An Roinn Sláinte
Department of Health

Stratification of clinical risk in pregnancy

National Clinical Guideline No. 23

Annex C: Systematic review of economic literature

National Patient Safety Office
Oifig Náisiúnta um Shábháilteacht Othar

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

HRB Health Research Board

CICER Collaboration in Ireland for Clinical Effectiveness Reviews

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Collaboration in Ireland for Clinical Effectiveness Reviews

Risk in pregnancy — systematic review of economic literature.

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HRB Health Research Board

NATIONAL CLINICAL EFFECTIVENESS COMMITTEE

RCSI

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About HRB-CICER

In 2016, the Department of Health requested the Health Research Board (HRB) to fund a dedicated multidisciplinary research group to support the activities of the Ministerial appointed National Clinical Effectiveness Committee (NCEC). Called HRB-CICER (Collaboration in Ireland for Clinical Effectiveness Reviews), a five-year contract (2017 to 2022) was awarded following a competitive process to the Health Information and Quality Authority (HIQA). The HRB-CICER team comprises a dedicated multidisciplinary research team (including expertise in health economics, qualitative and quantitative research methods and epidemiology) supported by staff from the Health Technology Assessment (HTA) team in HIQA and the HRB Centre for Primary Care Research at the Royal College of Surgeons in Ireland (RCSI), as well as national and international clinical and methodological experts.

Guideline development groups submit clinical guidelines for appraisal and endorsement by the NCEC as National Clinical Guidelines. HRB-CICER provides independent scientific support to guideline development groups tailored according to their specific needs. The main role of the HRB-CICER team is to undertake systematic reviews of the clinical effectiveness and cost-effectiveness of interventions included in the guidelines and to estimate the budget impact of implementing the guidelines. Additional support can be provided by HRB-CICER to guideline development groups, including providing tailored training sessions and working closely with the guideline development groups to develop clinical questions and search strategies; performing systematic reviews of international clinical guidelines; supporting the assessment of suitability of clinical guidelines for adaption to Ireland and assisting in the development of evidence-based recommendations.

Membership of the evaluation team

Members of the HRB-CICER Evaluation Team were Dr Barbara Clyne, Michelle O'Neill, Dr Christopher Fawsitt, Barrie Tyner, Professor Susan M. Smith and Dr Máirín Ryan.

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List of abbreviations that appear in this report

AGREE II	Appraisal of Guidelines for Research and Evaluation instrument version 2
DARE	Database of Abstracts of Reviews of Effects
DALYS	Disability-adjusted life years
ED	Emergency department
GDG	Guideline Development Group
HDU	High dependency unit
HRB-CICER	Health Research Board – Collaboration in Ireland for Clinical Effectiveness Reviews
HSE	Health Service Executive
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
ICU	Intensive care unit
NCEC	National Clinical Effectiveness Committee
NCG	National clinical guideline
NHS EED	National Health Service Economic Evaluation Database
NICU	Neonatal intensive care unit
PICOS	Population, intervention, comparator, outcome, study design
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
QALY	Quality-adjusted life year

Executive summary

Background and objectives

Creating a Better Future Together: National Maternity Strategy 2016–2026,[1] published in 2016, advocates a risk-based approach to ensure that women are provided with the most appropriate model of care in line with their clinical risk. The strategy highlighted the need to stratify pregnant women according to their clinical risk into three risk groups: normal risk, medium risk and high risk. Following publication of the National Maternity Strategy, the Minister for Health mandated the commissioning and quality assurance of prioritised national clinical guidelines through the National Clinical Effectiveness Committee (NCEC) to support its implementation.

The guideline to which this systematic review relates will focus on how to stratify women according to clinical risk during the antenatal period. This will include classification at the initial antenatal appointment and during all subsequent antenatal appointments. Stratification of risk during labour or post birth will not be considered within this clinical guideline. The purpose of this systematic review is to identify and evaluate economic evidence on the cost-effectiveness of using a formal risk stratification system during the antenatal period, which will inform the development of the national clinical guideline.

Methods

A systematic review of the literature was conducted.

Data sources: A comprehensive search of PubMed, EMBASE, and the Cochrane Library (which includes the Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the Health Technology Assessment Database and the National Health Service Economic Evaluation Database) was conducted in October 2018 using combinations of keywords and medical subject headings (MeSH) terms.

Selection criteria: Two reviewers independently screened studies.

