1. The provision of antenatal information for the NHS Newborn Bloodspot Screening Programme (NBSP) 11-62-02

2. Planned investigation

2.1 Research objectives

The overall study aim is to determine service providers' and users' views about the feasibility, cost, efficiency, impact on understanding and consent of current practice, and preference of alternative methods of conveying Newborn Bloodspot Screening Programme information antenatally. There are nine objectives:

Phase one: generation of alternative models, establishing costs and implications of current best practice for parent understanding

1. Collate characteristics of alternative communication and consent models for NBSPs via a realist review of current NBSP communication models within the UK and countries operating extended NBSPs [months 1-9];
2. Explore how providers and users envisage that information given antenatally can best meet the challenge of effectively and efficiently providing parents with sufficient understanding of an extended NBSP, including their reflections on the alternatives identified via the review [months 3-18]
3. Examine parents understanding and experience of NBSP communication to draw inferences regarding best practice within an extended NBSP [months 6-18];
4. Establish the resource use and costs associated with the current practice(s) of providing NBSP information antenatally [months 7-15];

Phase two: acceptability, preference, cost and broader impact of alternative communication models

5. Examine the preferences of midwives, parents and prospective parents, for different models of conveying NBSP information antenatally [months 16-21]
6. Establish the key parameters affecting the cost effectiveness of new modes compared with the current practice(s) of providing NBSP information antenatally [months 14-21];
7. Outline the key uncertainties in the current evidence base and what is the value of future research to evaluate the effectiveness and cost effectiveness of providing NBSP information antenatally [months 20-22] ;
8. Explore providers' and users' views on the study suggestions, focusing on acceptability, broader impact, effectiveness, efficiency and parent understanding [months 22-28];
9. Establish how generalisable the study findings are across conditions screened for in the UK NBSP [months 22-28].

2.2 Existing research

Newborn bloodspot screening is seen as one of the most significant public health achievements in the developed world.(1) The UK NBSP started in 1969 by screening for phenylketonuria (PKU)(2) and over the following 40 years four additional disorders were added: congenital hypothyroidism (CHT), cystic fibrosis (CF), sickle cell disorders (SCD) and medium chain acyl-CoA dehydrogenase deficiency (MCADD). Three of these disorders were added since 2007 in keeping with NBSPs worldwide, where panel expansion has been most noticeable in the last decade.(3) The UK NBSP involves collecting a blood sample between 5-8 days with the premise behind

screening for any of these diseases being that there is a clinical benefit to affected infants of being identified and potentially treated in the neonatal phase.(4) In 2010-11 over 814,000 babies were screened in the UK, of whom, 1,547 had a positive screening result, leading to an urgent referral for diagnostic tests and treatment where necessary.(5) The annual report for the UK NBSP stated the cost of screening for that year was £915,903.(5) Existing economic evaluations of NBSPs.[e.g. (6)] and other study designs, such as retrospective cohort studies(7) conclude that NBSPs are a cost effective use of resources. However, these conclusions are based on the assumption that NBSP information is communicated to parents in an efficient and cost effective manner.

Antenatal communication of NBSP information

The UK NBSP is introduced to parents as a recommended routine screen with the proviso that screening only occurs after parents have given informed consent both to the collection of the blood sample and for each individual test that will be performed on this sample.(8) Guidelines and training materials from the UK NBSP centre stress the importance of parents making an informed choice and the central role information provision plays in their ability to do so.(5, 9) Training slides infer that midwives invest time in conveying NBSP information and should cover that: testing is optional; the diseases screened for and the implications of having these diseases; the testing process and test detection rates; how results will be reported, what results may mean and options if results show increased risk; and that most pregnancies are normal. They must then check the parents' understanding and signpost them to further information. Notes alongside the slides state that "in order to make their choice parents need to be given information (hence the development of a national leaflet)"(10) which implies that the "national leaflet" (the aforementioned booklets) is the tool which conveys the information. The information booklets are available in 18 different languages.(5) Thus, ensuing parents are adequately informed appears to be midwives' responsibility with varying degrees of emphasis on the leaflet. Thus the current situation may leave midwives in a very difficult and ambiguous situation. They are told to recommend the tests and know that a high uptake is aimed for, but should also get the usual standard of consent; their communication is seen as crucial to the success of NBSPs and yet published figures regarding NBSP costs only covers the direct costs to the NBS Centre and does not consider the full cost to the NHS associated with the time midwives spend communicating with parents.(5) Indeed, at present the cost of current practice is unknown.

Acceptability, parental understanding, and broader impact of current consent and communication models

Concerns have been raised about the efficacy of the current model of informed consent as there is almost universal uptake.(4, 6, 11) Indeed, it has been argued that by making screening a routine part of postnatal care, and aiming for high uptake, the NBSP is incompatible with the sort of voluntary informed consent usually required for any medical treatment including testing for serious diseases and disorders.(12) There are additional concerns as although variance exists internationally in the diseases screened for, and communication and consent models used, there are repeat findings that parents whose children have been screened via a NBSP have limited knowledge about it.(13-18) Indeed some parents were unaware that their child had been screened.(16, 19-22) Within the UK a recent national HTA qualitative study reported concerns regarding whether parents

were adequately informed prior to screening.(23) Thus, providing parents with NBSP information appears complex, with no evidence-based, effective and standardised model in existence.

Further concerns stem from findings showing that *results* from NBSPs can trigger, sometimes profound, anxiety if misunderstood, or parents with children undergoing further testing related to carrier testing (CF) or false positive results (metabolic disorders) are not provided with timely and adequate information in an appropriate manner.(23-25) That such anxiety has been linked to impaired relationships with the baby (25-27) and stress-related problems enduring into childhood(28) demonstrate that the fears that historical lessons from PKU screening triggering the *vulnerable child syndrome* for some parents (29, 30) had not been learned. Unfortunately such distress commonly impacts on the wider family.(23) In these scenarios multiple and/or specialist health professional consultations are often needed to allay such anxiety.(23, 31) Yet, the resources related to this are often not included in NBSP cost estimates.(32)

Crucially research suggests that such distress may be avoidable as parents not only can understand NBSP information and assimilate it and the results into their lives with minimal distress, but they positively value the results.(23) The key difference between parents who report distress and those who received carrier results with minimal service need, is that parents who adapted well had a prior awareness of the disease and could understand the relevance of the information provided antenatally.(23) Parents who reported distress did not feel prepared for screening, felt overloaded by information provided antenatally,(17, 23) and the NBSP information provided did not meet their needs, or they did not perceive it as relevant.(18, 23) This fits with an argument made by Climb (an organisation which provides information on metabolic diseases for parents, children and health professionals) which holds that the NBSP leaflets require users to have pre-existing knowledge in order to appreciate their utility.(33) Importantly, parents whose children required further tests have also stressed that it was not the results *per se*, but the way in which they were communicated which triggered their anxiety.(23, 24) Thus, there appears to be a need to ensure that communication across the screening pathway is improved. Communication antenatally should convey the personal relevance of NBSP information to parents without overburdening them, whilst the process of communicating with parents after a positive screen also needs to be addressed.(23, 34) This is important as not only does inefficient communication lead to negative sequale for parents and their wider family, an increased need for support and resources, and long term breakdowns of relationships between parents and health professionals,(23) but it also represents a missed opportunity for NBSPs to have a positive impact.(35) Parents who are adequately informed and empowered via newborn screening report feeling a duty to inform other family members of potential risks, correct misperceptions and challenge stigma, and misunderstanding more widely in their communities.(35) Indeed within antenatal and newborn screening there is increasing recognition of the important role families and social networks can play in informing parents (35, 36) and shaping their choices about and adaptation to screening.(35) Thus optimising communication is likely to have a much broader impact than the proband's parents.

