WHO recommendations on
Choice of antiseptic agent
and method of application for
preoperative skin preparation
for caesarean section
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Acknowledgements

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 of the World Health Organization (WHO) gratefully acknowledge the contributions of many individuals and organizations to the updating of these recommendations. Work on this update was coordinated by Mercedes Bonet, Doris Chou, Tina Lavin, Olufemi Oladapo and Joshua Vogel of the Department of Sexual and Reproductive Health and Research.

WHO extends its sincere thanks to Fatima Adamu, Subha Sri Balakrishnan, Michelle Bazari, Maria Laura Costa, Jemima Dennis-Antiwi, Hadiza Galadanci, David Lissauer, Pisake Lumbiganon, Ashraf Nabhan, Hiromi Obara, Alfred Osoti, Haroon Saloojee, Sadia Shakoor, Rachel Smith and Joseph Solomkin who served as members of the Guideline Development Group (GDG), and to James Neilson (Chair) for leading the meeting. We also thank Ayse Akin, Justus Hofmeyr, Tina Lavender, Suneeta Mittal, Alan Tita, John Varallo and Khalid Yunis who were members of the External Review Group (ERG). WHO also gratefully acknowledges the contribution of the members of the Executive Guideline Steering Group (GSG).

Edgardo Abalos, Anna Cuthbert, Virginia Diaz, Katherine Eddy, Leanne Jones, Frances Kellie, Myfanwy Williams and Rana Zahroh reviewed the scientific evidence, prepared the Grading of Recommendations Assessment, Development and Evaluation (GRADE) tables and drafted the narrative summary of the evidence. Mercedes Bonet, Maurice Bucagu, Doris Chou, Christine Francis, Tina Lavin, Olufemi Oladapo and Joshua Vogel revised the narrative summaries and double-checked the corresponding GRADE tables and prepared the evidence-to-decision (EtD) frameworks. The ERG peer reviewed the final document before executive clearance by WHO and publication.

We acknowledge the various organizations that were represented by observers, including Deborah Armbruster (United States Agency for International Development [USAID]), Emma Clark (USAID), Jeanne Conry (International Federation of Gynecology and Obstetrics [FIGO]), Maria Fernanda Escobar (FIGO), Jeff Smith (Bill & Melinda Gates Foundation) and Ann Yates (International Confederation of Midwives [ICM]).

We also appreciate the contributions of staff at the WHO regional offices, including Bremen de Mucio, Karima Gholbzouri, Chandani Anoma Jayathilaka, Oleg Kuzmenko, Leopold Ouedraogo, Howard Sobel and Claudio Sosa. We appreciate the contributions of Willibald Zeck of the United Nations Population Fund (UNFPA).

WHO acknowledges the financial support for this work received from USAID and the UNDP-UNFPA-UNICEF-WHO-World Bank Special Programme of Research, Development and Research Training in Human Reproduction (HRP) of the Department of Sexual and Reproductive Health and Research. WHO emphasizes that donors do not participate in any decision related to the guideline development process, including the composition of research questions, membership of the guideline development groups, conducting and interpretation of systematic reviews, or formulation of the recommendations. The views of the funding bodies have not influenced the content of these recommendations.
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
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 recommendations on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section in response to the availability of new evidence. The recommendations in this document thus supersede the previous WHO recommendations for choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section as published in the 2015 guideline WHO recommendations for prevention and treatment of maternal peripartum infections.

Target audience
The primary audience for these recommendations 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 these recommendations 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 recommendations were 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 questions. 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 recommendations presented herein. The recommendations were 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 recommendations), recommended only in the context of rigorous research (implementation of the recommendations 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 issued these recommendations on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section with remarks and implementation considerations. To ensure that these recommendations are 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 recommendations on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section

Recommendation a: The use of alcohol-based chlorhexidine gluconate for skin preparation prior to elective or emergency caesarean section is recommended. (Recommended)

Recommendation b: The method of application of alcohol-based chlorhexidine gluconate prior to caesarean section should be based primarily on instructions for use, the clinician’s experience and preferences. (Recommended)

Remarks:
- There was a lack of evidence to recommend a specific concentration of chlorhexidine gluconate; however, most trials included used 2% chlorhexidine gluconate in 70% alcohol.
- Maternal allergy to alcohol-based chlorhexidine gluconate must be excluded before surgery. In women with no previous history of allergy to alcohol-based chlorhexidine gluconate, it should be noted that chlorhexidine gluconate can cause skin irritation.
- A standard preoperative skin preparation technique that is appropriate for the intended skin incision must be followed.
- As alcohol is highly flammable, alcohol-based antiseptic preparations may ignite if used in the presence of diathermy, and they must be allowed to dry by evaporation. It is advisable to ensure that the drapes are not saturated with alcohol or that the alcohol-based solution has not formed a pool underneath the woman before starting surgery. Particular care should be taken at emergency caesarean section.
- Where chlorhexidine gluconate is not available, other antiseptic agent such as povidone-iodine can be considered a suitable antiseptic agent for preoperative skin preparation, although it is not as effective as alcohol-based chlorhexidine gluconate.
- The Guideline Development Group noted that the current recommendation is consistent with the 2016 WHO global guidelines on the prevention of surgical site infection, which recommends chlorhexidine gluconate alcohol-based antiseptic solutions for surgical site skin preparation in individuals undergoing surgical procedures.
- These recommendations supersede Recommendation No. 17 of the 2015 WHO recommendations for prevention and treatment of maternal peripartum infections where this was considered a conditional recommendation based on low-quality evidence.
1. 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 initial 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). The risk of infection can be reduced through sound surgical techniques, correct use of topical antiseptic agents and antibiotic prophylaxis.

