Benefits and harms of antenatal and newborn screening programmes in health economic assessments: the VALENTIA systematic review and qualitative investigation

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Scientific summary

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Scientific summary

Background

National population screening programmes are implemented in the NHS on the advice of the United Kingdom National Screening Committee (UK NSC), which makes independent, evidence-based recommendations to ministers in the four countries of the UK. The recommendation to adopt a screening programme on a national scale is based on the premise that the benefits associated with the programme outweigh the harms to all relevant stakeholders. Screening committees require up-to-date evidence of these benefits and harms, as well as data demonstrating that the screening programme represents value for money. The latter is determined using a health economic assessment confirming that the additional costs to the NHS of implementing the programme and any unavoidable harms associated with it are justified by the benefits achieved, which are usually evaluated through outcome measures such as the incremental cost per quality-adjusted life-year (QALY) gained metric. Although there is established guidance on best practice for economic assessments of screening programmes in general (such as economic modelling), such guidance does not address the challenge of how the full range of potentially relevant benefits and harms can be incorporated into a single assessment, nor does it specifically focus on antenatal and newborn screening. Guidance in this area, therefore, remains limited.

Objectives

The overall objectives of this programme of work were to:

1. enhance knowledge about methods for the identification and valuation of benefits and harms within economic assessments of antenatal and newborn screening
2. identify attributes of relevance to stakeholders (parents/carers, health professionals, other relevant stakeholders) that should be considered for incorporation into future economic assessments using a range of qualitative research methods
3. make recommendations about the benefits and harms that should be considered by economic evaluations and the health economic tools that could be employed for this purpose.

Methods

Systematic review and development of thematic framework of benefits and harms to use in future health economic assessments

A systematic review of the published and grey literature of articles and reports published after January 2000 was conducted to identify health economic assessments evaluating antenatal and newborn screening programmes in one or more of the Organisation for Economic Co-operation and Development (OECD) countries (see *Chapter 3*). A protocol for this review was registered with PROSPERO (CRD42020165236) and published in January 2020. The Population, Intervention, Comparator, Outcome and Study design (PICOS) framework was used to develop the study eligibility criteria and applied to the literature searches. No language restrictions were imposed. The published literature was searched using a comprehensive selection of electronic bibliographic databases. The academic electronic database search was supplemented by manual reference searching of bibliographies, contacts with experts in the field and author searching. The list of sources of grey literature searched was informed by a recent systematic review of national policy recommendations on newborn screening. Two independent reviewers assessed the suitability for inclusion of outputs identified in the published and grey literature.

A data extraction sheet was created including: (1) items from the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) checklist, and (2) a bespoke form created by the research team to extract benefits and harms adopted by economic assessments evaluating antenatal and newborn screening programmes.

The information captured in the bespoke form was used to develop a framework of benefits and harms adopted by health economic assessments using a number of themes grouped into categories based on an integrative descriptive analysis (see *Chapter 4*). Benefits and harms reported by articles and reports were categorised into themes and subtheme(s) according to the condition and screening type, using this thematic framework.

Qualitative component

We conducted a qualitative study using multiple methods to capture stakeholders' views about the benefits and harms of antenatal and newborn screening that should be incorporated into future economic assessments. The qualitative study included:

1. a meta-ethnography of the existing literature on newborn screening experiences (see *Chapter 5*)
2. secondary analysis of existing individual interviews related to antenatal screening, newborn screening and living with screened-for conditions (see *Chapter 6*)
3. thematic analysis of primary data collected with stakeholders about their experiences with antenatal and newborn screening (see *Chapter 7*).

