>3 groups total:</p> <p>Intervention: vaginal washing with 10% povidone-iodine solution (n = 50)</p> <p>Control: 1 group had no washing (n = 50), 1 group had vaginal washing with 0.9% saline for 30 seconds (n = 50)</p> <p>Intention-to-treat: yes</p>
Outcomes	<ol style="list-style-type: none"> 1. Fever 2. Endometritis 3. Wound infection
Notes	<p>September 2015 to March 2016</p> <p>Funding source: not stated</p> <p>Authors' declaration of interest: no conflict of interests</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Used numbered patient' name list. Even - assigned to control (group 1); Odd - assigned to intervention group starting with group 2 then when complete went to the povidone-iodine group 3
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated, unlikely blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated

Hassan 2016 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Low risk	No apparent participant losses
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No evidence of other bias

Hodgetts 2019
Study characteristics

Methods	RCT
Participants	<p>328 women randomized (159 in vaginal cleansing group, 161 in control group)</p> <p>Inclusion: all women undergoing elective or emergency cesarean delivery, age ≥ 16 years</p> <p>Exclusion: known allergy to chlorhexidine, receiving intravenous antibiotics for GBS or other suspected infection, enrolled in another RCT aimed to decrease postop surgical site infections</p> <p>Setting: 4 UK maternity units</p>
Interventions	<p>Intervention: chlorhexidine 0.05% vaginal cleansing with a single swab/sponge mounted on a sponge holder soaked in 50 mL of the antiseptic</p> <p>Control: no vaginal wash</p> <p>Intention-to-treat analysis stated</p>
Outcomes	<ol style="list-style-type: none"> 1. Endometritis as defined by CDC criteria up to 30 days after delivery 2. Clinical diagnosis of endometritis 3. Maternal sepsis defined by NICE sepsis guideline 4. Length of hospital stay 5. Readmission to hospital 6. Antibiotic prescriptions 7. Need for critical care (level 2 or 3) 8. Patient-reported outcomes
Notes	<p>13 November 2017 to 3 March 2018</p> <p>Funding source: Birmingham Women's and Children's NHS Foundation Trust</p> <p>Authors' declaration of interest: no competing interests</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Secure automated telephone randomization system 24/7
Allocation concealment (selection bias)	Low risk	Central allocation not disclosed or recorded in the notes

Hodgetts 2019 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Attempts made to blind the women to the intervention, unable to blind the care providers
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All data collection from maternal notes were blinded, telephone follow-up by midwife blinded to the group
Incomplete outcome data (attrition bias) All outcomes	Low risk	Planned to recruit 250 women, but abstract says they 320 consented but that only 68% were followed up at the 14 and 30 day telephone interviews. However, medical note data were collected on > 96% of women so likely low risk for the main outcomes.
Selective reporting (reporting bias)	Low risk	No evidence of other bias
Other bias	Low risk	No evidence of other bias

Kiani 2018
Study characteristics

Methods	RCT
Participants	434 women randomized (217 in each group) Inclusion: women undergoing emergency cesarean in labor for more than 6 hours after admission with or without intact membranes Exclusion: gestational diabetes, severe anemia (Hgb < 7), placenta previa on ultrasound, obstructed labor or any preoperative febrile condition Setting: MCH unit 1 PIMS in Islamabad, Pakistan
Interventions	Intervention: vaginal cleansing with povidone-iodine Control: no vaginal cleansing Intention-to-treat: not specifically stated
Outcomes	1. Febrile morbidity 2. Endometritis 3. Wound infection
Notes	September 2014 to January 2015 Funding source: not stated Authors' conflict of interest: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated

Kiani 2018 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Allocation was not placed in medical record so unlikely outcomes assessor knew allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	No attrition bias
Selective reporting (reporting bias)	Low risk	Expected outcomes reported
Other bias	Low risk	No evidence of other bias.