The prevention, early diagnosis, and prompt management of sepsis are key factors in reducing sepsis-related morbidity and mortality, as reflected in the 2017 WHA70.7 Resolution: Improving the prevention, diagnosis and clinical management of sepsis (13). Globally, an effective intervention for reducing morbidity and mortality related to maternal infection is the prophylactic and therapeutic use of antibiotics, used in conjunction with sound surgical techniques and topical antiseptic agents. Antibiotics are widely used (and misused) for obstetric conditions (14, 15). 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.

The 2015 WHO global action plan on 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 (16). 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 (17, 18). 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 recommendations on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section after the publication of new evidence on this intervention.

These updated recommendations were 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 (19). The recommendations in this document thus supersede the previous WHO recommendations on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section as published in the 2015 guideline WHO recommendations for prevention and treatment of maternal peripartum infections (20).

The primary aim of these recommendations is to improve the quality of care and outcomes for women giving birth, as they relate to peripartum infection and its complications. These recommendations thus provide a foundation for sustainable implementation of skin antiseptics for preoperative skin preparation for 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.

These recommendations 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.

1.4 Scope of the recommendations

Framed using the population (P), intervention (I), comparator (C), outcome (O) (PICO) format, the questions for these recommendations were:

a. Among pregnant women undergoing caesarean section (P), is the use of a particular antiseptic agent for preoperative skin preparation (I), compared with other antiseptic agent(s) (C), more effective in preventing post-caesarean infectious morbidities (O)?

b. Among pregnant women undergoing caesarean section (P), is the use of a particular method of antiseptic application for preoperative skin preparation (I), compared with other methods of antiseptic application (C), more effective in preventing post-caesarean infectious morbidities (O)?

1.5 Persons affected by the recommendations

The population affected by these recommendations include all pregnant women in labour.

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\(^1\) Further information is available at: http://www.gradeworkinggroup.org/

\(^2\) Further information is available at: https://www.cerqual.org/.
2. Methods

These recommendations were developed using standardized operating procedures in accordance with the process described in the WHO *handbook for guideline development* (19). 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 recommendations; and (v) planning for the dissemination, implementation, impact evaluation and updating of the recommendations.

In 2019, the choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section was identified by the Executive GSG as a high priority for development of updated recommendations, 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 (17, 18).

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 these recommendations. 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 these recommendations 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 these recommendations,
advised on the interpretation of this evidence, formulated the final recommendations based on the draft prepared by the WHO Steering Group and reviewed and reached unanimous consensus for the recommendations 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 (21). 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 these 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 (20). 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 recommendations. 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 recommendations on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section

An existing systematic review on choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section was updated (21). Seven new studies involving 5416 women were added since the previous systematic review. This systematic review was the primary source of evidence of effectiveness for these recommendations. 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 recommendations 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 (22). 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 choice of antiseptic agent and method of application for preoperative skin preparation for caesarean section (23). This review included the 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 (24). Two studies on the perspectives and experiences of women and health-care providers with antiseptic use at birth were also identified and used to inform the acceptability domain (25, 26). Additionally, a systematic review of qualitative studies evaluating “what women want“ from intrapartum care was used to further inform the values and equity domains (27). Equity evidence was derived from two studies on availability and quality of antiseptic agents in low- and middle-income countries (28, 29).

The evidence for cost–effectiveness was derived from indirect cost-related evidence from a study on caesarean section (30) and a systematic review of multiple surgery types including caesarean section (31). The first study evaluated the cost and efficacy of dressings impregnated with dialkylicarbamoyl chloride compared with standard surgical dressings on preventing surgical site infections of women that gave birth by caesarian section (30). The second was a systematic review that compared chlorhexidine with povidone-iodine as preoperative skin antiseptics to prevent surgical site infection in a range of surgery types (foot/ankle, plastic, shoulder, vaginal, laparotomy, mastectomy and caesarean section) and included 9 trials (3614 patients) (31). Available evidence was assessed as low quality according to the Consensus Health Economic Criteria (CHEC) checklist (32).

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 (33). 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 recommendations were 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 (34), 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 CHEC checklist (32).

**2.5 Formulation of the recommendations**

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 use a specific antiseptic agent for preoperative skin preparation for 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 recommendations, to 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 recommendations 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 recommendations:

- **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 (19). All GDG members 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 (19). 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 meeting

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 recommendations. 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 recommendations.

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, recommendations 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 these recommendations 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 control precautions 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); and the 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.
  - 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.
  - 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, they 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 that are listed in the WHO model list of essential medicines for use in maternal and perinatal health-care, 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 Recommendations and supporting evidence

The following section outlines the recommendations 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 recommendations, is presented in the EtD framework (Annex 4).