We conducted a meta-ethnography to better understand what was known about the experiences of newborn bloodspot screening. The experiences of antenatal screening have been extensively investigated, but newborn screening experiences remained underexplored. In our secondary analysis, the goal was to bring together, examine and interpret the findings from disparate qualitative research studies and produce a richer and broader understanding than would be possible by looking at the studies individually. We drew on a large body of existing interview data reflecting a range of screening experiences, to better understand how individuals affected by screening discussed their experiences. What emerged was a complex web of individuals, organisations, technologies and discourses that shape the screening landscape. Finally, we conducted a thematic analysis of evidence generated from primary research with three groups of stakeholders (individuals, charity and policy professionals, and healthcare providers) to understand how these groups conceptualised the benefits and harms of screening. This primary data collection amplified concepts from our meta-ethnography and secondary analysis. By using a range of qualitative methods, we identified well-informed conclusions about not only the benefits and harms of screening as understood by a variety of stakeholders, but also concepts which do not fit neatly into that framework. We present the methods and findings for each of these pieces of work in individual chapters before summarising critical findings from across components of the qualitative study (see *Chapter 8*).

Blending benefits and harms taxonomy with qualitative evidence

A mapping exercise was carried out to identify levels of overlap between the outcomes of the systematic review and the qualitative component of the study. The aim of this exercise was to identify whether health economics assessments miss the adoption of key benefits and harms when evaluating antenatal and newborn screening programmes. We mapped the qualitative data (see *Chapters 5–7*) onto the completed thematic framework. In some cases, the qualitative data collected did not cover subcategories of the framework, and we noted the absence. There were also themes from the qualitative data that could not be easily mapped onto the thematic framework.

Stakeholder workshops

A scoping review of alternative methods to value benefits and harms associated with screening scenarios was conducted. The aim of this exercise was to clarify which valuation methods should be implemented to value antenatal and newborn benefits and harms in future studies. The final selected

alternatives were presented to our parent and public involvement (PPI) members to understand the feasibility of administering these valuation methods to relevant participants in future studies. This was supplemented by a separate workshop held with a broad set of stakeholders to review the findings of the VALENTIA research programme and contribute to a set of recommendations about approaches for the measurement and valuation of outcomes that should be considered by future economic assessments of antenatal and newborn screening, and to highlight areas for future methodological enquiry. The session was attended by healthcare professionals, representatives from relevant academic disciplines, representatives from charities, outreach services and support groups, and representatives from policy-making bodies.

Results

Systematic review and development of taxonomy of benefits and harms to use in future health economic assessments

We identified 52,244 articles and reports from the searches of the published and grey literature and included 336 records in the data extraction. The majority of the records were journal articles, with almost half conducted in the USA or UK. Genetic conditions and infectious diseases were the main areas covered by the articles and reports assessing antenatal screening, while metabolic and structural conditions were the main areas covered in the evaluations of newborn screening programmes. Decision-analytical models were employed in 272 (81.0%) of the articles and reports, while 117 (43.0%) used a lifetime time horizon. Almost half of the studies conducted a cost–utility analysis reporting incremental cost per QALY values (167, 49.4%). The costing perspective adopted was not stated in 117 (33.7%) articles and reports. Reporting quality assessed using the CHEERS checklist was heterogeneous. The top five items not satisfied among the studies for antenatal screening programmes were 'Abstract' (160, 88.4%), 'Time horizon' (153, 84.5%), 'Choice of model' (153, 84.5%), 'Discount rate' (130, 71.8%) and 'Study funding, limitation, generalisability and current knowledge' (123, 68.0%). The top six items not satisfied among newborn screening programme studies were 'Abstract' (69, 83.1%), 'Time horizon' (67, 80.7%), 'Study funding, limitation, generalisability and current knowledge' (59, 71.1%), 'Choice of model' (55, 66.3%), 'Discount rate' (53, 63.9%) and 'Setting and location' (53, 63.9%). The top five items satisfied among the studies for both antenatal and newborn screening programmes were 'Background and objectives' (264, 100%), 'Target population and subgroups' (264, 100%), 'Choice of health outcomes' (263, 99.6%), 'Measurement of effectiveness' (260, 98.5%) and 'Estimate resources and cost' (247, 93.6%).

