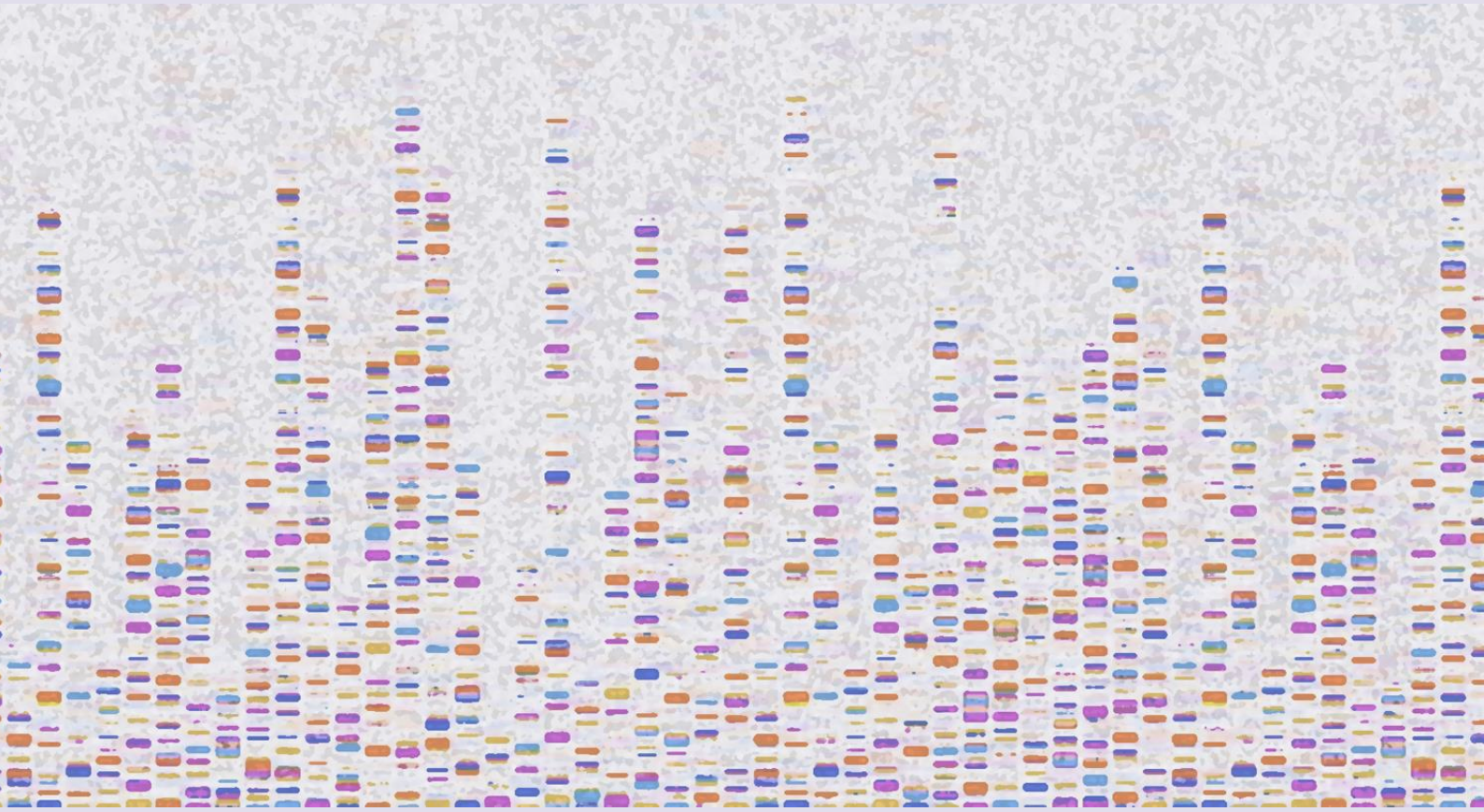
Implications of whole genome sequencing for newborn screening

A public dialogue



A Findings Report
Hopkins Van Mil
July 2021

Creating Connections
Hopkins Van Mil

Genomics england

UK National Screening Committee

sciencewise

UK Research and Innovation

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Foreword

UK National Screening Committee and Genomics England

There is no doubt that whole genome sequencing (WGS) has the potential to radically change the face of health screening in the UK and worldwide. To develop an evidence base to inform future UK National Screening Committee (UK NSC) recommendations, high quality, large-scale research programmes are needed to determine whether and how WGS can be implemented for screening in newborns. However, conventional scientific evidence is not the only criterion on which we base our recommendations. Society's values, beliefs and aspirations must be taken into account when considering the introduction of a screening programme. For this reason, the UK NSC decided to partner with Genomics England and Sciencewise to commission a public dialogue on the implications of WGS for newborn screening.

