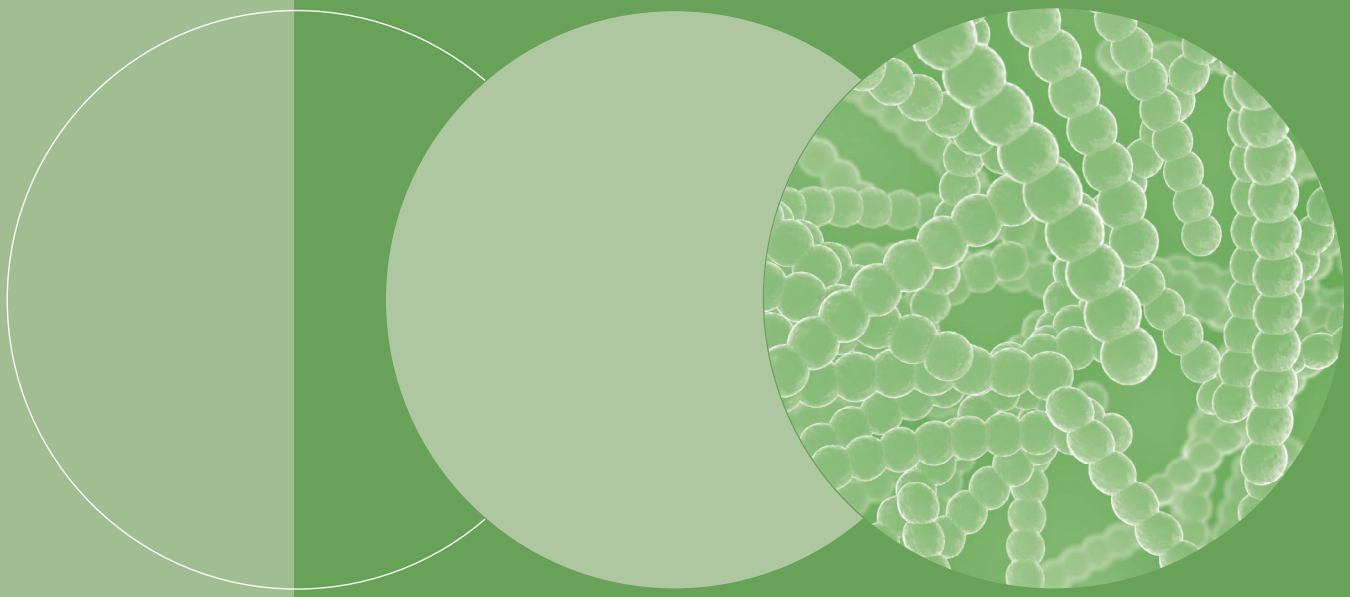
WHO recommendation on

Screening of pregnant women for intrapartum antibiotic prophylaxis for the prevention of early onset Group B streptococcus disease in newborns



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Acronyms and abbreviations

CerQUAL	Confidence in the Evidence from Reviews of Qualitative Research
CHEC	Consensus on Health Economic Criteria
CREP	Centro Rosarino de Estudios Perinatales
DG	Diagnosis Group
DOI	declaration of interest
EOGBS	Early onset group B streptococcus
ERG	Evidence Review Group
ESG	Evidence Synthesis Group
EtD	Evidence-to-decision
GBS	group B streptococcus
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GSG	Guideline Steering Group
HRP	UNDP–UNFPA–UNICEF–WHO–World Bank Special Programme of Research, Development and Research Training in Human Reproduction
IAP	intrapartum antibiotic prophylaxis
ICER	incremental cost–effectiveness ratio
IV	intravenous
MCA	Department of Maternal, Newborn, Child and Adolescent Health and Ageing (WHO)
MPH-GDG	Maternal and Perinatal Health Guideline Development Group
PICO	population (P), intervention (I), comparator (C), outcome (O)
pPROM	Preterm premature rupture of membranes
SRH	Department of Sexual and Reproductive Health and Research (WHO)
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

Group B streptococci (streptococcus agalactiae) (GBS) infection affects over 390 000 newborns per year. The leading cause of early-onset neonatal sepsis, early onset GBS (EOGBS) disease is defined by presence of GBS in the newborn's blood, cerebrospinal fluid or other usually sterile site within the first seven days following birth. EOGBS infection can be prevented through intrapartum antibiotic prophylaxis (IAP) administered to pregnant women prior to birth. There is a need, however, to determine whether screening for risk of EOGBS infection is effective in identifying women who are eligible for IAP. Risk for EOGBS infection can be ascertained either by presence of maternal GBS colonization in the vagina, perineum or rectum, or by maternal risk factors known to be associated with EOGBS disease.

Potential approaches for determining eligibility for IAP include: (i) universal screening: where all women undergo antepartum culture-based screening (rectovaginal swabbing is used to obtain a sample) and IAP is administered to those who have evidence of GBS colonization; (ii) risk factor-based screening: where IAP is administered to pregnant women when one or more risk-factors for EOGBS are present (no swabbing for maternal GBS colonization is carried out); (iii) a combined strategy of universal and risk-based screening programmes; and (iv) no specific screening strategy, with IAP administered based on individual assessment. Risk-factors typically considered in the risk-based approach include maternal fever, rupture of membranes, bacteriuria, and previous child with EOGBS, though these may vary across settings. Regardless of the strategy, most pregnant women with known GBS bacteriuria (for example, due to urine testing for urinary tract infection) or a previous child affected by an EOGBS infection will have IAP.

Target audience

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

The term "woman" includes individuals who have given birth, even if they may not identify as a woman or as a mother. It is recognized that some individuals who have given birth identify as gender diverse.

Guideline development methods

The guideline was developed using standard operating procedures in accordance with the process described in the *WHO handbook for guideline development*. Briefly, these procedures include: (i) identification of priority questions and outcomes; (ii) retrieval of evidence; (iii) assessment and synthesis of evidence; (iv) formulation of the recommendation; and (v) planning for the dissemination, implementation, impact evaluation and future updating of the recommendation.

The scientific evidence supporting the recommendation was synthesized using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach. A systematic review was used to prepare the evidence profiles for the prioritized questions. WHO convened a meeting on 5–6 December 2023 where the Guideline Development Group (GDG) members reviewed, deliberated and achieved consensus on the strength and direction of the recommendation presented herein. Through a structured process, the GDG reviewed the balance between the desirable and undesirable effects and the overall certainty of supporting evidence of effectiveness, values and preferences of women and families,

resource requirements and cost–effectiveness, impact on health equity, acceptability to stakeholders and feasibility of implementing the intervention.

Recommendation

The GDG issued the recommendation on screening of pregnant women for intrapartum antibiotic prophylaxis for the prevention of early onset Group B streptococcus disease in newborns with remarks, implementation considerations and research gaps. To ensure that the recommendation is correctly understood and applied in practice, guideline users are encouraged to refer to these remarks, as well as to the evidence summaries, including the considerations on implementation and research gaps.

Recommendation
Screening of pregnant women for intrapartum antibiotic prophylaxis is recommended for the prevention of early onset Group B streptococcus disease in newborns. Offer either universal antenatal testing for Group B streptococcus colonization and intrapartum antibiotic prophylaxis for women who screen positive (universal screening); or intrapartum assessment of risk factors and antibiotic prophylaxis for women at risk of having a newborn with early onset Group B streptococcus disease (risk-based approach). *(Recommended)*

- This recommendation was based on evidence from observational studies largely from high-income countries which show that either universal or risk-based screening strategies, compared with no screening strategy, may be associated with reduced risk of early onset Group B streptococcus (GBS) disease in newborns.
- While universal screening, as compared to a risk-based approach, is probably associated with reduced early onset GBS disease in newborns, the Guideline Development Group (GDG) acknowledged the challenges with costs and the feasibility of implementing antenatal universal screening, particularly in low-resource settings.
- Universal screening involves routine testing of all pregnant women during antenatal care, mostly conducted at 35–37 weeks using rectovaginal swabbing by a health worker or self-swabbing by the woman. Women who screened positive for GBS colonization, or with a previous infant with early onset GBS disease, or with known GBS bacteriuria (for example, due to urine testing for urinary tract infection) should be offered intrapartum antibiotic prophylaxis at the onset of labour.
- The risk-factor approach involves intrapartum assessment of women for any one risk factor associated with having a newborn with early onset GBS disease. The risk factors across observational studies were varied. The most common risk factors were preterm prelabour rupture of membranes, prolonged rupture of membranes (>18 hours), previous infant with early onset GBS disease, known maternal bacteriuria, maternal intrapartum fever (>38 °C), and chorioamnionitis. These risk factors are in keeping with indications for intrapartum antibiotics in the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections (1)*.
- Women with maternal intrapartum fever should be assessed for any diagnostic or clinical signs of infection with intrapartum antibiotics administered in line with existing WHO recommendations *(1)*.

- Few studies also included preterm labour <37 weeks (including women with intact membranes) as a risk-factor for early onset GBS disease in newborns. The GDG noted WHO does not recommend routine antibiotic administration for women in preterm labour with intact amniotic membranes, based on rigorous trial evidence, concluding that the potential risk of harm to the baby (i.e. cerebral palsy) outweighed any potential benefit of the intervention *(1)*.
- As the evidence came from studies that tested ampicillin or penicillin G, either antibiotic may be considered for treatment except where there are contraindications (e.g. allergy history) or GBS strain has been microbiologically shown to be penicillin-resistant, in keeping with the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections (1)*.
- Women should be provided with evidence-based, up-to-date information on the prevention of early onset GBS disease in newborns and the maternal screening offered in their setting before being offered screening. The information should facilitate an understanding of the purpose of screening, the procedure involved in obtaining swabs in their setting and the potential implications of a positive result including subsequent intrapartum antibiotic prophylaxis. Women should give consent for the procedure and be able to refuse without mistreatment.
- The GDG acknowledged that this recommendation may be updated following the conclusion of a large ongoing trial comparing universal screening (either antenatal testing at 35–37 weeks' gestation or rapid intrapartum testing) to maternal risk-based screening *(2)*. Future studies may also address the uncertainties on risk-factors to be assessed when a risk-based approach is used. The GDG also acknowledged the development of rapid intrapartum testing which may improve screening accuracy.

1. Introduction

1.1 Background

Group B streptococci (streptococcus agalactiae) (GBS) are gram-positive bacteria commonly found in human gastrointestinal and genital tracts. GBS colonization is found in around 13% of pregnant women, though colonization rates may be higher in certain subgroups *(3, 4)*. While GBS colonization is usually harmless among the general population, colonization during pregnancy increases the risk of maternal peripartum infections, preterm premature rupture of membranes, and preterm birth *(5)*. The newborn can become infected following aspiration of infected amniotic fluid or contact with the bacteria during birth *(5)*. Around half (40–50%) of babies born to colonized mothers will become colonized with GBS *(6)*.

GBS infection leads to substantial perinatal morbidity and mortality. It is a leading cause of serious neonatal infection, affecting over 390 000 newborns per year *(7)*. GBS infection was linked to an estimated 46 200 stillbirths and up to 91 900 infant deaths in the year 2020 *(7)*. In addition, 37 100 children who recovered from invasive GBS infection were predicted to develop moderate or severe neurodevelopmental impairment *(7)*. Early onset GBS (EOGBS) disease is the leading cause of early-onset neonatal sepsis *(8)*. It is defined by presence of GBS in the newborn's blood, cerebrospinal fluid or other usually sterile site within the first seven days following birth *(9)*.

EOGBS can be prevented through intrapartum antibiotic prophylaxis (IAP) administered to pregnant women prior to birth *(10)*. As part of its 2015 recommendations for the prevention and treatment of maternal peripartum infections *(1)*, the World Health Organization (WHO) currently recommends IAP for women with GBS colonization for the prevention of early neonatal GBS infection. However, this recommendation does not provide guidance on approaches to determine the presence of GBS colonization, or the risk of early onset GBS disease based on other factors.

Given the adverse effects of EOGBS disease for newborns and families, as well as ongoing debate about – and variation in – screening practices *(11, 12)*, there is a need to identify whether maternal screening strategies are effective in preventing EOGBS disease and improving maternal and neonatal outcomes. Maternal screening strategies assess risk for EOGBS infection either by presence of maternal GBS colonization or by maternal risk factors known to be associated with EOGBS disease. In this context, maternal screening strategies for EOGBS risk serve to identify women eligible for IAP, which can then prevent the transmission of GBS from the women to her newborn. It is important to note that EOGBS can occur with a negative maternal GBS culture *(13)*.

Potential approaches for assessing EOGBS risk in women (and thus determining eligibility for IAP) include: (i) universal screening: where all women undergo antepartum culture-based screening (rectovaginal swabbing is used to obtain a sample) and IAP is administered to those who have evidence of GBS colonization; (ii) risk factor-based screening: where IAP is administered to pregnant women when one or more risk-factors for EOGBS infection are present (no swabbing for GBS colonization is carried out); (iii) a combined strategy of universal and risk-based screening; and (iv) no specific screening strategy, with IAP administered based on individual assessment. Risk-factors typically considered in the risk-based approach include maternal fever, rupture of membranes, bacteriuria, and previous child with EOGBS *(13)*, though these may vary across settings. Regardless of the strategy, most pregnant women with known GBS bacteriuria (for example due to urine testing for urinary tract infection) or a previous child affected by an EOGBS infection will have IAP.

When considering the most effective method for reduction of EOGBS disease, contextual information such as local GBS prevalence and country income *(1)*, rising antimicrobial resistance *(14)*, and possible relationships between early antibiotic exposure and altered gut microbiome, asthma and obesity *(15, 16)* should be taken into account.

1.2 Rationale and objectives

WHO has established a process for prioritizing the development of maternal and perinatal health recommendations, whereby an international group of independent experts – the Executive Guideline Steering Group (GSG) – oversees a systematic prioritization of MPH recommendations in most urgent need of development *(17, 18)*. The Executive GSG prioritized development of the WHO recommendation on screening of pregnant women for intrapartum antibiotic prophylaxis for the prevention of early onset Group B streptococcus disease in newborns to complement the existing WHO recommendation supporting the provision of intrapartum antibiotic prophylaxis for women with GBS colonization *(1)*.

This recommendation was developed in accordance with the standards and procedures in the *WHO handbook for guideline development*, including synthesis of available research evidence, use of the Grading of Recommendations Assessment, Development and Evaluation (GRADE)[1] and GRADE Confidence in the Evidence from Reviews of Qualitative Research (GRADE-CerQUAL)[2] methodologies, and formulation of recommendations by a Guideline Development Group (GDG) composed of international experts and stakeholders *(19)*. The primary aim of this recommendation is to improve the quality of care and outcomes for women and newborns, as they relate to the prevention of EOGBS disease in newborns.

1.3 Target audience

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

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

The term "woman" includes individuals who have given birth, even if they may not identify as a woman or as a mother. It is recognized that some individuals who have given birth identify as gender diverse.

1.4 Scope of the recommendation

This recommendation specifically addresses GBS screening strategies to determine candidacy for intrapartum antibiotic prophylaxis in women at or near term. Vaccination, intrapartum rapid testing, and other methods to reduce GBS infection which are currently not readily implementable in health-care settings are beyond the scope of the recommendation.

Two questions guided the development of the recommendation. Framed using the Population (P), Intervention (I), Comparison (C), Outcome (O) (PICO) format, these questions were:

- *Among pregnant women at or near term (P) does a screening strategy for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with no screening strategy (C) improve maternal and neonatal outcomes (O)?*
- *Among pregnant women at or near term (P) does a screening strategy for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with another screening strategy (C) improve maternal and neonatal outcomes (O)?*

1.5 Persons affected by the recommendation

The population affected by this recommendation includes all pregnant women at or near term and their newborns.

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

2. Methods

The recommendation was 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 recommendation; and (v) planning for the dissemination, implementation, impact evaluation and updating of the recommendation.