Memon 2011

Study characteristics

Methods	RCT
Participants	200 women randomized (100 in each group) Inclusion: women > 18 years of age undergoing cesarean section Exclusion: allergy to iodine solution, bleeding placenta previa Setting: Hyderabad, Pakistan
Interventions	Intervention: 10% pyodine soaked pieces of gauze (3) used for vaginal scrub immediately before cesarean from vaginal apex to introitus with attention to vaginal walls Control: no vaginal cleansing Intention-to-treat: unclear
Outcomes	1. Postoperative febrile morbidity (oral temperature of 38 °C after 1st 24 hours of surgery) 2. Endometritis (postoperative fever with uterine tenderness and foul smelling lochia requiring broad spectrum antibiotic therapy) 3. Wound complications (infection at surgical site - seroma, hematoma, and disruption of abdominal incision - that required parenteral antibiotics and wound care) 4. Composite infectious morbidity - a sum of the 3 outcomes above
Notes	February 2010 to July 2010 Funding source: not stated Author declarations of interest: not stated

Risk of bias

Memon 2011 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Stated "randomly assigned" with no other details
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Stated that physician evaluating the data was unaware of any woman's participation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Appeared to be complete data on all participants
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Low risk	No evidence of other bias. Poorly defined composite infectious morbidity overall outcome appears to be the sum of endometritis, fever, and wound infection

Mohamed 2015
Study characteristics

Methods	Quasi-RCT
Participants	<p>200 women randomized (100 in each group)</p> <p>Inclusion: full term pregnant women, elective cesarean delivery, age 20 to 35 yo</p> <p>Exclusion: women at risk for developing postpartum infection as premature rupture of membranes, diabetes mellitus, anemia, history of post-cesarean section infection, obstructed labor, or pre-eclampsia, given history of being allergic to antiseptic cetrimide solutions</p> <p>Setting: single site in Mansoura University, Egypt</p>
Interventions	<p>Intervention: vaginal cleansing with cetrimide solution (diluted 0.5 cc cetrimide and 49.5cc of tap water) before cesarean. Authors note in their publication that cetrimide contains 0.3% chlorhexidine gluconate and 0.3% "Stremed"</p> <p>Control: no vaginal cleansing</p> <p>Intention-to-treat: not stated but no mention of women not getting the assigned intervention</p>
Outcomes	<ol style="list-style-type: none"> 1. Postpartum endometritis – presence of fever, purulent lochia and fundal tenderness, needed antibiotic therapy 2. Postoperative wound infection – erythema, purulent drainage from the site of operation and tenderness with or without fever, requiring antibiotic therapy

Mohamed 2015 (Continued)

3. Postoperative fever: > 38 °C

Notes	<p>May 2014 - August 2014</p> <p>Quasi-RCT due to odd and even number assignment</p> <p>Funding source: not stated</p> <p>Author declaration of interest: no conflicts of interest</p> <p>Included in chlorhexidine subgroup due to author note that the solution they used contained chlorhexidine</p>
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Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	By random assignment ...odd numbers were recruited as the intervention group and the even numbers are recruited as control group
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No evidence of other bias. Pilot study of 20 women for feasibility were later excluded from the study sample and not analyzed.

Mwangi 2013

Study characteristics

Methods	RCT
Participants	<p>397 women randomized (201 in vaginal cleansing group, 196 in control group)</p> <p>Inclusion: women undergoing elective and emergency cesarean delivery at gestational age of ≥ 28 weeks</p> <p>Exclusion: cord prolapse, placenta previa, antepartum hemorrhage of unknown cause, uterine rupture, chorioamnionitis, vulval/vaginal warts, low presenting part making it difficult to perform the intervention, fetal head descent 1/5, known hypersensitivity to povidone-iodine or related chemicals</p> <p>Setting: referral hospital in Nairobi, Kenya</p>

Mwangi 2013 (Continued)

Interventions	<p>Intervention: preoperative vaginal cleansing with povidone-iodine (2 lots of 4 x 4 cm gauze sponges soaked in solution)</p> <p>Control: no vaginal cleansing</p> <p>Intention-to-treat: yes</p>
Outcomes	<ol style="list-style-type: none"> 1. Post-cesarean endometritis 2. Fever 3. Surgical site infection 4. Side effects of povidone-iodine
Notes	<p>Abstract of results, dissertation thesis publication</p> <p>Study timeline for enrollment in appendix: July 2016 to October 2016</p> <p>Funding source: Kenyatta National Hospital</p> <p>Author declaration of interest: no conflicts of interest</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomization done by investigator with no clinical involvement using computer-generated random number sequences
Allocation concealment (selection bias)	Low risk	Cards in sealed opaque envelopes sequentially numbered
Blinding of participants and personnel (performance bias) All outcomes	Low risk	"single blind" that blinded study participants, did not mention blinding care providers
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Blinded research assistants that collected outcome data
Incomplete outcome data (attrition bias) All outcomes	Low risk	4 of 397 lost to follow-up (1%)
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	No evidence of other bias

