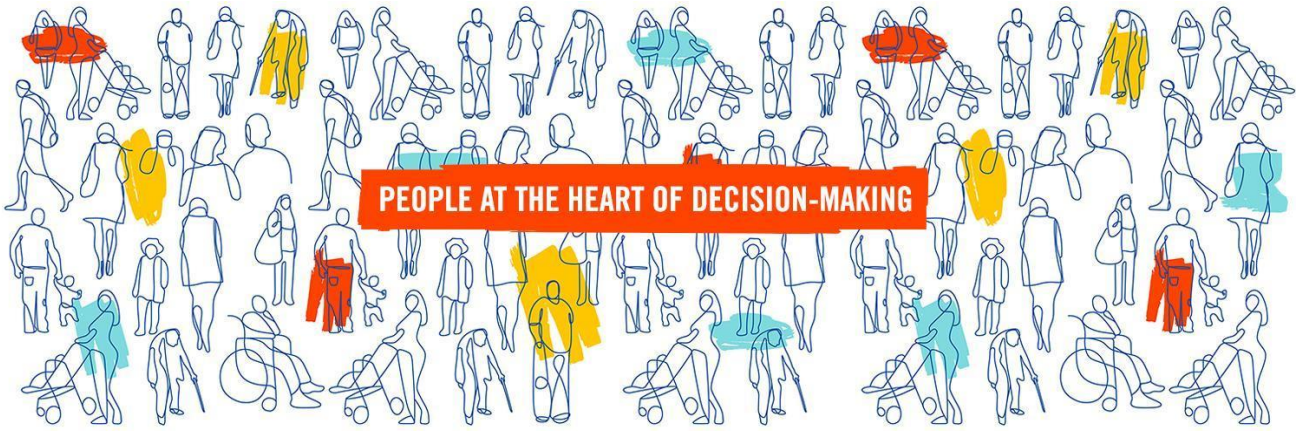
Newborn Genomes Programme: Establishing principles for feeding back results to families

Report on engagement with public, healthcare professionals and patient groups and representatives: phase 2

July 2022



About Involve

We're the UK's leading public participation charity, on a mission to put people at the heart of decision-making.

We believe that decision-making in the UK needs to be more:

- **Open** - so that people can understand, influence and hold decision-makers to account for the actions and inactions of their governments;
- **Participatory** - so that people have the freedom, support and opportunity to shape their communities and influence the decisions that affect their lives; and,
- **Deliberative** - so that people can exchange and acknowledge different perspectives, understand conflict and find common ground, and build a shared vision for society.

Our work seeks to create:

1. **New innovations** - to demonstrate better ways of doing democracy;
2. **New institutions** - to put people at the heart of decision-making;
3. **New norms** - to make democracy more open, participatory and deliberative.

Find out more about our work: www.involve.org.uk/our-work/

Our values

- **Collaboration** – because change comes when broad coalitions of people work towards a common vision.
- **Equality** – because everyone in society has an equal right to be listened to and participate in decisions that affect their lives. No one should be held back by societal divisions or prejudice.
- **Purpose** – because participation must have an impact. We reject tokenistic or ineffectual engagement.

Foreword

A key decision for the Newborn Genomes Programme is to determine which conditions, out of many potential options, should be looked for and fed back to parents as part of the research study. These choices will affect many people – the baby and their wider family, as well as healthcare professionals and others supporting those families. It is for this reason that, first, we felt it important to base these decisions on a set of agreed principles; and second, that we took the time to test and debate these principles through public deliberation with a diverse range of participants.

With the support of the team from Involve – particularly Sarah Castell, Juliet Swann, and Charlotte Obijaku – we have been able to engage with members of the general public, those with lived experience of rare condition, and healthcare professionals. Participants generously shared their experiences, feelings, and concerns through participating in our workshops or contributing to our online survey – and it has been our privilege to take these into consideration when determining our next steps in developing our principles. This task for us has been helped immeasurably by the clear direction participants gave us on how our principles might need to be refined. For this, I would like to extend our sincere gratitude and thanks.

I would also like to give my heartfelt thanks to all the members of the Conditions Working Group, listed in the appendix, for the considerable amount of time and hard work that was involved in bringing together the draft principles. I am grateful to our 'critical friends' whose support and guidance were invaluable in developing the workshops and survey so that they could elicit debate and discussion among our participants. Equally vital was the support we received from Genetic Alliance UK in ensuring that we included people with lived experience of rare conditions.

Genomics England's next task is to use these principles to identify the initial genes and conditions that will be included when the Newborn Genomes Programme's research study begins next year. Participants' contributions allow us to do this in the knowledge that our principles have been subject to rigorous and transparent discussion and debate.

This is not the end of the story – our list of genes and conditions, as well as the principles we've used to create it, will continue to evolve and be refined as our work progresses. But for our Programme's beginning, participants' contributions mean we can take those first steps with confidence.

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Contents

Executive summary 5

About Involve ..... Error! Bookmark not defined.

Executive summary

Background

Genomics England's Newborn Genomes Programme is embarking on an NHS-embedded research study to explore the benefits, challenges, and practicalities of sequencing and analysing the genomes of newborns.

Genomics England convened a working group with expertise from individuals with clinical, scientific, ethical, policy, patient and public backgrounds to inform the conditions (and the genes and variants which cause them) that will be included in the initial testing panel for newborn genome sequencing. Through work conducted between September 2021 and February 2022, this group drafted a set of five principles that could be used to assess which conditions would be looked for. This was Phase 1 of the engagement process, a report of which is available to download from Genomics England's website.

This report includes the findings from Phase 2 of the engagement process. Healthcare professionals, individuals with rare conditions and their family members, and the wider general public were invited to hear more about the Programme and the principles. Using three different methods of engagement, participants were invited to review, critique, and improve the principles based on their views on how decisions should be made on the conditions, genes, and variants which the study will screen for:

- A series of workshops run by Involve in May-June 2022, which were also attended by members of the working group and by the Genomics England team. Workshops were run using a deliberative methodology whereby participants are given evidence which they discussed in small groups and developed a consensus on recommendations. More information about their recruitment and design can be found in Appendix B.
- An online survey which included multiple choice and open ended questions. The survey was open to the public for 6 weeks in May-June 2022 and was completed by 440 people.
- Three "critical friend" interviews, where healthcare and science experts from outside the Working Group and Genomics England gave feedback on the principles and their engagement programme, with constructive suggestions for how to improve it.[1]

Recommendations for the final principles

The activities above have led to a series of recommendations for how the wording of the initial principles should be changed. These recommended changes are listed in Table 1 below.

Table 1: recommendations for the Newborn Genomes Programme's conditions principles

[1] We are grateful to Professor Anneke Lucassen, Chair in Clinical Genetics at the University of Southampton, Catherine Joynson, Associate Director at the Nuffield Council on Bioethics, and Dr Robin Lachmann, Consultant in Inherited Metabolic Disease at UCLH NHS Foundation Trust, for their time and considered thoughts.

Principle	*Final wording recommended* Include the genetic condition and variant(s) in the screening programme if…	*Initial wording for Phase 2*	*Key considerations from participants*
A	There is strong evidence that the genetic variant(s) causes the condition. *Could amend "strong" if the programme decides to accept more limited evidence about gene-disease association.*	There is strong evidence that the genetic variant(s) causes the condition.	Workshop participants would accept more limited evidence about gene-disease association than the Working Group. In the survey, the vast majority agreed it is better to have strong evidence; however, many – especially those with personal experience – also felt it acceptable to screen for variants where there is less evidence.
B	Individuals who have the genetic variant(s) would be expected to have symptoms that would significantly impact their quality of life if left **undiagnosed**. Satisfying criteria: • Symptoms have a significant impact on quality of life, **taking into consideration the testimony of people affected by the condition** • If left untreated, symptoms would **more likely than not start under 16 years.**	A high proportion of individuals who have the genetic variant(s) would be expected to have symptoms that would significantly impact their quality of life if left **untreated**. Satisfying criteria: • Symptoms have a significant impact on quality of life, **measured in QALYs where available or taking into consideration factors such as how serious the condition is and the testimony of people affected by the condition** • If left untreated, symptoms would **typically start [in childhood (less than 16**	The public and patient workshop groups in particular would accept conditions with lower penetrance* if there were lower-risk or less invasive treatments. Participants also felt that conditions where symptoms had higher impact on future quality of life could be subject to a lower threshold for penetrance because of the potential harm of having a condition and not knowing about it.

		years)]/ [early childhood]; or [by the age of 5]	
C	Early or pre-symptomatic intervention, management of the condition, or treatment(s) for the condition has been shown to lead to improved outcomes for the child, compared to after onset of symptoms.	Pre-symptomatic or early treatment(s) for the condition has been shown to lead to improved health outcomes for the child, compared to treatment after onset of symptoms.	Participants wanted to make it clear that this wasn't about just treatments, or pre-symptomatic treatment, but about lifestyle management too. People with personal experience of conditions wanted treatments to include anything that might make life better, not just medical options. Simply 'knowing' is worth screening for.
D	There is an appropriate confirmatory test, relative to the impact of that condition on the patient, that can establish whether or not the child has the condition.	There is a minimally invasive confirmatory test that can establish whether or not the child has the condition.	Confirmatory tests were desired by the majority of participants. It was felt that the invasiveness of the test should be considered relative to the level of harm that might be prevented by having the test, rather than just being as minimally invasive as possible.
E	Conditions screened for are only those for which the interventions are equitably accessible for all, including clinical trials and exploratory medicine. *Possibly exclude 'within NHS'*	Conditions screened for are only those for which the socially acceptable interventions are equitably accessible for all as standard of care within the NHS.	While participants appreciated the principle of equity, this was trumped by wanting as much knowledge as possible and wanting the choice to seek other interventions outside the NHS. This was an indication of a desire for personal autonomy vying with a desire for equity.

* Penetrance: the proportion of individuals with a particular variant(s) in a gene that have the condition associated with that variant(s)

Differences between groups, and the values they expressed

- **General public** – there were some differences between individuals who were parents and those who were not, but overall these groups indicated that *"knowledge is power"* and wanted to screen for as many conditions as possible. They prioritised the values of autonomy and transparency to help parents by empowering them to do as much as they could for themselves and their children.

- **Healthcare professionals (HCPs)** – this group had more practical considerations. Discussions focused on resourcing the Programme; communicating with, and caring for, parents and families; consent; and data security.

- **Individuals with rare conditions, and their family members**: this group emphasised the need to consider the emotional and wider support needs of families, considering the various impacts of information on overall wellbeing, including the mental health of children and parents. They also emphasised the need for patients to have the information they need to advocate for their condition and to increase the amount of new learning on rare conditions.

