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Conflict of interest

Anne-Marie Slowther (A-MS) and Jane Fisher (JF) sit on the UK National Screening Committee (UK NSC). Oliver Rivero-Arias (OR-A), Jane Fisher (JF), Basky Thilaganathan (BT) and Felicity Boardman (FB) are members of the Foetal, Maternal and Child Health reference group of the UK NSC. JF is a member of the NHS Foetal Anomaly Screening Programme Advisory Group. Sian Taylor-Phillips (ST-P) is a member of the UK NSC Adult Reference Group. Sam Oddie (SO) serves on the NSC expert group on implementing saturation screening. Basky Thilaganathan (BT) is the clinical lead for the SAFE test (NIPT) laboratory at St Georges Hospital (www.theSAFEtest.co.uk). BT has no pecuniary interest in this service.

Confidentiality Statement

This document contains confidential information that must not be disclosed to anyone other than the Sponsor, the Investigator Team, host organisation, and members of the Research Ethics Committee, unless authorised to do so.

Protocol amendment history (version control)

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
1	2	02 April 2020	May Ee Png/Oliver Rivero-Arias	PROSPERO reference number included. Study flowchart has been updated to improve the relationship between WS1, WS2, WS3 and PPI. The databases to search for published literature in WS1 has been updated as per the advice from SSC Information Specialist. The Cochrane Library has been removed as it contains systematic reviews and trials and is outside our scope. We have also removed the ASSIA database given its focus on social care unlikely to be relevant to our scope.

Table of contents

1 Scientific Summary

Background: Cost-effectiveness assessments of many forms of screening considered by the United Kingdom National Screening Committee (UK NSC) are conducted within a cost-utility framework and expressed in terms of incremental cost per quality-adjusted life year gained. However, a number of methodological factors, compounded by ethical challenges, have constrained capacity to evaluate antenatal and newborn screening programmes using standard cost-utility metrics. The consequence is that recommendations about antenatal and newborn screening are made on the basis of differing approaches to the construction and valuation of outcomes and without a common cost-effectiveness threshold that reflects opportunity cost in the health system. Invariably, this results in suboptimal levels of population health and wellbeing.

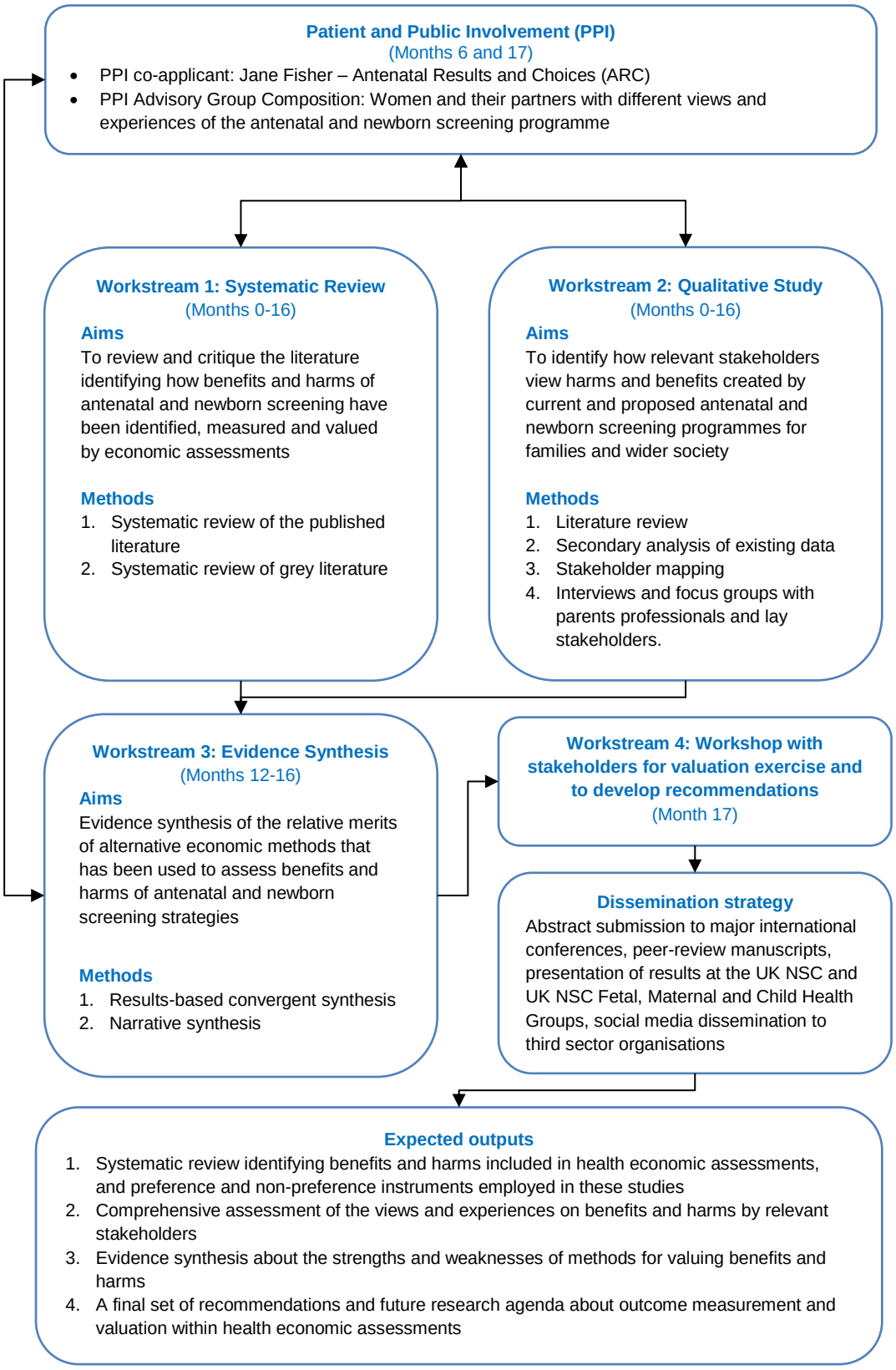
Aims and objectives: The overall aim of the proposed programme of work is to enhance knowledge about methods for valuing the benefits and harms of antenatal and newborn screening within economic assessments and make recommendations about health economic measurement tools that should be applied in this area in the future.

Methods: The programme of work will encompass four work-streams, including: 1) A systematic review of published and grey literature on methods for evaluating benefits and harms of antenatal and newborn screening programmes adopted by economic assessments; 2) A qualitative study to capture the perspectives of stakeholders (including parents/carers, professionals and other relevant stakeholders) about the value, benefits and harms of antenatal and newborn screening that should be incorporated into future economic assessments; 3) An evidence synthesis (encompassing a results-based convergent synthesis and a narrative synthesis) of the relative merits of alternative economic methods that have been used to assess antenatal and newborn screening strategies; and 4) A stakeholder workshop leading to a set of final recommendations for outcomes measurement and valuation within future economic assessments. Patient and public involvement (PPI) will draw upon different groups of women and their partners who could potentially have diverse views and experiences of antenatal and newborn screening, and will be integrated into each of the four work-streams.

Dissemination, outputs and anticipated impact: The results of the proposed research will be submitted to academic journals, and presented to UK NSC committees and at INVOLVE conferences. Bespoke strategies will be developed for dissemination to the third sector and for broader public dissemination. The findings will be used to inform methodological recommendations for future economic assessments of antenatal and newborn screening.

2 Study flowchart

Flowchart: Valuing the benefits and harms of antenatal and newborn screening programmes in health economic assessments



3 Background and rationale

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. Antenatal and newborn screening are covered by six of the eleven NHS screening programmes, namely fetal anomaly screening, infectious diseases in pregnancy screening, the newborn and infant physical examination, newborn blood spot screening, newborn hearing screening, and sickle cell and thalassaemia screening. They represent mainstays of national screening strategies with far-reaching implications for population health and wellbeing.[1]

The UK NSC considers cost-effectiveness assessments, as well as other criteria such as viability, effectiveness and appropriateness, in its regular reviews of a large number of conditions for continued or potential inclusion within the antenatal and newborn screening programmes.[2] The committee's recommendations are grounded in up-to-date evidence and influenced by the opinions of stakeholders. The number of conditions considered for inclusion within the antenatal and newborn screening programmes is likely to increase as a result of technological developments, such as next generation sequencing.[3]

Cost-effectiveness assessments of many forms of screening considered by the UK NSC (e.g. bowel cancer screening, abdominal aortic aneurysm screening) are conducted within a cost-utility framework and expressed in terms of incremental cost per quality-adjusted life year (QALY) gained, where the QALY combines preference-based health-related quality of life weights (health utilities) with data on length of time in the health states of interest.[4] This approach to cost-effectiveness assessment mirrors those recommended more broadly by health technology assessment agencies in the UK, such as the National Institute of Health and Care Excellence (NICE) in England and the Scottish Medicines Consortium (SMC) in Scotland.[5 6] It also mirrors the preferred form of cost-effectiveness assessment adopted by health technology assessment, pricing and reimbursement authorities in several other industrialised countries.[7-9]

A number of methodological factors have constrained capacity to evaluate antenatal and newborn screening programmes using the standard incremental cost per QALY gained metric. These include challenges surrounding the valuation of prenatal life when decisions following antenatal screening and diagnostic testing result in the termination of the fetus or unborn child,[10 11] the absence of a multi-attribute-utility measure validated for use in infancy and through early childhood,[12] and the challenges surrounding QALY aggregation across the mother, child and potentially other family members.[13] Furthermore, attributes of relevance to parents, such as the utility derived from information per se or reassurance following a screen-negative test result, and the disutility associated with a false positive test result or over-diagnosis of disease, are likely to be missed, or at least inadequately covered, by standard approaches to health utility measurement, such as available multi-attribute utility measures (e.g. EQ-5D, SF-6D, HUI Mark 3).[14 15] Moreover, a number of ethical challenges compound the technical complexities surrounding economic assessments of antenatal and newborn screening programmes. These emanate

from differences in moral perspectives on the status of the fetus or unborn child [11] and how society should value disability [16], and differing perspectives on the ownership of genetic information [17] and the potential harms of inadequately informed consent processes on parental autonomy [18].