We identified 86 unique descriptions of consequences associated with benefits and harms across all articles and reports. Our thematic analysis resulted in seven core themes of benefits and harms: (1) diagnosis of screened for condition, (2) life-years and health status adjustments, (3) treatment, (4) long-term costs, (5) overdiagnosis, (6) pregnancy loss and (7) spillover effects on family members. Diagnosis of screened-for condition (115, 47.5%), life-years and health status adjustments (90, 37.2%) and treatment (88, 36.4%) accounted for most of the benefits and harms evaluating antenatal screening. The same themes accounted for most of the benefits and harms included in studies assessing newborn screening. Overdiagnosis and spillover effects tended to be ignored. Only 10 out of the 242 (4.1%) antenatal screening evaluations adopted benefits and harms from all of themes 1–4, whereas only 9 out of the 95 (9.5%) newborn screening evaluations adopted benefits and harms from all of themes 1–4.

Qualitative component

By looking across a range of moments, outcomes and conditions across international contexts, our meta-ethnography identified that newborn screening experiences vary widely across families. We developed the concept of absorptive capacity – the ability to recognise, assimilate and apply new information – to capture the abilities of parents, and crucially also the limits of those abilities, to comprehend their child's screening results or condition. We explain the various ways that parents experience the expansion and

compression of time throughout and beyond the screening pathway, demonstrating the far-reaching implications of screening across time, as well as to wider family and kin.

Our secondary analysis brought together a large, rich data set and yielded a situational map. This map demonstrates that conversations about antenatal and newborn screening involve a complicated weaving of individuals, organisations, materials and discourses. We identified elements that may (or may not) be involved in an individual's situation and consider implicated environments that shape the landscape of screening. We generated a list of stakeholders that are central to screening conversations and uncovered temporal, spatial, economic and societal issues shaping screening experiences and debates.

We conducted in-depth interviews and focus groups with people who had recently made decisions about screening, charity and professional stakeholders and healthcare providers. While different stakeholders named different benefits and harms, there was a substantial amount of overlap between groups. Consistently named benefits included screening's ability to get information, prevent harm and provide reassurance. Consistently named harms included possible pressure to have termination of pregnancy, lack of preparation for unexpected results, emotional distress and a lack of understanding of the purposes and potential implications of screening tests.

Blending benefits and harms from the thematic framework with qualitative evidence

Our mapping exercise resulted in an overall good overlap between the quantitative and qualitative evidence, with elements of the qualitative evidence relevant to specific themes on the thematic framework identified. There was no suggestion that our thematic framework of benefits and harms excluded any important themes. Elements of the qualitative evidence not present in the thematic framework were also identified. For most of these elements, it was clear that they were not relevant for the development of health economic assessments (e.g. challenge of information provision to make sure choice is 'informed'). However, the area of wide-reaching family implications of screening was considered important to our stakeholders in the qualitative work but often overlooked by developers of health economic assessments evaluating antenatal and newborn screening programmes.

Stakeholder workshops

In the first workshop, concerns around the practicality of the number of valuation techniques that could be applied within the online workshops led to a focus on best–worst scaling and discrete choice experiments as the primary valuation techniques. The workshops highlighted a number of factors that can inform the design of future preference elicitation studies in this area. In the second workshop, we reviewed the findings of the VALENTIA research programme and informed the final set of recommendations about approaches for the measurement and valuation of outcomes that should be considered by future economic assessments of antenatal and newborn screening, and highlighted areas for future methodological enquiry.

Conclusions

Benefits and harms of antenatal and newborn screening are complex and multidimensional, and they have generally been incorporated in a haphazard manner into economic evaluations. Our work suggests that there is an immediate need to provide methods guidance for researchers conducting these types of studies in future work. Our proposed framework of benefits and harms can be used as a starting point to guide the development of health economic assessments evaluating antenatal and newborn screening for specific conditions and to prevent exclusion of important harms. It is important that future economic evaluations in this area incorporate benefits and harms of spillover effects to family members, as this was considered very important to the stakeholders consulted during the study. The QALY remains a common approach for capturing the benefits and harms associated with antenatal and newborn screening programmes. This study identifies a range of benefits and harms that should be considered for

inclusion within future economic assessments and provides preliminary evidence of the feasibility of applying alternative economic valuation methods in this area.

Study registration

This study is registered as PROSPERO CRD42020165236.

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