In April 2021, screening pregnant women for IAP for the prevention of early onset GBS disease in newborns was identified by the Executive GSG as a high priority for development of a new recommendation based on the current widespread use of different strategies, including no screening strategy in some settings. This recommendation was also prioritized in the context of the existing recommendation that intrapartum antibiotic prophylaxis should be administered to women with GBS colonization to prevent early neonatal GBS infection *(1)*.

Six main groups were involved in the guideline development 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, South-East Asia Region, European Region, Eastern Mediterranean 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 (SRH) and the Department of Maternal, Newborn, Child and Adolescent Health and Ageing (MCA) managed the development of the recommendation. 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, clinical practice, policy and programmes relating to maternal and perinatal health, as well as consumer representation. 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, 13 external experts and relevant stakeholders were invited to participate as members of the GDG for the current recommendation. Those selected formed a diverse group with expertise in research, guideline development methods, gender, equity and rights, clinical practice, policy and programmes and consumer representation relating to prevention and treatment of peripartum infection.

The GDG members for this recommendation were also selected in a way that ensured geographic representation and gender balance and there were no important conflicts of interest. The GDG appraised the evidence that was used to inform the recommendation, advised on the interpretation of this evidence, formulated the final recommendation based on the draft prepared by the WHO Steering Group and reviewed and reached unanimous consensus for the recommendation in the final document. The members of the GDG are listed in Annex 1.

2.1.4 Evidence Synthesis Group (ESG)

WHO convened an ESG to conduct systematic reviews, appraise the evidence and develop the Evidence to Decision (EtD) frameworks. A systematic review on the effect of GBS screening strategies on maternal and neonatal outcomes *(20)* was produced by a research team at Leiden University Medical Centre, Kingdom of the Netherlands. The WHO Steering Group reviewed and provided input into the updated protocol and worked closely with the ESG to appraise the evidence using the GRADE methodology. A rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS disease *(21)* was produced by a research team at the Centre for Maternal and Child Health Research at City, University of London, the United Kingdom. A systematic review of the cost–effectiveness of GBS screening programmes *(22)* was produced by a research team at the University of Melbourne, Australia. Further details on these reviews and how the reviews were used on the evidence synthesis process are provided under *Section 2.3 Evidence identification and retrieval* and *Section 2.4 Certainty assessment and grading of the evidence*.

An independent consultant from Australia served as the guideline methodologist and technical experts from the Centro Rosarino de Estudios Perinatales (CREP), Argentina, served as evidence synthesis experts. These individuals appraised the evidence, conducted GRADE assessments and developed the EtD frameworks with the WHO Steering Group. 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 Federation of Gynecology and Obstetrics and the Bill & Melinda Gates Foundation participated in the GDG meeting as observers. These organizations, with their long history of collaboration with WHO in maternal and perinatal health guideline dissemination and implementation, were identified to ensure the transparency of the processes, engage partners, and facilitate implementation of the recommendation. Observers were able to share information or opinions during the GDG meeting, but they did not participate in the formulation of recommendations. The observers who participated in the GDG meeting are listed in Annex 1.

2.1.6 External Review Group (ERG)

The ERG included three 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 the prevention and treatment for maternal peripartum infections (1)*. 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, maternal satisfaction was included as an important outcome in an attempt 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 recommendation would be woman-centred. All outcomes were included in the scope of this document for evidence searching, retrieval, synthesis, grading and formulation of the recommendation. The list of priority outcomes is provided in Annex 2.

2.3 Evidence identification and retrieval

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

2.3.1 Evidence on effectiveness of the intervention

A newly-developed systematic review on the effect of screening strategies on maternal and neonatal outcomes *(20)* was produced by Leiden University Medical Centre, Leiden, Kingdom of the Netherlands (PROSPERO [CRD42023411806]). This systematic review was the primary source of evidence of effectiveness for this recommendation. Studies relevant to the key question were screened by the review authors, and data on relevant outcomes and comparisons were entered into the statistical programme R. The review authors shared raw data exports from the R programme with the CREP team for data synthesis. The CREP team entered the data into Review Manager 5 (RevMan) software for the key comparisons and outcomes (those that were not relevant to the recommendation were excluded). The RevMan files were then exported to GRADE profiler software (GRADEpro), and GRADE criteria were used to critically appraise the retrieved scientific evidence. 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 newly developed rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS disease *(21)* was the primary source of evidence on acceptability and feasibility. This review included women's and providers' views and experiences with GBS screening and antibiotic prophylaxis. Evidence on values was obtained from a scoping review of what matters to women during antenatal care *(23)* as well as a systematic qualitative review on what matters to women during childbirth *(24)*, supplemented with findings from the rapid review of stakeholder perceptions of GBS screening *(21)*. The primary source of evidence for resources and cost–effectiveness was a review of cost–effectiveness of GBS screening programmes *(22)*.

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 *(25)*. 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 observational studies, certainty was first rated as "moderate" and then downgraded by one ("low") or two ("very low") levels, depending on the minimum criteria met by the majority of the studies contributing to the outcome.

Inconsistency of the results: The similarity in the results for a given outcome was assessed by exploring the magnitude of differences in the direction and size of effects observed in different studies. The certainty of evidence was not downgraded when the directions of the findings were similar and confidence limits overlapped, whereas it was downgraded when the results were in different directions and confidence limits showed minimal or no overlap.

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

Imprecision: Imprecision assesses 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 *(26)*. The GRADE-CERQual tool, which uses a similar conceptual approach to other GRADE tools, 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 according to the Consensus on Health Economic Criteria (CHEC) tool *(27)*.

2.5 Formulation of the recommendation

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

- **Effects:** The evidence on the priority outcomes was summarized in this domain to answer the questions: "What are the desirable and undesirable effects of the intervention?" and "What is the certainty of the evidence on effects?". Where benefits clearly outweighed

harms for outcomes that are highly valued by women, or vice versa, there was a greater likelihood of a clear judgement in favour of or against the intervention, respectively. Uncertainty about the net benefits or harms, or small net benefits, usually led to a judgement that did not favour the intervention or the comparator. The higher the certainty of the evidence of benefits across outcomes, the higher the likelihood of a judgement in favour of the intervention. In the absence of evidence of benefits, evidence of potential harm led to a recommendation against the intervention. Where the intervention showed evidence of potential harm and was also found to have evidence of important benefits, depending on the level of certainty and the likely impact of the harm, such evidence of potential harm was more likely to result in a context-specific recommendation, with the context explicitly stated within the recommendation.

- **Values:** This domain relates to the relative importance assigned to the outcomes associated with the intervention by those affected, how such importance varies within and across settings, and whether this importance is surrounded by any uncertainty. The question asked was: "Is there important uncertainty or variability in how much women value the main outcomes associated with the intervention?". When the intervention resulted in benefit for outcomes that most women consistently value (regardless of setting), this was more likely to lead to a judgement in favour of the intervention. This domain, together with the "effects" domain (see above), informed the "balance of effects" judgement.
- **Resources:** For this domain, the questions asked were: "What are the resources associated with the intervention?" and "Is the intervention cost–effective?". The resources required to implement screening for EOGBS risk and IAP candidacy are predominantly the costs of providing supplies, training, and equipment and infrastructure. A judgement in favour of, or against, the intervention was likely where the resource implications were clearly advantageous or disadvantageous, respectively.
- **Equity:** This domain encompasses evidence or considerations as to whether 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 inequities among different groups of women and their families.
- **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 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.

For each of the above domains, additional evidence of potential harms, unintended consequences or other information deemed important by the WHO Steering Group are described in the "Additional considerations" subsections. Such considerations were derived from evidence 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 two EtD frameworks, including evidence summaries, summary of findings tables and other documents related to the two PICO questions, to GDG members in advance of the GDG meeting. During the GDG meeting (5–6 December 2023), which was conducted under the leadership of the GDG chairperson, the GDG members collectively reviewed the EtD frameworks, and any comments received through preliminary feedback, and formulated the recommendation. The purpose of the meeting was to reach consensus on the recommendation and the specific context, based on explicit consideration of the range of evidence presented in the EtD frameworks and the judgement of the GDG members.

In formulating the recommendation, the GDG used the recommended GRADE EtD frameworks and considered separately the synthesized evidence on the effectiveness of the interventions, values, resource use and cost–effectiveness of the intervention, acceptability and feasibility of intervention, and the impact of the intervention on equity. For each of these domains, an appraisal of the certainty of evidence was performed using methods that were appropriate to the supporting evidence synthesis (e.g. GRADE or GRADE-CERQual). It was the view of the GDG that, as the certainty of the evidence was evaluated across several domains to arrive at the recommendation, not just for evidence on the effectiveness of the intervention, this cannot be captured within a single "certainty" rating. Providing the certainty of evidence for effectiveness alone within the text of the recommendations does not adequately demonstrate consideration of all types of evidence and could potentially confuse the target audience.

The GDG was asked to select one of the following categories for the recommendation:

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

2.6 Management of declarations of interests

WHO has a robust process to protect the integrity of its normative work, as well as to protect the integrity of individual experts with whom it collaborates. WHO requires that experts serving in an advisory role disclose any circumstances that could give rise to actual or ostensible conflict of interest. The disclosure and the appropriate management of relevant financial and non-financial conflicts of interest of GDG members and other external experts 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 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. All findings from the DOI statements received were managed in accordance with the WHO procedures to assure the work of WHO and the contributions of its experts is, actually and ostensibly, objective and independent. The names and biographies of individuals were published online two weeks prior to the meeting. Where a conflict of interest was not considered significant enough to pose any risk to the guideline development process or to reduce its credibility, the experts were only required to openly declare such conflicts of interest at the beginning of the GDG meeting, and no further actions were taken. Annex 3 shows a summary of the DOI statements and how conflicts of interest declared by invited experts were managed by the WHO Steering Group.

2.7 Decision-making during the GDG meetings

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

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

2.8 Document preparation

Prior to the online meeting, the WHO Steering Group prepared a draft version of the GRADE evidence profiles, the evidence summary and other documents relevant to the GDG's deliberation. The draft documents were made available to the participants before the meeting for their review. 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 GDG members, the final document was sent to six external independent experts (comprising 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, recommendations and supporting evidence

3.1 Guiding Principles

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 were adopted by the 2023 GDG. The principles are based on expert consensus and were not derived from a systematic process of evidence retrieval, synthesis and grading. They conform with the principles of good clinical practice that are needed to improve care related to the prevention or treatment of infectious morbidities around the time of childbirth. In addition to the strategies for implementation, monitoring and impact assessment presented later in this document, these principles are expected to guide end-users in the process of adapting and implementing this recommendation in a range of contexts and settings:

- Standard infection prevention and control precautions should be observed in the provision of maternity care to optimize the effects of the intervention recommended in this guideline *(28)*.
- 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 and sustain availability and equitable access of good-quality, affordable antibiotics for use in maternal and perinatal health care listed in the *WHO model list of essential medicines (29)* and to ensure that the necessary equipment is 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 *(14)*.
- 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. Additionally, the choice of antibiotics should be guided by maternal conditions and aimed at avoiding adverse effects. Ideally, the use of antimicrobials in any setting should be informed by local or national resistance surveillance data and treatment guidelines.

3.2 Recommendation and supporting evidence

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

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

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

Recommendation

Screening of pregnant women for intrapartum antibiotic prophylaxis is recommended for the prevention of early onset Group B streptococcus disease in newborns. Offer either universal antenatal testing for Group B streptococcus colonization and intrapartum antibiotic prophylaxis for women who screen positive (universal screening); or intrapartum assessment of risk factors and antibiotic prophylaxis for women at risk of having a newborn with early onset Group B streptococcus disease (risk-based approach). *(Recommended)*

- This recommendation was based on evidence from observational studies largely from high-income countries which show that either universal or risk-based screening strategies, compared with no screening strategy, may be associated with reduced risk of early onset Group B streptococcus (GBS) disease in newborns.
- While universal screening, as compared to a risk-based approach, is probably associated with reduced early onset GBS disease in newborns, the Guideline Development Group (GDG) acknowledged the challenges with costs and the feasibility of implementing antenatal universal screening, particularly in low-resource settings.
- Universal screening involves routine testing of all pregnant women during antenatal care, mostly conducted at 35–37 weeks using rectovaginal swabbing by a health worker or self-swabbing by the woman. Women who screened positive for GBS colonization, or with a previous infant with early onset GBS disease, or with known GBS bacteriuria (for example, due to urine testing for urinary tract infection) should be offered intrapartum antibiotic prophylaxis at the onset of labour.
- The risk-factor approach involves intrapartum assessment of women for any one risk-factor associated with having a newborn with early onset GBS disease. The risk factors across observational studies were varied. The most common risk factors were preterm prelabour rupture of membranes, prolonged rupture of membranes (>18 hours), previous infant with early onset GBS disease, known maternal bacteriuria, maternal intrapartum fever (>38 °C), and chorioamnionitis. These risk factors are in keeping with indications for intrapartum antibiotics in the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections (1)*.

- Women with maternal intrapartum fever should be assessed for any diagnostic or clinical signs of infection with intrapartum antibiotics administered in line with existing WHO recommendations *(1)*.
- Few studies also included preterm labour <37 weeks (including women with intact membranes) as a risk-factor for early onset GBS disease in newborns. The GDG noted WHO does not recommend routine antibiotic administration for women in preterm labour with intact amniotic membranes, based on rigorous trial evidence, concluding that the potential risk of harm to the baby (i.e. cerebral palsy) outweighed any potential benefit of the intervention *(1)*.
- As the evidence came from studies that tested ampicillin or penicillin G, either antibiotic may be considered for treatment except where there are contraindications (e.g. allergy history) or GBS strain has been microbiologically shown to be penicillin-resistant, in keeping with the 2015 *WHO recommendations for prevention and treatment of maternal peripartum infections (1)*.
- Women should be provided with evidence-based, up-to-date information on the prevention of early onset GBS disease in newborns and the maternal screening offered in their setting before being offered screening. The information should facilitate an understanding of the purpose of screening, the procedure involved in obtaining swabs in their setting and the potential implications of a positive result including subsequent intrapartum antibiotic prophylaxis. Women should give consent for the procedure and be able to refuse without mistreatment.
- The GDG acknowledged that this recommendation may be updated following the conclusion of a large ongoing trial comparing universal screening (either antenatal testing at 35–37 weeks' gestation or rapid intrapartum testing) to maternal risk-based screening *(2)*. Future studies may also address the uncertainties on risk-factors to be assessed when a risk-based approach is used. The GDG also acknowledged the development of rapid intrapartum testing which may improve screening accuracy.

4. Dissemination, adaptation and implementation of the recommendation

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

4.1 Recommendation dissemination

The recommendation will be disseminated through WHO regional and country offices, ministries of health, professional organizations, WHO collaborating centres, other United Nations agencies and nongovernmental organizations, among others. This recommendation will be published on the WHO SRH Department website and included in the WHO Human Reproduction Programme News bulletin which is disseminated to over 8000 subscribers, including clinicians, health programme managers, policy-makers and service users from all around the world. Updated recommendations are also routinely disseminated during meetings or scientific conferences attended by WHO maternal and perinatal health staff.

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

4.2 Adaptation

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

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

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

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

4.3 Implementation considerations

- To assess the suitability of implementation of universal screening, the following should be considered: (i) the incidence of GBS colonization, (ii) the availability of trained health workers to counsel pregnant women and ensure swab collection during antenatal

care, (iii) access and capacity of laboratories to process bacteriological cultures and (iv) continuity of care to ensure that all women who screen positive during pregnancy receive intrapartum antibiotic prophylaxis.