It has been a pleasure to be closely involved with this process. We were greatly impressed, not only by Hopkins Van Mil's approach to engaging with members of the UK population, but also by the enthusiasm and thoughtfulness displayed by all the participants. The discussions were expertly managed, everyone involved was able to express their opinions, and by the end of the process there was clearly a high level of understanding of the main issues. Some of these issues seem counter-intuitive but the participants understood and debated the fact that a genetic variation might or might not cause disease, and appreciated the difficulties of receiving results which do not give certainty to the individual but may confer stigma, risk many decades later, and consequences for family members.

Although the participants sometimes came to differing conclusions, there were some themes that stood out as universally important. In particular, there was a desire that truly informed consent to screening should be sought, that sufficient support should be available for those receiving a diagnosis, that access to data should be carefully controlled, and that inequalities in the distribution of the benefits of screening should be avoided. In addition, there was recognition that WGS should be used to expand the number of conditions screened for only when there are suitable interventions that can prevent, cure or ameliorate the conditions.

Obtaining the views of members of the public on very technical and sensitive issues represents a huge challenge, but this report demonstrates how well the project team have risen to it. The information gleaned will be of immense value to all the project partners and, we hope, others with an interest in this area. It will help shape future research and provides new and important information that will inform future UK NSC recommendations on the role of WGS in newborn screening.

Prof Bob Steele, Independent Chair
UK National Screening Committee

Prof Anne Mackie, Director of Programmes
UK National Screening Committee

In recent years it has been powerful to see patient and citizen voices come to the fore in healthcare research. This is certainly the case in genomics, where real engagement and involvement mean better decisions about how genomic medicine has an impact on our healthcare and our lives. It's important, and ongoing, both because of the positive benefits it can bring, and because it is the right thing to do.

Acting in a way that is worthy of public trust is existential for Genomics England. It lies at the heart of our behaviour, our systems, and our processes – for instance, the fact that our participant representatives have a veto on which research projects take place using their data.

Our knowledge of how the information in our DNA, our genome, affects our health and wellbeing over the course of our lives, is increasing all the time. We can only deploy that knowledge on the basis of public confidence and trust in what we do, and how we do it. And that confidence has to result from a genuine two-way conversation, listening as well as speaking.

This public dialogue is a striking example of how powerful that approach is, and I am deeply grateful to all the participants who made time to share their thinking with us.

Our primary goal in exploring this topic is to discover and diagnose serious genetic conditions earlier in life, because we know that for many conditions, each month that goes by can change outcomes for children. The earlier we catch these problems, the more we can do to help them. In future, as the dialogue covered, individuals may also choose to use their genetic information to inform their understanding of their own health over the course of their lives.

The potential use of whole genome sequencing in these ways raises a range of complex ethical, societal and technical challenges which are elegantly laid out in this report. The views of participants are proving invaluable in untangling those challenges.

So, while we need to be bold in our vision for encouraging research, innovation and new diagnostics, treatments and prevention, we need to be equally thoughtful in exploring the way forward, in a way that manages expectations, and provides transparency in how we do this.

We are already putting these dialogue findings to work as we explore the potential of both newborn screening, and the lifelong benefits of being able to use insights from our DNA to improve our health and wellbeing. As you would imagine, that preliminary thinking is being done in close collaboration with our partners in the NHS and a range of other stakeholders.

This report focuses our minds on the end-to-end support and service that participants expect. And we are committed to doing this with the families who might choose to have their child's genome sequenced at the heart of this conversation, and in a way that promotes diversity and equality – values that we recognise and to which we remain committed.

