FULL STUDY TITLE: Rethinking Strategies for Positive Newborn Screening Result (NBS+) Delivery (ReSPoND): a process evaluation of co-designing interventions to minimise impact on parental emotional well-being and stress.

SHORT STUDY TITLE / ACRONYM: Rethinking Strategies for Positive Newborn Screening Result Delivery / ReSPoND

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This is protocol has regard for the HRA guidance and order of content

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publically available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

For and on behalf of the Study Sponsor:

Signature: Date: 20/11/2017

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Name (please print):

....Professor Chris Hull.....

Position:

.... Associate Dean for Research and Enterprise.....

Chief Investigator:

Date: 20/11/2017

Signature:

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Name: (please print):

...Dr Jane Chudleigh.....

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SUMMARY:

Newborn blood spot screening (NBS) seeks to identify pre-symptomatic babies that are affected by genetic or congenital conditions(1). It is known that early diagnosis leads to better health outcomes for the child(1, 2).

Each year, around 10,000 parents[1] of babies born in the UK are given a positive newborn blood spot screening (NBS+) result. This initial NBS+ result occurs around 2-8 weeks, depending on the condition, after birth(3, 4). Despite guidance(1), NBS+ results are inconsistently delivered across UK-regions(5-8) and there is evidence that many parents are dissatisfied with how NBS+ results are communicated(6, 7, 9-13). As most infants will be asymptomatic when parents receive the NBS+ result(3, 4), it is vital that the process of communication is carried out carefully to avoid a negative effect on subsequent concordance with treatment and relationships with health professionals(6, 7, 13, 14). Concordance and trust (in health professionals and with the NBS result) are important considerations(15) to facilitate timely uptake of confirmatory diagnostic testing and treatment to maximise outcomes for the affected child(3, 4). Poor communication can also affect bonding between parents and their baby and ongoing parental and social relationships(6, 7, 16). Family systems theory will be used as a theoretical basis for this work because of its focus on communication, adaptation to new perspectives within the family and management of relationships(17). Enabling shared decision making in health care by incorporating patient/parent experiences is vital to ensure negative sequelae are minimised(18).

Since a recent expansion in January 2015, NBS in England and Wales now covers nine conditions. The NHS Newborn Blood spot Screening Programme (NBSP) recently discussed grouping these into four condition specific groups (CSGs) which will be used for this study (Table 1). The reasoning behind these categories is based on the urgency with which communication of the NBS+ result should occur.

This recent expansion of UK NBS to include nine conditions means there is added pressure for a cost-effective approach to the communication of NBS+ results. There are some data on the estimated cost of current models of information provision antenatally for the NBS programme but no data exist on the costs of providing NBS+ results or subsequent use of healthcare resources(19, 20).

[1] The term 'parents' refers to parents, carers or guardians.

Table 1: Condition specific groups (CSG) in the Newborn Bloodspot Screening Programme (NBSP)

Group	Conditions
Genetic/metabolic 'at immediate risk'	medium chain acyl CoA dehydrogenase deficiency (MCADD), maple syrup urine disease (MSUD), isovaleric aciduria (IVA)
Genetic/metabolic	Sickle Cell Disorder (SCD); Cystic Fibrosis (CF); phenylketonuria (PKU); homocystinuria (HCU); and glutaric aciduria type 1 (GA1)
Other affected	Hypothyroidism (CHT)
Carriers	SCD; CF

Primary research question: Can parents and staff[2] co-design interventions to improve delivery of initial positive NBS (NBS+) results to parents that can be successfully implemented into routine practice in a cost-effective manner?

Secondary research questions:

1. How are NBS+ results currently delivered to parents for the condition specific groups (CSGs) and what are the perceived benefits?
2. What are the current experiences of staff delivering, and parents receiving, NBS+ results for the CSGs?
3. What aspects of the new, co-designed interventions and local approaches to implementation are important in terms of improving the delivery of NBS+ results?
4. What are the costs associated with the delivery of the new, co-designed interventions and subsequent use of healthcare services and how does this compare with the costs associated with current strategies?
5. Which outcomes will be important to include in a subsequent evaluation study of the new, co-designed interventions from a stakeholder perspective?

Keywords: newborn screening, cystic fibrosis, sickle cell disease, metabolic disorders, congenital hypothyroid, communication.

[2] The term 'staff' refers to health professionals including, for instance, those employed in Newborn Screening Laboratories, Nurse Specialists, Consultants, Health Visitors, Midwives

FUNDING AND SUPPORT IN KIND

FUNDING and SUPPORT	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
NIHR Health Services and Delivery Research Programme, National Institute for Health Research, Evaluation, Trials and Studies Coordinating Centre, University of Southampton, Alpha House, Enterprise Road Southampton SO16 7NS	Funding the study
British Thyroid Foundation Suite 12, One Sceptre House, Hornbeam Square North, Hornbeam Park, Harrogate, HG2 8BP	Member of the Study Steering Committee and assistance with identification of PPI members
CLIMB Climb Building, 176 Nantwich Road, Crewe, Cheshire, CW2 6BG	Member of the Study Steering Committee and assistance with identification of PPI members
Cystic Fibrosis Trust One Aldgate, Second floor, London, EC3N 1RE	Member of the Study Steering Committee and assistance with identification of PPI members
National Society for Phenylketonuria PO Box 3143, Purley, CR8 9DD	Member of the Study Steering Committee and assistance with identification of PPI members
Sickle Cell Society 54 Station Road, London, NW10 4UA	Member of the Study Steering Committee and assistance with identification of PPI members

ROLE OF STUDY SPONSOR AND FUNDER

The Sponsor (City, University of London) and the funder (NIHR HS&DR) will abide by the terms set out in the 'research contract' between the Secretary of State for Health and City, University of London signed on 04 September 2017.

ROLES & RESPONSIBILITIES OF STUDY MANAGEMENT GROUPS

Dr Jane Chudleigh (JC) (PI) will oversee the conduct of the study and project manage its day to day conduct from recruitment to dissemination and co-ordinate management of the research team. A full-time research assistant will be recruited by City, University of London for 24 months to assist JC with data collection and analysis for phases 1-4. Professors Jill Francis (JF) and Alan Simpson (AS) 5% each, will support and mentor JC in leading and managing the study drawing on their experiences of conducting large, national studies. Professor Francis has extensive experience in implementation science (translating evidence into practice), in particular, using theories, evidence and methods for changing the clinical behaviours of healthcare professionals and applying and developing complex intervention methodology including, intervention design, intervention fidelity and feasibility and process evaluation. Professor Simpson has expertise in co-production and service user and carer involvement in research. He recently led and completed two NIHR HS&DR-funded cross-national studies in both community and inpatient settings and was co-investigator on the successful NIHR funded 'Safewards' programme of research. Simpson led and facilitated the high levels of co-production on all three studies. Both will therefore advise on data collection and facilitating the co-design process for this phase of the work. Professor Jim Bonham (JB) will assist with recruitment, data collection and collaboration with the NBSLs and provide input into the development and implementation of the intervention in practice and design of the definitive evaluation study. Dr Mandy Bryon (MB) and Dr Louise Moody (LM) will have an advisory role with regard to the intervention development and implementation into routine practice and LM will support the requirements gathering for the design of the intervention. Dr Fiona Ulph will assist with recruitment, data collection and qualitative data analysis and will have an advisory role with respect to the intervention development and implementation into routine practice. Dr Kevin Southern (KS) will advise on study site selection, the intervention development, dissemination and incorporation into practice as Chair of the UK NBS Programme Board. Professor Steve Morris will oversee the economic analysis assisted by a part time RA (50%FTE) during Phases 3 and 4.

The co-applicants are based in different institutions and so will communicate and monitor progress of the project via monthly, written project reports and monthly meetings via Skype.

Steering and Advisory Groups

In order to monitor the success and progress of the project, an independent study steering committee (SSC), a project advisory group (PAG) and a PPI advisory group (PPIAG) will be convened at the start of the study. The SSC, PAG and PPIAG will meet in person for a half day every six months. The research team will also liaise via telephone conference call monthly.

As per the NETSCC TSC SSC Guidance (2016), the SSC will consist of an independent Chair, external stakeholders (such as representatives from Public Health England and relevant charities), relevant methodologists (such a health economist) and a clinician. The purpose of the SSC will be to provide advice on aspects of the project to stakeholders, monitor the progress of the study, ensure the rights, well-being and safety of participants are maintained, ensure appropriate ethical and other approvals are obtained and agree substantial protocol amendments.

The PAG will include the research team, a PPI representative and a member of the SSC. The primary purpose of the PAG will be to monitor on-going progress of the study and resolve any issues that arise. The PAG will also review data collected, and provide feedback on manuscripts and dissemination plans.

The PPIAG will include PPI members (n=6 per meeting) and will provide feedback on documentation and data collected and data collection tools and eventually on manuscripts and dissemination plans. The PPIAG will be jointly chaired by a PPI member and the project lead JC.

The PAG and PPIAG will report directly to the SSC. The SSC will report directly to NIHR, and the study sponsor and will also provide feedback to the PAG and PPIAG where required.