The following recommendations were 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 recommendations are correctly understood and appropriately implemented in practice, additional remarks reflecting the summary of the discussion by the GDG are included under the recommendations.
Recommendation a: The use of alcohol-based chlorhexidine gluconate for skin preparation prior to elective or emergency caesarean section is recommended. (Recommended)

Recommendation b: The method of application of alcohol-based chlorhexidine gluconate prior to caesarean section should be based primarily on instructions for use, the clinician’s experience and preferences. (Recommended)

Remarks:

- There was a lack of evidence to recommend a specific concentration of chlorhexidine gluconate; however, most trials included used 2% chlorhexidine gluconate in 70% alcohol.
- Maternal allergy to alcohol-based chlorhexidine gluconate must be excluded before surgery. In women with no previous history of allergy to alcohol-based chlorhexidine gluconate, it should be noted that chlorhexidine gluconate can cause skin irritation.
- A standard preoperative skin preparation technique that is appropriate for the intended skin incision must be followed.
- As alcohol is highly flammable, alcohol-based antiseptic preparations may ignite if used in the presence of diathermy, and they must be allowed to dry by evaporation. It is advisable to ensure that the drapes are not saturated with alcohol or that the alcohol-based solution has not formed a pool underneath the woman before starting surgery. Particular care should be taken at emergency caesarean section.
- Where chlorhexidine gluconate is not available, other antiseptic agent such as povidone-iodine can be considered a suitable antiseptic agent for preoperative skin preparation, although it is not as effective as alcohol-based chlorhexidine gluconate.
- The Guideline Development Group noted that the current recommendation is consistent with the 2016 WHO global guidelines on the prevention of surgical site infection, which recommends chlorhexidine gluconate alcohol-based antiseptic solutions for surgical site skin preparation in individuals undergoing surgical procedures.
- These recommendations supersede Recommendation No. 17 of the 2015 WHO recommendations for prevention and treatment of maternal peripartum infections where this was considered a conditional recommendation based on low-quality evidence.
4. Dissemination, adaptation and implementation of the recommendations

The dissemination and implementation of these recommendations 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 these recommendations be translated into care packages and programmes at country, health-care facility and community levels, where appropriate.

4.1 Recommendation dissemination

These recommendations 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. These recommendations 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.

This 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 these recommendations based on an existing strategy. This process may include the development or revision of existing national guidelines or protocols based on the updated recommendations.

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 these recommendations, 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 recommendations 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 recommendations in humanitarian emergencies by stakeholders.

\(^1\) Available at: www.who.int/rlh.
4.3 Implementation considerations

- These recommendations should be implemented in line with the guiding principles and best practice statements outlined in these recommendations.
- Health-care providers and health services managers should ensure that alcohol-based chlorhexidine gluconate is available wherever caesarean section is performed.
- The availability of alcohol-based antiseptic solutions may be limited in some low- and middle-income countries. Commercial preparations of these solutions may represent a financial burden to health-care facilities and patients if they are required to procure care supplies. Local production may be a more affordable and feasible option in these settings, provided that adequate quality control is put in place.
- Women should be adequately counselled and engaged in shared decision-making around the use of antiseptic agents for skin preparation at caesarean section, including side-effects.

5. Research implications

The GDG did not identify any important knowledge gaps that need to be addressed, which may have an impact on the recommendations.

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 these recommendations. 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 the recommendations, health system stakeholders may wish to consider the following potential barriers to their application:

- lack of understanding of the value of alcohol-based chlorhexidine gluconate as an antiseptic agent for preoperative skin preparation for caesarean section among women giving birth, families or communities;
- lack of human resources with the necessary training and skills to use alcohol-based chlorhexidine gluconate as an antiseptic agent for preoperative skin preparation for caesarean section;
- concerns from skilled health-care personnel and health system managers regarding the safety of an alcohol-based chlorhexidine gluconate as an antiseptic agent for preoperative skin preparation for caesarean section;
- 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 the recommendations 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 recommendations 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 alcohol-based chlorhexidine gluconate for skin preparation, calculated as the number of women who received alcohol-based chlorhexidine gluconate for skin preparation 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 recommendations

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, these recommendations 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 recommendations may be updated. If no new reports or information is identified, the recommendations may be revalidated.

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

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


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

A. Participants at the WHO Guideline Development Group (GDG) meeting (19–20 October 2020)

<table>
<thead>
<tr>
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Annex 1. External Experts and WHO Staff Involved in the Preparation of the Recommendations
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 with/without salpingitis causing maternal febrile morbidity)
- Wound (surgical site) infection

Important outcomes:
- Maternal death
- Cost of care
- Allergy/irritation at operation site
- Maternal satisfaction
- Maternal well-being
- Neonatal infection
- Severe neonatal morbidity

¹ These outcomes reflect the prioritized outcomes used in the development of these recommendations, 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.
### Annex 3. Summary and management of declared interests from GDG members

<table>
<thead>
<tr>
<th>Name</th>
<th>Expertise contributed to guideline development</th>
<th>Declared interest</th>
<th>Management of conflict of interest</th>
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<td>Jemima Dennis-Antiwi</td>
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<tr>
<td>Alfred Osoti</td>
<td>Content expert and end-user</td>
<td>None declared</td>
<td>Not applicable</td>
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<tr>
<td>Haroon Saloojee</td>
<td>Content expert and end-user</td>
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<td>Not applicable</td>
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<tr>
<td>Sadia Shakoor</td>
<td>Content expert and end-user</td>
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<td>Not applicable</td>
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<tr>
<td>Rachel Smith</td>
<td>Content expert and end-user</td>
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<tr>
<td>Joseph Solomkin</td>
<td>Content expert and end-user</td>
<td>None declared</td>
<td>Not applicable</td>
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</table>
Annex 4. Evidence-to-decision framework

**Question**

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

a. Among pregnant women undergoing caesarean section (P), is the use of a particular antiseptic agent for preoperative skin preparation (I), compared with other antiseptic agents (C), more effective in preventing post-caesarean infectious morbidities (O)?

b. Among pregnant women undergoing caesarean section (P), is the use of a particular method of antiseptic application for preoperative skin preparation (I), compared with other methods of antiseptic application (C), more effective in preventing post-caesarean infectious morbidities (O)?