Nandi 2015
Study characteristics

Methods	RCT
Participants	294 women randomized (147 in each group)
	Inclusion: all women undergoing cesarean section over 18 years of age

Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections (Review)

Nandi 2015 (Continued)

Exclusion: cesarean section with deeply engaged head, bleeding placenta previa, active genital herpes, or allergy to iodine

Setting: single institution, India

Interventions	<p>Intervention: 5% povidone-iodine vaginal scrub</p> <p>Control: no vaginal scrub</p> <p>Intention-to-treat: not stated</p>
Outcomes	<ol style="list-style-type: none"> 1. Endometritis 2. Abdominal wound infection 3. Readmission due to late infection
Notes	<p>January 2013 to July 2014</p> <p>Funding source: not stated</p> <p>Authors' declaration of interest: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random numbers
Allocation concealment (selection bias)	Unclear risk	Not stated
Blinding of participants and personnel (performance bias) All outcomes	High risk	Surgeon and patient not blinded
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	9 women in intervention group and 11 in the control group lost to follow-up (6.8%)
Selective reporting (reporting bias)	Low risk	All expected outcomes reported
Other bias	Low risk	No other sources of bias identified

Olmez 2013

Study characteristics

Methods	RCT
Participants	667 women randomized (332 in vaginal wash group, 335 in control group)

Olmez 2013 (Continued)

Inclusion: > 37 weeks' gestation, emergency or elective cesarean

Exclusion: placental abruption, previa, and fever

Setting: single state hospital in Turkey

Interventions	<p>Inervention: povidone-iodine solution 30 seconds vaginal wash</p> <p>Control: no vaginal wash</p> <p>Intention-to-treat: not stated</p>
Outcomes	<p>1. Persistent fever at least 38 °C or above</p> <p>2. Partial or total separation of incision or induration, warmth or wound tenderness</p>
Notes	<p>Translated using online document translator from Turkish</p> <p>September 2009 to July 2010</p> <p>Funding source: not stated</p> <p>Author declarations of interest: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Only states "randomly divided"
Allocation concealment (selection bias)	Low risk	Sealed envelopes used
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not stated
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not stated
Incomplete outcome data (attrition bias) All outcomes	Low risk	No withdrawals noted
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No evidence of other bias

Reid 2001
Study characteristics

Methods	RCT
Participants	498 women randomized (247 in vaginal preparation group, 251 in control group)

Reid 2001 (Continued)

Inclusion: women admitted and mentally competent to consent for a cesarean delivery

Exclusion: medical contraindications to the cleansing - highly emergent cesarean, bleeding placenta previa, allergy to iodine or shellfish, active genital herpes

Setting: University of North Carolina Women's Hospital, North Carolina, USA

Interventions	<p>Intervention: 10% povidone-iodine surgical scrub solution vaginally immediately before cesarean</p> <p>Control: no vaginal cleansing</p> <p>Intention-to-treat analysis</p>
Outcomes	<ol style="list-style-type: none"> 1. Fever (38 °C or greater after the day of surgery) 2. Febrile morbidity (postoperative fever on 2 or more calendar days, excluding the day of surgery) 3. Endometritis (postoperative fever, with a physician's note indicating uterine or abdominal pain or tenderness, preceding an order for antibiotics and a statement indicating that the antibiotics were for uterine or pelvic infection and laboratory studies did not indicate other source for the infection) 4. Wound separation (defined by chart note reporting separation of the operative incision requiring intervention) 5. Number of postoperative days with fever 6. Average duration of antibiotic administration 7. Length of hospitalization
Notes	<p>Chorioamnionitis participants excluded from analysis</p> <p>May 1996 to September 1998</p> <p>Funding source: not stated</p> <p>Author declarations of interest: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated, permuted block randomization schedule
Allocation concealment (selection bias)	Low risk	Opaque sealed and numbered envelopes taped to abdominal prep packs
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not specifically stated. Cleansing done by residents during routine prep. These may have been the same surgeons who did the surgery and postoperative care.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcomes assessor masked
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 withdrawals lacked necessary charting information
Selective reporting (reporting bias)	High risk	Large number of participants excluded after randomization who had chorioamnionitis (a known risk factor for postoperative infectious morbidity) because their inclusion "distorted the absolute rates of fever and infectious morbidity." That trial states that when the 68 participants with antepartum infection were included, the estimates of effect of vaginal preparation were not

Reid 2001 (Continued)

meaningfully different. Thus they planned to exclude those participants from reports of outcomes. As this represented 13.5% of the originally randomized sample, however, there is a risk that this introduced selective reporting bias into the trial.

