National Institute for Health and Care Excellence

FINAL

Caesarean birth

Methods

NICE guideline NG192

Development of guideline and methods

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Final

Developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists

Disclaimer

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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Contents

Development of the guideline **5**
Remit 5
What this guideline update covers 5
Groups that are covered 5
Clinical areas that are covered 5
What this guideline update does not cover 5
Clinical areas that are not covered 5
Methods **6**
Developing the review questions and outcomes 6
Searching for evidence 7
Systematic literature search 7
Economic systematic literature search 8
Reviewing evidence 8
Systematic review process 8
Type of studies and inclusion/exclusion criteria 9
Methods of combining evidence 10
Appraising the quality of evidence 11
Reviewing economic evidence 16
Inclusion and exclusion of economic studies 16
Appraising the quality of economic evidence 17
Economic modelling 17
Cost effectiveness criteria 17
Developing recommendations 18
Updating existing recommendations 18
Guideline recommendations 18
Research recommendations 18
Validation process 18
Updating the guideline 19
Funding 19
References **20**

Development of the guideline

Remit

The National Institute for Health and Care Excellence (NICE) commissioned the National Guideline Alliance (NGA) to update the existing NICE clinical guideline on Caesarean section (CG132) (NICE 2011). As part of this update this guideline has been renamed Caesarean birth.

What this guideline update covers

Groups that are covered

- Women who have had a caesarean birth in the past and are now pregnant again
- Women who have a clinical indication for a caesarean birth
- Women who are considering a caesarean birth when there is no other indication

Clinical areas that are covered

The 2021 update to the guideline covers the following clinical issues:

- The risks and benefits of caesarean birth compared with planned vaginal birth for mothers and babies
- Methods to reduce infectious morbidity in women undergoing caesarean birth
- Prevention and management of hypothermia in women undergoing caesarean birth
- The efficacy of single-layer versus double-layer closure of the uterus after caesarean birth
- Monitoring after intrathecal opioids for caesarean birth
- Opioids for pain management after caesarean birth

For further details please refer to the surveillance report on the NICE website that defined which sections of this guideline should be updated.

What this guideline update does not cover

Clinical areas that are not covered

The guideline update does not cover the following clinical issues:

- Planned caesarean birth
- Factors affecting the likelihood of caesarean birth during intrapartum care
- Procedural aspects of caesarean birth (other than those listed above)
- Care of the baby born by caesarean birth
- Care of the woman after caesarean birth (other than those listed above|)
- Pregnancy and childbirth after caesarean birth

Methods

This section summarises methods used to identify and review the evidence, to consider cost effectiveness, and to develop guideline recommendations. This guideline was developed in accordance with methods described in Developing NICE guidelines: the manual (NICE 2014).

Declarations of interest were recorded and managed in accordance with NICE's Policy on declaring and managing interests for NICE advisory committees (NICE 2018)

Developing the review questions and outcomes

The 6 review questions developed for this update to the guideline were based on the key areas identified by the NICE surveillance program as requiring an update. Three questions were identified by a routine surveillance report, 2 questions were flagged by surveillance during development as requiring and update, and in addition, the committee highlighted 1 topic additional to those highlighted by the surveillance report (single-layer versus double-layer closure of the uterus) and an additional review question was agreed with NICE and included in the update. The review questions were drafted by NGA and were refined and validated by the committee.

The review questions were based on the following framework:

- intervention reviews: population, intervention, comparator and outcome (PICO)

This framework guided the development of the review protocols, the literature searching process, the critical appraisal and synthesis of evidence and facilitated the development of recommendations by the committee.

Full literature searches, critical appraisals and evidence reviews were completed for each review question.

The review questions and evidence reviews corresponding to each question (or group of questions) are summarised in **Error! Reference source not found.**.