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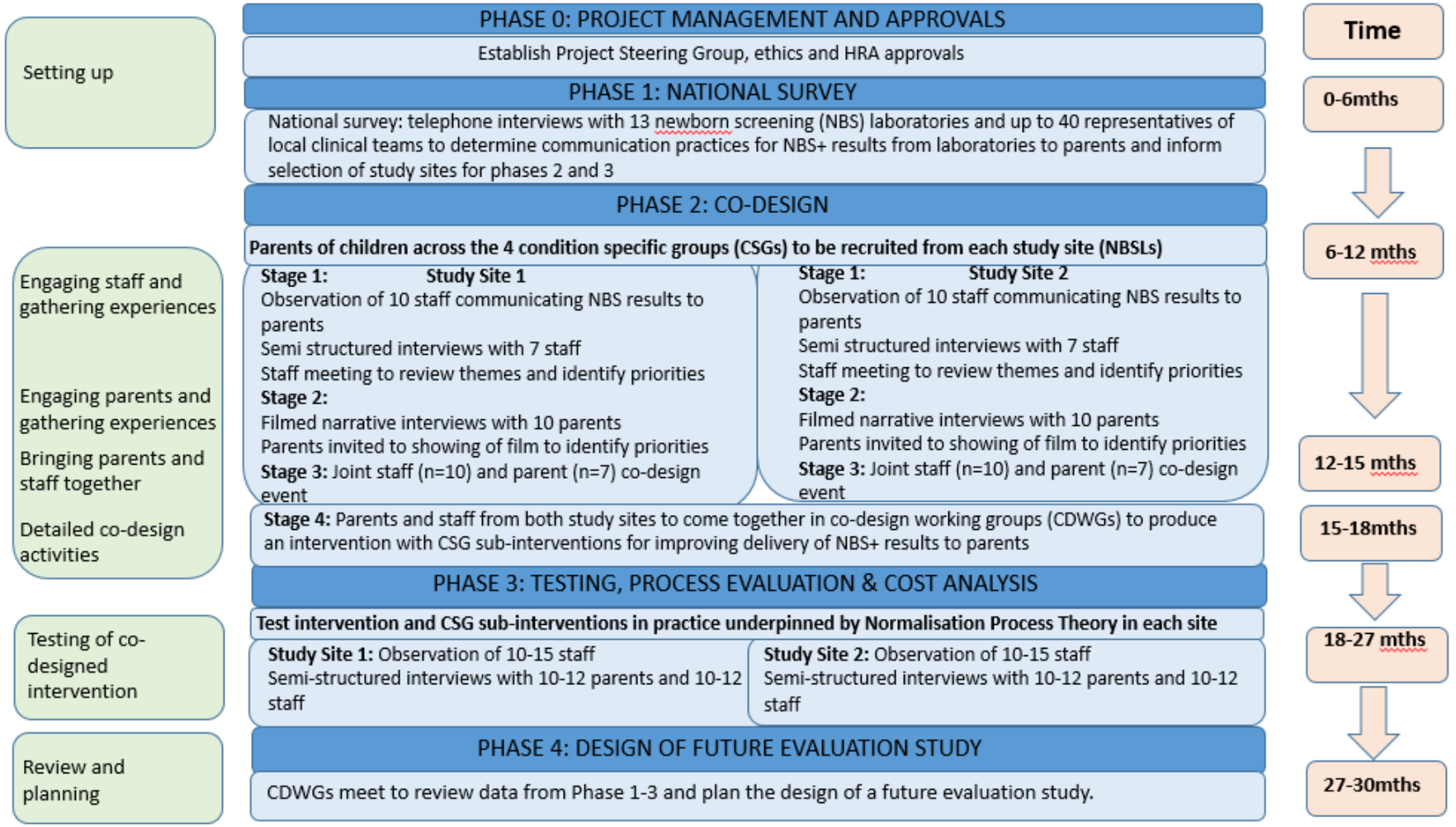
The PPI members of the advisory groups will attend training on their role at Guy's and St Thomas' NHS Trust Biomedical Research Centre. However, if individuals highlight specific training needs we will provide additional training via 1:1 supervision if relatively brief or they can access relevant modules and courses at City, University of London.

STUDY FLOW CHART



STUDY PROTOCOL

Rethinking Strategies for Positive Newborn Screening Result (NBS+) Delivery (ReSPoND): a process evaluation of co-designing interventions to minimise impact on parental emotional well-being and stress.

1. BACKGROUND AND RATIONALE

Each year in the UK, over 10,000 parents are informed of their child's positive NBS result around 2-8 weeks, depending on the condition, after birth (3, 4). Most babies with initial positive NBS (NBS+) results for SCD and approximately 10% of those with an NBS+ result for CF will later be confirmed as gene carriers but unaffected by the disease. However approximately 1,500 of the babies will eventually be diagnosed as being affected by one of the nine life changing conditions that are currently screened for(3, 4). The clinical spectrum in screen positive cases varies enormously and consequently the message to parents needs to be carefully crafted to prepare for a range of outcomes. Communication of NBS+ results is a subtle and skilful task which demands thought, preparation and evidence to minimise potentially harmful negative sequelae(6, 7, 13, 14, 16).

Current NBS+ Communication Practices

Generic guidelines for breaking bad news exist(21-24) but research to support them is lacking(25, 26). Much of the literature about breaking bad news comes from adult oncology(27-30) and paediatric palliative care settings(31, 32). Specific guidance regarding an initial NBS+ result currently focuses on the 'chain of communication' from the NBS laboratory to 'appropriately trained health professionals' and then to parents(1). This guidance does not define what is meant by 'appropriate' training for health professionals in this context. Much literature to date has focussed on the physician's role when breaking bad news(33-35) but often the delivery of NSB+ to parents is the role of other health professionals. When the NBS result suggests a child may be affected or a carrier, leaflets are available for each of the screened conditions and it is recommended parents receive these at the same time as receiving the NBS+ result[3]. Guidance regarding the content and best mode of communication between health professionals and parents is generic and vague(1) and is not evidence based. Consequently, communication occurs in a range of ways but these are not

[3] https://www.gov.uk/government/collections/newborn-blood-spot-screening-programme-supporting-publications

currently well defined. A recent quantitative stated preference study indicated that parents have clear preferences for how information should be provided antenatally as part of a NBS Programme (NBSP) and identified that these preferences differed from how this information is given in current UK practice(20). This study suggested a need to identify specific models of communication for sub-groups of parents and therefore a stratified approach to communication strategies that may be dependent on parent characteristics or the type of NBS condition(36). It is important therefore, that these information preferences are also clarified after NBS when a positive screening result is being communicated indicating a child may be a carrier or affected by one of these life changing conditions(20).

Similar challenges with communication of NBS+ results to parents are faced internationally. In the United States (US), findings from telephone interviews with 270 parents following communication of carrier status after NBS for CF and SCD indicated that content and knowledge of the person imparting the result, was vital in terms of parental experience of the process(12). This was supported in another study in the US where qualitative interviews with 28 parents following their child's positive NBS result for CF demonstrated communication of the positive NBS result resulted in parental uncertainty and emotional distress. This was strongly influenced by the physicians' approach to informing parents of the result with face-to-face communication (as opposed to use of the telephone) and the physician having time and knowledge to explain the results in detail being preferable(10). A more recent study in Switzerland exploring parents' perspective of NBS for CF found that parental dissatisfaction with the communication of the NBS result was associated with poor information provision about the screening result and the actual disease, again demonstrating the importance of ensuring the information is delivered by someone who is well-informed(37).

Studies in the US which explored parental experiences of receiving a positive NBS result for the metabolic conditions suggested that the communication of these results is highly stressful for parents and improvements are needed(11, 38). One of the studies involved observation and audio recording of clinical consultations as well as interviews with parents regarding communication of their child's initial NBS+ result for the metabolic conditions. It showed that the methods used to communicate the NBS result and the condition specific knowledge of the individual imparting the result influenced parental dissatisfaction, anxiety and distress; results delivered over the phone, by staff not known to the families or without condition specific knowledge were viewed less favourably(11).

All existing evidence supports the importance of ensuring the initial communication of NBS+ results is handled sensitively, and considers individual parent characteristics, to minimise parental distress and consequences of this distress.

Variation in Communication Practice in the UK

There is some evidence of regional variations in the UK with regard to the approaches used to communicate NBS+ results and in particular, suspected carrier status for CF and SCD following NBS. These approaches include receiving the result by letter to in-person communication during a home visit(5, 39). The findings of Kai et al's study(39) informed the development of the current national guidelines for the communication process in the NBSP(1), which recommend face-to-face communication by an appropriately trained health professional. Despite these guidelines, a recent study reporting the findings from 67 interviews with parents about their experience of receiving CF or SCD carrier results following NBS indicated that disparity continues to exist regarding how the guidelines are implemented in practice(6). The findings also indicated variability in the content and the way the result was communicated which led to increased parental anxiety and distress; the perceived lack of knowledge of the person communicating the result led to additional distress rather than the actual result *per se*(6). A scoping exercise at a national meeting of the CF NBS special interest group in 2014 and further informal discussion at the same group in 2016 indicated that communication of positive NBS results for CF in the UK remains variable. This ranges from initial telephone contact with CF Nurse Specialist to face-to-face contact with a Health Visitor (often without knowledge of CF) or CF Medical Consultant with the content not being clearly defined indicating very little has changed since the original work of Kai et al(39). The issue of guidelines written for staff but not meeting the needs of patients (or parents in this instance) is not unique to NBS. There is increasing recognition of the need to create guidelines that enable shared decision making in health care by incorporating patient/parent experiences(18), especially where it is likely to impact on the patient's well-being and family relationships.

Impact of Poor Communication Practices

Poor, or inappropriate, communication strategies for NBS+ can influence parental outcomes in the short term(6, 7, 11, 13, 14, 37) but may also have a longer-term impact on children and families(16). Evidence suggests the distress caused can manifest in several ways including arguments between couples including apportioning of blame(6, 7, 40), alteration of life plans and inability to conduct tasks of daily living such as going to work or socialising(6), long-

term alterations in parent-child relationships(16) and mistrust and lack of confidence affecting ongoing relationships with staff(7). There is also evidence of increased parental distress resulting in parents reducing their child's interaction with others, particularly in the case of CF(6). Parents also experienced poor intra and interpersonal relationships within their family system and more widely(41).This again highlights the importance of creating guidelines that inform shared decision making in health care by incorporating patient/parent experiences(18).