Other bias	Low risk	No evidence of other bias
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Rouse 1997
Study characteristics

Methods	RCT
Participants	<p>1024 women enrolled in the overall trial (508 to vaginal chlorhexidine wash, 516 to placebo/control wash)</p> <p>Inclusion: women admitted for delivery > 24 weeks' gestation</p> <p>Exclusion: contraindications to digital examinations, placenta previa, active herpes, chorioamnionitis before randomization or allergy to chlorhexidine</p> <p>Setting: University of Alabama - Birmingham, USA</p>
Interventions	<p>Intervention: 200 mL irrigation of 0.2% chlorhexidine solution in labor or if a planned cesarean then immediately before surgery</p> <p>Control: 200 mL sterile water placebo solution</p> <p>Intention-to-treat analysis</p>
Outcomes	1. Endometritis
Notes	<p>February 1994 to January 1996. 1024 women enrolled and trial designed for vaginal irrigation during labor. Trial did report on 14 women who had elective cesarean before labor and thus just got the irrigation before the procedure, thus qualifying the study for inclusion in the analysis for those 14 women only.</p> <p>Funding source: Agency for Health Care Policy Research Contract DHHS No. 290-92-0055</p> <p>Authors' declarations of interest: not stated</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated list
Allocation concealment (selection bias)	Low risk	Sequentially-numbered study labels on identical bottles prepared by Investigational Drug Service at the site.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Active and placebo solutions were clinically indistinguishable.
Blinding of outcome assessment (detection bias)	Low risk	Data collection was done before the assignment was known

Rouse 1997 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	10 total withdrawals, allocation not determined
Selective reporting (reporting bias)	Low risk	All outcomes reported
Other bias	Low risk	No evidence of other bias

Starr 2005
Study characteristics

Methods	RCT
Participants	308 women randomized (142 in vaginal preparation group, 166 in control group) Inclusion: women to undergo non-emergency cesarean delivery Exclusion: placenta previa, chorioamnionitis Setting: Chicago Lying-In Hospital, Illinois, USA
Interventions	Intervention: pre-packaged povidone-iodine solution (EZ Prep 200, 5%) vaginal preparation for 30 seconds Control: no preoperative vaginal cleansing
Outcomes	1. Febrile morbidity (any postoperative temperature > 38 °C) 2. Endometritis (temperature elevation > 38 °C beyond the first postoperative day, in association with uterine tenderness and foul lochia, in the absence of evidence of other infection; given at the time of clinical evaluation) 3. Wound infection (clinical diagnosis evidenced by erythema or wound edge separation with purulent drainage; including wound dehiscence and necrotizing fasciitis and excluding skin separation without evidence of cellulitis)
Notes	November 1997 to March 2000 Funding source: University of Chicago Hospitals Resident Research Fund Authors' declarations of interest: not stated

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random digit table
Allocation concealment (selection bias)	Low risk	Sequentially-numbered, opaque, sealed envelopes
Blinding of participants and personnel (performance bias)	Low risk	Not stated for participants, but treating providers at the time of fever were unaware of participation status

Starr 2005 (Continued)

All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Chart reviewer unaware of group
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Ultimately 92 participants excluded from analysis post-randomization (400 originally randomized), reasons explained: 33 due to lost envelopes, 6 for violations of inclusion criteria, and 53 because their hospital charts could not be located. Of all the women excluded, 54 were in the vaginal cleansing group and 38 were in the control group. Only outcomes for women for whom all data were available were reported. The large number of women excluded also makes this trial subject to an unclear risk of bias, however as there are no outcome data for the excluded participants, the potential impact is unclear. Unclear if exclusions impacted data
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Low risk	No evidence of other bias