Table 1: Summary of review questions and index to evidence reviews

Evidence review	Review question guideline	Type of review
A	What are the risks and benefits (short and long term) of planned caesarean birth compared with planned vaginal birth at term for women and neonates/infants/children?	Intervention
B	What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity in women undergoing caesarean birth?	Intervention
C	What are the procedures to prevent and manage hypothermia and shivering in women having a caesarean birth in the pre-	Intervention

Evidence review	Review question guideline	Type of review
	operative, peri-operative and post-operative periods?	
D	What is the efficacy of single-layer closure of the uterus as compared with two layer closure at caesarean birth?	Intervention
E	What post-operative monitoring is required for women who have received intrathecal or epidural opioids at the time of caesarean birth, to identify or prevent potential complications (including the duration, frequency and features to be monitored)?	Intervention
F	Are opioids safe and effective for pain management after caesarean birth?	Intervention

The COMET database was searched for core outcome sets relevant to this guideline. No core outcome sets were identified and therefore the outcomes were chosen based on committee discussions.

Additional information related to development of the guideline is contained in:

- Supplement 1 (Glossary and abbreviations)
- Supplement 2 (NGA staff list).

Searching for evidence

Systematic literature search

Systematic literature searches were undertaken to identify all published clinical evidence relevant to each review question. This is a partial update of an existing guideline. New review protocols were drafted for the updated guideline, but the review protocols for the 2011 version of the guideline were taken into consideration at this stage. Evidence presented in the existing guideline was considered according to the new review protocol, and included in the updated guideline if it met the inclusion criteria for an individual review.

Databases were searched using subject headings, free-text terms and, where appropriate, study type filters. Where possible, searches were restricted to retrieve articles published in English. All searches were conducted in the following databases: Medline, Medline-in-process, Embase, Cochrane Central Register of Controlled Trials (CCTR), and Cochrane Database of Systematic Reviews (CDSR). Some searches were conducted in the following databases: Health Technology Assessments (HTA), and Database of Abstracts of Reviews of Effects (DARE). No date restrictions were placed on the searches, unless otherwise stated (and explained) in the individual review protocols for each review.

Due to the short timeframe for updating this guideline all the final versions of the searches were just run on the databases once, with one exception. Any studies added to the databases after the date of the search (even those published prior to this date) were not included unless specifically stated in the text. With one exception,

no re-runs of searches were undertaken as it was not anticipated that additional evidence would be available that would lead to changes in the recommendations in the timeframe over which this update was carried out. The one exception was a targeted top up search just for negative pressure wound therapy using the relevant terms from the full searches, this was run on 10/12/2020. This was done in response to stakeholder consultation comments regarding potentially relevant publications that had been published since the full searches were run. See the Included Studies section of Evidence Report B for more details.

Details of the search strategies, including study type filters that were applied and databases that were searched, can be found in Appendix B of each evidence report.

Searching for grey literature or unpublished literature was not undertaken.

Economic systematic literature search

Systematic literature searches were also undertaken to identify published economic evidence. Databases were searched using subject headings, free-text terms and, where appropriate, an economic evaluations search filter.

Searches using the search strategies derived from the review questions, combined with a search filter for economic evaluations, were conducted in Medline, Medline in Process, CCTR and Embase. Some searches, using the population search terms used in the evidence reviews, were also conducted in the NHS Economic Evaluation Database (NHS EED) and HTA. Where possible, searches were limited to studies published in English.

Due to the short timeframe for updating this guideline all the final versions of the searches were just run on the databases once. No re-runs of searches were undertaken as it was not anticipated that additional evidence would be available that would lead to changes in the recommendations in the timeframe over which this update was carried out.

Quality assurance

Search strategies were quality assured by cross-checking reference lists of relevant studies, analysing search strategies from published systematic reviews and asking members of the committee to highlight key studies. The principal search strategies for each search were also quality assured by a second information scientist using an adaptation of the PRESS 2015 Guideline Evidence-Based Checklist (McGowan 2016).

Reviewing evidence

Systematic review process

The evidence was reviewed following these steps.

- Potentially relevant studies were identified from the search results for each review question by screening titles and abstracts. Full-text copies of the articles were then obtained.
- Full papers were reviewed against pre-specified inclusion and exclusion criteria in the review protocols (see appendix A of each evidence review).

- Key information was extracted on the study methods and results, in accordance with factors specified in the review protocol. The information was presented in a summary table in the corresponding evidence review and in a more detailed evidence table (see Appendix D of each evidence review).
- Included studies were critically appraised using an appropriate checklist as specified in Developing NICE guidelines: the manual (NICE 2014). Further detail on appraisal of the evidence is provided below.
- Summaries of evidence by outcome were presented in the corresponding evidence review and discussed by the committee.

