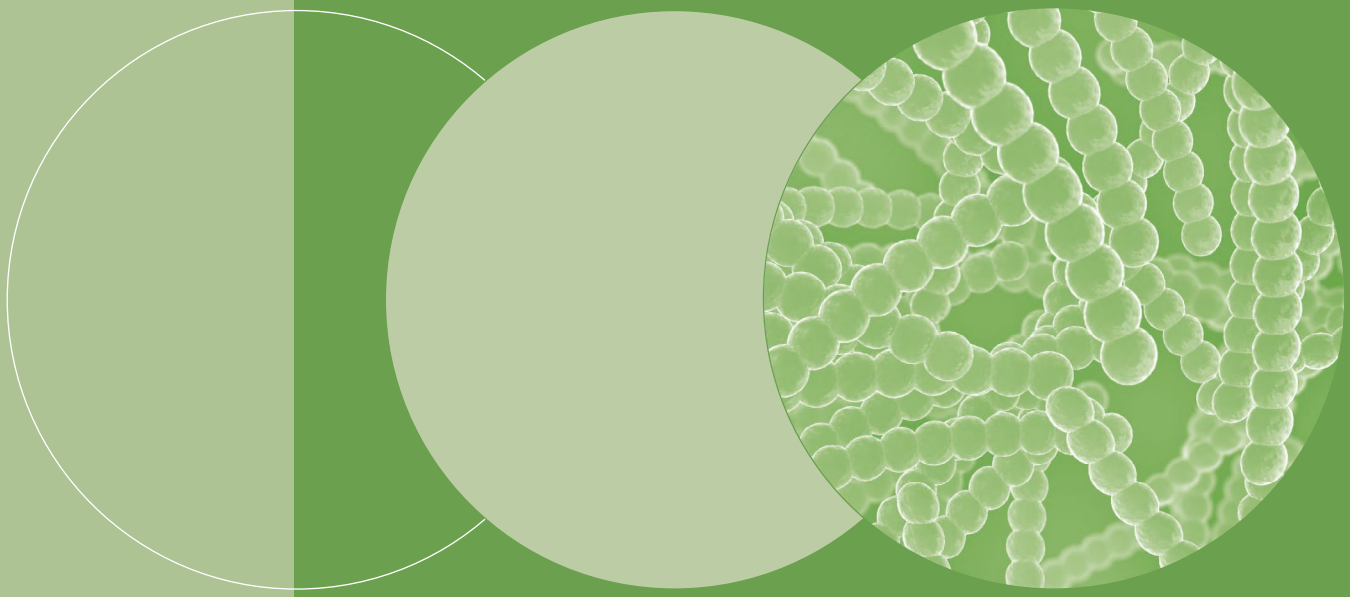
WHO recommendation on **Vaginal preparation with antiseptic agents for women undergoing caesarean section**



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Acronyms and abbreviations

CERQual	Confidence in the Evidence from Reviews of Qualitative Research
CHEC	Consensus Health Economic Criteria
DOI	declaration of interest
ERG	Evidence Review Group
ESG	Evidence Synthesis Group
EtD	evidence-to-decision
FIGO	International Federation of Gynecology and Obstetrics
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GSG	Guideline Steering Group
HRP	UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction
ICM	International Confederation of Midwives
MPH-GDG	Maternal and Perinatal Health Guideline Development Group
PICO	population (P), intervention (I), comparator (C), outcome (O)
UNDP	United Nations Development Programme
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Fund
USAID	United States Agency for International Development
WHO	World Health Organization

Executive summary

Introduction

Direct maternal infections around the time of childbirth account for about one tenth of the global burden of maternal death. Women who develop peripartum infections are also prone to severe morbidity, long-term disabilities such as chronic pelvic pain, fallopian tube blockage and secondary infertility. Maternal infections before or during childbirth are also associated with an estimated 1 million newborn deaths annually.

Several factors increase the risk of maternal peripartum infections, including pre-existing maternal conditions (e.g. malnutrition, diabetes, obesity, severe anaemia, bacterial vaginosis and group B streptococcus infections), as well as prelabour rupture of membranes, multiple vaginal examinations, manual removal of the placenta, operative vaginal birth and caesarean section. As such, the strategies to reduce maternal peripartum infections and their short- and long-term complications have been directed at improving infection prevention and control practices.

Globally, an effective intervention for preventing morbidity and mortality related to maternal infection is the use of antibiotics and antiseptics. However, the misuse of antibiotics for obstetric conditions and procedures is common in many settings. Inappropriate antibiotic use has implications for the global effort to prevent and reduce antimicrobial resistance. The *WHO global strategy for containment of antimicrobial resistance* underscores the importance of appropriate use of antimicrobials at different levels of the health system to reduce the impact of antimicrobial resistance, while ensuring access to the best treatment available.

In 2019, the Executive Guideline Steering Group (GSG) for World Health Organization (WHO) maternal and perinatal health recommendations prioritized updating of the existing WHO recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section in response to the availability of new evidence. The recommendation in this document thus supersedes the previous WHO recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section, as published in the 2015 guideline *WHO recommendations for prevention and treatment of maternal peripartum infections*.

Target audience

The primary audience for this recommendation includes health professionals who are responsible for developing national and local health-care guidelines and protocols (particularly those related to the prevention and treatment of peripartum infections) and those involved in the provision of care to women and their newborns during labour and childbirth, including midwives, nurses, general medical practitioners and obstetricians, as well as managers of maternal and child health programmes, and relevant staff in ministries of health and training institutions, in all settings.

Guideline development methods

The updating of this recommendation was guided by standardized operating procedures in accordance with the process described in the *WHO handbook for guideline development*. The recommendations were initially developed and updated using this process, namely: (i) identification of priority questions and outcomes; (ii) retrieval of evidence; (iii) assessment and synthesis of evidence; (iv) formulation of the recommendations; and (v) planning for the dissemination, implementation, impact evaluation and future updating of the recommendations.

The scientific evidence supporting the recommendation was synthesized using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. An updated systematic review was used to prepare the evidence profiles for the prioritized question. WHO convened a meeting on 19–20 October 2020 where the Guideline Development Group (GDG) members reviewed, deliberated and achieved consensus on

the strength and direction of the recommendation presented herein. The recommendation was formulated under one of the following categories: recommended, not recommended, recommended only in specific contexts (the intervention is applicable only to the condition, setting or population specified in the recommendation), recommended only in the context of rigorous research (implementation of the recommendation can still be undertaken provided it takes the form of research that addresses unanswered questions). Through a structured process, the GDG reviewed the balance between the desirable and undesirable effects and the overall certainty of supporting evidence, values and preferences of stakeholders, resource requirements and cost–effectiveness, acceptability, feasibility and equity.

Recommendations

The GDG reviewed the balance between the desirable and undesirable effects and the overall certainty of supporting evidence, values and preferences of stakeholders, resource requirements and cost–effectiveness, acceptability, feasibility and equity. The GDG issued the recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section with remarks and implementation considerations. To ensure that the recommendation is correctly understood and applied in practice, guideline users may want to refer to the remarks, as well as to the evidence summary, including the considerations on implementation.

WHO recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section

Recommendation: Vaginal preparation with chlorhexidine gluconate or povidone-iodine immediately before caesarean section is recommended. (Recommended)

Remarks:

- While the evidence on vaginal preparation before caesarean section was largely derived from trials using povidone-iodine, benefit was demonstrated overall for any antiseptic (either povidone-iodine or chlorhexidine gluconate) versus no antiseptic. Included trials used varying concentrations of chlorhexidine gluconate (0.05% to 0.25%) or povidone-iodine (1% to 10%), and the base (aqueous or alcohol) was not described. However, the Guideline Development Group agreed that alcohol-based antiseptic solutions should not be used for vaginal preparation because of concerns around irritation of mucosa.
- This recommendation pertains to all women undergoing caesarean section regardless of their baseline risk of infectious morbidity following surgery (i.e. for caesarean section in women before or during labour, and women with intact or ruptured membranes).
- Whilst available trials were not clear on the timing of vaginal preparation relative to the caesarean section, the Guideline Development Group suggested that vaginal preparation should be performed as close to the start of caesarean section as possible (e.g. directly following preoperative urinary bladder catheterization) to minimize the woman's discomfort.
- The most appropriate method of vaginal preparation is not known. Trials underpinning this evidence used various methods including irrigation, scrubbing, wiping or rotating soaked gauzes or sponges in the vagina. The duration of vaginal preparation varied from 30 seconds to one minute. The Guideline Development Group noted that shorter application and contact time are likely to be associated with less maternal and fetal exposure, which is desirable. The use of a high concentration and/or repeated applications of povidone-iodine should be avoided to minimize maternal and fetal exposure and possible interference with the results of neonatal thyroid screening.

- Vaginal preparation with an antiseptic agent could be perceived as an invasive procedure. The Guideline Development Group emphasized the importance of informing women on the beneficial effects of vaginal preparation and ensuring that this is included in the informed consent process for caesarean section. The method and timing of vaginal preparation should be applied in a manner that ensures women's privacy and dignity.
- This recommendation supersedes Recommendation No. 16 of the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections*, where this was considered a conditional recommendation based on moderate-quality evidence.

Introduction

1.1 Background

In 2017, an estimated 11.9 million cases of direct maternal infections occurred worldwide *(1)*. Maternal deaths due to infection occur mainly through maternal sepsis, a life-threatening condition defined as organ dysfunction resulting from infection during pregnancy, childbirth, post-abortion or postpartum period *(2)*. In 2017, an estimated 5.7 million women developed sepsis during pregnancy, childbirth or the postpartum period *(3)*. Infections during or following childbirth not only increase maternal mortality and short-term morbidities, but also can lead to long-term disabilities such as chronic pelvic pain, fallopian tube blockage and secondary infertility *(4)*. Maternal infections around childbirth also have a considerable impact on newborn mortality, causing an estimated 1 million newborn deaths annually *(5, 6)*. Infection-related morbidities and prolonged hospitalization can interfere with mother–infant bonding in the first days after birth *(7)*.

Several factors have been associated with increased risk of maternal infections, including pre-existing maternal conditions (e.g. malnutrition, diabetes, obesity, severe anaemia, bacterial vaginosis and group B streptococcus infections), as well as prelabour rupture of membranes, multiple vaginal examinations, manual removal of the placenta, severe perineal trauma, operative vaginal birth and caesarean section *(8, 9)*.

Caesarean section is notably the most important risk factor for infection in the immediate postpartum period, with a fivefold to 20-fold increased risk compared to vaginal birth *(8, 9)*. Peripartum infections associated with caesarean section include infection at the wound/incision site, endometritis and urinary tract infection. Rarer, more serious complications include pelvic abscesses, bacteraemia, septic shock, necrotising fasciitis and septic pelvic vein thrombophlebitis, which can lead to death *(10)*. Serious peripartum infections typically require therapeutic antibiotics, prolonged hospital stays and potentially additional surgery *(11)*. Globally, the incidence of post-caesarean infection varies from 2.5% to 20.5% *(12)*.

Endometritis after caesarean section is a particular concern due to bacteria present in vagina and cervix that move higher in the genital tract and uterus during surgery *(13, 14)*. Currently, vaginal preparation (i.e. application of an antiseptic agent to the vagina) is routinely used prior to obstetric and gynaecological surgical procedures, such as caesarean section or hysterectomy, to prevent post-operative infectious complications *(15)*. Antiseptic agents may be administered in a variety of ways, whether by washing, cleansing, painting or scrubbing. Gauzes, sponges or wipes soaked in antiseptic agents may be used. In addition to vaginal preparation with antiseptic, the risk of infection after caesarean section can be reduced by using sound surgical techniques, skin antiseptics and antibiotic prophylaxis.