The UK NSC has recognised the limitations of the economic assessments of antenatal and newborn screening programmes that it regularly considers. Assessments that have expressed cost-effectiveness in terms of incremental cost per QALY gained have tended to overlook relevant aspects of benefits and harms, and have been constrained by the tools available for the measurement, valuation and aggregation of those benefits and harms. Moreover, assessments that have resorted to framing cost-effectiveness in terms of narrow biomedical units of outcome, such as incremental cost per timely diagnosis [19] or incremental cost per case avoided,[20] are limited in two key respects. First, they do not allow decision-makers to draw cost-effectiveness comparisons with interventions in other areas of health care, resulting in a sub-optimal allocation of resources. Second, they overlook the preferences of patient groups or the general population for outcomes of interest.

There are over 650,000 births in England and over 750,000 births in the UK each year. Extensive resources and complex organisational arrangements are required to deliver antenatal and newborn screening programmes for this number of pregnant women and their babies. In 2016, the NHS screened approximately 660,000 pregnant women in England for a fetal anomaly, hepatitis B, HIV, syphilis, sickle cell disease and thalassaemia, and approximately 670,000 babies in England for 15 conditions.[1] Moreover, over one half of recommendations made by the UK NSC have focussed on the coverage of antenatal and/or newborn screening programmes,[21] a proportion likely to be magnified in the future by rapid technological developments.

Economic assessments of antenatal and newborn screening programmes have by and large adopted approaches to the identification, measurement and valuation of benefits and harms that preclude estimation of net health benefits within the QALY paradigm. Moreover, these economic assessments do not incorporate all factors of relevance to patients and their families within their cost-effectiveness calculus. In the context of antenatal screening, factors of relevance to patients and their families include anxiety generated by a positive screening result, time to wait for results, gestational age at which screening is performed and family preparedness,[22 23] whilst in the context of newborn screening, they include how and when information is provided, risk of over-diagnosis, factors associated with receipt of a false positive test result , identification of carrier status, and parents' ability to make a decision.[14 24 25] Arguably, economic assessments of antenatal and newborn screening should aim to maximise full economic utility using measures that encompass net health benefits as well as broader benefits and harms of importance to patients and their families. Conceptually, family-wide QALYs could be nested within full economic utility. In practice, economic analysts predominantly apply approaches that neither capture net health benefits using QALYs nor full economic utility also reflective of patient and family concerns. The consequence is that recommendations about antenatal and newborn screening are made on the basis of differing approaches to the construction and valuation of outcomes and without a common cost-

effectiveness threshold that reflects opportunity cost in the health system. Invariably, this results in suboptimal levels of population health and wellbeing.

Health economists have previously highlighted the methodological limitations of economic assessments of antenatal and newborn screening programmes.[11] In addition, attributes of screening of relevance to patients and members of the general public, which have largely been overlooked by economic assessments, have been highlighted by qualitative research [22] and stated preference [14 15] studies. A review of the literature on the ethical social and legal implications of extending the newborn blood spot test noted the complexity and inter-relatedness of benefits and harms of newborn screening.[26] We recently highlighted a range of harms that are not well reported in evidence reviews.[26] These include incidental detection of non-paternity, the potential detriment to parent-child bonding from false positive results, and the potential for consequent unnecessary treatment restricting children's lives. Other harms include potential for test developments to expand disease definitions into milder variants and increased incidental findings, thereby increasing the potential for over-diagnosis and over-treatment of clinically insignificant disease. Although taxonomies of the harms of screening have been proposed, encompassing domains such as physical effects, psychological effects, financial strain, and opportunity costs,[27] they arguably fail to capture the breadth of domains of interest within the antenatal and neonatal contexts. With regard to antenatal screening, for example, there is evidence that experience of the screened for condition influences perceptions of harms of screening.[28] Recent advances in non-invasive prenatal testing (NIPT) have prompted a review by the Nuffield Council on Bioethics of the ethical issues raised by this technology. The report comments on the potential wider societal harms of antenatal screening (and NIPT in particular) related to societal discrimination and stigmatisation of disability, and potential benefits in terms of reproductive choice and gender equality, adding further complexity to the task of weighing benefits and harms.[16]

Published primary and secondary research studies commissioned by the NIHR Health Technology Assessment programme have applied limited and inconsistent approaches to the measurement and valuation of benefits and harms of antenatal and newborn screening programmes. Benefit maximands applied within economic assessments include 'additional woman screened before 70 days' gestation' and 'extra unexpected affected live birth prevented' in an evaluation of antenatal screening for haemoglobinopathies,[29] 'spontaneous preterm birth avoided' and 'symptom avoided' in an evaluation of combinations of tests and treatments to predict and prevent spontaneous preterm birth,[20] and 'timely diagnosis' in an evaluation of pulse oximetry as a screening test for congenital heart disease.[19] Adoption of benefit maximands that take the form of uni-dimensional biomedical units of outcome of these types fail to capture the disutility associated with harms within the denominator of the incremental cost-effectiveness ratio. Assessments that have attempted to value the benefits and harms of screening in terms of QALYs highlight the limitations of available tools for QALY construction.[30] We are not aware of any studies that have attempted to estimate the full economic utility associated with antenatal or newborn screening, despite its increasing currency with policy makers.

4 Study objectives

The overall aim of the proposed programme of work is to enhance knowledge about methods for valuing benefits and harms within economic assessments of antenatal and newborn screening and make recommendations about health economic measurement tools that should be applied in this area in the future. Our specific objectives are:

(i) To systematically review and critique the published and grey literature on methods for identifying, measuring and valuing the benefits and harms of antenatal and newborn screening adopted by economic assessments;

(ii) Using a range of qualitative research methods, to identify attributes of relevance to stakeholders (parents/carers, health professionals, other relevant stakeholders) that should be considered for incorporation into future economic assessments; and

(iii) To make recommendations about approaches for the measurement and valuation of outcomes that should be considered by future economic assessments in these contexts.

To achieve these objectives, this study will encompass four work-streams, including: 1) A systematic review of published and grey literature on methods for evaluating benefits and harms of antenatal and newborn screening programmes adopted by economic assessments; 2) A qualitative study to capture the views of stakeholders about the impacts of screening that should be incorporated into future economic assessments; 3) An evidence synthesis of the relative merits of alternative economic methods that have been used to assess antenatal and newborn screening strategies; and 4) A stakeholder workshop leading to a set of final recommendations for outcome measurement and valuation within future economic assessments.

5 Work-stream 1: Systematic review

5.1 Aims

To systematically review and critique the published and grey literature on how the benefits and harms of antenatal and newborn screening have been identified, measured and valued by economic assessments.

5.2 Eligibility criteria

Evidence from both the published literature and grey literature will be included in the systematic review. The term 'published literature' is used broadly to encompass all literature controlled by commercial publishers and will primarily take the form of articles in peer-reviewed journals. The term 'grey literature' will encompass "documentation which is produced on all levels of government, academics, business and industry in print and electronic formats, but which is not controlled by commercial publishers" (http://www.greylit.org/about).

Studies reporting health economic assessments (e.g. economic evaluations, health technology assessments) of antenatal or newborn screening programmes will be included. We will include evidence in all languages and no restrictions will be imposed on publication dates. We will restrict eligible studies to those conducted in a developed country (defined, for the purposes of this review, as a member of the Organisation for Economic Co-operation and Development (OECD)).

5.3 Information sources

Two broad sources of information will be used to inform this systematic review: academic electronic databases and documentation from the grey literature. The academic electronic databases searched will include Medline, PsycINFO, Embase, EconLit, Web of Science and CINAHL. SCOPUS will be used to run forward and backward citation search once the included studies are identified. Supplementary search strategies targeted at the published literature will include manual reference searching of bibliographies, contacts with experts in the field, citation searching and author searching. We will work closely with local information specialists to develop and pilot bespoke combinations of free text and thesaurus search terms for each form of antenatal and newborn screening. We will build on previous search strategies that identified health economic evaluations of screening programmes,[31] the recent systematic review of national policy recommendations on screening newborn babies led by one of the co-applicants,[32] and an ongoing systematic review of the economic evidence surrounding newborn screening for tyrosinemia that we are conducting for the UK NSC.