Review questions selected as high priorities for economic analysis (and those selected as medium priorities and where economic analysis could influence recommendations) and complex review questions were subject to dual screening and study selection through a 10% random sample of articles. Any discrepancies were resolved by discussion between the first and second reviewers or by reference to a third (senior) reviewer. For the remaining review questions, internal (NGA) quality assurance processes included consideration of the outcomes of screening, study selection and data extraction and the committee reviewed the results of study selection and data extraction. The review protocol for each question specifies whether dual screening and study selection was undertaken for that particular question.

Drafts of all evidence reviews were checked by a senior reviewer.

Type of studies and inclusion/exclusion criteria

Inclusion and exclusion of studies was based on criteria specified in the corresponding review protocol.

Systematic reviews (SRs) with meta-analyses were considered the highest quality evidence to be selected for inclusion.

For intervention reviews, randomised controlled trials (RCTs) were prioritised for inclusion because they are considered to be the most robust type of study design that could produce an unbiased estimate of intervention effects. Where there was limited evidence from RCTs, non-randomised controlled trials were considered for inclusion.

The committee was consulted about any uncertainty regarding inclusion or exclusion of studies. A list of excluded studies for each review question, including reasons for exclusion is presented in appendix K of the corresponding evidence review.

Narrative reviews, posters, letters, editorials, comment articles, unpublished studies and studies published in languages other than English were excluded. Conference abstracts were not considered for inclusion because they typically provide insufficient detail to fully critically appraise the study methods.

For the review on the risks and benefits of caesarean birth, due to the large number of outcomes identified as important, a pragmatic approach was taken to inclusion of primary studies and systematic reviews. If a high quality systematic review was identified that covered an important outcome, the literature was only searched for that outcome from the date of the searches in that review onwards. If more recent primary evidence was identified that had no recommendation relevant impact on the outcomes reported by the systematic review (for example small primary studies, in

agreement with the findings of the review) then this evidence was documented in the appendix of the systematic review but not formally extracted or critically appraised. If more recent primary evidence was identified which could change the conclusion of the systematic review, the primary data included in the systematic review was updated.

Methods of combining evidence

When planning reviews (through preparation of protocols), the following approaches for data synthesis were discussed and agreed with the committee.

Data synthesis for intervention reviews

Pairwise meta-analysis

Meta-analysis to pool results from RCTs was conducted where possible using Cochrane Review Manager (RevMan5) software.

For dichotomous outcomes, such as mortality, the Mantel–Haenszel method with a fixed effect model was used to calculate risk ratios (RRs). For all outcomes with zero events in both arms the risk difference was presented. For outcomes in which the majority of studies had low event rates (<1%), Peto odds ratios (ORs) was calculated as this method performs well when events are rare (Bradburn 2007).

For continuous outcomes, measures of central tendency (mean) and variation (standard deviation; SD) are required for meta-analysis. Data for continuous outcomes, such as duration of hospital stay, were meta-analysed using an inverse-variance method for pooling weighted mean differences (WMDs). Where SDs were not reported for each intervention group, the standard error (SE) of the mean difference was calculated from other reported statistics (p values or 95% confidence intervals; CIs) and then meta-analysis was conducted as described above.

If a study reported only the summary statistic and 95% CI the generic-inverse variance method was used to enter data into RevMan5. If the control event rate was reported this was used to generate the absolute risk difference in GRADEpro. If multivariable analysis was used to derive the summary statistic but no adjusted control event rate was reported, no absolute risk difference was calculated.

When evidence was based on studies that reported descriptive data or medians with interquartile ranges or p values, this information was included in the corresponding GRADE tables (see below).

Subgroups for stratified analyses were agreed for some review questions as part of protocol development.

When meta-analysis was undertaken, the results were presented visually using forest plots generated using RevMan5 (see Appendix E of relevant evidence reviews).

Appraising the quality of evidence

Intervention studies

Pairwise meta-analysis

GRADE methodology for intervention reviews

For intervention reviews, the evidence for outcomes from included RCTs and comparative non-randomised studies was evaluated and presented using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology developed by the international GRADE working group.

