National Institute for Health and Care Excellence

Final

Abortion care

[Q] Supporting document for the recommendations on anti-D prophylaxis

NICE guideline NG140

Discussion underpinning recommendations 1.3.1 and 1.3.2 in the NICE guideline

May 2025

Final

This supporting document was developed by NICE

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The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

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Objective

The objective of this update is to revise recommendations on anti-D prophylaxis for pregnant women and people who are rhesus D negative and are having a medical or surgical abortion.

Introduction

Rhesus (Rh) D negative pregnant women exposed to the Rh D antigen may develop sensitisation due to fetal blood cell transfer during pregnancy. This immune response can lead to the production of antibodies against Rh D positive red blood cells, increasing the risk of fetal anaemia in subsequent pregnancies. To prevent sensitisation, anti-D prophylaxis is administered.

NICE guideline (NG140), developed in 2019, provides recommendations on the care of women of all ages seeking abortion services, including guidance on anti-D prophylaxis. Current recommendations specify that anti-D prophylaxis should be offered to Rh D negative women undergoing abortion after 10+0 weeks gestation and considered for those who are rhesus D negative and are having a surgical abortion up to and including 10+0 weeks' gestation. However, no prophylaxis is recommended for medical abortions up to and including 10+0 weeks gestation.

Since the publication of NG140, concerns have been raised regarding the alignment of its recommendations with emerging international guidelines and more recent scientific evidence. The guideline committee of NICE guideline NG140 has highlighted the potential cost-effectiveness implications for the NHS and proposed an update to recommendations on anti-D prophylaxis. In response to this proposal, an update is being undertaken to review and revise recommendations on anti-D prophylaxis.

Methods and process

In 2024, NICE conducted a surveillance review of the use of anti-D prophylaxis in its abortion care guideline to determine whether updates to current recommendations were necessary. No new relevant high-quality evidence was identified, and no ongoing studies currently being tracked by NICE were found to impact on the existing recommendations.

The surveillance review identified three external guidelines relevant to anti-D prophylaxis: the WHO guideline on abortion care[1] (2022), the Society of Family Planning (SFP) committee recommendations (2022)[9], and the Royal College of Obstetricians and Gynaecologists (RCOG) best practice in abortion care (2022)[11].

Both the RCOG best practice in abortion care and SFP committee recommendations align with the WHO guideline, as they are based on international guidelines and consensus. Given this alignment, a separate appraisal of these guidelines was not conducted. Instead, in accordance with NICE methods, the primary source the WHO guideline[1] was appraised.

Due to the lack of new relevant high-quality evidence, a formal evidence review was not conducted. Instead, it was decided to update the recommendations by cross-referencing the WHO guideline to ensure consistency with international best practices.

The WHO guideline on abortion care was critically appraised by 2 reviewers using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument. The AGREE II

instrument is an internationally validated tool that is used to assess the methodological rigour and transparency of clinical practice guidelines.

Methods for appraising quality of the external guideline, including a summary of the criteria for assessing the guideline using the AGREE II tool is included in Appendix A.

Included evidence

One external guideline on abortion care by the World Health Organization (WHO)[1] was included.

A summary of the external guideline and AGREE II tool assessment for the guideline is presented in Table 1.

Reviewer scoring of the WHO guideline using AGREE II tool can be found in Appendix B, and discussion points for assessing recommendations on anti-D prophylaxis are in Appendix C.

The WHO systematic review did not include cost-effectiveness in the protocol, but costs of the intervention and cost-effectiveness were at least qualitatively considered in making their recommendations.