- **Online survey**: survey respondents skewed significantly towards white women in England with experience of genetic conditions, whether through work, their own diagnosis, or as a parent and / or carer of someone with a genetic condition. Views on the principles were similar to those in the workshops; the online open-ended survey tended to have more nuance of the types of treatment they would find acceptable, and a few challenged the aims of the programme overall.

Compared with the working group, the groups and participants surveyed wanted the programme to cast a **slightly wider net** with respect to the range of conditions which should be screened for.

Taking the principles forward

Overall, the principles were seen as important and there was a clear understanding that the principles worked together as a group. If some genes are included that do not meet every principle, workshop participants wanted Genomics England to consider an interplay between principles A, B, and C.

The engagement revealed participants' desire to include elements not currently reflected in the principles, including explicit reference to "the parents' wishes," autonomy and freedom of choice, and the (future) desire of the person screened to have access to information about them.

Some participants (particularly members of the public and those with experience of a rare condition) argued that the Programme should screen for as much as possible, but ask parents to consent upfront to find out as much or as little as they want – even if it's uncertain and not clear what they might do with the results.

In contrast to the working group, participants were much more likely to embrace the risks associated with false positives, rather than focussing on effects on the wider health system of potential long-term impacts on families if diagnoses are not confirmed. This was in spite of case studies presented to participants that sought to make the consequences of false positives clear. Genomics England will need to examine this tension, and perhaps seek to fully explain the wider implications of false positives.

Some guidance on communicating the principles also emerged from this engagement:

- The principles must be presented in the context of how people in the Programme will be informed, asked to consent, followed up, and supported.
- It is important to talk about the outcomes for children in terms of their overall quality of life, closely connected to what kinds of interventions would support them in their development.
- Further exploration is needed regarding how to communicate the future potential of discovery research in the Programme and implications for participants beyond the initial screen.
- It is important to continue engaging and iterating the principles regularly to take account of the experiences of the initial study participants, and to account for any scientific advances arising from further discovery research in the Programme.
- While the principles form a crucial part of the Newborn Genomes Programme, it is important that the aims of the overall Programme also continue to be challenged through engagement with stakeholders

Next steps

Genomics England and the Working Group will now need to take these recommendations and finalise the principles, in order to initiate the task of selecting which conditions, genes and variants should be initially looked for in the study.

1. Introduction

1.1. Background

Genomics England's Newborn Genomes Programme is embarking on an NHS-embedded research study to explore the benefits, challenges, and practicalities of sequencing and analysing newborns' genomes. The study aims to generate evidence regarding whether whole genome sequencing (WGS) could complement (rather than replace) the existing NHS newborn screening service.

Whole genome sequencing (WGS) provides an opportunity to identify a large number of genetic conditions, but it is important to minimise feedback of information that may not be clinically useful, or place undue burden on families and the health system. A public dialogue conducted in 2021 commissioned by Genomics England, the UK National Screening Committee, and UK Research and Innovation's Sciencewise programme stated that the wider set of conditions that should be screened for should include those that "impact the infant in early childhood AND [where] there are treatments and interventions to cure, prevent, or slow progression of disease".

To provide more granularity and thinking on what this means for the research study, Genomics England convened a Working Group to provide the clinical, scientific, ethical, and public expertise to draft a number of principles, to inform which conditions will be looked for and fed back as part of the initial testing panel for newborn genome sequencing.

After these were drafted, the second phase of the project began. Various stakeholders, including members of the public, healthcare professionals from a non-geneticist background, and patient groups were engaged to gather opinions and feedback on the draft principles.

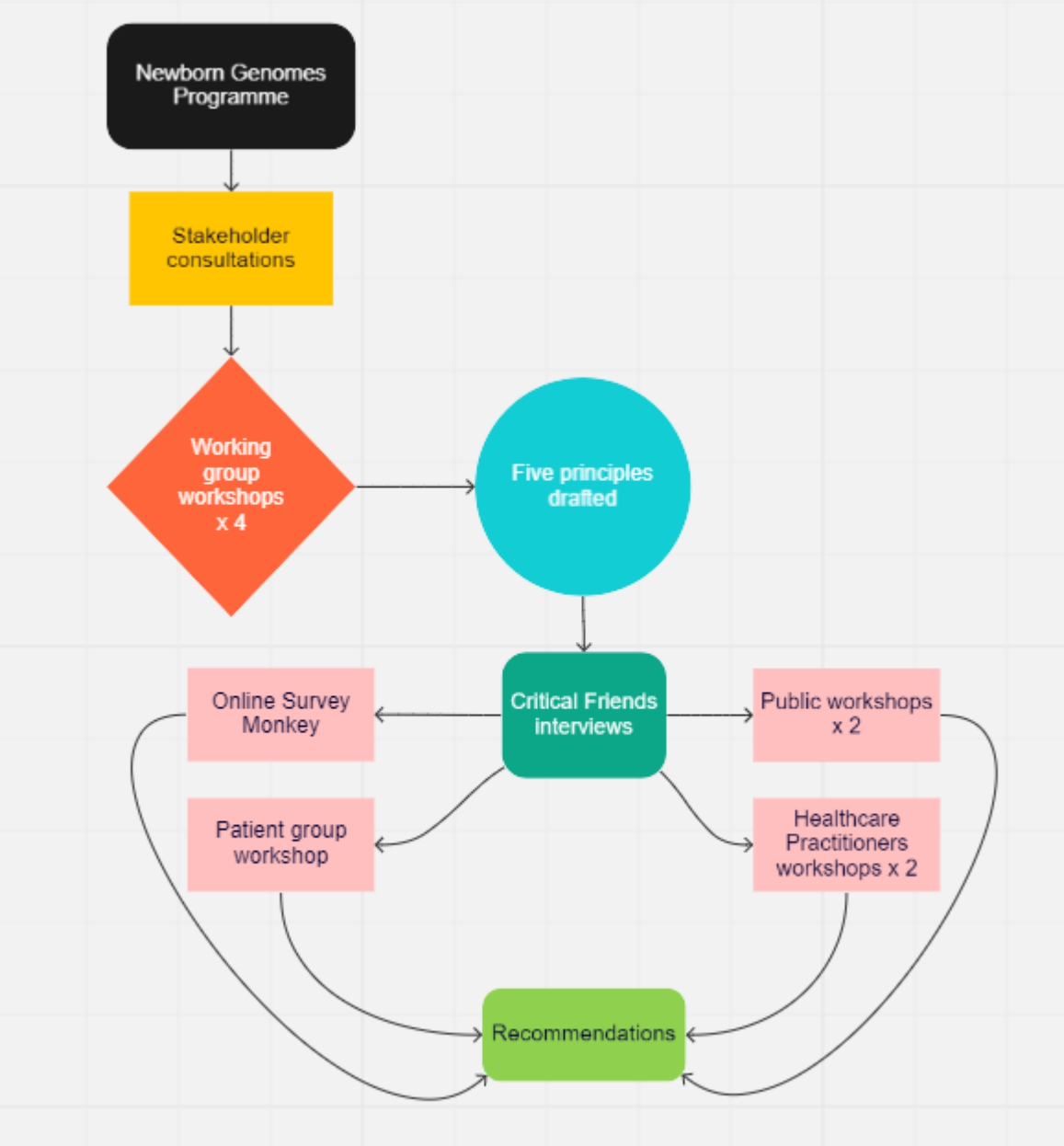
This report presents the findings from phase two of the engagement and makes recommendations on how the principles should be refined to take account of participants' feedback.

1.2. Purpose

While principles and criteria for screening already exist,[2] it was felt that a unique approach needed to be taken for this Programme, as it is a research study looking at the overall effectiveness of a specific technology (WGS). It is also important to ensure trust by the UK public and NHS, which can only be achieved if the voices of those that could be affected by this study and its findings are included in the conversation.

[2] See, for example, https://www.gov.uk/government/publications/evidence-review-criteria-national-screening-programmes; and https://apps.who.int/iris/handle/10665/37650.

1.3. Our approach



The **working group** consisted of 22 individuals from different backgrounds and four core Genomics England team members. The group met four times between September 2021 and February 2022 to discuss and achieve consensus on a set of five draft principles that could be used to determine which conditions would be included in the initial screen for babies in the Newborn Genomes Programme. This process is outlined in more detail in Involve's report of Phase 1, which is available to download on Genomics England's website.

After the five principles were drafted, Genomics England identified three '**critical friends**' who provided additional clinical, scientific, and ethical perspectives on the content and structure of the stakeholder workshops. They were selected because they were not involved in the working group, had previously advised caution about the aims of the programme, and had some prior experience with screening or genomic research. Each critical friend was

interviewed separately during the planning phase of this engagement and their comments and suggestions were integrated into the workshop sessions' plans.

Involve organised and hosted two sets of **public workshops,** each of which consisted of an evening and a Saturday full day session with two different cohorts of participants.[3]

Healthcare professionals from non-genetic specialist backgrounds were split into two different cohorts. Each cohort took part in one long evening workshop. **Patient groups** attended an evening and a Saturday full day session.

Each workshop was structured with a mix of presentations with explanatory videos on genetics and the Programme created by Genomics England and small group discussions with a facilitator where the participants had the chance to look at the issue more in-depth through the use of case studies. The aim of these deliberations was to review the draft principles and suggest specific amendments that would allow the principles to reflect the opinions of these stakeholders. The meetings provided ethical and practical recommendations for both the principles and the Programme as a whole.

At the same time, we ran an **online survey** made up of 18 questions. Most of the questions were multiple choice, but three included free text boxes. This was open to everyone publicly for six weeks via Survey Monkey and collected 440 full responses (316 of which gave permission for their demographic data to be analysed).[4] The survey was designed to pick up overall preferences on some of the decisions which remained to be made on the principles after the Phase 1 work with the working group. It also collected thematic inputs on quality of life, views on key issues related to each principle, and overall priorities across the principles.

1.4. How to interpret the findings in this report

This report presents the findings from the workshops, with reflection on the differences and similarities across the three stakeholder groups, as well as analysis of the results from the online survey.

Involve has collated feedback and used comments to illustrate key themes throughout. This was a qualitative piece of work where participants were able to engage directly in dialogue with members of the working group who participated in the discussions with them. While we can show that a point of view was present for participants, and indicate the strength of feeling that came along with it, we cannot extrapolate these views to the wider public as a whole or conclude that these views would be shared by wider patient or healthcare professional communities. While we talked to a diverse sample of healthcare professionals, these were still small-scale engagements and there will likely be a wider variety of views in the population as a whole.

[3] Full details of the recruitment process and the demographic make-up of the workshops is available at Appendix B.

[4] Full details of the survey findings and caveats on the use of the survey as quantitative data are in Appendix B.

When it comes to the online survey, care should be taken not to interpret percentages as representative. The overall numbers are too small for statistical validity.