When GRADE was applied, software developed by the GRADE working group (GRADEpro) was used to assess the quality of each outcome, taking account of individual study quality factors and any meta-analysis results. Results were presented in GRADE profiles (GRADE tables).

The selection of outcomes for each review question was agreed during development of the associated review protocol in discussion with the committee. The evidence for each outcome was examined separately for the quality elements summarised in **Error! Reference source not found.**. Criteria considered in the rating of these elements are discussed below. Each element was graded using the quality ratings summarised in Table 3. Footnotes to GRADE tables were used to record reasons for grading a particular quality element as having a 'serious' or 'very serious' quality issue. The ratings for each component were combined to obtain an overall assessment of quality for each outcome as described in Table 4

The initial quality rating was based on the study design: RCTs start as 'high' quality evidence and non-randomised studies as 'low' quality evidence. The rating was then modified according to the assessment of each quality element (Table 2). Each quality element considered to have a 'serious' or 'very serious' quality issue was downgraded by 1 or 2 levels respectively (for example, evidence starting as 'high' quality was downgraded to 'moderate' or 'low' quality). In addition, there was a possibility to upgrade evidence from non-randomised studies (provided the evidence for that outcome had not previously been downgraded) if there was a large magnitude of effect, a dose–response gradient, or if all plausible confounding would reduce a demonstrated effect or suggest a spurious effect when results showed no effect.

Table 2: Description of quality elements in GRADE for intervention reviews

Quality element	Description
Risk of bias ('Study limitations')	This refers to limitations in study design or implementation that reduce the internal validity of the evidence
Inconsistency	This refers to unexplained heterogeneity in the results
Indirectness	This refers to differences in study populations, interventions, comparators or outcomes between the available evidence and inclusion criteria specified in the review protocol
Imprecision	This occurs when a study has few participants or few events of interest, resulting in wide confidence intervals that cross minimally important thresholds

Quality element	Description
Publication bias	This refers to systematic under- or over-estimation of the underlying benefit or harm resulting from selective publication of study results

Table 3: GRADE quality ratings (by quality element)

Quality issues	Description
None or not serious	No serious issues with the evidence for the quality element under consideration
Serious	Issues with the evidence sufficient to downgrade by 1 level for the quality element under consideration
Very serious	Issues with the evidence sufficient to downgrade by 2 levels for the quality element under consideration

Table 4: Overall quality of the evidence in GRADE (by outcome)

Overall quality grading	Description
High	Further research is very unlikely to change the level of confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on the level of confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on the level of confidence in the estimate of effect and is likely to change the estimate
Very low	The estimate of effect is very uncertain

Assessing risk of bias in intervention reviews

Bias is a systematic error, or consistent deviation from the truth in results obtained. When a risk of bias is present the true effect can be either under- or over-estimated.

Risk of bias in RCTs was assessed using the Cochrane risk of bias tool as described in Appendix H in Developing NICE guidelines: the manual (NICE 2014).

The Cochrane risk of bias tool assesses the following possible sources of bias:

- selection bias
- performance bias
- attrition bias
- detection bias
- reporting bias.

A study with a poor methodological design does not automatically imply high risk of bias; the bias is considered individually for each outcome and it is assessed whether the chosen design and methodology will impact on the estimation of the intervention effect.

More details about the Cochrane risk of bias tool can be found in Section 8 of the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011, updated 2019).

For systematic reviews of RCTs the AMSTAR checklist was used and for systematic reviews of other study types the ROBIS checklist was used (see Appendix H in Developing NICE guidelines: the manual (NICE 2014).

For non-randomised studies the Newcastle-Ottawa checklist was used (see Appendix H in Developing NICE guidelines: the manual (NICE 2014).

Assessing inconsistency in intervention reviews

Inconsistency refers to unexplained heterogeneity in results of meta-analysis. When estimates of treatment effect vary widely across studies (that is, there is heterogeneity or variability in results), this suggests true differences in underlying effects. Inconsistency is, thus, only truly applicable when statistical meta-analysis is conducted (that is, results from different studies are pooled). When outcomes were derived from a single study the rating 'no serious inconsistency' was used when assessing this domain, as per GRADE methodology (Santesso 2016).