- Care providers' knowledge and skills should be strengthened regarding counselling, screening strategies and use of antibiotics and the provision of woman-centred, culturally-sensitive care around GBS screening, particularly as screening may lead to maternal anxiety.
- Settings may implement self-swabbing or swabbing by health-care workers, given evidence that women's preference for self-swabbing versus health-care professional swabbing varies *(21)* and self-swabbing remains accurate *(30)*. Lower vaginal and rectal swabbing should be used without a speculum. Clear information and decision-support about the screening procedure should be provided to women, including procedures for self-swabbing where needed.
- Health facilities using universal screening should ensure that they have adequately trained staff, clear protocols and the necessary equipment and supplies to store and process laboratory samples.
- To implement universal screening, a well-defined process to ensure continuity between antenatal care, receipt of test results and eligibility for intrapartum antibiotic prophylaxis at admission for birth is needed. Streamlined communication and coordination is required throughout the screening process. The *WHO recommendations for a positive pregnancy experience* recommend an antenatal contact at 36 weeks where GBS testing could occur.
- Health facilities providing intrapartum antibiotic prophylaxis should ensure that they have adequately trained staff, clear protocols and the necessary equipment and supplies to administer intravenous drugs safely and manage complications related to their use, should they arise.
- Antibiotic regimens should be determined according to local protocol. Settings may wish to consider: (i) 2 g of ampicillin IV followed by 1 g every 4 hours until birth; (ii) 500 mg of ampicillin IV every 6 hours until birth; or (iii) 5 million units of penicillin G IV every 6 hours during labour and, if labour lasts more than 18 hours, 1 million units of penicillin orally every 8 hours until birth *(1)*.
- Maternal screening strategies do not prevent all cases of early-onset GBS disease and do not reduce the risk for late-onset GBS disease. Prompt recognition and early initiation of appropriate antimicrobial therapy is necessary to minimize morbidity and mortality among the cases that continue to occur. WHO has existing recommendations for management of severe bacterial infection (0–59 days) in young infants *(31, 32)*.
- Mechanisms should be in place at health facilities to ensure that the necessary drugs are kept secure and in stock and can be dispensed when needed.
- A hospital committee is essential to monitor antimicrobial usage, including the quantity and patterns of use. The committee should report the results to the prescribers and regularly update the hospital antimicrobial formularies.
- Where penicillin and its derivatives are contraindicated, alternative antibiotics should be made available. Penicillin and ampicillin must be transported and stored according to supplier specifications. As penicillin and ampicillin are heat sensitive and may require refrigeration, proper storage may not be feasible in settings with no or inconsistent electricity supply.

5. Research gaps

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

- In low- and middle-income countries, is universal or risk-based screening more effective, acceptable, feasible and cost–effective?
- Is rapid intrapartum testing for GBS effective as compared with antepartum testing for IAP for the prevention of EOGBS in newborns?
- What is the short- and long-term impact of IAP on newborn and child health, including the impact on the intestinal microbiota of newborns, developmental outcomes and chronic disease?

6. Applicability issues

6.1 Anticipated impact on the organization of care and resources

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

- lack of understanding of GBS and of the purpose of GBS screening among health workers, women giving birth, families and/or communities;
- lack of opportunities for continuing education and professional development for health workers;
- lack of human resources with the necessary training and skills in patient communication and consent, infection control, rectovaginal swab technique and specimen handling, as well as in the administration of intravenous IAP;
- lack of infrastructure to support the interventions (such as lack of physical space to conduct individual care and counselling; lack of access to laboratory services to carry out culture-based testing; lack of electricity for refrigeration);
- concerns from skilled care personnel and system managers regarding the safety and potential consequences of intravenous IAP, including antimicrobial resistance;
- 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 (29)*; and
- lack of current systems in place to monitor the use of antibiotics and antimicrobial resistance.

6.2 Monitoring and evaluating guideline implementation

The implementation and impact of this recommendation will be monitored at the health service, country and regional levels, as part of broader efforts to monitor and improve the quality of maternal and newborn care. The WHO document *Standards for improving quality of maternal and newborn care in health facilities (33)* 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 Departments of SRH and MCA, data on country- and regional-level implementation of the recommendation can be collected and evaluated in the short to medium term to assess its impact on national policies of individual WHO Member States.

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

- Proportion of women undergoing screening for risk of early onset group B Streptococcus disease in newborns where intrapartum antibiotic prophylaxis was administered for eligible women, calculated as the number of women who undergo screening and have intrapartum antibiotic prophylaxis administered divided by the total number of birthing women.
- Incidence of early onset group B Streptococcus disease in newborns, calculated as the number of newborns diagnosed with early onset group B Streptococcus disease divided by the total number of live births.

The first indicator provides an assessment of the use of screening procedures among women, while the second provides information on the efficacy of the intervention in preventing early onset group B Streptococcus disease in newborns.

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, this recommendation will be reviewed along with other recommendations for prioritization by the Executive GSG.

If new evidence that could potentially impact the current evidence base is identified, the recommendation may be updated. If no new reports or information are identified, the recommendation may be revalidated. The GDG acknowledged the GBS3 trial anticipated for publication in 2026 which will provide new evidence on universal screening (including rapid intrapartum testing) as compared with risk-based screening (ISRCTN49639731) *(2)*. The GDG also noted the prioritized development of GBS vaccines suitable for maternal immunization in pregnancy and for use in low-and-middle-income countries by the WHO *(34)*. Following publication and dissemination of the updated recommendation, any concerns about the validity of the recommendation should be promptly communicated to the guideline implementers.

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

8. References

1. WHO recommendations for prevention and treatment of maternal peripartum infections. Geneva: World Health Organization; 2015. (https://iris.who.int/handle/10665/186171, accessed 15 August 2024).
2. ISRCTN Registry. Routine testing for Group B Streptococcus in pregnancy (GBS3 trial). ISRCTN49639731. [website]: BioMed Central; 2022 [updated 30 March 2022] doi: 10.1186/ISRCTN49639731 (accessed 15 June 2024).
3. Chen X, Cao S, Fu X, Ni Y, Huang B, Wu J, et al. The risk factors for group B Streptococcus colonization during pregnancy and influences of intrapartum antibiotic prophylaxis on maternal and neonatal outcomes. BMC Pregnancy Childbirth. 2023;23(1):207. doi: 10.1186/s12884-023-05478-9 (accessed 13 August 2024).
4. Khan MA, Faiz A, Ashshi AM. Maternal colonization of group B streptococcus: prevalence, associated factors and antimicrobial resistance. Ann Saudi Med. 2015;35(6):423–7. doi: 10.5144/0256-4947.2015.423 (accessed 13 August 2024).
5. Schuchat A. Group B streptococcus. Lancet. 1999;353(9146):51–6. doi: 10.1016/S0140-6736(98)07128-1 (accessed 13 August 2024).
6. Colbourn T, Gilbert R. An overview of the natural history of early onset group B streptococcal disease in the UK. Early Hum Dev. 2007;83(3):149–56. doi: 10.1016/j.earlhumdev.2007.01.004 (accessed 13 August 2024).
7. Gonçalves BP, Procter SR, Paul P, Chandna J, Lewin A, Seedat F, et al. Group B Streptococcus infection during pregnancy and infancy: estimates of regional and global burden. Lancet Glob Health. 2022;10(6):e807–e19. doi: 10.1016/S2214-109X(22)00093-6 (accessed 13 August 2024).
8. Luck S, Torny M, d'Agapeyeff K, Pitt A, Heath P, Breathnach A, et al. Estimated early-onset group B streptococcal neonatal disease. Lancet. 2003;361(9373):1953–4. doi: 10.1016/S0140-6736(03)13553-2 (accessed 13 August 2024).
9. Madrid L, Seale AC, Kohli-Lynch M, Edmond KM, Lawn JE, Heath PT, et al. Infant group B streptococcal disease incidence and serotypes worldwide: systematic review and meta-analyses. Clin Infect Dis. 2017;65(suppl_2):S160–S72. doi: 10.1093/cid/cix656 (accessed 13 August 2024).
10. Puopolo KM, Lynfield R, Cummings JJ, Committee on fetus and newborn, Newborn committee on infectious diseases, Hand I, et al. Management of infants at risk for group B streptococcal disease. Pediatrics. 2019;144(2):e20191881. doi: 10.1542/peds.2019-1881 (accessed 13 August 2024).
11. Le Doare K, O'Driscoll M, Turner K, Seedat F, Russell NJ, Seale AC, et al. Intrapartum antibiotic chemoprophylaxis policies for the prevention of Group B streptococcal disease worldwide: systematic review. Clin Infect Dis. 2017;65(suppl_2):S143–S51. doi: 10.1093/cid/cix654 (accessed 13 August 2024.
12. Rao GG, Khanna P. To screen or not to screen women for Group B streptococcus (streptococcus agalactiae) to prevent early onset sepsis in newborns: recent advances in the unresolved debate. Ther Adv Infect Dis. 2020;7:2049936120942424. doi: 10.1177/2049936120942424 (accessed 13 August 2024).
13. Hasperhoven GF, Al-Nasiry S, Bekker V, Villamor E, Kramer BWW. Universal screening versus risk-based protocols for antibiotic prophylaxis during childbirth to prevent early-onset group B streptococcal disease: a systematic review and meta-analysis. BJOG. 2020;127(6):680–91. doi: 10.1111/1471-0528.16085 (accessed 13 August 2024).

14. WHO global strategy for containment of antimicrobial resistance. Geneva: World Health Organization; 2001 (https://iris.who.int/handle/10665/66860, accessed 15 August 2024).

15. Li P, Chang X, Chen X, Wang C, Shang Y, Zheng D, et al. Early-life antibiotic exposure increases the risk of childhood overweight and obesity in relation to dysbiosis of gut microbiota: a birth cohort study. Ann Clin Microbiol Antimicrob. 2022;21(1):46. doi: 10.1186/s12941-022-00535-1 (accessed 13 August 2024).

16. Zhang Z, Wang J, Wang H, Li Y, Jia Y, Yi M, et al. Association of infant antibiotic exposure and risk of childhood asthma: a meta-analysis. World Allergy Organ J. 2021;14(11):100607. doi: 10.1016/j.waojou.2021.100607 (accessed 13 August 2024).

17. Vogel JP, Dowswell T, Lewin S, Bonet M, Hampson L, Kellie F, et al. Developing and applying a 'living guidelines' approach to WHO recommendations on maternal and perinatal health. BMJ Glob Health. 2019;4(4):e001683. doi: 10.1136/bmjgh-2019-001683 (accessed 13 August 202

18. Priority questions for WHO recommendations in maternal and perinatal health, 2024-2025 [website]. Geneva: World Health Organization; 2024 (https://www.who.int/news-room/articles-detail/priority-questions-who-recommendations-maternal-perinatal-health-2024-2025), accessed 18 June 2024.

19. WHO handbook for guideline development. Second edition. Geneva: World Health Organization; 2014 (https://iris.who.int/handle/10665/145714, accessed 15 August 2024).

20. Panneflek TJR, Hasperhoven GF, Chimwaza Y, Allen C, Lavin T, te Pas AB, et al. Intrapartum antibiotic prophylaxis to prevent Group B streptococcal infections in newborn infants: a systematic review and meta-analysis comparing various strategies. eClinicalMedicine. 2024;74:102748. doi: https://doi.org/10.1016/j.eclinm.2024.102748.

21. Constantinou G, Webb R, Ayers S. An evidence synthesis on parents' and healthcare providers' values and preferences for, and views on the acceptability, feasibility, equity and outcomes of screening strategies to prevent early-onset group B streptococcal disease in newborns [preprint version]. doi:10.1101/2024.06.28.24309381.

22. Allen C, Naznin E, Penneflek TJR, Lavin T, Hoque ME. The cost-effectiveness of Group B Streptococcus screening strategies: a systematic review [pre-print https://doi.org/10.1101/2024.08.25.24312541]

23. Downe S, Finlayson K, Tunçalp Ö, Metin Gülmezoglu A. What matters to women: a systematic scoping review to identify the processes and outcomes of antenatal care provision that are important to healthy pregnant women. BJOG. 2016;123(4):529–39. doi: 10.1111/1471-0528.13819 (accessed 13 August 2024).

24. Downe S, Finlayson K, Oladapo O, Bonet M, Gülmezoglu AM. What matters to women during childbirth: a systematic qualitative review. PLOS ONE. 2018;13(4):e0194906. doi: 10.1371/journal.pone.0194906 (accessed 13 August 2024).

25. Alonso-Coello P, Schünemann HJ, Moberg J, Brignardello-Petersen R, Akl EA, Davoli M, et al. GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction. BMJ. 2016;353:i2016. doi: 10.1136/bmj.i2016 (accessed 13 August 2024).

26. Lewin S, Booth A, Glenton C, Munthe-Kaas H, Rashidian A, Wainwright M, et al. Applying GRADE-CERQual to qualitative evidence synthesis findings: introduction to the series. Implement Sci. 2018;13(Suppl 1):2. doi: 10.1186/s13012–017-0688-3 (accessed 13 August 2024).

27. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care. 2005;21(2):240–5.

doi:10.1017/S0266462305050324 (accessed 13 August 2024).

28. Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/331750, accessed 15 August 2024).

29. Web Annex A. World Health Organization model list of essential medicines – 23rd list, 2023. In: The selection and use of essential medicines 2023. Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines, 24–28 April 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/bitstream/handle/10665/371090/WHO-MHP-HPS-EML-2023.02-eng.pdf, accessed 15 June 2024).

30. Odubamowo K, Garcia M, Muriithi F, Ogollah R, Daniels JP, Walker KF. Self-collected versus health-care professional taken swab for identification of vaginal-rectal colonisation with group B streptococcus in late pregnancy: a systematic review. Eur J Obstet Gynecol Reprod Biol 2023;286:95–101. doi: 10.1016/j.ejogrb.2023.05.027 (accessed 13 August 2024).

31. Recommendations for management of common childhood conditions: evidence for technical update of pocket book recommendations: newborn conditions, dysentery, pneumonia, oxygen use and delivery, common causes of fever, severe acute malnutrition and supportive care. World Health Organization; 2012 (https://apps.who.int/iris/handle/10665/44774, accessed 14 June 2024).

32. Guideline: Managing possible serious bacterial infection in young infants when referral is not feasible. World Health Organization. 2015 (https://www.who.int/publications/i/item/9789241509268, accessed 14 June 2024).

33. Standards for improving quality of maternal and newborn care in health facilities. Geneva: World Health Organization; 2016 (https://iris.who.int/handle/10665/249155, accessed 15 August 2024).

34. Group B streptococcus vaccine: full value of vaccine assessment. Geneva: World Health Organization; 2021 (https://iris.who.int/handle/10665/347595, accessed 15 August 2024).

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Annex 2. Priority outcomes used in decision-making

Priority outcomes (O):[1]

Critical outcomes:

1. Incidence of EOGBS infections[2] (as defined by study authors)
2. Perinatal mortality (composite of stillbirth and early neonatal death); early neonatal mortality (death within 7 days after birth)
3. Any early onset neonatal infection
4. Any early onset neonatal sepsis

Important outcomes:

5. Severe neonatal morbidity (such as neonatal ICU admission)
6. Maternal peripartum infection (chorioamnionitis, endometritis)
7. Maternal satisfaction with care
8. Cost of care
9. Early neonatal (≤7 days) therapeutic antibiotic use
10. Antimicrobial resistance (GBS resistant neonatal infection)
11. Maternal or neonatal anaphylaxis

[1] These outcomes reflect the prioritized outcomes used in the development of this recommendation, in the *WHO recommendations for prevention and treatment of maternal peripartum infections* (2015).

[2] Outcome adapted from the *WHO recommendations for prevention and treatment of peripartum infections* and critical to the current review question.