The prevention, early diagnosis and prompt management of sepsis are key factors for reducing related sepsis-related morbidity and mortality, as reflected in the 2017 *WHA70.7 Resolution: Improving the prevention, diagnosis and clinical management of sepsis (16)*. Globally, an effective intervention for reducing morbidity and mortality related to maternal infection is the prophylactic and therapeutic use of antibiotics in conjunction with the use of sound surgical techniques and topical antiseptic agents. Antibiotics are widely used (and misused) for obstetric conditions *(17, 18)*. Apart from poor outcomes associated with such practices, there is increasing concern that inappropriate use and misuse of antibiotics among women giving birth could compromise public health through the emergence of antibiotic-resistant bacterial strains.

According to the 2015 *WHO global action plan on antimicrobial resistance*, the global consumption of antibiotics in humans has risen in the past two decades, primarily driven by an increased use in low- and middle-income countries *(17, 18)*. The action plan underscores the importance of appropriate use of antimicrobials at different levels of the health system to reduce the impact of antimicrobial resistance, while ensuring access to the best treatment

available *(19)*. WHO guidelines for health-care professionals and policy-makers on strategies for the prevention and treatment of maternal infections, including topical antiseptic agents and antibiotic prophylaxis, align with the WHO strategy and, ultimately, improve maternal and newborn outcomes.

1.2 Rationale and objectives

WHO has established a new process for prioritizing and updating maternal and perinatal health recommendations, whereby an international group of independent experts – the Executive Guideline Steering Group (GSG) – oversees a systematic prioritization of maternal and perinatal health recommendations in most urgent need of updating (20, 21). Recommendations are prioritized for updating on the basis of changes or important new uncertainties in the underlying evidence based on benefits, harms, values placed on outcomes, acceptability, feasibility, equity, resource use, cost–effectiveness or factors affecting implementation. The Executive GSG prioritized updating of the existing WHO recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section after the publication of new evidence on this intervention.

This updated recommendation was developed in accordance with the standards and procedures in the *WHO handbook for guideline development*, including synthesis of available research evidence, use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE)[1] and GRADE Confidence in the Evidence from Reviews of Qualitative Research (GRADE-CERQual)[2] methodologies, and formulation of recommendations by a Guideline Development Group (GDG) composed of international experts and stakeholders *(22)*. The recommendation in this document thus supersedes the previous WHO recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section as published in the 2015 guideline *WHO recommendations for prevention and treatment of maternal peripartum infections (23)*. The primary aim of this recommendation is to improve the quality of care and outcomes for women giving birth, as they relate to peripartum infection and its complications. This recommendation thus provides a foundation for sustainable implementation of vaginal preparation with antiseptic agents for women undergoing caesarean section.

1.3 Target audience

The primary audience includes health professionals who are responsible for developing national and local health-care guidelines and protocols (particularly those related to the prevention and treatment of peripartum infections) and those involved in the provision of care to women during labour and childbirth, including midwives, nurses, general medical practitioners and obstetricians, as well as managers of maternal and child health programmes, and relevant staff in ministries of health and training institutions, in all settings.

This recommendation will also be of interest to women giving birth, as well as members of professional societies involved in the care of pregnant women, staff of nongovernmental organizations concerned with promoting people-centred maternal care, and implementers of maternal and perinatal health programmes.

[1] Further information is available at: http://www.gradeworkinggroup.org/.
[2] Further information is available at: https://www.cerqual.org/.

1.4 Scope of the recommendation

Framed using the population (P), intervention (I), comparator (C), outcome (O) (PICO) format, the question for this recommendation was:

- Among pregnant women undergoing caesarean section (P), does vaginal preparation with an antiseptic agent prior to caesarean section (I), compared with no vaginal preparation with an antiseptic agent (C), prevent post-operative maternal infectious morbidities (O)?

1.5 Persons affected by the recommendation

The population affected by this recommendation includes all pregnant women in labour.

2. Methods

The recommendation was developed using standardized operating procedures in accordance with the process described in the *WHO handbook for guideline development (22)*. In summary, the process included: (i) identification of the priority question and critical outcomes; (ii) retrieval of evidence; (iii) assessment and synthesis of evidence; (iv) formulation of the recommendation; and (v) planning for the dissemination, implementation, impact evaluation and updating of the recommendation.

In 2019, vaginal preparation with antiseptic agents for women undergoing caesarean section was identified by the Executive GSG as a high priority for development of an updated recommendation, in response to new evidence on this question. Six main groups were involved in this process, with their specific roles described below.

2.1 Contributors to the guideline

2.1.1 Executive Guideline Steering Group (GSG)

The Executive GSG is an independent panel of 14 external experts and relevant stakeholders from the six WHO regions: African Region, Region of the Americas, Eastern Mediterranean Region, European Region, South-East Asia Region and Western Pacific Region. The Executive GSG advises WHO on the prioritization of new and existing PICO questions in maternal and perinatal health for development or updating of recommendations *(20, 21)*.

2.1.2 WHO Steering Group

The WHO Steering Group, comprising WHO staff members from the Department of Sexual and Reproductive Health and Research, the Department of Maternal, Newborn, Child and Adolescent Health and Ageing and the Antimicrobial Resistance Division and Infection Prevention & Control Technical and Clinical Hub, managed the process of updating the recommendations. The WHO Steering Group drafted the key recommendation questions in PICO format, engaged the systematic review teams and guideline methodologists (that is, the Evidence Synthesis Group [ESG]), as well as the members of the GDG and the External Review Group (ERG) (see below). In addition, the WHO Steering Group supervised the retrieval and syntheses of evidence, organized the GDG meetings, drafted and finalized the guideline document, and will also manage the guideline dissemination, implementation and impact assessment. The members of the WHO Steering Group are listed in Annex 1.

2.1.3 Guideline Development Group (GDG)

The WHO Steering Group identified a pool of approximately 50 experts and relevant stakeholders from the six WHO regions to constitute the WHO Maternal and Perinatal Health Guideline Development Group (MPH-GDG). This pool consists of a diverse group of experts who are skilled in the critical appraisal of research evidence, implementation of evidence-informed recommendations, guideline development methods, and clinical practice, policy and programmes relating to maternal and perinatal health, as well as a consumer representative. Members of the MPH-GDG are identified in a way that ensures geographic representation and gender balance, and there were no perceived or real conflicts of interest. Members' expertise cuts across thematic areas within maternal and perinatal health.

From the MPH-GDG pool, 16 external experts and relevant stakeholders were invited to participate as members of the GDG for updating this recommendation. Those selected were a diverse group with expertise in research, guideline development methods, gender, equity and rights, clinical practice, policy and programmes, consumer representatives relating to prevention and treatment of peripartum infection.

The GDG members for this recommendation were also selected in a way that ensured geographic representation and gender balance and there were no important conflicts of

interest. The GDG appraised the evidence that was used to inform the recommendation, advised on the interpretation of this evidence, formulated the final recommendation based on the draft prepared by the WHO Steering Group and reviewed and reached unanimous consensus for the recommendation in the final document. The members of the GDG are listed in Annex 1.

2.1.4 Evidence Synthesis Group (ESG)

WHO convened an ESG composed of guideline methodologists and systematic review teams to conduct or update systematic reviews, appraise the evidence and develop the evidence-to-decision (EtD) frameworks. A systematic review on the effects of the intervention was updated, supported by the Cochrane Pregnancy and Childbirth Group *(24)*. The WHO Steering Group reviewed and provided input into the updated protocol and worked closely with the Cochrane Pregnancy and Childbirth Group and the guideline methodologist to appraise the evidence using the GRADE methodology. Representatives of the Cochrane Pregnancy and Childbirth Group and a methodologist attended the GDG meeting to provide an overview of the available evidence and GRADE tables and to respond to technical queries from the GDG.

All members of the ESG attended the GDG meetings to provide an overview of the synthesized evidence and to respond to technical queries from the GDG. The members of the ESG are listed in Annex 1.

2.1.5 External partners and observers

Representatives of the United States Agency for International Development (USAID), the International Confederation of Midwives (ICM), the International Federation of Gynecology and Obstetrics (FIGO) and the Bill & Melinda Gates Foundation participated in the GDG meetings as observers. These organizations, with their long history of collaboration with WHO in maternal and perinatal health guideline dissemination and implementation, were identified as potential implementers of the recommendations. The list of observers who participated in the GDG meetings is included in Annex 1.

2.1.6 External Review Group (ERG)

The ERG included eight technical experts with interests and expertise in the prevention and treatment of peripartum infections. The group was geographically diverse and gender balanced, and the members had no important conflicts of interest. The experts reviewed the final document to identify any factual errors and commented on the clarity of language, contextual issues and implications for implementation. They ensured that the decision-making processes had considered and incorporated contextual values and the preferences of persons affected by the recommendations, health-care professionals and policy-makers. It was not within the remit of this group to change the recommendations that were formulated by the GDG. Members of the ERG are listed in Annex 1.

2.2 Identification of priority questions and outcomes

The priority outcomes were aligned with those from the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections (23)*. These outcomes were initially identified through a search of scientific databases for relevant, published systematic reviews and a prioritization of outcomes by the GDG for the 2015 guideline. In recognition of the importance of women's experiences of care, two additional outcomes – maternal well-being and maternal satisfaction – were included for this update to ensure that evidence synthesis and recommendation decision-making by the GDG were driven by outcomes that are important to women and to ensure that the final set of recommendations would be woman-centred. All the outcomes were included in the scope of this document for evidence searching, retrieval, synthesis, grading and formulation of the recommendation. The list of priority outcomes is provided in Annex 2.

2.3 Evidence identification and retrieval

Evidence to support this update was derived from several sources by the ESG working in collaboration with the WHO Steering Group.

2.3.1 Evidence on recommendation on vaginal preparation with antiseptic agents for women undergoing caesarean section

An existing systematic review on vaginal preparation with antiseptic agents for women undergoing caesarean section was updated *(25)*. Fourteen trials (4443 women) have been added since the last systematic review. This systematic review was the primary source of evidence of effectiveness for this recommendation. Randomized controlled trials relevant to the key question were screened by the review authors, and data on relevant outcomes and comparisons were entered into the Review Manager 5 (RevMan) software. The RevMan file was retrieved from the Cochrane Pregnancy and Childbirth Group and customized to reflect the key comparisons and outcomes (those that were not relevant to the recommendation were excluded). The RevMan file was then exported to the GRADE profiler (GRADEpro) software, and GRADE criteria were used to critically appraise the retrieved scientific evidence *(26)*. Finally, evidence profiles (in the form of GRADE summary of findings tables) were prepared for comparisons of interest, including the assessment and judgements for each outcome and the estimated risks.