Health economic studies considered included economic evaluations (cost-effectiveness analysis, cost-utility analysis, cost-minimisation analysis and cost-benefit analysis) and comparative resource use studies evaluating any comprehensive system of classification or

identification of a woman's risk during the antenatal period (initial antenatal appointment and during all subsequent antenatal appointments).

Results

This systematic review identified no published economic evaluations related to the use of a comprehensive system of stratification or identification of a woman's risk during the antenatal period.

Conclusions

This review found no studies which met the inclusion criteria. This review is important because it might help encourage the economic evaluation of a comprehensive system of stratification of a woman's risk during the antenatal period.

Registration

This review was registered on PROSPERO: CRD42018114459.

1 Background

Creating a Better Future Together: National Maternity Strategy 2016–2026,[1] published in February 2016, advocates a risk-based approach to ensure that women are provided with the most appropriate model of care in line with their clinical risk. The strategy highlighted the need to stratify pregnant women according to their clinical risk into three risk groups: normal risk, medium risk and high risk. Following publication of the National Maternity Strategy, the Minister for Health mandated the commissioning and quality assurance of prioritised national clinical guidelines through the National Clinical Effectiveness Committee (NCEC) to support its implementation.

1.1 Description of the intervention

At the first meeting of the Childbirth Guideline Development Group (GDG) in June 2017, the scope of the first of a suite of national clinical guidelines (NCG) to be developed to support the implementation of the National Maternity Strategy was agreed. The guideline would focus on how to stratify women according to risk during the antenatal period. This would include stratification at the initial booking appointment and during all subsequent antenatal appointments. Stratification of risk during labour or post birth would not be considered within this clinical guideline.

A systematic review of existing clinical guidelines on risk in pregnancy was performed by HRB-CICER.[2] As no high-quality guideline with a three-level risk stratification (as described in the Irish Maternity Strategy) was identified, the GDG decided that adapting a single or a number of existing high-quality clinical guidelines using the ADAPTE process[3] was the preferred approach. Risk factors were extracted from three high-quality guidelines, identified through the systematic review and assessed according to the AGREE ll instrument. A three-step modified Delphi method was used to establish consensus on which risk factors should be included in the current guideline. Using this approach, the multidisciplinary GDG reached consensus on the risk factors to be used to stratify women according to risk within the Irish maternity services.

1.2 Purpose of this systematic review

The purpose of this systematic review is to identify and evaluate economic evidence on the cost-effectiveness of using a formal risk stratification system during the antenatal period to inform the development of an NCG on stratifying women according to risk during the antenatal period.

2 Methods

The reporting of this systematic review adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria.[4] The review also followed national guidelines for the retrieval and interpretation of economic literature.[5] The proposed methodology for the systematic review is outlined in a protocol which was agreed with the guideline development group (GDG) and registered on PROSPERO (CRD42018114459).

In general, it is considered best practice to develop the economic review questions in conjunction with the clinical review questions and to conduct the literature searches in tandem. Reviewing the evidence in this manner is more efficient and allows for explicit consideration of the economic evidence during formulation of the clinical recommendations. For this guideline, as an ADAPTE process was followed to generate the clinical recommendations, the economic review question was formulated based on the clinical evidence. In this regard, the review aims to identify economic evidence that will inform and support final guideline recommendations.

2.1 Review question

The question was formulated in line with the PICOS (population, intervention, comparator, outcome, study design) framework as presented in Table 2.1.

Economic review question:

- What is the cost-effectiveness of using a comprehensive system of stratification of risk during the antenatal period (classification at the initial antenatal appointment and during all subsequent antenatal appointments)?

Table 2.1 PICOS for review question

Population	Pregnant women during the antenatal period
Intervention	Any comprehensive system* of classification/stratification or identification of a woman's risk during the antenatal period (initial booking appointment and during all subsequent antenatal appointments) to determine the most appropriate model of care in community and outpatient settings
Comparator	Usual care, no formal system of risk classification/stratification
Outcomes	Any relevant measures of costs and benefits related to implementing a comprehensive system of classification, such as: • Implementation costs • Changes to the care pathway (that is, impact on consultation rates or duration with obstetricians, midwifery or primary care) • Additional screening and testing • Maternal and neonatal outcomes.
Study design	Systematic reviews of economic evaluations, full economic evaluation studies (cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis), costing studies and comparative resource use studies

* A comprehensive system is defined for this review as one that uses a formal questionnaire, documented list and or routine lab tests across potential risk categories including but not limited to medical history, obstetric history and lifestyle factors.