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

Name	Expertise contributed to guideline development	Declared interest	Management of conflict of interest
Felix Achana	Content expert and end-user	None declared	Not applicable
Subha Sri Balakrishnan	Content expert and end-user	None declared	Not applicable
Maria Laura Costa	Content expert and end-user	None declared	Not applicable
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Sadia Shakoor	Content expert and end-user	None declared	Not applicable
M Jeeva Sankar	Content expert and end-user	None declared	Not applicable

Annex 4. Evidence-to-Decision Frameworks

Framework 1: Screening strategies compared with no screening strategies

Question presented in PICO (population, intervention, comparator, outcome) format:

Among pregnant women at or near term (P) does a screening strategy for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with no screening strategy (C) improve maternal and neonatal outcomes (O)?*

* Screening strategy refers to a protocol to identify women eligible for IAP, and subsequent IAP administration to eligible women.

There are three specific PICOs under this question which relate to the different screening strategies:

- Among women at or near term (P) does **universal** screening for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with no screening strategy (C) improve maternal and neonatal outcomes (O)?
- Among women at or near term (P) does **risk-based** screening for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with no screening strategy (C) improve maternal and neonatal outcomes (O)?
- Among women at or near term (P) does a **combined/other** screening strategy for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with no screening strategy (C) improve maternal and neonatal outcomes (O)?

Problem: Prevention of early onset Group B streptococcus disease in newborns

Perspective: Clinical practice recommendation – population perspective

Population (P): All pregnant women at or near term

Intervention (I): Screening strategy for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns

Comparators (C): No screening strategy

Setting: Hospital setting

Subgroups: None

Priority outcomes (O):[1]

*Denotes outcomes deemed as "critical". All other outcomes deemed as "important".

Neonatal outcomes

1. *Incidence of EOGBS infections[2] (as defined by study authors)
2. *Perinatal mortality (composite of stillbirth and early neonatal death); early neonatal mortality (death within 7 days after birth)
3. *Any early onset neonatal infection
4. *Any early onset neonatal sepsis
5. Severe neonatal morbidity (e.g. neonatal ICU admission)

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[1] These outcomes reflect the prioritized outcomes used in the development of this recommendation, in the WHO recommendations for prevention and treatment of maternal peripartum infections (2015).

[2] Outcome adapted from the WHO recommendations for prevention and treatment of peripartum infections and critical to the current review question.

Maternal outcomes

6. Maternal peripartum infection (chorioamnionitis, endometritis)
7. Maternal satisfaction with care

Health service use

8. Cost of care
9. Early neonatal (≤7 days) therapeutic antibiotic use

Adverse effects

10. Antimicrobial resistance (GBS resistant neonatal infection)
11. Maternal or neonatal anaphylaxis

Assessment

Effects of interventions

Among pregnant women at or near-term women (P) does a screening strategy for intrapartum antibiotic prophylaxis for the prevention early onset GBS disease in newborns (I) compared with no screening strategy (C) improve maternal and neonatal outcomes (O)?

Research evidence

Summary of evidence

Source and characteristics of studies

Evidence was derived from a systematic review on the effect of different GBS screening strategies on maternal and neonatal outcomes *(1)*. In total, 65 studies were included which reported on the priority outcomes and compared two distinct screening strategies. In the 65 studies, data on the specified outcomes were available for more than 10 million women.

Comparison 1: Any screening strategy compared with no screening strategy

In total, 40 retrospective or prospective observational studies contributed to the comparison of any screening strategy compared with no screening strategy. The studies were published between the years 1994 and 2019 in high-income countries, including Australia (n=3), Chile (n=1), Chinese Taipei (n=1), Czechia (n=1), Denmark (n=1), Hungary (n=1), Italy (n=1), Japan (n=2), Kingdom of the Netherlands (n=1), New Zealand (n=2), Spain (n=2), Sweden (n=2), Switzerland (n=1), the United Kingdom and Ireland (n=1) and the United States of America (n=20). Sample sizes in the studies ranged from 3658 to 4 814 264 live births. Births occurred in the hospital or data was collected from nationwide birth/delivery data.

Of the 40 studies, six included data for women who birthed at or near term (defined as 35 weeks' gestation or more), and 34 did not describe the gestation at which the included women birthed. The data from these studies are presented separately in each of the comparisons in this evidence-to-decision-framework.

Screening strategies included universal screening, risk-based screening, and other/combined screening strategies. Universal screening involved screening all pregnant women antenatally via rectovaginal swab at 24–28 weeks' gestation or 35–37 weeks' gestation and providing IAP to women with GBS colonization. Risk-based screening consisted of administering IAP to pregnant women who presented with risk factors for EOGBS infection such as preterm premature rupture of membranes (pPROM), prolonged rupture of membranes, intrapartum fever and/or preterm labour. Combined/other screening included any combination of the risk-based and universal screening, or another strategy that did not align with either universal or risk-based

strategies. Regardless of the screening strategy, most pregnant women with GBS bacteriuria or a previous child affected by an EOGBS infection were given IAP.

EOGBS definitions varied between studies, including GBS in sterile fluids such as any combination of blood/cerebrospinal fluid/joint fluid/urine/sputum or specific Diagnosis Group (DG) codes for EOGBS within 2–7 days of birth with possible additional requirement of clinical symptoms of infection and antibiotic use.

At or near-term populations

Neonatal outcomes

Low-certainty evidence suggests any screening strategy may be associated with reduced EOGBS infections when compared with no screening strategy (6 studies, 943 373 newborns; RR 0.31, 95% CI 0.27 to 0.35 [common effects model] and RR 0.34, 95% CI 0.24 to 0.48 [random effects model]).

It is uncertain whether any screening strategy is associated with early onset non-GBS neonatal sepsis or any early onset neonatal sepsis when compared with no screening strategy *(very low certainty evidence)*.

Data on perinatal mortality could not be meta-analysed as there were no deaths reported in any study reporting the outcome. Data from three studies are presented descriptively. Simetka 2010 (Czechia) reported a GBS fatality incidence of 0/4901 for a universal screening and 0/3581 for no screening strategy. Katz 1994 (the USA) reported a GBS fatality incidence 0/1681 for a universal screening and 0/1977 for no screening strategy. Renner 2006 (the USA) reported a term GBS fatality incidence of 0/9385 in the period with a combined screening strategy and 0/16126 for no screening strategy.

Undetermined or combined term and preterm populations

Neonatal outcomes

It is uncertain whether any screening strategy is associated with EOGBS infections or early onset neonatal sepsis when compared with no screening strategy (very low certainty evidence).

Maternal outcomes

It is uncertain whether any screening strategy is associated with chorioamnionitis when compared with no screening strategy (very low certainty evidence).

Adverse effects

It is uncertain whether any screening strategy is associated with maternal anaphylaxis when compared with no screening strategy *(very low certainty evidence)*.

Health service use was not reported in the included studies.

Additional considerations

Case fatality: Eleven studies reported on case fatality in a period without a screening strategy and observed that case fatality was between 0% to 50% and mortality rate was 0/1000 live births to 0.52 per 1000 live births.

Antimicrobial resistance: Studies reporting on antimicrobial resistance to EOGBS isolates found that there was no resistance to ampicillin or penicillin during periods without screening strategies (7 studies), or during periods where screening strategies were implemented (universal screening = 4 studies; risk-based screening = 2 studies).

Summary of IAP proportion: Three studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis in the group where no screening strategy

was implemented. 7.9% of women in this group received antibiotics (0.0787 [0.0347; 0.1689] tau^2 = 0.5742; tau = 0.7578; I^2 = 99.8% [99.8%; 99.9%]; H = 25.52 [22.43; 29.03]). Fifteen studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis using any screening strategy. 19.3% of women in this group received antibiotics (0.1932 [0.1643; 0.2259] tau^2 = 0.1457; tau = 0.3817; I^2 = 99.7% [99.6%; 99.7%]; H = 17.68 [16.59; 18.84]).

Type of antibiotic: For women at or near term, the included studies prescribed ampicillin or penicillin G. For women where there were contraindications (such as allergy history), cefazolin/cefalotin, clindamycin or vancomycin were used.

Adverse effects: A systematic review of adverse events in women and children who have received IAP for the prevention of neonatal GBS disease concluded that the evidence base was limited *(2)*. Potential adverse effects included altered infant microbiome, of which the clinical significance could not be determined due to lack of follow-up. Observational evidence for increased antimicrobial resistance was limited by high or unclear risk of bias in the reporting studies. One randomized controlled trial with limited applicability reported potentially serious long-term adverse effects such as cerebral palsy, for which the biological plausibility was unclear, and the finding was not replicated in a similar trial *(2)*.

Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Comparison 1a: Universal screening compared with no screening strategy

Three retrospective cohort studies conducted in Czechia (n=1) and the USA (n=2) compared a period of universal screening with no screening strategy. Two studies were single facility studies, one study was multicentre. Two studies conducted screening at 35–37 weeks' gestation, one study at 24–28 weeks. Two studies defined EOGBS as the presence of GBS in blood under an unknown time after birth, or GBS in blood or cerebrospinal fluid <7 days after birth with clinical symptoms, or DG codes for GBS and lack of other DG codes that refer to non-GBS streptococcal bacteria. One single centre study in Australia also compared a period with universal screening to a period without a screening strategy. Screening was conducted at 28 weeks' gestation or 24 weeks'

gestation if the woman presented with a risk factor for preterm labour. This study only provided relevant data on maternal anaphylaxis.

At or near-term populations

Neonatal outcomes

Low-certainty evidence suggests universal screening may be associated with reduced EOGBS infections when compared with no screening strategy (3 studies, 490 024 newborns; RR 0.22, 95% CI 0.18 to 0.27 [common effects model] and RR 0.26, 95% CI 0.13 to 0.54 [random effects model]).

Data on perinatal mortality could not be meta-analysed. Simetka 2010 (Czechia) reported a GBS fatality incidence of 0/4901 for universal screening and 0/3581 for no screening strategy. Katz 1994 (the USA) reported a GBS fatality incidence 0/1681 for universal screening and 0/1977 for no screening strategy.

Undetermined or combined term and preterm populations

Neonatal outcomes

It is uncertain whether universal screening is associated with EOGBS infections or any early onset neonatal sepsis when compared with no screening strategy *(very low certainty evidence)*.

Adverse effects

It is uncertain whether universal screening is associated with maternal anaphylaxis when compared with no screening strategy (very low certainty evidence).

Maternal outcomes and health service use were not reported in the included studies.

Additional considerations

Case fatality: Nine studies reported on case fatality in a period with universal screening and observed that case fatality was between 0% and 10% and mortality rate was 0/1000 live births to 0.054/1000 live births.

Antimicrobial resistance: Studies reporting on antimicrobial resistance to EOGBS isolates found that there was no resistance to ampicillin or penicillin during periods without screening strategies (7 studies), or during periods where screening strategies were implemented (universal screening = 4 studies).

Summary of IAP proportion: Eleven studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis using universal screening. 20.6% of women in this group received antibiotics (0.2063 [0.1730; 0.2441] tau^2 = 0.1185; tau = 0.3443; I^2 = 99.1% [98.8%; 99.2%]; H = 10.34 [9.27; 11.54]).

Timing of screening: Katz 1994 screened at 24–28 weeks' gestation and reported a RR of 0.17 (95% CI 0.01 to 3.25) for EOGBS incidence compared to a period without a screening strategy. Eberly 2009 and Simetka 2010 both reported on the incidence of EOGBS for a period with universal screening at 35–37 weeks' gestation and a period without a screening strategy. The pooled RR was 0.3045 [0.1056; 0.8782] tau^2 = 0.3914, I^2=53.6% [0.0%-88.5%], H=1.47 [1.00-2.95]) for universal screening compared with no screening strategy.

Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Comparison 1b: Risk-based screening compared with no screening strategy

One prospective cohort study conducted in the USA compared risk-based screening (based on preterm birth <37 weeks' gestation, prolonged rupture of membranes, intrapartum fever or carriers of inconsistent screening for GBS colonization at 28 weeks' gestation/first prenatal visit) with no screening strategy. EOGBS was defined as the presence of GBS in blood <7 days after birth with clinical symptoms. One retrospective cohort study conducted in the USA compared risk-based screening (based on the Centers for Disease Control and Prevention [CDC] guidelines published in 1996) with no screening strategy.[1] EOGBS was defined as the presence of GBS in blood/cerebrospinal fluid <7 days after birth.

At or near-term populations

Neonatal outcomes

Low-certainty evidence suggests risk-based screening may be associated with reduced EOGBS infections when compared with no screening strategy (1 study, 46 959 newborns; RR 0.25, 95% CI 0.10 to 0.59).

Undetermined or combined term and preterm populations

Neonatal outcomes

It is uncertain whether risk-based screening is associated with EOGBS infections or any early onset neonatal sepsis when compared with no screening strategy *(very low certainty evidence)*.

Maternal outcomes

It is uncertain whether risk-based screening is associated with chorioamnionitis when compared with no screening strategy *(very low certainty evidence)*.

Health service use and adverse effects were not reported in the included studies.

[1] The same study also included a period with a combined/other screening strategy, but there were no data relevant to this evidence-to-decision framework from this comparison.

Additional considerations

Case fatality: Six studies reported on case fatality in a period with risk-based screening and observed that the case fatality rate was between 0% and 12.5% and the mortality rate was between 0/1000 live births and 0.033/1000 live births.

Antimicrobial resistance: Studies reporting on antimicrobial resistance to EOGBS isolates found that there was no resistance to ampicillin or penicillin during periods without screening strategies (7 studies), or during periods where screening strategies were implemented (risk-based screening = 3 studies, including one study conducted in India).

Summary of IAP proportion: Ten studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis using risk-based screening. 16.7% of women in this group received antibiotics (0.1677 [0.1363; 0.2046] tau^2 = 0.1403; tau = 0.3745; I^2 = 97.4% [96.4%; 98.1%]; H = 6.21 [5.29; 7.30]).

Lower-middle income country: One single-centre study conducted in India compared a period with risk-based screening (intrapartum ampicillin to pPROM, >3 gloved vaginal examinations, intrapartum fever, preterm labour, chorioamnionitis or GBS urinary tract infection during pregnancy) to a period without a screening strategy. The study period consisted of 107 692 live births and term incidence of EOGBS was reported to have decreased from a rate of 0.78/1000 live births (95% CI 0.51 to 1.05) to 0.56/1000 live births (95% CI 0.36 to 0.76), however actual numbers per period were not available.

Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Comparisons 1c–1f: Combined/other screening strategy compared with no screening strategy

Four studies provided data for women at, or near, term, including two retrospective cohort studies, one retrospective observational study, and one prospective cohort study published between the years 2002 and 2017. Two studies were conducted in the USA, and one each in Brazil and Switzerland. Definitions of EOGBS varied across studies and were defined as the possession of DG codes for streptococcal septicaemia, group B streptococcus, in conditions classified elsewhere, streptococcal meningitis, GBS pneumonia and lack of other DG codes that refer to non-GBS bacteria <7 days after birth, presence of GBS in blood <7 days after birth, presence of GBS in blood <7 days after birth with clinical symptoms, or presence of GBS in blood <72 hours after birth with antibiotic treatment >/=5 days or death <5 days while being treated with antibiotics.

Comparison 1c: Combined/other screening strategy compared with no screening strategy

Eberly 2009 compared a period without a screening strategy with a period with the CDC guidelines of 1996 which either recommend universal rectovaginal screening of all pregnant women at 35–37 weeks' gestation and IAP to all carriers of GBS, or IAP to pregnant women presenting with preterm delivery, intrapartum fever, prolonged rupture of membranes.

Neonatal outcomes

Low-certainty evidence suggests a combined/other screening strategy may be associated with reduced EOGBS infections when compared with no screening strategy (1 study, 570 038 newborns; RR 0.36, 95% CI 0.30 to 0.42).

Comparison 1d: Combined/other screening strategy compared with no screening strategy

Towers 2002 compared a period without a screening strategy with a period with IAP administered to carriers of GBS colonization determined via universal screening at 35–37 weeks' gestation or IAP to pregnant women presenting with preterm delivery <37 weeks' gestation, prolonged rupture of membranes, intrapartum fever or carriers of inconsistent screening for GBS colonization at 28 weeks' gestation/first prenatal visit were treated with IAP.