Expanded Newborn Bloodspot screening

The advent of tandem mass spectrometry (MS/MS) provided the means to screen for numerous disorders with few extra costs.(24) This grant's focus is that a further five disorders are being considered for inclusion in the panels including Maple Syrup Urine Disease (MSUD), Homocystinuria (pyridoxine unresponsive), Glutaric Aciduria Type I (GA1), Isovaleric Acidaemia (IVA), Long-chain 3-hydroxyacyl CoA dehydrogenase deficiency (LCHADD; includes trifunctional protein deficiency).(33) Currently a pilot study is being set up whereby approximately 400,000 babies from across six sites (two in London, Birmingham, Leeds, Manchester and Sheffield) will undergo expanded newborn screening from August 2012. We are aware that this pilot study plans to "develop and publish operational protocols and resources that will maximise benefit and minimise harm." We are in discussion with the PI Dr Jim Bonham to enable us to incorporate findings and minimise duplication.

As NBSPs include increasingly rare diseases with less clear treatment benefits, communication will become ever more critical.(33) Internationally there is increasing appreciation of the centrality of communication in ensuring that NBSP benefits are realised whilst reducing potential harms.(32, 34, 37-44) Specifically, there is a recognised need to inform parents prior to screening,(23, 24, 45) preferably antenatally.(23, 36). and that current models may not be meeting parents needs to clear and timely information.(23) Thus a potential expansion to the NBSP necessitates revisiting the efficacy of providing relevant information antenatally, and how best to provide support to parents whose child screens positive.(33)

NBSP information already represents one of the largest volumes of screening information people assimilate during their life time. This is complicated by the fact that this information is presented when parents commonly feel overloaded with information, and the decision about newborn screening is made when they are physically and emotionally exhausted, which reduces their ability to read(36) and assimilate information.(46, 47) Thus the challenge is how to ensure that health professionals or information materials are able to adequately inform parents of the diseases and screening process when each disease is rare and there are increasing numbers of diseases included in NBSPs. The introduction of an expanded NBSP, within the UK specifically, needs to be viewed in the context of providing a national health service from a finite budget and hence the requirement to consider opportunity cost. The additional cost of an expanded NBSP, potentially requiring extra input from midwives and removing them from other duties, needs to be worth the potential benefits for parents and babies. These benefits may come in the form of both health and non-health benefits, such as the value of the additional information *per se* that comes from a NBSP test result and the avoidance of distress.(23) Furthermore, efficiency must also be viewed alongside meeting parents' need for clear and timely information.(23)

Implications for this study

Compounding the complexity of the above issues are recognised gaps in the research regarding the effectiveness of NBSP information provision including: information provision antenatally;(48) optimal communication during follow-up testing(49) and conveying carrier results;(23, 50) effectiveness of alternative communication models;(49-51) and parents views.(23, 50) Thus, this project focuses on a need to develop the evidence base to produce acceptable, efficient, and effective models of NBSP communication both in the antenatal phase and continuing across the screening pathway. Existing research appears to show that the main additional

communication resources required during the NBSP pathway are for parents receiving carrier results or false positive results.(23, 24) Both were highlighted as important areas requiring further research into NBSP communication.(48) There are, however, large enough differences between the implications and experiences of receiving a carrier result and a false positive metabolic result to warrant detailed examination of these situations independently. Recent research conducted for the HTA has focused on the communication needs and experiences of parents receiving carrier test results from CF and SC screening which provided many findings relevant to the commissioning bid. The PI of this bid conducted this research and is fully aware of the issues in those screening programmes and will incorporate these into the current project. Thus this project will initially focus on screening for metabolic diseases, it will however, test out how transferable the findings are for screening of CF and SC diseases in the final study via consultation with relevant stakeholders.

Although there is a paucity of guidelines to develop communication and consent models for NBSPs, it has been suggested that the NICE report on guideline development(52) can be used as a model.(53) This project will use the definition used by Stewart, Hargreaves & Oliver of evidence based medicine as the template for the methods:

> 'the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. It requires a bottom-up approach that integrates the best external evidence with individual clinical expertise and patient-choice'

Thus, existing NBSP communication protocols and materials used in countries with expanded NBSP will be evaluated along with published research on the efficacy, impact and parent understanding of NBSP communication and consent. Parents and both front line and clinical specialists will then be engaged in qualitative research to develop alternative communication models for use with an expanded NBSP. These models will then be evaluated using quantitative and qualitative methods in the remainder of the project.

NBSP communication models

Although there is a paucity of work to generate testable alternative communication models there are inferences which could be made from existing literature to guide feasibility work and the development of alternative consent and communication models (see appendix a). Although many NBSPs appear to use leaflets which can support NBSPs with minimal resources, these only appear efficient for parents with a prior awareness of the disease and relevance of the programme.(23) For others, written leaflet are inefficient,(23) with parents reporting that whilst they understand the content they still feel ill equipped to understand newborn screening,(54) and approximately half parents surveyed reporting they did not use the leaflets.(36) Specifically, parents value face-to-face communication when seeking NBSP information.(23, 36) Yet, one outcome of an expanded NBSP is that the resultant increase of communication events linked to the programme may make it unfeasible and overly costly to convey pre-screening and all results in person. One alternative is videos which have been found to be useful within SCD screening,(51, 55) however, only 45% of the health professionals and parents in a consensus development study regarding NBSP information supported their use,(53) There are also concerns about using a static information material when NBSP information is prone to change with advances in

treatment and panel expansion. An alternative is to signpost parents to internet based information as this is a behaviour parents commonly undertake as soon as they receive a positive screening result.(23, 27, 33, 56) This is likely to be feasible as already half the NBSPs in the EU are supported by a website for parents to access information (41) and the majority of households now have direct access to the internet.(57)