Poor information provision when the initial NBS+ result is communicated to parents may also lead to identifiable, quantifiable and measurable consequences on healthcare systems and budgets such as additional consultations requested by parents to allay additional fears and impact on health status of the parent(6, 19). The process of delivering different approaches to information provision, involving a national strategy for all new births will also have a substantial impact on resource requirements, such as need for printing of leaflets and staff time to deliver information. In 2015, a systematic review summarised if, and how, information provision has been included in economic evaluations of NBSP(19). This review highlighted that only three studies included an estimate of the cost of information provision in their analysis and none of the studies captured the impact of information provision after screening(19). One study(42) referred to costs related to the impact of poor information provision specifically related to false-positive results rather than poor information provision at the time of communicating the initial NBS+ result *per se*. This review concluded that evidence existed that poor information provision in relation to NBS does impact on parents but there have been few attempts to quantify the impact of information provision in economic evaluations of NBS to date. Importantly this review confirmed that there are no current data on the long-term impact of poor information provision and subsequent use of healthcare resources and impact on parents' health and well-being. Following this review, Ulph et al(36) quantified the potential costs of different modes of information provision antenatally as part of the informed consent process for the UK-NBSP using mixed methods including telephone interviews and direct observation. This existing evidence base focussed on the informed consent process and did not identify the long-term costs of information provision in terms of the follow up use of healthcare resources.

With the expansion of the NBSP in 2015, now is the opportunity to ensure that the clinical advantages of this process continue to outweigh any long term possible negative psychosocial

consequences for the families involved. It is essential that approaches used to deliver this information to parents is informed by them and shaped to meet their needs. It may not be possible to remove parental distress completely from what is an upsetting time. However, it is important for staff to communicate NBS+ results in a manner that does not detrimentally affect parents' relationships with their child and other family members. Empirical evidence is lacking on the potential impact of information provision on parental well-being and decision-making strategies. Given the potential for the impact of information provision on finite budgets available to provide communication strategies on a national level, there is a need to understand both the short and long-term costs, of different aspects of the NBSP including the implications of providing NBS+ results, which have the potential to cause substantial parental distress thereby impacting on their well-being. A further consideration is ensuring parents are informed well enough to facilitate communication within and between family members. Most screened conditions are genetic in origin and therefore the NBS+ result can impact on cultural beliefs, future reproductive decisions and family communication(43-48).

2. THEORETICAL FRAMEWORK

The theory underpinning the proposed study is Family Systems Theory(17) because of the potential vulnerability of family relationships if the initial NBS+ information is not shared as effectively and empathetically as possible (51). This mixed-methods study will use four phases with defined outputs. The principles and methods of Experience-based Co-design (EBCD) will underpin intervention development(52-58). Normalisation Process Theory (NPT)(49, 50) will underpin the process evaluation of the new, co-designed interventions to improve delivery of NBS+ results to parents. An economic analysis will be undertaken to determine resource use and costs of current practice and implementing the new co-designed interventions. The nominal group technique(59, 60) will be used to inform selection of suitable outcome measures for a future evaluation study.

Family Systems Theory (FST)

Our initial work(7) and scoping of the literature showed that many parents were shocked to receive the initial NBS+ result. Despite consenting to the heel prick test immediately after their baby is born, most assume the test will come back negative. The initial NBS+ result can have significant impact on parents, and this has implications for their relationship with each other(6, 7, 40), within their family system and more widely(41, 61), with their newborn child(16) and their relationships with health professionals(7). Therefore, it is essential that

when parents are in receipt of a NBS+ result, they are helped to assimilate the information to enable them to cope and adapt as quickly as possible, to minimise distress and disruption to their relationships.

With the NBS+ result having consequences for more than one individual, it is appropriate to use Family Systems Theory (FST) as the theoretical basis for the study. FST focuses on the relationships between family members; between parents, parents and child but also with external relationships, in this case their relationships with health professionals because they will also influence how the family functions.

FST evolved from General Systems Theory one of the main tenets of which is *holism*, which states that a system (or in this instance family) cannot be understood by merely studying each of its components (or members) in isolation from each other. Therefore in order to understand the family and the way it functions, it is necessary to consider all members of the family and how they relate to each other as well as their responsiveness to external influences(62) cited in(63). It is also vital to remember that the family system is ongoing in that it has a past, present and future that will affect family functioning and how the NBS+ result is delivered may trigger many stressors that will not be immediately apparent(17, 64).

In FST all components of the family are regarded as interdependent. What happens to one member, will affect all other members of the family directly and indirectly(51, 64). However change is considered important and a normal part of families, which may result in both positive and negative consequences(17). It is how families deal with the change that is important. This is particularly true when this change is brought about because of potentially difficult news that family members may not be expecting to hear, such as initial NBS+ results.

FST postulates that family functioning has the potential to be affected by an event such as the communication of the initial NBS+ result and subsequently, facilitating the coping mechanisms used and adaptation of families to the NBS result is paramount. Therefore, the outcomes of communications about NBS+ results will be considered within the context of the family system; FST has guided our choice of data collection tools and questions. We will ask parents and staff to use a systemic approach to co-design the interventions, our process evaluation will view the factors affecting parents' coping and adaptation to the NBS+ result, the effects on their family and the impact of the intervention's delivery through this systemic family lens.

Experience-based Co-Design (EBCD)

EBCD is an approach to improving healthcare services that draws on participatory design and user experience design to bring about quality improvements in healthcare organisations(56). EBCD involves focussing on and designing patient/carer experiences rather than just systems and processes(52, 57, 58) and - through a 'co-design' process – enables staff, patients and carers to reflect on their shared experiences of a service and then work together to identify improvement priorities, devise and implement changes, and then jointly reflect on their achievements. EBCD was first piloted in an English head and neck cancer service in 2005(52). After a subsequent project in an integrated cancer unit, an online toolkit[4] was developed as a free guide to implement the approach. An international survey of EBCD projects in healthcare services identified 59 projects implemented in six countries (Australia, Canada, England, the Netherlands, New Zealand, and Sweden) during 2005-13 and a further 27 projects in the planning stage(55, 56, 65). The design of these studies has informed the sample size for the EBCD component of this work.

Normalisation Process Theory (NPT)

Research evidence needs to be translational; interventions can only have a significant impact on health and health care if they are shown to be effective, capable of being widely implemented and can be normalised into routine practice(49). For this reason, NPT(49, 50) will be used to study the implementation and assimilation of the co-designed interventions into routine practice in the two case study sites (NBSLs). NPT consists of four components that explain how interventions are embedded and 'normalised' into routine care. These are: coherence (how participants make sense of the new/different way of doing things), cognitive participation (committing to working in the new/different way), collective action (making the effort and working in that way) and reflexive monitoring (undertaking continuous evaluation and making adjustments if needed so that what was once a new intervention becomes a normal part of everyday practice). We will use NPT to guide and evaluate the translation of the co-designed interventions into routine practice.

Qualitative data collected during the process evaluation (non-participant observation and the semi-structured interviews) will be used to determine potential outcome measures for a future evaluation study. It is anticipated that there will be two main outcomes of interest; firstly, the impact on parents in terms of anxiety, stress, distress and well-being caused by communication of the NBS+ result (suitable measures might include GAD-7, PHQ-9, the

[4] http://www.kingsfund.org.uk/projects/ebcd

Parenting Stress Index(66), EQ5D[5] and/or ICECAP-A(67). Qualitative data from the observations and interviews will be used to determine where most overlap occurs and therefore which outcome measure(s) will be most suitable in a future evaluation study. Secondly, resource use, particularly, how frequently parents access different health services and the appropriateness of these consultations measured against national guidelines such as the Healthy Child Programme(68) and condition specific protocols, guidelines and standards. In addition, the nominal group technique(59, 60) will be used during Phase 4 to rank the components of the proposed outcome measures to determine their relevance and importance from a stakeholder perspective.

Economic Analysis

The aims of the economic analysis are to (1) calculate the costs of the proposed and current communication strategies (in Phase 3, but also using data collected in Phase 1), and (2) undertake a feasibility study for an economic evaluation of options to improve delivery of initial NBS+ results to parents (in Phase 4). With regards the latter, the objectives are to plan the economic evaluation that would accompany a full trial, identify potential sources of data, and how best to collect these. Hence the aim of the economic analysis in the present study is not to provide a definitive analysis of the costs, cost-effectiveness and budget impact of the planned interventions as that will not be possible until the full evaluation study (assuming this is shown to be feasible).

The economic analysis is underpinned by the need to consider opportunity cost when interventions to provide communication of NBS+ screening results will use finite healthcare resources (eg. laboratory time; NHS staff time) and influence subsequent use of resources caused by undue anxiety of parents receiving the result. Economic evaluations can provide decision makers with the required information to understand the opportunity cost of introducing a new intervention into a healthcare system. A full economic evaluation requires evidence of the incremental costs and consequences of a new intervention. A definitive economic evaluation is not feasible without a clear description of the current approach (comparator) or the proposed new intervention and potential pathways and resources involved; both aspects are the focus of this study.

3. AIMS AND OBJECTIVES

[5] http://www.euroqol.org/home.html

3.1 Aim: To co-design, implement and evaluate new interventions to improve delivery of initial positive newborn screening (NBS+) results to parents.