Neonatal outcomes

Low-certainty evidence suggests a combined/other screening strategy may be associated with reduced EOGBS infections when compared with no screening strategy (1 study, 47 334 newborns; RR 0.37, 95% CI 0.18 to 0.76).

Comparison 1e: Combined/other screening strategy compared with no screening strategy

Renner 2006 compared a period without a screening strategy to a period with IAP to carriers of GBS following universal screening at 35–37 weeks' gestation with prolonged rupture of membranes, preterm delivery or intrapartum signs of infection, when GBS carrier state is unknown, IAP to pregnant women presenting with prolonged rupture of membranes, preterm delivery or intrapartum signs of infection and IAP to pregnant women that had a previous infant affected by an EOGBS infection.

Neonatal outcomes

It is uncertain whether a combined/other screening strategy is associated with EOGBS infections when compared with no screening strategy *(very low certainty evidence)*.

Comparison 1f: Combined/other screening strategy compared with no screening strategy

Freitas 2017 compared a period without a screening strategy with a period with IAP to carriers if GBS following universal rectovaginal screening for GBS at 24 weeks' gestation or later with preterm labour and rupture of membranes and IAP to pregnant women with GBS bacteriuria or a previous child with GBS sepsis and IAP to pregnant women presenting with preterm labour, prolonged rupture of membranes, intrapartum fever if GBS colonization status was unknown.

Neonatal outcomes

It is uncertain whether a combined/other screening strategy is associated with EOGBS infections when compared with no screening strategy *(very low certainty evidence)*.

Maternal outcomes, health service use, and adverse effects were not reported in the included studies.

No data were reported for undetermined or combined term and preterm populations.

Additional considerations

Summary of IAP proportion: Seven studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis using a combined/other screening strategy. 18.3% of women in this group received antibiotics (0.1833 [0.1216; 0.2668] tau^2 = 0.4123; tau = 0.6421; I^2 = 99.8% [99.7%; 99.8%]; H = 21.40 [19.66; 23.30]).

Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Values

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

Research evidence

Findings from a scoping review of what matters to women during antenatal care *(3)* indicate that women from all resource settings value having a positive pregnancy experience, which includes the provision of effective clinical practices (interventions and tests), relevant and timely information, and psychosocial and emotional support *(high confidence in the evidence)*.

A systematic qualitative review on what matters to women during childbirth *(4)* indicates that most women are apprehensive about labour and childbirth, adverse birth outcomes and certain medical interventions, and they value the support and reassurance of health-care professionals who are sensitive to their needs *(high confidence in the evidence)*. Most women want a normal birth with good outcomes for mother and baby but acknowledge that medical intervention may sometimes be necessary. Where interventions are required, most women would like to receive relevant information from technically competent health care providers in a manner they can understand *(high confidence in the evidence)*. Women want to be in control of their birth process and involved in decision-making around the use of interventions *(high confidence in the evidence)*.

These findings are reinforced by those from a rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(5)* which indicate that women's knowledge and awareness of GBS, GBS testing, and antibiotic prophylaxis is low *(high confidence in the evidence)*. Women generally want more information about GBS screening, ideally provided face-to-face by a health-care professional. Information should be provided early and in sufficient detail to enable informed decision making *(moderate confidence in the evidence)*.

Additional considerations

None.

Judgement

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

Balance of effects

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

Judgement

— Don't know	— Varies	— Favours no screening strategy	— Probably favours no screening strategy	— Does not favour either	✔ Probably favours any screening strategy	— Favours any screening strategy

Resources

How large are the resource requirements (costs)?

Research evidence

Universal screening compared with no screening strategy: A review of cost-effectiveness of GBS screening strategies *(6)* identified four studies comparing universal screening with no screening strategy for which four incremental cost-effectiveness ratios (ICERs) were calculated. All four studies were conducted in high-income settings including Kingdom of the Netherlands, the United Kingdom, and the USA. Three studies calculated ICERs as cost per QALY gained, and one as cost per case of EOGBS averted as well as cost per death averted. Quality assessment using the Consensus on Health Economic Criteria (CHEC) tool *(7)* demonstrated that three studies were of high quality and one study was of low quality. No determination as to cost-effectiveness was made in two studies. Of the other two studies, universal screening was found to be cost-effective in one (US$ 11 900 per EOGBS case averted) and not cost-effective in the other (US$ 64 000 per QALY gained). The cost-effectiveness thresholds employed to make this determination were markedly heterogenous and ranged from US$ 27 900 to US$ 100 000 per QALY gained or used author determination for cost-effectiveness thresholds.

Two of the studies conducted sensitivity analyses investigating the impact of the prevalence of maternal GBS colonization on overall cost-effectiveness of screening. One found no relationship between the prevalence of GBS colonization and the overall cost of screening while the other found a direct inverse relationship: when the prevalence of GBS colonization was higher, costs were lower and therefore cost-effectiveness was improved (no threshold was reported in the study).

Risk-based screening compared with no screening strategy: The above-mentioned cost-effectiveness review identified seven studies comparing risk-based screening with no screening strategy from which a total of 13 ICERs were calculated. All seven studies were conducted in high-income settings including Australia, Kingdom of the Netherlands, the United Kingdom, and the USA. Quality assessment using the CHEC tool *(7)* demonstrated five studies were of high quality and two were of moderate quality. Four studies calculated ICERs as per QALY gained and five as per case of EOGBS prevented (two studies used both measures). Across the studies, no determination on cost-effectiveness was made for four ICERS, seven were deemed cost-effective (US$ 180 to US$ 8805 per EOGBS case averted; US$ 7600 per QALY gained to US$ 77 006 cost-savings per QALY gained and two not cost-effective (>US$ 63 000 per case of EOGBS averted). The cost-effectiveness thresholds were as defined by the authors except for one study that used US$ 31 704 per QALY gained and one study that used US$ 25 000 per EOGBS case averted.

Three of the seven studies conducted sensitivity analyses investigating the impact of prevalence of maternal GBS colonization on overall cost-effectiveness of risk-based IAP. One study found that prevalence rates did not impact the overall cost-effectiveness of risk-based IAP. Two studies found an inverse relationship between cost-effectiveness and prevalence: the intervention was more cost-effective when colonization rates were higher. Of these studies, one compared risk-based screening for women who developed labour complications with no screening strategy and found the cost-saving threshold to be 0.65 per 1000 live births. The other study found that risk-based screening remained cost-effective to an incidence rate of maternal GBS as low as 10%.

In summary, of the 17 ICERs calculated across both above comparisons, risk-factor screening or a universal screening strategy was found to be cost-effective for eight,

not cost-effective in three and undetermined in six. Of the eight instances in which the intervention was found to be cost-effective, four found it to be cost saving.

There were no economic evaluations of any screening strategy compared with no screening strategy.

Additional considerations

None.

Main resource requirements

Resource	Description
Staff	■ Specimen collection and administration of Intravenous (IV) antibiotics requires skilled health care personnel (doctors/ midwives/nurses)
Training	■ Practice-based training for maternity care providers including patient communication and consent, infection control, rectovaginal swab technique and specimen handling ■ Training to administer IV antibiotics and to monitor and manage expected and unexpected side-effects is part of standard maternity staff training
Supplies	■ *Swabbing for GBS colonization (universal screening)* ▪ Gloves ▪ Sterile cotton swabs ▪ Specimen collection vials/biohazard bags ▪ Labels ■ *Intrapartum antibiotic prophylaxis* ▪ IV antibiotics: — Benzylpenicillin (penicillin G or PenG) = US$ 0.2404 per 3 g vial (injectable) / cost per regimen approximately US$ 2.40 *(8)* — Ampicillin = US$ 0.1507 per 500 mg vial (injectable) *(8)* ▪ Alcohol wipes ▪ IV catheter or cannula and tubing ▪ IV pole/stand
Equipment and infrastructure	■ Access to laboratory with facilities to carry out testing of swab samples ■ On-site pharmacy and/or medicine stock management system that is managed by a trained pharmacist or dispenser ■ Rectovaginal culture ranges from US$ 6.15 to 18.44 for a negative result and US$ 13.63 to $ 40.89 for a positive result *(9)*
Time	■ Laboratory processing time varies according to the specific methods used, laboratory workload and sample transportation time. Results may be available from after several hours to after several days ■ IV antibiotics dispensing time estimated to be 2–5 minutes
Supervision and monitoring	■ Ongoing intrapartum care and monitoring of the woman and baby during labour and after birth, as for usual care

Resources required

Judgement – Any screening strategy vs no screening strategy

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

Judgement – Universal screening vs no screening strategy

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

Judgement – Risk-based screening vs no screening strategy

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

Judgement – Combined/other screening strategy vs no screening strategy

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

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Any screening strategy vs no screening strategy

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

Cost–effectiveness

Judgement – Any screening strategy vs no screening strategy

✔ Don't know	— Varies	— Favours no screening strategy	— Probably favours no screening strategy	— Does not favour either	— Probably favours any screening strategy	— Favours any screening strategy

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Universal screening vs no screening strategy

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

Cost-effectiveness

Judgement – Universal screening vs no screening strategy

— Don't know	✔ Varies	— Favours no screening strategy	— Probably favours no screening strategy	— Does not favour either	— Probably favours universal screening	— Favours universal screening

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Risk-based screening vs no screening strategy

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

Cost-effectiveness

Judgement – Risk-based screening vs no screening strategy

— Don't know	— Varies	— Favours no screening strategy	— Probably favours no screening strategy	— Does not favour either	✔ Probably favours risk-based screening	— Favours risk-based screening

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Combined/other screening strategy vs no screening strategy

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

Cost-effectiveness

Judgement – Combined/other screening strategy vs no screening strategy

✔ Don't know	— Varies	— Favours no screening strategy	— Probably favours no screening strategy	— Does not favour either	— Probably favours combined/ other screening	— Favours combined/ other screening

Equity

What would be the impact on health equity?

Research evidence

A rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(5)* found no direct evidence on the impact of GBS screening on health equity. The 2015 WHO state of inequality report *(10)* indicates that women who are poor, least educated and who reside in rural areas have lower coverage of health interventions and worse health outcomes than more advantaged women. Availability of GBS testing services and of IAP is likely to vary widely by geographical location and income setting. IAP is likely to be available for facility births only.

Additional considerations

The rapid review *(5)* found that knowledge and awareness of GBS is influenced by maternal education, with higher levels of education associated with higher knowledge. Younger women found the test less acceptable, found vaginal and rectal swabbing more embarrassing, and found vaginal swabs less comfortable than older women. The review suggested that ethnicity may influence acceptability of GBS testing, though research is limited.

The review also suggested that obstetricians have higher knowledge of GBS and may be more likely to discuss, screen for, and follow policies related to GBS than nursing and midwifery professionals. It is therefore possible that access to GBS screening and prophylaxis may vary by health service according to workforce structure/composition.

Judgement

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

Acceptability

Is the intervention acceptable to key stakeholders?

Research evidence

A rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(5)* indicates that most women (at least 80%) find GBS swabbing acceptable *(moderate confidence in the evidence)*. Evidence from four studies indicates that most women are in favour of universal screening *(moderate confidence in the evidence)*. Some report negative views of GBS testing, often related to embarrassment, fear of birth plans being altered, overmedicalization of birth, and implications for the baby *(both moderate confidence in the evidence)*. Screening may increase maternal anxiety, particularly the combination strategy in which all women are screened, but only those who test positive for GBS and have a risk factor are provided with antibiotics *(low confidence in the evidence)*. Provision of clear information is vital in mitigating such anxiety *(high confidence in the evidence)*.

Preference for self-swabbing versus swabbing by a health-care professional varies. Women value the comfort, privacy, and sense of control afforded by self-swabbing *(low confidence in the evidence)* and generally find self-swabbing easy and comfortable *(moderate confidence in the evidence)*. Others are not comfortable with the thought of

touching their genitals and feel more confident in the accuracy of the process and of the swab when done by a health-care professional *(moderate confidence in the evidence)*. Vaginal swabbing generally appears more acceptable than rectal swabbing *(moderate confidence in the evidence)*.

The review suggests that most health professionals view GBS screening as important and beneficial to pregnant women *(moderate confidence in the evidence)*. The review could not determine whether universal or risk-based screening approaches are more acceptable to health professionals. Rectal swabs are generally less acceptable to health professionals than vaginal swabs. Midwives are generally opposed to universal antibiotic use, whereas obstetricians may find this more acceptable *(latter findings all low confidence in the evidence)*.

Additional considerations

A qualitative study in the United Kingdom of Great Britain and Northern Ireland on the acceptability of different methods of routine testing found routine GBS testing was well received by both women and health-care professionals. Most participants found the procedure acceptable and were willing to receive or offer testing in the future. Preferences for different methods of testing varied, with participants emphasizing the importance of evidence and informed choice. Clear communication and information were important for women and health-care professionals *(11)*.

Judgement

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

Feasibility

Is the intervention feasible to implement?

Research evidence

Views from health professionals collated in a rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(5)* suggest that barriers to carrying out GBS screening and prophylaxis include organizational impediments, fear of consequences such as anxiety and overmedicalization of birth, lack of clarity around guidelines, medicolegal reasons, and lack of training *(moderate confidence in the evidence)*. Facilitators to GBS screening and prophylaxis include patient request, presence of guidelines, adherence to guideline among peers, and personal reasons such as a past negative experience with GBS *(very low confidence in the evidence)*.

In terms of administration of antibiotic prophylaxis, the review found that 50–87% of health professionals would treat with antibiotics if women tested positive for GBS. 13–99% would treat with antibiotics if women had a positive screen and a positive risk factor. 38–80% would treat if women had no positive GBS screen, but risk factors were present *(low confidence in the evidence)*. Health professionals conduct screening at the recommended time in 47.5–82% of cases *(low confidence in the evidence)*.

There is some evidence that obstetricians and gynaecologists are more likely to discuss, screen for, and follow policies related to GBS than nursing and midwifery professionals, and some evidence that those with fewer years of experience are more likely to screen than those with more years of experience *(low confidence in the evidence)*.

Views from women indicate reasons for not swabbing vary, but may include not being offered swabbing, lack of understanding about swabbing, and giving birth prior to the scheduled swab *(low confidence in the evidence)*.

Additional considerations

Lack of access to skilled intrapartum care and higher proportion of home births, particularly in low-income countries, is likely to limit the feasibility of IAP.

Ampicillin and penicillin are heat sensitive and may require refrigeration and protection from light. Ampicillin (powder for injection: 500 mg; 1 g [as sodium] in vial) and benzylpenicillin/penicillin G (powder for injection: 600 mg [= 1 million IU]; 3 g [= 5 million IU] [sodium or potassium salt] in vial) are listed in the *WHO model list of essential medicines (12)*.

Judgement

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

Summary of judgements tables

Any screening strategy vs no screening strategy

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

Universal screening vs no screening strategy

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

Risk-based screening vs no screening strategy

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

Combined/other screening strategy vs no screening strategy

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

Summary of findings tables

Question: Any screening strategy compared with no screening strategy – term population
Setting: Brazil, Czechia, Switzerland, the USA

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any screening strategy	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – COMMON EFFECTS MODEL												
6	observational studies	very serious[a]	not serious	not serious	not serious	none	354/650350 (0.1%)	487/293023 (0.2%)	**RR 0.31** (0.27 to 0.35)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTIONS – RANDOM EFFECTS MODEL												
6	observational studies	very serious[a]	not serious	not serious	not serious	none	354/650350 (0.1%)	487/293023 (0.2%)	**RR 0.34** (0.24 to 0.48)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL
EARLY ONSET NON-GBS NEONATAL SEPSIS – COMMON EFFECTS MODEL												
2	observational studies	very serious[a]	not serious	not serious	serious[b,c]	none	12/46999 (0.0%)	4/24008 (0.0%)	**RR 1.57** (0.38 to 6.55)	**0 fewer per 1000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
EARLY ONSET NON-GBS NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
2	observational studies	very serious[a]	not serious	not serious	serious[b,c]	none	12/46999 (0.0%)	4/24008 (0.0%)	**RR 1.42** (0.31 to 6.62)	**0 fewer per 1000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
2	observational studies	very serious[a]	not serious	not serious	serious[b]	none	27/46999 (0.1%)	14/24008 (0.1%)	**RR 0.72** (0.34 to 1.49)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
2	observational studies	very serious[a]	not serious	not serious	serious[b]	none	26/46999 (0.1%)	14/24008 (0.1%)	**RR 0.75** (0.36 to 1.58)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] The pooled effect is provided by studies "C".
[b] Wide confidence interval crossing the line of no effect.
c Few events but large sample size.