2.3.2 Evidence on values, resource use and cost–effectiveness, equity, acceptability and feasibility

A mixed-methods systematic review was the primary source of evidence on values, acceptability and feasibility as they relate to the EtD framework on vaginal preparation for women undergoing caesarean section *(27)*. This review included views and experiences of women and health-care providers with antiseptics for preventing infection at birth. The review identified one qualitative study with 21 women who had undergone caesarean section in the United Kingdom of Great Britain and Northern Ireland *(28)*. Additionally, a systematic review of qualitative studies evaluating "what women want" from intrapartum care was used to further inform the values and equity domains *(29)*. Equity evidence was derived from two studies on availability and quality of antiseptic agents in low- and middle-income countries (30, 31). The included trials in the Cochrane review did not report on cost or resource-related outcomes. In addition, a structured search was conducted (up to 17 July 2020), and no studies were identified. Therefore, expert opinion was used, and the GDG agreed that implementation of this intervention was likely to slightly increase costs where it is not currently in practice, due to use of additional antiseptic agents. However, the increase may be cost-effective due to the low costs of antiseptic agents already available in maternity settings and the low resources in terms of staff time or skills needed to implement the intervention.

2.4 Certainty assessment and grading of the evidence

The certainty assessment of the body of evidence on effects for each outcome was performed using the GRADE approach *(32)*. Using this approach, the certainty of evidence for each outcome was rated as "high", "moderate", "low" or "very low" based on a set of established criteria. The final rating of certainty of evidence was dependent on the factors briefly described below.

Study design limitations: The risk of bias was first examined at the level of each individual study and then across the studies contributing to the outcome. For randomized trials, certainty was first rated as "high" and then downgraded by one ("moderate") or two ("low") levels, depending on the minimum criteria met by the majority of the studies contributing to the outcome.

Inconsistency of the results: The similarity in the results for a given outcome was assessed by exploring the magnitude of differences in the direction and size of effects observed in different studies. The certainty of evidence was not downgraded when the directions of the

findings were similar and confidence limits overlapped, whereas it was downgraded when the results were in different directions and confidence limits showed minimal or no overlap.

Indirectness: The certainty of evidence was downgraded when there were serious or very serious concerns regarding the directness of the evidence, that is, whether there were important differences between the research reported and the context for which the recommendation was being prepared. Such differences were related, for instance, to populations, interventions, comparisons or outcomes of interest.

Imprecision: This assessed the degree of uncertainty around the estimate of effect. As this is often a function of sample size and number of events, studies with relatively few participants or events, and thus wide confidence intervals around effect estimates, were downgraded for imprecision.

Publication bias: The certainty rating could also be affected by perceived or statistical evidence of bias to underestimate or overestimate the effect of an intervention as a result of selective publication based on study results. Downgrading evidence by one level was considered where there was strong suspicion of publication bias.

Certainty of evidence assessments are defined according to the GRADE approach:

- **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.

The findings of the qualitative reviews were appraised for quality using the GRADE-CERQual tool *(33)*, which uses a similar conceptual approach to other GRADE tools and provides a transparent method for assessing and assigning the level of confidence that can be placed in evidence from reviews of qualitative research. The systematic review team used the GRADE-CERQual tool to assign a level of confidence (high, moderate, low and very low) to each review finding according to four components: methodological limitations of the individual studies; adequacy of data; coherence; and relevance to the review question of the individual studies contributing to a review finding. Findings from individual cost–effectiveness studies were reported narratively for each comparison of interest. Available evidence was assessed using the Consensus Health Economic Criteria (CHEC) checklist *(34)*.

2.5 Formulation of the recommendation

The WHO Steering Group supervised and finalized the preparation of summary of findings tables and narrative evidence summaries in collaboration with the ESG using the GRADE EtD framework. EtD frameworks include explicit and systematic consideration of evidence on prioritized interventions in terms of specified domains: effects, values, resources, equity, acceptability and feasibility. For the priority questions, judgements were made on the impact of the intervention on each domain to inform and guide the decision-making process. Using the EtD framework template, the WHO Steering Group and ESG created summary documents for each priority question covering evidence on each domain:

- **Effects:** The evidence on the priority outcomes was summarized in this domain to answer the questions: "What are the desirable and undesirable effects of the intervention?" and "What is the certainty of the evidence on effects?" Where benefits clearly outweighed harms for outcomes that are highly valued by women, or vice versa, there was a greater likelihood of a clear judgement in favour of or against the intervention, respectively. Uncertainty about the net benefits or harms, or small net benefits, usually led to a

judgement that did not favour the intervention or the comparator. The higher the certainty of the evidence of benefits across outcomes, the higher the likelihood of a judgement in favour of the intervention. In the absence of evidence of benefits, evidence of potential harm led to a recommendation against the intervention. Where the intervention showed evidence of potential harm and was also found to have evidence of important benefits, depending on the level of certainty and the likely impact of the harm, such evidence of potential harm was more likely to result in a context-specific recommendation, with the context explicitly stated within the recommendation.

- **Values:** This domain relates to the relative importance assigned to the outcomes associated with the intervention by those affected, how such importance varies within and across settings, and whether this importance is surrounded by any uncertainty. The question asked was: "Is there important uncertainty or variability in how much women value the main outcomes associated with the intervention?" When the intervention resulted in benefit for outcomes that most women consistently value (regardless of setting), this was more likely to lead to a judgement in favour of the intervention. This domain, together with the "effects" domain (see above), informed the "balance of effects" judgement.
- **Resources:** For this domain, the questions asked were: "What are the resources associated with the intervention?" and "Is the intervention cost-effective?" The resources required to implement vaginal preparation with antiseptic agents for women undergoing caesarean section, training, and monitoring and evaluation. A judgement in favour of or against the intervention was likely where the resource implications were clearly advantageous or disadvantageous, respectively.
- **Acceptability:** For this domain, the question was: "Is the intervention acceptable to women and health-care providers?" The lower the acceptability, the lower the likelihood of a judgement in favour of the intervention.
- **Feasibility:** The feasibility of implementing this intervention depends on factors such as the resources, infrastructure and training requirements, and the perceptions of health-care providers responsible for administering it. The question addressed was: "Is it feasible for the relevant stakeholders to implement the intervention?" Where major barriers were identified, it was less likely that a judgement would be made in favour of the intervention.
- **Equity:** This domain encompasses evidence or considerations as to whether or not the intervention would reduce health inequities. Therefore, this domain addressed the question: "What is the anticipated impact of the intervention on equity?". The intervention was likely to be recommended if its proven (or anticipated) effects reduce (or could reduce) health inequalities among different groups of women and their families.

For each of the above domains, additional evidence of potential harms or unintended consequences are described in the Additional considerations subsections. Such considerations were derived from studies that might not have directly addressed the priority question but provided pertinent information in the absence of direct evidence. These were extracted from single studies, systematic reviews or other relevant sources.

The WHO Steering Group provided the EtD framework, including evidence summaries, summary of findings tables and other documents related to the recommendation, to the GDG members two weeks in advance of the GDG meeting. The GDG members were asked to review and provide comments (electronically) on the documents before the GDG meeting. During the GDG meeting (19–20 October 2020), which was conducted under the leadership of the GDG chairperson, the GDG members collectively reviewed the EtD framework, and any comments received through preliminary feedback, and formulated the recommendations. The purpose of the meeting was to reach consensus on the recommendation and the specific context, based on explicit consideration of the range of evidence presented in the EtD framework and the judgement of the GDG members. The GDG was asked to select one of the following categories for the recommendation:

- **Recommended:** This category indicates that the intervention should be implemented.
- **Not recommended:** This category indicates that the intervention should not be implemented.
- **Recommended only in specific contexts ("context-specific recommendation"):** This category indicates that the intervention is applicable only to the condition, setting or population specified in the recommendation and should only be implemented in these contexts.
- **Recommended only in the context of rigorous research ("research-context recommendation"):** This category indicates that there are important uncertainties about the intervention. With this category of recommendation, implementation can still be undertaken on a large scale, provided it takes the form of research that addresses unanswered questions and uncertainties related both to effectiveness of the intervention or option, and its acceptability and feasibility.

2.6 Management of declarations of interests

WHO has a robust process to protect the integrity of its normative work, as well as to protect the integrity of individual experts with whom it collaborates. WHO requires that experts serving in an advisory role disclose any circumstances that could give rise to actual or ostensible conflict of interest. The disclosure and the appropriate management of relevant financial and non-financial conflicts of interest of GDG members and other external experts, including external reviewers and contributors are a critical part of guideline development at WHO. According to WHO regulations, all experts must declare their interests prior to participation in WHO guideline development processes and meetings according to the guidelines for declaration of interest (DOI) for WHO experts *(22)*. All GDG and ERG members were therefore required to complete a standard WHO DOI form before engaging in the guideline development process and before participating in the guideline-related processes. The WHO Steering Group reviewed all declarations before finalizing the experts' invitations to participate. Where any conflict of interest was declared, the WHO Steering Group determined whether such conflicts were serious enough to affect an expert's objective judgement in the guideline and recommendation development process. To ensure consistency, the WHO Steering Group applied the criteria for assessing the severity of conflict of interests as outlined in the *WHO handbook for guideline development* to all participating experts *(22)*. All findings from the DOI statements received were managed in accordance with the WHO procedures to assure the work of WHO and the contributions of its experts is, actually and ostensibly, objective and independent. The names and biographies of individuals were published online two weeks prior to the meeting. Where a conflict of interest was not considered significant enough to pose any risk to the guideline development process or to reduce its credibility, the experts were only required to openly declare such conflicts of interest at the beginning of the GDG meeting, and no further actions were taken. Annex 3 shows a summary of the DOI statements and how conflicts of interest declared by invited experts were managed by the WHO Steering Group.

2.7 Decision-making during the GDG meetings

During the meeting, the GDG reviewed and discussed the evidence summary and sought clarification. In addition to evaluating the balance between the desirable and undesirable effects of the intervention and the overall certainty of the evidence, the GDG applied additional criteria based on the GRADE EtD framework to determine the direction and strength of the recommendation. These criteria included stakeholders' values, resource implications, acceptability, feasibility and equity. Considerations were supported by evidence from a literature search as described in section 2.3.2 and the experience and opinions of the GDG members. EtD tables were used to describe and synthesize these considerations.

Decisions were made based on consensus, defined as the agreement by three quarters or more of the participants. None of the GDG members expressed opposition to the recommendation.

2.8 Document preparation

Prior to the online meeting, the WHO Steering Group prepared a draft version of the GRADE evidence profiles, the evidence summary and other documents relevant to the GDG's deliberation. The draft documents were made available to the participants of the meeting two weeks before the meeting for their comments. During the meeting, these documents were modified in line with the participants' deliberations and remarks. Following the meeting, members of the WHO Steering Group drafted a full guideline document to accurately reflect the deliberations and decisions of the participants. The draft document was sent electronically to the GDG and the ERG for their final review and approval.

2.9 Peer review

Following review and approval by the GDG members, the final document was sent to eight external independent experts of the ERG who were not involved in the guideline panel for peer review. The WHO Steering Group evaluated the inputs of the peer reviewers for inclusion in this document. After the meeting and external peer review, the modifications made by the WHO Steering Group to the document consisted only of the correction of factual errors and improving language to address any lack of clarity.