2.2 Types of studies

The review aimed to identify health economic studies such as economic evaluations (cost-effectiveness analysis, cost-utility analysis, cost-minimisation analysis and cost-benefit analysis) and comparative resource use studies.

2.3 Types of participants

The population of interest was pregnant women during the antenatal period in community and outpatient settings. In-patient systems of classification or identification of a woman's risk were not included.

2.4 Types of outcome measures

The following is a non-exhaustive list of economic outcome measures applicable to this review:

Economic evaluations

Cost-utility and or cost-effectiveness analysis:

- incremental cost-effectiveness ratio (ICER)
- cost per unit of effect (such as cost per life year gained) or effects per unit cost (for example, life years gained per Euro spent) (maternal and or neonatal)
- quality-adjusted life years (QALYs), disability-adjusted life years (DALYs) or health/life years equivalent (maternal and or neonatal)
- incremental net monetary benefit.

Cost-benefit and or cost-minimisation analysis:

- net monetary benefit
- incremental costs.

Other economic outcome measures

Costs and resource use:

- direct (for example, cost of changes to treatment pathway such as consultation rates with obstetricians, midwifery, primary care) and indirect medical costs (for example, out-of-pocket patient expenses for attending additional consultations or attending for additional tests)
- intensive care unit (ICU)/high dependency unit (HDU)/emergency department (ED)/neonatal intensive care unit (NICU) admissions
- length of stay (hospital or ICU/HDU)
- implementation costs (for example, training and education or changes to referral pathway)
- service utilisation costs (for example, additional screening tests, lab resources, additional treatment and monitoring)

- cost savings or offsets.

2.5 Search methods for identification of studies

Electronic searches were conducted in October 2018 in PubMed, Embase and the Cochrane Library (which includes the Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, the Health Technology Assessment Database and the National Health Service Economic Evaluation Database) using a search strategy outlined in Appendix 1. A grey literature search was also conducted, as described in Appendix 2.

2.6 Exclusion criteria

The following exclusion criteria were applied:

- studies related to screening for individual specific risk factors (for example, individual medical factors such as hypertension or risk relating specifically to previous obstetric complications or psychosocial problems)
- studies outside of the antenatal period
- studies that were published before 2008 (a 10-year time limit was applied to the search to insure identified economic literature was applicable to current practice)
- conference papers and abstracts where the full paper was unobtainable.

2.7 Data collection and analysis

Selection of studies

Citations were screened by two reviewers to eliminate clearly irrelevant studies. Two people independently reviewed the remaining citations per the inclusion criteria, with any disagreements being resolved by discussion.

Data extraction and management

Data extraction was planned to be performed independently by two people with any disagreements being resolved by discussion; however, due the lack of data, this step did not take place.

Assessment of risk of bias in included studies

Risk of bias was planned to be assessed using the CHEC-list quality appraisal tool[6] and evaluation of transferability was planned to be conducted using the International Society for Pharmacoeconomics (ISPOR) questionnaire,[7] independently performed by two people; however, due the lack of data, this step did not take place.