Our timing in jointly commissioning this work is deliberate: it comes right at the beginning of our work to explore and understand the opportunities, risks, regulatory and ethical implications of using genomics to expand diagnosis in early life where something can be done to reduce harm or avoid unnecessary interventions. It is the start of an ongoing conversation we are beginning, using this report as a solid first step.

This report is required reading for anyone working in genomics, or newborn screening, or both – and is hopefully a useful template for how public dialogue can be done both rapidly and robustly. It builds on Genomics England's strong track record in starting and sustaining conversations about the implications of genomic medicine – and provides a basis for building on and expanding our engagement and dialogue as we continue. My thanks again to all involved.

Chris Wigley, Chief Executive
Genomics England

Executive Summary

The implications of whole genome sequencing (WGS) for newborn screening public dialogue was commissioned in September 2020 by Genomics England and the UK National Screening Committee (UKNSC) with support from UKRI's Sciencewise programme[1]. It was designed and delivered by the deliberative engagement specialists Hopkins Van Mil.

1. The public dialogue research question

The research question for the public dialogue was as follows:

What are the implications for the NHS and society of using whole genome sequencing (WGS) for newborn screening?

The question was explored in two contexts:

1. The potential use of WGS as a technology **in addition to or to replace** some parts of the current NHS newborn screening programme (which has defined purposes and criteria). What might be the potential benefits and harms for the baby throughout their lifetime, for parents and the wider family, for others in society, and for the NHS?

2. The potential **novel or alternative** uses of WGS in newborns – going beyond traditional screening and exploring different purposes (e.g. lifetime monitoring, pharmacogenomics, family planning, research, information only), and the potential benefits and harms for the baby throughout their lifetime, for parents and the wider family, and for others in society, and for the NHS.

2. The dialogue process

The dialogue process involved the following people:

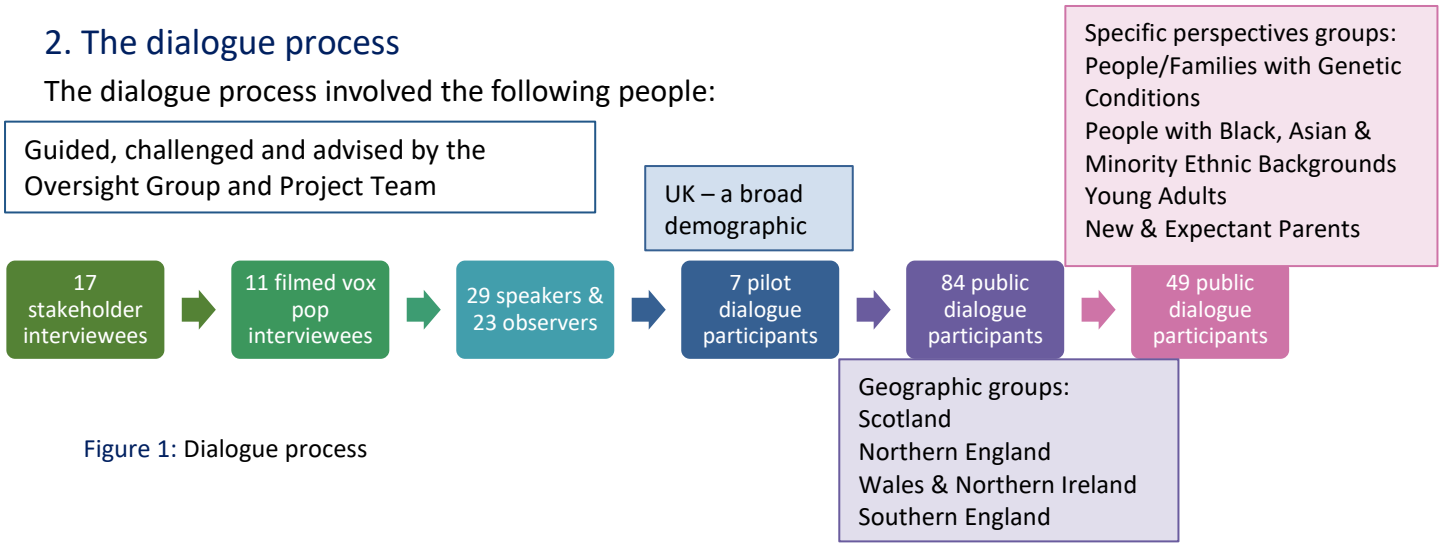


Figure 1: Dialogue process

Participants took part in five online dialogue events with reflective tasks between each workshop in a dedicated online space. Each workshop was a mix of plenary and break out discussions. The fieldwork took place between February and March 2021 using public dialogue best practice in line with Sciencewise Guiding Principles[2]. Participants reflected on the research question at each workshop drawing on expert presentations, case studies and lived experience examples.

[1] www.sciencewise.org.uk
[2] https://sciencewise.org.uk/about-sciencewise/our-guiding-principles/

Public dialogue is a qualitative methodology. In this report the subtleties and nuances of participants' views, concerns, hopes and aspirations are presented. These will inform the development of a pilot research study on using WGS as a technology for newborn screening; discussions about the potential for its use in population screening programmes; and ongoing public involvement in these activities.

3. Key findings

Participants were supportive of the potential use of WGS for newborn screening. They expected proper consideration to be given to designing and planning any future use of this technology. This includes involving the public in integration of the technology into any future research or newborn screening and ensuring appropriate resources, investment and safeguards are in place. The following key findings are to be found in the report:

1. It would be acceptable to use WGS to identify a wider set of conditions than the current NHS newborn screening programme *if*:

    - the conditions impact the infant in early childhood *and*
    - there are treatments and interventions to cure, prevent, or slow progression of the conditions.

    There is also potential for WGS in newborn screening to bring health benefits to parents, siblings and the wider family.

2. Genetic counselling and mental health assistance must be available for those who receive a confirmed diagnosis to help them understand the health condition and to provide emotional and psychological support.

3. A comprehensive genetic database should be established so that people from ethnic minority backgrounds are not disadvantaged by receiving more uncertain, or less accurate, diagnoses than the rest of the population from newborn screening - and the accuracy of diagnosis for everyone is improved.

4. The full complexities of WGS must be recognised when designing consent processes including:

    - the implications of WGS for the wider family
    - that 21st century families come in many forms
    - that parents give consent on behalf of their child, but the child may have different views as they grow up, including on their genomic data being used for research
    - and that the screening test has potential to look for many more conditions than current newborn screening tests.

5. If consent is sought for WGS data to be used for research: the data must be anonymised and used to deliver improved diagnoses, treatment and care.

4. Responding to the research question

The implications of WGS for newborn screening that participants identified, and their reactions to them, filter throughout the report.

Significant implications and reactions include:

Implications	Reactions
The NHS should be prepared to shift to a more prevention focused approach	Implement staff training and awareness raising throughout the system
The cost of an equitable national roll-out could be prohibitive	Time the programme correctly, making sure cost benefit analyses are drawn from the pilot research study
Take-up could be affected in a similar way to COVID-19 vaccine scepticism Conspiracy theories and fake news discourage people from taking part and jeopardise a national implementation plan People might have unrealistic expectations of what WGS for newborn screening can reveal	Instigate an early programme of engagement, communication and awareness raising and act with transparency Provide robust evidence of benefits and assessed risks using results from the pilot study Make sure realistic expectations are set out from the beginning
Safeguard WGS results from use by insurance/ marketing companies & employers What society agrees to over the next few years could be over-turned by changes in government	Ensure future-proofed legislation and governance procedures are in place Involve the public in meaningful ways in governance and decision making
Discrimination could filter in through the back door A postcode lottery or a two tier system of health care could emerge	Diverse genomic data sets and global collaboration should be sought and supported Raise awareness of disabilities and genetic conditions

Figure 2: Implications of and reactions to WGS for newborn screening

5. A future with WGS for newborn screening

Participants felt that a future which included WGS as a technology within newborn screening offered interlinked opportunities for society and the NHS.