Yildirim 2012
Study characteristics

Methods	RCT
Participants	670 women randomized (335 in each group) Inclusion: women undergoing either a scheduled or emergency cesarean delivery Exclusion: umbilical cord prolapse, placenta previa, or known allergy to povidone-iodine Setting: Istanbul, Turkey
Interventions	Intervention: 30 second vaginal cleansing with 2 prepackaged povidone-iodine solution-soaked foam sponges preoperatively performed in conjunction with the abdominal preparation with 2 prepackaged foam sponges that contained the solution, rotated 360 degrees Control: no preoperative vaginal preparation
Outcomes	1. Postpartum endometritis (primary outcome) body temperature > 38.5 °C with concomitant foul-smelling discharge or abnormally tender uterus on bimanual examination) 2. Wound infection (partial or total separation of the incision, as well as the presence of purulent or serous wound discharge, with induration, warmth, and tenderness) 3. Fever (elevated temperature of 38 °C or higher for a minimum of 24 hours following surgery not associated with signs of infection)
Notes	January 2011 to August 2011 Funding source: not stated Authors' declarations of interest: no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
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Yildirim 2012 (Continued)

Random sequence generation (selection bias)	Low risk	Quote: "Computer generated randomization process."
Allocation concealment (selection bias)	Low risk	Sealed envelopes containing random numbers. Assignment based on those numbers
Blinding of participants and personnel (performance bias) All outcomes	High risk	The researchers in the study were not blinded and the assignment was written in the medical record.
Blinding of outcome assessment (detection bias) All outcomes	High risk	The researchers in the study were not blinded and the assignment was written in the medical record.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Only one participant withdrew.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	Low risk	No evidence of other bias

CDC: Centers for Disease Control and Prevention

CRP: C-reactive protein

GBS: Group B streptococcal infection

Hb: hemoglobin

NICE: National Institute for Health and Care Excellence

Plt: platelets

PROM: premature rupture of membranes

RCT: randomized controlled trial

WBC: white blood cell

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Abdallah 2015	Study retracted
Dudko 2018	Wrong comparison - compared vaginal cleansing with iodine versus chlorhexidine
Lakhi 2016	Wrong comparison - compared vaginal cleansing with iodine versus chlorhexidine
NCT03133312	Wrong comparison - compared vaginal cleansing with iodine versus chlorhexidine
NCT03925155	Wrong comparison - compared vaginal cleansing with iodine versus chlorhexidine
Pitt 2001	Not all women received surgical prophylactic antibiotics. 79% of 1 group and 85% of the other group received antibiotics and results were not stratified.
Sweeten 1997	Use of vaginal wash during labor
Tewfik 2015	Wrong comparison - compared vaginal cleansing with iodine versus chlorhexidine

Characteristics of studies awaiting classification *[ordered by study ID]*

IRCT201105146467N1

Methods	RCT
Participants	526 women getting cesarean at term, excluding chorioamnionitis
Interventions	Intervention: vaginal irrigation with povidone-iodine Control: no vaginal preparation
Outcomes	Primary: fever (body temperature)
Notes	Iranian Clinical Trials Registry record says complete. Emailed study contact 7 December 2017: no response as of September 2019

IRCT2016061425292N6

Methods	RCT
Participants	400 women getting elective cesarean delivery at term, Iran
Interventions	Intervention: vaginal washing with 2 gauze with 10% povidone-iodine for 30 seconds Control: no vaginal preparation
Outcomes	Primary: fever, uterine tenderness, tachycardia, foul-smelling lochia
Notes	Iranian Clinical Trials Registry record says complete. Emailed study contact 7 December 2017: no response

NCT03442218

Methods	RCT
Participants	203
Interventions	Intervention: vaginal wash with chlorhexadine solution prior to cesarean Control: vaginal wash with saline solution
Outcomes	Primary: endometritis
Notes	ClinicalTrials.gov record says completed. Last update December 9, 2019. Email sent to author in September 2019, no reply

NCT03640507

Methods	RCT
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NCT03640507 (Continued)

Participants	30
Interventions	Intervention: vaginal preparation with chlorhexadine-alcohol Intervention 2: vaginal preparation with povidine-iodine Control: vaginal preparation with sterile saline
Outcomes	Change in bacterial colony counts
Notes	ClinicalTrials.gov record states completed (record last updated July 24, 2019) and notes actual study completion date as June 14, 2019. emailed author in September 2019, no reply.