3. Guiding principles, best practice, recommendation and supporting evidence

3.1 Guiding principles and best practice

The participants in the 2015 technical consultation on prevention and treatment of peripartum infection agreed that the following overarching principles were applicable to the recommendations on prevention and treatment of peripartum infections. These guiding principles and best practice statements were adopted by the 2020 GDG panel. The principles and best practice statements are based on expert consensus and are not derived from a systematic process of evidence retrieval, synthesis and grading. They conform with the principles of good clinical practice that are needed to improve care related to the prevention or treatment of infectious morbidities around the time of childbirth. In addition to the strategies for implementation, monitoring and impact assessment presented later in this document, these principles are expected to guide end-users in the process of adapting and implementing this recommendation in a range of contexts and settings:

- Avoidance of infection by identifying and correcting predisposing factors to infection (e.g. by providing nutritional advice and addressing nutritional deficiencies, anaemia and other maternal medical conditions such as diabetes) during antenatal care.
- Standard infection prevention and precautions measures should be observed in the provision of maternity care to optimize the effects of interventions recommended in this guideline. These measures should include:
  - Promoting high quality standards of hand hygiene for the sterilization and storage of instruments and supplies and use of clean equipment; promoting aseptic surgical practices (e.g. following standard skin preparation techniques and proper use of antiseptic agents for surgical site preparation); use of personal protection equipment (for example, gloves and aprons, or surgical gowns); and use of safe products (e.g. blood products). Local protocols on infection prevention and control practices should be developed and implemented in accordance with existing WHO guidance *(35)*.
  - Improvement of health-care facilities physical environments (e.g. clean water, appropriate waste disposal and sanitation).
  - Clinical monitoring of women for signs of infection throughout labour and the postpartum period and early detection of infection by laboratory investigation as needed. This is particularly crucial for women who present with any form of illness around the time of childbirth, as poor monitoring and late detection of severe infection are known contributory factors to infection-related severe maternal morbidity and death. Before hospital discharge, women should be counselled on how to identify and promptly seek care for any danger signs of infection during the postpartum period *(36)*.
  - Clear guidance and protocols are needed for the prompt recognition, timely management and transfer to specialized services (e.g. intensive care unit) of women with maternal sepsis (organ dysfunction resulting from infection) and septic shock (hypotension due to sepsis not reversed with fluid resuscitation) and ensure availability of a protocol on resuscitation, antimicrobial therapy and subsequent supportive therapies. This protocol should be informed by internationally recommended guidelines and adapted to the local obstetric population and available skills and resources.
  - When transmission-based precautions are necessary to reduce or prevent nosocomial transmission of infections for women with peripartum infections, women should be provided care and support, while in an isolation ward, by appropriately trained health-care staff.

— Care should be organized in a way that facilitates staff behavioural change and encourages compliance with the hospital infection control measures. These should include but not be limited to staff training and feedback, use of information and educational materials, appropriate distribution of infection control equipment and materials, establishment of local protocols, infection surveillance, and clinical audit and feedback.

— National health systems need to ensure reliable supply systems, sustain availability and equitable access of good-quality, affordable antibiotics for use in maternal and perinatal health-care that are listed in the *WHO model list of essential medicines*, and ensure that the necessary equipment are available wherever maternity services are provided. They also need to ensure that the core list of first-line and second-line antibiotics on the *WHO model list of essential medicines* are available at maternity care facilities. This includes establishing robust and sustainable regulatory, procurement and logistics processes that can ensure good-quality medicines and equipment are obtained, transported and stored correctly.

- As part of the global efforts to reduce antimicrobial resistance, antibiotics should be administered only when there is a clear medical indication (as recommended in this guideline) and where the expected benefits outweigh the potential harms within the local context. It is essential to establish a hospital committee that monitors antimicrobial usage, including the quantity and patterns of use, feeds back the results to the prescribers and regularly updates the hospital antimicrobial formularies *(37)*.
- To the extent possible, prophylactic and therapeutic use of antibiotics should be informed by the narrowest antibacterial spectrum, the woman's history (including drug intolerance), the simplest effective dose in terms of antibiotic class and regimen, cost–effectiveness, bacterial agents most likely to cause infection and local susceptibility patterns in the hospital and in the community. Bacterial culture samples should be obtained before initiating antibiotics therapy, but this should not prevent prompt administration of antibiotics. Additionally, the choice of antiseptics and antibiotics should be guided by maternal conditions and aimed at avoiding adverse effects. Ideally, the use of antimicrobials in any setting should be informed by local or national resistance surveillance data and treatment guidelines.

3.2 Recommendation and supporting evidence

The following section outlines the recommendation and the corresponding narrative summary of evidence for the prioritized question. The EtD table, summarizing the balance between the desirable and undesirable effects and the overall certainty of the supporting evidence, values and preferences of stakeholders, resource requirements, cost–effectiveness, acceptability, feasibility and equity that were considered in determining the strength and direction of the recommendation, is presented in the EtD framework (Annex 4).

The following recommendation was adopted by the GDG. Evidence on the effectiveness of this intervention was derived from the updated systematic review and summarized in GRADE tables (Annex 4).

To ensure that the recommendation is correctly understood and appropriately implemented in practice, additional remarks reflecting the summary of the discussion by the GDG are included under the recommendation.

Recommendation: Vaginal preparation with chlorhexidine gluconate or povidone-iodine immediately before caesarean section is recommended. *(Recommended)*

Remarks:

- While the evidence on vaginal preparation before caesarean section was largely derived from trials using povidone-iodine, benefit was demonstrated overall for any antiseptic (either povidone-iodine or chlorhexidine gluconate) versus no antiseptic. Included trials used varying concentrations of chlorhexidine gluconate (0.05% to 0.25%) or povidone-iodine (1% to 10%), and the base (aqueous or alcohol) was not described. However, the Guideline Development Group agreed that alcohol-based antiseptic solutions should not be used for vaginal preparation because of concerns around irritation of mucosa.
- This recommendation pertains to all women undergoing caesarean section regardless of their baseline risk of infectious morbidity following surgery (i.e. for caesarean section in women before or during labour, and women with intact or ruptured membranes).
- Whilst available trials were not clear on the timing of vaginal preparation relative to the caesarean section, the Guideline Development Group suggested that vaginal preparation should be performed as close to the start of caesarean section as possible (e.g. directly following preoperative urinary bladder catheterization) to minimize the woman's discomfort.
- The most appropriate method of vaginal preparation is not known. Trials underpinning this evidence used various methods including irrigation, scrubbing, wiping or rotating soaked gauzes or sponges in the vagina. The duration of vaginal preparation varied from 30 seconds to one minute. The Guideline Development Group noted that shorter application and contact time are likely to be associated with less maternal and fetal exposure, which is desirable. The use of a high concentration and/or repeated applications of povidone-iodine should be avoided to minimize maternal and fetal exposure and possible interference with the results of neonatal thyroid screening.
- Vaginal preparation with an antiseptic agent could be perceived as an invasive procedure. The Guideline Development Group emphasized the importance of informing women on the beneficial effects of vaginal preparation and ensuring that this is included in the informed consent process for caesarean section. The method and timing of vaginal preparation should be applied in a manner that ensures women's privacy and dignity.
- This recommendation supersedes Recommendation No. 16 of the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections*, where this was considered a conditional recommendation based on moderate-quality evidence.

4. Dissemination, adaptation and implementation of the recommendation

The dissemination and implementation of this recommendation are to be considered by all stakeholders involved in the provision of care for pregnant women at the international, national and local levels. There is a vital need to increase women's access to maternal health-care at community level and to strengthen the capacity at health-care facilities of all levels to ensure they can provide high-quality services and information to all women giving birth. It is therefore crucial that this recommendation be translated into care packages and programmes at country, health-care facility and community levels, where appropriate.

4.1 Recommendation dissemination

The recommendation will be disseminated through WHO regional and country offices, ministries of health, professional organizations, WHO collaborating centres, other United Nations agencies and nongovernmental organizations, among others. This recommendation will also be available on the WHO website and the WHO Reproductive Health Library.[1] Updated recommendations are also routinely disseminated during meetings or scientific conferences attended by WHO maternal and perinatal staff.

The executive summary and recommendation from this publication will be translated into the six United Nations languages and disseminated through the WHO regional offices.

4.2 Adaptation

National and subnational subgroups may be established to adapt and implement this recommendation based on an existing strategy. This process may include the development or revision of existing national guidelines or protocols based on the updated recommendation.

The successful introduction of evidence-based policies (relating to updated recommendations) depends on well-planned and participatory consensus-driven processes of adaptation and implementation. These processes may include the development or revision of existing national or local guidelines and protocols, often supported by ministries of health, United Nations agencies, local professional societies and other relevant leadership groups. An enabling environment should be created for the use of this recommendation, including changes in the behaviour of health-care practitioners to enable the use of evidence-based practices.

This recommendation should be adapted into documents and tools that are appropriate for different locations and contexts, to meet the specific needs of each country and health service. Modifications to the recommendations, where necessary, should be justified in an explicit and transparent manner.

In the context of humanitarian emergencies, the adaptation of the current recommendation should consider the integration and alignment with other response strategies. Additional considerations to the unique needs of women in emergency settings, including their values and preferences, should be made. Context-specific tools and toolkits may be required in addition to standard tools to support the implementation of the recommendation in humanitarian emergencies by stakeholders.

4.3 Implementation considerations

- This recommendation should be implemented in line with the guiding principles and best practice statements outlined in this recommendation

[1] Available at: www.who.int/rhl.

- Prior to caesarean section, women should be advised in the benefits and possible side-effects of vaginal preparation using an antiseptic agent. Informed consent should be obtained prior to its use.
- Health-care services should ensure that antiseptic agents in appropriate concentrations (aqueous chlorhexidine gluconate or povidone-iodine) are available wherever caesarean section is performed. Managers should be aware that chlorhexidine gluconate solutions should be stored and labelled as distinct products.

5. Research implications

The GDG identified important knowledge gaps that need to be addressed through primary research, which may have an impact on this recommendation. The following questions were identified as those that demand urgent priority:

- What is the most effective vaginal preparation (in terms of dose, method of application and duration) before caesarean section?
- Is vaginal preparation with antiseptic agents before caesarean section acceptable to women?

6. Applicability issues

6.1 Anticipated impact on the organization of care and resources

A number of factors (barriers) may hinder the effective implementation and scale-up of this recommendation. These factors may be related to the behaviours of patients (women or families) or health-care professionals and to the organization of care or health service delivery. As part of efforts to implement this recommendation, health system stakeholders may wish to consider the following potential barriers to their application:

- lack of understanding of the value of vaginal preparation with antiseptic agents for women undergoing caesarean section among women giving birth, families or communities;
- lack of human resources with the necessary training and skills to use antiseptic agents for vaginal preparation for women undergoing caesarean section;
- concerns from women, families or skilled health-care personnel and health system managers regarding the safety of vaginal preparation with antiseptic agents for women undergoing caesarean;
- lack of reliable supply systems and sustained availability and equitable access to antibiotics for use in obstetrics listed in the *WHO model list of essential medicines*;
- lack of current systems in place to monitor the use of antibiotics and antiseptic agents and antimicrobial resistance;
- lack of effective referral mechanisms and care pathways for women identified as needing additional care.

6.2 Monitoring and evaluating guideline implementation

The implementation and impact of this recommendation will be monitored at the health service, country and regional levels, as part of broader efforts to monitor and improve the quality of maternal and newborn care. The WHO document *Standards for improving quality*

of maternal and newborn care in health facilities (38) provides a list of prioritized input, output and outcome measures that can be used to define quality of care criteria and indicators and that should be aligned with locally agreed targets. In collaboration with the monitoring and evaluation teams of the WHO Department of Sexual and Reproductive Health and Research and the WHO Department of Maternal, Newborn, Child and Adolescent Health and Ageing, data on country- and regional-level implementation of the recommendation can be collected and evaluated in the short to medium term to assess its impact on national policies of individual WHO Member States.