Summary of the evidence

Table 1 Summary of the guideline and the AGREE II quality assessment

Study	Population, intervention, comparison and outcomes (PICO)	Recommendations	Quality assessment with AGREE II
WHO 2022[1] Abortion care guideline Study type: Guideline Aim: The objective of this guideline is to present the complete set of all WHO recommendations and best practice statements relating to abortion, with the goal of enabling evidence-based quality abortion care globally.	**Rh immunisation** PICO: No anti-D administration in unsensitised Rh-negative individuals seeking abortion. PICO question: For an unsensitised Rh-negative individual seeking abortion at < 12 weeks of gestation, is no administration of anti-D a safe and effective alternative to routine anti-D administration? P: Unsensitised Rh-negative individuals seeking abortion at < 12 weeks (undergoing either medical or surgical abortion) I: No anti-D administration C: Routine anti-D administration O: • Rate of isoimmunisation in subsequent pregnancy • Rate of antibody formation after initial pregnancy	**Rh isoimmunisation for abortion at gestational ages < 12 weeks** For both medical and surgical abortion at < 12 weeks: Recommend against anti-D immunoglobulin administration. <u>Remark:</u> • Standard of care applies for anti-D administration at gestational ages ≥ 12 weeks	**Scope and Purpose** **97%** The guideline states that the objective of this guideline is to present the complete set of all WHO recommendations and best practice statements relating to abortion, with the goal of enabling evidence-based quality The guideline provides a detailed research question (RQ) addressing Rh immunisation and anti-D prophylaxis. It defines the target population as unsensitised Rh-negative individuals seeking abortion at less than 12 weeks of gestation, whether undergoing medical or surgical abortion. Age is not specified in the RQ, but the guideline includes a Law and policy recommendation regarding gestational age limits. The RQ does not specify additional characteristics of the target population, such as presence of comorbidities, or any excluded groups. **Stakeholder Involvement** **92%** The guideline development group (GDG) includes a

Study	Population, intervention, comparison and outcomes (PICO)	Recommendations	Quality assessment with AGREE II
			comprehensive list of members, detailing their names, institutional affiliations, locations, and roles. The composition of the GDG is well-suited to the topic; however, the group lacks lay members and patient representatives. To ensure a broader understanding of the values and preferences of individuals seeking abortion care, the guideline reports conducting a global survey. Additionally, a technical meeting was held with 19 participants from 15 different countries and organisations. Key themes emerging from this consultation emphasised equity, inclusivity, and the importance of addressing the needs of vulnerable and marginalised populations. The guideline clearly defines its target users and outlines its intended application.
			Rigour of Development **97%** The guideline provides details on the databases searched, search terms and the time periods covered. however, the full search strategy is archived for reference.

Study	Population, intervention, comparison and outcomes (PICO)	Recommendations	Quality assessment with AGREE II
			A summary of the evidence is provided, and the recommendation is supplemented with a justification that details the availability of data, study designs, and the consistency of results across studies. The justifications also explain how the evidence was interpreted to inform the recommendations. All referenced studies are cited in a comprehensive reference list. The quality of evidence was assessed using the GRADE methodology, with evidence quality levels clearly indicated for each discussion. The Evidence-to-Decision frameworks for clinical service recommendations outline the process by which recommendations were formulated. In cases where evidence is lacking, recommendations were instead based on expert opinion, with a clear distinction between evidence-based and consensus-based recommendations. The WHO-INTEGRATE framework (balance of health benefits and harms; human rights and sociocultural acceptability; health equity, non-discrimination and equality; societal implications; financial

Study	Population, intervention, comparison and outcomes (PICO)	Recommendations	Quality assessment with AGREE II
			and economic considerations and feasibility and health system considerations and quality of evidence) was used as a basis for deciding on the direction and strength of each recommendation. The guideline is designed as a living guideline ensuring that new research evidence is continuously reviewed and incorporated as necessary. The guideline underwent external review by an independent review group (ERG), with all feedback from ERG members systematically evaluated by the WHO Steering Group.
			Clarity of Presentation **97%** The recommendations are clear, specific, unambiguous, and easily identifiable in the guideline. However, caveats or qualifying statements e.g., patients or conditions for whom the recommendations would not apply is not stated in the recommendation.
			Applicability **88%**

Study	Population, intervention, comparison and outcomes (PICO)	Recommendations	Quality assessment with AGREE II
			The guideline discusses in detail the barriers and facilitators to implementation of the recommendations in the guideline. Resource impact and cost-effectiveness was considered for the recommendation. .
			Editorial Independence **88%** The guideline states that no conflicts of interest were declared by any members of the Evidence and Recommendation Review Groups (ERRGs) and guideline development group (GDG). Funding for the development of the guideline was provided by Development and Research Training in Human Reproduction (HRP). The guideline however does not explicitly state that the funding body did not influence the content of the guideline.
Overall score			**Overall quality of the guideline: 6** (1 lowest possible quality and 7 highest possible quality) **I would recommend this guideline for use.** - Yes

Discussion of external guidance and the rationale for recommendations

This section discusses the updated recommendations for anti-D prophylaxis in NICE guideline NG140 for pregnant women and people undergoing a medical or surgical abortion.