**Problem:** Preventing infectious morbidities amongst women undergoing caesarean section

**Perspective:** Clinical practice recommendation – population perspective

**Population (P):** Pregnant women undergoing caesarean section

**Intervention (I):**

a) Antiseptic agents: Parachlorometaxylenol plus povidone-iodine (PVP-I); Chlorhexidine gluconate (CHX) plus alcohol; PVP-I; isopropyl alcohol plus iodophor

b) Methods of application: scrub; paint

**Comparators (C):**

a) Other antiseptic agents

b) Methods of application

**Setting:** Hospital setting

**Subgroups:** by type of solution (alcohol-based versus aqueous-based)

**Priority outcomes (O):**

**Critical outcomes:**

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

**Important outcomes:**

- Maternal death
- Cost of care
- Allergy/irritation at operation site
- Maternal satisfaction
- Maternal well-being
- Neonatal infection
- Severe neonatal morbidity

---

1 These outcomes reflect the prioritized outcomes used in the development of these recommendations, 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.
Assessment

Effects of interventions

a) What is the effect of a particular antiseptic agent for preoperative skin preparation compared to other antiseptic agents for prevention of post-caesarean infectious morbidities?

b) What is the effect of a particular method of application of antiseptic agent for preoperative skin preparation compared to other methods for prevention of post-caesarean infectious morbidities?

Research evidence

Summary of evidence

Source and characteristics of studies

Evidence on the effects of different skin preparation agents and methods of application prior to caesarean section was derived from a Cochrane systematic review of 13 trials involving 6938 women (1). One trial conducted in France did not contribute any data to the meta-analysis because it did not report any pre-specified outcomes. One trial, which did contribute data to the analysis, was only in abstract form with limited information available.

Included trials used different combinations of antiseptic agents and methods of application. The review pooled data from trials that used the same antiseptic agents, as follows:

- CHX with alcohol versus PVP-I in aqueous- or alcohol-based solution
- parachlorometaxylenol with PVP-I versus scrubbing with PVP-I alone
- isopropyl alcohol plus iodophor

The 10 trials (4461 women) that contributed relevant data to the meta-analysis were published between 1988 and 2019. Six trials were conducted in the United States of America (USA), and one each in Egypt, India, Indonesia and Nigeria. Six were single-centre trials, three were conducted in multiple centres (in Egypt, Indonesia and the USA), and one did not describe the trial’s setting.

Five trials (2610 women) included women having pre-labour or intrapartum caesarean section, one trial (932 women) included women undergoing intrapartum caesarean section only, and one trial (60 women) included women undergoing pre-labour caesarean section only. The remaining trials (859 women) did not report on timing of caesarean section.

Prophylactic antibiotics were administered to all women in 8 out of the 10 trials included: preoperatively (six trials) or after cord clamping (one trial). A small number of women received antibiotics preoperatively or intraoperatively (one trial). Two trials did not report whether prophylactic antibiotics were administered.

All 10 trials contributed data for surgical site infection, but definitions used varied across trials. Four trials included symptoms of redness, heat and swelling around the wound, presence of discharge, skin separation or wound breakdown. Fever, or need for antibiotics, were also included in two of these trials. Five trials specified the use of the Center for Disease Control and Prevention criteria; one trial did not describe how they defined this outcome. Trials used a range of time points in the definition: 3 and 7 days (one trial); 3 and 14 days (one trial); 7 days (one trial); 30 days (five trials). Two trials did not specify a time period. Appendix 1 has a detailed description of CHX versus PVP-I and their methods of application used in the included trials.


**Effects of interventions**

a) Antiseptic agents versus other antiseptic agents

1) Chlorhexidine gluconate (CHX) versus povidone-iodine (PVP-I)

Eight trials (4332 women) compared CHX with alcohol versus PVP-I. The trials varied in the concentrations of antiseptic agents and solutions used, and also in the method of application. See Appendix I for a detailed summary of the bases, concentrations and methods of application in the included studies.

**Puerperal infection:** Low certainty evidence suggests CHX may make little or no difference to rates of *endometritis* when compared with PVP-I (3 trials, 2484 women; RR 0.95, 95% CI 0.49 to 1.86).

**Wound (surgical site) infection:** Moderate certainty evidence suggests that CHX probably reduces *surgical site infection* when compared with PVP-I (8 trials, 4323 women; RR 0.72, 95% CI 0.58 to 0.91).

**Cost of care:** Low certainty evidence suggests CHX may make little or no difference to re-admissions resulting from infection when compared with PVP-I (3 trials, 2484 women; RR 0.51, 95% CI 0.25 to 1.02).

**Allergy/irritation at operation site:** Low certainty evidence suggests CHX may make little or no difference to rates of *erythema* when compared with PVP-I (2 trials, 1521 women; RR 1.13, 95% CI 0.57 to 2.26). It is unclear whether CHX reduces *skin irritation* or *allergic skin reaction* when compared with PVP-I (very low certainty evidence).

The priority outcomes *maternal satisfaction* and *maternal well-being* were not reported in the Cochrane review, while *severe infectious morbidity*, *maternal death*, *neonatal infection* and *severe neonatal morbidity* were not reported by any included studies.