Many economic models used to inform clinical decision-making are reported only in the grey literature. We will therefore also search recognised grey literature databases, including but not restricted to TRIP, Open Grey and the University of York Centre for Reviews and Dissemination database. Screening decision-making is

a niche area with many models that guide decision-making not indexed in any search engine for grey literature, but appearing only on websites of national screening organisations, medical societies or health technology assessment agencies. Recent research led by one of the co-applicants of this proposal (ST-P) has identified 30 websites of national and regional screening organisations with documentation about antenatal and/or newborn screening recommendations.[32] Integrating the database from this research with the Canadian Agency for Drugs and Technology in Health Grey Matters checklist and searches of websites of several international organisations, we have identified health technology assessment agencies, obstetrics and gynaecology societies and paediatrics societies in OECD countries (see Appendix 1 for a the list of sources for grey literature). We will expand these lists and consider international decision-making bodies (e.g. WHO, the European Council, European Commission and the European Observer) at the start of the project. We will systematically search the websites of these organisations as the main sources of grey literature in our review. We will adapt the search terms developed for academic electronic databases for application to websites. Our experience suggests that entering keywords sequentially into both the search engines of websites and using the google engine directed exclusively at each website yields the most comprehensive results, so we will take this approach. Finally, some economic models used to influence national policy, particularly in other European countries, are not published at all, and will therefore be obtained through personal communication. We have developed a contact directory of national screening organisations worldwide in collaboration with the UK NSC. The development of this directory was informed by our previous research and the research of others,[33 34] our experience of organising international meetings with the UK NSC, as well as Dr Taylor-Phillips's fellowship investigating screening evidence review methods internationally. As a result, we have contact details of committee members across 30 countries, and will make contact more widely through the International Society for Prenatal Diagnosis and the International Society for Neonatal Screening. We will also email each organisation and corresponding authors of the final reports enquiring about further documentation not identified through the main grey literature sources. Contact details we hold for national screening organisations are not attached as we do not have permission to share them with third parties.

5.4 Study selection and data collection process

The study selection process will follow PRISMA guidelines [35] and will be managed using Endnote software. The stages involved in selecting studies for inclusion in the systematic review will include: (i) examining titles and abstracts to remove obviously irrelevant reports; (ii) retrieving full texts of potentially relevant reports; (iii) translation, where necessary, of non-English language reports into the English language using a combination of the google translate facility and a professional translation service; (iv) linking together multiple reports of the same economic assessment; (v) examining full-text reports for compliance of studies with study eligibility criteria; (vi) corresponding with study authors, where appropriate, to clarify study eligibility; and (vii) making final decisions on study inclusion before proceeding to data extraction and assessment. Assessments at each of the two stages of the review process (title and abstracts, full reports) will be undertaken independently by

two health economists, one based at the University of Warwick and the other based at the University of Oxford. Disagreements will be resolved by discussion with the two co-principal investigators during regular face-to-face and Skype meetings, and if necessary seeking advice from other members of the co-applicant research team.

5.5 Data extraction and presentation

A data extraction sheet, which will be piloted and refined using 5-10 randomly selected studies identified in either the academic databases or the grey literature, will be created using recommendations from the Cochrane Handbook for Systematic Reviews of Interventions.[36] The data extraction process will be conducted independently by two health economists, followed by a reconciliation process. The list of variables that will be extracted from each report included at the final stage of the review process will be finalised following the piloting and refinement of the data extraction sheet. However, it is anticipated that these variables will broadly fall into the following categories: bibliographic details, geographical jurisdiction, health care context, disease area, type of study and where appropriate decision problem, type of screening, disaggregated benefits measured, disaggregated harms measured, data source(s) for benefits, data source(s) for harms, methods of measurement of benefits, methods of measurement of harms, methods of valuation of benefits, methods of valuation of harms, non-preference based methods of aggregation and valuation of benefits and harms, preference-based methods of aggregation and valuation of benefits and harms, coverage of benefits and harms within aggregation processes, instruments and underpinning tariffs applied within preference-based approaches, whether spillover effects were accounted for, scope of spillover effects, and methods used to measure and value spillover effects.

5.6 Assessment of risk of bias of individual studies

We will assess the quality of the contributing evidence on the measurement and valuation of benefits and harms in economic assessments of antenatal and newborn screening programmes using a risk of bias exercise. The evidence will be drawn from different study designs, suggesting that use of a single risk of bias tool would not be appropriate. The risk of bias will therefore be based on evidence from a number of tools, including the Cochrane Risk of Bias Tool for randomised studies,[37] the ROBINS-I for non-randomised studies,[38] the CHEERS statement for economic evaluations [39] and recently developed tools that consider factors related to the utility assessment process, for example, respondent selection and recruitment, response rates to the instrument used, and levels of missing data and how they were dealt with.[40 41] A particular feature of relevance when assessing the quality of contributing studies will be their face validity, for example, whether they generated economic or cost-effectiveness outcomes that vary in an expected direction in response to a change in screening policy.[42]

5.7 Presentation of results

The study will conform to PRISMA guidelines when reporting the results of this review.[35]

6 Work-stream 2: Qualitative study

6.1 Aim

To identify how (prospective) parents/carers offered screening, professionals and other relevant stakeholders view current and possible antenatal and newborn screening programmes, in particular the benefits and harms they create for families and wider society. By engaging with relevant lay stakeholders, we will explore understandings of the practical, social and ethical issues raised by these programmes, as well as their perspectives on the value, benefits and harms of these programmes.

6.2 Methods

We will undertake a multi-method qualitative study in two stages to explore the perspectives of relevant stakeholders. These stakeholders will include (prospective) parents, health professionals and adults living with genetic and screened-for conditions. The range of impacts associated with antenatal and newborn screening, as well as the issues and concerns they raise for families, health professionals and wider society will be explored. The methods will include in Stage 1 a scoping literature review, secondary analysis of existing qualitative data sources (in-depth research interviews) and stakeholder mapping. These methods, in addition to consultation with our PPI group, will be used to identify further relevant stakeholder groups for primary data collection in Stage 2. With each stakeholder group, we will explore the practical, clinical, social and ethical issues associated with antenatal and newborn screening. The identification of participants for Stage 2 will be an iterative process undertaken through Stage 1. Consultation with our PPI group, through face to face meeting (in month 6) and ongoing telephone/email discussions, will also be key to scoping Stage 2.

6.2.1 Stage 1: Literature review, secondary analysis and stakeholder mapping

Stage 1 will include the following components:
i) Scoping review of the literature on the views of (prospective) parents/carers offered screening as well as professional/stakeholder (e.g. policy makers, support group staff) on national antenatal and newborn screening programmes.

ii) Secondary analysis of existing interview data. We will re-analyse 256 interviews from previously conducted studies. These in-depth narrative interviews were all conducted over the last 13 years by co-applicant FB based at the University of Warwick, and co-applicant LH and other social scientists based at the Health

Experience Research Group, University of Oxford. They include the perspectives of people with a wide range of experiences in relation to screening, testing, pregnancy termination and continuation, as well as parents and affected adults living with genetic and chromosomal abnormalities (see Appendix 2 for a summary of data sources).

We will additionally review comments sent to the UK NSC for all previous UK NSC reviews of antenatal and newborn screening that went to consultation within the last five years. This includes 25 antenatal screening programmes, 23 newborn screening programmes and two joint antenatal/newborn programmes. Such information is available at https://legacyscreening.phe.org.uk/screening-recommendations.php.

iii) Finally, we will conduct stakeholder mapping exercises with knowledgeable participants.

We will conduct a thematic secondary analysis [43] to explore discussions of screening, benefits and harms, across these rich and varied data sets of narrative interviews, which cover experiences of parents both affected and not affected by rare conditions, those who have continued with, and those who have terminated a pregnancy following a prenatal diagnosis, and those who have accepted, as well as those who have declined, antenatal and/or newborn screening. Furthermore, the dataset also includes the perspectives of people diagnosed with rare or screened-for conditions themselves, perspectives that are frequently omitted in screening debates.

Some of these interviews were conducted over 10 years ago, but the majority were conducted in the last 1-4 years. While some specific aspects of testing have changed during this period (for example, combined nuchal scan and blood test rather than older triple test), we anticipate that these data are still highly relevant. The data contain rich insights into people's feelings about risk, weighing up the value of screening compared to firm diagnosis, decision-making in the case of a foetal abnormality, and relational care. These are all areas that are primarily emotional and moral, and are not driven solely by specific technical processes. However, as the field is constantly evolving (e.g. NIPT, expansions in field of genetics), we will also conduct primary data collection (Stage 2).

In parallel with the literature review and secondary analysis, and building on all current UK NSC registered stakeholders, we will also undertake an informal stakeholder analysis in order to identify any stakeholders whose perspectives have not been captured through the literature review and secondary data analysis.[44] We do not propose a formal stakeholder mapping exercise, but rather an amended approach that includes brainstorming with knowledgeable participants and our advisory panel in addition to our literature review and secondary analyses.

The results from this first stage will be used to inform the identification of participant groups for primary data collection in Stage 2, as well as the sampling and interview/focus group schedules.

6.2.2 Stage 2: Primary data collection

We will conduct focus groups and interviews with three groups. For the focus groups, we propose using innovative online methods that have been used previously,[54] supplemented by face-to-face methods.

Sampling and recruitment: Here, we indicate the samples we anticipate using, but this will be refined during Stage 1. We are mindful that this is ethically contentious terrain with groups and individuals that hold strong views. We therefore propose

using a variety of data collection approaches to allow us to explore how views on screening are socially and culturally shaped without exposing participants to confrontation. Sampling widely will be paramount, so that we capture the seldom heard voices as well as those more readily captured. Therefore, while we will recruit through support groups and established stakeholder routes, we will also use a variety of other routes to include a wide range of perspectives, both lay and expert. We will use our established networks of clinical and lay representatives, in particular informed by our grey literature and stakeholder mapping, social media and snow-balling techniques.