Providing information via the internet may address a related issue which is there appears to be lack of a consensus regarding the desired content and language of NBSP information.(43, 53) People may actually have different information needs, both in the content and language used, but also the amount of information sought. This fits with theories of psychology(58) information use and communication.(59) Indeed, findings cited above including that parents with a prior level of awareness seem to be those best served by current NBSP information, seeking information from social networks, and needing to appreciate the personal relevance of information to assimilate it, fits with Johnson's Comprehensive Model of Information Seeking (CMIS)(60) This model also explains that when people seek information they are less concerned about the content and more concerned with how that information is conveyed, with a strong preference for personal interaction (59) again the links between this and previous findings(23) are clear. Incorporating this theory into this field of research would introduce a move to understand that seeking to ensure that all parents are *fully* informed may go against some parent's natural coping and information processing styles(59) and therefore may actually be unfeasible. Thus, rather than striving to guarantee all parents reach a certain level of understanding, ensuring they receive information and support at a level they require may be not only a more effective use of resources, but ensure that the broader impact of NBSPs is positive. Providing tailored information via the internet may not only give parents a more acceptable service, but it may be necessary given the documented need for timely information from specialists(23) to whom access is often delayed,(61) and the lack of specialist IMD services and patchy provision.(62) Using developments in internet based behaviour change interventions[1],(63) NBSP websites could be supported by centralised specialists who could meet parents desire to contact someone who could answer their questions in a timely manner.(23, 36) This would build on an idea generated and discussed by parents in the recent HTA report on communication of carrier results generated via newborn screening.(23)

NBSP consent models

NBSP consent models determine the level of information provided and thus potentially the mode of information provision too. As NBSPs aim to greatly improve prognosis by early diagnosis, mandatory screening may be justified if serious harm can be avoided. In debates about the genetic profiling of children it has been argued that in the scenario where doctors need test results in order to trigger treatment, it is ethical to encourage parents to provide consent to the tests.(64) This is justification given in the US for making newborn screening mandatory in most states, yet even in this scenario there is a belief that parents should be fully informed.

A middle ground between this and the current UK model is generic consent mooted by Elias and Annas.(65) This uses analogies with communication and consent models for biobanking and genetic profiling, both

[1] Discussions with Yardley suggest that benefits from this field could be easily transferred to the situation of NBSP information support.

situations where the potential information to convey is vast and evolving, prohibiting in-person communication in terms of time, money and potential utility for the recipient of each piece of information. There are caveats with this model, however, that parents should be enabled to ask questions and additional information to be provided by those who need it. It also should not be used for testing for untreatable fatal diseases. It is accepted, however that generic consent still needs empirical testing,(65) as it is not clear that this would achieve sufficiently informed parents.(64) Although such concerns are warranted, it should be noted that numerous studies report that parents feel overwhelmed by information provided during pregnancy,(23) and that providing too much information can be counterproductive to the goal of informed consent.(66, 67) Also, providing complete NBSP information may already be unfeasible without a significant increase in midwives.(68)

Another option is to continue using an informed consent or informed choice model, yet with expanded screening this is going to be extremely challenging.(69-72) Indeed, there is concern that even with the current number of diseases, parents information needs may not be being met.(23) Thus, there is a need to understand how best to convey timely information to parents, to ensure that they appreciate the personal relevance, without feeling overwhelmed, and still provide in-person communication to those who most need it within NHS resources.

2.3 Research methods

The provision of NBSP information antenatally meets many of the criteria of the MRC's definition of a complex intervention.(73) At present there are insufficient data to effectively design a comparison of alternative communication models. Therefore this project focuses on providing the necessary data to facilitate such evaluation via a two phase sequential exploratory mixed methods project(74) using qualitative, quantitative, observational, survey and economic modelling studies in a complementarity style(75) to address the research objectives. Phase one involves a realist review, a survey and observational study of current practice, an in-depth qualitative study to generate alternative communication and consent models informed by health professionals' and parents' experiences and international evidence. Phase two uses quantitative methods to explore preferences and costs of alternative communication models. This is followed by a final qualitative study which will examine the implication of the study findings from the viewpoint of parents, service providers and key stakeholders. Further information is provided below with indication in brackets of which research objective is being met:

1. Realist literature review to collate characteristics of alternative communication and consent models for NBSPs [RO1]. A realist literature review will establish what works, for who, under what circumstances(76) to assimilate suggestions for alternatives to the current UK NBSP communication model. This work will inform the qualitative interviews [study 2] and the discrete choice experiment [study 4]. The search strategy is likely to be wide given that few studies have specifically addressed this topic, and suggestions for inclusion in this study are as likely to come from inferences based on what is known not to work, known gaps in current models, or analogous situations such as genetic profiling. This will be supplemented by information from researchers, with whom the PI already has communicated, from US, Canada and Australia regarding ongoing research, searches of policy documents, websites and other grey literature. Additionally a full and systematic review of existing

communication materials will be undertaken, as this is seen as a key step in developing evidence based communication guidelines and materials.(53)

2. Interviews with service providers and parents regarding experiences and views of current practice and alternative communication and consent models [RO2&3]. Service providers: Telephone interviews will be conducted nationally with all national newborn screening co-ordinators, and purposively sampled hospital screening co-ordinators, community midwives and hospital based midwives. Telephone interviews enable busy health professionals to participate in health service research.(77, 78) Parents: Parents from across the screening pathway will be purposively sampled via screening co-ordinators and midwives to participate in in-depth face-to-face or telephone interviews and through newborn screening laboratories across England.(79). In addition, we will also involve local 'sure start' and family centres to reach more diverse parents.(79) We will also recruit parents from parent pages on social media websites such as Facebook, Twitter, Mumsnet, Babycentre and Tommies to enhance the geographical diversity of our sample. We will also tweet about the study through our own twitter account @PINSAStudy. The study poster will be attached to tweets and posts.

The interview schedules for this study will be developed by FU who has qualitative expertise related to communication of NBSP information.(23) The schedules will be informed by study 1, guided by the scientific advisory panel, parent reference group and advisors, and piloted with two parents. All participants will be asked for their views on alternative models, with prompts directing them to discuss factors which might affect acceptability or recipients' understanding within each model. Parents will be asked to report how they were informed antenatally and asked to reflect on their level of understanding and whether/how this was affected by content or mode of information provision. This will allow inferences to be made about factors which contribute to understanding and acceptability which will be used to further the development of alternative models for phase 2 of this project.

3. Resource use and potential variation in the costs of current practice [RO4]. This study will identify resource use and key cost drivers of current practice using the perspective of the NHS. The time frame for the analysis will start from initial information provision and informed consent process, through to use of diagnostic tests and potential use of subsequent healthcare services and treatments. Three types of direct healthcare costs will be identified and quantified (a) fixed costs such as consultation room and equipment requirements (b) semi-fixed costs such as staff times and (c) variable costs such as number of screening tests, subsequent use of diagnostic tests and treatments. Two modes of data collection will be used (i) Telephone survey of midwives, (ii) direct observation of midwife practice in hospitals, ante-natal clinics and in patient homes. The survey will aim to identify current practice, any regional variation in current practice and the key costs drivers of current practice including use of subsequent resources and referral to other services such as primary care or specialist genetics services, using the views of a national sample of midwives. The observational studies will provide

micro-costing data of the resource requirements for current models of service delivery but also aim to identify which resources would need modifying to provide proposed new models of information provision. These studies will place a researcher alongside a sample of practicing midwives. The researcher will shadow each midwife for one week to allow time for acclimatisation with the aim of minimising the Hawthorne effect [this process has been successfully used in previous HTAs see (80)]. This process of direct observation will allow the researcher to make accurate recordings of the staff grade and time taken to perform duties associated with the provision of NBSP information.