Inconsistency was assessed visually by inspecting forest plots and observing whether there was considerable heterogeneity in the results of the meta-analysis (for example if the point estimates of the individual studies consistently showed benefits or harms). This was supported by calculating the I-squared statistic for the meta-analysis with an I-squared value of more than 50% indicating considerable heterogeneity, and more than 80% indicating very serious heterogeneity. When considerable or very serious heterogeneity was observed, possible reasons were explored and subgroup analyses were performed as pre-specified in the review protocol where possible. In the case of heterogeneity unexplained by subgroup analyses, sensitivity analyses were conducted based on the quality of studies, eliminating studies at high risk of bias (in relation to randomisation, allocation concealment and blinding, and/or missing outcome data).

When considerable unexplained heterogeneity was still present following subgroup and sensitivity analyses, the meta-analysis was re-run using the Der-Simonian and Laird method with a random effects model and this was used for the final analysis.

When no plausible explanation for the heterogeneity could be found, the quality of the evidence was downgraded in GRADE for inconsistency.

Assessing indirectness in intervention reviews

Directness refers to the extent to which populations, interventions, comparisons and outcomes reported in the evidence are similar to those defined in the inclusion criteria for the review and was assessed by comparing the PICO elements in the studies to the PICO defined in the review protocol. Indirectness is important when such differences are expected to contribute to a difference in effect size, or may affect the balance of benefits and harms considered for an intervention.

Assessing imprecision and clinical importance in intervention reviews

Imprecision in GRADE methodology refers to uncertainty around the effect estimate and whether or not there is an important difference between interventions (that is, whether the evidence clearly supports a particular recommendation or appears to be consistent with several candidate recommendations). Therefore, imprecision differs from other aspects of evidence quality because it is not concerned with whether the point estimate is accurate or correct (has internal or external validity). Instead, it is

concerned with uncertainty about what the point estimate actually represents. This uncertainty is reflected in the width of the CI.

The 95% CI is defined as the range of values within which the population value will fall on 95% of repeated samples, were the procedure to be repeated. The larger the study, the smaller the 95% CI will be and the more certain the effect estimate.

Imprecision was assessed in the guideline evidence reviews by considering whether the width of the 95% CI of the effect estimate was relevant to decision making, considering each outcome independently. This is illustrated in Figure 1, which considers a positive outcome for the comparison of treatment 'A' versus treatment 'B'. Three decision-making zones can be differentiated, bounded by the thresholds for minimal importance (minimally important differences; MIDs) for benefit and harm. The MID for harm for a positive outcome means the threshold at which treatment A is less effective than treatment B by an amount that is important to people with the condition of interest (favours B).

When the CI of the effect estimate is wholly contained in 1 of the 3 zones there is no uncertainty about the size and direction of effect, therefore, the effect estimate is considered precise; that is, there is no imprecision.

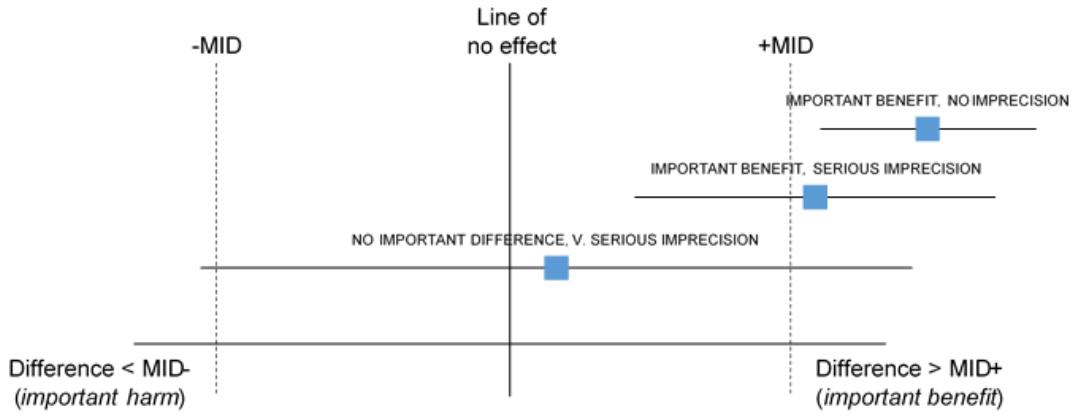
When the CI crosses 2 zones, it is uncertain in which zone the true value of the effect estimate lies and therefore there is uncertainty over which decision to make. The CI is consistent with 2 possible decisions, therefore, the effect estimate is considered to be imprecise in the GRADE analysis and the evidence is downgraded by 1 level ('serious imprecision').