Parents/carers: Focus groups with individuals with perspectives that we identify as missing from our secondary analysis. This would potentially include: women who are currently pregnant, parents of young children, parents who have sought antenatal or newborn screening beyond those offered within standard NHS care, parents who have received false positive and false negative screening results, as well as individuals who have not yet started a family, but for whom screening is likely to be relevant in the future (n=6 per group, to include up to 30/40 parent and carer voices). We have chosen focus groups, especially those conducted online, as the primary means of data collection as they will allow for an open discussion of sensitive topics and how they are socially shaped without over-exposing participants. However, to increase participation rates and minimise the risk of emotional harm, individual interviews (telephone or online) will be offered to those wishing to participate in an interview, but for whom a group setting would not be appropriate or feasible (for example, recently bereaved parents). As the study develops, we will discuss with the PPI advisory group, co-applicants and the Independent Oversight Committee the appropriate balance between online and face to face groups. Where the anonymity offered by online discussions is felt to be the most productive, we will hold a series of online focus groups conducted via a custom-built platform to support live chat and forum discussions designed and built for the study by the DIPEx Charity. Each focus group will have between 6-8 participants, who will be given anonymous identities and sampled so that the views within each group are complementary rather than oppositional. The discussion will start with an hour-long live web chat, moderated and facilitated by applicant LH, which will include introductions and a description of how the online focus group will run. Participants will then be encouraged to discuss particular questions that will be posted on the discussion forum at various stages throughout the week. These questions and discussions will be captured for analysis. Where face-to-face focus groups are felt to be appropriate, we will convene small groups (no more than 6 per group) moderated by LH with support from the full time qualitative researcher. Face to face focus groups will be audio recorded and transcribed for analysis. This primary data collection will not only enable us to build on the gaps identified by our secondary analysis, but also allow us to explore some of the early findings from work-stream 1.

Professionals: Telephone or Skype interviews (n=20) with health care professionals (to include midwives, sonographers, obstetricians, genetic counsellors and neonatologists) and private screening companies.

Other relevant stakeholders: Telephone or Skype interviews (n=20) with patient support groups (both those aimed at pregnant women and their partners such as ARC, but also those supporting people and families with screened-for conditions),

charities, religious and community leaders, policy and advisory groups and others identified in the stakeholder mapping.

6.2.2.1 Analysis

All focus groups and interviews will be audio recorded for transcription and analysis, and anonymised. We will undertake a thematic analysis [55, 56] to identify key themes, which will then be collated into meta-matrices (separately for alternative forms of antenatal and newborn screening) to form visual representation and analysis tools for the identified benefits and harms (on the horizontal) as perceived by each relevant stake holder group (on the vertical). The meta-matrices will be used to undertake comparative analysis [57] exploring the concordance and discordance between each of the stakeholder groups and to highlight the range of priorities and perspectives across stakeholder groups, in particular a patient-professional comparison. Finally, the meta-matrices will be used to produce a framework of results to contribute to the overall project recommendations.

7 Work-stream 3: Evidence synthesis of the relative merits of economic methods

We will conduct an evidence synthesis of the relative merits of alternative economic methods that have been used to assess antenatal or newborn screening strategies, describing the strengths and weaknesses of each approach. We will begin with a results-based convergent synthesis [58 59] that will juxtapose the quantitative evidence generated by the systematic review (work-stream 1) against the qualitative evidence generated by our thematic analysis (work-stream 2). We will assess the extent to which each economic assessment included within the systematic review addressed the themes/factors of importance to stakeholders as reflected by the meta-matrices for alternative forms of antenatal and newborn screening.

We will then additionally assess each economic study included within the systematic review (work-stream 1) against a number of criteria, including its compatibility with the theoretical basis for QALY construction, whether the scope of impacts on all affected individuals was captured in terms of full economic utility, compatibility with the methodological requirements of health technology assessment agencies, and whether or not the methods were compatible with broader policy goals of the UK NSC. Economic studies that applied preference-based approaches to the measurement and valuation of outcomes will also be assessed using established checklists that encompass concepts of economic validity such as theoretical validity and empirical validity.[42] We will draw together our review with a narrative synthesis of the relative merits of the alternative economic methods that have already been applied within the field.

8 Work-stream 4: Stakeholder workshop and final recommendations

A crucial final requirement will be to assess whether and how economic valuation methods can be used to elicit preferences for scenarios of benefits and harms associated with antenatal and newborn screening. The intention here is to test the feasibility of applying alternative economic valuation methods in future economic assessments of antenatal and newborn screening. Plausible scenarios of benefits and harms will be developed, each reflecting a range of the types of attributes (themes) represented in the meta-matrices developed in work-stream 2 of the research programme. We will consult with our PPI group and our independent oversight committee to ensure that the scenarios developed are reflective of patient experiences. We will hold a workshop in month 17 with stakeholders encompassing patient and public representatives, health professionals, religious and community representatives, policy and advisory groups, and representatives of relevant academic disciplines. We will replicate the planned methods for recruiting alternative stake-holder groups described in work-stream 2, and supplement these with recruitment of individuals through our academic and professional networks. We will aim to recruit a total of 30 individuals to participate in the workshop.

Potential participants will be sent information about the study and a brief outline of what they will be asked to do during the workshop. People who express an interest in taking part will be sent more detailed information prior to the workshop with a background to the study, preliminary findings of the work carried out, and descriptions of the tasks that will be undertaken during the workshop. Prior to participation in the group activities, participants will be asked to consent to their participation and for any data collected to be used for analysis and reporting of the study. Any participant will be able to decline to consent to a particular activity and withdraw from part or all of the workshop.

Participants in the workshop will be asked to undertake valuation exercises that explore the use of alternative economic (preference-based) techniques to value plausible scenarios of benefits and harms. It is anticipated that different scenario sets will be developed for alternative forms of antenatal and newborn screening. Participants will be divided into small groups, each with approximately four to five people of different backgrounds. Each small group will be facilitated by a member of the research team. Details of the study context and preliminary findings of the work carried out will be described in detail at the outset of the workshop, thereby providing exposition to the written materials that participants would have been asked to read beforehand. Members of the research team will subsequently provide overviews of economic valuation methods and provide guidance on how to complete the valuation tasks. The range of economic valuation methods will include those identified in work-stream 1 of the research programme, but these will be supplemented by other valuation methods that have yet to be applied within the context of antenatal and newborn screening. The process of selection of valuation methods will be informed by reviews of economic valuation methods applied in public decision-making.[60 61] However, it is anticipated that the valuation methods will draw from a pool of the following alternatives: rating scales, the standard gamble approach, the time trade-off approach, the person trade-off approach, discrete choice experiments, best-worst

scaling, contingent valuation, an analytical hierarchical process and allocation of points.[61] A filtering process that balances relevance to health economic assessments of antenatal and newborn screening and participant burden will guide the final selection of valuation methods applied. Participants will be encouraged to complete the valuation methods individually, followed by group discussions at the end of each session. Group discussions will be audio-recorded for transcription and analysis. Participants will also be invited to send their retrospective reflections on the tasks following the workshop. We will undertake a thematic analysis of the data to generate key themes arising from the workshop deliberations and the post-workshop reflections.[55 56]

The health economists and qualitative researchers will subsequently use the results from the workshop to develop final 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.

9 Patient and public involvement (PPI)

We have worked closely with our PPI co-applicant Jane Fisher, who is the director of the organisation Antenatal Results and Choices (ARC), and who has extensive experience providing support to women and their partners during antenatal screening and its consequences. She has provided valuable insights into the understanding of the complexity of PPI in the context of antenatal and newborn screening. Because screening is optional and the experiences of mothers and their partners vary depending on the results of the test, there are potentially several PPI groups of interest for this study. To identify these different PPI groups, we have created the diagram presented in Appendix III. We identified up to fifteen groups of women and their partners who could potentially have different views and experiences of the antenatal and newborn screening programme. The diagram identifies groups of women depending on whether they opt-in or opt-out of antenatal or newborn screening and depending on the results of the screening test. It was clear from this exercise that the perceptions about benefits and harms of the antenatal and newborn screening programmes can vary substantially depending on parental experiences. Women who, for example, opted-in for antenatal screening, had a screen positive test result, had further tests and a true positive confirmation have a different personal experience and therefore are likely to have different perceptions of benefits and harms than women given a screen negative result. Similarly, the views on benefits and harms of parents who opted-in for newborn screening, had a screen positive test result but decided not to have any further tests are expected to be different from parents who decide to have further testing.

We also had access to the parent advisory group of the British Association of Paediatric Surgeons Congenital Anomalies Surveillance System (BAPS-CASS) and circulated a letter among their members asking their views about the aims of our study and whether it was worthwhile investing NHS resources in this type of research. We received one response from a parent of a child with a diagnosis of Exomphalos who was supportive. She explained to us that, in her experience, providing early signposting to support groups after a positive antenatal screening result has contributed positively to the development of her child and her own mental health. She also suggested that there are possible harms difficult to capture through formal research including out of date information about treatment options, survival rates and long-term outcomes.

Conducting the diagram exercise with ARC and the feedback from the member of the advisory group of BAPS-CASS have been very useful to appreciate the breadth of experiences from women and their partners needed for our qualitative study. It has also highlighted the possibility that the benefits and harms included in health economic assessments to date might not include all elements of importance to women, their partners and relatives. This is an important aspect to consider in the design of the systematic review and it will assist in the preparation of the search strategies.

We will aim to engage parents from as many groups as possible as identified in the diagram of potential PPI groups (see Appendix III) throughout our proposed research. We acknowledge that it will be complicated to identify women and partners for some of these groups. For instance, there are no specific groups or fora for

parents where screening is done privately or that do not screen at all (Groups 7, 8, 14 and 15). We are currently collaborating with Antenatal Results and Choices (ARC) and the BAPS-CASS parental advisory group, which will assist in the identification of parents in Groups 3, 4, 5 and 6 and Groups 11, 12 and 13, respectively. For the two groups representing the views of parents with screen true negative and false negative antenatal or newborn results (Groups 1, 2, 9 and 10), we are thinking using our social media channels on Facebook and Twitter to identify at least one PPI member in each group. It is important that the true negative group is properly represented as they contain the highest numbers of women. We are aiming to have at least one individual representing each of these groups.