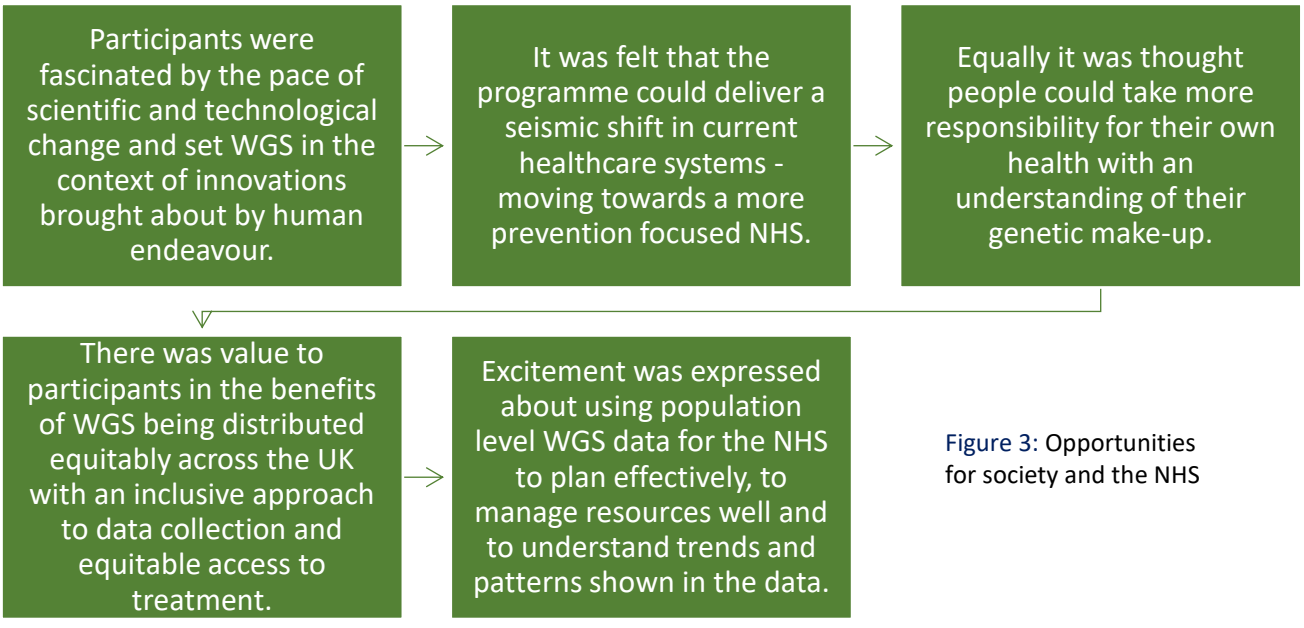


Figure 3: Opportunities for society and the NHS

Participants expressed their desire for a pilot research study on using WGS for newborn screening to be thoroughly planned and well executed. They want to avoid an unthought through pilot study that could damage the potential for benefits to be realised and undermine the existing high level of uptake of newborn screening. They expressed the expectation that the pilot study will:

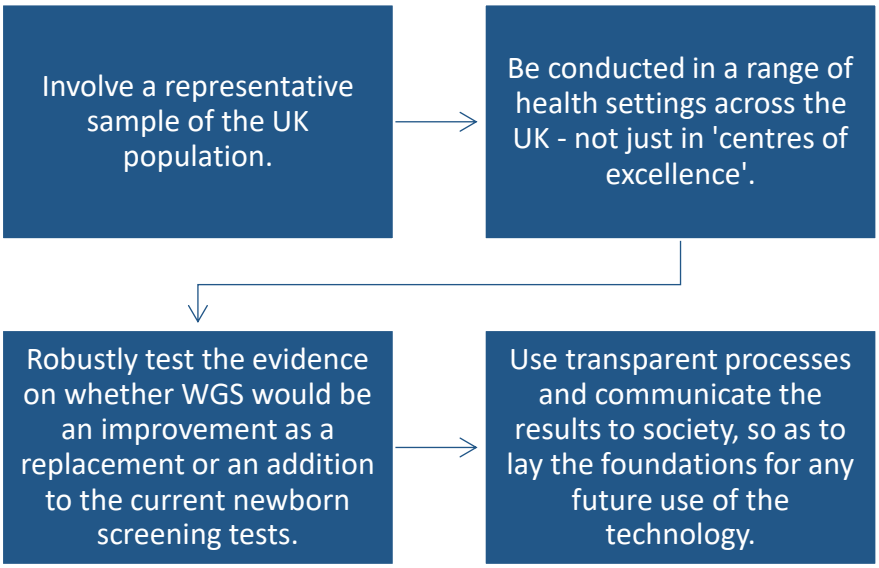


Figure 4: Expectations of the pilot research study

In summary, participants were supportive of the potential use of WGS for newborn screening but only if proper consideration is given to the design and planning of any use of this technology; the public is involved; and appropriate resources, investment and safeguards are in place. The elements that participants would like to see included in any future use of WGS for newborn screening are illustrated in figure 5.

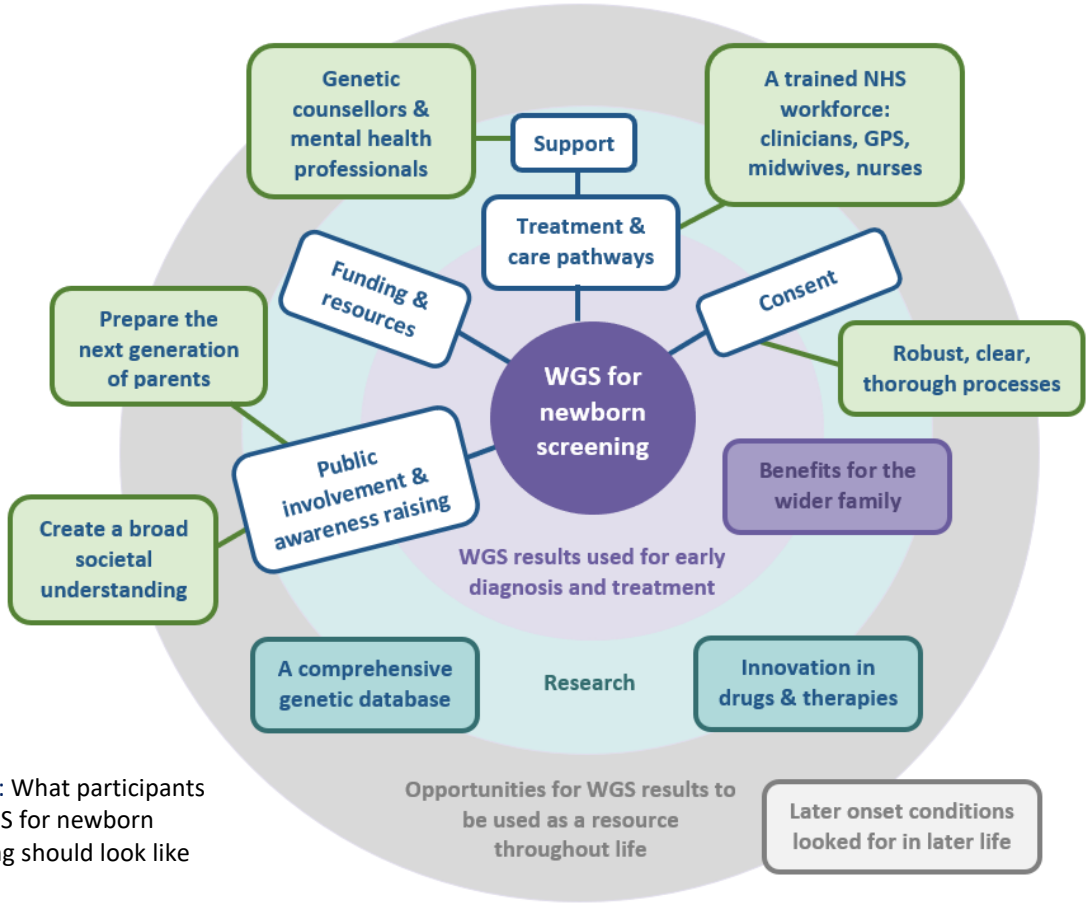


Figure 5: What participants said WGS for newborn screening should look like

Part A: Dialogue scene setting

This section of the report will be of particular interest to those wishing to understand the detail of the public dialogue methodology. Part B will be of interest to those who wish to turn immediately to the analysis of public dialogue findings.