3.2 Objectives:

This study has the following objectives:

1. Identify and quantify the costs and benefits of approaches currently used to deliver NBS+ results to parents.
2. Select two case study sites (newborn screening laboratories (NBSLs)) in which to co-design interventions for communicating NBS+ results to parents.
3. Develop co-designed interventions in two case study sites for improving delivery of NBS+ results using Experience-based Co-design (EBCD) by:
    a. observing current practices for the delivery of NBS+ results to parents
    b. exploring the experiences of parents' receiving and staff delivering NBS+ results
    c. producing a composite film of key themes or 'touch points' from parents' perspectives
    d. enabling parents and staff to identify together, priorities for improving the delivery of NBS+ results
    e. co-designing interventions for the delivery of NBS+ results.
4. Implement the new interventions in the selected case study sites.
5. Undertake a parallel process evaluation underpinned by Normalisation Process Theory (NPT)(49, 50).
6. Explore which outcome measures best capture the impact on parents of the new co-designed interventions for use in a future evaluation study.
7. Quantify the resources required to deliver the co-designed interventions in the selected case study sites and compare these with the costs associated with current strategies.
8. Quantify the subsequent use of healthcare resources following the implementation of the co-designed interventions in selected case study sites.
9. Decide if further evaluation is needed, and if so plan the economic evaluation that would accompany a full trial.

3.3 Outcome

The main output from the research described will be co-designed and evaluated(49, 50) CSG interventions for the initial communication of NBS+ results to parents ready to be evaluated in a definitive evaluation study. These interventions will be co-produced with parents and

therefore will inform future shared-decision making between health professionals and parents(18). The proposed research could lead to exploration of the usefulness of general principles of communicating results that emerge from this work for other conditions where screening is recommended in children as well as breaking bad news in general. This might include conditions that may or may not be life altering/threatening but nevertheless can be distressing for parents. For example, delivering results of newborn hearing screening(82), findings from the physical examination of newborn babies (at birth and 6-8 weeks of age) including congenital cardiac abnormalities, congenital cataracts, cryptorchidism, developmental dislocation of the hip and findings from screening of children's eyes at 4-5 years of age. It may also be possible to extrapolate findings from the present study for the delivery of bad news to parents in instances such as children newly diagnosed with cancer or following diagnosis of chronic conditions such as diabetes or epilepsy.

Important and useable outcomes from Phases 1-4

Phase 1: (i) Description of current communication practice (ii) data from this Phase will be used in Phase 3 to compare costs of current practice with costs of the new co-designed interventions (iii) Inform the selection of relevant study sites for Phases 2-3.

Phase 2: Co-designed interventions for the four condition specific groups.

Phase 3: (i) Data will establish the cost of current communication strategies (using data from Phase 1) and costs associated with the co-designed interventions (ii) the acceptability and feasibility of the of the co-designed interventions (iii) inform choice of potential outcomes measures (GAD 7 PHQ 9 PSI(66) EQ5D[6] and ICECAP-A(67)) for use in a future evaluation study.

Phase 4: (i) Need for and design of a future evaluation study (ii) choice of relevant outcome measures and (iii) list of relevant resource use and costs to identify and quantify in a future evaluation study.

4. STUDY DESIGN

Phase 0: 0-6 Months Project Management and Approvals

Establish governance and project management arrangements, and secure ethics and HRA approvals. Appoint Research Assistant (RA) for phases 1-4.

[6] http://www.euroqol.org/home.html

Phase 1: 0-6 Months Identifying Current NBS+ Communication Strategies

Data Collection: A national survey will be used to define examples of current approaches, and associated resource use, for communication of NBS+ results from all 13 laboratories via clinical teams to parents for each condition specific group (CSG) in England. The survey will be informed by the literature and piloted before use in the main study. The survey, comprising closed and open-ended questions, will be conducted using semi-structured telephone interviews. The survey will identify all the ways NBS+ results are communicated from the NBSLs to parents via a range of health professionals by collecting data on: the mode of communication strategy (face-to-face; letter; telephone; e-mail); the resources involved in each communication strategy; who provides the information and their role; location (co-located or alternative site) of relevant services for the CSG. The communication pathway currently used in the UK setting will be identified from the point at which the laboratory produces the test result to when the parents are told the definitive result.

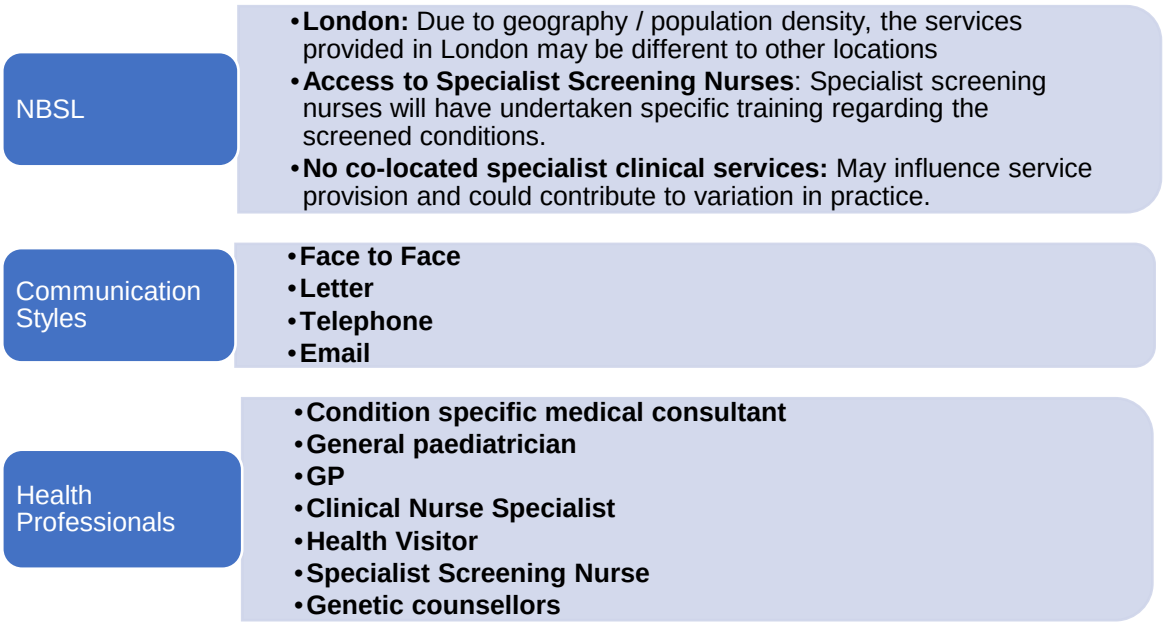
Setting / Context: Surveys will be completed by directors of all NBS-laboratories (NBSLs; n=13) in England and up to 40 representative members (10 for each CSG) of local clinical teams (medical consultants; general paediatricians; nurse specialists; health visitors; specialist screening nurses, genetic counsellors) who receive laboratory results and are identified as being involved in the 'chain of communication' from NBSL to parent.

Data Analysis: The aim of the data analysis is to describe and identify variation in approaches to communicating the NBS+ results and identify potential study sites for Phase 2. Quantitative data collected from the closed-ended questions will be analysed using descriptive statistics. Qualitative data from the open-ended questions will be analysed using content analysis(69). Communication pathways for each of the 13 NBSL will be described, by combining quantitative and quantitative data. Data collected during this Phase will be used in Phase 3 to determine the total cost of existing communication strategies, assuming the NHS perspective. Study sites for phase 2 will be identified using pre-defined criteria (see Figure 1) and selected using input from members of the research team and members of the PPI Advisory Group (PPIAG).

Sampling: To construct a sampling framework to inform selection of study sites for Phase 2 from the national survey, we will consider possible characteristics that are likely to differentiate communication of the NBS+ results. We will ask the PPIAG to review data collected and consider which are deemed to be the most influential in terms of being

representative of the range of approaches and resources used. An example of what these might include can be seen in see Figure 1.

Figure 1: Exemplar Framework: Features of the communication process for NBS+ results to parents



Phase 2: 6-18 Months Co-Design of New CSG-NBS+ Communication Interventions

This phase will consist of implementing the EBCD approach(54, 57) and will be guided by the EBCD Toolkit[7].

Stage 1: 6-12 months Engaging Staff and Gathering Experiences

Data Collection:

Non-participant observation: Staff responsible for communicating the initial NBS+ result to parents will be contacted and invited to participate. The process of communicating the result and the parents' initial reactions, how the health professional responded, questions asked and information and resources provided will be observed. These observations will provide insight into the procedures and practices and their relationships with the outcomes for the parent(70-73). All observations will be written up as field notes immediately after completion of the encounter, and a separate reflective researcher diary will record personal views or thoughts(74).

[7] https://www.kingsfund.org.uk/projects/ebcd

Semi-structured interviews: Semi-structured interviews will be undertaken with the staff responsible for communicating the initial NBS+ result to parents. They will be asked about their experiences of giving parents the screening result, their reactions, what makes the process easier or harder and any suggestions they have for improving practice.
Staff meeting: After the interviews, staff will be invited to attend a meeting to review themes arising from the observation and interviews and identify their priorities for improving delivery of NBS+ results.

Sampling:
Non-participant observation: A purposeful sample of 20 staff delivering NBS+ results to parents across the two study sites to ensure representation of all CSGs and to conceptualise and understand processes for delivery of NBS+ results.
Semi-structured interviews: A purposeful sample of 15 staff (NBSL staff, Nurse Specialists, Consultants, Health Visitors, Midwives, Genetic Counsellors) involved in communicating NBS+ results in the preceding 6 months. Previous work has identified that 12-15 interviews are sufficient to inform the co-design process(54).

Setting/ context: Staff involved in communicating the initial NBS+ result in the preceding 6 months in the two study sites.

Data Analysis:
Non-participant observation: The transcribed notes and observations will be thematically analysed(75) to provide rich accounts of the initial NBS+ result communication process for discussion in the subsequent stages and in the co-design working groups (CDWGs). An inductive approach to data analysis will be used and themes will be generated using a manifest approach(75).
Semi-structured interviews: All the interviews will be audio-recorded and transcribed and thematic analysis used to detail and describe the patterns emerging from the data as above(75)

<u>Stage 2: 6-12 months Engaging Patient/Carers and Gathering Experiences</u>
Data Collection:
Filmed narrative unstructured interviews: Filmed, narrative interviews with 20 parents (ensuring representation of CSGs) across the two study sites exploring their experiences receiving NBS+ results to identify key themes (touch points). Parents will be identified by the

person communicating the NBS+ result as a potential participant as this has previously been shown to be an effective recruitment method(7).