- Throughout this report, we indicate whether we are using the base of 316 or 440 survey participants depending on how far we are analysing demographic data. We also asked workshop participants to complete the survey. This means that some survey responses are from those who might have a more informed perspective. However, findings were reasonably consistent without the strong outliers that were observed among workshop participants.
- Gender: responses were dominated by females – more than 80% of respondents were female. This is not representative of the overall UK population.
- Age: responses were reasonably spread, albeit with a marked lack of responses from people under 25. Less than 2% of respondents were from this age range compared to 12% of the adult population.
- Location: just under 90% of respondents were from England. This is representative of the UK population, although the North of England was underrepresented.
- Ethnicity: more than 86% of respondents identified as "White or Caucasian", which broadly reflects the UK population.
- Reason for interest: responses were dominated by people directly affected by rare disease: more than 84% of respondents were in the first three categories (have a rare disease/ family member has a rare disease/ work involves rare diseases). In addition, of the 6% of respondents who clicked "Other", more than half were directly affected by the issue (sometimes in more than one way – e.g., family/ work). More than 54% of respondents' work involves rare diseases. This is not representative of the general UK population.

This means that the online survey data should be seen as indicative of the attitudes of people with a direct connection to the issue, as opposed to the attitude of the general public.

1.5. Next steps

This report will aid Genomics England and the Working Group in refining and applying the principles to define a list of conditions, genes, and variants that will be included in the research study.

Throughout this period, the Genomics England team also engaged with healthcare professional and rare disease patient groups, as well as members of the Newborn Genomes Programme NHS Steering Group and working group, to gain feedback on the draft principles.

This report has been shared with participants who have been engaged so far.

2. What was important to participants?

This chapter summarises the areas which were most important for the different participant groups in the engagement process, and what this revealed about the underlying values which emerged as important during discussions.

2.1. Overview

Participants expressed appreciation for being asked about the Programme and understood how important it was. The word cloud below shows some of the words used by participants to summarise their experience.

Fig 1: How participants felt about taking part in the workshops

General public: there were some differences between parents and non-parents, but overall these groups felt that *"knowledge is power"* and erred on the side of screening for as many conditions as possible. This includes those conditions where knowledge about penetrance is uncertain, those which might not have a curative treatment, or might not present symptoms until later in life. At the same time, there were concerns about the Programme bringing additional stress for parents, especially with young children, so **the way the Programme was delivered, including support offered to families, was felt to be important**. Overall, though they did not necessarily express it in these terms, they prioritised the values of **autonomy** and **transparency** as the best ways to help parents by **empowering** them.

> *"No matter how stressful it is at the beginning, I think that information is a reassurance to a new parent going through that (health problems with your child)"* Public workshop participant.

Healthcare professionals (HCPs): this group had more practical considerations than the other workshop groups. The focus of the discussions was on the benefits and implications

of the Programme, including resourcing; communicating with, and caring for, parents and families; consent; and data security. As a key point of contact for parents, HCPs were particularly interested in what the implications would be for the care of parents and newborns, and how they might be able to support them. Similarly to the public, HCPs believed that parents' anxieties should be adequately addressed, and valued giving parents support. They also valued empowering parents by giving them choice; feeling they have the right to know and choose the best intervention for their child.

> *"We are empowering people - no matter when the conditions start, the only thing we are doing is identifying that there is a condition to see if we can treat or manage it."* HCP workshop participant.

A few HCPs also mentioned the need to link the Programme to known screening principles, either Wilson & Jungner, or more recent suggestions.[5]

Individuals with rare conditions, and their family members: this group emphasised the need to consider families' emotional and wider support needs, and the impact of information on overall wellbeing, including the mental health of children and parents. This included, but went beyond, clinical intervention. Overall, the group also felt *"knowledge is power"* and preferred having information. They were very clear that they wanted information, even if it was uncertain or resulted in a greater number of false positives. Several highlighted that in emerging fields such as rare diseases, transparency is essential, ensuring there isn't a discrepancy between information held by the clinician, and research and information provided to the patient.

> *"Does testing automatically mean all information is communicated, with all areas of grey, to the family member? Is some information kept locked behind a data wall - with an AI decision tree choosing when it is released to a professional?"* Comment from online feedback

Such views might be related to participants' own experiences with a rare condition, rather than having had a false positive result through screening. They brought to the discussion their own experiences of how eventual diagnoses had improved their quality of life. They also emphasised the value of considering the whole family – especially for future family planning and the different decisions that might be made if parents have a very ill child.

> *"No one wants to see suffering, any parent will tell you the anxiety exists no matter how well or unwell your children are. If they are unwell it goes through the roof, so if you can remove suffering and pain through early diagnosis and treatment then it's a win-win."* Patient workshop participant.

[5] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5893317/

Online survey: survey respondents skewed significantly towards white women with experience of genetic conditions, whether through work, their own diagnosis, or as a parent and / or carer of someone with a genetic condition. Data from this survey should therefore be seen as indicative of the attitudes of people with a direct connection to the issue, as opposed to the attitude of the general public.

In the workshops, we also observed that in the general public groups, group members deferred to women and parents – especially mothers of young children. It may be that when discussing issues concerning newborns, mothers are felt to be the key stakeholders, which could be considered for future communication.

Similarly Principles D and E were lower priorities for all groups.

2.2. Shared ethical concerns and values

As indicated above, some values and ethical concerns emerged as important across the four groups of participants. These do not directly inform the principles, but offer a steer as to how the Programme might be shaped as a whole.

- Choice and knowledge was important to all; most participants would err on the side of giving as much knowledge as possible of conditions and treatment/intervention options; even if this was uncertain knowledge. This was seen as empowering for patients and parents to make decisions about their own/their child's heath. .
- The sentiment above related to an underlying sense that healthcare is a marketplace; and that people with rare conditions need to advocate for themselves and tend to educate HCPs and researchers on their own conditions. Patients pointed out that rare conditions have historically not been given sufficient attention; therefore, the more conditions which could be screened for, the more information there would be about rare conditions, whether this information was complete or not.
- It was seen as important that patients should self-define and self-determine issues like quality of life or what they wanted to get out of treatment, rather than this being decided for them.
- Putting resources into the Programme was seen as important; so that as well as providing an early diagnosis, the Programme could adequately communicate with and care for families.
- Participants also discussed the idea of testing as more than a one-time event, suggesting that genomic data should be reviewed at key life stages to address early, mid, and late onset conditions. This might negate the need to test for everything at birth and could potentially help deal with ethical issues around consent.
- Non-curative treatments were welcomed by all groups as something the Programme should also consider. Medical interventions were seen as not the only way to manage a genetic condition.

> *"All interventions are acceptable. Any intervention that will, or may, increase quality of life is acceptable."* Online survey response

- Equity was an important point for participants, but was one of the ethical concepts with high levels of disagreement. Participants understood its relevance but many were still inclined to have the option to access treatments outside the NHS after diagnosis. This reinforces the sense from participants that parental autonomy is important.
- Informed choice to take part in the Programme; in particular, choice about what might happen with the data about the newborn in the future, and in the light of new scientific advances or medico-legal changes. Participants queried whether this had been thought through enough. They asked whether parents with a newborn would have the emotional and physical energy and space to take on board some of these complex concepts at the moment of consent.
- Additionally, there was a strong sense that **"socially acceptable"** did not hold much meaning or seem to be a relevant criterion for participants. This is covered in more detail in section 3.6 on Principle E.

2.3. Managing false positives

Participants **embraced the risks associated with having false positives;** they wanted the Programme to prioritise avoiding missing cases, even where that would mean some parents would receive false positive results.

> *"Which would be worse, me worrying and then nothing happening or having the opportunity to know but not finding out, and that they are sick and worse than if we knew? I'd rather have the worry rather than have missed an opportunity to save or improve the life of my child."* Public workshop participant.

The public group did acknowledge that worry and stress of false positives could harm the parent and child but this was not usually the first reaction.

> *"Should be some certainty, I had a relatively new test that came back positive, because it was new the nurses couldn't say as much, and there wasn't much I could do. There was so much uncertainty. For the rest of the pregnancy, I was on edge … it turned ok but it was a lot of worry "* Public workshop participant

his was in contrast to the perspective from the Working Group which sought to minimise false positives as much as possible to avoid potentially negative impacts on families, the health system and society if a diagnosis was not confirmed and/or unnecessary treatment was provided. In workshop discussions, false positives were seen as a price to pay for information, choice and autonomy. It will be important to also consider the findings from the broader public dialogue which can be found here.

3. The principles

3.1. How the principles work together, what's missing, and what to do with edge cases

All of the principles were seen as important and there was a clear understanding that the principles worked together as a group. Participants provided insights on how to approach edge cases, and whether there might be elements that the principles are missing in their current iteration.

If some genes are to be included that do not meet every principle, workshop participants wanted Genomics England to consider an interplay between the most important principles of A, B and C.

- Where the variant has *strong evidence* of causing the condition [A], AND the effect on the person is significant [B], especially where this would affect the child's development and their future life; then participants would overall loosen the criteria around treatment [C] and accept a *lower threshold* of types of treatment available (for example treatments could be more experimental, or related to wider wellbeing rather than curative or halting the progress of the disease).
- Where the variant has *low evidence* of causing the condition [A] AND the effect on the person is significant [B], participants again would loosen the criteria around treatment [C] as the person's experience was seen as part of the journey to find more knowledge about the condition and what might work. This is because any treatment was seen as better than not knowing, or not having treatment.
- People with personal experience of a rare condition also particularly highlighted Principle A and B, with the importance of avoiding feedback of a condition that a child may be unlikely to develop. E.g., *"Must avoid identifying a theoretical disease where there is no certainty that the child will develop the phenotype*" (Online survey response).
- Principle C was more likely to be the highest priority for those with experience of rare diseases through their work, perhaps relating to the fact that Principle C looks at the types of treatments and interventions that are available and links screening to the possibility of treatment and positive outcomes.
- When there is a highly effective treatment available [C], participants would accept a lower threshold at [B] – i.e., less of a requirement for the person to be impacted significantly.
    - This is because participants wanted treatments that were certain to make a difference to be available to people who might be impacted by the condition, not just those most significantly affected.

- If there were a highly reliable, non-distressing or painful confirmatory test available [D] and some treatment fairly available [E], participants thought that the genes/variants/conditions could be included in the Programme even if the treatment available [C] was not likely to ameliorate the condition.
    - This was because participants believed that information may be enough to help reduce harm even if no treatments are available.

Participants felt that **explicit reference to 'the parents' wishes' and freedom of choice was missing from the principles**, as well as the (future) desire of the person screened to have access to the information about them.

