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

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[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, and twice in 2014.

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 Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (10 July 2017), and reference lists of retrieved studies.

Selection criteria

We included randomized trials and one quasi-randomized trial 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-randomized trials were eligible for inclusion but none were identified. 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.

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 11 trials reporting results for 3403 women evaluating the effects of vaginal cleansing (eight using povidone-iodine, two chlorhexidine, one benzalkonium chloride) on post-cesarean infectious morbidity. Additionally, some trials used vaginal preparations using sponge sticks, douches, or soaked gauze wipes. The control groups were typically no vaginal preparation (eight trials) or the use of a saline vaginal preparation (three trials). The risk of bias in the studies reduced our confidence in the results for endometritis outcomes.

Vaginal preparation with antiseptic solution immediately before cesarean delivery probably reduces the incidence of post-cesarean **endometritis** from 8.7% in control groups to 3.8% in vaginal cleansing groups (average risk ratio (RR) 0.36, 95% confidence interval (CI) 0.20 to 0.63, 10 trials, 3283 women, moderate quality of evidence). Subgroup analysis could not rule out larger reductions in endometritis with antiseptics in women who were in labor or in women whose membranes had ruptured when antiseptics were used. Risks of **postoperative fever** and **postoperative wound infection** may be slightly lowered by antiseptic preparation, but the confidence intervals around the effects for both outcomes are consistent with a large reduction in risk and no difference between groups (fever: RR 0.87 (0.72 to 1.05; wound infection: RR 0.74 (95% CI 0.49 to 1.11), both moderate-quality evidence). Two trials reported 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, two trials, 499 women, moderate-quality evidence). No **adverse effects** were reported with either the povidone-iodine or chlorhexidine vaginal cleansing.

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. Subgroup analysis could not rule out larger reductions in endometritis with antiseptics in women who were in labor or in women whose membranes had ruptured when antiseptics were used.

The quality of the evidence using GRADE was moderate for all reported outcomes. We downgraded the outcome of post-cesarean endometritis and composite of wound complications or endometritis for risk of bias and postoperative fever and postoperative wound infections for wide CIs.

As a simple, generally inexpensive intervention, providers may consider implementing preoperative vaginal cleansing with povidone-iodine or chlorhexidine before performing cesarean deliveries.

PLAIN LANGUAGE SUMMARY

Vaginal cleansing with antiseptic solution before cesarean delivery to reduce post-cesarean infections

What is the issue?

We set out to determine if cleansing the vagina with an antiseptic solution before a cesarean delivery decreases the risk of maternal infections, including infection of the lining of the uterus and wound complications. Cleansing the vagina before the cesarean delivery can reduce the number of bacteria in the vagina. Bacteria are naturally present in the vagina and cervix and can move up to infect the uterus during the procedure. Antibiotics are routinely given before or during the surgery to reduce the risk of infections, but some women still suffer from these complications. Some antibiotics do not consistently eradicate all bacteria and antibiotic-resistant bacteria may also be present.

Why is this important?

Cesarean deliveries are common, with almost one in three babies born by cesarean in some countries such as the USA. Between one in four and one in 10 women having a cesarean delivery develop an infection of the uterus (endometritis) or a problem with their skin incision, respectively. The risk of infection is greater if a woman's waters have already broken or she is in labor before the cesarean section. These complications slow a woman's recovery from the surgery and may affect her ability to take care of her baby. This is a Cochrane Review first published in 2010 and then subsequently updated in 2012 and twice in 2014.

What evidence did we find?

We searched for evidence on July 10, 2017. In this update, we have included 11 randomized controlled studies, involving a total of 3403 women undergoing cesarean section. Eight studies used povidone-iodine for vaginal cleansing, two chlorhexidine, and one benzalkonium chloride. The quality of the evidence using GRADE was moderate for the reported outcomes.

We found that cleansing the vagina with an antiseptic solution compared to not cleansing or using saline or water immediately before the cesarean delivery more than halved the risk of post-cesarean infection of the uterus from a rate of 8.7% down to a rate of 3.8% (10 studies, 3283 women). While we should be cautious about results found for women in certain groups, we did also find that the benefit was also seen if the woman's waters had already broken (from 17.9% to 4.3% with vaginal cleansing; three studies, 272 women) and if women were already in labor at the time of the cesarean delivery (from a rate of 11.1% down to 4.7% with vaginal cleansing; four studies, 960 women women). The benefits were similar using both povidone-iodine and chlorhexidine.

The risk of experiencing a fever (eight studies, 3109 women) or wound infection (eight studies, 2839 women) after the cesarean delivery may be slightly lowered by antiseptic preparation, but the results were not entirely clear. Only the composite outcome of wound complication or endometritis was reduced overall for women receiving preoperative vaginal cleansing (two studies, 499 women).

None of the reports mentioned that any women had adverse events such as an allergic reaction to the cleansing solution or irritation.

What does this mean?

Cleansing the vagina immediately before a cesarean delivery with either an iodine-based or chlorhexidine-based solution probably reduces the risk of infection of the uterus after a cesarean section. This benefit may be greater for women who have their cesarean delivery after their membranes have already ruptured or they are already in labor. This is a generally simple, well-tolerated way to lower the chances of developing an infection after having a baby by cesarean.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

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

Patient or population: pregnant women who were about to receive a cesarean delivery. This included women receiving elective, laboring, or urgent cesareans
Setting: multiple countries (United States-5, Pakistan-2, Turkey-2, Iran-1, Saudi Arabia-1) mostly in academic centers or large hospitals
Intervention: vaginal preparation - 9 trials using iodine solution and 2 using chlorhexidine solution
Comparison: control - 9 trials with no vaginal cleansing and 2 with a saline vaginal cleansing

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evi- dence (GRADE)	Comments
	Risk with control	Risk with vaginal preparation				
Post-cesarean endometritis	Study population		Average RR 0.36 (0.20 to 0.63)	3283 (10 RCTs)	⊕⊕⊕◯ MODERATE [1]	
	86 per 1000	31 per 1000 (17 to 54)				
Postoperative fever	Study population		RR 0.87 (0.72 to 1.05)	3109 (8 RCTs)	⊕⊕⊕◯ MODERATE [2]	
	125 per 1000	109 per 1000 (90 to 131)				
Postoperative wound infection	Study population		RR 0.74 (0.49 to 1.11)	2839 (8 RCTs)	⊕⊕⊕◯ MODERATE [2]	
	36 per 1000	27 per 1000 (18 to 41)				
Composite wound com- plication or endometri- tis	Study population		RR 0.46 (0.26 to 0.82)	499 (2 RCTs)	⊕⊕⊕◯ MODERATE [1]	
	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; **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

[1] Over 40% of included studies had some design limitations.
[2] Wide confidence intervals in included studies.

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 can lead to significant delay in a 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*), 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

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; Zuarez-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 1984). Vaginal preparation has not typically been included in evidence-based bundles to reduce post-cesarean infectious morbidity (Carter 2017; Hsu 2016; NICE 2012). 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.

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.

Why it is important to do this review

Cesarean delivery is increasing, particularly in the developed world. Postoperative infectious morbidity after cesarean delivery impacts the woman's return to normal function and potentially her bonding with the newborn. It can also cause major medical problems and sequelae. Finding an easy, inexpensive method to reduce this risk could have major public health impact in both developed and developing countries.

OBJECTIVES

Our objective was 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 studies and one quasi-randomized study. Cluster-randomized trials were eligible for inclusion, but none were identified.

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.

Types of outcome measures

Primary outcomes

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 degrees C or 100.4 degrees 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 (allergy, irritation). As these solutions are applied gently and not absorbed, there should be no adverse fetal/neonatal effects. We did not anticipate or find mention of adverse neonatal effects 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

We searched Cochrane Pregnancy and Childbirth's Trials Register by contacting their Information Specialist (10 July 2017).

The Register is a database containing over 23,000 reports of controlled trials in the field of pregnancy and childbirth. For full search methods used to populate the 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 to the editorial information about the Cochrane Pregnancy and Childbirth in the Cochrane Library and select the '***Specialized Register***' section from the options on the left side of the screen.

Briefly, the 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 (10 July 2017) using the terms given in Appendix 1

Searching other resources

We searched the reference lists of retrieved studies.

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 2014b.

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

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

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 (RevMan 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:

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

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

- low, high or unclear risk of bias for participants;
- 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:

- 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 re-include missing data in the analyses that we undertook.

We assessed methods as being at:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- 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);
- 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:

- 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);
- 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);
- 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 judgements 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).

Assessment of the quality of the evidence using the GRADE approach

For this update the quality of the evidence was assessed using the GRADE approach as outlined in the GRADE handbook in order to assess the quality of the body of evidence relating to the following outcomes for the main comparisons.

1. Post-cesarean endometritis: defined as a clinical diagnosis, usually involving fever, uterine fundal tenderness, or purulent lochia requiring antibiotic therapy.
2. Postoperative wound infection: defined as erythema, tenderness, purulent drainage from the incision site, with or without fever, requiring antibiotic therapy.
3. Postoperative fever: defined as greater than 38 degrees C or 100.4 degrees F.
4. Composite wound complications or endometritis.

We used the GRADEpro Guideline Development Tool to import data from Review Manager 5.3 (RevMan 2014) in order to create a 'Summary of findings' table. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' 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.

Measures of treatment effect

Dichotomous data

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

Continuous data

For continuous data, we planned to use the mean difference (MD) if outcomes were measured in the same way between trials. We planned 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

No cluster-randomized trials were identified. If, in future updates some are identified, we will include cluster-randomized trials 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 included one quasi-randomized trial but noted their increased risk of bias in this design.

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 analysis.

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 Tau^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if the I^2 was greater than 30% and either a Tau^2 was greater than zero, or there was a low P value (less than 0.10) in the Chi^2 test for heterogeneity.

Assessment of reporting biases

There are 11 included studies. Since there are 10 or more studies in the meta-analysis, we would have investigated reporting biases (such as publication bias) using funnel plots, however only nine trials contributed estimates and thus we did not perform formal assessment of reporting bias. In future updates, if 10 or more trials contribute estimates for the primary outcome, we will assess for reporting bias by inspecting the funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, exploratory analyses will be undertaken to investigate reporting bias in the results.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2014). We used 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 substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated 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, the results are presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau^2 and I^2.

Subgroup analysis and investigation of heterogeneity

In future updates, if we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

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.
3. Women with chorioamnionitis preoperatively versus women without chorioamnionitis.
4. Women undergoing emergency cesarean versus those undergoing unscheduled cesarean versus those undergoing scheduled cesarean.
5. Women with internal fetal or uterine monitors in place versus those with only external monitors in place before the cesarean.

All reported outcomes in the primary analysis were used in the subgroup analyses.

We assessed subgroup differences by interaction tests available within RevMan (RevMan 2014). We reported the results of subgroup analyses quoting the Chi^2 statistic and P value, and the interaction test I^2 value.

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, with poor quality studies being excluded from the analyses, in order to assess whether this makes any difference to the overall result.