RCT: randomized controlled trial

Characteristics of ongoing studies [ordered by study ID]

NCT02495753

Study name	Vaginal cleansing before cesarean delivery to reduce infection: a randomized trial
Methods	RCT
Participants	608 women undergoing cesarean
Interventions	Intervention: vaginal cleansing with 2 sponge sticks soaked in 1% povidone-iodine Control: no cleansing All will receive standard abdominal cleansing using chlorhexidine or Betadine per provider preference
Outcomes	Primary: composite postoperative infectious morbidity up to 30 days - fever, endometritis, infection or abscess, wound complications or infection
Starting date	August 2015
Contact information	Lorene Temming, Washington University, St. Louis
Notes	Recruitment status is recruiting. Anticipated completion is December 2020. Last update posted July 16, 2019. NCT02495753

NCT02693483

Study name	Preoperative vaginal cleansing with povidone-iodine and the risk of post-cesarean endometritis
Methods	RCT
Participants	306 women undergoing cesarean
Interventions	Intervention: vaginal cleansing with 3 gauze pieces soaked in 10% povidone-iodine from vaginal apex to introitus Control: no vaginal cleansing

NCT02693483 (Continued)

Outcomes	Primary outcome: post-cesarean endometritis diagnosed by fever 38.4 °C or greater in first 48 hours with either uterine tenderness, foul smelling lochia or positive C-reactive protein
Starting date	April 2015
Contact information	Amer Ahmed Mahmoud Riad, Ain Shams Maternity Hospital
Notes	Listed as recruiting as of February 2016

NCT03093194

Study name	Vaginal antimicrobial preparation before cesarean section for endometritis prevention
Methods	RCT
Participants	1040 women getting a cesarean delivery
Interventions	Intervention: vaginal preparation with septal soap before cesarean Control: no vaginal preparation
Outcomes	Primary: endometritis
Starting date	April 2017, anticipated completion April 2020
Contact information	Hila Ben-Asher, Rambam Health Care
Notes	Not yet recruiting, verified in ClinicalTrials.gov by PI April 2017. Estimated completion date listed as April 30, 2020

NCT03397615

Study name	Effect of Vaginal Douching With Betadine Before CS for Prevention of Post Operative Infections
Methods	RCT
Participants	1200
Interventions	Intervention: vaginal preparation with betadine douches before cesarean Control: no vaginal preparation
Outcomes	Primary: postpartum endometritis
Starting date	January 3, 2019, anticipated completion December 2019
Contact information	Ahmed Maged, MD, Cairo University
Notes	ClinicalTrials.gov record says recruiting (record last updated July 26, 2019) but estimated completion date is December 2019. Email sent to author (September 13, 2019), no reply.

NCT03423147

Study name	Preoperative application of chlorhexidine to reduce infection with cesarean section after labor (PRACTICAL)
Methods	RCT
Participants	800 women getting a cesarean delivery in labor
Interventions	Intervention: 4% chlorhexidine gluconate vaginal scrub prior to cesarean Control: no vaginal cleansing
Outcomes	Primary: rate of surgical site infection up to 6 weeks postpartum: composite of wound infection and postpartum endometritis, defined as fever of 100.4 °F or more 24 hours after delivery associated with uterine tenderness and persistent foul-smelling lochia requiring broad spectrum intravenous antibiotic administration
Starting date	March 2018, anticipated completion March 2020
Contact information	Angela Bianco at Icahn School of Medicine at Mount Sinai, New York
Notes	Status is 'recruiting' (last update posted March 2, 2020). Estimated completion date is October 2021

PACTR201709002597110

Study name	Effectiveness of preoperative vaginal cleansing with povidone-iodine in post-caesarean infectious morbidity; a randomized controlled trial
Methods	RCT
Participants	180
Interventions	Intervention: vaginal cleansing with 50 ml povidone- iodine for 30 seconds Control: no vaginal preparation
Outcomes	Post-caesarean endometritis
Starting date	December 1, 2017 anticipated
Contact information	Benjamin Ozumba, University of Nigeria
Notes	Pan African Clinical Trials Registry record states not yet recruiting Last updated July 5, 2018 Email sent to author (September 2019), no reply

RCT: randomized controlled trial

DATA AND ANALYSES

Comparison 1. Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Post-cesarean endometritis	20	6918	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.29, 0.58]
1.1.1 Iodine-based solution	16	6197	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.28, 0.60]
1.1.2 Chlorhexidine-based solution	4	721	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.16, 0.89]
1.2 Postoperative fever	16	6163	Risk Ratio (M-H, Random, 95% CI)	0.64 [0.50, 0.82]
1.2.1 Iodine-based solution	14	5763	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.50, 0.87]
1.2.2 Chlorhexidine-based solution	2	400	Risk Ratio (M-H, Random, 95% CI)	0.44 [0.23, 0.83]
1.3 Postoperative wound infection	18	6385	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.50, 0.77]
1.3.1 Iodine-based solution	15	5767	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.50, 0.81]
1.3.2 Chlorhexidine-based solution	3	618	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.31, 0.90]
1.4 Composite wound complication	2	729	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.37, 1.07]
1.5 Composite wound complication or endometritis	2	499	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.26, 0.82]