Data synthesis

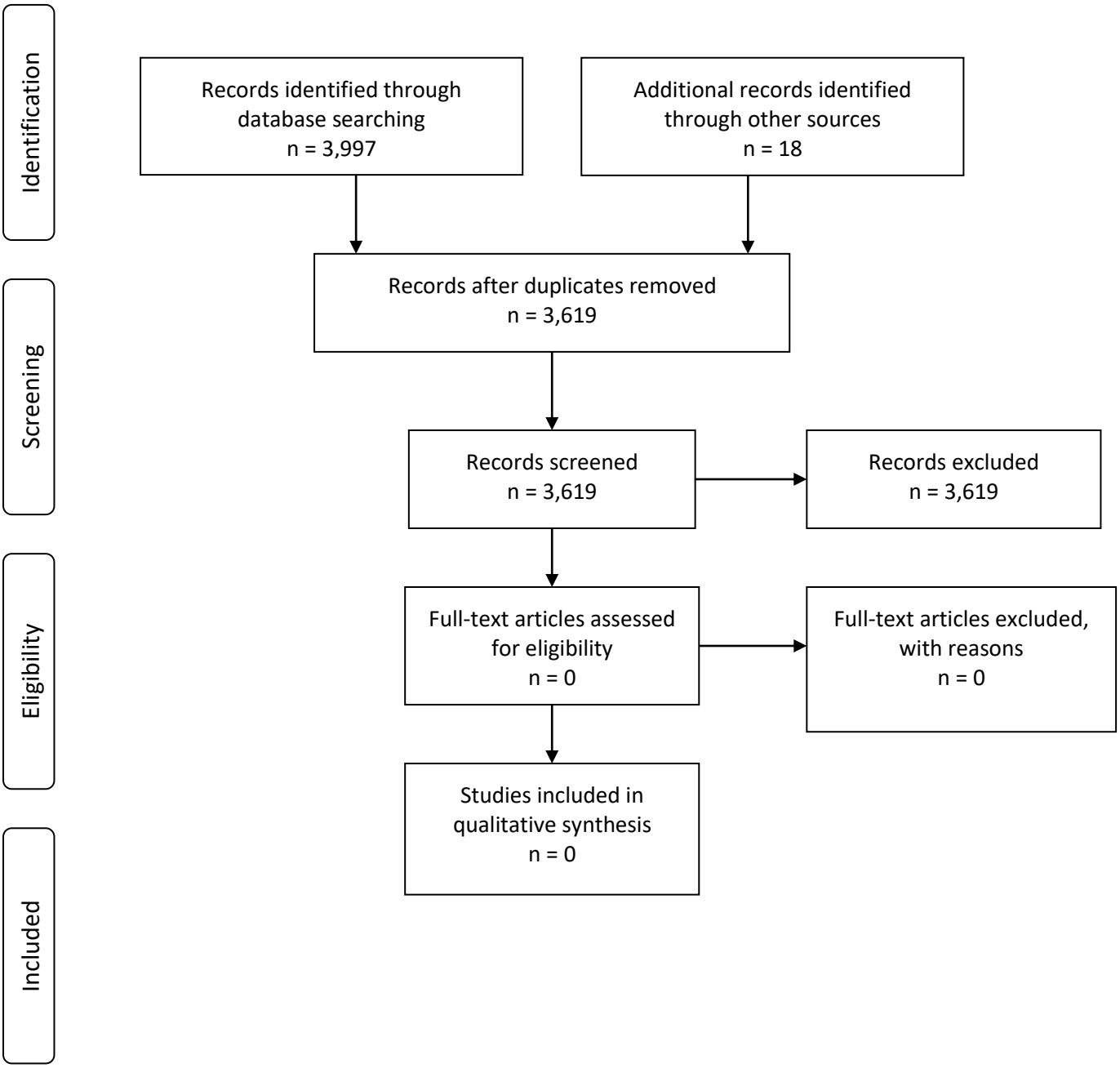
A narrative synthesis of the results of economic studies was planned; however, due the lack of data, this step did not take place.

3 Results

3.1 Search results

The search strategy identified 4,015 potentially relevant references through searching listed databases and grey literature. After the exclusion of duplicates, 3,619 records were screened. All 3,619 records were excluded based on a review of the titles and abstracts (see Figure 3.1). A number of economic evaluations related to clinical outcomes and costs of screening for specific risk factors (for example, individual medical factors such as hypertension, risk relating specifically to previous obstetric complications or psychosocial problems) were identified; however no studies focused on a comprehensive system of stratification of a woman's risk during the antenatal period.

Figure 3.1 PRISMA flow diagram



4 Discussion

The purpose of this systematic review was to identify and evaluate economic evidence on the cost-effectiveness of using a formal risk stratification system during the antenatal period. The current review is an empty review given no studies met the eligibility criteria.

Empty reviews are not uncommon and account for 8.7–12% of published Cochrane systematic reviews.[8, 9] Reasons for an empty review include novel research areas and the use of strict inclusion criteria.[8] One reason for this review being empty relates to the field of study. Economic evaluation literature tends to be published after initial clinical literature. Given there has been little evaluation of the effectiveness of comprehensive risk stratification systems on patient and health system outcomes, the lack of economic evidence is unsurprising. A number of economic evaluations related to costs of screening for specific risk factors (for example individual medical factors such as hypertension, risk relating specifically to previous obstetric complications or psychosocial problems); however, no studies focused on a comprehensive system of stratification of a woman's risk during the antenatal period.

4.1 Limitations of the study

This review was carried out in accordance with national guidelines for the retrieval and interpretation of economic literature, and reporting adhered to the PRISMA criteria. Potential limitations in the search process relate to the lack of medical subject headings (MeSH) for a comprehensive system of stratification or identification of a woman's risk during the antenatal period. Broad search terms related to antenatal screening were, therefore, used, resulting in a high yield of citations to be searched but without any studies being identified for inclusion.