Many patients with rare conditions and some members of the public suggested a shift in emphasis on the whole approach to the principles. They argued that the Programme's research study should **screen for as much as possible**, but think more carefully about consent; perhaps offering choice to parents upfront to find out as much as you want – even if it's uncertain and not clear what you might do with the results. When more discussion took place, participants did acknowledge the harm of finding out uncertain results but, as discussed above, it was very hard to trade this off against a perception that **more information would lead to better personal agency and control** and this would improve life for those tested.

A further emerging principle was the idea of **testing as more than a one-time event**. Participants suggested that we should sequence the whole genome, gather the genomic data and review at key life stages – ensuring the data is used and reviewed regularly over the lifetime of an individual to address early, mid, and late onset conditions. This might negate the need to test for everything at birth and could potentially help deal with some ethical issues around consent.

3.2. PRINCIPLE A

Participants were asked to discuss a current version of Principle A:

Include the genetic variant in the screening programme if… there is strong evidence that the genetic variant(s) causes the condition.

Generally Principle A was agreed to be clear and useful but there was a strong sense that even imperfect knowledge was better than none and that parents could make better informed decisions if they were given as much information as possible. Support for parents to understand any results was a clear priority.

> *"The question is about how much info you give to parents? A diagnosis can be life changing, or maybe there's not enough known to be life changing. It's how to give that information to parents and kids."* Patient workshop participant

Across the three workshop cohorts, there were different views on the level of evidence required on gene-disease association. The public, patients and HCPs all had a higher acceptance of screening for variants with less evidence of a gene-disease association than the working group.

In the patient group, there was a desire for more information about genetic variants that are less associated with developing conditions in the hope that rare conditions would then become more researched and more knowledge generated about them.

The online survey asked for responses to the following statements:

'It is better to look for only the variants with strong evidence that they cause the condition, because then we will not create uncertainty for parents and children.'

76% of respondents chose agree or strongly agree with a consistent response across most demographics. The notable exceptions are people with personal experience (lower at 54%) and people with work involvement (higher at 85%).

' It is better to look for a wider range of variants, even if we don't know as much about the relationship between the variant and the condition, because this might lead to more research in areas we know less about.'

45% of respondents chose agree or strongly agree with a consistent response across all demographics except those with personal experience, where 75% chose agree or strongly agree.

Principle A: wording recommendation

Accepted by most – 'strong evidence' could change to reflect different thresholds of penetrance acceptable for different conditions.

3.3. PRINCIPLE B

Participants were asked to discuss a current version of Principle B.

Include the genetic variant in the screening programme if… A high proportion of individuals who have the genetic variant(s) would be expected to have symptoms that would significantly impact their quality of life if left untreated. Satisfying criteria:

- Symptoms have a significant impact on quality of life, measured in QALYs where available or taking into consideration factors such as how serious the condition is and the testimony of people affected by the condition

- If left untreated, symptoms would typically start [in childhood (less than 16 years)]/ [early childhood]; or [by the age of 5]

There was no clear view on how sensitive and specific the test should be, and generally participants felt the risk of missing diagnosis of a condition outweighed the risk of a false positive.

Both the patient and public groups wanted the programme to prioritise avoiding missing potential conditions, even where that might mean more parents would receive false positive results.

> *"Which would be worse, me worrying and then nothing happening or having the opportunity to know but not finding out, and that they are sick and worse than if we knew? I'd rather have the worry rather than have missed an opportunity to save or improve the life of my child."* Public workshop participant.

The public group did acknowledge that worry and stress of false positives could harm the parent and child but this was not usually their first reaction.

> *"Should be some certainty, I had a relatively new test that came back positive, because it was new the nurses couldn't say as much, and there wasn't much I could do. There was so much uncertainty. For the rest of the pregnancy, I was on edge … it turned ok but it was a lot of worry "* Public workshop participant

'High proportion' was seen as problematic and it was suggested it be removed. Patients particularly felt that this might mean rare conditions were overlooked which might not affect many people but could have a significant impact on those it did affect. Nonetheless, there was a recognition that if the incidence of a condition was higher in certain communities the 'high proportion' qualifier could be helpful.

> *"Perhaps "high proportion" is not required?...If we know the genetic variant is likely to cause disease which is significant in the individual, then it should be screened for."* HCP workshop participant.

Some consideration was given to the idea that conditions where symptoms had higher impact on future life could be subject to a lower threshold for penetrance – because the harm of having it, and not knowing about it, was seen as higher. Public workshop participants broadly felt that more serious conditions should be prioritised; this impact was described as "*life threatening versus not"* and questions often related to how the Programme might prioritise more serious conditions.

> *"It would be a terrible thing to digest, if screening was possible but it wasn't used and if it could have cured, prevented or mitigated part of an illness"* Public workshop participant.

Patients were especially unhappy with quality-adjusted life years (QALYs) being used as impact measurements. While other groups wanted some way of judging severity of

symptoms, they also recognised it was a subjective measure even where they saw the value of including it:

> *"We had the screening before birth and was told QALY would be poor- she wouldn't eat, talk, walk. Now she does all of it. So I don't think you can say their QALY will be bad in all situations. So I don't like it."* Patient workshop participant.

The use of the word 'treatment' was questioned, with 'diagnosis' being a preferred qualifier.

> *"What does treatment mean anyway?…does it include psychiatric and developmental? …the phrase perhaps steers us too much towards medical and clinical interventions and doesn't seem to include support and other developmental therapies that may also be very useful/helpful"* Patient workshop participant.

Views on when symptoms should start varied, but generally perceiving 'childhood' as representing those under-16 was agreed with.

The online survey asked for responses to the following statements:

Q: The programme should only look for conditions where we would expect most people that have the condition to have symptoms that would significantly impact their quality of life.

76% of respondents chose 'agree' or 'strongly agree', but here the percentage of people with personal experience making that choice was lower (57%). We might infer from the workshop discussions that this relates to the need to find out more information about rare conditions overall even if they impact a small number of people.

Q: The programme should look for conditions even if most people who have the condition do not experience symptoms that significantly impact their quality of life.

Only 27% of respondents chose 'agree' or 'strongly agree' in response to this statement, with the greatest variation being between people with personal experience (49%) and people with work involvement (13%). There was a decrease in 'agree + strongly agree' percentages as respondents' ages increases.

On further deliberation, workshop respondents from the public groups also wanted some judgement on the severity of symptoms to be part of the screening criteria. These participants all wanted those with symptoms to contribute information on their severity. This aligns with the quantitative findings from the survey.

Principle B: wording recommendations

Remove 'high proportion' or change perhaps to 'significant proportion'. Change 'untreated' to 'undiagnosed'. In the satisfying criteria, change 'typically' to 'more likely than not'. Remove the references to QALYs and seriousness in the definition of impact, and rely on 'the testimony of those affected'.

3.4. PRINCIPLE C

Participants were asked to discuss a current version of Principle C.

Include the genetic variant in the screening programme if… Pre-symptomatic or early treatment(s) for the condition has been shown to lead to improved health outcomes for the child, compared to treatment after onset of symptoms.

HCPs made the connection between pre-symptomatic treatment and QALYs. In contrast, the public and patient groups concentrated on the 'improved outcomes' aspect of this principle, regardless of whether this was pre or post onset of symptoms.

As in the discussions around Principle B, QALY was not liked by patients as it was felt to be judgemental and not a helpful way to evaluate the lives of their loved ones – especially with rare conditions. The patient group highlighted the subjective experience of quality of life, and how this could fluctuate day to day, and throughout the course of the disease.

In relation to treatments, interventions, and timing of treatments, 'diagnosis' was again preferred to 'treatment'. There was significant recognition that treatment might mean something other than a medical intervention. Generally participants were keen that lifestyle management and access to potential future treatments.

The HCP group discussed that the principle would need to be flexible enough to include new developments in treatments.

The public and patient groups felt that even simply "knowing" justifies screening, as it enables parents to make changes to theirs and their newborns' lives, even if no treatment is available.

> *"Even if it means your child will not live and there might not be a cure now, but in the future there might be a treatment your child could be part of"* Public workshop participant.

The online survey asked for responses to the following statements and questions:

Q: The programme needs to look for diseases where symptoms appear early and where treatment can be started early, to bring the most benefit to parents and children and to justify the investment in the programme. Which of the following[6] is closest to your view?

Responses to this question showed fairly strong consistency for all large demographic categories. The most significant variation is shown by the set of respondents who have a rare disease, although this demographic category was small (15). Nonetheless, it is notable that people who have a rare disease typically wanted screening for diseases with a wider range of onset ages. This preference was not shared by people who have a family member with a rare disease. The same group expressed a weaker preference for linking screening to treatments that have an impact before symptoms start, as compared with the overall population.

Q: The programme should only screen for conditions where there are treatments that can cure or significantly affect the course of the condition.

55% of respondents chose 'agree' or 'strongly agree', but amongst those with personal experience, this fell to 32%, compared to 69% for those who work in rare disease contexts.

Q: The programme should screen for conditions where there are interventions that can affect the course of the condition, even if there may not be a significant improvement for all.

75% of respondents chose 'agree' or 'strongly agree' in response to this question. Responses to this question are unusual in that they show remarkable consistency across many categories including, in particular, "people with personal experience of rare diseases" and people who work in rare disease contexts.

Q: The programme should screen for conditions where there are options available which make life better for the patient, even if they do not modify the course of the condition or cure it.

With 75% of respondents choosing 'agree' or 'strongly agree', this statement showed greater consistency of response than many of the previous statements. "People with personal experience" were a significant outlier, with 94% of respondents in this group choosing 'agree' or 'strongly agree'.

Q: In addition to improving health outcomes for the child, the Programme needs to be economically responsible because it represents an investment of taxpayers' money. How far

[6] Options that respondents could choose from were:

A. The programme should look for diseases where the symptoms start before age 5
B. The programme should look for diseases where symptoms typically start in early childhood
C. The programme should look for diseases where symptoms typically start in childhood (less than 16 years).
D. The programme should look for diseases where there are treatments available which have more impact if they are given before symptoms start.

do you agree with the following statement? 'The programme should prioritise finding conditions where the cost to the NHS is greatest if the diagnosis or treatment is delayed.'

Respondents did not respond strongly to this statement. People with personal experience tended to agree less with the statement than the average, most other notable extremal cases involved small demographic categories, with the notable exception of "Other demographic groups".

Principle C: wording recommendations

C: Add 'early intervention or management of symptoms for the condition' alongside pre-symptomatic or early treatment(s). Remove the word 'health' (as an acknowledgement that outcomes are not only health related).

3.5. PRINCIPLE D

Participants were asked to discuss a current version of Principle D.

Include the genetic variant in the screening programme if… There is a minimally invasive confirmatory test that can establish whether or not the child has the condition.