Rationale

The World Health Organization (WHO) guideline on abortion care was developed following its established guideline development process, with recommendations based on the best available evidence and consensus from the Guideline Development Group (GDG). An assessment using the AGREE II tool rated the guideline as high quality, leading NICE to cross-refer to the WHO recommendations on anti-D prophylaxis. While ongoing research may provide further insights, no new high-quality evidence has emerged, and no large-scale clinical trials are expected to publish in the near future. The WHO guideline is structured as a living guideline, ensuring that new evidence will be continuously reviewed and incorporated as needed.

To inform its recommendations on anti-D prophylaxis, the WHO guideline incorporated a systematic review[2] evaluating the impact of routine anti-D administration in Rh-negative individuals without prior sensitisation who were undergoing an abortion. However, only two studies, one conducted in Israel[3] and another in the United States[4] met the inclusion criteria, both published in 1972. These studies suggested that anti-D administration reduced the likelihood of antibody development following a first pregnancy, with no adverse effects. Additionally, a comparative study[6] examining Rh alloimmunisation rates in Canada and Netherlands found no increased risk of sensitisation among Rh negative individuals with spontaneous abortion before 10 weeks of gestation without receiving anti D prophylaxis. Despite the evidence suggesting potential benefits for the intervention in the 2 included studies, the WHO expert panel considered multiple factors, including resource allocation, cost-effectiveness, and feasibility, alongside the very low certainty of the evidence. Ultimately, the panel concluded that the overall evidence did not strongly support routine anti-D administration, and they recommended against its use for gestational ages under 12 weeks, modifying the previous guidance from 2012[5], which had set the threshold at 9 weeks.

The WHO recommendations on anti-D prophylaxis have been widely adopted by health organisations worldwide, influencing national and international clinical guidelines. Notably, the Royal College of Obstetricians and Gynaecologists 2022[8], The American College of Obstetricians and Gynaecologists, 2024[9] , Society for Maternal–Fetal Medicine, 2024[10] and Society of Family Planning,2022[11] have issued guidance consistent with the recommendations outlined in the WHO abortion care guideline.

Further supporting these recommendations, data from the Serious Hazards of Transfusion (SHOT) database recorded 133 cases of Rh D sensitisation following pregnancy between 2002 and 2015, of which only 3 were associated with abortions, with one occurring at 11 weeks gestation. Despite the considerable number of abortions in the UK during this time (over 1.6 million), primarily in the first trimester, this low incidence indicates that abortion before 10 weeks' gestation is unlikely to pose a significant risk for Rh D sensitisation.

Considering these findings, NICE decided to cross-refer to the WHO guideline to ensure that its recommendations on anti D prophylaxis align with international best practices.

The adoption of these recommendations could result in fewer women and people requiring anti-D prophylaxis. This could potentially reduce the workload of clinical staff and minimise the burden associated with testing, venepuncture, and anti D immunoglobulin administration in abortion care.

Only editorial changes were made to recommendation 1.3.2 in this update (to align with the changes to recommendation 1.3.1). When the recommendations were drafted by the committee in the previous version, they agreed that continuing to test and use anti-D for surgical procedures that are not same day would have little impact. However, they emphasised that providers should ensure their systems for doing so do not deter them from offering efficient pathways.

Cost effectiveness and resource use

At the time of writing the cost of anti-D was £54 (https://bnf.nice.org.uk/drugs/anti-d-rh0-immunoglobulin/medicinal-forms/) and treatment would also require a small amount of staff time to administer an injection. Given the uncertainty surrounding the evidence on the effectiveness of treatment before 12 weeks and the cost of treatment, it is reasonable to conclude that the cost-effectiveness of the intervention has not been demonstrated.

Adoption of WHO recommendations could lead to some savings compared to previous NICE guidance. Anti-D would no longer be offered to a cohort of rhesus D negative women who are between 10+0 weeks and 11+6 weeks gestation. In addition, anti-D would no longer be considered for rhesus D negative women having a surgical abortion up to and including 10+0 weeks gestation. In addition, savings from a reduced need for rhesus D testing are anticipated in women up to 11+6 weeks gestation.