Analysis 1.1. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 1: Post-cesarean endometritis

Analysis 1.2. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 2: Postoperative fever

Analysis 1.3. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 3: Postoperative wound infection

Analysis 1.4. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 4: Composite wound complication

Analysis 1.5. Comparison 1: Vaginal preparation with antiseptic solution before cesarean section versus control (no preparation or saline preparation), Outcome 5: Composite wound complication or endometritis

Comparison 2. Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Post-cesarean endometritis	7	2677	Risk Ratio (M-H, Random, 95% CI)	0.47 [0.27, 0.81]
2.1.1 Women in labor	6	1634	Risk Ratio (M-H, Random, 95% CI)	0.35 [0.19, 0.67]
2.1.2 Women not in labor	5	1043	Risk Ratio (M-H, Random, 95% CI)	0.86 [0.33, 2.21]
2.2 Postoperative fever	5	2233	Risk Ratio (M-H, Fixed, 95% CI)	0.72 [0.55, 0.95]
2.2.1 Women in labor	5	1415	Risk Ratio (M-H, Fixed, 95% CI)	0.61 [0.42, 0.87]
2.2.2 Women not in labor	3	818	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.60, 1.43]
2.3 Postoperative wound infection	5	2233	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.37, 0.88]
2.3.1 Women in labor	5	1415	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.30, 0.90]
2.3.2 Women not in labor	3	818	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.35, 1.31]
2.4 Composite wound complication	2	729	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.38, 1.09]
2.4.1 Women in labor	2	314	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.36, 1.61]
2.4.2 Women not in labor	2	415	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.25, 1.16]
2.5 Composite wound complication or endometritis	2	499	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.27, 0.85]
2.5.1 Women in labor	2	164	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.13, 0.87]
2.5.2 Women not in labor	2	335	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.29, 1.26]

Analysis 2.1. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 1: Post-cesarean endometritis

Analysis 2.2. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 2: Postoperative fever

Analysis 2.3. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 3: Postoperative wound infection

Analysis 2.4. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 4: Composite wound complication

Analysis 2.5. Comparison 2: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 5: Composite wound complication or endometritis

Comparison 3. Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Post-cesarean endometritis	9	2634	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.30, 0.55]
3.1.1 Women with ruptured membranes	5	552	Risk Ratio (M-H, Fixed, 95% CI)	0.23 [0.12, 0.45]
3.1.2 Women with intact membranes	8	2082	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.34, 0.68]
3.2 Postoperative fever	8	2474	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.38, 0.78]
3.2.1 Women with ruptured membranes	4	480	Risk Ratio (M-H, Random, 95% CI)	0.42 [0.22, 0.80]
3.2.2 Women with intact membranes	7	1994	Risk Ratio (M-H, Random, 95% CI)	0.70 [0.49, 0.99]
3.3 Postoperative wound infection	9	2634	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.47, 0.91]
3.3.1 Women with ruptured membranes	5	552	Risk Ratio (M-H, Random, 95% CI)	0.54 [0.19, 1.50]
3.3.2 Women with intact membranes	8	2082	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.50, 1.07]
3.4 Composite wound complication	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.28, 1.44]
3.4.1 Women with ruptured membranes	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.15, 1.89]
3.4.2 Women with intact membranes	1	224	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.25, 2.10]
3.5 Composite wound complication or endometritis	2	500	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.27, 0.85]
3.5.1 Women with ruptured membranes	2	134	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.13, 1.13]
3.5.2 Women with intact membranes	2	366	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.26, 1.04]

Analysis 3.1. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 1: Post-cesarean endometritis

0.01 0.1 1 10 100
Favors vaginal Favors control

Analysis 3.2. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 2: Postoperative fever

Analysis 3.3. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 3: Postoperative wound infection

Analysis 3.4. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 4: Composite wound complication

Analysis 3.5. Comparison 3: Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 5: Composite wound complication or endometritis