When the CI crosses all 3 zones, the effect estimate is considered to be very imprecise because the CI is consistent with 3 possible decisions and there is therefore a considerable lack of confidence in the results. The evidence is therefore downgraded by 2 levels in the GRADE analysis ('very serious imprecision').

When the point estimate was between the MIDs and the CI crossed the line of no effect, this was considered to be precise evidence of no difference between interventions.

Implicitly, assessing whether a CI is in, or partially in, an important zone, requires the guideline committee to estimate an MID or to say whether they would make different decisions for the 2 confidence limits.

Figure 1: Assessment of imprecision and importance in intervention reviews using GRADE



MID, minimally important difference

Defining minimally important differences for intervention reviews

The committee was asked whether there were any recognised or acceptable MIDs in the published literature and community relevant to the review questions under consideration.

For the majority of reviews, in the absence of published or accepted MIDs, the committee agreed to use the GRADE default MIDs to assess imprecision. For dichotomous outcomes minimally important thresholds for a RR of 0.8 and 1.25 respectively were used as default MIDs in the guideline. The committee also chose to use 0.8 and 1.25 as the MIDs for ORs & HRs in the absence of published or accepted MIDs. While the GRADE default MIDs were originally intended for use on RRs, no default MIDs exist for OR or HR and as these measures are mathematically similar (particularly OR at low event rates) the committee agreed for consistency to continue to use 0.8 and 1.25 for these outcomes.

The same thresholds were used as default MIDs in the guideline for all dichotomous outcomes considered in intervention evidence reviews except for future rupture/morbidly adherent placenta/hysterectomy and all outcomes in the review on the benefits and risks of caesarean birth. In these two situations any statistically significant difference was judged to be important. For the placenta related outcomes that was because the consequences of each individual event are so serious. For the benefits and risks question that is because the aim of the review is to inform women rather than recommend one intervention or other. For continuous outcomes default MIDs, equal to half the median SD of the control groups at baseline (or at follow-up if the SD is not available a baseline), were used for all outcomes except for temperature in the review of hypothermia and shivering. For temperature the committee used two ranges of clinical importance: below 36.0°C, a difference between intervention and control of 0.2°C or more was considered important; above 36.0°C, a difference of 0.5°C was clinically important. These thresholds were used for consistency with the NICE guideline on Hypothermia: prevention and management in adults having surgery (NICE 2016).

For outcomes where 95% CI around ratios or mean differences were not readily available (for example those based on risk differences or medians), imprecision was assessed against pragmatic sample size thresholds based loosely on the principle of

optimal information size. A sample size of <300 was considered to represent very serious imprecision and between 300 and 500 was considered to represent serious imprecision.

Assessing publication bias in intervention reviews

Where 10 or more studies were included as part of a single meta-analysis, a funnel plot was produced to graphically assess the potential for publication bias. Where fewer than 10 studies were included for an outcome, the committee subjectively assessed the likelihood of publication bias based on factors such as the proportion of trials funded by industry and the propensity for publication bias in the topic area.

Reviewing economic evidence

Inclusion and exclusion of economic studies

Titles and abstracts of articles identified through the economic literature searches were independently assessed for inclusion using the predefined eligibility criteria listed in Table 5.

Table 5: Inclusion and exclusion criteria for the systematic reviews of economic evaluations

Inclusion criteria
Studies from Organisation for Economic Co-operation and Development (OECD) countries were included, as the aim of the review was to identify economic information transferable to the UK context.
Study population matches scope.
Clinical condition and interventions assessed identical to those considered in the clinical evidence review.
Studies include sufficient details regarding methods and results to enable methodological quality to be assessed and results to be extracted.
Full economic evaluations (cost utility, cost effectiveness, cost benefit or cost consequence analyses) that assess both the costs and outcomes associated with the interventions of interest.
Exclusion criteria
Conference abstracts, poster presentations or dissertation abstracts with insufficient methodological details
Cost-of-illness type studies
Non-English language study

Once the screening of titles and abstracts was completed, full-text copies of potentially relevant articles were requested for detailed assessment. Inclusion and exclusion criteria were applied to articles obtained as full-text copies.