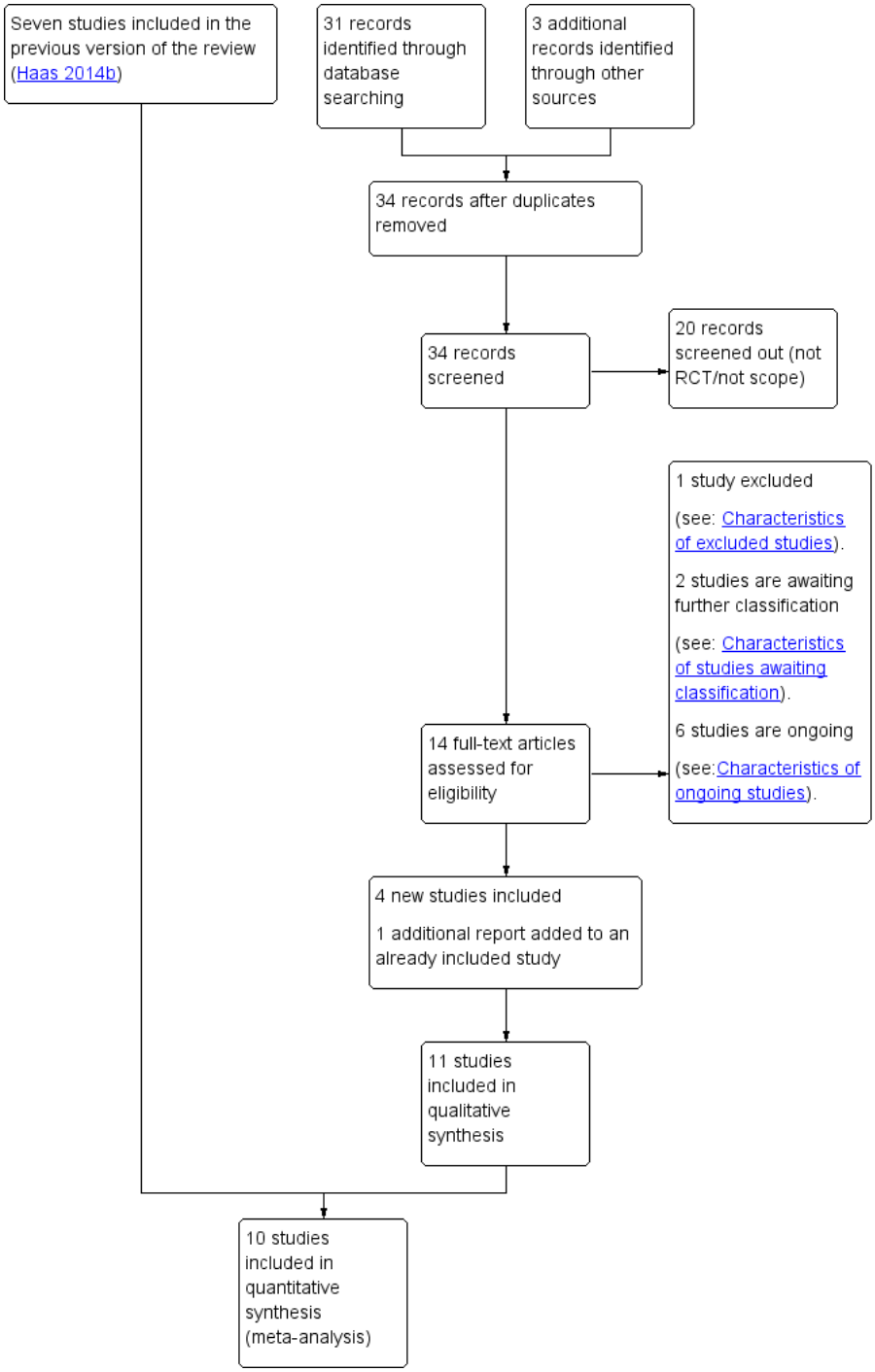
RESULTS

Description of studies

Results of the search

See: Figure 1.

Figure 1. Study flow diagram.



An updated search in July 2017 retrieved 14 new trial reports to assess. After assessing these new trial reports we identified four new included studies (plus one report of a study that was already included), one excluded studies (two reports), and four new ongoing studies. Two studies are awaiting classification pending further information.

This updated review is comprised of 11 included studies (Characteristics of included studies), two excluded studies (Characteristics of excluded studies), six ongoing studies (Characteristics of ongoing studies) and two studies awaiting classification (see Characteristics of studies awaiting classification).

Included studies

Methods

In this updated review we include 11 studies, reporting results for 3403 women. All trials were randomized controlled trials.

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), two in Packistan (Asad 2017; Memon 2011), two in Turkey (Goymen 2017; Yildirim 2012), one in Iran (Asghania 2011), and one in Saudi Arabia (Ahmed 2017).

Participants

Two trials only included women for scheduled or elective cesareans (Ahmed 2017; Goymen 2017). One trial only included women who were in labor (Asad 2017), and the remainder of the studies included women both in labor and for scheduled cesareans (Asghania 2011; Guzman 2002; Haas 2010; Memon 2011; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012). Two trials specifically excluded women with ruptured membranes (Ahmed 2017; Goymen 2017). Four trials excluded women with chorioamnionitis (Asad 2017; Reid 2001; Starr 2005; Goymen 2017). Two trials excluded women undergoing emergency cesarean deliveries (Guzman 2002; Reid 2001).

Interventions and comparisons

One study compared chlorhexidine cleansing versus no cleansing (Ahmed 2017). One study compared chlorhexidine solution versus a saline solution (Rouse 1997). 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. The other seven trials compared the vaginal cleansing with no vaginal cleansing (Asad 2017; Asghania 2011; Haas 2010; Memon 2011; 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 pre-specified 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 eight studies reported on postoperative fever and 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

Three trials reported sources of funding. Haas 2010 and Starr 2005 reported internal institutional funding. Rouse 1997 received federal funding from the United States Department of Health and Human Services. All other reports did not list any sources of funding.

Declarations of interest

Four trials (Ahmed 2017; Goymen 2017; Haas 2010; Yildirim 2012) specified no conflicts of interest from the authors. The remainder of the trials did not specify any declarations of interest.

Excluded studies

One trial was excluded as the journal retracted the publication (Abdallah 2015).

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.

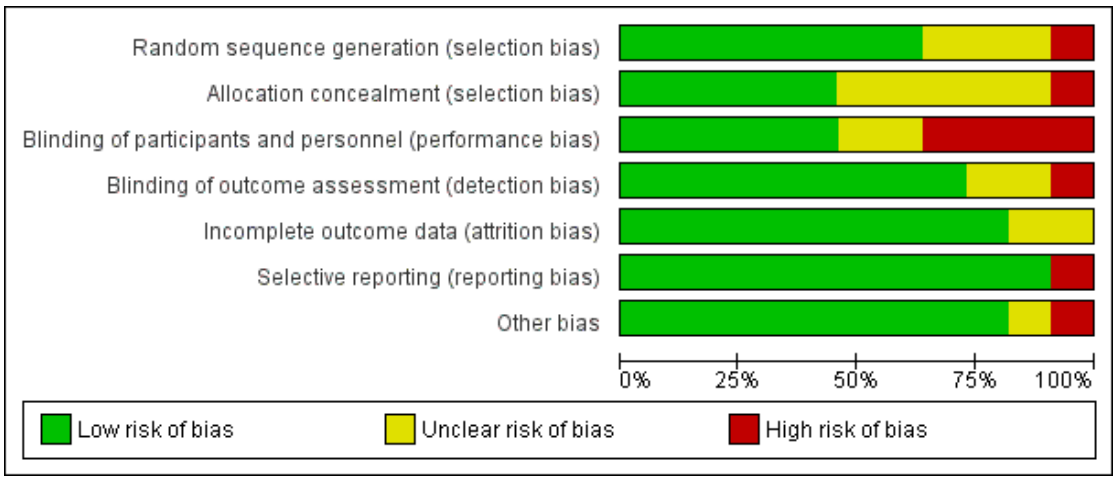
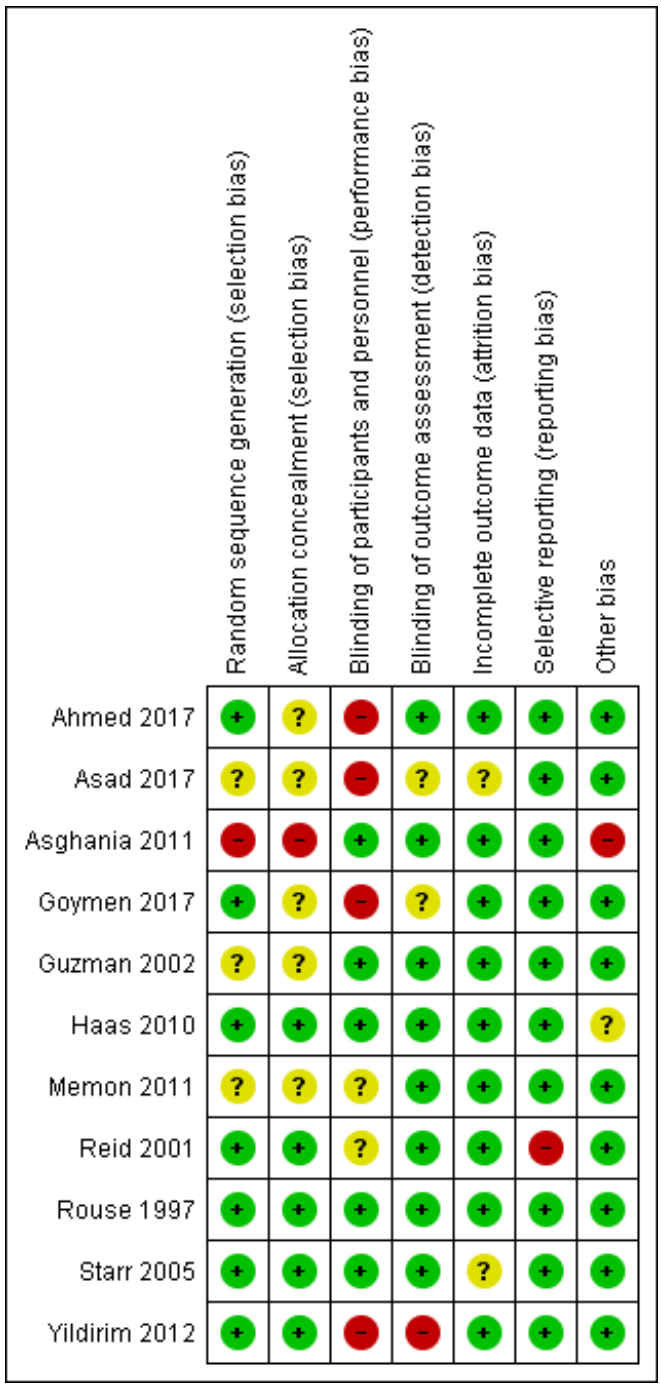


Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Overall, the quality of these 11 studies was generally moderate as defined by Higgins 2011.