Patient / Carer feedback Event: Parents (n=20) will view a composite film of the interviews to ensure it is a fair and valid representation of their shared experiences, leading to a facilitated group discussion to highlight emerging issues and priorities for improvement.

Sampling: Informed by previous successful EBCD projects(55, 56, 65), a purposeful sample of 20 parents who have received a NBS+ result for their child in the previous 3-12 months ensuring representation of the CSGs. Where screened conditions are particularly prevalent in certain ethnic groups such as CF and SCD, purposive sampling will ensure representation of these groups and their experiences.

Setting/ Context: Volunteer parents in each of the two study sites who have infants who have received a NBS+ result in the preceding 3-12 months ensuring representation of each of the CSGs.

Analysis: Themes (touch points) identified from parent interviews developed into a 30-minute composite film.

Stage 3: 12-15 months Bringing Staff and Patients/Carers Together

Data Collection: Mixed staff and parent focus groups(76) using issues highlighted in the film with priorities from separate staff and parent meetings to facilitate discussion and to help identify joint priorities for improving delivery of NBS+ results.

Sampling: Informed by previous successful EBCD projects(55, 56, 65), a purposeful sample of participants from stages 1 and 2 consisting of 20 parents and 15 staff across both study sites

Setting/context: Joint staff and parent event to share experiences, view composite film and identify priorities for the co-design working groups (CDWGs).

Analysis: Focus groups will be audio-recorded and transcribed and thematic analysis used to detail and describe the patterns emerging from the data and identify joint priorities(75). In this instance, a deductive approach to data analysis will be used to identify the joint priorities of staff and parents. Themes will be generated using a latent approach(75).

Stage 4: 15-18mths Co-design Working Groups (CDWGs)

Data Collection: Parents and staff from both study sites come together in 4 CDWGs (6-8 members each) to consider how different components might be combined to produce interventions for improving delivery of NBS+ results to parents

Sampling: Informed by previous successful EBCD projects(55, 56, 65)**.** Four CDWGs consisting of parents and staff from stages 1-3 comprising of 6-8 members each.

Setting / Context: Staff who have been involved in the delivery of NBS+ results in the previous 6 months. Parents who have received a NBS+ result in the preceding 3-12 months.

Analysis: Parents and staff will use data collected in Phases 1-3 to work on their designated work stream to produce interventions for improving delivery of condition-specific NBS+ results to parents.

Phase 3 (18-27 Months) Implementation and Evaluation of New Interventions

Staff (n=20-30) identified as being involved in the delivery of initial NBS+ results (Phase 1) will be recruited. Each member of staff will receive training about the co-designed CSG NBS+ interventions. Members of the research team will visit each study site and provide clinical teams for the CSGs with 2 face-to-face training sessions during Phase 3 and follow-up support including resource packs of information to support the use of the new co-designed interventions in practice, online resources made available to staff via a study specific website and remote support via telephone/email. The face-to-face training will include a didactic approach but also include the use of role play. Staff will be asked to evaluate the training to ensure it has met their needs and identify areas for improvement. A parallel process evaluation underpinned by NPT(49, 50) will also be conducted.

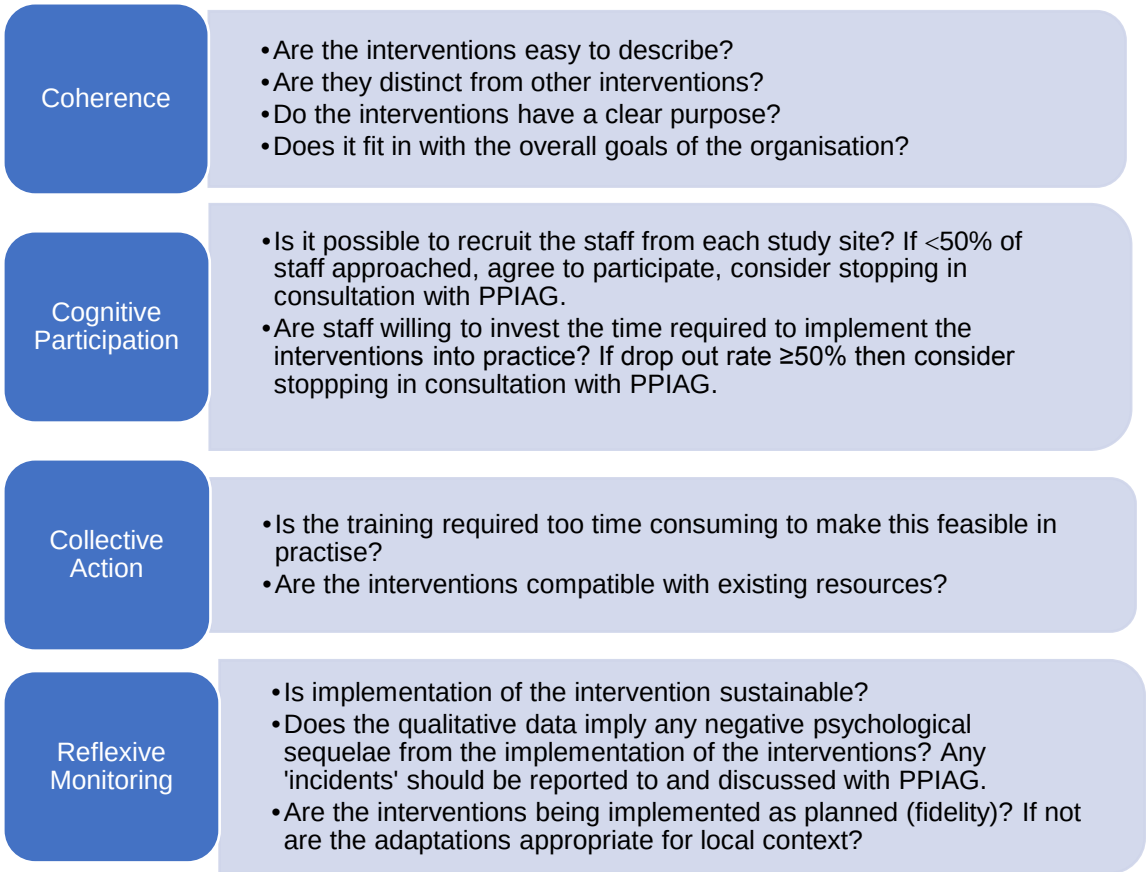
Success criteria (Figure 2) will be defined to ensure that implementation of the co-designed interventions is acceptable and feasible. This will be monitored by the research team on a weekly basis and if the answer to any of the questions contained within the success criteria is ‘no’, the study steering committee (SSC) and PPIAG will convene to discuss whether the testing of the interventions in practice should continue in its initial form.

Data Collection:

Non-participant observation: 20-30 staff, trained in the use of the new, co-designed CSG-NBS+ communication interventions will be observed delivering NBS+ results to parents ensuring representation of all condition-specific groups (CSGs) across the two selected study sites (NBSLs). The observer will observe the process of communicating the result and the

parents' initial reactions, how the health professional responded, questions asked and information and resources provided. These observations will provide insight into the procedures and practices and their relationships with the outcomes for the parent(70-73). All observations will be written up as field notes immediately after completion of the encounter and items of resource use recorded using a structured data collection tool, and a separate reflective researcher diary will record personal views or thoughts(74).

Figure 2: Success Criteria for Testing the Co-Designed Interventions in Routine Practice (49)



Semi-structured interviews: 20-25 parents and 20-25 staff will be interviewed across the two case study sites. These will be based on the questions proposed by the developers of the NPT approach(49, 50) and also include structured questions on healthcare resources use from the point of receiving the NBS+ result and the subsequent definitive result. The purpose will be to explore the views of the interventions, perceptions of factors that were influential (mechanisms of impact and context) and impact of a NBS+ on subsequent use of healthcare resources(77, 78). Parents and staff will also be asked for their views regarding other scenarios / conditions with ill children where they feel the interventions may be of use.

Economic data: Data collected in Phase 1 regarding costs associated with current communication practices will be compared with costs associated with the new co-designed interventions. The same time horizon will be used for both; the time from the point at which the laboratory produces the test result to when the parents receive the definitive result. This is consistent with the purpose of the study to co-design, implement and evaluate new interventions to improve delivery of initial NBS+ results to parents. For current communication practices and the new co-designed interventions, the resources required for each identified communication pathway / co-designed intervention will be defined and combined with unit costs to produce a total cost. Unit costs will be identified from published sources (79-81). Resource use data (e.g. type of NHS staff; time to deliver intervention; subsequent GP consultations, outpatient appointments and consultations with NHS services such as emergency departments and emergency hospital admissions) will be collected where possible using bespoke structured data collection tools. The data will be identified assuming the NHS perspective and reflect the time horizon from producing the NBS+ result to receiving a definitive result. We do not expect there to be costs incurred beyond this time point, but will explore this in the semi-structured interviews described above.

Sampling:

Non-participant observation: A purposeful sample of 20-30 staff implementing the co-designed interventions for the delivery of NBS+ results to parents across the two study sites (ensuring representation of all CSGs and specific ethnic groups where some of these diseases are more prevalent).

Semi-structured interviews: In order to achieve saturation, a purposeful sample of approximately 20-25 parents who have received their child's NBS+ result using the co-designed interventions and approximately 20-25 staff who have used the co-designed interventions to deliver the NBS+ result to parents.

Setting / Context: Two selected case study sites (NBSLs) from Phase 1.