Given the sensitive nature of the conversations that are likely to occur during PPI meetings, we will meet participants for specific groups separately. We will give the opportunity for PPI members to meet with the study team face-to-face or use the online platform that we will be using during the qualitative study. PPI groups will be divided as follows:

- **Group 1:** Parents who opt-in for antenatal or newborn screening with a screen true negative result (Groups 1 and 9)
- **Group 2:** Parents who opt-in for antenatal or newborn screening with a screen false negative result (Groups 2 and 10)
- **Group 3:** Parents who opt-in for antenatal or newborn screening with a screen positive result and decline any further tests (Groups 3 and 11)
- **Group 4:** Parents who opt-in for antenatal or newborn screening with a false positive result (Groups 4 and 12)
- **Group 5:** Parents who opt-in for antenatal screening with a true positive result and continue pregnancy (Group 5)
- **Group 6:** Parents who opt-in for antenatal screening with a true positive result and end pregnancy (Group 6)
- **Group 7:** Parents who opt-in for newborn screening with a true positive result (Group 13)

Participants will be reimbursed in in recognition of time, skills and expertise and we have costed PPI support using the INVOLVE guidance. In addition, we will provide up to one-hour training session about the use of health economic assessments in screening programmes in the UK during our first meeting. The health economics team in Warwick and Oxford have extensive experience delivering courses about cost-effectiveness analysis to non-economists. The training will cover an introduction to cost-effectiveness analysis to evaluate value for money of existing or new screening programmes.

We will present PPI in our study in the final report using the GRIPP2 reporting checklist. [62]

10 Ethical considerations

Ethical approval will not be required in work-streams 1 and 3 as no original data from human participants will be collected.

10.1 Work-stream 2 ethical considerations

10.1.1 Stage 1: Literature review, secondary analysis and stakeholder mapping

The literature review, review of comments sent to the UK NSC and stakeholder mapping exercise will not require ethical approval.

Secondary analysis of existing interview data (see Appendix II)

a) Data from the Health Experiences Research Group, University of Oxford are available for data sharing and secondary analysis. The data included are covered by two approvals:

i) Study title DIPEx: personal experiences of health and illness. Study approved by Anglia and Oxford MREC originally granted 8th September 1999 (reference 99/5/17) extended to cover all adult health conditions in 2003 ref (03/5/016) Eastern MREC. This approval covers:

- Parents who have undergone antenatal screening/newborn screening Healthtalk (http://healthtalk.org/peoples-experiences/pregnancy-children/antenatal-screening/topics)
- Parents whose foetus received a diagnosis of thalassaemia following antenatal screening (http://healthtalk.org/peoples-experiences/pregnancy-children/screening-sickle-cell-and-beta-thalassaemia/topics)
- Parents who have undergone pregnancy termination for foetal anomaly (screening or family history) (http://healthtalk.org/peoples-experiences/pregnancy-children/ending-pregnancy-fetal-abnormality/topics)

ii) Study title: Narratives of health and illness for www.healthtalkonline.org(formerly DIPEx) and www.youthhealthtalk.org . Study approved by NRES Committee South Central 12/SC/0495. Approval covers the following:

- Parents with experience of neonatal surgery (http://healthtalk.org/peoples-experiences/pregnancy-children/parents-experiences-neonatal-surgery/topics)
- Parents with experience of late miscarriage (http://healthtalk.org/peoples-experiences/pregnancy-children/losing-baby-20-24-weeks-pregnancy/topics)

b) Data from Dr Boardman's two studies, 'Pre-conception genetic screening for conditions of variable or uncertain prognosis: social and ethical implications' (2017-2021) Wellcome Trust Grant (203384/Z/16/Z) and 'Imagining Futures: the social and ethical implications of genetic screening' (2013-2017) ESRC Grant (ES/K002090/1) are being included for this secondary analysis. This secondary analysis is covered by the following ethical approval:

i) University of Warwick Biomedical and Scientific Research Ethics Committee (Ethical Application Reference: BSREC 105/18-19) (15/9/19).

This approval covers secondary analysis of all data from these studies as per Appendix II.

10.1.2 Stage 2: Primary data collection

We will require new approvals for interviews and focus groups for primary data collection. These will be applied for in first half of 2020.

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12 Appendices

12.1 Appendix I: Sources for grey literature

12.1.1 National and Regional Screening Organisations

Country	Organisation	Website	National or Regional
Australia	Australian Government department of health Standing Committee on Screening	http://www.cancerscreening.gov.au/internet/screening/publishing.nsf/Content/standing-committee-on-screening	National
Australia	Australian Department of Health Medical Services Advisory Committee	http://www.msac.gov.au/internet/msac/publishing.nsf/Content/about-msac http://www.msac.gov.au/internet/msac/publishing.nsf/Content/completed-assessments	National
Australia	Australian COAG Health Council Health Technology Reference Group	https://www.coaghealthcouncil.gov.au/Health-Technology-Reference-Group/Reports-and-Briefs/Technology-Briefs-by-specialty	National
Belgium	Superior Health Council (Hoge Gezondheidsraad/Conseil Supérieur de la Santé)	https://www.health.belgium.be/en/superior-health-council	National
Canada	Public Health Agency of Canada	https://www.canada.ca/en/public-health/corporate/mandate/about-agency.html	National
Canada	Canadian Task Force on Preventative Health Care	https://canadiantaskforce.ca/	National
Canada	Alberta Health	http://www.health.alberta.ca/about-us.html	Regional
Canada	Health Quality Council of Alberta (HQCA)	http://www.hqca.ca/about/	Regional
Canada	Health Quality Ontario	http://www.hqontario.ca/about-us	Regional
Canada	Institut national d'excellence en santé et en services sociaux (INESSS) [formerly AETMIS]	https://www.inesss.qc.ca/en/home.html	Regional
Canada	Toronto Health Economics and Technology Assessment (THETA) Collaborative	http://theta.utoronto.ca/c.php?g=700781&p=4976503	Regional
Denmark	National Board of Health (Sundhedsstyrelsen)	https://www.sst.dk/	National
Finland	National Screening Committee, Ministry of Health and Social Affairs (Social- och hälsovårdsministeriet)	http://stm.fi/en/frontpage	National

France	Haute Autorité de Santé	https://www.has-sante.fr/	National
Germany	German Institute of Medical Documentation and Information (DIMDI)	https://www.dimdi.de/dynamic/en/dimdi/	National
Germany	The Federal Joint Committee (Gemeinsamer Bundesausschuss)	https://www.g-ba.de/	National
Ireland	Health Information and Quality Authority (HIQA)	https://www.hiqa.ie/about-us	National
Netherlands	The Health Council (Gezondheidsraad)	https://www.gezondheidsraad.nl/	Regional
Netherlands	Zorginstituut Nederland (National Health Care Institute Netherlands)	https://www.zorginstituutnederland.nl/	National
New Zealand	National Screening Advisory Committee, National Screening Unit	https://www.nsu.govt.nz/	National
Norway	Norwegian Institute of Public health (NIPH)	https://www.fhi.no/sys/ks/	National
Spain	Instituto de Salud Carlos III (Institute of Health Carlos III, ISCIII)	http://www.eng.isciii.es/ISCIII/es/contenidos/fd-el-instituto/quienes-somos.shtml	Regional
Spain	Ministry of Health, Social Services and Equality (Ministerio de Sanidad, Servicios Sociales E Igualdad)	http://www.msssi.gob.es/en/ http://www.idi.mineco.gob.es/	National
Sweden	The National Board of Health and Welfare (Socialstyrelsen)	http://www.socialstyrelsen.se/	National
UK	UK National Screening Committee	https://legacyscreening.phe.org.uk/screening-recommendations.php	National
UK	Healthcare Improvement Scotland	http://www.healthcareimprovementscotland.org/about_us.aspx	National
USA	U.S. Preventive Services Task Force	https://www.uspreventiveservicestaskforce.org/	National
USA	Advisory Committee on Heritable Disorders in Newborns and Children: Bloodspot	https://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/	National
USA	American College of Medical Genetics and Genomics (ACMG): Bloodspot	http://www.acmg.net/	National
USA	Washington State Health Care Authority (HCA)	https://www.hca.wa.gov/about-hca	Regional

Regional organisations included as some countries such as Spain with autonomous regions produce a different economic model for each region.