Information on recommended indicators can also be obtained at the local level by interrupted time series or clinical audits. In this context, the GDG suggests the following indicators to be considered:

- Proportion of women giving birth by caesarean section who received vaginal preparation with chlorhexidine gluconate or povidone-iodine, calculated as the number of women who received vaginal preparation with chlorhexidine gluconate or povidone-iodine divided by the total number of women giving birth by caesarean section.
- Incidence of peripartum infection among women giving birth by caesarean section, calculated as the number of women with peripartum infection after caesarean section divided by the total number of women giving birth by caesarean section.

The first indicator provides an assessment of the use of evidence-based practices among women considered at higher risk of infection around childbirth, while the second indicator provides information on the efficacy of the intervention. WHO has developed specific guidance for evaluating the quality of care for severe maternal complications (including sepsis) based on the near-miss and criterion-based clinical audit concepts *(39)*.

7. Updating the recommendation

The Executive GSG convenes annually to review WHO's current portfolio of maternal and perinatal health recommendations and to help WHO prioritize new and existing questions for recommendation development and updating. Accordingly, this recommendation will be reviewed along with other recommendations for prioritization by the Executive GSG. If new evidence that could potentially impact the current evidence base is identified, the recommendation may be updated. If no new reports or information is identified, the recommendation may be revalidated.

Following publication and dissemination of the updated recommendation, any concerns about the validity of the recommendation should be promptly communicated to the guideline implementers, in addition to any plans to update the recommendation.

WHO welcomes suggestions regarding additional questions for inclusion in the updated recommendation. Please email your suggestions to srhmph@who.int.

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Annex 1. External experts and WHO staff involved in the preparation of the recommendation

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Annex 2. Priority outcomes used in decision-making

Priority outcomes (O):[1]

Critical outcomes:

- Severe infectious morbidity (sepsis, septic shock, laparotomy/hysterectomy for infection, maternal intensive care unit admission)
- Puerperal infection (endometritis with/without myometritis and with/without salpingitis causing maternal febrile morbidity)

Important outcomes:

- Wound infection[2]
- Side-effects of antiseptics (vaginal irritation/allergy)
- Maternal satisfaction
- Maternal well-being
- Cost of care

[1] These outcomes reflect the priority outcomes used in the development of this recommendation, in the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections*. The outcomes "maternal well-being" and "maternal satisfaction" have been added as part of this update. The labels of the outcomes "severe infectious morbidity" and "puerperal infection" were updated to reflect the current WHO definition of maternal sepsis.

[2] In this framework, the outcomes "post-operative wound infection" and "composite wound complications" (defined as the presence of any one of: wound infection, seroma, haematoma, wound separation) have been considered within the important outcome "wound infection".

Annex 3. Summary and management of declared interests from GDG members

Name	Expertise contributed to guideline development	Declared interest	Management of conflict of interest
Fatima Adamu	Content expert and end-user	None declared	Not applicable
Subha Sri Balakrishnan	Content expert and end-user	Senior Technical Officer, Centre for Maternal and Newborn Health (CMNH), Liverpool School of Tropical Medicine (March 2018–March 2020). CMNH received grants from United Nations Children's Fund (UNICEF), WHO India and National Health Mission Madhya Pradesh during this period.	The conflict was not considered serious enough to affect Guideline Development Group (GDG) membership or participation.
Michelle Bazari	Women's representative	None declared	Not applicable
Maria Laura Costa	Content expert and end-user	None declared	Not applicable
Jemima Dennis-Antiwi	Content expert and end-user	None declared	Not applicable
Hadiza Galadanci	Content expert and end-user	None declared	Not applicable
David Lissauer	Content expert and end-user	None declared	Not applicable
Pisake Lumbiganon	Content expert and end-user	None declared	Not applicable
Ashraf Nabhan	Content expert and end-user	None declared	Not applicable
James Neilson	Content expert and end-user	None declared	Not applicable
Hiromi Obara	Content expert and end-user	None declared	Not applicable
Alfred Osoti	Content expert and end-user	None declared	Not applicable
Haroon Saloojee	Content expert and end-user	None declared	Not applicable
Sadia Shakoor	Content expert and end-user	None declared	Not applicable
Rachel Smith	Content expert and end-user	None declared	Not applicable
Joseph Solomkin	Content expert and end-user	None declared	Not applicable

Annex 4. Evidence-to-decision framework

Question

The question of interest in PICO (population (P), intervention (I), comparator (C), outcome (O)) format:

- Among pregnant women undergoing caesarean section (P), does vaginal preparation with an antiseptic agent prior to caesarean section (I), compared with no vaginal preparation with an antiseptic agent (C), prevent post-operative maternal infectious morbidities (O)?

Problem: Preventing maternal infections at caesarean section

Perspective: Clinical practice recommendation – population perspective

Population (P): All pregnant women undergoing caesarean section

Intervention (I): Vaginal preparation with an antiseptic agent

Comparators (C): No vaginal preparation or vaginal preparation with saline solution

Setting: Hospital setting

Subgroups:

- Type of antiseptic agent
- Presence of labour
- Rupture of amniotic membranes

Priority outcomes (O):[1]

Critical outcomes:

- Severe infectious morbidity (sepsis, septic shock, laparotomy/hysterectomy for infection, maternal intensive care unit admission)
- Puerperal infection (endometritis with/without myometritis and with/without salpingitis causing maternal febrile morbidity)

Important outcomes:

- Wound infection[2]
- Side-effects of antiseptics (vaginal irritation/allergy)
- Maternal satisfaction
- Maternal well-being
- Cost of care

[1] These outcomes reflect the priority outcomes used in the development of this recommendation, in the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections*. The outcomes "maternal well-being" and "maternal satisfaction" have been added as part of this update. The labels of the outcomes "severe infectious morbidity" and "puerperal infection" were updated to reflect the current WHO definition of maternal sepsis.

[2] In this framework, the outcomes "post-operative wound infection" and "composite wound complications" (defined as the presence of any one of: wound infection, seroma, haematoma, wound separation) have been considered within the important outcome "wound infection".

Assessment

Effects of interventions

What is the effect of vaginal preparation with antiseptic solution before caesarean section versus the comparison (no preparation or saline preparation)?

Research evidence

Summary of evidence

Source and characteristics of studies

Evidence on the effects of vaginal preparation prior to caesarean section is from a Cochrane systematic review that included 21 trials with 7038 women *(1)*. The trials were published between 1997 and 2019 and were conducted in low-, middle- and high-income countries (United States of America, five trials; Turkey, three trials; Pakistan, three trials; Saudi Arabia, two trials; Egypt, two trials; Iran, two trials; one trial each in India, Kenya, Thailand and United Kingdom of Great Britain and Northern Ireland).

Fourteen trials (6157 women) compared vaginal preparation using an iodine-based solution versus no vaginal preparation, and four trials (721 women) compared vaginal preparation using chlorhexidine versus no preparation. One trial each compared chlorhexidine solution (14 women) or iodine-based solution (160 women) versus a saline solution. Another three-arm trial (150 women) compared povidone-iodine versus saline solution versus no washing. The review authors commented that this may lead to a lower baseline incidence of post-operative morbidity. One report had two intervention groups compared with controls without preparation – one group received povidone-iodine preparation (120 women) and one group received benzalkonium chloride preparation (150 women).

Most trials describe the intervention as vaginal washing, cleansing, preparation, painting or scrubbing. Preparations were administered by irrigation (one trial) or by using gauzes (four trials), sponges (three trials) or wipes (one trial), soaked in the intervention and/or control solutions. The technique for application was described in five trials: by scrubbing the vaginal walls (two trials), by rotating the gauze or sponge in the vagina 360 degrees (two trials) or just by introducing embedded wipes in the vagina (one trial) for one minute. The duration of the intervention also varied from 30 seconds (five trials) to one minute (two trials).

Six trials (1295 women) included women undergoing pre-labour caesarean section, twelve trials (5175 women) included women undergoing either pre-labour or intrapartum caesarean section, and two trials (868 women) included women who were in labour. The status of amniotic membranes varied among trials. Eight trials (1633 women) included women with intact membranes.[1] Eleven out of 21 trials reported they gave antibiotic prophylaxis to the participants; eight of these reported when it was administered (five prior to skin incision and three after cord clamping).

Effects of interventions

1) Vaginal preparation with antiseptic solution before caesarean section compared to no preparation or saline preparation

Severe infectious morbidity: Low certainty evidence suggests that there is no difference in the incidence of **maternal sepsis**[2] between the vaginal preparation with

[1] The Cochrane review authors indicated that for those trials that did not explicitly state the status of membranes, they assumed that all women presenting for a pre-labour caesarean section would have had intact membranes at time of enrolment.

[2] These outcomes reflect the priority outcomes used in the development of this recommendation, in the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections*. The outcomes "maternal well-being" and "maternal satisfaction" have been added as part of this update. The labels of the outcomes "severe infectious morbidity" and "puerperal infection" were updated to reflect the current WHO definition of maternal sepsis.

chlorhexidine compared to no intervention (1 trial, 309 women; RR 1.06, 95% CI 0.23 to 4.94).

Puerperal infection: Moderate certainty evidence suggests that vaginal preparation with antiseptic solution prior to caesarean section probably reduces **post-caesarean endometritis**, when compared to no vaginal preparation or preparation with saline solution (20 studies, 6918 women; RR 0.41, 95% CI 0.29 to 0.58). Moderate certainty evidence suggests vaginal preparation with antiseptic solution prior to caesarean section probably reduces the risk of **post-operative fever** when compared to no vaginal preparation or preparation with saline solution (16 trials, 6163 women; RR 0.64, 95% CI 0.50 to 0.82).

Wound infection: Moderate certainty evidence suggests that vaginal preparation with antiseptic solution probably reduces the risk of **post-operative wound infection** when compared to no vaginal preparation or preparation with saline solution (19 studies, 6385 women; RR 0.62, 95% CI 0.50 to 0.77). It is unclear whether vaginal preparation with an antiseptic agent affects the incidence of **composite wound complication**[1] (as defined by authors) as the certainty of the evidence is very low.

Side-effects: Low certainty evidence suggests that vaginal preparation may make little or no difference on side-effects of the intervention when compared to no vaginal preparation or preparation with saline solution.[2]

The outcomes **maternal satisfaction**, **maternal well-being** and **cost of care** were not reported in the Cochrane review.

Subgroup analyses

Even though there are well-described limitations in the use of subgroup analysis, the Guideline Development Group (GDG) opted to explicitly consider the subgroups (type of antiseptic agent, presence of labour, membrane status) due to:

- The 2015 GDG that formulated the previous version of this recommendation pre-specified the subgroup analyses as an integral part of the PICO questions;
- These subgroup analyses were not conducted to investigate heterogeneous results, but to (if possible) answer specific questions about benefits and possible harms in clinically important patient groups.

The subgroup analyses below should be interpreted with caution as the subgroups represent non-randomized comparisons that may have different abilities to detect effects. Their characteristics may overlap, and their influences on the intervention effect cannot be disentangled. For example, subgroup analysis by status of membranes might be influenced by presence of labour (i.e. it is likely that most of the 552 women with rupture of membranes were amongst the group of 1634 women in labour).

Subgroup analysis by type of antiseptic agent:

Twenty trials (6918 women) contributed data to this subgroup analysis.

- Vaginal preparation with iodine-based solution compared to no vaginal preparation or preparation with saline solution:
  - Probably reduces the risk of **post-operative endometritis** (16 studies, 6197 women; RR 0.41, 95% CI 0.28 to 0.60, moderate certainty evidence).
  - Probably reduces the risk of **post-operative fever** (14 studies, 5763 women; RR 0.66, 95% CI 0.50 to 0.87, moderate certainty evidence).