APPENDICES

Appendix 1. Search terms used in ClinicalTrials.gov and ICTRP

Each line was run separately

ICTRP

cesarean AND vaginal AND cleanse
caesarean AND vaginal AND cleanse
cesarean AND vaginal AND cleansing
caesarean AND vaginal AND cleansing
cesarean AND vaginal AND preparation
caesarean AND vaginal AND preparation
cesarean AND vaginal AND antiseptic(s)
caesarean AND vaginal AND antiseptic(s)
cesarean AND vaginal AND chlorhexidine
caesarean AND vaginal AND chlorhexidine
cesarean AND vaginal AND iodine
caesarean AND vaginal AND iodine
cesarean AND vaginal AND antimicrobial
cesarean AND vaginal AND antimicrobial

ClinicalTrials.gov

vaginal | Interventional Studies | cesarean | preparation
vaginal | Interventional Studies | cesarean | cleanse
vaginal | Interventional Studies | cesarean | chlorhexidine
vaginal | Interventional Studies | cesarean | iodine
vaginal | Interventional Studies | cesarean | antiseptic

WHAT'S NEW

Date	Event	Description
7 July 2019	New citation required but conclusions have not changed	We have incorporated data from new included trials for this update. The primary outcome conclusion is more supported now and more of the subgroup comparisons demonstrate improved outcomes with vaginal cleansing for multiple outcomes. In total, these additions strengthen the overall conclusions supporting the benefit of vaginal cleansing.
7 July 2019	New search has been performed	We updated the search and included 10 new trials. The conclusions changed for subgroups and were strengthened for the primary outcome.

HISTORY

Protocol first published: Issue 3, 2009

Review first published: Issue 3, 2010

Date	Event	Description
10 July 2017	New search has been performed	Search updated and six new studies added.
10 December 2014	New search has been performed	Search updated. Two new reports of trials identified (Memon 2011 ; Yildirim 2012).
10 December 2014	New citation required but conclusions have not changed	Review updated. Two new trials included. Conclusions strengthened and one additional subgroup of women in labor now shows a significant reduction in endometritis.
21 July 2014	New search has been performed	Search updated. No new trial reports identified.
21 July 2014	New citation required but conclusions have not changed	Review updated.
14 September 2012	New search has been performed	Search updated. One new trial included (Asghania 2011) and the published report of Haas 2010 added.
14 September 2012	New citation required but conclusions have not changed	Review updated.

CONTRIBUTIONS OF AUTHORS

David Haas is the guarantor for the review. Drs. Haas, Morgan, and Contreras developed the original protocol, data extraction sheet, and preparation of results and final original report and previous updates. Dr Kimball (nee Enders) was added for the 2018 update and all four authors contributed to study selection, data extraction, and preparation of results and final report for this update.

DECLARATIONS OF INTEREST

David Haas is the Principal Investigator for a randomized trial included in this review ([Haas 2010](#)). He holds grants from the US National Institute of Health for work unrelated to this review. He has no financial conflicts of interest to disclose.

Sarah Morgan is also an investigator in the [Haas 2010](#) trial. She has no financial conflicts of interest to disclose.

Trial authors for [Haas 2010](#) were not involved in assessing trial quality or extracting data from the [Haas 2010](#) study. This task was carried out by Karenrose Contreras and a third party (Dr Jon Hathaway, MD, PhD).

Karenrose Contreras has no financial conflicts of interest to disclose.

Savannah Enders Kimball has no financial conflicts of interest to disclose.

SOURCES OF SUPPORT

Internal sources

- Indiana University School of Medicine, Indianapolis, USA

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We were unable to perform three of the planned subgroup analyses as they were not reported in the trials.

In the 2018 update, we added an additional search of [ClinicalTrials.gov](https://clinicaltrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform ([ICTRP](https://www.trials.gov)) for unpublished, planned and ongoing trial reports.

In the 2018 update, we edited the list of outcomes for use in GRADE. We edited, postpartum endometritis, postoperative wound infection and postoperative fever to include definitions as per the list of outcomes in the main methods/types of outcomes. We also added 'Composite wound complications or endometritis' to our list of outcomes for use in GRADE.

INDEX TERMS

Medical Subject Headings (MeSH)

Administration, Intravaginal; Anti-Infective Agents, Local [*administration & dosage]; Benzalkonium Compounds [administration & dosage]; Cesarean Section [*adverse effects]; Chlorhexidine [administration & dosage]; Disinfection [*methods]; Endometritis [*prevention & control]; Fever [prevention & control]; Povidone-Iodine [administration & dosage]; Preoperative Care [*methods]; Randomized Controlled Trials as Topic; Surgical Wound Infection [*prevention & control]

MeSH check words

Female; Humans; Pregnancy