Data Analysis: ***Non-participant observation:*** Data from the non-participant observation will be analysed thematically(75). A deductive approach to data analysis will be used and themes will be generated using a manifest and latent approach(75). These might include the structures (processes) and use of healthcare resources (type and time) required for delivery of the interventions, how parents and staff respond (implementation and mechanism of impact) and how external factors (language barriers, cultural difference) influence implementation of the intervention(s) (context)(77, 78).

Semi-Structured Interviews: All interviews will be audio-recorded and transcribed. A deductive approach to thematic analysis will be and themes will be generated using both a manifest and latent approach as above(75).

Qualitative data collected during the observation and semi structured interviews will be used to identify factors that influence experiences during the delivery of NBS+ results. These will be compared with the content of measures such as GAD-7, PHQ-9, the Parenting Stress Index(66), EQ5D[8] and ICECAP-A(67) to determine where most overlap occurs and therefore which outcomes might be most suitable in a future evaluation study.

Economic analysis: Resource use will be measured against national guidelines such as the Healthy Child Programme(68) and condition specific protocols, guidelines and standards. The resource use data will be combined with unit cost data identified from published resources to calculate the total cost of providing each intervention.

Phase 4: 27-30 Months Design of an Evaluation Study

Data Collection: A meeting of key stakeholders (NBS co-ordinators, directors of NBSLs, health visitors, midwives, genetic counsellors, parents) will be convened and the nominal group technique (NGT)(59, 60) used, to reach consensus about the need for, and potential design, of an evaluation study of the co-designed interventions.

Key stakeholders will be asked to consider pre-defined questions about (i) need for a definitive study (ii) selection of the co-designed interventions to include in an evaluation (iii) selection of relevant outcome measures, (iv) selection of relevant time horizon and resource use data to collect in a definitive evaluation (v) choice of future study design. The stakeholders will be presented with data collated from Phases 1 to 3 to inform each question.

Also in this phase, we will plan the economic evaluation for the main evaluation study. This will be based on the idea that we wish to estimate the lifetime incremental cost per quality-adjusted life year (QALY) gained. Within this framework the objectives are to identify: (1) the main cost components; (2) the resource use and unit cost data required for each of these cost components and how best to source these data; (3) potential sources of health-related quality of life data suitable for estimating QALYs in this patient group and, if primary data collection is required, how best to do this; (4) alternative outcome measures that might be suitable for the economic analysis; and, (5) potential sources that could be used to estimate long term outcomes. Examples of potentially relevant sources of unit cost data are the Unit Costs of Health and Social Care (79-81) and NHS Reference Costs. This will all be achieved

[8] http://www.euroqol.org/home.html

by reviewing previous and similar economic evaluations in this area (e.g., Bessey et al, 2014 (81)) and also via discussion in the stakeholder meetings described above.

Sample: A purposeful selection of up to 10 staff and parents involved in Phase 2 as well as representatives of the charities mentioned previously and members of the research team will be invited.

Data analysis: Qualitative data collated during the NGT will be analysed using thematic analysis(75). Quantitative data, such as ranking or rating data will be summarised using descriptive statistics.

5. RECRUITMENT and INFORMED CONSENT

5.1 Recruitment

Participants will be recruited as follows:

Phase 1: Contact details of Directors of newborn screening laboratories will be identified through the relevant website (http://newbornscreening.org/site/index.asp). The Directors of newborn screening laboratories will be invited to be the Lead Investigator for the research site and will be asked to provide names and contact details of staff within the laboratory who meet the inclusion criteria for the study. These staff members will then be contacted via email and invited to participate. Members of relevant clinical teams will be identified through the individual trust websites.

Phase 2: Staff identified in Phase 1 as being involved in the communication of positive newborn screening results to parents in the selected study sites will be contacted via email and invited to participate in this phase of the study.

Parents who fit the inclusion criteria will be identified by the relevant clinical nurse specialist (CNS). Once eligible parents have been identified, a member of the clinical team (CNS or doctor) will provide the parent with a participant information sheet at their next routine clinic appointment and ask the parents' permission to provide their name and telephone number to a member of the research team. At least 24 hours later, a member of the research team will telephone the parents, give them the opportunity to ask questions about the study, ask if they wish to proceed and if so, an appointment will be made to conduct the interview. Parents will be given a choice of location for the interviews, e.g. the hospital setting or the child/parent’s home.

Phase 3: Staff identified in Phases 1 and 2 as being involved in the communication of positive newborn screening results to parents in the selected study sites will be contacted via email and invited to participate in this phase of the study.

Parents who fit the inclusion criteria will be identified by the relevant clinical nurse specialist. Once eligible parents have been identified, a member of the clinical team (CNS or doctor) will provide the parent with a participant information sheet at their next routine clinic appointment and ask the parents' permission to provide their name and telephone number to a member of the research team. At least 24 hours later, a member of the research team will telephone the parents, give them the opportunity to ask questions about the study, ask if they wish to proceed and if so, an appointment will be made to conduct the interview. Parents will be given a choice of location for the interviews, e.g. the hospital setting or the child/parent's home.

Phase 4: Key stakeholders will be identified by the study steering committee.

5.2 Consent

All potential participants will receive a written participant information sheet (PIS) and have a least 24 hours to consider the information within the PIS before being asked to provide written informed consent. All participants will have the opportunity to ask questions prior to being asked to provide written informed consent The Chief Investigator or research assistant will obtain written, informed consent from all research participants.

6. ELIGIBILITY CRITERIA

6.1 Inclusion criteria for parents:

- Parents of children who have received a NBS+ result in the previous 3-12 months including true positives, false positives and children who later have a cystic fibrosis screen positive, inconclusive diagnosis (CFSPID).

This time frame has been chosen as the focus for this research based on feedback from parents of children who have previously received a NBS+ result. It has also been demonstrated that positive NBS can impact on child-parent relationships during the first year of life(16).

- If a parent/parents are already involved in the study and their baby dies, advice will be sought from the baby's health visitor and specialist team as to the appropriateness of their continued involvement in the study

6.2 Exclusion criteria for parents:

- Parent of children who have received a negative NBS result.

- Parents of children with co-morbidities that are likely to influence their perception of receiving their NBS+ result
- Inability of parents to understand and give informed consent
- Parents whose baby has died prior to being approached to be involved in the study
- Parents whose recruitment is contra indicated on psychosocial grounds (identified by their health visitor or specialist nurse).

6.3 Inclusion criteria for health professionals:

- Staff employed in NBS laboratories and involved in the processing of NBS+ results
- Staff who have been involved in communicating NBS+ results to parents in the last 6 months.

6.4 Exclusion criteria for health professionals:

- Staff who have not been involved in communicating NBS+ results to parents in the last 6 months.
- Staff who have personal experience of receiving a NBS+ result

7. ETHICAL AND REGULATORY CONSIDERATIONS

7.1 Assessment and management of risk

We appreciate the highly sensitive nature of the research that for parents and staff, recalling details of receiving or delivering NBS+ results may be highly emotive and potentially distressing. The project team have worked in this areas for many years and will ensure all new researchers are suitably trained. One of the project team (MB) is a Consultant Clinical Psychologist with over 10 years' experience working with families following NBS and will provide advice and support should any difficult situations arise during data collection. Also, as the data collected will be highly sensitive, issues such as anonymity, confidentiality and informed consent will be addressed in the recruitment of all participants, data collection processes and data storage.

The project involves a number of different data collection techniques. The project team is experienced in NHS research and research ethics applications, including recruitment, access and data collection such as observation of practice, interviews, and questionnaire design, the EBCD process and health economic processes.

As this is a national study involving health professionals and parents of patients from a multitude of NHS sites, gaining HRA approval and access is going to be labour intensive and

time consuming. For this reason, the ethical approval process commenced immediately after funding was secured. HRA approval and access will be sought as soon as ethical approval has been granted.

7.2 Research Ethics Committee (REC) and other Regulatory review & reports

Before the start of the study, a favourable opinion will be sought from a REC for the study protocol, informed consent forms and other relevant documents. Substantial amendments that require review by NHS REC will not be implemented until that review is in place and other mechanisms are in place to implement at site. All correspondence with the REC will be retained. The Chief Investigator will notify the REC of the end of the study. An annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the study is declared ended. The Chief Investigator's will be responsible for producing the annual reports as required. If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC.

Before any site can enrol patients into the study, the Chief Investigator or designee will ensure that appropriate approvals from participating organisations are in place.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. Available guidelines will be followed at all times (https://www.hra.nhs.uk/approvals-amendments/amending-approval/). The Chief Investigator or designee will work with sites so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

7.3 Peer Review

The study has been peer reviewed by RDS London, the study team and the funder, NIHR HS&DR Programme.

7.4 Patient and Public Involvement

Relevant organisations and charities including; The Cystic Fibrosis Trust, the Sickle Cell Society, the National Society for PKU, The British Thyroid Foundation, Children Living with Inherited Metabolic Diseases (CLIMB), the National Newborn Screening Programme and the NHS Sickle Cell Disease and Thalassaemia Screening Programme were all involved in the

original design of this project and will continue to be involved through the Independent Study Steering Committee (SSC) which will meet six monthly for the duration of the project.

Ongoing patient and public involvement will be vital to the success of the proposed work. As such this will include:

Management: Parent representatives for each screened condition will form a Patient and Public Involvement Advisory group (PPI), where members will chair and meet every 6 months to advise on the project. Parents will be invited to participate via charities for the screened conditions. Members of PPIAG will be invited to join the main steering group for all meetings.

The PPIAG will assist on designing the study's implementation and advise on parental recruitment, data collection and findings and discuss whether it is compatible with their experiences. The PPIAG and the charities involved will assist in developing lay summaries for dissemination of the findings and contribute to presentations at conferences.