Whilst participants understood the trade-off represented by this principle, they strongly felt that it was something that would vary according to the given situation; that the baby would have little memory of this period of time, so *"knowing would always be better"* even if the test was uncomfortable or even painful. In general, they felt if confirmation could be provided, it should be for the parents to decide whether to have the test or not.

We would also reflect that especially in the public groups, very little was understood about the role of the confirmatory test, so any research study would need to explain this aspect of the process.

There was substantial discussion and concern about the term 'minimally invasive', with some members of the patient group suggesting it should be completely removed from the list. Others suggested that this principle should be firmly aligned with screening being prioritised where a treatment is available - so that the invasive test is a gateway to treatment rather than undertaken 'with nothing to show for it'. That said, as before, the idea that knowing was better than not knowing still ran through the discussions.

> *"Even with an invasive test, if you can give a firmer yes/no, surely that has to be better?"* HCP workshop participant

The online survey asked for responses to the following statements:

Q: There should always be a confirmatory test that can establish whether or not the child has the condition.

Responses to this question were very high and very consistent across all categories. 80% of respondents chose 'agree' or 'strongly agree' and 93% of people with a rare condition did so.

Q: The test should always be minimally invasive.

The responses to this question tended towards 'neither agree nor disagree' indicating a less firmly held position in relation to this question.

Q: The invasiveness of the test should be considered relative to the level of harm that might be prevented by having the test (e.g. a biopsy is invasive but if it can treat a life limiting condition it might be worth it).

An extremely high and consistent positive response with 94% of respondents choosing agree or strongly agree.

Principle D: wording recommendations

Remove 'minimally invasive' and replace it with 'an appropriate test, relative to the impact of that condition on the patient'.

3.6. PRINCIPLE E

Participants were asked to discuss a current version of Principle E:

Include the genetic variant in the screening programme if… Conditions screened for are only those for which the socially acceptable interventions are equitably accessible for all as standard of care within the NHS.

Participants understood the equitable access part of the principle. However, they were pessimistic as to its practicability, with repeated references to the 'postcode lottery' of existing healthcare in the UK, but they felt that parents would want to know about an available intervention regardless. Clinical studies, crowdfunding and international treatment were all mentioned.

The public group did consider how much stress would come from knowing there was a treatment but not being able to access it, especially financially.

> *"For me, if I knew there was a treatment that I could never afford, it would be a lot more stress in that situation than not knowing"* Public workshop participant.

But they also saw that equity demanded others are not judged by a person's own situation, and they spoke about the responsibility parents would feel to do anything possible for their child.

> *"I don't think it's right to be based on the minimum. If there's other treatments across the UK, it's like cutting your nose off to spite your face, it's like you're cutting other families off from accessing those treatments. Just because you have it, and I can't, I don't want anybody to have it, which is really difficult."* Public workshop participant.

> *"As parents you just do what you have to do for your kids."* Public workshop participant.

The participants in the patient workshop were much more definitive about knowing about a condition, regardless of the accessibility of treatment.

> *"The vast majority of parents will turn themselves inside out and re-mortgage their house, etc, to get/provide care/treatment for their child… but many simply do not have the resources/ability/opportunity and should not be discriminated against due to their social or economic circumstances."* Patient workshop participant.

> *"The world is already unequal. As a parent with a child under the NHS I should still have the right to raise the money to treat him privately / in another country. Don't take this knowledge away based on what the NHS can / cannot offer. That feels more unethical."* Patient workshop participant.

This was not just because they wanted to be able to seek alternative treatment options, but also because they wanted to be able to make other lifestyle choices in the light of the diagnosis.

> *"Time is the most precious thing you have with your child and you appreciate all that you have and can make the most of that time."* Patient workshop participant.

The HCP workshop participants were pragmatic about the NHS and the reality that travelling to specialist centres is already part of treatment plans. But they agreed a postcode lottery was undesirable. They also recognised the value to additional research studies of being able to recruit patients from this programme, suggesting that the treatment did not need to necessarily be part of the mainstream NHS offer - essentially that research studies looking into the ongoing impact of genetic conditions would have a pool of available patients if screening was widespread.

The term 'socially acceptable' was problematic - and the patient group particularly felt it was a term that implied a value judgement about certain treatments.

The patient group struggled to find a shared definition of 'socially acceptable' and the public group agreed that it was a subjective term that would mean different things to different people.

> *"If no one understands "socially acceptable" it's probably not the right wording."* Patient workshop participant.

> *"'Socially acceptable'… what does this mean? - it raises questions and is too open to negative interpretation."* Patient workshop participant.

> *"What might be socially acceptable for one may not for a.n.other."* Public workshop participant.

The HCP group felt the term added confusion rather than clarity, and prioritised equitable access.

> *"This should probably be less about socially acceptable and more about equitable access for all."* HCP workshop participant.

The online survey asked for responses to the following statements and questions:

Q: The Programme should not look for conditions if the NHS would not be able to provide everyone with the same access to treatment and care, regardless of where they live.

Responses here were generally consistent with most demographics showing an "agree + strongly agree" percentage of around 50%. There are two notable points to observe.

First, for nearly all other questions, there has been strong correlation between the responses of "people with a rare disease" and "people with a family member with a rare disease". For this question, this correlation disappears: people who have a family member with a rare disease were far more willing to overlook inequality in access to treatment compared to all other demographics, including those people who have a rare disease.

Second, very few people who identify as Asian or Asian British disagreed with this statement but a notably large proportion of this demographic did not have strong feelings either way ("neither agree nor disagree").

Q: The programme should also look for conditions where the only intervention is an experimental treatment or clinical research study available in the NHS.

Responses here were relatively consistent and, like the previous, "agree + strongly agree" hovered around 50%.

Q: What factors do you think are important when thinking about the quality of life of the newborns who will be tested in this programme?

The most striking fact about these responses is the difference in attitude towards treatment considerations. Approximately 44% of respondents with work involvement raised treatment considerations compared to 16% of respondents with personal experience. There was a similar proportional difference in lived experience: around 8.9% of respondents who work in a rare disease context raised this, compared to 3.4% of respondents with personal experience (although note that the raw numbers were much smaller for this code).

In sum, when considering the quality of life for the newborns who might take part in the research study, availability of treatment is much more at the forefront of considerations for people with work involvement, compared to those with personal experience.

Q: Please give any examples of what you think are acceptable and unacceptable interventions.

This was a much more difficult question to analyse as many of the responses interpreted the question as asking for specific examples of acceptable / unacceptable interventions, rather than principles describing such interventions.

Principle E: wording recommendations

Remove ‘socially acceptable’. Include clinical trials and exploratory medicine. Re-consider ‘within the NHS’.

4. Putting the principles into practice

In designing this engagement, we reflected the way that Genomics England and the working group framed the key ethical challenges of setting up the Programme. All questions and discussions that formed the engagement started from a relatively abstract premise: that the Programme's research study should be based on principles to create the most learning for society and maximise the benefits of the new technology, while helping parents and babies, and, crucially, doing no harm – including through making sure no additional worry or distress were caused by false positives.

However, public, healthcare professionals (HCPs), and patients had a different starting point. When introduced to the Programme, the majority reflected on what it might feel and look like to be part of it. They wanted to know how it might change the experience of patients on the ground; how it would take place in practice; and how the journey of new parents from birth through various touchpoints with medicine might be changed by the Programme.

Therefore, for these groups to understand and trust the principles, it will be key to ground communication about them, and the Programme in general, in a description of how the principles will play out in real life.

The workshops generated several points:

- Parents and some frontline HCPs needed reassurance that any new testing would be designed in conjunction with support services for patients. They wanted assurance that a test result would automatically come alongside a prognosis, a roadmap for treatment, counselling, and advice. These groups did not focus on the systems integration needed to provide this, they simply wanted it to happen. Participants did not go so far as to say that a condition should be excluded if there wasn't a comprehensive plan for support; but they wanted to see evidence that Genomics England had thought through what would happen to patients after screening and what the impacts might be on the wider system.
- HCPs also wanted to know about next steps on the clinical side, in particular if GPs and others would be armed with the right information to know what to do with their patients who had screening results; e.g., what if multiple conditions emerge from screening? This also aligned with findings from responses to the online survey, where those who said they were connected by *work* to rare diseases tended to prioritise the need for evidence-based interventions (as opposed to those who said they had *personal* connections with rare diseases, who focused more on offering any intervention which would make life better for the patient).
- Further priorities in the online survey included the need to look at the developmental outcomes of the child when considering quality of life – a factor considered most important by those with personal experience. Workshop participants similarly indicated that there was no such thing as a static finding from a test for newborns, because their rapid development was almost the whole measure of their life at that

stage and there could be little quality of life for a baby without development of some kind. There is a need to frame communications in the context of the potential developmental outcomes for the baby, as well as in terms of diagnosing the condition.

- Consent process and how data would be used needs to be clear. The first questions from many in the workshops were around how the screening would happen, how it would work with the current newborn blood spot test, , and how consent would be obtained.

- The public understood the cost-benefit analysis of screening earlier and how it might minimise the time and financial cost of a diagnostic odyssey or treating the newborn later. Three-quarters of those responding online agreed that the Programme needed to prioritise screening for those conditions for which treatments would be the most if delayed. However, workshop participants did not respond well to this prioritisation, which suggests this should not be presented as the main aim of the Programme, as it can seem too calculated to focus upon financial cost/benefit analyses.

- Glossary notes and technical criteria should be presented in plain English.

- Continuous evaluation will be important. All participants wanted the principles to be kept under review and indicated they would be reassured to see a plan for going back and checking how they are working and how the Programme is operating. A few workshop participants who also completed the online survey commented that the questions put to them were too limited and focused narrowly on the principles rather than collecting views on how the overall Programme should be run. While this engagement was about the principles, participants nevertheless strongly made the point that they should be able to feed in more widely, on an ongoing basis.

- Participants felt they did not have enough information on how the screening and wider health research aspects of the Programme's research study would work together. This suggests there may be a need to explore how to communicate the future potential of discovery research in the programme and implications for those who take part, beyond immediate clinical need. Connected to this, the public and patients felt that genetic screening should not be a one-time event – though this Programme focused on newborns, several participants queried whether the later stages of life had been thought through. More engagement could be important, especially around how to protect the principle of autonomy and informed consent for the children as they grow up with the Programme having already created potentially large stores of data about them which could have considerable implications for later life.

- Participants told us that the Programme and its principles should be subject to a flexible policy with respect to new treatments and new best practice for all the conditions it includes.

  "As science moves on we will need to revisit everything." Public workshop participant.