Allocation

Random sequence generation

The Asad 2017, Guzman 2002 and Memon 2011 studies were unclear about the randomization sequence generation and allocation concealment. One study (Asghania 2011) was a quasi-randomized trial with alternate allocation, earning a high risk of bias rating. The remaining seven trials (Ahmed 2017; Goymen 2017; Haas 2010; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012) were at a low risk of bias due to random sequence generation.

Allocation concealment

Five of the reports were unclear about allocation concealment (Ahmed 2017; Asad 2017; Goymen 2017; Guzman 2002; Memon 2011), mainly due to no mention of that in the publication. One trial (Asghania 2011) had a high risk of bias due to alternating sequence. The other five trials had low risk of allocation bias (Haas 2010; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012).

Blinding

Blinding of participants and personnel (performance bias)

Four trials had a high risk of bias regarding blinding of the participants and care providers (Ahmed 2017; Asad 2017; Goymen 2017; 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. Two trials (Memon 2011; Reid 2001) were unclear risk of bias because it was not stated.
Five 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 prep) (Asghania 2011; Guzman 2002; Haas 2010; Rouse 1997; Starr 2005).

Blinding of outcome assessment (detection bias)

Seven trials blinded outcomes assessors (Ahmed 2017; Asghania 2011; Guzman 2002; Haas 2010; Memon 2011; Reid 2001; Rouse 1997; Starr 2005). One trial (Yildirim 2012) stated that the researchers were not blinded and that the assignment was written in the medical records so outcomes assessors were unlikely to be blinded either. Two studies did not state blinding of outcomes assessors (Asad 2017; Goymen 2017).

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). One other trial had a potential 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 is no outcome data for the excluded participants, the potential impact is unclear (Starr 2005). Nine studies had a low risk of attrition bias (Ahmed 2017; Asghania 2011; Goymen 2017; Guzman 2002; Haas 2010; Memon 2011; Reid 2001; Rouse 1997; Yildirim 2012).

Selective reporting

One trial (Reid 2001) 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". 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 (Reid 2001). The other 10 trials were at low risk of reporting bias (Ahmed 2017; Asad 2017; Asghania 2011; Goymen 2017; Guzman 2002; Haas 2010; Memon 2011; Rouse 1997; Starr 2005; Yildirim 2012).

Other potential sources of bias

One trial (Haas 2010). was stopped early at a planned safety analysis due to difficulty recruiting participants; we assessed this trial as 'unclear' risk of reporting 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. This trial was assessed as having a high risk of potential bias. The other nine trials were at low risk of other sources of bias (Ahmed 2017; Asad 2017; Goymen 2017; Guzman 2002; Memon 2011; Reid 2001; Rouse 1997; Starr 2005; Yildirim 2012).

As only nine trials contributed estimates toward the primary analysis, a funnel plot for formal assessment of publication bias was not generated.

Effects of interventions

See: **Summary of findings for the main comparison** 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 (comparison 1)

Primary outcome - post-cesarean endometritis

Vaginal cleansing with povidone-iodine solution reduced the risk of post-cesarean endometritis from 8.7% in control groups to 3.8% in vaginal cleansing groups (average risk ratio (aRR) 0.36, 95% confidence interval (CI) 0.20 to 0.63, 10 trials, 3283 women; moderate-quality evidence). Random-effects meta-analysis was utilized for this outcome because of high heterogeneity (I^2 = 59% and Tau^2 = 0.35), *see* 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 0.38, 95% CI 0.21 to 0.69, eight trials, 3069 women for iodine; aRR 0.22, 95% CI 0.07 to 0.75, two trials, 214 women for chlorhexidine) Analysis 1.1.

Secondary outcomes

Vaginal cleansing did not lead to a clear reduction in the outcomes of **postoperative fever** (risk ratio (RR) 0.87, 95% CI 0.72 to 1.05, eight trials, 3109 women; moderate-quality evidence, Analysis 1.2), **postoperative wound infection** (RR 0.74, 95% CI 0.49 to 1.11, eight trials, 2839 women; moderate-quality evidence, Analysis 1.3), or **composite wound complication** (RR 0.63, 95% CI 0.37 to 1.07, two trials, 729 women, Analysis 1.4), but did lead to a clear reduction in the **composite wound complication or endometritis** outcome (RR 0.46, 95% CI 0.26 to 0.82, two trials, 499 women; moderate-quality evidence, Analysis 1.5). None of the trials noted any **side effects of vaginal preparation** in either the intervention or control groups.

There was no evidence of any differences between subgroups according to the test for subgroup differences performed.

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

Four trials (Haas 2010; Memon 2011; Reid 2001; Yildirim 2012) stratified data for women in labor versus not in labor, while one trial only included women in labor (Asad 2017). One trial included 14 women receiving irrigation before elective cesareans not in labor and only reported on endometritis outcome for the group (Rouse 1997). Two trials (Haas 2010; Reid 2001) reported on the outcomes of post-cesarean endometritis and composite wound complication. Two studies reported on stratified outcomes for post-cesarean endometritis, postoperative fever, and postoperative wound infection (Asad 2017; 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 11.1% in the control group to 4.7% in the vaginal preparation group (aRR 0.41, 95% CI 0.19 to 0.89, four trials, 960 women; Analysis 2.1). There was not a clear difference in rates of post-cesarean endometritis for women who were not in labor (aRR 1.00, 95% CI 0.35 to 2.84, four trials, 886 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: Chi^2 = 1.80, df = 1 (P = 0.18), I^2 = 44.3%).

Secondary outcomes

Women in labor had a reduction in rates of postoperative fever (RR 0.64, 95% CI 0.43 to 0.96, three trials, 741 women; Analysis 2.2),and the composite wound complication or endometritis (RR 0.34, 95% CI 0.13 to 0.87, two trials, 164 women; Analysis 2.5). The small number of women in these groups limit this conclusion. There were no clear differences in rates of other secondary outcomes for women in labor who received vaginal cleansing (postoperative wound infection: RR 0.54, 95% CI 0.23 to 1.24, three trials, 741 women; postoperative wound complication: RR 0.77, 95% CI 0.36 to 1.61, two trials, 314 women), *see* Analysis 2.3; 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 0.96, 95% CI 0.61 to 1.49, two trials, 661 women; postoperative wound infection: RR 0.65, 95% CI 0.27 to 1.57, two trials, 661 women; postoperative wound complication: RR 0.54, 95% CI 0.25 to 1.16, two trials, 415 women; composite wound complication or endometritis: RR 0.60, 95% CI 0.29 to 1.26, two trials, 335 women), *see* Analysis 2.2; Analysis 2.3; Analysis 2.4; Analysis 2.5.

There was no evidence of any differences between subgroups according to the test for subgroup differences performed.

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

Four trials (Guzman 2002; Haas 2010; Memon 2011; Yildirim 2012) stratified data for women with ruptured membranes versus women without ruptured membranes. One trial excluded women with ruptured membranes (Ahmed 2017). Two trials (Guzman 2002; Haas 2010) reported on the outcomes of post-cesarean endometritis and postoperative fever. Two studies reported on stratified outcomes for post-cesarean endometritis, postoperative fever, and postoperative wound infection (Ahmed 2017; 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 (4.3% in the vaginal cleansing group versus 17.9% in the control group; RR 0.24, 95% CI 0.10 to 0.55, three trials, 272 women), *see* 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 (RR 0.50, 95% CI 0.31 to 0.82, four trials, 1057 women) and the subgroup interaction test indicated no difference between these two subgroups (Test for subgroup differences: $Chi^2 = 2.28$, df = 1 (P = 0.13), $I^2 = 56.1\%$).

Secondary outcomes

There were no clear differences between the vaginal preparation and control groups in the other outcomes for women with ruptured membranes (postoperative fever: RR 0.62, 95% CI 0.34 to 1.12, two trials, 200 women; postoperative wound infection: aRR 1.04, 95% CI 0.16 to 6.70, three trials, 272 women; composite wound complication: RR 0.53, 95% CI 0.15 to 1.89, 1 trial, 76 women; composite wound complication or endometritis: RR 0.39, 95% CI 0.13 to 1.13, two trials, 134 women), *see* Analysis 3.2; Analysis 3.3; Analysis 3.4; Analysis 3.5. All of the reported outcomes for women without ruptured membranes were not clearly different between the vaginal preparation and control groups (postoperative fever: RR 0.89, 95% CI 0.61 to 1.30, three trials, 969 women; postoperative wound infection: aRR 0.68, 95% CI 0.36 to 1.28, four trials, 1057 women; postoperative wound complication: RR 0.73, 95% CI 0.25 to 2.10, one trial, 224 women; composite wound complication or endometritis: RR 0.52, 95% CI 0.26 to 1.04, two trials, 336 women), *see* Analysis 3.2; Analysis 3.3; Analysis 3.4; Analysis 3.5.

There was no evidence of any differences between subgroups according to the test for subgroup differences performed.

Other planned subgroup analysis - 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 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.

No adverse events were noted in the four trials commenting on possible adverse effects 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.

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. The heterogeneity in the results for this variable may be explainable by the study design and patient populations. The Guzman 2002 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 other studies contained a majority of 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 the Summary of findings for the main comparison.

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 several ongoing trials.

Quality of the evidence

The risk of bias of the 11 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 a 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 of unclear risk of bias, often in allocation concealment. 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 quality of the evidence using GRADE was moderate for all outcomes (Summary of findings for the main comparison).

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 low-, middle-, and high-income countries.

Agreements and disagreements with other studies or reviews

Several new trials were added to this update. However, this review is still somewhat limited by the number of trials of preoperative vaginal preparation immediately before cesarean delivery. However, the addition of the new trials strengthen the conclusions of the earlier versions of this review (Haas 2010a; Haas 2013; Haas 2014a; Haas 2014b). The findings of lower risk of post-cesarean endometritis is consistent with a recently published meta-analysis (Caissutti 2017). While the data point to a reduction in post-cesarean endometritis with the intervention, it is possible that with more trial data, we will find more clarity in the subgroup comparisons, or for secondary outcomes. The addition of data from currently ongoing trials in future updates is planned. 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. No adverse effects were noted in any of the trials. Subgroup analysis could not rule out larger reductions in endometritis with antiseptics in women who were in labor or in women whose membranes had ruptured when antiseptics were used. As a simple, generally inexpensive intervention, 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.

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'Summary of findings' table for the previous version of this review (Haas 2014b). At that time, Erika Ota's work was financially supported by the UNDP/UNFPA/UNICEF/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP), Department of Reproductive Health and Research (RHR), World Health Organization.

The 'Summary of findings' table in this update was prepared by the current review team using GradePro software.