12.1.2 HTA Organisations

Country	Organisation	Website	National or Regional
Austria	Institute of Technology Assessment (ITA) of the Austrian Academy of Sciences	https://www.oeaw.ac.at/ita/en/about-us	National
Belgium	Federal Knowledge Center for Health Care (KCE)	https://kce.fgov.be/nl/content/wat-is-het-kce/onze-missie	National
Canada	Canadian Agency for Drugs and Technologies in Health (CADTH)	https://www.cadth.ca/about-cadth	National
Canada	Alberta Health Evidence Reviews	http://www.health.alberta.ca/initiatives/health-evidence-reviews-list.html	Regional
Canada	Institute of Health Economics Alberta Canada (IHE)	https://www.ihe.ca/about/about-ihe	Regional
Finland	Finnish Office for Health Technology Assessment (Finohta), National Institute for Health and Welfare	https://www.thl.fi/en/finohta	National
France	Committee for Evaluation and Dissemination of Innovative Technologies (CEDIT)	http://cedit.aphp.fr/cedit-hta-agency/	Regional
Ireland	National Centre for Pharmacoeconomics (NCPE Ireland)	http://www.ncpe.ie/about/	National
Spain	Department of Health of Galicia (conducts HTAs for Spain)	http://avalia-t.sergas.es/	National
Spain	Health and Quality Assessment Agency of Catalonia (AQuAS)	http://aquas.gencat.cat/ca/sobre_aquas/	Regional
Sweden	Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU)	http://www.sbu.se/en/	National
Sweden	Sahlgrenska Universitetssjukhuset - HTA-centrum	https://www.sahlgrenska.se/forskning/htacentrum/	Regional
UK	National Institute for Health and Care Excellence (NICE)	https://www.nice.org.uk/about	National
UK	NIHR Journals Library - HTA programme	https://www.journalslibrary.nihr.ac.uk/programmes/	National
USA	Agency for Healthcare Research and Quality (AHRQ)	https://www.ahrq.gov/cpi/about/index.html	National

12.1.3 Pediatrics Organisations

Country	Association name	Website
Albania	Albanian Pediatric Society	http://www.aps.al
Algeria	Societe Algerienne de Pediatrie.	http://www.ands.dz/sap/accueil.html
Angola	Sociedade Angolana de Pediatria	http://sociedadeangolanadepediatria.com/
Argentina	Sociedad Argentina de Pediatra	www.sap.org.ar
Australia	Paediatrics & Child Health Division, The Royal Australasian College Of Physicians (2016-2018)	https://www.racp.edu.au/about/racps-structure/paediatrics-child-health-division
Austria	Austrian Society of Pediatrics & Adolescent Medicine	http://www.docs4you.at/
Bangladesh	Bangladesh Paediatrics Association (BPA)	http://www.bpabd.org/
Belgium	Belgian Society of Pediatrics	http://www.bvksbp.be/
Bolivia	Sociedad Boliviana de Pediatra	http://www.bago.com.bo/sbp
Bosnia And Herzegovina	Pediatric Society of Bosnia and Herzeqovina (UPUBiH)	http://upubih.org
Brazil	Sociedad Brasilera de Pediatra	http://www.sbp.com.br/
Bulgaria	Bulgarian Pediatric Association (Association Bulgare de Pediatrie)	http://www.pediatria-bg-ed
Cambodia	Cambodian Pediatric Association	http://cpa-cambodia.org/
Cameroon	Societe Camerounaise de Pediatrie	http://www.socaped.org/
Canada	Canadian Paediatric Society (CPS)	http://www.cps.ca/
Chile	Sociedad Chilena De Pediatria (Pediatric Society of Chile)	http://sochipe.cl/ver2/index.php
China	Chinese Society of Pediatrics	hppt://cps.cma.org.cn
Colombia	Sociedad Colombiana de Pediatra	http://www.scp.com.co/
Congo, Republic of	Societe Congolaise de Pediatrie	http://www.fleuvecongoped.net
Costa Rica	Asociacin Costarricense de Pediatra (ACOPE)	http://www.acopecr.com/
Cote D'Ivoire	Societe Ivoirienne de Pediatrie (SIP)	http://sip.ci/
Croatia	Croatian Pediatric Society (Hrvatski Luecnicki Zbor Subiceva)	http://www.hpd.com.hr/
Cuba	Sociedad Cubana de Pediatra	http://www.sld.cu/sitios/pediatria/
Cyprus	Cyprus Pediatric Society	www.child.org.cy
Czech Republic	Czech National Pediatric Society	http://www.cpsjep.cz/
Denmark	Dansk Paediatrisk Selskab (Danish Paediatric Society)	http://www.paediatri.dk
Dominican Republic	Sociedad Dominicana de Pediatra	www.pediatriadominicana.org

Ecuador	Sociedad Ecuatoriana de Pediatra	http://www.pediatria.org.ec/
Egypt	Egyptian Pediatric Society	http://www.egyptpediatrics.org/
El Salvador	Asociacion de Pediatria de El Salvador	http://www.asopedes.org.sv/
Ethiopia	Ethiopian Pediatric Society	http://www.epseth.org
Finland	Finnish Paediatric Association	http://www.suomenlastenlaakariyhdistys.fi/
France	Socit Franaise de Pdiatrie (SFP)	http://www.SFPediatrie.com
Germany	German Society of Pediatrics & Adolescent Medicine (DGKJ)	http://www.dgkj.de
Ghana	Paediatric Society of Ghana	http://pedsgh.com/
Greece	Hellenic Pediatric Society (Greek Pediatric Society)	www.e-child.gr
Haiti	Societe Haitienne de Pediatrie (Haitian Pediatric Society)	http://www.pediatriehaiti.org/
Hong Kong	Hong Kong Paediatric Society	www.medicine.org.hk/hkps
Hungary	Hungarian Pediatric Association	http://www.gyermekorvostarsasag.hu
India	Indian Academy of Pediatrics	http://www.iapindia.org
Indonesia	Indonesian Pediatric Society	http://www.idai.or.id
Iran, Islamic Republic Of	Iranian Society Of Pediatrics	http://www.irpediatrics.com
Ireland	Irish Paediatric Association (IPA)	http://www.irishpaediatricassociation.ie/
Israel	Israel Paediatric Association	http://www.pediatrics.org.il/english.asp
Italy	Societa Italiana di Pediatria (Italian Society of Pediatrics)	http://www.sip.it
Jamaica	Paediatric Association of Jamaica	http://www.paedassocja.org/
Japan	The Japan Pediatric Society (JPS)	http://www.jpeds.or.jp/
Jordan	Jordan Pediatric Society	http://www.jps.org.jo
Kenya	Kenya Paediatric Association (KPA)	http://kenyapaediatric.org/
Korea, Republic Of	The Korean Pediatric Society	http://www.pediatrics.or.kr/
Latvia	Latvian Pediatric Association	http://www.lpa.lv
Lebanon	Lebanese Pediatric Society(LPS)	http://www.lebpedsoc.org/
Lithuania	Lithuanian Paediatric Association	http://www.pediatrija.org
Macedonia, The Former Yugoslav Republic Of	Pediatric Association of Macedonia	http://www.zpm.org.mk
Malaysia	Malaysian Paediatric Association	mpaweb.org.my
Mexico	Asociacion Mexicana de Pediatria A.C.(AMP)	http://www.amp.org.mx
Mexico	Confederacin Nacional de Pediatra de Mexico (CONAPEME)	http://www.conapeme.org
Morocco	Societe Marocaine de Pediatrie	http://www.smpediatrie.ma/
Nepal	Nepal Paediatric Society (NEPAS)	http://www.nepas.org.np/

Netherlands	Nederlandse Vereniging voor Kindergeneeskunde (Paediatric Association of the Netherlands) NVK	http://www.nvk.nl/
New Zealand	Paediatric Society of New Zealand	www.paediatrics.org.nz
Nicaragua	Sociedad Nicaragense de Pediatra	http://www.soniped.org/
Nigeria	Paediatric Association of Nigeria	http://www.pan-ng.org/
Norway	Norwegian Pediatric Association	http://www.barnelegeforeningen.no
Pakistan	Pakistan Paediatric Association(PPA)	http://ppa.org.pk
Panama	Sociedad Panamena de Pediatria	http://spponline.net
Papua New Guinea	PNG PAEDIATRIC SOCIETY	http://pngpaediatricsociety.org/
Paraguay	Sociedad Paraguaya de Pediatria	http://www.spp.org.py/
Peru	Sociedade Peruana de Pediatria	http://www.pediatriaperu.org/
Philippines	Philippine Pediatric Society(PPS)	http://www.pps.org.ph/
Poland	Polish Pediatric Society	www.ptp.edu.pl
Portugal	Sociedade Portuguesa de Pediatria (Portuguese Society of Pediatrics)	http://www.spp.pt/
Puerto Rico	Sociedad de Pediatra de Puerto Rico	http://www.pediatraspr.org/
Romania	Romanian Society of Pediatrics	http://srped.ro/
Romania	Societe Roumaine de Pediatrie Sociala (Romanian Society of Social Pediatrics)	http://www.pediatriesociala.ro
Russian Federation	Union of Paediatricians of Russia	http://www.pediatr-russia.ru
Saudi Arabia	Saudi Paediatric Association	http://www.speda.org.sa/
Serbia And Montenegro	Paediatric Association of Serbia	http://www.imd.org.rs
Singapore	Singapore Paediatric Society	http://www.sps.org.sg/
Slovakia	Slovak Pediatric Society	http://www.sls-sps.sk
Slovenia	Slovenian Paediatric Society	http://www.zzp.si
South Africa	South African Paediatric Association (SAPA)	http://www.paediatrician.co.za
Sri Lanka	Sri Lanka College of Paediatricians (SLCP)	www.slcp.lk
Sweden	Swedish Pediatric Society	http://www.barnlakarforeningen.se
Taiwan ROC	Taiwan Pediatric Association	http://www.pediatr.org.tw
Tunisia	Societe Tunisienne de Pediatrie	http://www.stp.tn/
Turkey	Turkish National Pediatric Society(TNPS)	http://www.millipediatri.org.tr
Turkey	Turkish Pediatric Association (Turk Pediatri Kurumu)	http://www.turkpediatri.org.tr
Uganda	Uganda Paediatric Association	http://upauganda.org/

United Arab Emirates	Emirates Medical Association - Pediatric Society	http://www.ema.ae
United Kingdom	Royal College of Paediatrics and Child Health (RCPCH)	http://www.rcpch.ac.uk/
Uruguay	Sociedad Uruguaya de Pediatria (SUP)	http://www.sup.org.uy/
USA	American Academy of Pediatrics (AAP)	http://www.aap.org
USA	Academic Pediatric Association (APA)	http://www.academicpeds.org
USA	American Pediatric Society (APS)	http://www.aps-spr.org/
Uzbekistan	Uzbekistan Pediatric Association	http://www.tashpmi.uz/new/index.php
Venezuela	Sociedad Venezolana de Puericultura y Pediatria	http://www.svpediatria.org/