When commenting on the structure of the engagement, the critical friends also pointed out some communications needs. They commented that the wider medical community would need to know how and why the principles differ from other screening criteria already in use. Two of the three also pointed out that WGS as an approach would need to defend its investment as a better way to create clinical diagnosis than, for example, ramping up existing programmes of diagnosis from phenotype or biochemical testing. More engagement with the medical and research community was felt to be needed so that the purpose of the Programme and the benefits of both research and clinical contexts were clear. Critical friends also noted, in a final review of this document, that public enthusiasm for 'as much knowledge as possible' has been seen in other research and testing contexts in the past; and this sometimes does not translate to patients wanting the knowledge in the context of need. Therefore, parents and patients will need support to understand the complexities of such knowledge through the programme.

5. Conclusions and next steps

The views of the public, patients, healthcare professionals, and critical friends were clearly set out through this process, and the suggestions for redrafting the principles were relatively consistent and clear.

Genomics England should be mindful that participants suggested casting a wider net with broader consideration of conditions to be included in the research study, compared to the views of the working group. However, this suggestion was accompanied by participants' indications that support can be provided for each condition and clinical pathway. A balance will need to be struck.

The working group will also need to consider the participants' feedback and consolidate with other engagement work that Genomics England is doing.

For each condition which may be investigated as part of the Programme, it would be wise to develop the next steps for babies and families in parallel. Finally, it is important for dialogue to continue, and for the principles to be reviewed in the light of any emerging tensions or challenges.

Appendices

Appendix A – working group membership and additional resources

Working group membership

** Indicates that Working Group members are also a member of the NHS Steering Group*

- Chair: Dr Emma Baple, Medical Lead for Rare Disease, SW GLH (CHAIR)*
- Professor Elijah Behr, Professor of Cardiovascular Medicine, St George's University of London
- Dr Felicity Boardman, Professor in Medicine, Ethics and Society, Warwick Medical School
- Dr Mike Champion, Consultant in Children's Inherited Metabolic Diseases And Clinical Lead, Evelina London Children's Hospital
- Dr Ngozi Edi-Osagie, Consultant Neonatologist, Manchester University NHS Foundation Trust*
- Dr David Elliman, Clinical Lead for NHS Newborn Infant Physical Examination Programme and NHS Newborn Blood Spot Screening Programme, Public Health England*
- Dr Francis Elmslie, Consultant Clinical Geneticist, St George's University Hospitals NHS Foundation Trust*
- Brad Gudger, Founder and Director, Alike
- Alison Hall, Senior Advisor (Humanities), PHG Foundation
- Georgia Hayes, Institute of Health Visiting
- Michelle Lyne, Royal College of Midwives*
- Dr Emma McCann, Medical Director, North West Genomics Laboratory Hub
- Dominic McMullan, Consultant Clinical Scientist, Central and South Genomics Laboratory Hub
- Simon Ramsden, Consultant Clinical Scientist, North West Genomics Laboratory Hub
- Jo Revill, CEO, Royal College of Paediatrics and Child Health*
- Professor Rob Taylor, Head of Highly Specialised Mitochondrial Laboratory, Newcastle upon Tyne Hospitals NHS Foundation Trust
- Sally Shillaker, Institute of Health Visiting
- Professor Caroline Wright, Professor in Genomic Medicine, University of Exeter
- Sarah Wynn, CEO, Unique

NHS England & NHS Improvement team

- Sarah Jevons, Head of Policy and Strategy
- Donna Kirwan, Genomics Midwifery Lead
- Alexandra Pickard, Deputy Director for Genomics*
- Laurence Russell, Senior Policy and Strategy Manager

Genomics England Team

- Arzoo Ahmed, Ethics Lead
- Dr David Bick, Principal Clinician
- Dasha Deen, Genome Data Scientist
- Kate Harvey, Engagement Manager
- Dalia Kasperaviciute, Head of Rare Disease Analysis
- Alice Tuff-Lacey, Programme Lead*
- Amanda Pichini, Clinical Lead for Genetic Counselling*
- Dr Richard Scott, Chief Medical Officer*
- Simon Wilde, Engagement Director

Appendix B - Workshop recruitment, attendance and design

All the workshops relied on the same information, which had been prepared in collaboration between GEL and Involve. The precise format varied slightly to reflect the cohort of participants and the time frame. In the breakout sessions, participants were shown sections of a video from the Genomics England website and the associated case studies. These materials can be reviewed at the Genomics England's Newborn Genomes Programme website.[7]

Public workshops

Recruitment and demographics

Criteria Qualitative Fieldwork were commissioned to recruit for the two sets of public workshops. Criteria carried out all participant contact and processed incentives.

The workshops took place on a weekday evening (2 hours) and two sessions on Saturday (5 hours with a lunch break). Participants were split into three breakout groups where they undertook a facilitated discussion prompted by the short videos and case studies prepared by the Genomics England team.

Seventeen participants were male and 22 were female. They represented social groups B-E.

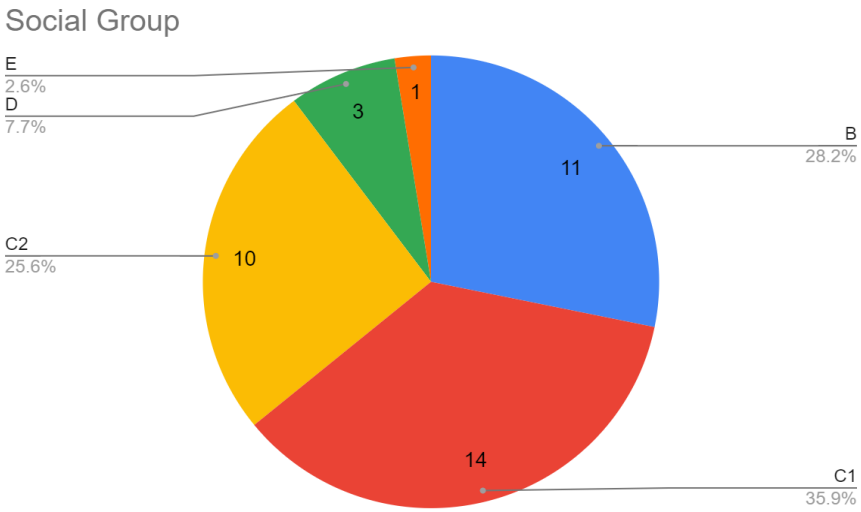


Fig 2: Breakdown of social groups represented at public workshop

Participants came from across the UK and Ireland, although Scotland was overrepresented.

[7] Web address https://www.genomicsengland.co.uk/initiatives/newborns/engagement (accessed 18/07/22)

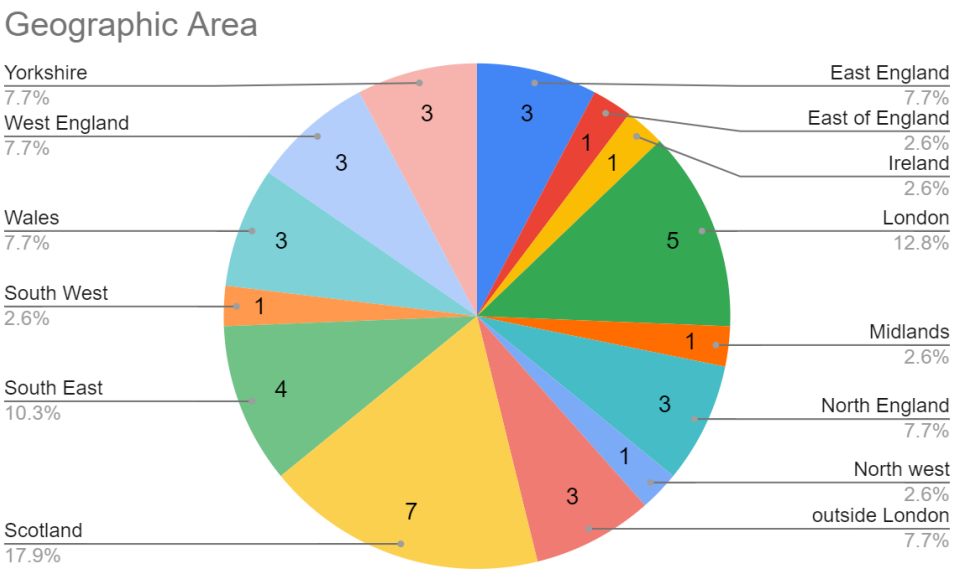


Fig 3: Geographic range of public workshop participants

Ethnicity was more diverse than the general population, but White British remained the dominant ethnicity represented.

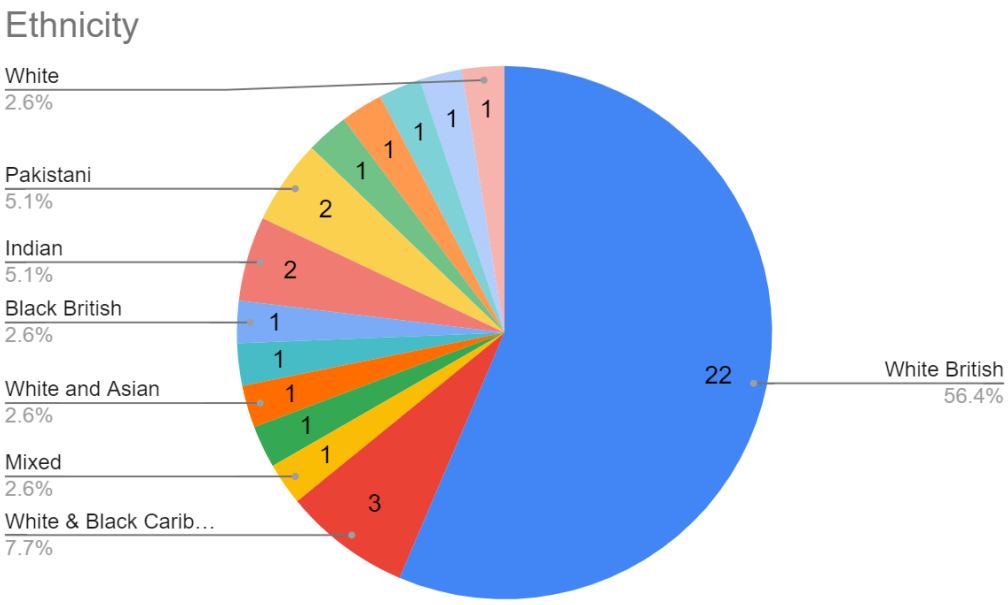


Fig 4: Ethnicity represented by public workshop participants

Sixteen participants had one child, nine had two children (one set of twins), five had three children and one participant had five children. Seven identified as being 'pre-family' and one that their family was older. The children ranged in age from 5 months to 23 years old.