4.2 Implications and conclusion

Empty reviews can identify gaps in the evidence in particular areas of interest. This review is important because it highlights a current gap in the evidence. There is a lack of studies on the clinical effectiveness of a comprehensive system of stratification of a woman's risk

during the antenatal period. Furthermore, there is a lack of economic evaluations to establish the cost-effectiveness and resource implications related to the implementation of such systems. There is, therefore, a need for further research evaluating both the clinical effectiveness and cost-effectiveness of a comprehensive system of stratification of a woman's risk during the antenatal period to underpin further development of the guideline recommendations.

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10. Scottish Intercollegiate Guidelines Network. Search filters. [Available from: http://www.sign.ac.uk/search-filters.html]. 2018.

Appendix 1: Search terms

The economic search was conducted by combining a generic clinical search to each database and applying the relevant economic filter.[10] The search terms for the Pubmed are presented below.

PubMed	
1.	Pregnancy
2.	Hospitals, Maternity"[MeSH]
3.	"Maternal Health Services"[MeSH]
4.	"Gynecology"[MeSH]
5.	"Obstetrics"[MeSH]
6.	"prenatal care"[MeSH Terms]
7.	"antenatal care"
8.	OR /1-7
9.	risk stratification
10.	risk assessment
11.	risk management
12.	OR /10-11
13.	8 AND 12
14.	13 AND economic filter (described below)
15.	Limits published in the last 10 years, humans

Economic filter

PubMed	
1.	Economics/
2.	"costs and cost analysis"/
3.	Cost allocation/
4.	Cost-benefit analysis/
5.	Cost control/
6.	Cost savings/

PubMed	
7.	Cost of illness/
8.	Cost sharing/
9.	"deductibles and coinsurance"/
10.	Medical savings accounts/
11.	Health care costs/
12.	Direct service costs/
13.	Drug costs/
14.	Employer health costs/
15.	Hospital costs/
16.	Health expenditures/
17.	Capital expenditures/
18.	Value of life/
19.	Exp economics, hospital/
20.	Exp economics, medical/
21.	Economics, nursing/
22.	Economics, pharmaceutical/
23.	Exp "fees and charges"/
24.	Exp budgets/
25.	(low N1 cost).mp.
26.	(high N1 cost).mp.
27.	(healthcare N1 cost*).mp.
28.	(fiscal or funding or financial or finance).tw.
29.	(cost N1 estimate*)
30.	(cost N1 variable)
31.	(unit N1 cost*)
32.	(economic* or pharmacoeconomic* or price* or pricing).tw.
33.	Or/1-32

Appendix 2: Grey literature search

The following electronic sources were searched for economic evaluations relevant to the research questions of this systematic review:

- Andalusian Agency for Health Technology Assessment, which can be found at http://www.aetsa.org/
- Australian National Health and Medical Research Council Clinical Practice Guidelines, which can be found at https://www.nhmrc.gov.au/guidelines
- Belgian Health Care Knowledge Centre, which can be found at https://kce.fgov.be/language_selection
- Centre for Health Economics and Policy Analysis, which can be found at http://www.chepa.org/
- Cost Effectiveness Analysis Registry, which can be found at http://healtheconomics.tuftsmedicalcenter.org/cear4/SearchingtheCEARegistry/SearchtheCEARegistry.aspx
- HTAi vortal, which can be found at https://www.htai.org/index.php?id=579
- Google Scholar and Google, which can be found at https://scholar.google.com/ and https://www.google.ie
- Health Service Executive, which can be found at https://www.hse.ie/eng/
- Health Information and Quality Authority, which can be found at https://www.hiqa.ie/
- Health Research Board, which can be found at http://www.hrb.ie/home/
- Institute of Health Economics (Alberta Canada), which can be found at https://www.ihe.ca/
- Lenus, which can be found at http://www.lenus.ie/hse/
- National Centre for Pharmacoeconomics, which can be found at http://www.ncpe.ie/

- National Coordinating Centre for Health Technology Assessment, which can be found at https://www.nihr.ac.uk/funding-and-support/funding-for-research-studies/funding-programmes/health-technology-assessment/
- National Institute for Health and Clinical Excellence, which can be found at https://www.nice.org.uk/
- NHS Evidence database (UK), which can be found at https://www.evidence.nhs.uk/
- Open Grey, which can be found at http://www.opengrey.eu/
- World Health Organization, which can be found at http://www.who.int/en/

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