However, the overall number of women impacted by the change in NICE recommendations is relatively small and the savings realised would be modest. Furthermore, it is thought that current practice in some NHS settings already reflects the WHO guidance which would mean that not all these savings would be realised.

Recommendations supported by this supporting document

This supporting document supports recommendations 1.3.1 to 1.3.2.

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Appendices

Appendix A Appraising the quality of external guideline

The external guideline was appraised using a two-stage process. The first stage assessed whether the external guideline development process was robust and high quality. This was conducted using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.

The second stage of the appraisal process assessed the applicability and acceptability of the external recommendations themselves. It covered areas that are important for NICE such as the quality of the guideline development process, barriers to implementation, compatibility with cultures and values and health inequalities.

First stage assessment using the AGREE II instrument:

The Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument was developed to address the issue of variability in guideline quality. To that end, the AGREE instrument is a tool that assesses the methodological rigour and transparency in which a guideline is developed. The original AGREE instrument has been refined, which has resulted in the new AGREE II.

AGREE II has six domains and an overall assessment. The domains are listed below:

- Domain 1. **Scope and Purpose** is concerned with the overall aim of the guideline, the specific health questions, and the target population.
- Domain 2. **Stakeholder Involvement** focuses on the extent to which the guideline was developed by the appropriate stakeholders and represents the views of its intended users.
- Domain 3. **Rigour of Development** relates to the process used to gather and synthesise the evidence, the methods to formulate the recommendations, and to update them.
- Domain 4. **Clarity of Presentation** deals with the language, structure, and format of the guideline.
- Domain 5. **Applicability** pertains to the likely barriers and facilitators to implementation, strategies to improve uptake, and resource implications of applying the guideline.
- Domain 6. **Editorial Independence** is concerned with the formulation of recommendations not being unduly biased with competing interests.
- Overall assessment includes the rating of the overall quality of the guideline and whether the guideline would be recommended for use in practice.
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- For further details on each domain see the agree reporting checklist at agreetrust.org

Each of the 23 AGREE II items were rated on a 7-point scale (1 indicating strong disagreement and 7 indicating strong agreement). An overall rating for each of the 6 AGREE II domains was then calculated by summing all the scores of the individual items in a domain and then calculating the total as a percentage of the maximum possible score for that domain, as follows:

$$\frac{\text{Obtained score} - \text{Minimum possible score}}{\text{Maximum possible score} - \text{Minimum possible score}} \times 100$$

An overall rating for all domains was then determined (score 1 to 7) and finally an overall percentage rating was calculated for each guidance document based on the following equation: (overall score – 1)/6.

The AGREE II also suggests an overall assessment which includes a rating of the overall quality of the guideline and whether the guideline would be recommended for use in practice. The overall assessment requires the user to make a judgment as to the quality of the guideline, taking into account the criteria considered in the assessment process.

Table 2: Interpretation of overall score

Assessment	**Score**
Not met	equivalent to an AGREE II score of approximately 3 or less
Partially met	equivalent to an AGREE II score of approximately 4-5
No major concerns / fully met	equivalent to an AGREE II score of approximately 6-7

<u>Second stage appraisal of the guideline using NICE checklist:</u>

For the external guideline assessed to be high quality using the AGREE II instrument, the suitability of specific recommendations for cross-referencing in a NICE guideline was assessed using a NICE checklist. The checklist includes discussion points that were developed to provide a structured framework for assessing issues not covered by AGREE II. It was developed by NICE as no checklists were identified that fully covered all relevant.

The discussion points were used to assess the recommendations in more detail in terms of applicability and acceptability. For example, they include questions on health inequality considerations, applicability to UK settings, compatibility with cultures and values and consideration of health economics. Please see Appendix C for discussion points for assessing recommendations on anti-D prophylaxis.