[1] Defined as the presence of any one of the following: wound infection, seroma, haematoma, separation.

[2] The Cochrane review authors indicated that four of the included trials commented on possible adverse events from the vaginal preparation solution; however, no adverse events were reported on the studies. They did not include this data on the meta-analysis, no reason was given.

- Probably reduces the risk of **post-operative wound infection** (15 studies, 5767 women; RR 0.64, 95% CI 0.50 to 0.81, moderate certainty evidence).

- Vaginal preparation with chlorhexidine-based solution compared to no vaginal preparation or preparation with saline solution:
  - May reduce the risk of **post-caesarean endometritis** (4 studies, 721 women; RR 0.38, 95% CI 0.16 to 0.89, low certainty evidence).
  - May reduce the risk of **post-operative fever** (2 studies, 400 women; RR 0.44 (95% CI 0.23 to 0.83, low certainty evidence).
  - Probably reduces the risk of **post-operative wound infection** (3 trials, 618 women; RR 0.53, 95% CI 0.31 to 0.90, moderate certainty evidence).

The outcomes **severe infectious morbidity**, **side-effects of antiseptics**, **maternal satisfaction**, **maternal well-being** and **cost of care** were not reported in the Cochrane review.

Subgroup analysis by presence of labour

The Cochrane review included 7 trials (2677 women) in this subgroup analysis comparing vaginal preparation with antiseptic versus no preparation or preparation with saline solution.

- For women **in labour**, vaginal preparation with antiseptic solution versus no vaginal preparation or preparation with saline solution:
  - Probably reduces the risk of **post-caesarean endometritis** (6 studies, 1634 women; RR 0.35, 95% CI 0.19 to 0.67, moderate certainty evidence).
  - Probably reduces the risk of **post-operative fever** (5 studies, 1415 women; RR 0.61 95% CI 0.42 to 0.87, moderate certainty evidence).
  - Probably reduces the risk of **post-operative wound infection** (5 studies, 1415 women; RR 0.52, 95% CI 0.30 to 0.90, moderate certainty evidence).

- For women **not in labour**, vaginal preparation with antiseptic solution versus no vaginal preparation or preparation with saline solution:
  - May make little or no difference in the risk of **post-caesarean endometritis** (5 trials, 1043 women; RR 0.86, 95% CI 0.33 to 2.21, low certainty evidence).
  - May make little or no difference in the risk of **post-operative fever** (3 trials, 818 women; RR 0.93, 95% CI 0.60 to 1.43, low certainty evidence).
  - The effect on **post-operative wound infection** is unclear as the evidence is very low certainty.

The priority outcomes **severe infectious morbidity**, **side-effects of antiseptics**, **maternal satisfaction**, **maternal well-being** and **cost of care** were not reported in the Cochrane review.

Subgroup analysis by amniotic membrane status (ruptured or not)

Vaginal preparation with antiseptic solution probably reduces the risk of **post-caesarean endometritis** regardless of membrane status, when compared to no vaginal preparation or preparation with saline solution:

- **women with ruptured membranes** (5 trials, 552 women; RR 0.23, 95% CI 0.12 to 0.45, moderate certainty evidence)

- **women with intact membranes** (8 trials, 2082; RR 0.48, 95% CI 0.34 to 0.68, moderate certainty evidence).

Vaginal preparation with antiseptic solution probably reduces the risk of **post-caesarean fever** regardless of membrane status, when compared to no vaginal preparation or preparation with saline solution:

- **women with ruptured membranes** (4 studies, 480 women; RR 0.42, 95% CI 0.22 to 0.80, moderate certainty evidence)
- **women with intact membranes** (7 trials, 1994 women; RR 0.70, 95% CI 0.49 to 0.99, moderate certainty evidence)

Vaginal preparation with antiseptic solution may reduce the risk of **composite wound complication** regardless of membrane status, when compared to no vaginal preparation or preparation with saline solution:

- **women with ruptured membranes** (1 trial, 76 women; RR 0.53, 95% CI 0.15 to 1.89, low certainty evidence)
- **women with intact membranes** (1 trial, 224 women; RR 0.73, 95% CI0.25 to 2.10, low certainty evidence).

Vaginal preparation with antiseptic solution probably reduces the risk of **post-operative wound infection** regardless of membrane status, when compared to no vaginal preparation or preparation with saline solution:

- **women with ruptured membranes** (5 studies, 552 women; RR 0.54, 95% CI 0.19 to 1.50, moderate certainty evidence)
- **women with intact membranes** (8 trials, 2082 women; RR 0.73, 95% CI 0.50 to 1.07, moderate certainty evidence)

The priority outcome **severe infectious morbidity** (sepsis, septic shock, laparotomy/ hysterectomy for infection, maternal intensive care unit admission), **side-effects**, **maternal satisfaction**, **maternal well-being** and **cost of care** were not reported in the Cochrane systematic review.

Additional considerations

- Three small trials evaluated saline solution as the control group, out of the 21 included in the review. The comparisons included: povidone-iodine (n = 80) versus saline solution (n = 80) *(2)*; povidone-iodine (n = 50) versus saline solution (n = 50) versus no washing (n = 50) *(3)*; chlorhexidine (n = 6) versus saline solution (n = 8) *(4)*. Exclusion of these three trials yielded to no differences in the results for post-caesarean endometritis, post-operative fever or post-operative wound infection. None of these trials reported data on side-effects of the intervention or use of saline solution for vaginal cleansing.
- A systematic review and meta-analysis on the comparative efficacy of antiseptic formulations and their concentrations for vaginal preparation before caesarean delivery in the prevention of endometritis and other infectious complications was considered *(5)*. The review found that povidone-iodine 1% is the most effective vaginal antiseptic for preventing post-caesarean endometritis.
- The purpose of this study was to review the literature systematically and quantitate and summarize indirectly the comparative efficacy of antiseptic formulations and their concentrations that are used for the preparation of the vagina before caesarean delivery in the prevention of endometritis and other infectious complications.
- In the 2015 recommendation, the GDG added a remark that "the use of a high concentration and/or repeated applications of povidone-iodine should be avoided to minimize maternal and fetal exposure and possible interference with the results

of neonatal thyroid screening". This comes from a rapid review of literature that identified three randomized controlled trials and six cohort studies investigating the effect of vaginal exposure to povidone-iodine at delivery and maternal and newborn iodine levels and/or thyroid function. For this update, we conducted a new rapid review for evidence on neonatal risks of povidone-iodine antenatal exposure. The available evidence is indirect, coming from studies where povidone-iodine was applied for abdominal skin preparation prior to caesarean section (two studies) or vaginal preparation in women with lacerations prior to vaginal births (one study):

- A systematic review on the effects of povidone-iodine exposure in preterm neonates that included 14 studies *(6)*. Two were cohort studies where povidone-iodine was used for abdominal skin preparation prior to caesarean section. One included 73 babies exposed to povidone-iodine and 55 exposed to chlorhexidine, and the other included 24 babies exposed to povidone-iodine and 22 exposed to chlorhexidine. The babies were also exposed to povidone-iodine directly to the cord or the skin.
- A cohort study of 326 women in Iran described the effect of iodine containing disinfectants in preparation for caesarean section *(7)*.
- A case series of nine women in Italy described the effect of long-term (six months) vaginal application of povidone-iodine in pregnant women with vaginal infections *(8)*.

None of the aforementioned studies provided clear evidence regarding impairment of thyroid function in the neonates. These studies found that there was only a transient descent in thyroid-stimulating hormone (TSH) levels. However, iodine absorption from the intact vaginal mucosa may be different.

- A search of the literature identified a further three trials that compared vaginal preparation with chlorhexidine solution compared to povidone-iodine solution before caesarean section. Meta-analysis of these trials indicates that wound infection is probably reduced with chlorhexidine compared to povidone-iodine (3 studies, 1540 women; RR 0.43, 95%CI 0.22 to 0.85, moderate certainty evidence).

Desirable effects

How substantial are the desirable anticipated effects?

Judgement

— Don't know	— Varies	— Trivial	— Small	— Moderate	✓ Large

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

✓ Don't know	— Varies	— Large	— Moderate	— Small	— Trivial

Certainty of the evidence

What is the overall certainty of the evidence on effects?

— No included studies	— Very low	— Low	✓ Moderate	— High

Values

Is there important uncertainty about, or variability in, how much women (and their families) value the main outcomes?

Research evidence

A systematic review was conducted on the perspectives and experiences of women and health-care providers with antibiotics and antiseptics for preventing infection at birth. The review identified one qualitative study with 21 women who had undergone caesarean section in the United Kingdom *(9)*.Women's descriptions of recovery after caesarean section focused on their experiences of pain, the impact on mobility and care-giving and their concerns on the risks of wound infection or non-healing. Women described receiving inadequate information on the risk of post-operative infections, not being aware that endometritis was a possible complication or that endometritis could be prevented through vaginal cleansing.

A 2018 core outcome set for caesarean delivery maternal infectious morbidity outcomes was proposed on the basis of a systematic review of outcomes in 452 trials and a Delphi survey of 40 review authors *(10)*. The proposed core outcome set included endometritis (primary outcome), maternal mortality, wound infection, wound complications, febrile morbidity and neonatal morbidity.

Additional considerations

A 2018 systematic review of qualitative studies of "what women want" from intrapartum care found that most women want a positive birth experience (with good outcomes for mother and baby) but acknowledge that medical intervention may sometimes be necessary (*high confidence*) *(11)*. Most women, especially those giving birth for the first time, are apprehensive about labour and birth (*high confidence*) and wary of medical interventions, although in certain contexts and/or situations, women welcome interventions to address recognized complications (low confidence). Where interventions are introduced, women would like to receive relevant information from technically competent health-care providers who are sensitive to their needs (*high confidence*).

Judgement

— Important uncertainty or variability	— Possibly important uncertainty or variability	✓ Probably no important uncertainty or variability	— No important uncertainty or variability

Balance of effects

Does the balance between desirable and undesirable effects favour the intervention or the comparison?

Judgement

— Don't know	— Varies	— Favours no treatment	— Probably favours no treatment	— Does not favour either	— Probably favours vaginal preparation	✓ Favours vaginal preparation

Resources

How large are the resource requirements (costs)?

Research evidence

The included trials in the Cochrane review did not report on cost or resource-related outcomes. A structured search was conducted (up to 17 July 2020), and no studies were identified.

Additional considerations

Implementation of this intervention is likely to slightly increase costs where it is not currently in practice, due to use of additional antiseptic agents. However, the increase may be cost-effective due to the low costs of antiseptic agents, ready availability in maternity settings and low resources in terms of staff time or skills needed to implement the intervention.

Main resource requirements

Resource	Description
Staff	No additional staff requirements beyond theatre staff
Training	Some training required in addition to standard surgical sterile techniques and surgical site preparation for vaginal preparation technique and to monitor and manage expected and unexpected maternal and neonatal side-effects.
Supplies	Swabs Antiseptic solution: ■ Povidone-iodine solution (10%) – median price of $6.30 per L *(12)*. ■ Chlorhexidine (4%) – median price of $5.30 per L *(13)*.
Equipment and infrastructure	Minimal
Time	Minimal
Supervision and monitoring	Minimal

Resources required

Judgement

— Don't know	— Varies	— Large costs	— Moderate costs	✓ Negligible costs or savings	— Moderate savings	— Large savings

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement

✓ No included studies	— Very low	— Low	— Moderate	— High

Cost–effectiveness

Judgement

✓ Don't know	— Varies	— Favours no UBT treatment	— Probably favours no UBT treatment	— Does not favour either	— Probably favours vaginal preparation	— Favours vaginal preparation

Equity

What would be the impact on health equity?