**Subgroup analysis by type of antiseptic solution (alcohol-based versus aqueous-based)**

All trials used CHX with alcohol but varied in the use of alcohol- versus aqueous-based PVP-I. The Cochrane review included a subgroup analysis by alcohol-based (4 trials, 2663 women) versus aqueous-based (4 trials, 1660 women) PVP-I solution for the surgical site infection outcome. Although this analysis did not identify a difference between these subgroups, there were relatively few studies and the subgroups were not balanced in size and, therefore, the subgroup analysis could not be expected to provide a reliable indication of differences by alcohol-based versus aqueous-based PVP-I.

2) Parachlorometaxylenol with PVP-I scrub versus PVP-I scrub alone

One trial (50 women) compared parachlorometaxylenol with PVP-I versus PVP-I alone. Women in the intervention group received a 5-minute scrub with parachlorometaxylenol (concentration not described), and women in the control group received a 30–60-second scrub with 7.5% PVP-I. All women subsequently received a 10% PVP-I scrub for 30–60 seconds and normal saline irrigation of the pelvis and subcutaneous tissue at uterine and fascial closure.

**Puerperal infection:** It is unclear whether parachlorometaxylenol with PVP-I reduces *endometritis* when compared with PVP-I alone (very low certainty evidence).

**Wound infection:** It is unclear whether parachlorometaxylenol with PVP-I reduces *surgical site infection* when compared with PVP-I alone (very low certainty evidence).

3) Isopropyl alcohol scrub plus iodophor-impregnated incise drape versus iodophor scrub

One trial (79 women) compared a 1-minute circular scrub with 70% isopropyl alcohol followed by application of an iodophor-impregnated antimicrobial incise drape versus a 5-minute iodophor scrub followed by application of iodophor solution (this appears to have been a wash, but method was not explicit).
Puerperal infection: It is unclear whether isopropyl alcohol scrub plus iodophor-impregnated antimicrobial skin sealant reduces metritis when compared with iodophor scrub (very low certainty evidence).

Wound infection: It is unclear whether an isopropyl alcohol scrub plus iodophor-impregnated antimicrobial skin sealant reduces surgical site infection in comparison with iodophor scrub (very low certainty evidence).

The priority outcomes maternal satisfaction, maternal well-being and cost of care were not reported in the Cochrane review, while severe infectious morbidity, maternal death, allergy/irritation at operation site, neonatal infection and severe neonatal morbidity were not reported by any included studies.

b) Methods of application

Included trials used different combinations of antiseptic agents and methods of application. No trials were identified comparing different methods of application (e.g. scrub versus paint) for the same antiseptic agent.

Additional considerations

- For comparison of CHX versus PVP-I, the trials varied in the method of application both within and between trials. It is possible that variation in methods within the arms of individual trials could have confounded the effect estimates in these analyses. However, it should be noted that the method of application recommended by manufacturers differs for CHX and PVP-I.

- The Cochrane review included an additional comparison on the use of incise drapes versus non-incise drapes (three trials). Data from one of these trials is included in the Antiseptic agents versus other antiseptic agents subsection of this evidence summary as it compared different antiseptic agents (isopropyl alcohol scrub plus iodophor-impregnated drape versus iodophor scrub) alongside the use of incise drape. The remaining two trials compared the application of the antiseptic agent with or without an incise drape, but using the same antiseptic agents in both arms, and therefore were not included in this framework.

- In 2016, WHO released guidelines on the prevention of surgical site infections (2). The panel considered the following available evidence from 17 trials on antiseptic agents for skin preparation for any surgery:
  - Moderate quality evidence showed that alcohol-based antiseptic solutions are overall more effective compared to aqueous solutions in reducing the risk of surgical site infection (OR 0.60; 95% CI 0.45–0.78).
  - Low quality of evidence showed a significant reduction in the risk of surgical site infections with the use of alcohol-based CHX compared to PVP-I in alcohol-based solutions (OR 0.58; 95% CI 0.42–0.80).
  - Moderate quality evidence showed a significant benefit in using CHX alcohol-based solutions compared to aqueous PVP-I for the reduction of surgical site infections (OR 0.65; 95% CI 0.47–0.90).
  - Very low-quality evidence suggests that there is no significant difference between PVP-I alcohol-based solutions and PVP-I aqueous solutions (OR 0.61; 95% CI 0.19–1.92).

However, three trials investigating the effect of the application technique with comparable antiseptic compounds showed no difference in surgical site infection rates (3, 4). Despite current knowledge of the antimicrobial activity of many antiseptic
agents and application techniques, it remains unclear what is the best approach to surgical site preparation (5, 6).

The panel recommended alcohol-based antiseptic solutions based on CHX for surgical site skin preparation in patients undergoing surgical procedures (strong recommendation, low to moderate quality of evidence).

Desirable effects
How substantial are the desirable anticipated effects?

Judgement

<table>
<thead>
<tr>
<th></th>
<th>Don’t know</th>
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<th>Trivial</th>
<th>Small</th>
<th>Moderate</th>
<th>Large</th>
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</table>

Undesirable effects
How substantial are the undesirable anticipated effects?

Judgement

<table>
<thead>
<tr>
<th></th>
<th>Don’t know</th>
<th>Varies</th>
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Certainty of the evidence
What is the overall certainty of the evidence on effects?

<table>
<thead>
<tr>
<th></th>
<th>No included studies</th>
<th>Very low</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
</tr>
</thead>
</table>

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 of Great Britain and Northern Ireland (7). Women’s descriptions of recovery after caesarean section focused on their experiences of pain, the impact on mobility and caregiving and their concerns on the risks of wound infection or non-healing. Women described receiving inadequate information on the risk of post-operative infections and not being aware that endometritis was a possible complication.