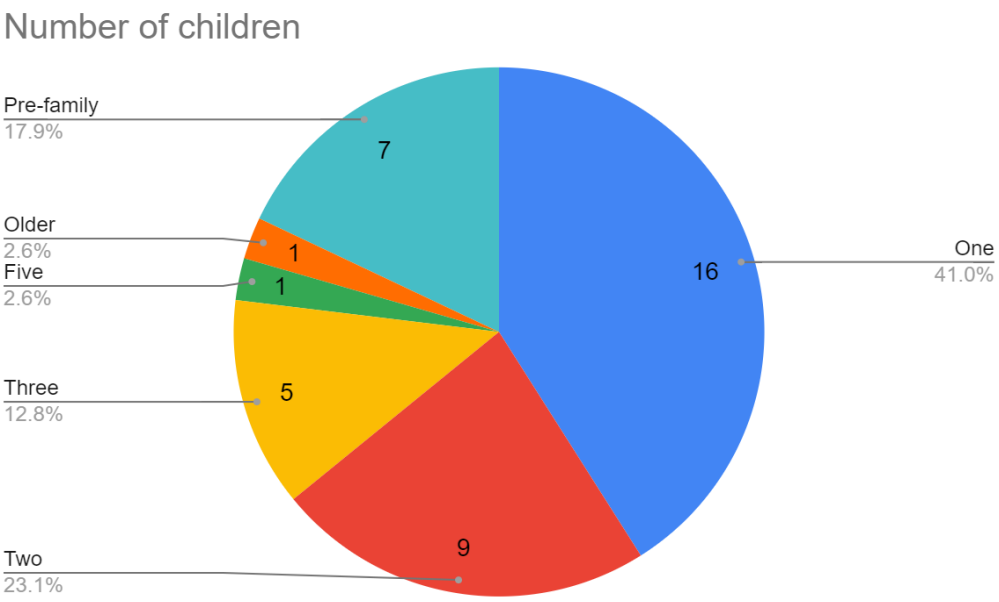


Fig 5: Number of children of public workshop participants

A variety of health conditions were reported but over half of participants reported as having no health conditions or impairments, and none considered themselves, their partner or children to have a rare condition.

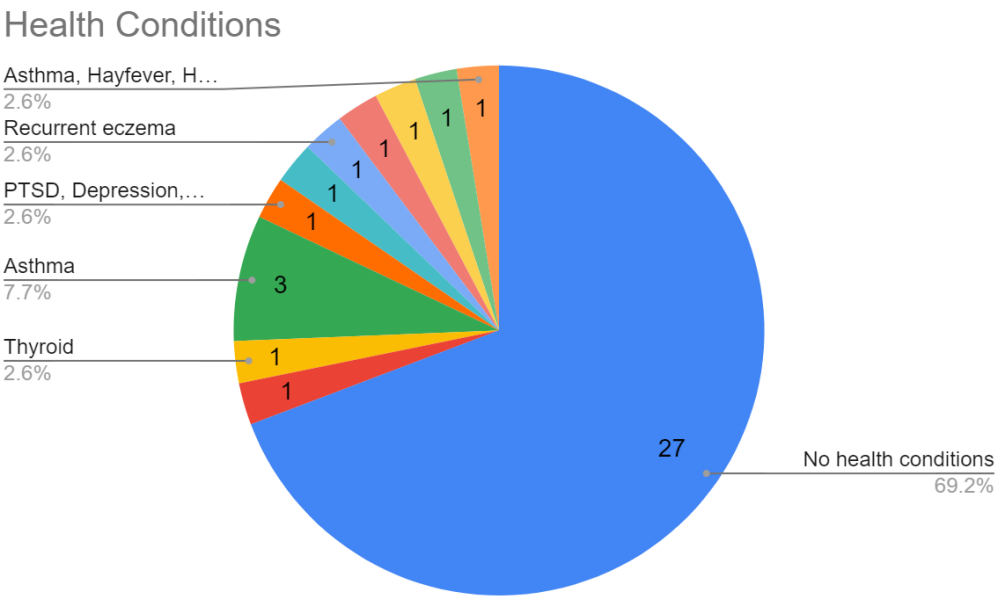


Fig 6: Reported health condition status of public workshop participants

Agenda

The public workshops both followed the same agenda:

Evening session	
Time	**Exercise**
6pm - 6:20pm	Welcome and Presentation including Genomics England films 'About the Newborn Genome Programme' and 'A basic introduction to genomics'. Opportunity to add any questions to Jamboard. Background to the study, recap of work so far and objectives for the workshop.
6:20pm - 7pm	Breakout Groups Introductions, Questions and first section of video from Genomics England website. Case Study 1 (these were rotated so different groups discussed different case studies). Case Study 2.
7:40pm - 8pm	Plenary feedback

Saturday session	
Time	**Exercise**
10am - 10:20am	Intros and icebreaker
10:20 - 10:50am	Objectives for today
10:50am - 3pm	Breakout Groups Facilitators were able to pace these sessions at a rate that suited participants. Part 1: Reflections from last session and introductions Part 2: Exploring the principles one at a time – first session (2 x principles) BREAK Part 3: Exploring the principles – second session (2 x principles) LUNCH Part 4: Exploring the principles – third session (1 x principle) and overview plus suggested changes
3pm - 3:40pm	Feedback in plenary Next steps, thanks and resources.

Some of the questions posted on the Jamboard were responded to in plenary, the full posting is included here for completeness.

Fig 7: Questions about genomics and the newborn screening programme asked at the public workshop

Feedback

Only 11 participants completed the post-workshop feedback survey. The word cloud below captures their responses when asked: *What three words would you use to describe your experience of being part of the Newborn Genomes Programme workshops?*

Fig 8: word cloud of feedback from participants at public workshop

All of those who completed the feedback survey agreed or strongly agreed with the statement: 'I have learned a lot about genomics and rare diseases.' 9/11 agreed or strongly agreed with the statement: 'My views about genomics and the importance of testing have changed.' 9 /11 thought their recommendations were likely or very likely to contribute to the principles final wording.

Healthcare professionals workshop

Recruitment and demographics

Gillian Kenny Associates were commissioned to recruit for the two sets of healthcare professionals' (HCP) workshops. GKA is a medical research recruitment agency specialising in the healthcare industry.

The workshops took place over two separate evening sessions lasting 3 hours. Participants were split into three breakout groups where they undertook a facilitated discussion prompted by the short videos and case studies prepared by the Genomics England team.

The first workshop consisted of GPs (5), paediatric nurses (5) and paediatricians (5). The second workshop was attended by health visitors (5); practice nurses (5) and midwives (4).

The number of years attendees had been practising ranged from 5.5 to 27. Attendees were predominantly female (all but 6), and were evenly spread between the 18-45 age bracket and over 45.

A third of the participants were practising in London, one was located in Glasgow and the others broadly represented other areas of England.

About half of the attendees identified as White British. Other ethnicities included Caribbean; African; Indian; Bangladeshi and Pakistani.

Agenda

The two HCP workshops followed the same agenda:

Time	**Exercise**
6pm - 6:40pm	Welcome and Presentation including GEL films 'About the Newborn Genome Programme' and 'A basic introduction to genomics'. Mini breakout for participants to meet each other and share any immediate questions about the study and genomics in general (shared to a Jamboard). Background to the study, recap of work so far and objectives for the workshop.
6:40pm - 8:45pm	Breakout Groups Facilitators were able to pace these sessions at a rate that suited participants. Part 1: Intro to the study Part 2: First two principles (these were rotated so were not covered in any particular order). This included a short video introduction and discussion of a case study with facilitators prompting attendees for their reflections and taking notes. BREAK

	Part 3: Next three principles
8:45pm - 9pm	Feedback in plenary. Next steps and thanks.

Some of the questions posted on the Jamboard were responded to in plenary, the full posting is included here for completeness.

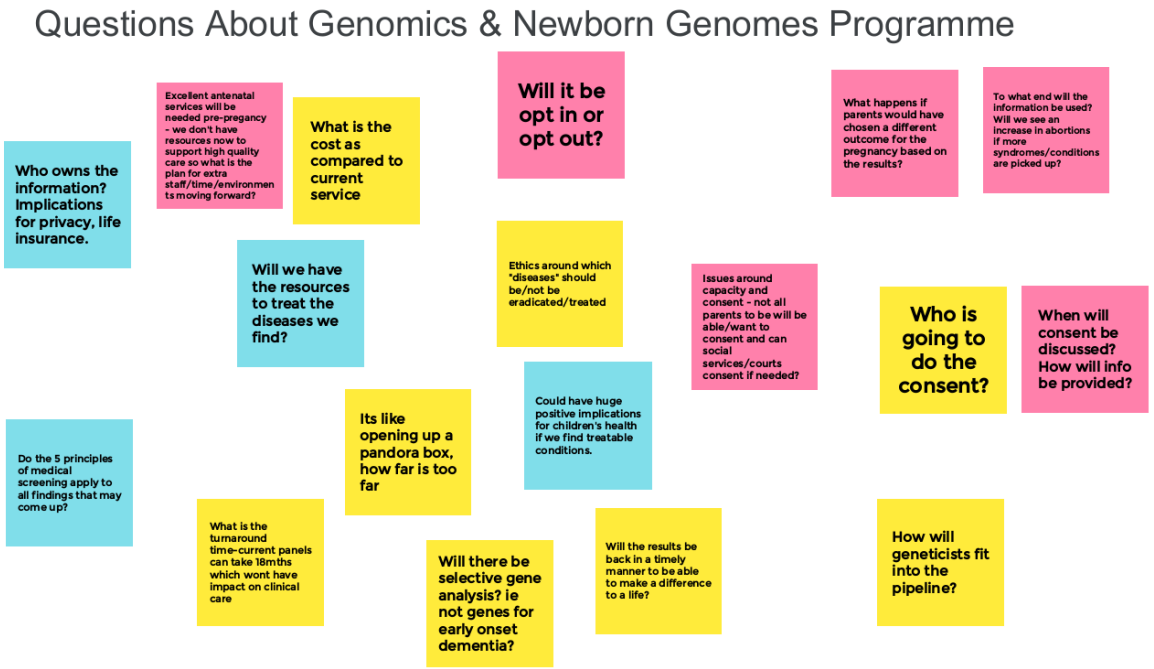


Fig 9: Questions about genomics and the newborn screening programme asked at the HCP workshop

Feedback

Of the 29 participants, 20 chose to complete a feedback form after the workshop. The word cloud below captures their responses when asked: *What three words would you use to describe your experience of being part of the Newborn Genomes Programme workshops?*

Fig X: word cloud of feedback from participants at HCP workshop

12/20 agreed or strongly agreed with the statement: 'I have learned a lot about genomics and rare diseases.' 11/20 agreed with the statement: 'My views about genomics and the importance of testing have changed.' 14/20 thought their recommendations were likely or very likely to contribute to the principles final wording.