As part of the pre-publication editorial process, this review has been commented on by three peers (an editor and two referees who are external to the editorial team) and the Group's Statistical Adviser.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Ahmed 2017

Methods	RCT.
Participants	Inclusion: pregnant women schedule for term elective cesarean section - indications were prior cesarean, abnormal presentation, maternal request, prior cystocele repair or prior perineal tear Exclusion: emergency cesarean, premature ruptured membranes, placenta previa, immunocompromised status Setting: Saudi Arabia
Interventions	Intervention: chlorhexidine 0.25% antiseptic wipes in vagina (3 10 cm x 10 cm pieces used from apex to introitus including fornices for approximately 1 minute total time) Control: no vaginal cleansing. Intention-to-treat analysis.
Outcomes	Outcomes: infectious morbidities - endometritis, fever, wound infection Endometritis - fever with tenderness and offensive lochia. Febrile morbidity - fever of 38 degrees 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	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 Funding source: not stated Author declarations of interest: no conflicts of interest

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 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.

Ahmed 2017 (*Continued*)

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

Asad 2017

Methods	RCT.
Participants	Inclusion: 434 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 (n = 217 randomized) Control: no vaginal cleansing (n = 217 randomized).
Outcomes	Fever, wound infection, endometritis.
Notes	February 1 to July 31, 2016. 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

Methods	Double blind quasi-RCT.
Participants	Inclusion: women undergoing non-emergent or laboring cesarean delivery Exclusion: iodine sensitivity, chorioamnionitis, gestational herpes, abnormal vaginal discharge, emergency cesarean (due to fetal distress, placenta previa) Setting: Iran.
Interventions	Intervention: 2 4 x 4 gauze sponges soaked in 10% povidone -iodine solutions rotated 360 degrees for 30 seconds from vault to introitus (n = 284) Control: no vaginal cleansing (n = 284). Intention-to-treat analysis.
Outcomes	Febrile morbidity, endometritis, wound infection.
Notes	May 2007-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

Goymen 2017

Methods	RCT.
Participants	Inclusion: 120 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 degrees celsius, severe anemia, allergic reaction to agents Setting: Sanko University.
Interventions	Intervention group 1: povidone-iodine vaginal cleansing for 30 seconds (n = 41) Intervention group 2: benzalkonium chloride vaginal cleansing for 30 seconds (n = 39) Control: no vaginal cleansing (n = 40). Intention-to-treat analysis.
Outcomes	Postoperative pain evaluation, time to flatulence and defecation, and Hb, WBC, Plt, CRP in 24 hours
Notes	July to August 2014. Funding source: not stated Author declarations of interest: no conflicts of interest

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

Methods	RCT.
Participants	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) (n = 80) Control: saline vaginal wash (n = 80).
Outcomes	Endometritis (temperature > 100.4 degrees F at least twice > 24 hours after surgery or of 101 degrees F any time after surgery, with abdominal/uterine tenderness) Cellulitis (advancing erythema around the incision).
Notes	March 2000 to July 2001. 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	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

Methods	RCT.
Participants	Inclusion: all women undergoing cesarean delivery, age ≥ 18 years Exclusion: emergency cesarean delivery, allergy to iodine. Setting: academic medical center in Indiana, USA.
Interventions	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 (n = 155) Control: no preoperative vaginal cleansing (n = 145). Intention-to-treat analysis.
Outcomes	Post-cesarean endometritis (uterine tenderness plus postoperative fever requiring antibiotics) Postoperative fever (> 38 degrees Celcius, > 24 hours after surgery) Wound infection requiring antibiotics. Wound separation, seroma, hematoma, or need for debridement. Composite infectious morbidity outcome: either endometritis, fever, sepsis, hospital readmission, wound infection, or wound complication
Notes	The trial was stopped early due to difficulty recruiting. September 2006 to January 2009 Funding source: Internally funded. Author declarations of interest: no conflicts of interest

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

Memon 2011

Methods	RCT.
Participants	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 (n = 100) Control: no vaginal cleansing (n = 100). Intention to treat - unclear.
Outcomes	Postoperative febrile morbidity (oral temperature of 38 degrees C after 1st 24 hours of surgery) Endometritis (postoperative fever with uterine tenderness and foul smelling lochia requiring broad spectrum antibiotic therapy) Wound complications (infection at surgical site - seroma, hematoma, and disruption of abdominal incision - that required parenteral antibiotics and wound care Composite infectious morbidity - a sum of the 3 outcomes above
Notes	February to July 2010. 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	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

Reid 2001

Methods	RCT.
Participants	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	Intervention: 10% povidone-iodine surgical scrub solution vaginally immediately before cesarean (n = 247) Control: no vaginal cleansing (n = 251). Intention-to-treat analysis.
Outcomes	Fever (38 degrees C or greater after the day of surgery). Febrile morbidity (postoperative fever on 2 or more calendar days, excluding the day of surgery) 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) Wound separation (defined by chart note reporting separation of the operative incision requiring intervention) Number of postoperative days with fever. Average duration of antibiotic administration. Length of hospitalization.
Notes	Chorioamnionitis participants excluded from analysis. May 1996 to September 1998. Funding source: not stated Author declarations of interest: not stated

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.

Reid 2001 (*Continued*)

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 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.

Rouse 1997

Methods	RCT.
Participants	Inclusion: women admitted for delivery > 24 weeks' gestation Exclusion: contraindications to digital examinations, placenta previa, active herpes, chorioamnionitis before randomization or allergy to chlorhexidine Setting: University of Alabama - Birmingham, USA.
Interventions	Intervention: 200 mL irrigation of 0.2% chlorhexidine solution in labor or if a planned cesarean then immediately before surgery Control: 200 mL sterile water placebo solution. Intention-to-treat analysis.
Outcomes	Endometritis.
Notes	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 Funding source: Agency for Health Care Policy Research Contract DHHS No. 290-92-0055 Author declarations of interest: not stated

Risk of bias

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

Rouse 1997 (*Continued*)

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) All outcomes	Low risk	Data collection done before the assignment was known.
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

Methods	RCT.
Participants	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 (n = 142) Control: no preoperative vaginal cleansing (n = 166).
Outcomes	Febrile morbidity (any postoperative temperature > 38 degrees C) Endometritis (temperature elevation > 38 degrees 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) 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 Author declarations of interest: not stated

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random digit table.

Starr 2005 (*Continued*)

Allocation concealment (selection bias)	Low risk	Sequentially-numbered, opaque, sealed envelopes.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Not stated for participants but treating providers at the time of fever were unaware of participation status
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 posts-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 is 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

Methods	RCT.
Participants	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 (n = 335) Control: no preoperative vaginal preparation (n = 335).
Outcomes	Postpartum endometritis (primary outcome) body temperature > 38.5 degrees C with concomitant foul-smelling discharge or abnormally tender uterus on bimanual examination) 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) Fever (elevated temperature of 38 degrees C or higher for a minimum of 24 hours following surgery not associated with signs of infection)

Yildirim 2012 (*Continued*)

Notes	January to August 2011. Funding source: not stated Author declarations of interest: no conflicts of interest

Risk of bias

Bias	Authors' judgement	Support for judgement
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 1 participant withdrew.
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting.
Other bias	Low risk	No evidence of other bias.

CRP: C-reactive protein
Hb: hemoglobin
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.

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

Ghanbarpour 2016

Methods	RCT
Participants	400 women getting elective cesarean delivery at term, Iran
Interventions	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 trial registry says complete. Emailed study contact 7/12/2017, no response

Ghomian 2011

Methods	RCT
Participants	526 women getting cesarean at term, excluding chorioamnionitis
Interventions	Vaginal irrigation with povidone-iodine Control: no vaginal preparation
Outcomes	Primary- fever (body temperature)
Notes	Iranian trial registry says complete. Emailed study contact 7/12/2017, no response

RCT: randomized controlled trial

Characteristics of ongoing studies *[ordered by study ID]*

Ben-Asher 2017

Trial name or title	Vaginal antimicrobacterial preparation before cesarean section for endometritis prevention
Methods	RCT
Participants	1040 women getting a cesarean delivery
Interventions	Vaginal preparation with septal soap before cesarean Control: no vaginal preparation
Outcomes	Primary- endometritis
Starting date	April 2017, anticipated completion April 2020

Ben-Asher 2017 (*Continued*)

Contact information	Hila Ben-Asher, Rambam Health Care
Notes	Not yet recruiting, verified in clinicaltrials.gov by PI April 2017

Bianco 2018

Trial name or title	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	4% chlorhexidine gluconate vaginal scrub prior to cesarean ControlL 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 degrees 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	Not yet recruiting as of posting February 6, 2017

Irving 2017

Trial name or title	Chlorhexidine gluconate versus povidone-iodine as vaginal preparation antiseptics prior to cesarean delivery
Methods	RCT
Participants	100 women getting a scheduled cesarean delivery at least 37 weeks' gestation (not in labor or with ruptured membranes)
Interventions	Group 1: 4% chlorhexidine gluconate preoperative vaginal preparation Group 2: 10% povidone-iodine preoperative vaginal preparation with scrub and paint
Outcomes	Primary: bacterial load immediately postoperative prior to exit from operating room- outcome is change in total bacterial load from preoperative sampling Secondary outcomes include length of hospital stay and postoperative infections including endometritis, pelvic abscesses, and skin/wound infection
Starting date	May 2017, anticipated completion December 2019
Contact information	Lauryn Przeslawski at Metro Health in Michigan

Irving 2017 (*Continued*)

Notes	Currently recruiting as of August 30, 2017

Lakhi 2016

Trial name or title	Chlorhexidine gluconate vs povidone-iodine vaginal cleansing solution prior to cesarean delivery
Methods	RCT
Participants	1500 women getting non-emergent cesarean delivery, chorioamnionitis excluded
Interventions	Group 1: 10% povidone-iodine solution for vaginal cleansing with 4 minutes of drying time before draping Group 2: 4% chlorhexidine gluconate solution for vaginal cleansing
Outcomes	Primary outcome: postpartum endometritis 0-3 days postpartum with diagnosis involving fever, uterine fundal tenderness, or purulent lochia requiring antibiotic therapy
Starting date	December 2016, anticipated completion May 2018
Contact information	Nisha Lakhi, MD at Richmond University Medical Center, New York
Notes	Currently recruiting as of February 16, 2018

Riad 2016

Trial name or title	Preoperative vaginal cleansing with povidone iodine and the risk of post-cesarean endometritis
Methods	RCT
Participants	306 women undergoing cesarean
Interventions	Vaginal cleansing with 3 gauze pieces soaked in 10% povidone-iodine from vaginal apex to introitus Control: no vaginal cleansing
Outcomes	Primary outcome: postcesarean endometritis diagnosed by fever 38.4 degrees 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	Currently recruiting as of February 2016.