Research evidence

A structured literature search identified no direct evidence on this question. However, the GDG considered that given the health benefits, if implemented, the intervention is likely to increase health equity.

Additional considerations

The availability of supplies required to observe infection control procedures in maternity care settings (such as antiseptic solution, gloves and running water) varies across low- and middle-income country settings *(14)*. The quality of antiseptic solution may also vary across settings *(14, 15)*. Overall, this intervention will likely increase health equity by preventing death and serious health consequences of peripartum infection with an inexpensive and easily implemented intervention. However, in settings where good-quality antiseptic solutions are not routinely stocked or available, the benefits of antibiotic prophylaxis may not be fully realized.

Judgement

— Don't know	— Varies	— Reduced	— Probably reduced	— Probably no impact	✓ Probably increased	— Increased

Acceptability

Is the intervention acceptable to key stakeholders?

Research evidence

A systematic review on the perspectives and experiences of women and health-care providers with antiseptic use at birth identified two relevant studies (Nigeria and Ireland) *(16–18)*. The evidence was somewhat indirect – the study in Nigeria pertained to infection control guidelines (including use of antiseptics), while the study in Ireland pertained to use of antiseptic agents for neuraxial procedures.

The review found a preference for specific antiseptic regimens as being due to health-care providers' beliefs about its benefits and some influence of local guidelines.

Additional considerations

The panel considered that this intervention is likely to be acceptable, considering that it is a common practice in many clinical settings and within the scope of practice of skilled health personnel performing caesarean section. The GDG also considered that vaginal preparation maybe viewed by some women as an invasive procedure.

Judgement

— Don't know	✓ Varies	— No	— Probably No	— Probably Yes	— Yes

Feasibility

Is the intervention feasible to implement?

Research evidence

A systematic review on the perspectives and experiences of women and health-care providers with antiseptic use at birth identified that health-care providers' non-compliance with antiseptic guidelines is affected by a lack of supervision and training, inadequate supply, absence of relevant policies or protocols, doubt about benefits, perceived lack of clinical evidence and lack of examples or directives from senior colleagues *(16)*.

Additional considerations

The panel considered that this intervention is likely to be feasible, considering that antiseptic agents are used routinely in maternity care settings. It is within the scope of practice of skilled health personnel performing caesarean section.

Judgement

— Don't know	— Varies	— No	— Probably No	✓ Probably Yes	— Yes

Summary of judgements table

Desirable effects	— Don't know	— Varies		— Trivial	— Small	— Moderate	✓ **Large**
Undesirable effects	✓ **Don't know**	— Varies		— Large	— Moderate	— Small	— Trivial
Certainty of the evidence	— No included studies			— Very low	— Low	✓ **Moderate**	— High
Values				— Important uncertainty or variability	— Possibly important uncertainty or variability	✓ **Probably no important uncertainty or variability**	— No important uncertainty or variability
Balance of effects	— Don't know	— Varies	— Favours no vaginal preparation	— Probably favours no vaginal preparation	— Does not favour either	— Probably favours vaginal preparation	✓ **Favours vaginal preparation**
Resources required	— Don't know	— Varies	— Large costs	— Moderate costs	✓ **Negligible costs or savings**	— Moderate savings	— Large savings
Certainty of the evidence on required resources	✓ **No included studies**			— Very low	— Low	— Moderate	— High
Cost–effectiveness	✓ **Don't know**	— Varies	— Favours no vaginal preparation	— Probably favours no vaginal preparation	— Does not favour either	— Probably favours vaginal preparation	— Favours vaginal preparation
Equity	— Don't know	— Varies	— Reduced	— Probably reduced	— Probably no impact	✓ **Probably increased**	— Increased
Acceptability	Don't know	✓ **Varies**		— No	— Probably No	— Probably Yes	— Yes
Feasibility	— Don't know	— Varies		— No	— Probably No	✓ **Probably Yes**	— Yes

Summary of findings tables

Question: Vaginal preparation with antiseptic solution before caesarean section compared to control (no preparation or saline preparation) for preventing post-operative infections.
Setting: Egypt, Iran, Kenia, Pakistan, Saudi Arabia, Thailand, Turkey, United Kingdom, United States of America.
Bibliography: Haas DM, Morgan S, Contreras K, Kimball S. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections. Cochrane Database Syst. Rev. 2020; 4:CD007892. doi:10.1002/14651858.CD007892.pub7.

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution before caesarean section	Control (no preparation or saline preparation)	Relative (95% CI)	Absolute (95% CI)		
COMPOSITE WOUND COMPLICATION												
2	randomized trials	serious[a]	serious[b]	not serious	serious[c]	none	21/372 (5.6%)	32/357 (9.0%)	RR 0.63 (0.37 to 1.07)	**33 fewer per 1000** (from 56 fewer to 6 more)	⨁◯◯◯ VERY LOW	CRITICAL
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS												
2	randomized trials	not serious	not serious	not serious	not serious	none	16/255 (6.3%)	33/244 (13.5%)	RR 0.46 (0.26 to 0.82)	**73 fewer per 1000** (from 100 fewer to 24 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
POST-CAESAREAN ENDOMETRITIS												
20	randomized trials	serious[a]	not serious	not serious	not serious	asymmetry in funnel plot[d]	105/3430 (3.1%)	252/3488 (7.2%)	RR 0.41 (0.29 to 0.58)	**43 fewer per 1000** (from 51 fewer to 30 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-CAESAREAN ENDOMETRITIS – IODINE-BASED SOLUTION												
16	randomized trials	serious[a]	not serious	not serious	not serious	none	94/3070 (3.1%)	222/3127 (7.1%)	RR 0.41 (0.28 to 0.60)	**42 fewer per 1000** (from 51 fewer to 28 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution before caesarean section	Control (no preparation or saline preparation)	Relative (95% CI)	Absolute (95% CI)		
POST-CAESAREAN ENDOMETRITIS – CHLORHEXIDINE-BASED SOLUTION												
4	randomized trials	very serious[e]	not serious	not serious	not serious	none	11/360 (3.1%)	30/361 (8.3%)	RR 0.38 (0.16 to 0.89)	**52 fewer per 1000** (from 70 fewer to 9 fewer)	⨁⨁◯◯ LOW	CRITICAL
POST-OPERATIVE FEVER												
16	randomized trials	serious[a]	not serious	not serious	not serious	none	238/3056 (7.8%)	374/3107 (12.0%)	RR 0.64 (0.50 to 0.82)	**43 fewer per 1000** (from 60 fewer to 22 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE FEVER – IODINE-BASED SOLUTION												
14	randomized trials	serious[a]	not serious	not serious	not serious	none	226/2854 (7.9%)	347/2909 (11.9%)	RR 0.66 (0.50 to 0.87)	**41 fewer per 1000** (from 60 fewer to 16 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE FEVER – CHLORHEXIDINE-BASED SOLUTION												
2	randomized trials	very serious[e]	not serious	not serious	not serious	none	12/202 (5.9%)	27/198 (13.6%)	RR 0.44 (0.23 to 0.83)	**76 fewer per 1000** (from 105 fewer to 23 fewer)	⨁⨁◯◯ LOW	CRITICAL
POST-OPERATIVE WOUND INFECTION												
18	randomized trials	serious[a]	not serious	not serious	not serious	none	127/3166 (4.0%)	209/3219 (6.5%)	RR 0.62 (0.50 to 0.77)	**25 fewer per 1000** (from 32 fewer to 15 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution before caesarean section	Control (no preparation or saline preparation)	Relative (95% CI)	Absolute (95% CI)		
POST-OPERATIVE WOUND INFECTION – IODINE-BASED SOLUTION												
15	randomized trials	serious[a]	not serious	not serious	not serious	none	108/2853 (3.8%)	174/2914 (6.0%)	RR 0.64 (0.50 to 0.81)	21 fewer per 1000 (from 30 fewer to 11 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT
POST-OPERATIVE WOUND INFECTION – CHLORHEXIDINE-BASED SOLUTION												
3	randomized trials	not serious	serious[b]	not serious	not serious	none	19/313 (6.1%)	35/305 (11.5%)	RR 0.53 (0.31 to 0.90)	54 fewer per 1000 (from 79 fewer to 11 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT
SIDE-EFFECTS												
2	randomised trials	not serious	not serious	not serious	very serious[a]	none	Two trials stated that none of the women included in these studies referred side effects or local reaction on the vaginal mucosa; however, this data was not included in the analysis (0/303 women vs 0/294 women)				⨁⨁◯◯ LOW	CRITICAL
MATERNAL SEPSIS												
1	randomized trial	not serious	not serious	not serious	very serious[b,c]	none	3/153 (2.0%)	3/156 (1.9%)	RR 1.06 (0.23 to 4.94)f	1 more per 1000 (from 15 fewer to 76 more)	⨁⨁◯◯ LOW	CRITICAL

CI: Confidence interval; RR: Risk ratio.

[a] Most of the pooled effect provided by studies "B" or "C" but without a substantial proportion (i.e. < 50%) from studies "C".

[b] Statistical heterogeneity ($Chi^2 \leq 0.05$)

[c] Wide confidence interval crossing the line of no effect

[d] Asymmetry is evident in funnel plot. However, not downgraded because, after some test run by the authors, they excluded possible publication bias. The authors stated that: "it is possible that some of the funnel plot asymmetry is present due to the wide variation in apparent population risk among the trials... These different baseline population risk differences may have contributed to the asymmetry".

[e] Most of the pooled effect provided by studies "B" or "C" but with a substantial proportion (i.e. > 50%) from studies "C".

[f] Maternal sepsis, reported in a single study, was not included in the review as the main paper was published after the data extraction. Authors reported three cases among the 153 women in the vaginal preparation with chlorhexidine group and three cases among the 156 women in the no intervention group.

Question: Vaginal preparation with antiseptic solution compared to control (no preparation or saline preparation) – stratified by presence of labour for preventing post-operative infections.
Setting: Egypt, Iran, Kenia, Pakistan, Saudi Arabia, Thailand, Turkey, United Kingdom, United States of America.
Bibliography: Haas DM, Morgan S, Contreras K, Kimball S. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections. Cochrane Database Syst. Rev. 2020; 4:CD007892. doi:10.1002/14651858.CD007892.pub7.