Training/Support: The PPIAG will have an introductory session to explain the details about the project and the conduct of the research. Group members will also attend a training day for lay members involved in research[9]. Additionally, each PPIAG member will have a mentor in the steering group to advise them on the research processes and governance. Parents will receive payment for time and work undertaken in accordance with current INVOLVE guidance.

7.5 Protocol Compliance

Accidental protocol deviations can happen at any time. If they do occur, they will be adequately documented on the relevant forms and reported to the Chief Investigator and Sponsor immediately.

Deviations from the protocol which are found to frequently recur, will require immediate action and could potentially be classified as a serious breach.

7.6 Data protection and patient confidentiality

9 http://www.guysandstthomasbrc.nihr.ac.uk/PatientsPublic/Getinvolved/Haveyoursay/HaveYourSay.aspx

All investigators and study site staff will comply with the requirements of the Data Protection Act 1998 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Data Protection Act's core principles.

Pseudonymised identification numbers will be used to ensure individual's data cannot be identified in public documents. A project code will be allocated to every individual recruited to the study. There will be secure storage of paper and electronic records; interview and focus group recordings will be stored in a locked room, in a locked filing cabinet at the university. Files stored on university computers will be password protected.

Interviews and focus groups containing pseudonymised data will be transcribed by a professional transcription company.

Only the research team including the Chief Investigator (with the prior consent of the participants), Consultant and Clinical Nurse Specialists will have access to personal data during the study.

It is anticipated that these results will be used to inform a future evaluation study. Therefore, the data will be stored for 10 years and in line with City, University of London's data storage policy. Dr Jane Chudleigh (Chief Investigator) will be the data custodian.

7.7 Indemnity

In order to meet to meet the potential legal liability of the sponsors or employers for harm to participants arising from the management and design of the research, City, University of London has the following insurance in place: Public Liability: up to £50,000,000 any one event, Products Liability: up to £50,000,000 for all claims in the Pollution, aggregate during period of insurance, Employers' Liability: up to £50,000,000 any one event, Professional Indemnity: up to £10,000,000.

In order to meet to meet the potential legal liability of the sponsors or employers for harm to participants arising from the conduct of the research, NHS indemnity scheme or professional indemnity will apply

7.8 Access to the final study dataset

Only the research team and the study steering committee will have access to the full study dataset.

8 DISSEMINATION POLICY

Our study findings will be disseminated on the national NBS websites (https://www.gov.uk/topic/population-screening-programmes/newborn-blood-spot, https://www.gov.uk/topic/population-screening-programmes/sickle-cell-thalassaemia) so that it may be available to HPs such as health visitors, midwives and clinical nurse specialists who will be involved in the delivery of the initial positive NBS result.

Additionally, the findings will be disseminated via the website of the relevant charities and support groups associated with these conditions all of whom have been contacted and provided their endorsement for this study (CF Trust, Sickle Cell Society, British Thyroid Foundation, National Society for Phenylketonuria, CLIMB).

Furthermore, the results will be disseminated at relevant conferences nationally and internationally. The findings will also be published in high impact, peer reviewed journals including the NIHR HS&DR journal.

Parents involved in the study and those who form the advisory group will also be sent a summary of the research findings.

9 REFERENCES

1. UK Newborn Screening Programme Centre. Health Professional Handbook: A guide to newborn blood spot screening for healthcare professionals. London: UK Newborn Screening Programme Centre; 2012.
2. Bush A. Newborn screening for cystic fibrosis – benefit or bane? Paediatric respiratory reviews. 2008;9:301-2.
3. Public Health England. Data Collection and Performance Analysis Report Newborn blood spot screening in the UK 2014/15. London; 2016.
4. Public Health England. NHS Sickle Cell and Thalassaemia Screening Programme Data Report 2014/15: Trends and performance analysis. London; 2016.
5. Parker H, Qureshi N, Ulph F, Kai J. Imparting carrier status results detected by universal newborn screening for sickle cell and cystic fibrosis in England: a qualitative study of current practice and policy challenges. BMC Health Serv Res. 2007;7:203.
6. Ulph F, Cullinan T, Qureshi N, Kai J. Parents' responses to receiving sickle cell or cystic fibrosis carrier results for their child following newborn screening. Eur J Hum Genet. 2015;23(4):459-65.
7. Chudleigh J, Buckingham S, Dignan J, O'Driscoll S, Johnson K, Rees D, et al. Parents' Experiences of Receiving the Initial Positive Newborn Screening (NBS) Result for Cystic Fibrosis and Sickle Cell Disease. J Genet Couns. 2016.
8. Finan C, Nasr SZ, Rothwell E, Tarini BA. Primary care providers' experiences notifying parents of cystic fibrosis newborn screening results. Clin Pediatr (Phila). 2015;54(1):67-75.
9. Parsons EP, Bradley DM. Psychosocial issues in newborn screening for cystic fibrosis. Paediatric respiratory reviews. 2003;4(4):285-92.
10. Tluczek A, Koscik RL, Farrell PM, Rock MJ. Psychosocial risk associated with newborn screening for cystic fibrosis: parents' experience while awaiting the sweat-test appointment. Pediatrics. 2005;115(6):1692-703.
11. Buchbinder M, Timmermans S. Newborn screening for metabolic disorders: parental perceptions of the initial communication of results. Clin Pediatr (Phila). 2012;51(8):739-44.
12. Collins JL, La Pean A, O'Tool F, Eskra KL, Roedl SJ, Tluczek A, et al. Factors that influence parents' experiences with results disclosure after newborn screening identifies genetic carrier status for cystic fibrosis or sickle cell hemoglobinopathy. Patient Educ Couns. 2012.
13. Salm A, Yetter E, Tluczek A. Informing parents about positive newborn screening results: Parents' recommendations Journal of Child Health Care. 2012;16(4):367-81.
14. Ulph F, Cullinan T, Qureshi N, Kai J. The impact on parents of receiving a carrier result for sickle cell or cystic fibrosis for their child via newborn screening. Eur J Hum Genet. 2014;22.
15. Steuten L, Buxton M. Economic evaluation of healthcare safety: which attributes of safety do healthcare professionals consider most important in resource allocation decisions? Quality & safety in health care. 2010;19(5):e6.
16. Tluczek A, Clark R, McKechnie AC, Brown RL. Factors affecting parent-child relationships one year after positive newborn screening for cystic fibrosis or congenital hypothyroidism. J Dev Behav Pediatr. 2015;36(1):24-34.
17. Segrin C, Flora J. Family Communication. 2nd ed. London: Routledge; 2011.
18. Elwyn G, Quinlan C, Mulley A, Agoritsas T, Olav Vandvik P, Guyatt G. Trustworthy guidelines – excellent; customized care tools – even better. BMC Medicine. 2015;13(199).

19. Wright SJ, Jones C, Payne K, Dharni N, Ulph F. The Role of Information Provision in Economic Evaluations of Newborn Bloodspot Screening: A Systematic Review. Appl Health Econ Health Policy. 2015;13(6):615-26.
20. Wright SJ, Ulph F, Dharni N, Payne K. Eliciting Preferences for Information Provision in Newborn Bloodspot Screening Programmes. Value in Health. 2016;In Press.
21. Baile WF, Buckman R, Lenzi R, Glober G, Beale EA, Kudelka AP. SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer. Oncologist. 2000;5(4):302-11.
22. Narayanan V, Bista B, Koshy C. 'BREAKS' Protocol for Breaking Bad News. Indian J Palliat Care. 2010;16(2):61-5.
23. Hollis R, Corkin D, Crawford D, Campbell M, Coad J, Davies J, et al. Breaking bad news: supporting parents when they are told of their child's diagnosis. London: Royal College of Nursing; 2013.
24. Widdas D, McNamara K, Edwards F. A Core Care Pathway for Children with Life-limiting and Life-threatening Conditions Bristol; 2013.
25. Paul CL, Clinton-McHarg T, Sanson-Fisher RW, Douglas H, Webb G. Are we there yet? The state of the evidence base for guidelines on breaking bad news to cancer patients. Eur J Cancer. 2009;45(17):2960-6.
26. Porensky EK, Carpenter BD. Breaking bad news: Effects of forecasting diagnosis and framing prognosis. Patient Educ Couns. 2016;99(1):68-76.
27. Fujimori M, Uchitomi Y. Preferences of cancer patients regarding communication of bad news: a systematic literature review. Jpn J Clin Oncol. 2009;39(4):201-16.
28. Innes S, Payne S. Advanced cancer patients' prognostic information preferences: a review. Palliat Med. 2009;23(1):29-39.
29. Martins RG, Carvalho IP. Breaking bad news: patients' preferences and health locus of control. Patient Educ Couns. 2013;92(1):67-73.
30. Mishelmovich N, Arber A, Odelius A. Breaking significant news: The experience of clinical nurse specialists in cancer and palliative care. Eur J Oncol Nurs. 2016;21:153-9.
31. Contro NA, Larson J, Scofield S, Sourkes B, Cohen HJ. Hospital staff and family perspectives regarding quality of pediatric palliative care. Pediatrics. 2004;114(5):1248-52.
32. Bower P. Breaking disability news. The Practicing Midwife. 2009;12(4):18-9.
33. Fallowfield L, Jenkins V. Communicating sad, bad, and difficult news in medicine. Lancet. 2004;363(9405):312-9.
34. Shaw J, Dunn S, Heinrich P. Managing the delivery of bad news: an in-depth analysis of doctors' delivery style. Patient Educ Couns. 2012;87(2):186-92.
35. Reed S, Kassis K, Nagel R, Verbeck N, Mahan JD, Shell R. Breaking bad news is a teachable skill in pediatric residents: A feasibility study of an educational intervention. Patient Educ Couns. 2015;98(6):748-52.
36. Ulph F, Wright S, Dharni N, Lavender T, Bennett R, Roberts S, et al. Provision of Information about newborn screening antenatally: a sequential exploratory mixed methods project.; (In press)
37. Rueegg CS, Barben J, Hafen GM, Moeller A, Jurca M, Fingerhut R, et al. Newborn screening for cystic fibrosis - The parent perspective. Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society. 2016;15(4):443-51.
38. DeLuca JM, Kearney MH, Norton SA, Arnold GL. Parents' experiences of expanded newborn screening evaluations. Pediatrics. 2011;128(1):53-61.
39. Kai J, Ulph F, Cullinan T, Qureshi N. Communication of carrier status information following universal newborn screening for sickle cell disorders and cystic fibrosis: qualitative study of experience and practice. Health Technol Assess. 2009;13(57):1-82, iii.