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 (8). 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) (9). 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

<table>
<thead>
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<th>Important uncertainty or variability</th>
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</tr>
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<tr>
<td>—</td>
<td>—</td>
<td>✓</td>
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</table>

Balance of effects

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

Judgement

<table>
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<th>Don’t know</th>
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<th>Favours no skin preparation</th>
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<tr>
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<td></td>
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</table>

Resources

How large are the resource requirements (costs)?

Research evidence

The Cochrane systematic review providing effectiveness evidence pre-specified the outcome cost of care; however, no direct evidence was identified in the included trials.

Additional considerations

A systematic search of the literature (17 July 2020) identified one cost-effectiveness study that compared the use of dressings impregnated with dialkylcarbamoyl chloride (DACC) to standard surgical dressing following skin closure in women giving birth by caesarean section (10). This study was assessed as low quality according to Consensus Health Economic Criteria (CHEC) checklist (11). Surgical site infection rates were lower in the DACC group (1.8%) compared to the standard surgical dressing group (5.2%) ($P = 0.04$). The total cost of prophylaxis and treatment of surgical site infections was lower in the DACC group compared with the standard surgical dressing group (£1065 versus €5775).

A systematic review compared the use of CHX with PVP-I for preoperative skin antiseptics to prevent surgical site infection in a range of surgery types (foot/ankle, plastic, shoulder, vaginal, laparotomy, mastectomy and caesarean section) and
included 9 trials (3614 patients) (12). None of the included studies looked separately at caesarean section. A separate cost analysis was then conducted using the probability of developing a surgical site infection, and then determined the mean costs associated with patients who did and patients who did not develop surgical site infection at Hospital of the University of Pennsylvania. CHX antisepsis was associated with significantly fewer surgical site infections (aRR 0.64; 95% CI 0.51–0.80) and positive skin culture results (aRR 0.44; 95% CI 0.35–0.56) than PVP-I antisepsis. In the cost–benefit model baseline scenario, switching from PVP-I to CHX resulted in a net cost savings of $16–$26 per surgical case in a single hospital setting in the USA. Sensitivity analyses showed that these savings persisted under most circumstances.

A systematic review of the economic burden of surgical site infections in low- and middle-income countries found the range of additional cost of surgical site infections (presented in 2017 international dollars) was similar in the low- and middle-income countries ($174–$29 610) to European countries ($21–$34 000) (13).

Main resource requirements

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<td>Staff</td>
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<tr>
<td>Training</td>
<td>No additional training required beyond standard surgical sterile techniques and surgical site preparation</td>
</tr>
<tr>
<td>Supplies</td>
<td>Antiseptic solution</td>
</tr>
<tr>
<td></td>
<td>PVP-I US$ 0.75 per 100 mL (14)</td>
</tr>
<tr>
<td></td>
<td>CHX surgical scrub US$ 0.54 per 100 mL (15)</td>
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<tr>
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<td>Time</td>
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<tr>
<td>Supervision and monitoring</td>
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Resources required

Judgement

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Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement

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Cost–effectiveness

Judgement

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<th>— Does not favour either</th>
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<th>— Favours skin preparation</th>
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</table>
Equity
What would be the impact on health equity?

Research evidence

A structured literature search identified no direct evidence on this question.

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 (16). The quality of antiseptic solution may also vary across settings (16, 17).

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 antiseptic use may not be fully realized.

Judgement

<table>
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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) (18–20). 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.

WHO guidelines on surgical site infections note that the use of alcohol as an antiseptic agent might be refused by patients and/or health-care workers because of religious reasons (2). A chapter on this topic is included in the WHO guidelines on hand hygiene in health care (15), which recommends the preferred use of alcohol-based hand rub (ABHR) for hand cleansing. The engagement of cultural and religious leaders (for example, in the hand hygiene campaign in health-care facilities) proved useful to overcome such barriers, and positive solutions were found. Indeed, an encouraging example is the statement issued by the Muslim Scholars’ Board of the Muslim World
League during the Islamic High Council’s meeting held in Mecca, Saudi Arabia, in January 2002: “It is allowed to use medicines that contain alcohol in any percentage that may be necessary for manufacturing if it cannot be substituted. Alcohol may be used as an external wound cleanser, to kill germs, and in external creams and ointments.” There may be a necessity to resume the discussion with religious leaders and individual patients with regards to the recommendation to use alcohol-based solutions for surgical site skin preparation.

Judgement

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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 (18).

Additional considerations
The panel considered that this intervention is likely to be feasible, considering that skin preparation agents are used routinely prior to incision. It is within the scope of practice of skilled health personnel performing caesarean section.

Judgement

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<td>Values</td>
<td>Balance of effects</td>
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Summary of judgements table

Desirable effects
- Don’t know
- Varies
- Trivial
- Small
- Moderate
- Large

Undesirable effects
- ✓
- 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
- ✓
- Probable no important uncertainty or variability
- No important uncertainty or variability

Balance of effects
- Don’t know
- Varies
- Favours no particular agent
- Probable no particular agent
- Does not favour either
- Probable favours a particular agent
- Favour an agent

Resources required
- Don’t know
- Varies
- Large costs
- Moderate costs
- Negligible costs or savings
- Moderate savings
- Large savings

Cost-effectiveness
- Don’t know
- Varies
- Favours no particular agent
- Probable no particular agent
- Does not favour either
- Probable favours a particular agent
- Favour a particular agent

Equity
- Don’t know
- Varies
- Reduced
- Probable reduced
- Probable no impact
- Probable increased
- Increased