4. A discrete choice experiment (DCE) of preferences for alternative models [RO5]. DCEs are commonly used to value different models of healthcare programmes and allow measurement of preferences using a method underpinned by robust economic theories.(81) A DCE is a form of survey which identifies and measures what outcomes or aspects of service delivery service users or providers prefer and value the most and can be used to incorporate patient stated preferences into resource allocation decisions.(81) Importantly, a DCE enables identification of the trade-offs people make between different attributes of a service, such as being prepared to wait longer to achieve better quality information. The aim of this DCE is to determine parent and midwives preferences and trade-offs between service and outcome attributes for alternative communication and consent models. This will allow quantification of preferences for different models and allow comparison between the views of midwives and parents. A DCE survey generally comprises up to a maximum of 16 'choice' questions that asks the respondent to choose between one of two alternatives, describing the process of service delivery and possible outcomes in terms of attributes and levels.(81) This DCE will also include an 'opt out' choice to allow for respondents to not choose one of the offered potential models of service delivery described to enable people to indicate if they do not like any of the proposed models. The creation of the choice questions will be informed by mathematical design properties to ensure the main effects and any appropriate interaction between attribute effects can be estimated. This DCE will be web-based and contain three parts: 1. the discrete choice questions; 2. basic socio economic and demographic information about the respondent and 3. Standardised measures of health (EQ-5D) status; and a psychological measure of preferences for level of information when faced with health threats the Monitor and Blunter style scale (MBSS), will be collated for each respondent to use as a variable in the analysis of factors possibly affecting heterogeneity in preferences.(58)

A key component of designing a DCE is the selection of the relevant attributes and levels describing the service and outcomes. The team has expertise in designing DCEs and will use similar methods to those used by Al-Janabi, Coast and Flynn (82) with studies 1 and 2 informing the service delivery and outcome attributes. Although it is not possible at this stage to state what the attributes will be, we have identified some possible examples of the service attributes (and levels) to include such as: mode of information provision (face to face; telephone or internet); person giving the information (local known midwife; screening specialist; disorder specialist); waiting time (immediate access, 48 hours, one week, two weeks); whether informed consent is required (yes; no); how conditions are explained (for example: each condition explained in detail and individually; condition explained in terms of general terms eg. Genetic); cost to the parents of information provision (£ reflecting time and travel costs). An example of a possible outcome attribute to include is: whether the service affects levels of uncertainty about whether to take the screening test. Advice will be sought from the

scientific advisory panel, parent reference groups and advisors to refine the phrasing of the DCE before a pilot study. This will involve conducting cognitive interviews with a small sample of student midwives and members of the patient reference group in order to verify that participants can fully understand the DCE followed by a test of the survey amongst a slightly larger sample. Following the successful completion of the pilot work, the link to the on-line DCE will be sent to the study sample which will include midwives, prospective parents and parents with experience of the NBSP.

5. A preliminary economic model of the proposed alternative methods of communication [RO6,7]. Data collected from phase 1 will be used to structure and populate a simple decision analytic model that compares current practice with the alternatives for a hypothetical cohort of parents. The model structure is likely to be a decision tree and will be informed by a systematic review and critical appraisal of existing economic models relevant to NBSPs. It is likely that existing model structures will require modifications to allow the incremental costs and benefits of new communication models to be evaluated. The scientific advisory panel will be asked to ratify the final model structure. The model will assume the viewpoint of the NHS and use a 3-month time horizon. It will be populated from cost data from study 3. The selection of the appropriate outcome to value the benefits of information provision models has been recognised to be a challenge(3) for this reason, we will conduct a cost consequence analysis. We will also review the relevant literature to better inform the most appropriate outcome measure. If feasible, published utility values will be identified to weight the life years gained and generate quality adjusted life years for each model of information provision. Other possible measures of outcome to be estimated in the model include (a) proportion of parents who feel sufficiently informed to make a decision about the NBSP (b) proportion of parents who feel empowered, as measured by a standardised measure of empowerment [for example see the GCOS-24(83)]. Outcome data will be identified from systematic reviews of the published NBSP literature. These systematic reviews will be supplemented by expert elicitation methods where published data is not available to estimate the difference in costs or benefits. The key drivers of cost and benefits will be identified using sensitivity analyses. The type and degree of parameter (using probabilistic sensitivity analysis) and model structure (using scenario analysis) uncertainty will be identified. If appropriate, formal value of information methods will be used to quantify potential value of future research and inform research prioritisation in the context of NBSP.

6. Respondent feedback to study findings [RO8&9]. Three focus groups will be run providing a chance to check the team's interpretation of the qualitative data, the participants' views regarding the study's conclusions, and gather suggestions for future research. This approach has been used previously(84) and follows recommendations of how to test NBSP materials.(49) To do this the PI will give a short presentation to the group including a brief overview of the study aims, the results of the empirical studies and the recommendations and range of policy options and alternative models to be presented to the HTA. Within this presentation we will highlight any uncertainties or contradictions in the results, or any aspects where we seek clarification of the meaning of responses or suggestions made by participants to ensure this is discussed by the group. Whilst presentation content will be standard across the group, they will be tailored so as to be accessible to all. The focus of the groups will be to gain consensus views on the acceptability, broader impact, impact on parent understanding, effectiveness and efficiency of each of the alternative models. Whilst the aforementioned will

have been examined in detail within the project, this phase will enable the holistic evaluation of the alternative models and recommendations. This model of modifying research based policy recommendations via focus groups with providers and users has been used previously by the PI when making recommendations about NBSP communication issues.(23) Further, as focus groups will enable the observation of how such alternatives are discussed and concerns negotiated in social settings these data will provide insight into the implicit processes and potential barriers which may affect the success of alternative models of communication.(85) The groups will be hosted at the University with refreshments provided, and travel expenses covered. Additionally, participants who agreed to be re-contacted, but did not participate in the focus groups, will be sent a summary of the study findings, and offered the opportunity to provide their views during a telephone interview. Thus, enabling involvement via group discussion and "private" interviews, in keeping with best practice of developing guidance.(86) Finally key stakeholders in NBSP for cystic fibrosis and sickle cell will be invited to participate in a virtual focus group to discuss the study findings in relation to screening for these diseases to check how generalisable our project findings based on metabolic disorders are to the wider NBSP.

2.4 Planned Intervention

Phase one and the DCE will generate alternative models of consent and communication which will be ratified during the final study. One of the outputs of the study is an intervention that can be evaluated.