Details of the economic evidence study selection for each question, list of excluded studies, economic evidence tables, the results of quality assessment of economic evidence (see below) and health economic evidence profiles are presented in appendices G, K, H and I of the evidence report. Existing economic evidence considered in the guideline is provided in the respective evidence chapters.

Appraising the quality of economic evidence

The quality of economic evidence was assessed using the economic evaluations checklist specified in Developing NICE guidelines: the manual (NICE 2014).

Economic modelling

The aims of the economic input to the guideline were to inform the guideline committee of potential economic issues to ensure that recommendations represented a cost effective use of healthcare resources. Economic evaluations aim to integrate data on healthcare benefits (ideally in terms of quality-adjusted life-years; QALYs) with the costs of different options. In addition, the economic input aimed to identify areas of high resource impact; these are recommendations which (while cost effective) might have a large impact on NHS finances and so need special attention.

The committee prioritised the following review question where it was thought that economic considerations would be particularly important in formulating recommendations:

- What methods, apart from prophylactic antibiotics, should be used to reduce infectious morbidity at caesarean section?

A model on negative pressure wound therapy (NPWT) dressings after caesarean section was initially planned but ultimately deemed unnecessary as there was a cost analysis done as part of NICE medical technology guidance (mtg43) and other published economic evidence. When new economic analysis was not prioritised, the committee made a qualitative judgement regarding cost effectiveness by considering existing economic evidence, expected differences in resource and cost use between options, alongside clinical effectiveness evidence identified from the clinical evidence review.

Cost effectiveness criteria

NICE's report Social value judgements: principles for the development of NICE guidance sets out the principles that committees should consider when judging whether an intervention offers good value for money. In general, an intervention was considered to be cost effective if any of the following criteria applied (given that the estimate was considered plausible):

- the intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more effective compared with all the other relevant alternative strategies), or
- the intervention cost less than £20,000 per QALY gained compared with the next best strategy, or
- the intervention provided clinically significant benefits at an acceptable additional cost when compared with the next best strategy.

The committee's considerations of cost effectiveness are discussed explicitly in the committee's discussion of the evidence section on 'Cost effectiveness and resource use'.

Developing recommendations

Updating existing recommendations

Although a number of sections of the 2011 guideline had not been prioritised for updating by the NICE surveillance report, the committee identified some recommendations in these sections where practice had changed, new technology had become available, or health policy had changed. In addition, the committee identified a number of recommendations which were not written in the current NICE style or terminology. As part of the update process the committee therefore reviewed the sections of the guideline which were not being formally updated and made minor edits to some of the recommendations to improve clarity, ensure they reflected current best practice, or correct recommendations that no longer were applicable. These changes are clearly marked in yellow in the guideline version for consultation, and the changes and reasons for them summarised in Table 2 of the update information at the end of the guideline.

Guideline recommendations

Recommendations were drafted on the basis of the committee's interpretation of the available evidence, taking into account the balance of benefits, harms and costs between different courses of action. When effectiveness and economic evidence was of poor quality, conflicting or absent, the committee drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential benefits and harms, the economic costs or implications compared with the economic benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues.

The main considerations specific to each recommendation are outlined under the 'The committee's discussion of the evidence' within each evidence review.

For further details please refer to Developing NICE guidelines: the manual (NICE 2014).

Research recommendations

When areas were identified for which good evidence was lacking, the committee considered making recommendations for future research. For further details please refer to Developing NICE guidelines: the manual (NICE 2014).

Validation process

This guidance was subject to a 6-week public consultation and feedback process. All comments received from registered stakeholders are responded to in writing and posted on the NICE website at publication. For further details please refer to Developing NICE guidelines: the manual (NICE 2014).

Updating the guideline

Following publication, and in accordance with the NICE guidelines manual, NICE will undertake a review of whether the evidence base has progressed significantly to alter the guideline recommendations and warrant an update. For further details please refer to Developing NICE guidelines: the manual (NICE 2014).

Funding

The NGA was commissioned by NICE to develop this guideline.

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