40. Kladny B, Williams A, Gupta A, Gettig EA, Krishnamurti L. Genetic counseling following the detection of hemoglobinopathy trait on the newborn screen is well received, improves knowledge, and relieves anxiety. Genet Med. 2011;13(7):658-61.
41. Tluczek A, Orland KM, Cavanagh L. Psychosocial consequences of false-positive newborn screens for cystic fibrosis. Qual Health Res. 2011;21(2):174-86.
42. Schoen EJ, Baker JC, Colby CJ, To TT. Cost-benefit analysis of universal tandem mass spectrometry for newborn screening. Pediatrics. 2002;110(4):781-6.
43. Marsh VM, Kamuya DM, Molyneux SS. 'All her children are born that way': gendered experiences of stigma in families affected by sickle cell disorder in rural Kenya. Ethn Health. 2011;16(4-5):343-59.
44. Metcalfe A, Haydon J, Bennett C, Farndon P. Midwives' view of the importance of genetics and their confidence with genetic activities in clinical practice: implications for the delivery of genetics education. J Clin Nurs. 2008;17(4):519-30.
45. Plumridge G, Metcalfe A, Coad J, Gill P. Parents' communication with siblings of children affected by an inherited genetic condition. J Genet Couns. 2011;20(4):374-83.
46. Metcalfe A, Plumridge G, Coad J, Shanks A, Gill P. Parents' and children's communication about genetic risk: a qualitative study, learning from families' experiences. Eur J Hum Genet. 2011;19(6):640-6.
47. Socio-Psychological Research in Genomics C, Eisler I, Ellison M, Flinter F, Grey J, Hutchison S, et al. Developing an intervention to facilitate family communication about inherited genetic conditions, and training genetic counsellors in its delivery. Eur J Hum Genet. 2015.
48. Ulph F, Cullinan T, Qureshi N, Kai J. Informing children of their newborn screening carrier result for sickle cell or cystic fibrosis: qualitative study of parents' intentions, views and support needs. J Genet Couns. 2014;23(3):409-20.
49. Murray E, Treweek S, Pope C, MacFarlane A, Ballini L, Dowrick C, et al. Normalisation process theory: a framework for developing, evaluating and implementing complex interventions. BMC Med. 2010;8:63.
50. May CR, Finch T, Ballini L, MacFarlane A, Mair F, Murray E, et al. Evaluating complex interventions and health technologies using normalization process theory: development of a simplified approach and web-enabled toolkit. BMC Health Serv Res. 2011;11:245.
51. Rolland JS, Williams JK. Toward a biopsychosocial model for 21st-century genetics. Fam Process. 2005;44(1):3-24.
52. Bate SP, Robert G. Bringing user experience to health care improvement: the concepts, methods and practices of experience-based design. Oxford: Radcliffe Publishing 2007.
53. Tsianakas V, Robert G, Maben J, Richardson A, Dale C, Wiseman T. Implementing patient centred cancer care: using experience-based co-design to improve patient experience in breast and lung cancer services. Support Care Cancer. 2012;20(11):2639-47.
54. Robert G. Participatory action research: using Experience-based Co-design (EBCD) to improve the quality of health care services. In: Ziebland S, Coulter A, Calabrese J, Locock L, editors. Understanding and Using Health Experiences: Improving patient care. Oxford: Oxford University Press; 2013.
55. Locock L, Robert G, Boaz A, Vougioukalou S, Shuldham C, Fielden J, et al. Using a national archive of patient experience narratives to promote local patient-centered quality improvement: an ethnographic process evaluation of 'accelerated' experience-based co-design. J Health Serv Res Policy. 2014;19(4):200-7.

56. Donetto S, Pierri P, Tsianakas V, Robert G. Experience-based Co-design and healthcare improvement: realising participatory design in the public sector. The Design Journal. 2015;18(2):227-48.
57. Robert G, Cornwell J, Locock L, Purushotham A, Sturmey G, Gager M. Patients and staff as codesigners of healthcare services. BMJ. 2015;350:g7714.
58. Tsianakas V, Robert G, Richardson A, Verity R, Oakley C, Murrells T, et al. Enhancing the experience of carers in the chemotherapy outpatient setting: an exploratory randomised controlled trial to test impact, acceptability and feasibility of a complex intervention co-designed by carers and staff. Support Care Cancer. 2015.
59. Jones J, Hunter D. Qualitative Research: Consensus methods for medical and health services research. Br Med J (Clin Res Ed). 1995;311:4.
60. Fink A, Kosecoff J, Chassin M, Brook R. Consensus methods: characteristics and guidelines for use. . Am J Public Health. 1984;74(9):4.
61. Dheensa S, Metcalfe A, Williams RA. Men's experiences of antenatal screening: a metasynthesis of the qualitative research. Int J Nurs Stud. 2013;50(1):121-33.
62. Bateson G. Steps to an Ecology of Mind. New York: Ballentine; 1972.
63. Carr A. Family Therapy Concepts, Process and Practice. 2nd ed. Chichester: John Wiley and Sons Ltd; 2006.
64. Carter B, McGoldrick M. The changing family life cycle: A framework for family therapy. . Boston: Allyn & Bacon; 1989.
65. Jones F, Clarke D, Robert G, Harris R, McKevitt C, Macdonald A, et al. 'CREATE' Collaborative Rehabilitation Environments in Acute sTrokE': Using co-production to improve patient carer and staff experiences in health care organizations: a multi-centre, mixed methods evaluation in inpatient stroke units.: NIHR- HS&DR Project 13/114/95; 2016. Contract No.: Project 13/114/95.
66. Abidin RR. Parenting Stress Index, Fourth Edition Short Form (PSI-4 SF). Florida: Psychological Assessment Resources Inc.; 2012.
67. Al-Janabi H, Flynn TN, Coast J. Development of a self-report measure of capability wellbeing for adults: the ICECAP-A. Qual Life Res. 2012;21(1):167-76.
68. Department of Health. Healthy Child Programme Pregnancy and the first five years of life 2009.
69. Krippendorff K. Content analysis : an introduction to its methodology. 3rd edition ed. Los Angeles: SAGE; 2013.
70. Emerson RM, Fretz I, Shaw L. Writing ethnographic fieldnotes. London: The Chicago University Press; 2011.
71. Bernard H. Research methods in anthropology: Qualitative and quantitative methods. Newbury Park CA: Sage; 2002.
72. Falzon M. Multi-sited ethnography: Theory, praxis and locaility in contemporary research. . Burlington VT: Ashgate; 2009.
73. Marcus G. Ethnography in / of the world system: The emergence of multi-sited ethnography. Annual Review of Anthropology. 1995;24:95-117.
74. Atkinson P. For Ethnography. Los Angeles: SAGE; 2015.
75. Braun V, Clarke V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3(2):77-101.
76. Krueger RA, Casey MA. Focus groups : a practical guide for applied research. LinkLos Angeles: Sage; 2009.
77. Moore G, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions. London: MRC Population Health Science Research Network; 2014.

78. Moore GF, Audrey S, Barker M, Bond L, Bonell C, Hardeman W, et al. Process evaluation of complex interventions: Medical Research Council guidance. BMJ. 2015;350:h1258.
79. Curtis L, Burns A. Unit Costs of Health and Social Care. . Kent; 2015.
80. Department of Health. National Schedule of Reference Costs London; 2015.
81. Bessey A, Chilcott J, Pandor A, Paisley S. The Cost-Effectiveness of Expanding the NHS Newborn Bloodspot Screening Programme To Include Homocystinuria (Hcu), Maple Syrup Urine Disease (Msud), Glutaric Aciduria Type 1 (Ga1), Isovaleric Acidaemia (Iva), and Long-Chain Hydroxyacyl-Coa Dehydrogenase Deficiency (Lchadd). . Value in Health. 2014;17(7):A531.
82. Gilbey P. Qualitative analysis of parents' experience with receiving the news of the detection of their child's hearing loss. Int J Pediatr Otorhinolaryngol. 2010;74(3):265-70.

9. APPENDICES

9.1 Appendix 1 – Required Documentation

Protocol

CVs of the research team

Patient Information Sheets (PIS) (on headed paper)

Consent forms (on headed paper)

Data collection tools

Poster advertising the study

Schedule of Events

Statement of Activities

9.2 Appendix 2 – Schedule of Procedures

Procedure	Time (months									
	0-3	3-6	6-9	9-12	12-15	15-18	18-21	21-24	24-27	27-30
Phase 1										
Ethics and HRA approvals	X	X								
National survey		X								
Phase 2										
Observation of staff			X	X						
Semi structured			X	X						
interviews with staff			X	X						
Staff meeting			X	X						
Narrative interviews with parents			X	X						
Parent meeting			X	X						
Joint parent and staff meeting					X	X				
Co-design working groups						X				
Phase 3										
Training of staff							X	X	X	
Implementation of co-designed interventions							X	X	X	
Observation of staff							X	X		
Interviews with staff							X	X	X	
Interviews with parents							X	X	X	
Phase 4										
Design of a future evaluation study										X
Final report										X
Dissemination										X

9.3 Appendix 3 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made