2.5 Planned inclusion and exclusion criteria

Inclusion criteria [study number indicated in brackets]:

[2] Health professionals: All regional screening co-ordinators. Midwives with experience of providing NBSP information in the community or a hospital. Parents: a sampling framework will be constructed to ensure maximum variation. Parents will be included from across the screening pathway (e.g. antenatally, screening conducted but results not received, post results) as research suggests that parents ability to process information during this time are reduced(46, 47) increasing the likelihood of recollection biases, making the use of whole pathway recollection designs problematic as they are likely to capture particularly salient recollections, rather than a realistic assessment of information needs. Using immediacy recall has been advocated in this setting.(61) Parents will be sought with a range of results including negative, positive and false positives (for each disorder). Parents of children with positve results will be identified through the charity CLIMB (Children Living with Inherited Metablic Diseases). Participation of parents who do not speak fluent English will be facilitated by offering study materials in their own language and providing interpreters. Specific attempts will also be made to ensure participation of fathers, young parents and those with lower education achievement as these are commonly underrepresented in the research(23) or may have different communication needs.

[3] practising midwives of any grade

[4] practising midwives of any grade and adults of child bearing age (18+ years)

[5] a hypothetical cohort of parents and up to five NBSP experts

[6] Participants from study 2. Key stakeholders for cystic fibrosis and sickle cell NBSPs.

Exclusion criteria

[2] Parents whose child has died or their child was born prematurely; who had newborn screening performed >180 days, or where multiple abnormalities were identified. Parents who do not have the capacity to consent.

[4] Parents who do not read English fluently due to the linguistic demands of the DCE
[6] Parents who require interpreters will be excluded from focus groups due to the fast paced discussion style of focus groups. Low participation rates of non-English speakers in research are likely to make it impractical to run language specific groups. These parents' views will be collected via interviews with translators.

2.6 Ethical arrangements

Risks and anticipated benefits for participants including how benefits justify risks.

In any interview there is a chance that interviewees may become distressed. The questions asked in the interviews will be designed by team members experienced in collecting sensitive data, and training and support will be provided to the interviewers to ensure that data is collected professionally. Written records of the interviews will have any identifiable information removed to protect participants' identities.

It is impossible to guarantee confidentiality of focus group data due to the group setting. Participants will be asked to respect others' views and maintain confidentiality of data, but will also be advised that as this cannot be guaranteed they should not discuss issues which they feel uncomfortable being disclosed outside the group.

It is our experience that although parents may become distressed when participating in research about newborn screening, they value the opportunity to discuss their experiences. They do, occasionally, however require more support. A formal distress policy will be formulated and agreed upon prior to study commencement. It is our experience that when researching actual service provision health professionals may disclose that the service is not being provided in a way that fits with guidance. Thus, all data will either be collected anonymously or the identity of those observed will be protected. The sounding out of study findings with health professionals in study six will help the project team report any such findings in a sensitive manner.

The project team includes a psychologist, lawyer, health economist, statistician, professor of midwifery, and neonatologist. All have experience of a conducting research with parents and health professionals and the PI has expertise in research about NBSP communication and the ethical issues such research entails.

Informing potential participants of possible benefits and known risks.

All participants in all studies will receive information outlining the possible benefits and known risks. Study materials will be designed by the team, reviewed by the scientific advisory group, parent reference group, and local NBSP advisors and approved by an ethics committee. They will receive information via a number of routes depending on the recruitment strategy, as outlined below [study number]:
[2] Health professionals will receive study materials direct from the team. Parents will receive study materials via health professionals (midwives for prospective parents, health visitors for parents post result) as well through subscription to the mailing list of the CLIMB charity to protect potential participants' identities. Administrators of each parenting page on social media websites will be contacted and asked to post a study

poster to their members. Interested parents will then contact the research team who will send them a participant information sheet. In order to facilitate recruitment of parents who are still pregnant, the Research Associate (RA), will attend antenatal clinics at Central Manchester Hospitals Foundation NHS Trust. Potential participants will be handed a study information sheet, consent to contact form and translation request leaflet in the clinic waiting room. No personally identifiable information of attending parents will be sought as the only inclusion criterion is that parents would have received the information about newborn screening at 9 weeks gestation. [3] Matrons and screening coordinators will be informed about the study and asked to inform colleagues who are members of the RCM about the study. Any midwives who express an interest in the study will be sent more information. [4] Participants will receive information either at midwife study days run by the British Journal of midwifery (midwives), an international midwifery conference (midwives), parenting clubs or Research Now (prospective parents) or from the study team (parents with experiences of false or true positive results). [5] Experts will receive information direct from the team. The team has experience of all these recruitment methods. The study information will be provided at least 24 hours before participation with the exception of the survey and DCE where there is no control over how long participants leave between reading study information and choosing to participate.

Obtaining informed consent from participants whenever possible or proposed action where fully informed consent is not possible (e.g. emergency settings).

Health professionals who wish to be interviewed [2], participate in the observation studies [3] or expert elicitation exercise [5] will return a consent form to the team. The RA will contact the health professional to arrange a suitable time for the interview or observation study. Health professionals participating in the telephone interviews or telephone survey will be asked to confirm their consent verbally once the recording equipment has started including whether they are happy to be contacted by the team for study 6.

Parents who are interested in being interviewed will return a "consent to contact**"** form to the team. The RA will then contact the parents to discuss the study and where appropriate arrange an interview. Confirmation will be sent with a second copy of the participant information sheet (PIS) in case the first is lost. Before the interview commences salient aspects of the study information will be discussed and time provided for participants to ask questions. Parents will be asked to sign a consent form before the interview begins. The consent forms will include consent to be re-contacted by the team for studies 4 (where appropriate) and 6. Where parents do not speak or read English the information within the PIS and consent form will be verbally translated by an interpreter. Three way telephone conversations will be held before the interviews to discuss the study. All other consent practices will remain the same.

Participants completing the DCE [study 4] will indicate consent by completing the measure.

[6] Participants from study 2 who agreed to be re-contacted and NBSP stakeholders will be sent a project findings summary and a PIS. They will be informed that the RA will contact them within a fortnight of sending the information to discuss the information, provide an opportunity to ask questions, establish whether they wish

to participate in a focus group and where appropriate book them into the next available group. Where this is not appropriate/accessible parents will be offered the opportunity to arrange a telephone interview. Confirmation will be sent with a repeat copy of the PIS. Before the group or telephone interview begins salient aspects of the study information will be discussed, including confidentiality issues inherent in focus groups. Participants will be able to ask questions and then asked to sign a consent form, or confirm their consent verbally for telephone interviews and the stakeholders' virtual focus group.

Proposed time period for retention of relevant trial documentation.

Documentation will be stored for five years in keeping with the University of Manchester's policy.

2.7 Proposed sample size

Qualitative studies

Whilst it is not possible to be certain of sample sizes for qualitative research, we have outlined approximate sample sizes below, based on our experience of conducting similar studies. All regional NBSP co-ordinators will be invited to participate (N=9) as previous work(78) evidenced variation in NBSP communication practice and discussions with co-ordinators about the design of this project suggests variance in practice persists. Current communication practice will affect views of alternative models, thus we will seek to capture maximum variation in practice. Midwives in the community and hospital setting will be sampled nationally, proportional to those involved in newborn screening and purposively to capture variance in experience. Preliminary discussions with screening co-ordinators and research midwives suggests the following numbers will provide a sample which proportionally represents front-line professionals involved in communication of NBSP information : 18 hospital screening co-ordinators, 14 community midwives and 4 hospital based midwives.