Patient workshop

Recruitment and demographics

The recruitment for this workshop was very different from that undertaken for the public and HCP workshops. Involve and Genomics England asked umbrella organisations that support people living with rare genetic conditions to share information about the workshop with their networks. Those who were interested were asked to complete a data protection form and a short questionnaire to determine their eligibility to participate. This was administered by Involve.

The workshop took place over the course of a weekday evening (2 hours) and a Saturday (5 hours including a longer lunch break. The longer break was in recognition of the emotional labour that would be required of these participants in particular. Involve also provided a counsellor who was available to participants both during and for a short time after the sessions.

Attendees at the patient workshop skewed female, with 20 of 27 participants identifying as female. Geographically, the South of England was somewhat overrepresented but there was decent attendance from across the country, albeit with no residents of Wales or Northern Ireland.

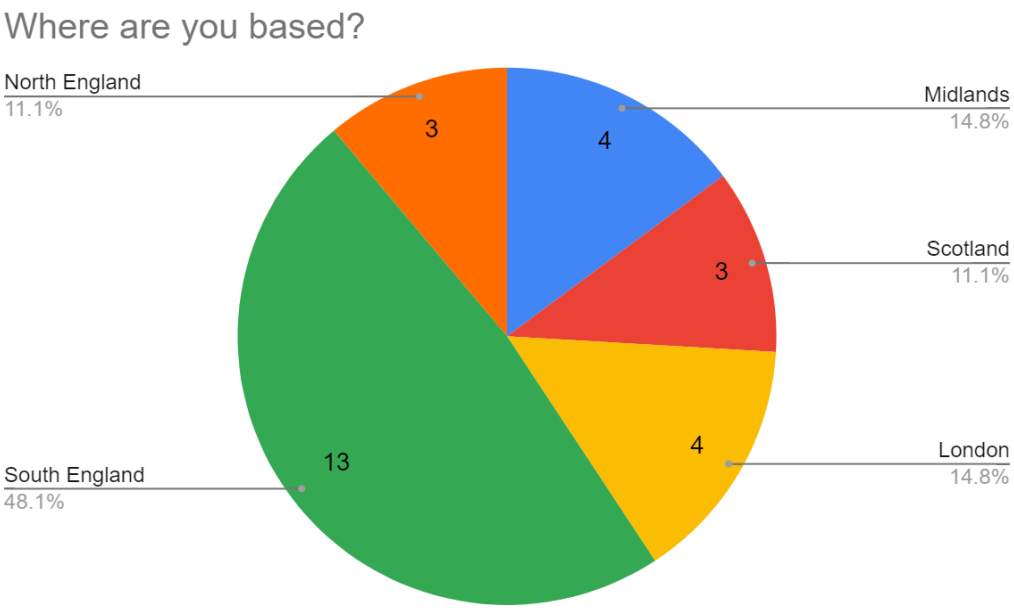


Fig 11: Geographic range of patient workshop participants

Despite Involve reaching out to specific groups including those with experience of sickle cell, ethnicity was overwhelmingly white / Caucasian (26/27) with only one participant defining themselves as having a 'mixed / multiple ethnic background'.

Age groups at the patient workshop were varied, and spread across all brackets.

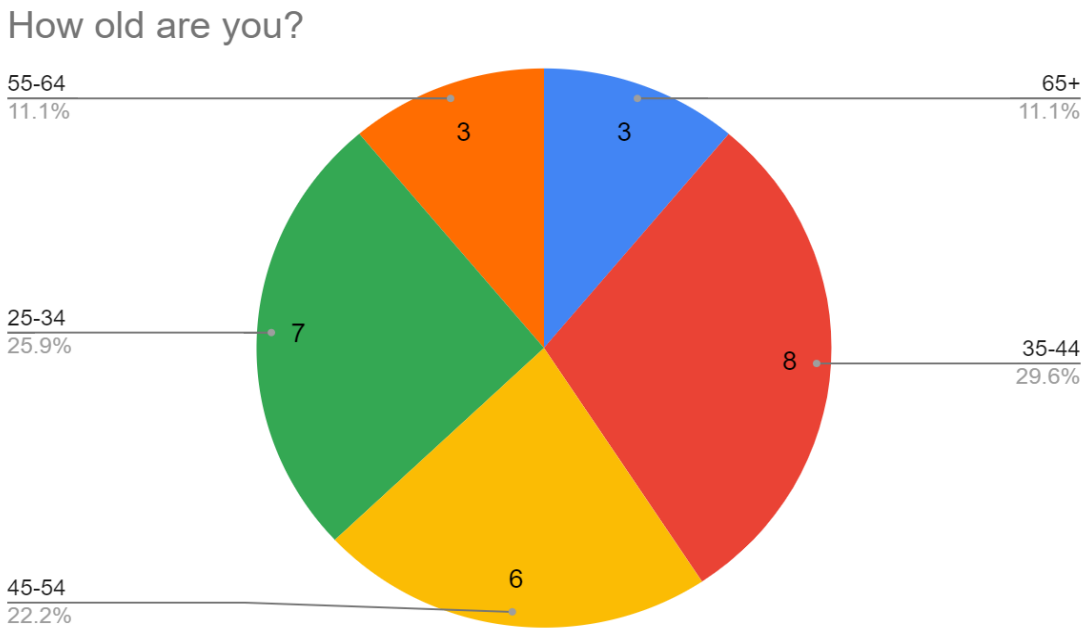


Fig 12: Age groups represented by participants at patient workshop

As we wanted this workshop to be made up of people with direct knowledge of rare genetic conditions, we also asked them why they were interested in attending. We allowed applicants to select more than one of the statements recognising that there would be overlap. Therefore these responses add up to more than 27. It is worth noting that only one participant selected 'My work involves supporting individuals and families affected by rare and/or genetic diseases' and did not select any of the additional statements. Eleven people who selected 'My work involves supporting individuals and families affected by rare and/or genetic diseases' also either themselves had a rare genetic disease (4) or their child (10) and / or another family member (2) had a rare genetic disease.

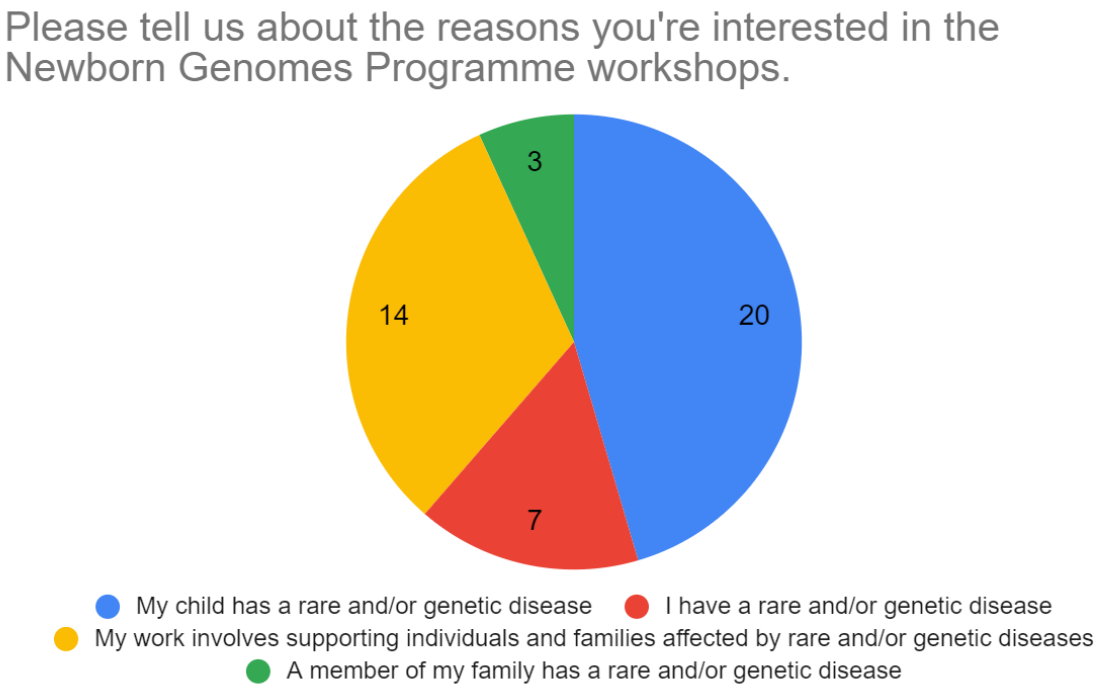


Fig 13: Reasons for attending patient workshop

Agenda

Evening Session	
Time	**Exercise**
6.00 - 6.30pm	Welcome and introduction to the project. Presenting background on the Newborn Screening pilot, two films about what the Newborn Screening Programme is and about genomics.
6.30 - 7.25pm	Breakouts in small groups with facilitators, to introduce everyone to one another, and reflect on genomics or rare conditions. Also, identifying questions about genomics or the Newborn Screening programme.
7.25 - 8.00pm	Breakouts exploring a case study provided by Genomics England of how parents might hear about the results of screening. Each breakout group discussed a different example and what the experience may be like for families in that situation. Plenary with feedback from groups.

Saturday session	
Time	**Exercise**
10.00 - 10.55	Welcome to session, with ice breaker and presentation of session's aim to help define the wording of principles so that they meet the aims of the programme. Presentation of the five principles for if a gene or variant would be included in the programme, using a Genomics England film. Breakout groups reflecting on the previous session.
10.55 - 2.35	Exploring the principles in facilitated breakout rooms. Groups shared their initial thoughts, their concerns and suggested amendments for each of the principles in turn. Facilitators were able to pace these sessions at a rate that suited participants. Part 1: Exploring the principles one at a time - first session (3x principles) LUNCH Part 2: Exploring the principles - second session (2x principles) BREAK Part 3: Exploring the principles - overview of if they are comprehensive and if anything else should be included
2.35 - 3.00	Plenary feedback from facilitators. Next steps, thanks and resources shared.

Feedback

6 participants completed the post-workshop feedback form.

The word cloud below captures their answers to the question: *What three words would you use to describe your experience of being part of the Newborn Genomes Programme workshops?*

Fig 14: Word cloud of feedback from participants at Patients workshop

Half of them Strongly Agreed or Agreed with the statement *I have learned a lot about genomics and rare diseases*. Again, 3 / 6 of them strongly agreed or agreed that their views about genomics and the importance of testing have changed. 3 / 6 strongly agreed or agreed that they knew how the decisions and recommendations made are going to be taken forward by Genomics England. 4 people felt their recommendations will contribute to the final principles' wording.

Detailed analysis of the online feedback is available from Involve on request: info@involve.org.uk

Further information about the Newborn Genome Programme can be found at https://www.genomicsengland.co.uk/initiatives/newborns