Appendix B AGREE II tool reviewer scoring

Table 3: Reviewer scoring of WHO guideline on abortion care

	1. Scope and purpose				2. Stakeholder involvement				3. Rigour of development									4. Clarity of presentation				5. Applicability					6. Editorial independence			Overall assessment
Reviewer & guideline	Objectives	Question	Population	Total	Group membership	Target population	Target users	Total	Search methods	Evidence selection criteria	Evidence strengths and limitations	Formulation of recs	Considerations of benefits / harms	Link between recommendations & evidence	External review	Updating procedure	Total	Specific & unambiguous recs	Management options	Identifyable key recs	Total	Facilitators & barriers to application	Implementation advice/tools	Resource implications	Monitoring/auditing criteria	Total	Funding body	Competing interests	Total	
Reviewer 1	7	7	6	**20**	6	6	7	**19**	6	7	7	7	7	7	7	7	**55**	6	7	7	**20**	7	7	5	7	**27**	6	7	**13**	**6**
Reviewer 2	7	7	7	**21**	7	6	7	**20**	7	7	7	7	7	7	6	6	**54**	7	7	7	**21**	6	7	4	6	**23**	5	7	**12**	**6**
Score				**97%**				**92%**									**97%**				**97%**					**88%**			**88%**	

Appendix C Discussion points for assessing anti-D prophylaxis recommendations

	Details
Were the recommendations developed in accordance with the external organisation's development process (i.e., the process that has been assessed by either the NICE accreditation programme or AGREE II)?	The WHO guideline was developed following its prescribed development process, with recommendations based on current evidence and consensus from the Guideline Development Group (GDG). The guideline was assessed by two reviewers from the NICE team using the AGREE II tool. This evaluation included a rating of the overall quality of the guideline and an assessment of whether it should be recommended for use in practice. The guideline was deemed to be of "high quality''. Additionally, the WHO guideline is widely adopted and applicable to UK settings. Therefore, NICE decided to cross-refer to the recommendations.
Is the recommendation and the guideline development process low risk to NICE (this may be informed by other processes for example risk categories for QA or the multi criteria decision framework for updates)?	The recommendations are low risk to NICE. They are in line with current clinical practice and recent international guideline recommendations.
Is the recommendation and underpinning evidence current? Things to consider include:	*Whether the recommendation is likely to change over time (for example, information and support recommendations are more likely to be static and the evidence may need to be less up to date, whereas a recent evidence base is likely to be more important for recommendations on diagnosis and management):* Currently, there is limited high quality evidence available in this area. The recommendations are based on the available evidence and

	expert consensus. While new evidence may emerge, there are currently no known large clinical trials that are due to publish soon. *How recently were searches performed or updated for the underlying evidence base?* The WHO guideline has archived its date of search and full search strategy, so this information is not available. The WHO guideline is a living guideline, allowing for continuous review of new research evidence. *Has there been a recent check that the recommendation is up to date?* The relevant recommendations are up to date and in line with current clinical practice. *How recent evidence searches or checks need to be may depend on, for example, how fast-moving or high-volume the evidence base is:* NICE is not aware of any large clinical trials being conducted in this area that are publishing soon. *Is the recommendation based on evidence that would be considered of appropriate quality within the area of the review question?* Although evidence on the effectiveness of anti-D prophylaxis suggested potential benefits, it was assessed as being of very low certainty. Considering the limited confidence in the evidence, as well as the resources required, cost-effectiveness, and the feasibility of administering anti-D, the WHO expert panel concluded that the evidence does not support the intervention. Consequently, they recommended against its use for gestational ages< 12 weeks.

Was health economics (health economic studies, and/or an economic model) taken into account? If not, is the recommendation likely to be a low resource impact? [Ignore this question if health economics is not a relevant consideration for the recommendation, for example qualitative or signs and symptoms questions]	Resource impact and cost-effectiveness was considered for the recommendation.
If health inequality issues relevant to the recommendation were identified by the EHIA for the NICE guideline, does the committee think the recommendation is likely to adversely impact on the identified health inequality issues? If yes, are additional recommendations required to address the unmet need or should the committee develop their own recommendations?	No equalities or health inequalities issues relevant to this topic were identified.
Is the recommendation likely to be acceptable to the NHS and / or social care services? Things to consider include:	*Population(s) in the evidence base for the source recommendation vs the target population of the NICE recommendation:* The population in the recommendations is the same target population as the NICE recommendations. *Patient/service user views and preferences:* The WHO Guideline Development Group (GDG) did not include a patient representative. However, to ensure that the values and preferences of individuals seeking abortion care were considered, the guideline development process incorporated a global survey aimed at gaining a deeper understanding of patient perspectives. *Constraints, organisational barriers, legislation, policy, or any other issues that could impede implementation:* There is no anticipated constraints or barriers as the recommendations are reflective of current clinical practice. *Compatibility with cultures and values:* We do not anticipate there to be any issues of compatibilities with cultures and values