Within our parent interviews we want to represent views from parents across the screening pathway and with experience of different outcomes. Estimates are based on discussions with our local NBSP advisors, data from previous annual reports for the North West newborn screening laboratory, and experience of conducting interview studies with parents regarding NBSP communication. Based on this the following will be purposively sampled: 15 prospective parents after the initial time they should have received NBSP information, but prior to screening and birth of child; 15 parents following the heel prick test, but prior to results; 15 parents who receive normal results; 20 parents who receive a false positive result and 12 parents who receive a positive result for one of the metabolic disorders currently screened for. Parents will be identified by midwives (pre-NBSP result), health visitors or newborn screening labortatory staff (post NBSP result) a method of recruitment within the North West SHA a method of recruitment used by the PI in previous studies.(23) We will endeavour to also include parents with false and true positive results from the pilot study of the expanded NBSP. Given the timing of the pilot study relative to this project and the low numbers identified for each disease, this may be challenging, but would ultimately strengthen the design. Parents of babies with a positive result will be identified by the charity CLIMB.

Higher numbers of false positive parents are being sampled as they have the highest communication and support needs . Whilst many of the salient support needs may be common across false positive results, previous experience of parents awaiting carrier results for CF suggests that idiosyncratic personal experiences shape support needs and views of services. This indicates a need for larger samples to ensure saturation occurs. We have based the recruitment strategy, costs and timetable of the study on a 30% participation rate based on previous research using interviews.(45) Where possible we will strive to ensure all participants who have received results have done so in the previous year to minimise recall bias and control for changes in communication practice which have weakened previous studies.(23) If necessary, and theoretically appropriate, however we may augment this sample by inviting parents with children identified in previous years to participate. Whilst the overall number of parents is large (N=77) especially in comparison to previous studies adopting in-depth interviewing techniques, there is a desire to capture viewpoints across the screening pathway as parents report that screening is a continuous process, and to ensure that within each subsample something substantive can be said about suitability and preference for communication models.

Whilst all participants in study 2 will receive a summary of project findings we will aim to gather views from approximately one third of that sample in keeping with other studies in the field.(23) Thus we plan to run one focus group with service providers (N=10-12) and two with parents (N=~20). Telephone interviews (N=~7) will augment this data, target negative cases or facilitate parents who need interpreters to participate.

Expertise in qualitative methods, knowledge of the relevant literature and experience of previous health service research related to NBSP suggests the above sample sizes will enable data saturation. The project has been designed to ensure this by basing costs and timescales on higher numbers to ensure sufficient resources, if the data do not reach saturation before this point. Sampling frameworks for the interviews will be designed to ensure maximum variation(87) whilst using previous experience and the advisory groups to make pragmatic decisions to ensure the project is deliverable. In all instances sampling will be theoretically driven (88) and constantly reviewed to ensure that the balance is met between capturing a rich account of the social process whilst minimising redundancy and repetition in the data generation phase.

Quantitative studies

[3 i] The telephone survey will seek to interview midwives who have expressed an interest in being interviewed, having previously received information from contacts of the team (screening coordinators and matrons). Midwives (n=30) will be sought in a variety of trusts with different underlying demographics and the different aspects of the information pathway will be accounted for. For example, both community and hospital based midwives will be interviewed.
[3 ii] Data from study 2 and study 3i will direct purposive sampling of 5-8 midwives in the North West SHA to be directly observed for one week each. This will give a reasonable view of the breadth of current practice and feasibility of recruitment and observation has been discussed with the local NBSP advisors.

[4] Sample sizes of published DCEs range from ~30 to 100+(81) with no guidance existing on the ideal sample size. The planned sample size for the DCE study is 250 midwives and 500 parents, which will be a sufficiently large sample size to understand service provider and parents' preferences and compare the preferences of these groups. Using an appropriate mathematical design this sample size will also allow exploration of preference heterogeneity. These samples should be sufficient to estimate preferences in a study design comprising ~6 attributes, but pilot study data will also be used to inform the final sample size required. To obtain the sample of midwives, the Royal College of Midwives will email the heads of midwifery at a number of trusts and ask that if they would like to be involved in the study, that they email the researchers. The researchers will then give them a pre-written email, including a link to the online survey, to circulate to their teams. We will ask how many midwives are in these teams to obtain a response rate. After two weeks we will provide trusts who are taking part with follow up letters to distribute to their teams in order to boost recruitment. The first 100 midwives who complete the survey will be sent a £10 amazon voucher by email. They will have to provide their RCM membership number so that the researchers can verify they are midwives. Adverts highlighting the midwives DCE will be placed in the British Journal of Midwifery and the RCM magazine and the links will also be distributed to midwives using social media (twitter and facebook) to maximise survey completion. To achieve a sample size of 500 current and prospective parents two sampling frames will be used: existing collaborative links with the parenting clubs and *Research Now* who provide access to a panel of respondents through which participants with specific characteristics can be targeted. Such companies have been used in previous research to generate samples to examine public preferences.(84) The survey will be pre-piloted by a group of approximately six student midwives and members of the parent advisory group before it is later externally piloted by approximately 50 midwives and members of the public.

[5] The economic model will estimate the incremental costs and benefits of all models assuming an annual cohort of ~800,000 babies and one set of parents per baby in accordance with the predicted number of parents whose babies are screened via the NBSP.(5) Five NBSP experts will participate in an expert elicitation exercise. This number is based on previous experience of running such studies.

2.8 Data analysis

Qualitative analyses

The qualitative data will be audio recorded and transcribed verbatim with identifying material removed. One third of the interview transcripts and recordings will be reviewed by FU to ensure data quality. These data will be analysed using thematic analysis which seeks and reports the patterns inherent within the data collected.(89). Thematic analysis is a commonly used method that results in a rich, complex, yet accessible account of the data.(89) Aspects of grounded theory which enhance rigour will be used such as iterative data generation and analysis, constant comparative analysis, in-depth reflexive accounts,(90) and detailed line-by-line coding.

The data will be coded by the qualitative research fellow and the emerging coding framework will be developed with guidance from FU. To develop recommendations on alternative NBSP communication models, most themes will be coded at the manifest level,(91) however where appropriate a latent analysis will be conducted

enhance the depth of the analysis, utilising the flexibility inherent in thematic analysis.(92) Coding will be conducted systematically and iteratively. Deviant cases will be sought to test the emerging framework. Regular coding meetings will be held with the team, drawing on the strength of multidisciplinary viewpoints, to refine the coding structure.(93) Coding will continue until the team are satisfied that the framework adequately describes and captures the data and saturation has been achieved. The coding of data by independent researchers may be used to check reliability in thematic analysis(94) and ensures that the fit between data and analysis is maximised.(95) Data excerpts will be given to two independent researchers to code using codebooks. Percentage agreement on presence will be calculated (91). "Member checking" is a form of validation in qualitative research,(96) whereby initial findings are reported to participants to elicit feedback, as detailed above. This process is inherent in the final study. Data will be stored and organised within Nvivo software.