Temming 2015

Trial name or title	Vaginal cleansing before cesarean delivery to reduce infection: a randomized trial
Methods	RCT
Participants	608 women undergoing cesarean
Interventions	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	Anticipated completion August 2018, verified 2/22/18- NCT02495753

RCT: randomized controlled trial

DATA AND ANALYSES

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

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post-cesarean endometritis	10	3283	Risk Ratio (M-H, Random, 95% CI)	0.36 [0.20, 0.63]
1.1 Iodine-based solution	8	3069	Risk Ratio (M-H, Random, 95% CI)	0.38 [0.21, 0.69]
1.2 Chlorhexidine-based solution	2	214	Risk Ratio (M-H, Random, 95% CI)	0.22 [0.07, 0.75]
2 Postoperative fever	8	3109	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.72, 1.05]
2.1 Iodine-based solution	7	2909	Risk Ratio (M-H, Fixed, 95% CI)	0.87 [0.72, 1.06]
2.2 Chlorhexidine-based solution	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.09, 2.56]
3 Postoperative wound infection	8	2839	Risk Ratio (M-H, Fixed, 95% CI)	0.74 [0.49, 1.11]
3.1 Iodine-based solution	7	2639	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.50, 1.19]
3.2 Chlorhexidine-based solution	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.55 [0.17, 1.82]
4 Composite wound complication	2	729	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.37, 1.07]
5 Composite wound complication or endometritis	2	499	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.26, 0.82]

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
1 Post-cesarean endometritis	5	1846	Risk Ratio (M-H, Random, 95% CI)	0.58 [0.32, 1.06]
1.1 Women in labor	4	960	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.19, 0.89]
1.2 Women not in labor	4	886	Risk Ratio (M-H, Random, 95% CI)	1.00 [0.35, 2.84]
2 Postoperative fever	3	1402	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.57, 1.03]
2.1 Women in labor	3	741	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.43, 0.96]
2.2 Women not in labor	2	661	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.61, 1.49]
3 Postoperative wound infection	3	1402	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.32, 1.08]
3.1 Women in labor	3	741	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.23, 1.24]
3.2 Women not in labor	2	661	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.27, 1.57]
4 Composite wound complication	2	729	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.38, 1.09]
4.1 Women in labor	2	314	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.36, 1.61]
4.2 Women not in labor	2	415	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.25, 1.16]
5 Composite wound complication or endometritis	2	499	Risk Ratio (M-H, Fixed, 95% CI)	0.47 [0.27, 0.85]
5.1 Women in labor	2	164	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.13, 0.87]
5.2 Women not in labor	2	335	Risk Ratio (M-H, Fixed, 95% CI)	0.60 [0.29, 1.26]

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

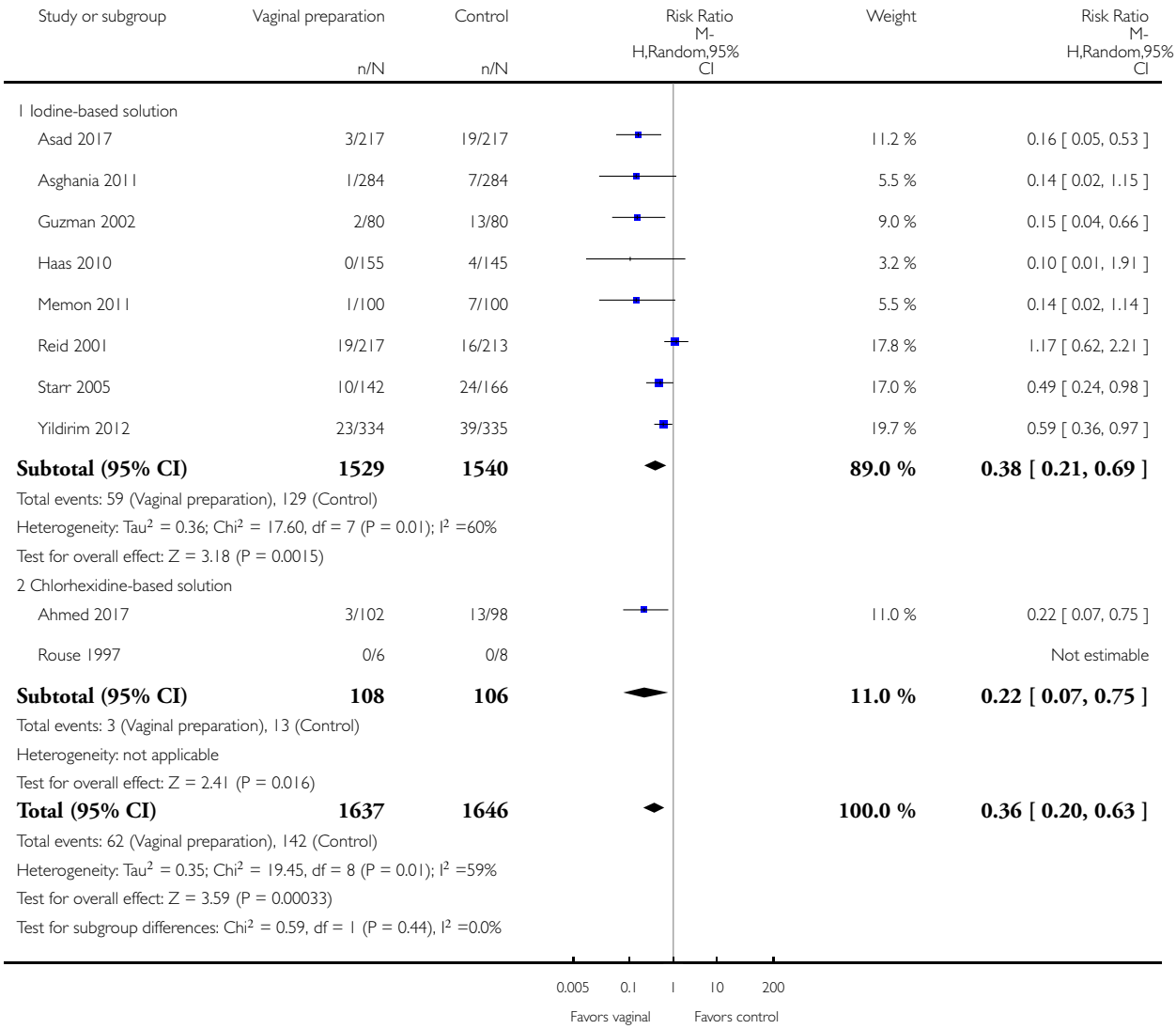
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Post-cesarean endometritis	4	1329	Risk Ratio (M-H, Fixed, 95% CI)	0.41 [0.27, 0.62]
1.1 Women with ruptured membranes	3	272	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.10, 0.55]
1.2 Women with intact membranes	4	1057	Risk Ratio (M-H, Fixed, 95% CI)	0.50 [0.31, 0.82]
2 Postoperative fever	3	1169	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.59, 1.11]
2.1 Women with ruptured membranes	2	200	Risk Ratio (M-H, Fixed, 95% CI)	0.62 [0.34, 1.12]
2.2 Women with intact membranes	3	969	Risk Ratio (M-H, Fixed, 95% CI)	0.89 [0.61, 1.30]
3 Postoperative wound infection	4	1329	Risk Ratio (M-H, Random, 95% CI)	0.74 [0.43, 1.30]
3.1 Women with ruptured membranes	3	272	Risk Ratio (M-H, Random, 95% CI)	1.04 [0.16, 6.70]
3.2 Women with intact membranes	4	1057	Risk Ratio (M-H, Random, 95% CI)	0.68 [0.36, 1.28]
4 Composite wound complication	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.64 [0.28, 1.44]
4.1 Women with ruptured membranes	1	76	Risk Ratio (M-H, Fixed, 95% CI)	0.53 [0.15, 1.89]
4.2 Women with intact membranes	1	224	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.25, 2.10]
5 Composite wound complication or endometritis	2	500	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.27, 0.85]
5.1 Women with ruptured membranes	2	134	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.13, 1.13]
5.2 Women with intact membranes	2	366	Risk Ratio (M-H, Fixed, 95% CI)	0.52 [0.26, 1.04]

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

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

Comparison: 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation)

Outcome: 1 Post-cesarean endometritis



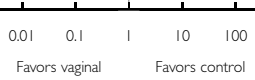
Analysis 1.2. Comparison 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation), Outcome 2 Postoperative fever.

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

Comparison: 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation)

Outcome: 2 Postoperative fever

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Iodine-based solution					
Asad 2017	9/217	16/217		8.3 %	0.56 [0.25, 1.25]
Asghania 2011	14/284	17/284		8.9 %	0.82 [0.41, 1.64]
Haas 2010	2/155	7/145		3.8 %	0.27 [0.06, 1.27]
Memon 2011	4/100	6/100		3.1 %	0.67 [0.19, 2.29]
Reid 2001	44/217	37/213		19.5 %	1.17 [0.79, 1.73]
Starr 2005	34/142	47/166		22.6 %	0.85 [0.58, 1.24]
Yildirim 2012	55/334	61/335		31.7 %	0.90 [0.65, 1.26]
Subtotal (95% CI)	**1449**	**1460**		**97.9 %**	**0.87 [0.72, 1.06]**
Total events: 162 (Vaginal preparation), 191 (Control)					
Heterogeneity: Chi^2 = 5.76, df = 6 (P = 0.45); I^2 =0.0%					
Test for overall effect: Z = 1.38 (P = 0.17)					
2 Chlorhexidine-based solution					
Ahmed 2017	2/102	4/98		2.1 %	0.48 [0.09, 2.56]
Subtotal (95% CI)	**102**	**98**		**2.1 %**	**0.48 [0.09, 2.56]**
Total events: 2 (Vaginal preparation), 4 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.86 (P = 0.39)					
Total (95% CI)	**1551**	**1558**		**100.0 %**	**0.87 [0.72, 1.05]**
Total events: 164 (Vaginal preparation), 195 (Control)					
Heterogeneity: Chi^2 = 6.28, df = 7 (P = 0.51); I^2 =0.0%					
Test for overall effect: Z = 1.49 (P = 0.14)					
Test for subgroup differences: Chi^2 = 0.49, df = 1 (P = 0.49), I^2 =0.0%					



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

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

Comparison: 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation)

Outcome: 3 Postoperative wound infection

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Iodine-based solution					
Asad 2017	3/217	8/217		15.3 %	0.38 [0.10, 1.39]
Asghania 2011	10/284	9/284		17.2 %	1.11 [0.46, 2.69]
Guzman 2002	7/80	4/80		7.6 %	1.75 [0.53, 5.75]
Haas 2010	7/155	10/145		19.8 %	0.65 [0.26, 1.67]
Memon 2011	1/100	3/100		5.7 %	0.33 [0.04, 3.15]
Starr 2005	1/142	2/166		3.5 %	0.58 [0.05, 6.38]
Yildirim 2012	6/334	9/335		17.2 %	0.67 [0.24, 1.86]
Subtotal (95% CI)	**1312**	**1327**		**86.3 %**	**0.77 [0.50, 1.19]**
Total events: 35 (Vaginal preparation), 45 (Control)					
Heterogeneity: Chi^2 = 4.41, df = 6 (P = 0.62); I^2 =0.0%					
Test for overall effect: Z = 1.17 (P = 0.24)					
2 Chlorhexidine-based solution					
Ahmed 2017	4/102	7/98		13.7 %	0.55 [0.17, 1.82]
Subtotal (95% CI)	**102**	**98**		**13.7 %**	**0.55 [0.17, 1.82]**
Total events: 4 (Vaginal preparation), 7 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.98 (P = 0.33)					
Total (95% CI)	**1414**	**1425**		**100.0 %**	**0.74 [0.49, 1.11]**
Total events: 39 (Vaginal preparation), 52 (Control)					
Heterogeneity: Chi^2 = 4.71, df = 7 (P = 0.69); I^2 =0.0%					
Test for overall effect: Z = 1.44 (P = 0.15)					
Test for subgroup differences: Chi^2 = 0.27, df = 1 (P = 0.60), I^2 =0.0%					