Question: Any screening strategy compared with no screening strategy – undetermined or combined preterm/term population
Setting: Australia, Chile, Chinese Taipei, Denmark, France, Hungary, Ireland, Italy, Japan, Netherlands (Kingdom of the), New Zealand, Spain, Sweden, the United Kingdom, the USA

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any screening strategy	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTION – COMMON EFFECTS MODEL												
27	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	1470/4504081 (0.0%)	1554/4492926 (0.0%)	**RR 0.81** (0.75 to 0.87)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
EOGBS INFECTION – RANDOM EFFECTS MODEL												
27	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	1470/4504081 (0.0%)	1554/4492926 (0.0%)	**RR 0.46** (0.34 to 0.62)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
13	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	16048/2063804 (0.8%)	16924/1803736 (0.9%)	**RR 0.75** (0.73 to 0.76)	**2 fewer per 1000** (from 3 fewer to 2 fewer)	⨁◯◯◯ Very low	CRITICAL
EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
13	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	16048/2063804 (0.8%)	16924/1803736 (0.9%)	**RR 0.49** (0.34 to 0.70)	**5 fewer per 1000** (from 6 fewer to 3 fewer)	⨁◯◯◯ Very low	CRITICAL
MATERNAL PERIPARTUM INFECTION – CHORIOAMNIONITIS – COMMON EFFECTS MODEL												
2	observational studies	very serious[d]	not serious	serious[c]	not serious	none	281/9048 (3.1%)	588/15620 (3.8%)	**RR 0.84** (0.73 to 0.97)	**6 fewer per 1000** (from 10 fewer to 1 fewer)	⨁◯◯◯ Very low	IMPORTANT
MATERNAL PERIPARTUM INFECTION – CHORIOAMNIONITIS – RANDOM EFFECTS MODEL												
2	observational studies	very serious[d]	not serious	serious[c]	not serious	none	281/9048 (3.1%)	588/15620 (3.8%)	**RR 0.84** (0.73 to 0.97)	**6 fewer per 1000** (from 10 fewer to 1 fewer)	⨁◯◯◯ Very low	IMPORTANT
MATERNAL ANAPHYLAXIS – COMMON EFFECTS MODEL												
1	observational study	very serious[d]	not serious	serious[c]	serious[e,f]	none	1/36342 (0.0%)	0/5732 (0.0%)	**RR 0.47** (0.02 to 11.62)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	IMPORTANT

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any screening strategy	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
MATERNAL ANAPHYLAXIS – RANDOM EFFECTS MODEL												
1	observational study	very serious[d]	not serious	serious[c]	serious[e,f]	none	1/36342 (0.0%)	0/5732 (0.0%)	**RR 0.47** (0.02 to 11.61)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; RR: risk ratio
[a] Most of the pooled effect provided by studies "C".
[b] Statistical heterogeneity (I2≥60%).
[c] Data provided by studies with undetermined or mixed population of preterm and at/near term pregnancies.
[d] The pooled effect is provided by study "C".
[e] Wide confidence interval crossing the line of no effect.
[f] Few events but large sample size.

Question: Universal screening compared with no screening strategy – term population
Setting: Czechia, the USA

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Any screening strategy	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – COMMON EFFECTS MODEL												
3	observational studies	very serious[a]	not serious	not serious	not serious	none	105/254197 (0.0%)	441/235827 (0.2%)	**RR 0.22** (0.18 to 0.27)	**1 fewer per 1000** (from 2 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTIONS – RANDOM EFFECTS MODEL												
3	observational studies	very serious[a]	not serious	not serious	not serious	none	105/254197 (0.0%)	441/235827 (0.2%)	**RR 0.26** (0.13 to 0.54)	**1 fewer per 1000** (from 2 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] The pooled effect is provided by studies "C".

Question: Universal screening compared with no screening strategy – undetermined or combined preterm/term population
Setting: Australia, Chinese Taipei, France, Spain, the USA

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – COMMON EFFECTS MODEL												
13	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	249/564224 (0.1%)	438/551262 (0.1%)	**RR 0.35** (0.30 to 0.41)	**1 fewer per 1000** (from 1 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
EOGBS INFECTIONS – RANDOM EFFECTS MODEL												
13	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	249/564224 (0.1%)	438/551262 (0.1%)	**RR 0.37** (0.25 to 0.55)	1 fewer per 1000 (from 1 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
8	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	6563/881307 (0.7%)	16442/1298615 (1.3%)	**RR 0.71** (0.69 to 0.73)	**4 fewer per 1000** (from 4 fewer to 3 fewer)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
8	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	6563/881307 (0.7%)	16442/1298615 (1.3%)	**RR 0.43** (0.24 to 0.78)	**7 fewer per 1000** (from 10 fewer to 3 fewer)	⨁◯◯◯ Very low	CRITICAL
MATERNAL ANAPHYLAXIS – COMMON EFFECTS MODEL												
1	observational study	very serious[d]	not serious	serious[c]	serious[e,f]	none	1/36342 (0.0%)	0/5732 (0.0%)	**RR 0.47** (0.02 to 11.62)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	IMPORTANT
MATERNAL ANAPHYLAXIS – RANDOM EFFECTS MODEL												
1	observational study	very serious[d]	not serious	serious[c]	serious[e,f]	none	1/36342 (0.0%)	0/5732 (0.0%)	**RR 0.47** (0.02 to 11.61)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; RR: risk ratio
[a] Most of the pooled effect is provided by studies "C".
[b] Statistical heterogeneity ($I^2 \geq 60\%$).
[c] Data provided by studies with undetermined or mixed population of preterm and at/near term pregnancies.
[d] The pooled effect is provided by study "C".
[e] Wide confidence interval crossing the line of no effect.
[f] Few events but large sample size.

Question: Risk-based screening compared with no screening strategy – term population
Setting: The USA

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk-based screening	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS												
1	observational study	very serious[a]	not serious	not serious	not serious	none	6/19516 (0.0%)	34/27443 (0.1%)	**RR 0.25** (0.10 to 0.59)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; RR: risk ratio

[a] The pooled effect is provided by study "C".

Question: Risk-based screening compared with no screening strategy – undetermined or combined preterm/term population
Setting: Denmark, Ireland, Italy, New Zealand, Sweden, the United KingdomK, the USA

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Risk-based screening	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – COMMON EFFECTS MODEL												
10	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	854/1709405 (0.0%)	742/1387394 (0.1%)	**RR 0.87** (0.79 to 0.96)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
EOGBS INFECTIONS – RANDOM EFFECTS MODEL												
10	observational studies	very serious[a]	serious[b]	serious[c]	not serious	none	854/1709405 (0.0%)	742/1387394 (0.1%)	**RR 0.60** (0.43 to 0.83)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
5	observational studies	very serious[a]	not serious	serious[c]	not serious	none	275/169900 (0.2%)	355/147315 (241.5%)	**RR 0.72** (0.61 to 0.84)	**676 fewer per 1000** (from 942 fewer to 386 fewer)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
5	observational studies	very serious[a]	not serious	serious[c]	not serious	none	275/169900 (0.2%)	355/147315 (0.2%)	**RR 0.72** (0.58 to 0.88)	**1 fewer per 1000** (from 1 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
MATERNAL PERIPARTUM INFECTION – CHORIOAMNIONITIS												
1	observational study	very serious[d]	not serious	serious[c]	very serious[e,f]	none	6/150 (4.0%)	10/300 (3.3%)	**RR 1.20** (0.44 to 2.37)	**7 more per 1000** (from 19 fewer to 46 more)	⨁◯◯◯ Very low	IMPORTANT

CI: confidence interval; RR: risk ratio
[a] Most of the pooled effect is provided by studies "C".
[b] Statistical heterogeneity ($I^2 \geq 60\%$).
[c] Data provided by studies with undetermined or mixed population of preterm and at/near term pregnancies.
[d] The pooled effect is provided by study "C".
[e] Wide confidence interval crossing the line of no effect.
[f] Few events.

Question: Combined/other screening strategy compared with no screening strategy – term population
Setting: Brazil, the USA, Switzerland

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Combined/ other screening strategy	No screening strategy	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTION – EBERLY 2009												
1	observational study	very serious[a]	not serious	not serious	not serious	none	229/339769 (0.1%)	435/230269 (0.2%)	**RR 0.36** (0.30 to 0.42)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTION – TOWERS 2002												
1	observational study	very serious[a]	not serious	not serious	not serious	none	9/19891 (0.0%)	34/27443 (0.1%)	**RR 0.37** (0.18 to 0.76)	**1 fewer per 1000** (from 1 fewer to 0 fewer)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTION – RENNER 2006												
1	observational study	very serious[a]	not serious	not serious	serious[b,c]	none	5/9385 (0.1%)	9/16126 (0.1%)	**RR 0.95** (0.32 to 2.85)	**0 fewer per 1000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
EOGBS INFECTION – FREITAS 2017												
1	observational study	very serious[a]	not serious	not serious	serious[b,c]	none	0/7592 (0.0%)	3/13627 (0.0%)	**RR 0.26** (0.01 to 4.96)	**0 fewer per 1000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] The pooled effect is provided by study "C".
[b] Wide confidence interval crossing the line of no effect.
[c] Few events but large sample size

References – Evidence-to-Decision Framework 1

1. Panneflek TJR, Hasperhoven GF, Chimwaza Y, Allen C, Lavin T, te Pas AB, et al. Intrapartum antibiotic prophylaxis to prevent Group B streptococcal infections in newborn infants: a systematic review and meta-analysis comparing various strategies. eClinicalMedicine. 2024;74:102748. doi: https://doi.org/10.1016/j.eclinm.2024.102748 (accessed 13 August 2024).
2. Seedat F, Stinton C, Patterson J, Geppert J, Tan B, Robinson ER, et al. Adverse events in women and children who have received intrapartum antibiotic prophylaxis treatment: a systematic review. BMC Pregnancy Childbirth. 2017;17(1):247. doi:10.1186/s12884-017-1432-3 (accessed 13 August 2024).
3. Downe S, Finlayson K, Tunçalp Ö, Metin Gülmezoglu A. What matters to women: a systematic scoping review to identify the processes and outcomes of antenatal care provision that are important to healthy pregnant women. BJOG. 2016;123(4):529-39. doi: 10.1111/1471-0528.13819 (accessed 13 August 2024).
4. Downe S, Finlayson K, Oladapo O, Bonet M, Gülmezoglu AM. What matters to women during childbirth: a systematic qualitative review. PLOS ONE. 2018;13(4):e0194906. doi: 10.1371/journal.pone.0194906 (accessed 13 August 2024).
5. Constantinou G, Webb R, Ayers S. An evidence synthesis on parents' and healthcare providers' values and preferences for, and views on the acceptability, feasibility, equity and outcomes of screening strategies to prevent early-onset group B streptococcal disease in newborns [preprint verion]. doi:10.1101/2024.06.28.24309381.
6. Allen C, Naznin E, Penneflek TJR, Lavin T, Hoque ME. The cost-effectiveness of Group B Streptococcus screening strategies: a systematic review [pre-print https://doi.org/10.1101/2024.08.25.24312541].
7. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care. 2005;21(2):240-5. doi:10.1017/S0266462305050324 (accessed 13 August 2024).
8. MSH (Management Sciences for Health). International medical products price guide, 2015 edition. Medford: Medical Sciences for Health; 2016 (https://msh.org/resources/international-medical-products-price-guide-2/, accessed 15 June 2024).
9. Williams M, Zantow E, Turrentine M. Cost effectiveness of latest recommendations for group B streptococci screening in the United States. Obstet Gynecol. 2020;135(4):789-98. doi: 10.1097/AOG.0000000000003649.
10. State of inequality: reproductive, maternal, newborn and child health. Geneva: World Health Organization; 2015 (https://iris.who.int/handle/10665/164590, accessed 15 August 2024).
11. Constantinou G, Ayers S, Mitchell EJ, Walker KF, Daniels J, Moore S, et al. Women and healthcare professionals' experiences of GBS testing as part of the GBS3 Trial: a qualitative study (under review).
12. Web Annex A. World Health Organization model list of essential medicines – 23rd list, 2023. In: The selection and use of essential medicines 2023. Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines, 24–28 April 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/handle/10665/371090, accessed 15 August 2024).

Framework 2: Screening strategies compared with other screening strategies

Question presented in PICO (population, intervention, comparator, outcome) format:

Among pregnant women at or near term (P) does a screening strategy for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared to another screening strategy (C) improve maternal and neonatal outcomes (O)?

* Screening strategy refers to a protocol to identify women eligible for IAP, and subsequent IAP administration to eligible women.

There are three specific PICOs under this question which relate to the different screening strategies:

- Among women at or near term (P) does **universal** screening for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with **risk-based** screening (C) improve maternal and neonatal outcomes (O)?
- Among women at or near term (P) does **universal** screening for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with a **combined/other** screening strategy (C) improve maternal and neonatal outcomes (O)?
- Among women at or near term (P) does **risk-based** screening for intrapartum antibiotic prophylaxis for the prevention of early onset GBS disease in newborns (I) compared with **combined/other** screening (C) improve maternal and neonatal outcomes (O)?

Problem: Prevention of early onset Group B streptococcus disease in newborns

Perspective: Clinical practice recommendation – population perspective

Population (P): All pregnant women at or near term

Intervention (I): Screening strategy for intrapartum antibiotic prophylaxis for the prevention early onset GBS disease in newborns

Comparators (C): Another screening strategy

Setting: Hospital setting

Subgroups: None

Priority outcomes (O):[1]

*Denotes outcomes deemed as "critical". All other outcomes deemed as "important".

Neonatal outcomes

1. *Incidence of EOGBS infections[2] (as defined by study authors)
2. *Perinatal mortality (composite of stillbirth and early neonatal death); early neonatal mortality (death within 7 days after birth)
3. *Any early onset neonatal infection
4. *Any early onset neonatal sepsis
5. Severe neonatal morbidity (e.g. neonatal ICU admission)

Maternal outcomes

6. Maternal peripartum infection (chorioamnionitis, endometritis)
7. Maternal satisfaction with care

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[1] These outcomes reflect the prioritized outcomes used in the development of this recommendation, in the *WHO recommendations for prevention and treatment of maternal peripartum infections* (2015).

[2] Outcome adapted from the *WHO recommendations for prevention and treatment of peripartum infections* and critical to the current review question.

Health service use

8. Cost of care
9. Early neonatal (≤7 days) therapeutic antibiotic use

Adverse effects

10. Antimicrobial resistance (GBS resistant neonatal infection)
11. Maternal or neonatal anaphylaxis

Assessment

Effects of interventions

Among pregnant women at or near-term women (P) does a screening strategy for intrapartum antibiotic prophylaxis for the prevention early onset GBS disease in newborns (I) compared with another screening strategy (C) improve maternal and neonatal outcomes (O)?

Research evidence

Summary of evidence

Source and characteristics of studies

Evidence was derived from a systematic review of the effect of different GBS screening strategies on maternal and neonatal outcomes *(1)*. In total, 65 studies were included which reported on the outcomes specified above and compared two distinct screening strategies. In the 65 studies, data on the specified outcomes were available for more than 10 million women.