Quantitative analyses

[3] Descriptive statistics summarising the mean costs with variation and distribution will be produced to estimate the total (and fixed, semi-fixed and variable) costs for current models of information provision.
[4] Appropriate regression methods taking into account the need to include an opt-out question in the design (based on conditional logit models) will be used to analyse the DCE data. The preferences of midwives and parents will be compared. In addition, more advanced regression methods (such as latent class analysis) will be used to identify heterogeneity in preferences in sub-groups of the sample who show particular preferences for different types of communication or consent models.
[5] The decision analytic model will estimate the mean expected costs and benefits (using selected outcome measures) for each communication and consent alternative. An incremental analysis will compared the costs and benefits between the models. The scenario analysis will show the key structural drivers of cost effectiveness. The probabilistic sensitivity analysis will be used to show the variation around the mean costs and benefits and also be used to generate an estimate of the value of perfect information.

2.9 Proposed outcome measures

This is a mixed methods project which will generate a range out outcomes. The qualitative work will provide an outline of parents' and health professionals' views of alternative communication and models grounded in their personal experience of the NBSP. In the final phase focus groups will seek a consensus view on the preference, feasibility, acceptability and possible impact on parents' understanding of nascent models of communication and consent. These data will also illustrate how such preferences are shaped by social group processes. Telephone interviews will permit the inclusion of views from participants who are unable to participate in focus groups. This will also enable an in-depth and personal reflection at the idiopathic case study level of the implications of the study findings. This phase will be conducted 9-15 months after the parents were initially interviewed. It is our experience from previous work that returning to parents in this fashion enables them to reflect on their earlier accounts and also add to the depth of the data by reflecting on their current adaptation to NBSP information.(23) This will be crucial as work suggests that the mode in which parents are informed may be used by parents to in turn convey information to the wider family. Thus, whilst changes in communication

models may be sufficient for individuals at the time of testing, it is important to look at the wider implications of this communication event which commonly occurs many months after initial screening.(97)

The costing study will provide a description of the types of resources driving the total cost of current models of communication and consent. The primary outcome will be the mean costs (total, fixed, semi-fixed and variable) with a description of the variation and distribution of the mean costs. The DCE will provide a measure of stated preferences that reflect a quantitative description of the trade-offs that people make between service and outcome attributes when valuing preferences for a model of communication or consent. The economic model will provide a measure of the expected incremental costs and benefits of proposed new models of communication or consent compared with a standardised description of current practice. It will also provide a measure of the uncertainty and key parameters driving cost effectiveness and the value of future research.

2.10 Research Governance –

NHS NREC approval will be sought via IRAS for studies 2-6. University of Manchester ethical approval will be sought for inclusion of prospective parents in study 4. The University of Manchester will act as sponsor in this project.
As this is not a trial, a trial steering committee and data monitoring and ethics committee will not be convened. Rather we have confirmed appointments of the following advisory groups:

3. ***Project timetable and milestones:***
See overleaf

4. Expertise:
Dr Fiona Ulph is a senior qualitative methods advisor for the NIHR North West Research Design Service and a chartered health psychologist. She has extensive experience of using qualitative methods and has conducted research into the understanding and communication related to the UK NBSP for the past nine years. She has delivered relevant projects for the HTA [e.g Communication of carrier status following universal newborn screening for sickle cell and cystic fibrosis(76)] and the Department of Health.

She will have overall responsibility for running the project, including managing the study budget, maintaining research quality whilst ensuring objectives are delivered on time, and creating clear lines of communication between all members of the team. She will act as line manager for the qualitative researcher and directly supervise the literature review, design of qualitative measures, provide additional qualitative training, audit interview and focus group practice, contribute to the data analysis, draft publications and oversee dissemination. She has convened the advisory groups and will ensure there is clear communication between them and the research team. She will ensure that all aspects of the project are conducted in line with research governance and ensure that data and documents are available for audit. She will maintain communication with the HTA, prepare and approve reports for the HTA and notify them of any changes in the project. Although she has relevant

experience and expertise she will be mentored by Professor Katherine Payne throughout this project, with additional team members providing guidance when appropriate. Additional time and costings have been provided for this work.

Professor Katherine Payne, a health economist, has experience designing and conducting DCEs, using national surveys to identify use of resources and variation in costs, designing and populating economic models and using expert opinion to populate economic models in the absence of robust published data. She will act as line manager for the health economic researcher, mentor to FU and be a member of the scientific advisory group.

Professor Kieran Walshe, a professor of Health Policy and Management, works at the interface between research and practice. He is an associate director of the National Institute of Health Research health services and delivery research programme, which exists to serve the research needs of managers and clinicians in the NHS. He will provide expertise in evidence synthesis to guide the work on the realist review and will provide ongoing support with study management and dissemination.

Professor Tina Lavender, a international leader of maternity care research, is CI for a number of research grants in this field. She will provide expertise in research within the perinatal field, and will provide ongoing support with study design, management and dissemination

Steve Roberts, a medical statistician, has extensive experience in observational and experimental studies in health services research and integrating statistical modelling with qualitative work. He will support the quantitative study design and analysis, and contribute to the study management and dissemination.

Fiona Ulph, Katherine Payne, Tina Lavender and Steve Roberts, have experience of mixed-methods studies.

Rebecca Bennett, a senior lecturer in bioethics, specialises in analysing policy regarding screening newborns to clarify whether the standard of consent is ethically defendable. She will advise on the consent models and contribute to drafting of reports.

Suresh Victor, an Honorary consultant neonatologist, has experience of neonatal research. He will advise on medical aspects of the disorders and contribute to study management and drafting of reports.

A research fellow with qualitative experience will work full time on this project to conduct the literature and communication protocols review (study 1) and collect and analyse the data for studies 2 and 6.