Acceptability
- Don’t know
- Varies
- No
- Probable No
- ✓
- Probable Yes
- Yes

Feasibility
- Don’t know
- Varies
- No
- Probable No
- ✓
- Probable Yes
- Yes
## Summary of findings tables

**Question:** Chlorhexidine gluconate compared to povidone-iodine for preventing infection following caesarean section

**Setting:** Hospital (Egypt, India, Indonesia, Nigeria, United States of America)


<table>
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<th>Effect</th>
<th>Certainty</th>
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<td><strong>PUERPERAL SEPSIS: ENDOMETRITIS</strong></td>
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<td>not serious</td>
<td>serious(^b)</td>
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</tbody>
</table>

| **WOUND (SURGICAL SITE) INFECTION** | | | | |
| 8 randomized trials | serious\(^a\) | not serious | not serious | not serious | none | 117/2160 (5.4%) | 162/2163 (7.5%) | RR 0.72 (0.58 to 0.91) | 21 fewer per 1000 (from 31 fewer to 7 fewer) | ◇◇◇◇ MODERATE | CRITICAL |

| **MATERNA L DEATH – NOT REPORTED** | | | | |
| | | | | |
| | | | | |

| **COST OF CARE: RE-ADMISSION RESULTING FROM INFECTION** | | | | |
| 3 randomized trials | serious\(^a\) | not serious | not serious | serious\(^d\) | none | 29/1237 (2.3%) | 54/1247 (4.3%) | RR 0.51 (0.25 to 1.02) | 21 fewer per 1000 (from 32 fewer to 1 more) | ◇◇◇◇ LOW | IMPORTANT |

| **ALLERGY/IRRITATION AT OPERATION SITE: ERYTHEMA** | | | | |
| 2 randomized trials | serious\(^a\) | not serious | not serious | serious\(^d\) | none | 17/760 (2.2%) | 15/761 (2.0%) | RR 1.13 (0.57 to 2.26) | 3 more per 1000 (from 8 fewer to 25 more) | ◇◇◇◇ LOW | IMPORTANT |
### ALLEGY/IRRITATION AT OPERATION SITE: SKIN IRRITATION OR ALLERGIC SKIN REACTION

<table>
<thead>
<tr>
<th>No. of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Chlorhexidine gluconate</th>
<th>Povidone-iodine</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>randomized trials</td>
<td>serious(^a)</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious(^c)</td>
<td>none</td>
<td>9/964 (0.9%)</td>
<td>14/962 (1.5%)</td>
<td>RR 0.64 (0.28 to 1.46)</td>
<td>5 fewer per 1000 (from 10 fewer to 7 more)</td>
<td>☢☢☢☢  VERY LOW</td>
<td>IMPORTANT</td>
</tr>
</tbody>
</table>

**Certainty assessment**
- **No. of patients**
- **Effect**
- **Certainty**
- **Importance**

<table>
<thead>
<tr>
<th>CI: Confidence interval; RR: Risk ratio; OR: Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>(^a) All of pooled effect provided by studies at moderate risk of bias.</td>
</tr>
<tr>
<td>(^b) Wide confidence interval including appreciable benefit and appreciable harm with chlorhexidine gluconate.</td>
</tr>
<tr>
<td>(^c) Majority of pooled effect provided by studies at moderate risk of bias.</td>
</tr>
<tr>
<td>(^d) Wide confidence interval including appreciable benefit with chlorhexidine gluconate and also crossing the line of no effect.</td>
</tr>
<tr>
<td>(^e) Few events.</td>
</tr>
</tbody>
</table>
**Question:** Parachlorometaxylenol with povidone-iodine compared to povidone-iodine alone for preventing infection following caesarean section

**Setting:** Hospital (United States of America)


<table>
<thead>
<tr>
<th>Certainty assessment</th>
<th>No. of participants</th>
<th>Effect</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEVERE INFECTION MORBIDITY (SEPTICAEMIA, SEPTIC SHOCK, LAPAROTOMY/HYSTERECTOMY FOR INFECTION, MATERNAL INTENSIVE CARE UNIT ADMISSION) - NOT REPORTED</strong></td>
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<tr>
<td><strong>PUERPERAL SEPSIS: ENDOMETRITIS</strong></td>
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<tr>
<td>1 randomized trial</td>
<td>serious&lt;sup&gt;a&lt;/sup&gt;</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>WOUND (SURGICAL SITE) INFECTION</strong></td>
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<td></td>
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<tr>
<td>1 randomized trial</td>
<td>serious&lt;sup&gt;a&lt;/sup&gt;</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious&lt;sup&gt;b,d&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>MATERNAL DEATH - NOT REPORTED</strong></td>
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<tr>
<td><strong>COST OF CARE - NOT REPORTED</strong></td>
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<tr>
<td><strong>ALLERGY/IRRITATION AT OPERATION SITE - NOT REPORTED</strong></td>
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<tr>
<td><strong>MATERNAL SATISFACTION - NOT REPORTED</strong></td>
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<tr>
<td><strong>MATERNAL WELL-BEING - NOT REPORTED</strong></td>
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</tbody>
</table>
### Annex 4. Evidence-to-Decision Framework

#### Certainty assessment no. of patients effect

<table>
<thead>
<tr>
<th>No. of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Parachlorometaxyleol with povidone-iodine</th>
<th>Povidone-iodine alone</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NEONATAL INFECTION – NOT REPORTED</strong></td>
<td></td>
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<td>--</td>
<td>IMPORTANT</td>
</tr>
<tr>
<td><strong>SEVERE NEONATAL MORBIDITY – NOT REPORTED</strong></td>
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<td>--</td>
<td>--</td>
<td>IMPORTANT</td>
</tr>
</tbody>
</table>

CI: Confidence interval; RR: Risk ratio; OR: Odds ratio

- All of pooled effect provided by study at moderate risk of bias.
- **Wide confidence interval including both appreciable benefit and appreciable harm with parachlorometaxyleol.**
- Single study with small sample size.
- Single study, few events, and small sample size.