Comparison 1: Universal screening compared with risk-based screening

In total, 17 studies contributed data to the comparison of universal screening compared with risk-based screening. The studies consisted out of retrospective and prospective observational, mixed and quasi-experimental studies. Fifteen studies were conducted in high-income countries and three were conducted in high-middle income countries, published between the years 1998 and 2023.

Data from the following countries were extracted: China (n=2), Finland (n=1), Qatar (n=1), Saudi Arabia (n=1), Türkiye (n=1), the Republic of Korea (n=1) and the USA (n=10). Sample sizes ranged from 1100 to 629 912 live births. Live births/deliveries occurred in the hospital or data was collected from nationwide birth/delivery data. Of the 17 studies, eight included data on outcome of women who birthed at or near term (defined as 35 weeks' gestation and up), and nine did not describe the gestation at which the included women birthed. The data from these studies are presented separately in each of the comparisons in this evidence-to-decision-framework.

Universal screening included screening all pregnant women antenatally via rectovaginal swab (at 24–28 weeks' gestation; or at 35–37 weeks' gestation) and providing IAP to those with GBS colonization. Risk-based screening consisted of IAP for pregnant women who presented with risk factors for EOGBS infection such as preterm premature rupture of membranes (pPROM), prolonged rupture of membranes, intrapartum fever and preterm birth.

EOGBS definitions included GBS in sterile fluids such as any combination of blood/cerebrospinal fluid/joint fluid/urine/sputum or specific DG codes for EOGBS within 2–7 days of birth with possible additional requirement of clinical symptoms of infection and antibiotic use.

At or near-term populations

Neonatal outcomes

Moderate-certainty evidence suggests universal screening is probably associated with reduced EOGBS infections when compared with risk-based screening (8 studies, 709 956 newborns; RR 0.24, 95% CI 0.18 to 0.31 [common effects model]. Low certainty evidence suggests universal screening may be associated with reduced EOGBS infections when compared with risk-based screening (8 studies, 709 956 newborns; RR 0.29, 95% CI 0.17 to 0.51 [random effects model]).

It is uncertain whether universal screening is associated with non-GBS early onset neonatal sepsis or any early onset neonatal sepsis when compared with risk-based screening *(very low certainty evidence)*.

Maternal outcomes

Low certainty evidence suggests universal screening may have no association with maternal peripartum infection (combined chorioamnionitis and endometritis) when compared with risk-based screening (1 study, 1654 women; RR 0.99, 95% CI 0.63 to 1.57). Low certainty evidence suggests universal screening may have no association with chorioamnionitis when compared with risk-based screening (1 study, 827 women; RR 1.19, 95% CI 0.67 to 2.11). It is uncertain whether universal screening is associated with endometritis when compared with risk-based screening *(very low certainty evidence)*.

Undetermined or combined term and preterm populations

Neonatal outcomes

Low certainty evidence suggests universal screening may be associated with reduced EOGBS infections when compared with a risk-based screening (9 studies, 1 089 105 newborns; RR 0.47, 95% CI 0.40 to 0.56 [common effects model]). It is uncertain whether universal screening is associated with EOGBS infections when compared with risk-based screening *(very low certainty evidence [random effects model])*.

Low certainty evidence suggests universal screening may be associated with reduced any early onset neonatal sepsis when compared with risk-based screening (4 studies, 654 621 newborns; RR 0.70, 95% CI 0.63 to 0.78).

Health service use and adverse effects were not reported in the included studies.

Additional considerations

Case fatality: Six studies reported on case fatality in a period with risk-based screening and observed that case fatality was between 0% and 12.5% and mortality rate was between 0/1000 live births and 0.033/1000 live births. Nine studies reported on case fatality in a period with universal screening and observed that case fatality was between 0% and 10% and mortality rates were 0/1000 live births to 0.054/1000 live births.

Antimicrobial resistance: Studies reporting on antimicrobial resistance to EOGBS isolates found that there was no resistance to ampicillin or penicillin during periods of universal screening (4 studies) or risk-based screening (2 studies).

Summary of IAP proportion: Eleven studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis using universal screening. 20.6% of women in this group received antibiotics (0.2063 [0.1730; 0.2441]). Ten studies reported on the proportion of women receiving intrapartum antibiotic prophylaxis using risk-based screening. 16.8% of women in this group received antibiotics (0.1677 [0.1363; 0.2046]).

Ongoing trial: The routine testing for group B Streptococcus in pregnancy (GBS3 trial) is currently underway in the United Kingdom *(2)*. This large, multicentre randomized trial will compare universal GBS screening with risk-based screening (the current local standard of care). The universal screening arm will be further randomly divided into testing via vaginal and rectal swab at approximately 35–37 weeks' gestation and via rapid test during labour. The primary outcome is all-cause early neonatal sepsis. Results are expected in the year 2026.

Adverse effects: A systematic review of adverse events in women and children who have received IAP for the prevention of neonatal GBS disease concluded that the evidence base was limited *(3)*. Potential adverse effects included altered infant microbiome, of which the clinical significance could not be determined due to lack of follow-up. Observational evidence for increased antimicrobial resistance was limited by high or unclear risk of bias in the reporting studies. One randomized control with limited applicability reported potentially serious long-term adverse effects such as cerebral palsy, for which the biological plausibility was unclear, and the finding was not replicated in a similar trial *(3)*.

Desirable effects

How substantial are the desirable anticipated effects?

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Comparison 2: Universal screening compared with a combined/other screening strategy

Two cohort studies conducted in the USA contributed data to the comparison universal screening compared with a combined/other screening strategy.

Locksmith 1999 included 15 582 live births and compared a period with universal screening where IAP was administered to carriers of GBS colonization determined by universal screening at 35–37 weeks' gestation; pregnant women with risk factors when carrier state was unknown; and to pregnant women with maternal fever indicative of chorioamnionitis or when a previous infant was affected by a GBS infection, with two distinct periods of other screening strategies. In the first period, IAP was administered to carriers of screening at the hospital for pPROM and preterm delivery. In the second period, which occurred after 1993, IAP was admitted to these same pregnant women

but also when carrier state was unknown to pregnant women with preterm delivery, prolonged rupture of membranes, intrapartum fever and a previous infant affected by a GBS sepsis.

Eberly 2009 included 587 382 live births and compared a period where IAP was administered according to the CDC guidelines from the year 2002 comprising IAP administration to carriers of GBS following universal rectovaginal screening at 35–37 weeks' gestation to a period when IAP was administered according to the CDC guidelines from 1996 comprising IAP administration according to the aforementioned CDC 2002 guidelines or IAP administered to pregnant women presenting with preterm delivery, intrapartum fever and prolonged rupture of membranes.

EOGBS was defined as GBS in sterile fluids such as any combination of blood/cerebrospinal fluid or specific codes for EOGBS within 7 days of birth with additional clinical symptoms.

Neonatal outcomes

Locksmith 1999; combined study periods 1 and 2: Low certainty evidence suggests universal screening may have no association with EOGBS infections when compared with a combined/other screening strategy (1 study, 15 582 newborns; RR 0.49, 95% CI 0.17 to 1.38).

Eberley 2009: Low certainty evidence suggests universal screening may be associated with reduced EOGBS infections when compared with a combined/other screening strategy (1 study, 587 382 newborns; RR 0.61, 95% CI 0.48 to 0.77).

Results by study period:

Locksmith 1999 (1st): Low certainty evidence suggests universal screening may have no association with EOGBS infections when compared with a combined/other screening strategy (1 study, 9425 newborns; RR 0.41, 95% CI 0.14 to 1.22).

Locksmith 1999 (2nd): Low certainty evidence suggests universal screening may have no association with EOGBS infections when compared with a combined/other screening strategy (1 study, 9333 newborns; RR 0.60, 95% CI 0.19 to 1.83).

Maternal outcomes, health service use, and adverse effects were not reported in the included studies.

Additional considerations

None.

Desirable effects

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Comparison 3: Risk-based screening compared with a combined/other screening strategy

One prospective cohort study conducted in the USA contributed descriptive data to the comparison of risk-based screening compared with a combined/other screening strategy.

Towers 2002 included 39 407 live births and compared a period where IAP was administered to pregnant women presenting with preterm delivery <37 weeks' gestation, prolonged rupture of membranes, intrapartum fever or carriers of inconsistent screening for GBS colonization at 28 weeks' gestation/first prenatal visit were treated with IAP, to a period where antibiotics were administered to the aforementioned screening strategy but also to carriers of universal screening at 35–37 weeks' gestation.

EOGBS was defined as GBS in sterile fluids such as any combination of blood/cerebrospinal fluid or specific codes for EOGBS within 7 days of birth with additional clinical symptoms.

Neonatal outcomes

It is uncertain whether risk-based screening is associated with EOGBS infections when compared with combined/other screening strategy *(very low certainty evidence)*.

Maternal outcomes, health service use and adverse effects were not reported in the included studies.

Additional considerations

None.

Desirable effects

Judgement

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

Undesirable effects

How substantial are the undesirable anticipated effects?

Judgement

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

Certainty of the evidence

What is the overall certainty of the evidence on effects?

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

Values

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

Research evidence

Findings from a scoping review of what matters to women during antenatal care *(4)* indicate that women from all resource settings value having a positive pregnancy experience, which includes the provision of effective clinical practices (interventions and tests), relevant and timely information, and psychosocial and emotional support *(high confidence in the evidence)*.

A systematic qualitative review on what matters to women during childbirth *(5)* indicates that most women are apprehensive about labour and childbirth, adverse birth outcomes and certain medical interventions, and they value the support and reassurance of health-care professionals who are sensitive to their needs *(high confidence in the evidence)*. Most women want a normal birth with good outcomes for mother and baby but acknowledge that medical intervention may sometimes be necessary. Where interventions are required, most women would like to receive relevant information from technically competent health care providers in a manner they can understand *(high confidence in the evidence)*. Women want to be in control of their birth process and involved in decision-making around the use of interventions *(high confidence in the evidence)*.

These findings are reinforced by those from a rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(6)* which indicate that women's knowledge and awareness of GBS, GBS testing, and antibiotic prophylaxis is low *(high confidence in the evidence)*. Women generally want more information about GBS screening, ideally provided face-to-face by a health-care professional. Information should be provided early and in sufficient detail to enable informed decision making *(moderate confidence in the evidence)*.

Additional considerations

None.

Judgement

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

Balance of effects

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

Judgement – Universal screening compared with risk-based screening

— Don't know	— Varies	— Favours risk-based screening	— Probably favours risk-based screening	— Does not favour either	✔ Probably favours universal screening	— Favours universal screening

Judgement – Universal screening compared with a combined/other screening strategy

— Don't know	✔ Varies	— Favours combined/ other screening	— Probably favours combined/ other screening	— Does not favour either	— Probably favours universal screening	— Favours universal screening

Judgement – Risk-based screening compared with a combined/other screening strategy

✔ Don't know	— Varies	— Favours combined/ other screening	— Probably favours combined/ other screening	— Does not favour either	— Probably favours risk-based screening	— Favours risk-based screening

Resources

How large are the resource requirements (costs)?

Research evidence

None.

Additional considerations

A systematic review of cost–effectiveness of GBS screening strategies *(7)* identified one study comparing universal screening with risk-based screening. The study was conducted in the USA and pertained specifically to women with a singleton pregnancy presenting for repeat caesarean births. Quality assessment using the Consensus on Health Economic Criteria (CHEC) tool *(8)* demonstrated that the study was of high quality. This study identified that universal screening in this population was not cost–effective. Sensitivity analyses demonstrated that universal screening would only become cost–effective if the more than 28% of women were GBS-positive, more than 29% laboured before their scheduled delivery, or more than 10% had vaginal births *(9)*.

A separate study conducted in the Kingdom of the Netherlands (assessed as high quality) reported on ICERs for per QALY gained for universal screening as compared with no screening strategy; and risk-based screening as compared with no screening strategy. Risk-based screening was found to be cost–effective (US$ 8200 per QALY gained) while there was no determination as to whether universal screening was cost–effective (US$ 64 482 per QALY gained) *(10)*.

Main resource requirements

Resource	Description
Staff	■ Specimen collection and administration of IV antibiotics requires skilled health care personnel (doctors/midwives/nurses)
Training	■ Practice-based training for maternity care providers including patient communication and consent, infection control, rectovaginal swab technique and specimen handling ■ Training to administer IV antibiotics, and to monitor and manage expected and unexpected side-effects, is part of standard maternity staff training
Supplies	■ *Swabbing for GBS colonization (universal screening)* ▪ Gloves ▪ Sterile cotton swabs ▪ Specimen collection vials/biohazard bags ▪ Labels ■ *Intrapartum antibiotic prophylaxis* ▪ IV antibiotics: — Benzylpenicillin (penicillin G or PenG) = US$ 0.2404 per 3 g vial (injectable) / cost per regimen approximately US$ 2.40 *(11)* — Ampicillin = US$ 0.1507 per 500 mg vial (injectable) *(11)* ▪ Alcohol wipes ▪ IV catheter or cannula and tubing ▪ IV pole/stand
Equipment and infrastructure	■ Access to laboratory with facilities to carry out testing of swab samples. ■ On-site pharmacy and/or medicine stock management system that is managed by a trained pharmacist or dispenser ■ Rectovaginal culture ranges from US$ 6.15 to 18.44 for a negative result and US$ 13.63 to $ 40.89 for a positive result *(12)*
Time	■ Laboratory processing time varies according to the specific methods used, laboratory workload and sample transportation time. Results may be available from after several hours to after several days ■ IV antibiotics dispensing time estimated to be 2–5 minutes
Supervision and monitoring	■ Ongoing intrapartum care and monitoring of the woman and baby during labour and after birth, as for usual care

Resources required

Judgement – Universal screening compared with risk-based screening

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

Judgement – Universal screening compared with a combined/other screening strategy

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

Judgement – Risk-based screening compared with a combined/other screening strategy

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

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Universal screening compared with risk-based screening

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

Cost–effectiveness

Judgement – Universal screening compared with risk-based screening

✔ Don't know	— Varies	— Favours risk-based screening	— Probably favours risk-based screening	— Does not favour either	— Probably favours universal screening	— Favours universal screening

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Universal screening compared with a combined/other screening strategy

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

Cost–effectiveness

Judgement – Universal screening compared with a combined/other screening strategy

✔ Don't know	— Varies	— Favours combined/ other screening	— Probably favours combined/ other screening	— Does not favour either	— Probably favours universal screening	— Favours universal screening

Certainty of the evidence on required resources

What is the certainty of the evidence on costs?

Judgement – Risk-based screening compared with a combined/other screening strategy

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

Cost–effectiveness

Judgement – Risk-based screening compared with a combined/other screening strategy

✔ Don't know	— Varies	— Favours combined/ other screening	— Probably favours combined/ other screening	— Does not favour either	— Probably favours universal screening	— Favours universal screening

Equity

What would be the impact on health equity?

Research evidence

A rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(6)* found no direct evidence on the impact of GBS screening on health equity. The 2015 WHO state of inequality report *(13)* indicates that women who are poor, least educated and who reside in rural areas have lower coverage of health interventions and worse health outcomes than more advantaged women. Availability of GBS testing services and of IAP is likely to vary widely by geographical location and income setting. IAP is likely to be available for facility births only.

Additional considerations

The rapid review *(6)* found that knowledge and awareness of GBS is influenced by maternal education, with higher levels of education associated with higher knowledge. Younger women found the test less acceptable, found vaginal and rectal swabbing more embarrassing, and found vaginal swabs less comfortable than older women. The review suggested that ethnicity may influence acceptability of GBS testing, though research is limited.

The review also suggested that obstetricians have higher knowledge of GBS and may be more likely to discuss, screen for, and follow policies related to GBS than nursing and midwifery professionals. It is therefore possible that access to GBS screening and prophylaxis may vary by health service according to workforce structure/composition.