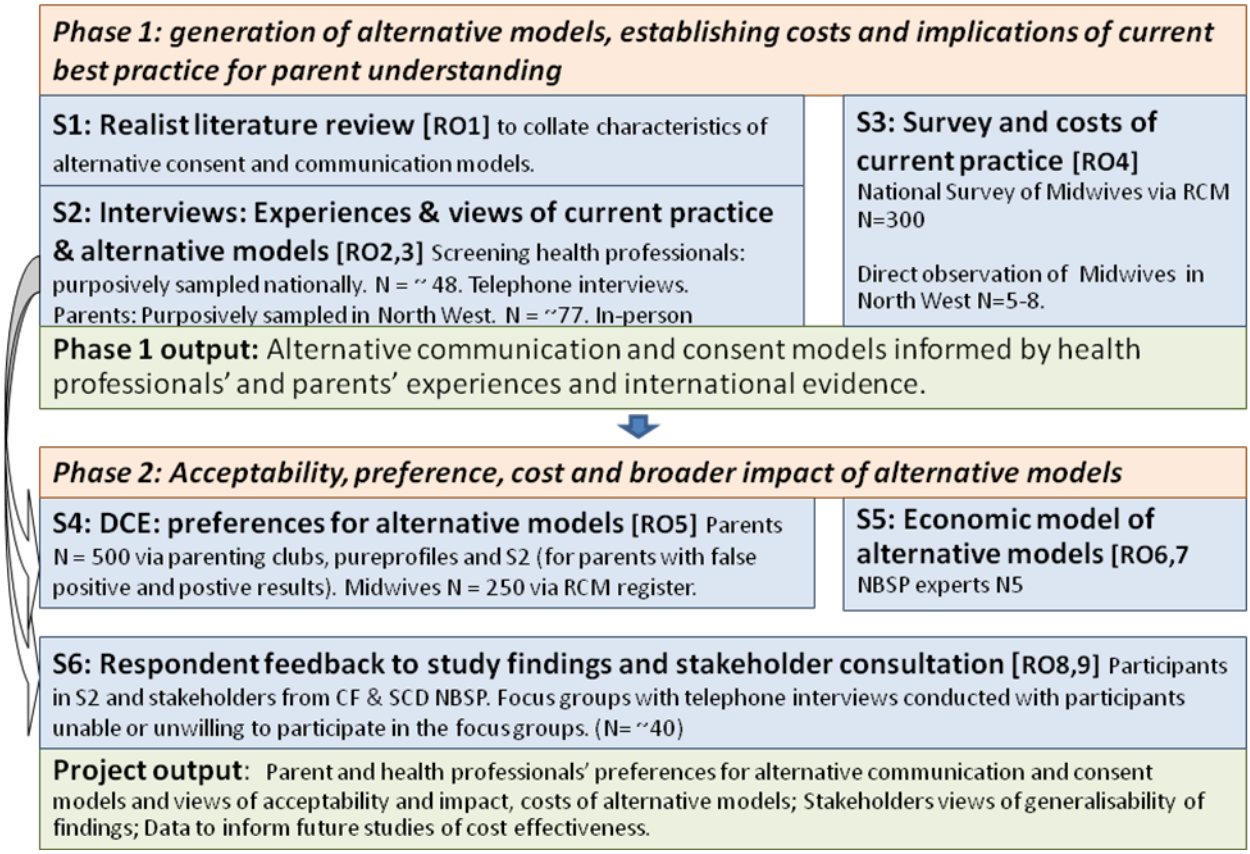
A research associate with health economic experience will work full time on the study and will collect and analyse data for studies 3-5.Both researcher will attend all team meetings, write draft reports and publications, and contribute to dissemination activities.

5. Service Users:

This proposal has been informed by a Parent Reference Group (PRG). The PRG members are drawn from St Mary's Hospital, Manchester, which has an active research user forum. Members are parents of newborn children who will therefore have a recent experience of newborn screening. In constructing this group, we have taken advice from the Greater Manchester, Lancashire and South Cumbria Medicines for Children Research Network. We have also followed guidance from INVOLVE and will be using a consultation model to PPI (98)

Feedback from the PRG will occur via the group lead. Members will be informed of areas for discussion and asked to review and comment on various documentation produced. Regular two-way communications between the RUG and research team will ensure consensus on appropriate modifications and provide the research team with an opportunity to report back to the group about changes made in light of their recommendations. This group has been consulted at the research design stage and have worked alongside researchers in developing this proposal. This collaboration will continue throughout the research period. PRG members will actively participate in shaping the patient information sheets, consent forms, interview schedule, data analysis and dissemination. The group will also be particularly valuable in assisting with the interpretation of the findings and subsequent recommendations. The group will meet at around the same time as the Steering Committee. The research team will update them regarding progress since the last meeting including, rate of recruitment and other study related issues. The group will then be encouraged to discuss the project independently with no researchers present. Following the discussion, the group will be given an opportunity to provide their feedback; this will be done through the group lead. Appropriate costs have been included to cover travel costs and costs of carers.

6. Flow diagram:


Phase 1: generation of alternative models, establishing costs and implications of current best practice for parent understanding
S1: Realist literature review [RO1] to collate characteristics of alternative consent and communication models.
S2: Interviews: Experiences & views of current practice & alternative models [RO2,3] Screening health professionals: purposively sampled nationally. N = ~ 48. Telephone interviews. Parents: Purposively sampled in North West. N = ~77. In-person
S3: Survey and costs of current practice [RO4]
National Survey of Midwives via RCM N=300
Direct observation of Midwives in North West N=5-8.
Phase 1 output: Alternative communication and consent models informed by health professionals' and parents' experiences and international evidence.
Phase 2: Acceptability, preference, cost and broader impact of alternative models
S4: DCE: preferences for alternative models [RO5] Parents N = 500 via parenting clubs, pureprofiles and S2 (for parents with false positive and postive results). Midwives N = 250 via RCM register.
S5: Economic model of alternative models [RO6,7
NBSP experts N5
S6: Respondent feedback to study findings and stakeholder consultation [RO8,9] Participants in S2 and stakeholders from CF & SCD NBSP. Focus groups with telephone interviews conducted with participants unable or unwilling to participate in the focus groups. (N= ~40)
Project output: Parent and health professionals' preferences for alternative communication and consent models and views of acceptability and impact, costs of alternative models; Stakeholders views of generalisability of findings; Data to inform future studies of cost effectiveness.

	-10	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Ethics & R+D approval	FU/KP																														
Recruit Staff	FU/KP																														
STUDY 1 *Review*																															
Review conducted		All	RAs	RAs	RAs	HE	HE	HE																							
Publication									FU/KP	FU/KP																					
STUDY 2 *Interview*																															
Inform regional co-ordinators				Q																											
Regional co-ordinator interview					Q																										
Arrange MW interviews						Q	Q																								
Conduct MW interviews							Q	Q	Q																						
Send study packs to recruiters							Q	Q	Q																						
Arrange parent interviews							Q	Q	Q	Q																					
Conduct parent interviews							Q	Q	Q	Q	Q																				
Transcribe Interviews					£	£	£	£	£	£	£	£																			
Analyse interviews					Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q	Q															
Write up												Q	Q	Q	Q	Q	Q	Q	Q												
STUDY 3 *MW survey & Obs*																															
Draft, pilot and send out survey								HE																							
Data entry									HE	HE	HE																				
Recruitment observation study									HE	HE	HE																				
Conduct observation study										HE	HE	HE	HE																		
Analysis of observation study											HE	HE	HE	HE																	
Write up														HE	HE	HE															
STUDY 4 *DCE*																	HE	HE	HE	HE	HE	HE									
STUDY 5 *Economic modelling*															HE	HE	HE	HE	HE	HE	HE	HE	HE								
STUDY 6 *Qualitative*																															
Convene Focus groups																							Q								
Run Focus groups																								Q							
Conduct telephone interviews																									Q	Q	Q				
Transcribe data																									£	£	£				
Analyse data																									Q	Q	Q	Q	Q		
DISEMINATION																															
Final report																				Q	Q	Q	Q	HE	HE	HE	HE	HE	All	All	All

FU/KP Fiona Ulph and Katherine Payne with guidance from wider team; Q= qualitative research fellow; HE= health economist research fellow; £ = outsourced task; All – team lead by PI with RAs doing fieldwork/drafting

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