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

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

Comparison: 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation)

Outcome: 4 Composite wound complication

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Haas 2010	9/155	14/144		44.4 %	0.60 [0.27, 1.34]
Reid 2001	12/217	18/213		55.6 %	0.65 [0.32, 1.33]
Total (95% CI)	**372**	**357**		**100.0 %**	**0.63 [0.37, 1.07]**

Total events: 21 (Vaginal preparation), 32 (Control)

Heterogeneity: $Chi^2 = 0.03$, df = 1 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 1.71 (P = 0.087)

Test for subgroup differences: Not applicable

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

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

Comparison: 1 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation)

Outcome: 5 Composite wound complication or endometritis

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Haas 2010	10/155	17/144		52.4 %	0.55 [0.26, 1.15]
Memon 2011	6/100	16/100		47.6 %	0.38 [0.15, 0.92]
Total (95% CI)	**255**	**244**		**100.0 %**	**0.46 [0.26, 0.82]**

Total events: 16 (Vaginal preparation), 33 (Control)

Heterogeneity: $Chi^2 = 0.40$, df = 1 (P = 0.53); $I^2 = 0.0\%$

Test for overall effect: Z = 2.62 (P = 0.0087)

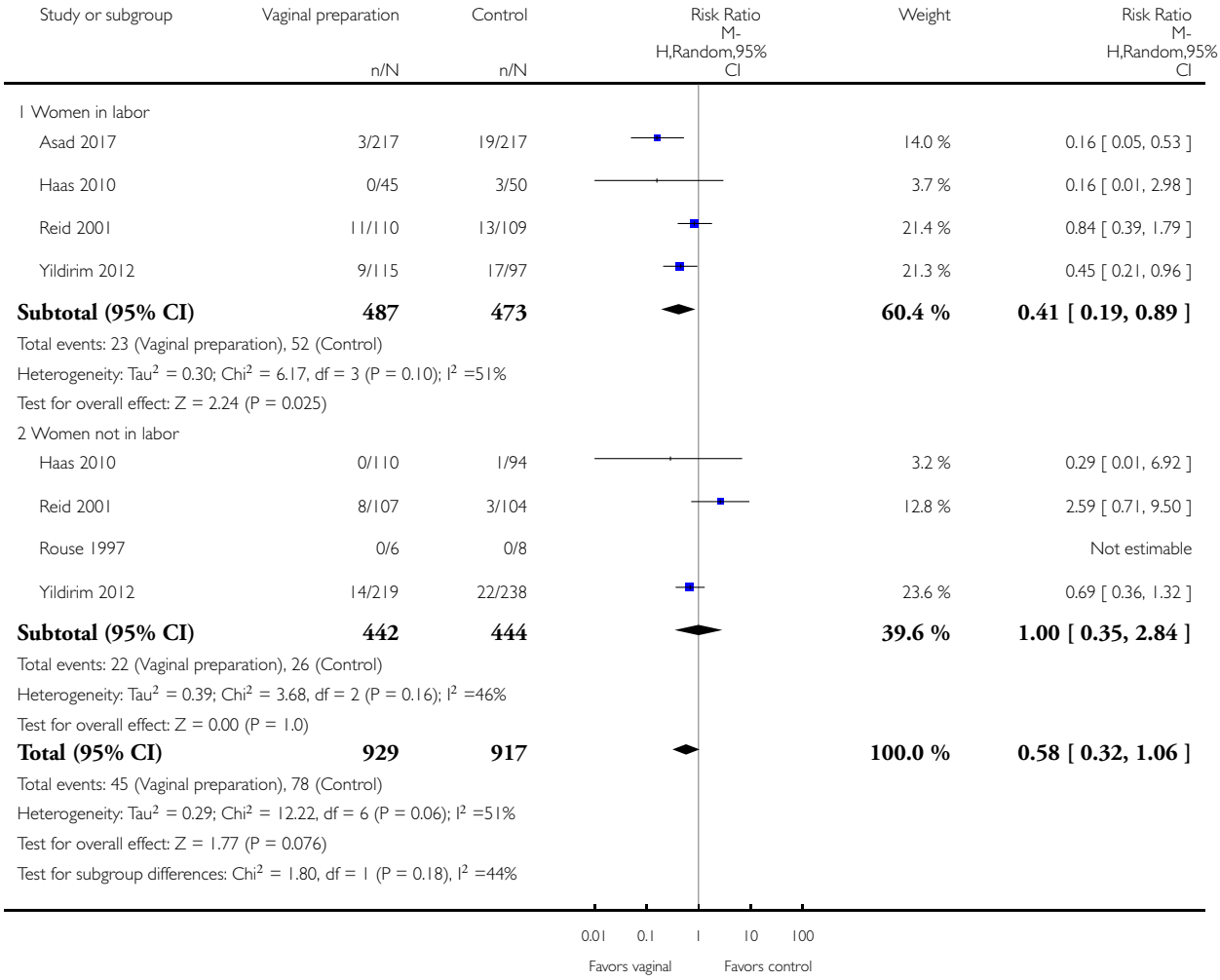
Test for subgroup differences: Not applicable

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.

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

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

Outcome: 1 Post-cesarean endometritis

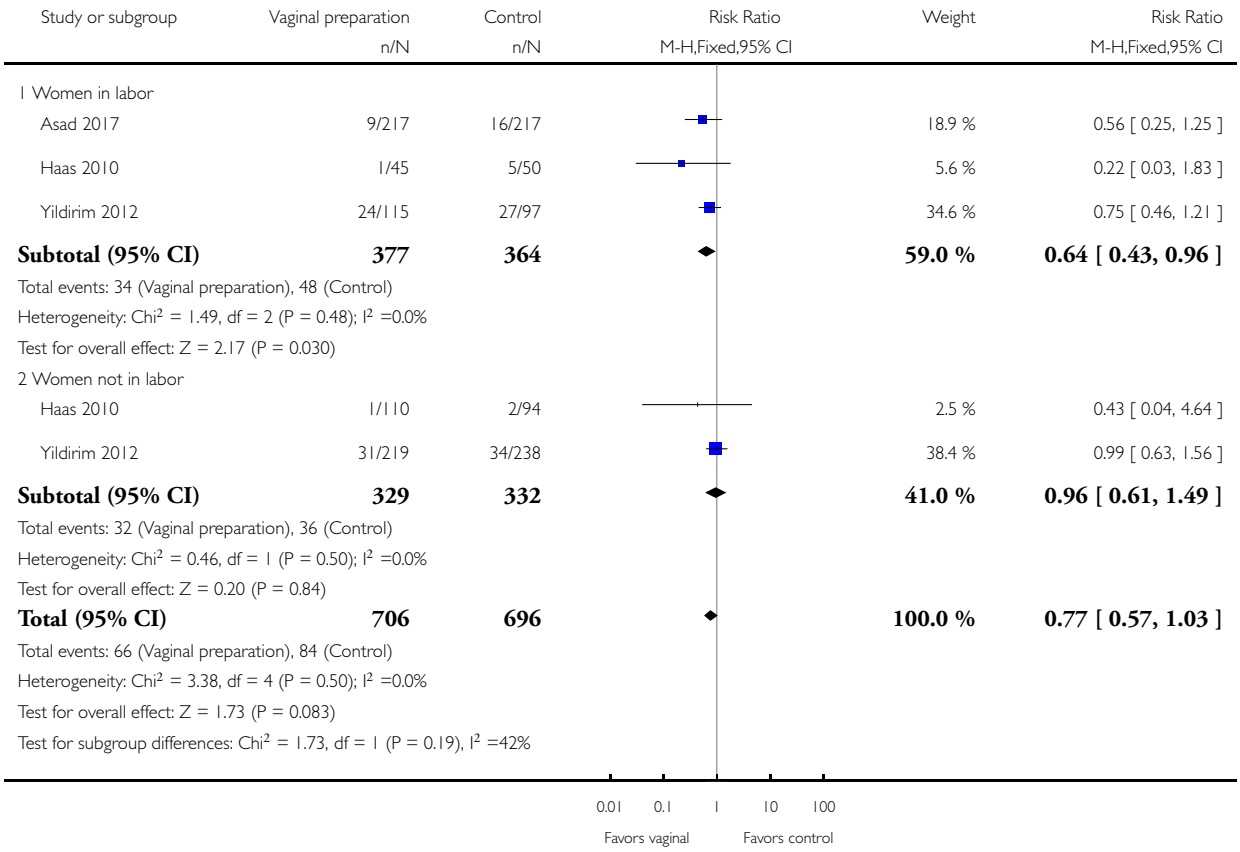


Analysis 2.2. Comparison 2 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 2 Postoperative fever.

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

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

Outcome: 2 Postoperative fever

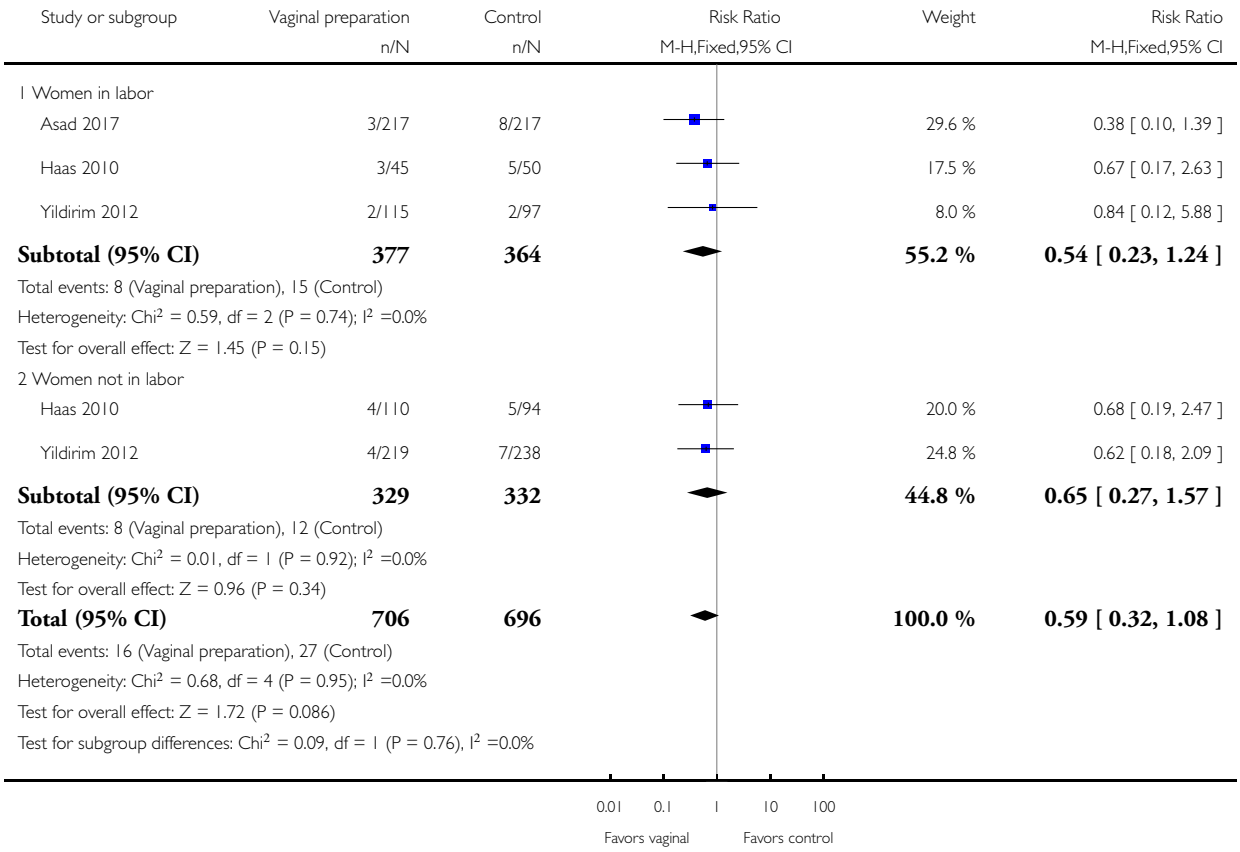


Analysis 2.3. Comparison 2 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 3 Postoperative wound infection.