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of labour	Relative (95% CI)	Absolute (95% CI)		
COMPOSITE WOUND COMPLICATION												
2	randomized trials	serious[a]	not serious	not serious	serious[b]	none	21/372 (5.6%)	32/357 (9.0%)	RR 0.64 (0.38 to 1.09)	**32 fewer per 1000** (from 56 fewer to 8 more)	⨁⨁◯◯ LOW	CRITICAL
COMPOSITE WOUND COMPLICATION – WOMEN IN LABOUR												
2	randomized trials	very serious[c]	not serious	not serious	very serious[b,d]	none	11/155 (7.1%)	15/159 (9.4%)	RR 0.77 (0.36 to 1.61)	22 fewer per 1000 (from 60 fewer to 58 more)	⨁◯◯◯ VERY LOW	CRITICAL
COMPOSITE WOUND COMPLICATION – WOMEN NOT IN LABOUR												
2	randomized trials	serious[a]	not serious	not serious	very serious[b,d]	none	10/217 (4.6%)	17/198 (8.6%)	RR 0.54 (0.25 to 1.16)	**39 fewer per 1000** (from 64 fewer to 14 more)	⨁◯◯◯ VERY LOW	CRITICAL
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS												
2	randomized trials	not serious	not serious	not serious	not serious	none	16/255 (6.3%)	33/244 (13.5%)	RR 0.47 (0.27 to 0.85)	**72 fewer per 1000** (from 99 fewer to 20 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of labour	Relative (95% CI)	Absolute (95% CI)		
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS – WOMEN IN LABOUR												
2	randomized trials	not serious	not serious	not serious	serious[d,e]	none	5/76 (6.6%)	17/88 (19.3%)	RR 0.34 (0.13 to 0.87)	**127 fewer per 1000** (from 168 fewer to 25 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS – WOMEN NOT IN LABOUR												
2	randomized trials	serious[a]	not serious	not serious	very serious[b,d,e]	none	11/179 (6.1%)	16/156 (10.3%)	RR 0.60 (0.29 to 1.26)	41 fewer per 1000 (from 73 fewer to 27 more)	⨁◯◯◯ VERY LOW	CRITICAL
POST-CAESAREAN ENDOMETRITIS												
7	randomized trials	serious[a]	not serious	not serious	not serious	none	50/1347 (3.7%)	104/1330 (7.8%)	RR 0.47 (0.27 to 0.81)	**41 fewer per 1000** (from 57 fewer to 15 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-CAESAREAN ENDOMETRITIS – WOMEN IN LABOUR												
6	randomized trials	serious[a]	not serious	not serious	not serious	none	28/824 (3.4%)	76/810 (9.4%)	RR 0.35 (0.19 to 0.67)	**61 fewer per 1000** (from 76 fewer to 31 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-CAESAREAN ENDOMETRITIS – WOMEN NOT IN LABOUR												
5	randomized trials	serious[a]	not serious	not serious	serious[b]	none	22/523 (4.2%)	28/520 (5.4%)	RR 0.86 (0.33 to 2.21)	**8 fewer per 1000** (from 36 fewer to 65 more)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of labour	Relative (95% CI)	Absolute (95% CI)		
POST-OPERATIVE FEVER												
5	randomized trials	serious[a]	not serious	not serious	not serious	none	76/1124 (6.8%)	104/1109 (9.4%)	RR 0.72 (0.55 to 0.95)	**26 fewer per 1000** (from 42 fewer to 5 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE FEVER – WOMEN IN LABOUR												
5	randomized trials	serious[a]	not serious	not serious	not serious	none	43/714 (6.0%)	66/701 (9.4%)	RR 0.61 (0.42 to 0.87)	**37 fewer per 1000** (from 55 fewer to 12 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE FEVER – WOMEN NOT IN LABOUR												
3	randomized trials	serious[a]	not serious	not serious	serious[b]	none	33/410 (8.0%)	38/408 (9.3%)	RR 0.93 (0.60 to 1.43)	**7 fewer per 1000** (from 37 fewer to 40 more)	⨁⨁◯◯ LOW	CRITICAL
POST-OPERATIVE WOUND INFECTION												
5	randomized trials	not serious	not serious	not serious	not serious	none	32/1124 (2.8%)	55/1109 (5.0%)	RR 0.57 (0.37 to 0.88)	**21 fewer per 1000** (from 31 fewer to 6 fewer)	⨁⨁⨁⨁ HIGH	IMPORTANT
POST-OPERATIVE WOUND INFECTION – WOMEN IN LABOUR												
5	randomized trials	serious[a]	not serious	not serious	not serious	none	18/714 (2.5%)	35/701 (5.0%)	RR 0.52 (0.30 to 0.90)	**24 fewer per 1000** (from 35 fewer to 5 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of labour	Relative (95% CI)	Absolute (95% CI)		
POST-OPERATIVE WOUND INFECTION – WOMEN NOT IN LABOUR												
3	randomized trials	serious[a]	serious[f]	not serious	serious[b]	none	14/410 (3.4%)	20/408 (4.9%)	RR 0.67 (0.35 to 1.31)	**16 fewer per 1000** (from 32 fewer to 15 more)	⨁◯◯◯ VERY LOW	IMPORTANT

CI: Confidence interval; RR: Risk ratio.

[a] Most of the pooled effect provided by studies "B" or "C" but without a substantial proportion (i.e. < 50%) from studies "C".

[b] Wide confidence interval crossing the line of no effect.

[c] Most of the pooled effect provided by studies "B" or "C" but with a substantial proportion (i.e. > 50%) from studies "C".

[d] Few events.

[e] Small samples size.

[f] Statistical heterogeneity.

Question: Vaginal preparation with antiseptic solution compared to control (no preparation or saline preparation) – stratified by presence of ruptured membranes for preventing post-operative infections.
Setting: Egypt, Iran, Kenia, Pakistan, Saudi Arabia, Thailand, Turkey, United Kingdom, United States of America.
Bibliography: Haas DM, Morgan S, Contreras K, Kimball S. Vaginal preparation with antiseptic solution before cesarean section for preventing postoperative infections. Cochrane Database Syst. Rev. 2020; 4:CD007892. doi:10.1002/14651858.CD007892.pub7.

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of ruptured membranes	Relative (95% CI)	Absolute (95% CI)		
COMPOSITE WOUND COMPLICATION												
1	randomized trial	not serious	not serious	not serious	very serious[a,b]	none	9/155 (5.8%)	14/145 (9.7%)	RR 0.64 (0.28 to 1.44)	**35 fewer per 1000** (from 70 fewer to 42 more)	⨁⨁◯◯ LOW	CRITICAL
COMPOSITE WOUND COMPLICATION – WOMEN WITH RUPTURED MEMBRANES												
1	randomized trial	not serious	not serious	not serious	very serious[a,b]	none	3/34 (8.8%)	7/42 (16.7%)	RR 0.53 (0.15 to 1.89)	**78 fewer per 1000** (from 142 fewer to 148 more)	⨁⨁◯◯ LOW	CRITICAL
COMPOSITE WOUND COMPLICATION – WOMEN WITH INTACT MEMBRANES												
1	randomized trial	not serious	not serious	not serious	very serious[a,b]	none	6/121 (5.0%)	7/103 (6.8%)	RR 0.73 (0.25 to 2.10)	**18 fewer per 1000** (from 51 fewer to 75 more)	⨁⨁◯◯ LOW	CRITICAL
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS												
2	randomized trials	not serious	not serious	not serious	not serious	none	16/255 (6.3%)	33/245 (13.5%)	RR 0.48 (0.27 to 0.85)	**70 fewer per 1000** (from 98 fewer to 20 fewer)	⨁⨁⨁⨁ HIGH	CRITICAL
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS – WOMEN WITH RUPTURED MEMBRANES												
2	randomized trials	not serious	not serious	not serious	very serious[a,b]	none	4/59 (6.8%)	13/75 (17.3%)	RR 0.39 (0.13 to 1.13)	**106 fewer per 1000** (from 151 fewer to 23 more)	⨁⨁◯◯ LOW	CRITICAL

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of ruptured membranes	Relative (95% CI)	Absolute (95% CI)		
COMPOSITE WOUND COMPLICATION OR ENDOMETRITIS – WOMEN WITH INTACT MEMBRANES												
2	randomized trials	serious[c]	not serious	not serious	serious[a]	none	12/196 (6.1%)	20/170 (11.8%)	RR 0.52 (0.26 to 1.04)	**56 fewer per 1000** (from 87 fewer to 5 more)	⨁⨁◯◯ LOW	CRITICAL
POST-CAESAREAN ENDOMETRITIS												
9	randomized trials	serious[c]	not serious	not serious	not serious	none	53/1348 (3.9%)	125/1286 (9.7%)	RR 0.41 (0.30 to 0.55)	**57 fewer per 1000** (from 68 fewer to 44 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-CAESAREAN ENDOMETRITIS – WOMEN WITH RUPTURED MEMBRANES												
5	randomized trials	serious[c]	not serious	not serious	not serious	none	10/296 (3.4%)	35/256 (13.7%)	RR 0.23 (0.12 to 0.45)	**105 fewer per 1000** (from 120 fewer to 75 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-CAESAREAN ENDOMETRITIS – WOMEN WITH INTACT MEMBRANES												
8	randomized trials	serious[c]	not serious	not serious	not serious	none	43/1052 (4.1%)	90/1030 (8.7%)	RR 0.48 (0.34 to 0.68)	**45 fewer per 1000** (from 58 fewer to 28 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE FEVER												
8	randomized trials	serious[c]	not serious	not serious	not serious	none	90/1268 (7.1%)	132/1206 (10.9%)	RR 0.54 (0.38 to 0.78)	**50 fewer per 1000** (from 68 fewer to 24 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE FEVER – WOMEN WITH RUPTURED MEMBRANES												
4	randomized trials	serious[c]	not serious	not serious	not serious	none	25/260 (9.6%)	39/220 (17.7%)	RR 0.42 (0.22 to 0.80)	**103 fewer per 1000** (from 138 fewer to 35 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL

Certainty assessment							No. of patients		Effect		Certainty	Importance
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Vaginal preparation with antiseptic solution	Control (no preparation or saline preparation) – stratified by presence of ruptured membranes	Relative (95% CI)	Absolute (95% CI)		
POST-OPERATIVE FEVER – WOMEN WITH INTACT MEMBRANES												
7	randomized trials	serious[c]	not serious	not serious	not serious	none	65/1008 (6.4%)	93/986 (9.4%)	RR 0.70 (0.49 to 0.99)	**28 fewer per 1000** (from 48 fewer to 1 fewer)	⨁⨁⨁◯ MODERATE	CRITICAL
POST-OPERATIVE WOUND INFECTION												
9	randomized trials	serious[c]	not serious	not serious	not serious	none	61/1348 (4.5%)	85/1286 (6.6%)	RR 0.66 (0.47 to 0.91)	**22 fewer per 1000** (from 35 fewer to 6 fewer)	⨁⨁⨁◯ MODERATE	IMPORTANT
POST-OPERATIVE WOUND INFECTION – WOMEN WITH RUPTURED MEMBRANES												
5	randomized trials	not serious	not serious	not serious	serious[a]	none	16/296 (5.4%)	25/256 (9.8%)	RR 0.54 (0.19 to 1.50)	**45 fewer per 1000** (from 79 fewer to 49 more)	⨁⨁◯◯ LOW ⨁⨁⨁◯ MODERATE	IMPORTANT
POST-OPERATIVE WOUND INFECTION – WOMEN WITH INTACT MEMBRANES												
8	randomized trials	serious[c]	not serious	not serious	not serious	none	45/1052 (4.3%)	60/1030 (5.8%)	RR 0.73 (0.50 to 1.07)	**16 fewer per 1000** (from 29 fewer to 4 more)	⨁⨁⨁◯ MODERATE	IMPORTANT

CI: Confidence interval; RR: Risk ratio.

[a] Wide confidence interval crossing the line of no effect.

[b] Small sample size and few events.

[c] Most of the pooled effect provided by studies "B" or "C" but without a substantial proportion (i.e. < 50%) from studies "C".

[d] Most of the pooled effect provided by studies "B" or "C" but with a substantial proportion (i.e. > 50%) from studies "C".

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