Judgement

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

Acceptability

Is the intervention acceptable to key stakeholders?

Research evidence

A rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(6)* indicates that most women (at least 80%) find GBS swabbing acceptable *(moderate confidence in the evidence)*. Evidence from four studies indicates that most women are in favour of universal screening *(moderate confidence in the evidence)*. Some report negative views of GBS testing, often related to embarrassment, fear of birth plans being altered, overmedicalization of birth, and implications for the baby *(both moderate confidence in the evidence)*. Screening may increase maternal anxiety, particularly the combination strategy in which all women are screened, but only those

who test positive for GBS and have a risk factor are provided with antibiotics *(low confidence in the evidence)*. Provision of clear information is vital in mitigating such anxiety *(high confidence in the evidence)*.

Preference for self-swabbing versus swabbing by a health-care professional varies. Women value the comfort, privacy, and sense of control afforded by self-swabbing *(low confidence in the evidence)* and generally find self-swabbing easy and comfortable *(moderate confidence in the evidence)*. Others are not comfortable with the thought of touching their genitals and feel more confident in the accuracy of the process and of the swab when done by a health-care professional *(moderate confidence in the evidence)*. Vaginal swabbing generally appears more acceptable than rectal swabbing *(moderate confidence in the evidence)*.

The review suggests that most health professionals view GBS screening as important and beneficial to pregnant women *(moderate confidence in the evidence)*. The review could not determine whether universal or risk-based screening approaches are more acceptable to health professionals. Rectal swabs are generally less acceptable to health professionals than vaginal swabs. Midwives are generally opposed to universal antibiotic use, whereas obstetricians may find this more acceptable *(latter findings all low confidence in the evidence)*.

Additional considerations

A qualitative study in the United Kingdom of Great Britain and Northern Ireland on the acceptability or different methods of routine testing found routine GBS testing was well received by both women and health care professionals. Most participants found the procedure acceptable and were willing to receive or offer testing in the future. Preferences for different methods of testing varied, with participants emphasizing the importance of evidence and informed choice. Clear communication and information were important for women and health care professionals *(14)*.

Judgement

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

Feasibility

Is the intervention feasible to implement?

Research evidence

Views from health professionals collated in a rapid review of stakeholder perceptions of GBS screening strategies to prevent EOGBS *(6)* suggest that barriers to carrying out GBS screening and prophylaxis include organizational impediments, fear of consequences such as anxiety and overmedicalization of birth, lack of clarity around guidelines, medicolegal reasons, and lack of training *(moderate confidence in the evidence)*. Facilitators to GBS screening and prophylaxis include patient request, presence of guidelines, adherence to guideline among peers, and personal reasons such as a past negative experience with GBS *(very low confidence in the evidence)*.

In terms of administration of antibiotic prophylaxis, the review found that 50–87% of health professionals would treat with antibiotics if women tested positive for GBS. 13–99% would treat with antibiotics if women had a positive screen and a positive risk factor. 38–80% would treat if women had no positive GBS screen, but risk factors were

present *(low confidence in the evidence)*. Health professionals conduct screening at the recommended time in 47.5–82% of cases *(low confidence in the evidence)*.

There is some evidence that obstetricians and gynaecologists are more likely to discuss, screen for, and follow policies related to GBS than nursing and midwifery professionals, and some evidence that those with fewer years of experience are more likely to screen than those with more years of experience *(low confidence in the evidence)*.

Views from women indicate reasons for not swabbing vary, but may include not being offered swabbing, lack of understanding about swabbing, and giving birth prior to the scheduled swab *(low confidence in the evidence)*.

Additional considerations

Lack of access to skilled intrapartum care and higher proportion of home births, particularly in low-income countries, is likely to limit the feasibility of IAP.

Penicillin and ampicillin are heat sensitive and may require refrigeration and protection from light. Ampicillin (powder for injection: 500 mg; 1 g [as sodium] in vial) and benzylpenicillin/penicillin G (powder for injection: 600 mg [= 1 million IU]; 3 g [= 5 million IU] [sodium or potassium salt] in vial) are listed in the *WHO Model List of Essential Medicines (15)*.

Judgement

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

Summary of judgements tables

Universal screening vs risk-based screening

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

Universal screening vs a combined/other screening strategy

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

Risk-based screening vs a combined/other screening strategy

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

Summary of findings tables

Question: Universal screening compared with risk-based screening– term population
Setting: China, Finland, Israel, Republic of Korea, Singapore, the USA

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	Risk-based screening	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – COMMON EFFECTS MODEL												
8	observational studies	serious[a]	not serious	not serious	not serious	none	91/468662 (0.0%)	186/241294 (0.1%)	**RR 0.24** (0.18 to 0.31)	**1 fewer per 1.000** (from 1 fewer to 1 fewer)	⨁⨁⨁◯ Moderate	CRITICAL
EOGBS INFECTIONS – RANDOM EFFECTS MODEL												
8	observational studies	very serious[b]	not serious	not serious	not serious	none	91/468662 (0.0%)	186/241294 (0.1%)	**RR 0.29** (0.17 to 0.51)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL
NON-GBS EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
2	observational studies	very serious[c]	not serious	not serious	serious[d,e]	none	6/9824 (0.1%)	6/9588 (0.1%)	**RR 1.02** (0.33 to 3.13)	**0 fewer per 1000** (from 0 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
NON-GBS EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
2	observational studies	very serious[c]	not serious	not serious	serious[d,e]	none	6/9824 (0.1%)	6/9588 (0.1%)	**RR 1.10** (0.34 to 3.54)	**0 fewer per 1000** (from 0 fewer to 2 more)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
2	observational studies	very serious[c]	not serious	not serious	serious[d]	none	12/9824 (0.1%)	19/9588 (0.2%)	**RR 0.62** (0.30 to 1.28)	**1 fewer per 1000** (from 1 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
2	observational studies	very serious[c]	not serious	not serious	serious[d]	none	12/9824 (0.1%)	19/9588 (0.2%)	**RR 0.65** (0.31 to 1.34)	1 fewer per 1000 (from 1 fewer to 1 more)	⨁◯◯◯ Very low	CRITICAL
MATERNAL PERIPARTUM INFECTION												
1	observational study	serious[f]	not serious	not serious	serious[d]	none	39/840 (4.6%)	38/814 (4.7%)	**RR 0.99** (0.63 to 1.57)	**0 fewer per 1000** (from 17 fewer to 27 more)	⨁⨁◯◯ Low	IMPORTANT

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	Risk-based screening	Relative (95% CI)	Absolute (95% CI)		
MATERNAL PERIPARTUM INFECTION – CHORIOAMNIONITIS												
1	observational study	serious[f]	not serious	not serious	serious[d]	none	28/420 (6.7%)	23/407 (5.7%)	**RR 1.19** (0.67 to 2.11)	**11 more per 1000** (from 19 fewer to 63 more)	⨁⨁◯◯ Low	IMPORTANT
MATERNAL PERIPARTUM INFECTION – ENDOMETRITIS												
1	observational study	serious[f]	not serious	not serious	very serious[d,g]	none	11/420 (2.6%)	15/407 (3.7%)	**RR 0.70** (0.32 to 1.55)	**11 fewer per 1000** (from 25 fewer to 20 more)	⨁◯◯◯ Very low	IMPORATNT

CI: confidence interval; RR: risk ratio

[a] Most of the pooled effect provided by studies "B" or "C" but without a substantial proportion (i.e. < 50%) from studies "B".
[b] Most of the pooled effect provided by studies "B" or "C" but with a substantial proportion (i.e. > 50%) from studies "C".
[c] The pooled effect is provided by studies "C".
[d] Wide confidence interval crossing the line of no effect.
[e] Few events but large sample size.
[f] The pooled effect is provided by study "B".
[g] Few events.

Question: Universal screening compared with risk-based screening – undetermined or combined preterm/term population
Setting: Austria, China, Qatar, Saudi Arabia, Türkiye, the United Kingdom, the USA

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	Risk-based screening	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTION – COMMON EFFECTS MODEL												
9	observational studies	serious[a]	not serious	serious[b]	not serious	none	225/618386 (0.0%)	378/470719 (0.1%)	**RR 0.47** (0.40 to 0.56)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTION – RANDOM EFFECTS MODEL												
9	observational studies	very serious[c]	not serious	serious[b]	not serious	none	225/618386 (0.0%)	378/470719 (0.1%)	**RR 0.46** (0.32 to 0.67)	**0 fewer per 1000** (from 1 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – COMMON EFFECTS MODEL												
4	observational studies	serious[a]	not serious	serious[b]	not serious	none	973/462362 (0.2%)	592/192259 (0.3%)	**RR 0.70** (0.63 to 0.78)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL
ANY EARLY ONSET NEONATAL SEPSIS – RANDOM EFFECTS MODEL												
4	observational studies	serious[a]	not serious	serious[b]	not serious	none	973/462362 (0.2%)	592/192259 (0.3%)	**RR 0.70** (0.63 to 0.78)	**1 fewer per 1000** (from 1 fewer to 1 fewer)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] Most of the pooled effect provided by studies "B".
[b] Data provided by studies with undetermined or mixed population of preterm and at/near term pregnancies.
[c] Most of the pooled effect provided by studies "C".

Question: Universal screening compared with a combined/other screening strategy (combined study periods 1 and 2 for Locksmith 1999) – term population
Setting: The USA

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	Combined/ other screening	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – LOCKSMITH 1999												
1	observational study	serious[a]	not serious	not serious	serious[b]	none	4/3176 (0.1%)	32/12406 (0.3%)	**RR 0.49** (0.17 to 1.38)	**1 fewer per 1000** (from 2 fewer to 1 more)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTIONS – EBERLY 2009												
1	observational study	very serious[c]	not serious	not serious	not serious	none	102/247613 (0.0%)	229/339769 (0.1%)	**RR 0.61** (0.48 to 0.77)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] The pooled effect is provided by study "B".
[b] Wide confidence interval crossing the line of no effect.
[c] The pooled effect is provided by study "C".

Question: Universal screening compared with a combined/other screening strategy (results by study period) – term population
Setting: The USA

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	Combined/ other screening	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS – LOCKSMITH 1999 (1ST)												
1	observational study	serious[a]	not serious	not serious	serious[b,c]	none	4/3176 (0.1%)	19/6249 (0.3%)	**RR 0.41** (0.14 to 1.22)	**2 fewer per 1000** (from 3 fewer to 1 more)	⨁⨁◯◯ Low	CRITICAL
EOGBS INFECTIONS – LOCKSMITH 1999 (2ND)												
1	observational study	serious[a]	not serious	not serious	serious[b,c]	none	4/3176 (0.1%)	13/6157 (0.2%)	**RR 0.60** (0.19 to 1.83)	**1 fewer per 1000** (from 2 fewer to 2 more)	⨁⨁◯◯ Low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] The pooled effect is provided by study "B".
[b] Wide confidence interval crossing the line of no effect.
[c] Few events but large sample size.

Question: Risk-based screening compared with a combined/other screening strategy – term population
Setting: The USA

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Universal screening	Combined/ other screening	Relative (95% CI)	Absolute (95% CI)		
EOGBS INFECTIONS												
1	observational study	very serious[a]	not serious	not serious	serious[b,c]	none	6/19516 (0.0%)	9/19891 (0.0%)	**RR 0.68** (0.24 to 1.91)	**0 fewer per 1000** (from 0 fewer to 0 fewer)	⨁◯◯◯ Very low	CRITICAL

CI: confidence interval; RR: risk ratio
[a] The pooled effect is provided by study "C".
[b] Wide confidence interval crossing the line of no effect.
[c] Few events but large sample size

References – Evidence-to-Decision Framework 2

1. Panneflek TJR, Hasperhoven GF, Chimwaza Y, Allen C, Lavin T, te Pas AB, et al. Intrapartum antibiotic prophylaxis to prevent Group B streptococcal infections in newborn infants: a systematic review and meta-analysis comparing various strategies. eClinicalMedicine. 2024;74:102748. doi: https://doi.org/10.1016/j.eclinm.2024.102748.
2. ISRCTN Registry. Routine testing for Group B Streptococcus in pregnancy (GBS3 trial). ISRCTN49639731. [website]: BioMed Central; 2022 [updated 30 March 2022] doi: 10.1186/ISRCTN49639731 (accessed 15 June 2024).
3. Seedat F, Stinton C, Patterson J, Geppert J, Tan B, Robinson ER, et al. Adverse events in women and children who have received intrapartum antibiotic prophylaxis treatment: a systematic review. BMC Pregnancy Childbirth. 2017;17(1):247. doi:10.1186/s12884-017-1432-3.
4. Downe S, Finlayson K, Tunçalp Ö, Metin Gülmezoglu A. What matters to women: a systematic scoping review to identify the processes and outcomes of antenatal care provision that are important to healthy pregnant women. BJOG. 2016;123(4):529–39. doi: 10.1111/1471-0528.13819.
5. Downe S, Finlayson K, Oladapo O, Bonet M, Gülmezoglu AM. What matters to women during childbirth: a systematic qualitative review. PLOS ONE. 2018;13(4):e0194906. doi: 10.1371/journal.pone.0194906.
6. Constantinou G, Webb R, Ayers S. An evidence synthesis on parents' and healthcare providers' values and preferences for, and views on the acceptability, feasibility, equity and outcomes of screening strategies to prevent early-onset group B streptococcal disease in newborns [preprint verion]. doi:10.1101/2024.06.28.24309381.
7. Allen C, Naznin E, Penneflek TJR, Lavin T, Hoque ME. The cost-effectiveness of Group B Streptococcus screening strategies: a systematic review [pre-print https://doi.org/10.1101/2024.08.25.24312541].
8. Evers S, Goossens M, de Vet H, van Tulder M, Ament A. Criteria list for assessment of methodological quality of economic evaluations: Consensus on Health Economic Criteria. Int J Technol Assess Health Care. 2005;21(2):240-5. doi:10.1017/S0266462305050324.
9. Albright CM, MacGregor C, Sutton D, Theva M, Hughes BL, Werner EF. Group B streptococci screening before repeat cesarean delivery: a cost-effectiveness analysis. Obstet Gynecol. 2017;129(1):111–9. doi: 10.1097/AOG.0000000000001800.
10. van den Akker-van Marle ME, Rijnders MEB, van Dommelen P, Fekkes M, van Wouwe JP, Amelink-Verburg MP, et al. Cost-effectiveness of different treatment strategies with intrapartum antibiotic prophylaxis to prevent early-onset group B streptococcal disease. BJOG. 2005;112(6):820– 6. doi: 10.1111/j.1471-0528.2005.00555.x.
11. MSH (Management Sciences for Health). International medical products price guide, 2015 edition. Medford: Medical Sciences for Health; 2016 (https://msh.org/resources/international-medical-products-price-guide-2/, accessed 15 June 2024).
12. Williams M, Zantow E, Turrentine M. Cost effectiveness of latest recommendations for group B streptococci screening in the United States. Obstet Gynecol. 2020;135(4):789–98. doi: 10.1097/AOG.0000000000003649.
13. State of inequality: reproductive, maternal, newborn and child health. Geneva: World Health Organization; 2015 (https://www.who.int/publications/i/item/9789241564908, accessed 15 June 2024).

14. Constantinou G, Ayers S, Mitchell EJ, Walker KF, Daniels J, Moore S, et al. Women and healthcare professionals' experiences of GBS testing as part of the GBS3 Trial: a qualitative study (under review).

15. Web Annex A. World Health Organization model list of essential medicines – 23rd list, 2023. In: The selection and use of essential medicines 2023. Executive summary of the report of the 24th WHO Expert Committee on the Selection and Use of Essential Medicines, 24–28 April 2023. Geneva: World Health Organization; 2023 (https://iris.who.int/bitstream/handle/10665/371090/WHO-MHP-HPS-EML-2023.02-eng.pdf, accessed 15 June 2024).

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