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

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

Outcome: 3 Postoperative wound infection



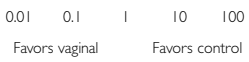
Analysis 2.4. Comparison 2 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of labor, Outcome 4 Composite wound complication.

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

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

Outcome: 4 Composite wound complication

Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women in labor					
Haas 2010	4/45	8/50		23.5 %	0.56 [0.18, 1.72]
Reid 2001	7/110	7/109		21.8 %	0.99 [0.36, 2.73]
Subtotal (95% CI)	**155**	**159**		**45.3 %**	**0.77 [0.36, 1.61]**
Total events: 11 (Vaginal preparation), 15 (Control)					
Heterogeneity: Chi^2 = 0.56, df = 1 (P = 0.46); I^2 =0.0%					
Test for overall effect: Z = 0.70 (P = 0.48)					
2 Women not in labor					
Haas 2010	5/110	6/94		20.1 %	0.71 [0.22, 2.26]
Reid 2001	5/107	11/104		34.6 %	0.44 [0.16, 1.23]
Subtotal (95% CI)	**217**	**198**		**54.7 %**	**0.54 [0.25, 1.16]**
Total events: 10 (Vaginal preparation), 17 (Control)					
Heterogeneity: Chi^2 = 0.37, df = 1 (P = 0.54); I^2 =0.0%					
Test for overall effect: Z = 1.58 (P = 0.11)					
Total (95% CI)	**372**	**357**		**100.0 %**	**0.64 [0.38, 1.09]**
Total events: 21 (Vaginal preparation), 32 (Control)					
Heterogeneity: Chi^2 = 1.31, df = 3 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 1.63 (P = 0.10)					
Test for subgroup differences: Chi^2 = 0.41, df = 1 (P = 0.52), I^2 =0.0%					



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.

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

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

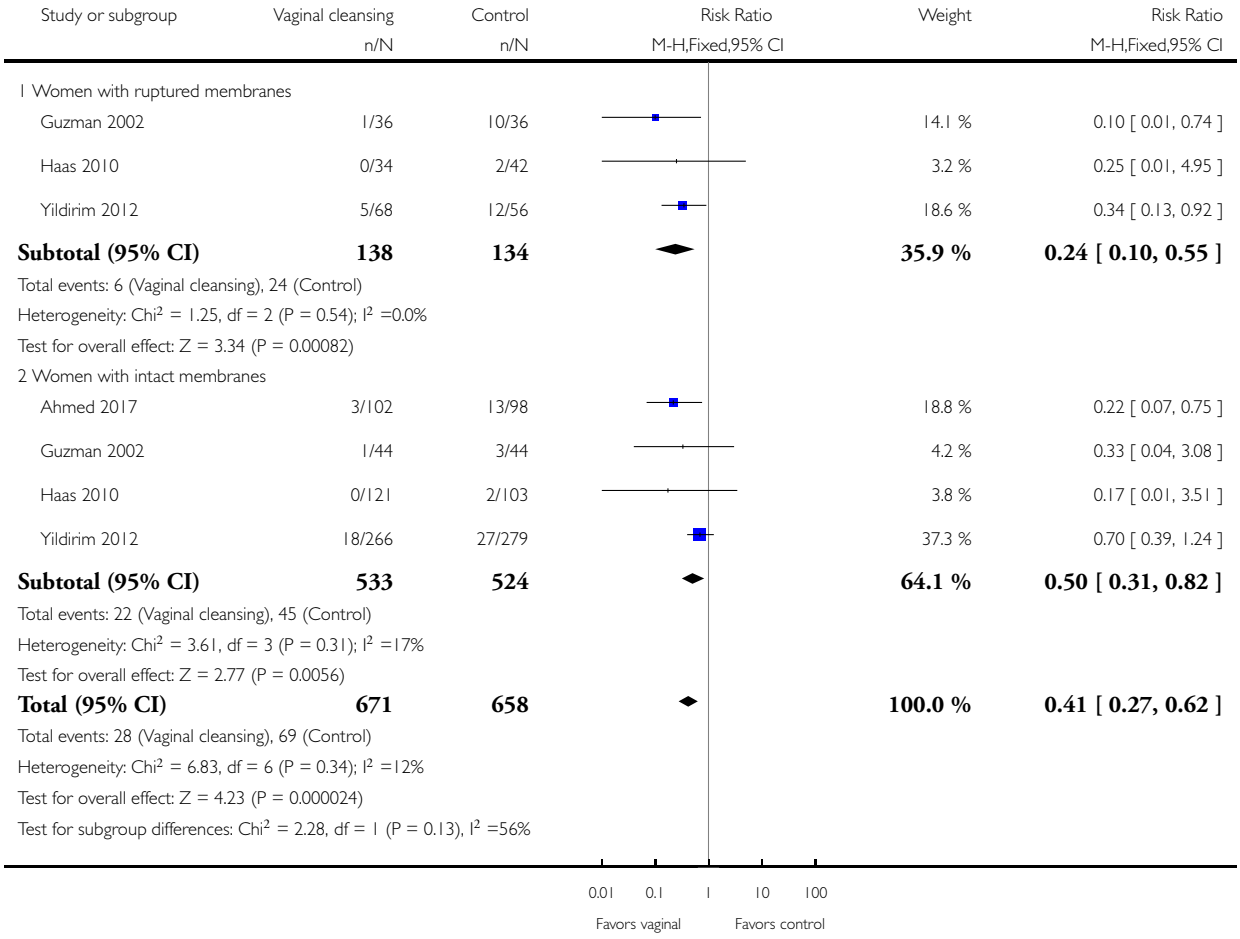
Study or subgroup	Vaginal preparation n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women in labor					
Haas 2010	4/45	11/50		31.8 %	0.40 [0.14, 1.18]
Memon 2011	1/31	6/38		16.4 %	0.20 [0.03, 1.61]
Subtotal (95% CI)	**76**	**88**		**48.2 %**	**0.34 [0.13, 0.87]**
Total events: 5 (Vaginal preparation), 17 (Control)					
Heterogeneity: Chi^2 = 0.34, df = 1 (P = 0.56); I^2 =0.0%					
Test for overall effect: Z = 2.25 (P = 0.024)					
2 Women not in labor					
Haas 2010	6/110	6/94		19.7 %	0.85 [0.29, 2.56]
Memon 2011	5/69	10/62		32.1 %	0.45 [0.16, 1.24]
Subtotal (95% CI)	**179**	**156**		**51.8 %**	**0.60 [0.29, 1.26]**
Total events: 11 (Vaginal preparation), 16 (Control)					
Heterogeneity: Chi^2 = 0.71, df = 1 (P = 0.40); I^2 =0.0%					
Test for overall effect: Z = 1.34 (P = 0.18)					
Total (95% CI)	**255**	**244**		**100.0 %**	**0.47 [0.27, 0.85]**
Total events: 16 (Vaginal preparation), 33 (Control)					
Heterogeneity: Chi^2 = 1.84, df = 3 (P = 0.61); I^2 =0.0%					
Test for overall effect: Z = 2.53 (P = 0.011)					
Test for subgroup differences: Chi^2 = 0.91, df = 1 (P = 0.34), I^2 =0.0%					

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.

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

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

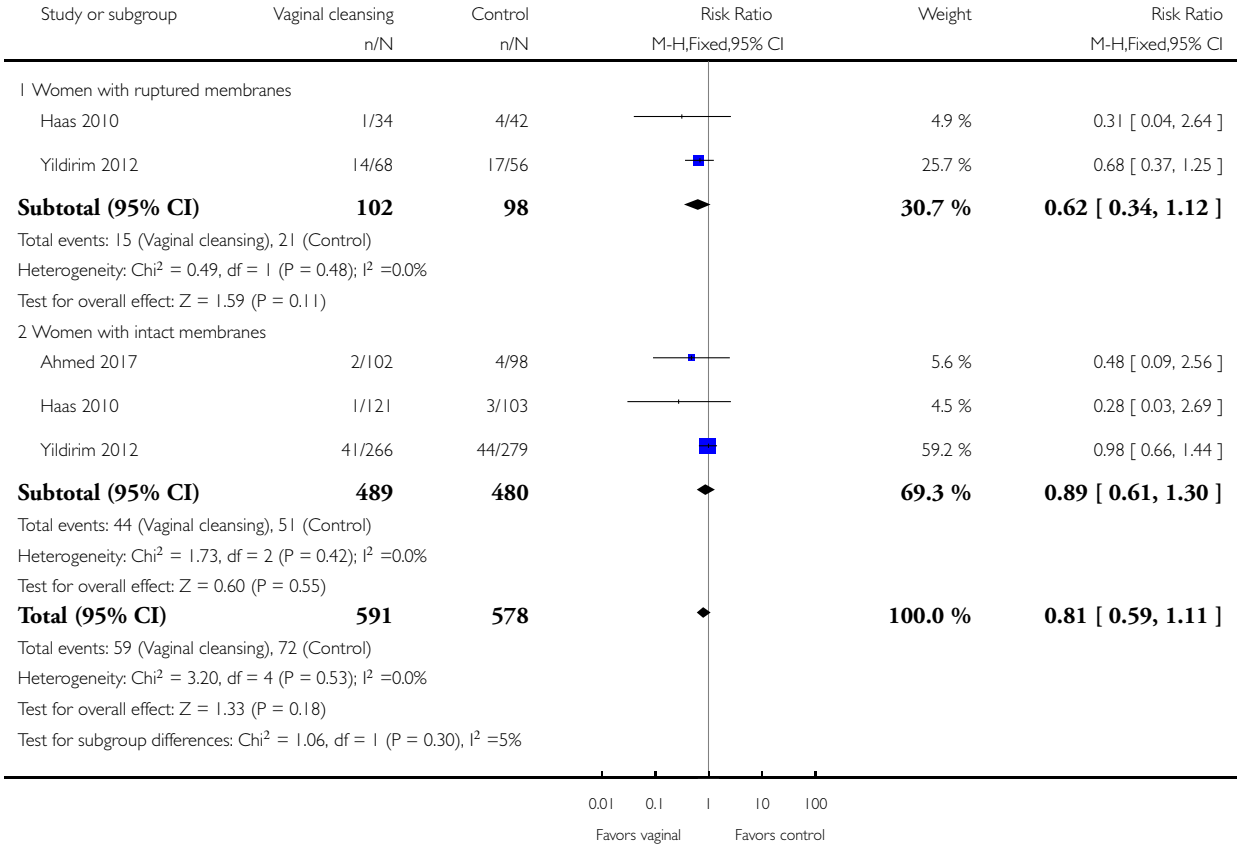


Analysis 3.2. Comparison 3 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 2 Postoperative fever.