12.1.4 Obstetrics and Gynaecology Organisations

Country	Organisation	Website
Afghanistan	Afghan Society Obstetricians Gynaecologists	https://www.figo.org/societies/afghan-society-obstetricians-and-gynaecologists
Albania	Albanian Association Obstetrics Gynecology	www.ssognet.org
Algeria	Societé Algérienne de Gynécologye-Obstétrique	https://www.figo.org/societies/societé-algérienne-de-gynécologye-obstétrique
Argentina	Federación Argentina de Sociedades de Ginecología y Obstetricia	www.fasgo.org.ar/
Armenia	Republic Armenia Association Obstetricians/Gynecologists Neonatologists	https://www.figo.org/societies/republic-armenia-association-obstetriciansgynecologists-and-neonatologists
Australia	Royal Australian New Zealand College Obstetricians Gynaecologists	www.ranzcog.edu.au
Austria	Oesterreichische Gesellschaft fur Gynakologie und Geburtshilfe Austrian Society Gynaecology Obstetrics	www.oeggg.at
Azerbaijan	Azerbaijan	egip-az.com
Bangladesh	Obstetrical Gynaecological Society Bangladesh	www.ogsb.org
Belgium	Royal Belgian Society for Obstetrics Gynaecology	www.rbsog.be
Benin	Societe de Gynecologie et dObstetrique du Benin et du Togo CUGO-CNHU	https://www.figo.org/societies/societe-de-gynecologie-et-dobstetrique-du-benin-et-du-togo-cugo-cnhu
Bolivia	Sociedad Boliviana de Obstetricia y Ginecología	http://www.sbgob.com/
Brazil	Federaçao Brasileira das Associações de Ginecologia e Obstetricia FEBRASGO	www.febrasgo.org.br
Bulgaria	Bulgarian Society Obstetrics Gynecology	www.bsobgyn.com
Burkina Faso	Societé de Gynécologues et Obstétriciens du Burkina SOGOB	www.sogob-bf.org/
Cambodia	Societe Cambodyenne de Gynecology et Obstetrique	https://www.figo.org/societies/societe-cambodyenne-de-gynecology-et-obstetrique
Cameroon	Society Gynecologists Obstetricians Cameroon SOGOC	www.sogoc.org
Canada	Society Obstetricians Gynaecologists Canada/Societé des Obstétriciens et Gynécolgues du Canada	www.sogc.org

Chile	Sociedad Chilena de Obstetricia y Ginecología	www.sochog.cl/
China	Chinese Society Obstetrics Gynecology	https://www.figo.org/societies/chinese-society-obstetrics-and-gynecology
Colombia	Federación Colombiana de Asociaciones de Obstetricia y Ginecología	www.fecolsog.org/
Costa Rica	Asociacion de Obstetricia y Ginecologia de Costa Rica	www.aogcr.com
Croatia	Croatian Society Gynecologists Obstetricians	https://www.figo.org/societies/croatian-society-gynecologists-and-obstetricians
Cuba	Sociedad Cubana de Obstetricia y Ginecología	www.scog.sld.cu
Cyprus	Cyprus Gynaecological Obstetrics Society	https://www.figo.org/societies/cyprus-gynaecological-and-obstetrics-society
Czech Republic	Czech Gynecological Obstetrical Society	www.cgps.cz
Denmark	Dansk Selskab for Obstetric og Gynaekologi	www.dsog.dk
Dominican Republic	Sociedad Dominicana de Obstetricia y Ginecologia	www.sdog.org.do
Ecuador	Federación Ecuatoriana de Sociedades de Ginecología y Obstetricia	https://www.figo.org/societies/federación-ecuatoriana-de-sociedades-de-ginecología-y-obstetricia
Egypt	Egyptian Society Gynaecology Obstetrics	https://www.figo.org/societies/egyptian-society-gynaecology-and-obstetrics
El Salvador	Asociación de Ginecología y Obstetricia de El Salvador	https://www.figo.org/societies/asociación-de-ginecología-y-obstetricia-de-el-salvador
Eritrea	Eritrean Medical Association ERIMA	https://www.figo.org/societies/eritrean-medical-association-erima
Estonia	Society Estonian Gynaecologists	www.ens.ee/
Ethiopia	Ethiopian Society Obstetricians Gynecologists	www.esog.org.et/
Fiji	Fiji Obstetrics Gynaecology Society FOGS	https://www.figo.org/societies/fiji-obstetrics-and-gynaecology-society-fogs
Finland	Finnish Gynecological Association	www.gynekologiyhdistys.fi
France	Collège National des Gynécologues et Obstétriciens Français	https://www.figo.org/societies/collège-national-des-gynécologues-et-obstétriciens-français
Gabon	Société Gabonaise de Gynécologie Obstétrique et de la Reproduction SGGOR	https://www.figo.org/societies/société-gabonaise-de-gynécologie-obstétrique-et-de-la-reproduction-sggor
Georgia	Georgian Obstetricians Gynecologists Association GOGA	www.goga.org.ge
Germany	Deutsche Gesellschaft für Gynäkologie und Geburtshilfe	www.dggg.de
Ghana	Society Gynaecologists Obstetricians Ghana Ghana Medical Association	https://www.figo.org/societies/society-gynaecologists-and-obstetricians-ghana-ghana-medical-association
Greece	Hellenic Obstetrical Gynaecological Society	www.hsog.gr

Guatemala	Asociacion de Ginecologia y Obstetricia de Guatemala AGOG	www.agog.org.gt
Guinea	Société Guinéenne de Gynécologie-Obstétrique	https://www.figo.org/societies/société-guinéenne-de-gynécologie-obstétrique
Haiti	Societe Haitienne d'Obstetrique et de Gynecologie	www.shog.org
Honduras	Sociedad de Ginecología y Obstetricia de Honduras	https://www.figo.org/societies/sociedad-de-ginecología-y-obstetricia-de-honduras
Hong Kong S.A.R., China	Obstetrical & Gynaecological Society Hong Kong	www.ogshk.org
Hungary	Hungarian Society Obstetrics Gynaecology	www.mnt.hu
Iceland	Icelandic Society Obstetrics Gynecology	https://www.figo.org/societies/icelandic-society-obstetrics-and-gynecology
India	Federation Obstetrics & Gynaecological Societies India FOGSI	www.fogsi.org/
Indonesia	Perkumpulan Obstetri Dan Ginekologi Indonesia Indonesian Society Obstetrics & Gynecology	www.pogi.or.id
Iran	National Association Iranian Obstetricians & Gynecologists NAIGO	https://www.figo.org/societies/national-association-iranian-obstetricians-gynecologists-naigo
Iraq	Iraqi Society Obstetrics & Gynecology ISOG	https://www.figo.org/societies/iraqi-society-obstetrics-gynecology-isog
Ireland	Institute Obstetricians Gynaecologists the Royal College Physicians Ireland	www.rcpi.ie
Israel	Israel Society Obstetrics Gynecology	www.obgyn.org.il
Italy	Società Italiana di Ginecologia e Ostetricia	www.sigo.it
Ivory Coast	Societe de Gynecologie et d'Obstetrique de Cote d'Ivoire	https://www.figo.org/societies/societe-de-gynecologie-et-d'obstetrique-de-cote-d'ivoire
Jamaica	Grabham Society Obstetricians Gynaecologists	https://www.figo.org/societies/grabham-society-obstetricians-and-gynaecologists
Japan	Japan Society Obstetrics Gynecology	www.jsog.or.jp/
Jordan	Jordanian Society Obstetricians Gynaecologists	www.jsog.org
Kenya	Kenya Obstetrical Gynaecological Society	https://www.figo.org/societies/kenya-obstetrical-and-gynaecological-society
Kuwait	Kuwait Medical Association: The Profession Obstetrics Gynaecology	https://www.figo.org/societies/kuwait-medical-association-profession-obstetrics-and-gynaecology
Kyrgyzstan	Kyrgyz Association Obstetricians, Gynecologists Neonatologists KOAGN	https://www.figo.org/societies/kyrgyz-association-obstetricians-gynecologists-and-neonatologists-koagn