---

**Question:** Isopropyl alcohol scrub plus iodophor-impregnated antimicrobial skin sealant compared to iodophor scrub for preventing infection following caesarean section.

**Setting:** Hospital (United States of America)


#### Puerperal Sepsis: Metritis

<table>
<thead>
<tr>
<th>No. of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Isopropyl alcohol scrub + iodophor-impregnated drape</th>
<th>Iodophor scrub versus</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>randomized trial</td>
<td>serious&lt;sup&gt;a&lt;/sup&gt;</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious&lt;sup&gt;b,c&lt;/sup&gt;</td>
<td>none</td>
<td>3/38 (7.9%)</td>
<td>2/41 (4.9%)</td>
<td>RR 1.62 (0.29 to 9.16)</td>
<td>30 more per 1000 (from 35 fewer to 398 more)</td>
<td>◆◆◆◆</td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>

---

**Wound (Surgical Site) Infection**

<table>
<thead>
<tr>
<th>No. of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Isopropyl alcohol scrub + iodophor-impregnated drape</th>
<th>Iodophor scrub versus</th>
<th>Relative (95% CI)</th>
<th>Absolute (95% CI)</th>
<th>Certainty</th>
<th>Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>randomized trial</td>
<td>serious&lt;sup&gt;a&lt;/sup&gt;</td>
<td>not serious</td>
<td>not serious</td>
<td>very serious&lt;sup&gt;d&lt;/sup&gt;</td>
<td>none</td>
<td>0/38 (0.0%)</td>
<td>0/41 (0.0%)</td>
<td>not estimable</td>
<td>—</td>
<td>◆◆◆◆</td>
<td>VERY LOW</td>
</tr>
</tbody>
</table>

CI: Confidence interval; RR: Risk ratio

- All pooled effect provided by study at moderate risk of bias.
- **Wide confidence interval including both appreciable benefit and appreciable harm with isopropyl alcohol plus iodophor-impregnated drape.**
- Single study, small sample size, and few events.
- Single study, small sample size, and no events.
### Appendix 1

#### a) Chlorhexidine gluconate vs povidone-iodine: summary of interventions and comparators

<table>
<thead>
<tr>
<th>Base</th>
<th>Concentration</th>
<th>Method of application</th>
<th>No. of trials (women)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>2% CHX in 70% alcohol</td>
<td>Scrub</td>
<td>1 (572)</td>
</tr>
<tr>
<td></td>
<td>Paint (26 mL single step applicator)</td>
<td></td>
<td>1 (461)</td>
</tr>
<tr>
<td></td>
<td>Unclear: 3x 'applications' CHX; then 3x 'applications' alcohol</td>
<td></td>
<td>1 (204)</td>
</tr>
<tr>
<td></td>
<td>Not described</td>
<td></td>
<td>2 (240)</td>
</tr>
<tr>
<td></td>
<td>Unclear, probably 2% CHX in 70% alcohol</td>
<td>Not described</td>
<td>1 (21)</td>
</tr>
<tr>
<td></td>
<td>0.3% CHX plus 3% cetrimide</td>
<td>Scrub (CHX plus cetrimide in water; then 95% isopropyl alcohol scrub)</td>
<td>1 (188)</td>
</tr>
<tr>
<td></td>
<td>Not described</td>
<td>Not described</td>
<td>1 (474)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Base</th>
<th>Concentration</th>
<th>Method of application</th>
<th>No. of trials (women)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol</td>
<td>8.3% PVP-I in 72.5% alcohol</td>
<td>Scrub</td>
<td>1 (575)</td>
</tr>
<tr>
<td></td>
<td>10% PVP-I in 70% alcohol</td>
<td>Scrub (PVP-I scrub with applicator x3; then 3x 'applications' PVP-I with alcohol)</td>
<td>1 (201)</td>
</tr>
<tr>
<td></td>
<td>10% PVP-I (alcohol concentration not described)</td>
<td>Not described</td>
<td>1 (87)</td>
</tr>
<tr>
<td></td>
<td>Not described</td>
<td>Not described</td>
<td>1 (463)</td>
</tr>
<tr>
<td>Aqueous</td>
<td>0.75% PVP-I (scrub), then 1% PVP-I (paint)</td>
<td>Scrub and paint</td>
<td>1 (471)</td>
</tr>
<tr>
<td></td>
<td>10% PVP-I (aqueous base assumed)</td>
<td>Paint</td>
<td>1 (186)</td>
</tr>
<tr>
<td></td>
<td>Not described</td>
<td>Not described</td>
<td>1 (158)</td>
</tr>
<tr>
<td></td>
<td>Not described (aqueous base assumed)</td>
<td>Not described</td>
<td>1 (22)</td>
</tr>
</tbody>
</table>
References


For more information, please contact:

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Avenue Appia 20, CH-1211 Geneva 27, Switzerland

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Website: www.who.int/reproductivehealth

Department of Maternal, Newborn, Child and Adolescent Health and Ageing
Email: mncah@who.int.
Website: www.who.int/maternal_child_adolescent