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

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

Outcome: 2 Postoperative fever

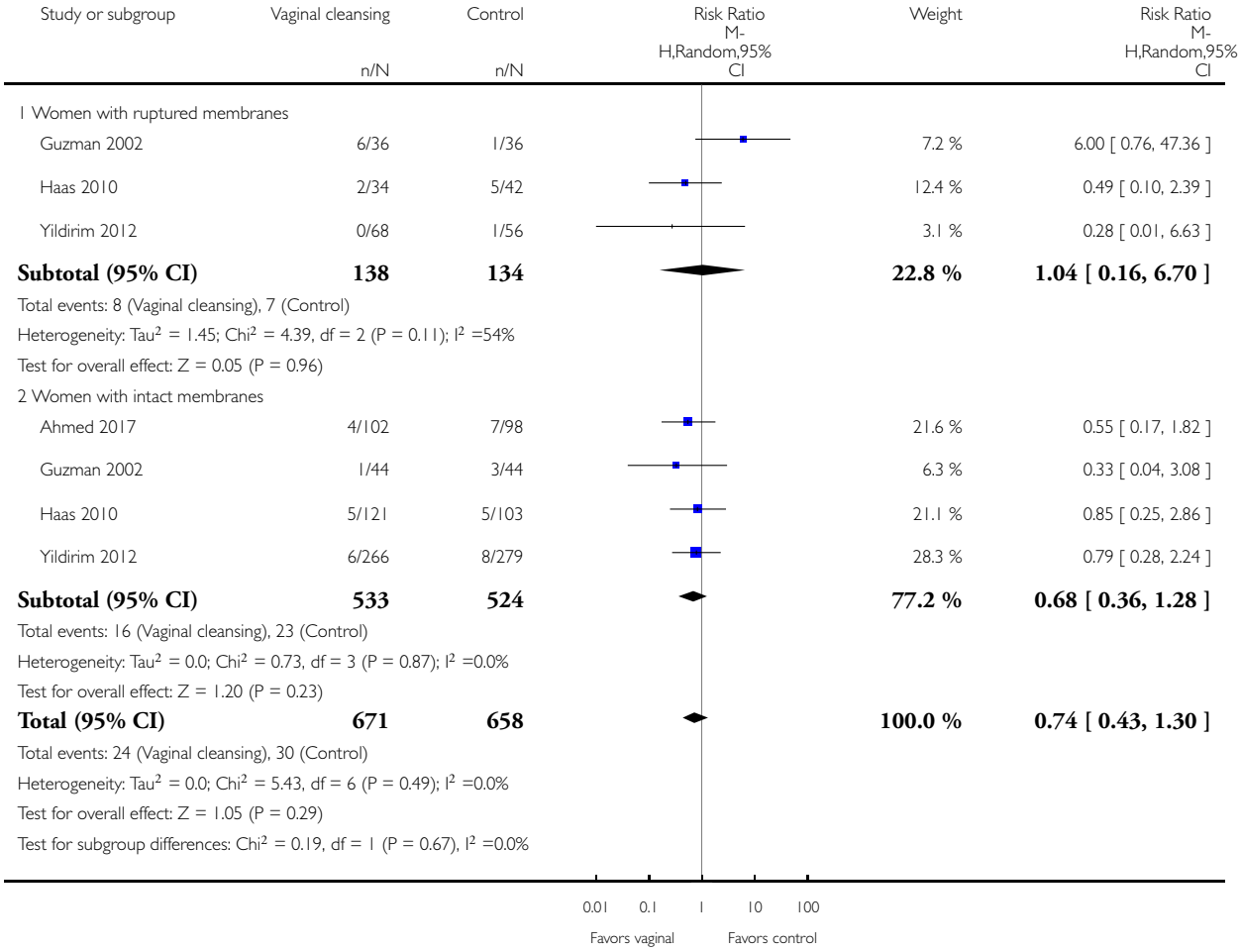


Analysis 3.3. Comparison 3 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 3 Postoperative wound infection.

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

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

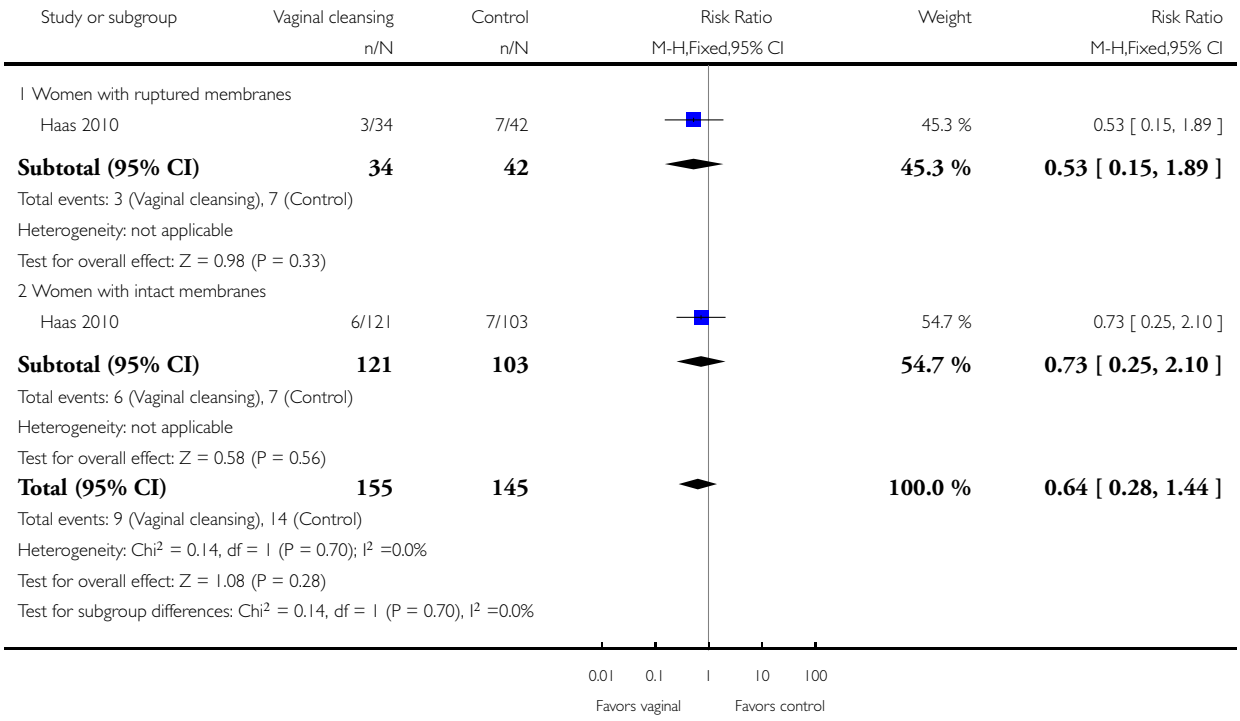


Analysis 3.4. Comparison 3 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 4 Composite wound complication.

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

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



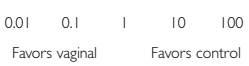
Analysis 3.5. Comparison 3 Vaginal preparation with antiseptic solution versus control (no preparation or saline preparation) - stratified by presence of ruptured membranes, Outcome 5 Composite wound complication or endometritis.

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

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

Study or subgroup	Vaginal cleansing n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Women with ruptured membranes					
Haas 2010	3/34	8/42		21.8 %	0.46 [0.13, 1.61]
Memon 2011	1/25	5/33		13.1 %	0.26 [0.03, 2.12]
Subtotal (95% CI)	**59**	**75**		**35.0 %**	**0.39 [0.13, 1.13]**
Total events: 4 (Vaginal cleansing), 13 (Control)					
Heterogeneity: Chi^2 = 0.21, df = 1 (P = 0.65); I^2 =0.0%					
Test for overall effect: Z = 1.74 (P = 0.083)					
2 Women with intact membranes					
Haas 2010	7/121	9/103		29.6 %	0.66 [0.26, 1.72]
Memon 2011	5/75	11/67		35.4 %	0.41 [0.15, 1.11]
Subtotal (95% CI)	**196**	**170**		**65.0 %**	**0.52 [0.26, 1.04]**
Total events: 12 (Vaginal cleansing), 20 (Control)					
Heterogeneity: Chi^2 = 0.48, df = 1 (P = 0.49); I^2 =0.0%					
Test for overall effect: Z = 1.85 (P = 0.064)					
Total (95% CI)	**255**	**245**		**100.0 %**	**0.48 [0.27, 0.85]**
Total events: 16 (Vaginal cleansing), 33 (Control)					
Heterogeneity: Chi^2 = 0.87, df = 3 (P = 0.83); I^2 =0.0%					
Test for overall effect: Z = 2.53 (P = 0.012)					
Test for subgroup differences: Chi^2 = 0.21, df = 1 (P = 0.65), I^2 =0.0%					



APPENDICES

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

[cesarean OR caesarean] AND [vaginal cleanse OR vaginal cleansing OR vaginal preparation OR antiseptic(s) OR chlorhexidine OR iodine OR disinfectant(s) OR antimicrobial OR antimicrobacterial]

WHAT'S NEW

Last assessed as up-to-date: 10 July 2017.

Date	Event	Description
10 July 2017	New search has been performed	Search updated and six new studies added.
10 July 2017	New citation required but conclusions have not changed	We have incorporated data from new included trials for this update and the overall conclusions are unchanged, however the support for the intervention for women who are in labor now shows a clear benefit to vaginal cleansing

HISTORY

Protocol first published: Issue 3, 2009

Review first published: Issue 3, 2010

Date	Event	Description
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.

(*Continued*)

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. Ms. Enders was added for this 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 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 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

Three of the planned subgroup analyses were unable to be performed as they were not reported in the trials.

In the 2017 update, we added an additional search of ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for unpublished, planned and ongoing trial reports.

A new co-author (Savannah Enders) has joined the review team for this update.

We have edited the list of outcomes for use in GRADE. We have 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 have 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]; Vagina

MeSH check words

Female; Humans; Pregnancy