Latvia	Latvian Association Gynaecologists Obstetricians	https://www.figo.org/societies/latvian-association-gynaecologists-and-obstetricians
Lebanon	Société Libanaise dObstétrique et de Gynécologie Lebanese Society Obstetrics & Gynecology	www.lsog.org.lb
Libya	Libyan Obstetrical Gynaecological Association	https://www.figo.org/societies/libyan-obstetrical-and-gynaecological-association
Lithuania	Lithuanian Association Obstetricians Gynecologists	www.lagd.lt
Luxembourg	Société Luxembourgeoise de Gynécologie et d'Obstétrique	https://www.figo.org/societies/société-luxembourgeoise-de-gynécologie-et-d'obstétrique
Macao S.A.R., China	Macau Association Obstetric Gynaecology	http//www.aogm.org.mo
Macedonia	Association Gynecologists Obstetricians Macedonia	https://www.figo.org/societies/association-gynecologists-and-obstetricians-macedonia
Malawi	Association Obstetricians Gynaecologists Malawi AOGM	https://www.figo.org/societies/association-obstetricians-and-gynaecologists-malawi-aogm
Malaysia	Obstetrical & Gynaecological Society Malaysia	www.ogsm.org.my
Mali	Societé Malienne de Gynécologie Obstétrique SOMAGO	https://www.figo.org/societies/societé-malienne-de-gynécologie-obstétrique-somago
Malta	Malta College Obstetricians Gynaecologists	https://www.figo.org/societies/malta-college-obstetricians-and-gynaecologists
Mexico	Federación Mexicana de Colegios de Obstetricia y Ginecologia FEMECOG	www.femecog.org.mx
Moldova	Society Obstetricians Gynecologists Republic Moldova	https://www.figo.org/societies/society-obstetricians-and-gynecologists-republic-moldova
Mongolia	Mongolian Association Obstetrics, Gynecology Neonatology MOGNA	https://www.figo.org/societies/mongolian-association-obstetrics-gynecology-and-neonatology-mogna
Morocco	Société Royale Marocaine de Gynécologie Obstétrique	https://www.figo.org/societies/société-royale-marocaine-de-gynécologie-obstétrique
Mozambique	Associação Moçambicana de Obstetras e Ginecologistas AMOG	https://www.figo.org/societies/associação-moçambicana-de-obstetras-e-ginecologistas-amog
Myanmar	Myanmar Medical Association	https://www.figo.org/societies/myanmar-medical-association
Nepal	Nepal Society Obstetricians Gynaecologists NESOG	www.nesog.org.np
Netherlands	Dutch Society Obstetrics Gynaecology	www.nvog.nl
Nicaragua	Sociedad Nicaragüense de Ginecología y Obstetricia SONIGOB	https://www.figo.org/societies/sociedad-nicaragüense-de-ginecología-y-obstetricia-sonigob

Niger	Societé de Gynécologie et Obstétrique du Niger SGON	https://www.figo.org/societies/societé-de-gynécologie-et-obstétrique-du-niger-sgon
Nigeria	Society Gynaecology Obstetrics Nigeria SOGON	www.sogon.org
Norway	Norsk gynekologisk Forening Norwegian Society for Gynecology Obstetrics	https://legeforeningen.no/Fagmed/Norsk-gynekologisk-forening/
Pakistan	Society Obstetricians & Gynaecologists Pakistan	www.sogp.org
Palestinian Territory	Society Palestinian Gynaecologists Obstetricians	https://www.figo.org/societies/society-palestinian-gynaecologists-and-obstetricians
Panama	Sociedad Panamenã de Obstetricia y Ginecología	www.spogpanama.org/
Papua New Guinea	Papua New Guinea Obstetrics Gynaecology Society	https://www.figo.org/societies/papua-new-guinea-obstetrics-and-gynaecology-society
Paraguay	Sociedad Paraguaya de Ginecología y Obstetricia	www.spgo.org.py
Peru	Sociedad Peruana de Obstetricia y Ginecología	www.spog.org.pe
Philippines	Philippine Obstetrical & Gynecological Society, INC	www.pogsinc.org
Poland	Polish Society Gynecologists Obstetricians.	www.ptgin.pl
Portugal	Federação das Sociedades Portuguesas de Obstetricia e Ginecologia FSPOG	www.fspog.com
Romania	Romanian Society Obstetrics Gynecology	www.sogr.ro
Russia	Russian Society Obstetricians Gynaecologists	https://www.figo.org/societies/russian-society-obstetricians-and-gynaecologists
Rwanda	Rwanda Society Obstetricians Gynecologists RSOG	https://www.figo.org/societies/rwanda-society-obstetricians-and-gynecologists-rsog
Saudi Arabia	Saudi Obstetrical Gynaecological Society	http://www.ssog.org.sa/
Senegal	Association Sénégalaise de Gynécologie-Obstétrique ASGO	https://www.figo.org/societies/association-sénégalaise-de-gynécologie-obstétrique-asgo
Serbia	Association Gynecologists Obstetricians Serbia, Montenegro Republic Srpska UGOSCGRS	https://www.figo.org/societies/association-gynecologists-and-obstetricians-serbia-montenegro-and-republic-srpska-ugoscgrs
Serbia	Shoqata e Obstetërve dhe Gjinekologëve te Kosovës/Kosovo Obstetrics Gynaecology Association KOGA	https://www.figo.org/societies/shoqata-e-obstetërve-dhe-gjinekologëve-te-kosovëskosovo-obstetrics-and-gynaecology
Sierra Leone	Sierra Leone Association Gynaecologists Obstetricians	https://www.figo.org/societies/sierra-leone-association-gynaecologists-and-obstetricians
Singapore	Obstetrical & Gynaecological Society Singapore	www.ogss.net

Slovakia	Slovak Society Gynecology Obstetrics	www.sgps.sk
Slovenia	Slovene Association Gynaecologists Obstetricians	https://www.figo.org/societies/slovene-association-gynaecologists-and-obstetricians
South Africa	South African Society Obstetricians Gynaecologists SASOG	www.sasog.co.za
South Korea	Korean Society Obstetrics Gynecology	www.ksog.org
Spain	Sociedad Espanõla de Ginecología y Obstetricia	www.sego.es
Sri Lanka	Sri Lanka College Obstetricians Gynaecologists	www.slcog.lk
Sudan	Obstetrical & Gynaecological Society the Sudan	https://www.figo.org/societies/obstetrical-gynaecological-society-sudan
Sweden	Svensk Förening För Obstetrik & Gynekologi The Swedish Society Obstetrics Gynecology	www.sfog.se
Switzerland	Schweizerische Gesellschaft für Gynäkologie Geburtshilf/Société Suisse de Gynécologie & Obstétrique	www.sggg.ch
Syria	Syrian Society Obstetricians & Gynecologists	https://www.figo.org/societies/syrian-society-obstetricians-gynecologists
Taiwan	Taiwan Association Obstetrics Gynecology	www.taog.org.tw/
Tanzania	Association Gynaecologists Obstetricians Tanzania AGOTA	https://www.figo.org/societies/association-gynaecologists-and-obstetricians-tanzania-agota
Thailand	Royal Thai College Obstetricians Gynaecologists	www.rtcog.or.th
Tunisia	Société Tunisienne de Gynécologie et d'Obstétrique	www.stgo.org.tn/fr/
Turkey	Turkish Society Obstetrics Gynecology	www.tjod.org
Uganda	Association Obstetricians Gynaecologists Uganda	www.sogc.org/aogu
Ukraine	Ukrainian Association Obstetricians Gynaecologists	https://www.figo.org/societies/ukrainian-association-obstetricians-and-gynaecologists
United Arab Emirates	Emirate Medical Association	www.ema.ae
United Kingdom	Royal College Obstetricians Gynaecologists UK	www.rcog.org.uk
United States	American College Obstetricians Gynecologists	www.acog.org
Uruguay	Sociedad Ginecotocologica del Uruguay	www.sguruguay.org
Uzbekistan	Obstetricians Gynecologists Uzbekistan	https://www.figo.org/societies/obstetricians-and-gynecologists-uzbekistan
Venezuela	Sociedad de Obstetricia y Ginecología de Venezuela	www.sogvzla.org

Vietnam	Vietnam Gynaecology Obstetrics Association VINAGOFPA	https://www.figo.org/societies/vietnam-gynaecology-and-obstetrics-association-vinagofpa
Zambia	Zambia Association Gynaecologists & Obstetricians ZAGO	https://www.figo.org/societies/zambia-association-gynaecologists-obstetricians-zago
Zimbabwe	Zimbabwe Society Obstetricians Gynaecologists	https://www.figo.org/societies/zimbabwe-society-obstetricians-and-gynaecologists

12.2 Appendix II: Data sources for secondary analysis of existing interview data

Type of Participant	Number of interview transcripts	Source of data	Year of data collection
Parents who have undergone antenatal screening/newborn screening	45 (37 women, 8 couples)	Healthtalk (http://healthtalk.org/peoples-experiences/pregnancy-children/antenatal-screening/topics)	2005
Parents whose child received a diagnosis of cystic fibrosis following newborn screening	6	FB study, under development	2018
Parents whose foetus received a diagnosis of thalassaemia following antenatal screening	5	FB study[45] Healthtalk (http://healthtalk.org/peoples-experiences/pregnancy-children/screening-sickle-cell-and-beta-thalassaemia/topics)	2017-18
Parents who have undergone pregnancy termination for foetal anomaly (screening or family history)	48 (40 Healthtalk, 12 FB study)	FB studies [28 46] Healthtalk (http://healthtalk.org/peoples-experiences/pregnancy-children/ending-pregnancy-fetal-abnormality/topics)	2006-2018
Parents who refused prenatal testing for condition in family	12	FB study [28]	2012-2018
Parents who continued with a pregnancy following prenatal diagnosis	9	FB studies [47 48]	2012-2018
Adults living with conditions that are currently screened for (either antenatal or newborn screening)	20 (10 cystic fibrosis, 10 thalassaemia)	FB studies [28 48]	2017-2018
Parents of children with conditions that are currently screened for	20 (6 Down's Syndrome, 7 cystic fibrosis, 7 thalassaemia)	FB study [45]	2017-2018
Parents with experience of neonatal surgery	13	Healthtalk (http://healthtalk.org/peoples-experiences/pregnancy-children/parents-experiences-neonatal-surgery/topics)	2017

Participants with experience of late miscarriage	3	Healthtalk (http://healthtalk.org/peoples-experiences/pregnancy-children/losing-baby-20-24-weeks-pregnancy/topics)	2018
Families (parents and affected adults) living with genetic diseases that are not yet screened for	75 (22 haemophilia, 17 fragile X syndrome, 36 spinal muscular atrophy)	FB studies [28 46-53]	2012-2018
Total	**256**		

FB denotes Felicity Boardman

12.3 Appendix III: Potential PPI Advisory Group Composition