Part A contains the following chapters:

1. Introduction

The Whole Genome Sequencing (WGS) for newborn screening public dialogue was commissioned in October 2020 by Genomics England and the UK National Screening Committee with support from UKRI's Sciencewise[3] programme. It was designed and delivered by the deliberative engagement specialists Hopkins Van Mil.

1.1 Public dialogue partners

Genomics England successfully led the world-leading 100,000 Genomes Project, which compared and analysed individuals' genetic codes to help diagnose, treat and prevent illness. It now works with the NHS to further develop and embed genomic healthcare and research in Britain. Genomics England's next chapter involves working with patients, doctors, scientists, government and industry to improve genomic testing, and help researchers access the health data and technology they need to make new medical discoveries and create more effective, targeted medicines for everybody.

The UK National Screening Committee (UKNSC) is a Scientific Advisory Committee that provides independent advice to Ministers and the NHS on all aspects of national population screening. The UK NSC secretariat is hosted by Public Health England.

Sciencewise is an internationally recognised public engagement programme which enables policy makers to develop socially informed policy with a particular emphasis on science and technology. Sciencewise helps to ensure policy is informed by the views and aspirations of the public. The programme is led and funded by UK Research and Innovation (UKRI) with support from BEIS.

Hopkins Van Mil (HVM) facilitates engagement so that voices are heard, learning is shared, and understanding achieved. In practice this means finding the process by which people can explore their hopes, fears, challenges and aspirations for the future. HVM's work enables stakeholders, technical specialists, and a diversity of publics to work together as equals to make actionable, better informed, and powerful decisions.

[3] www.sciencewise.org.uk

1.2 Project aim and scope

The project aim and objectives were developed in collaboration with the project partners and Oversight Group[4] members. The aim was to carry out a public dialogue to gain an understanding of the diverse public perspectives around Whole Genome Sequencing (WGS) for newborn screening, in order that future policies and decisions can better reflect societal views, hopes, concerns and aspirations.

This aim was explored in two contexts:

1. The potential use of WGS as a technology **in addition to or to replace** some parts of the current NHS newborn screening programme (which has defined purposes and criteria). What might be the potential benefits and harms for the baby throughout their lifetime, for parents and the wider family, for others in society, and for the NHS?

2. The potential **novel or alternative** uses of WGS in newborns – going beyond traditional screening and exploring different purposes (e.g. lifetime monitoring, pharmacogenomics, family planning, research, information only), and the potential benefits and harms for the baby throughout their lifetime, for parents and the wider family, and for others in society, and for the NHS.

Leading to the research question:

> **What are the implications for the NHS and society of using whole genome sequencing (WGS) for newborn screening?**

The commissioning partners intend to use the results of the dialogue to inform the development of a pilot study on WGS for newborn screening. Plans for this pilot study are in their initial stages and the timescale is yet to be determined.

1.3 Dialogue against the backdrop of COVID-19

2020 was a year like no other in the social and economic shifts caused by the global pandemic. The COVID-19 crisis shone a light on science and technology, health, health monitoring and genomics in ways which were new to everyone in society. Planning for the public dialogue began in October 2020. Fieldwork began in early February 2021 and was completed in mid-March 2021. As such the dialogue was delivered in a time when developments in health and genomics were in the public eye. Given COVID-19 the dialogue was delivered online. Whilst the vaccination programme and genome sequencing were in the minds of some dialogue participants, reflections in the dialogue went far beyond the immediate impact of the pandemic.

[4] The full list of Oversight Group members is listed in Chapter 11.

1.4 How to read this report

This report distils the findings from the public dialogue. In Part A we describe how the public dialogue was designed and delivered including the materials used, the role of specialist expertise, and details of the public dialogue participants and locations from which they were recruited. Part B of this report starts with a section on the context of the dialogue including participants' initial understanding and awareness of screening and genomics. We consider here the impact of COVID-19 on participants' views and their feelings about science and technology developments in healthcare more generally. Part B continues with the dialogue findings. Readers are encouraged to read Part A of the report if they are interested in how the dialogue came about, but to turn to Part B to go straight to the findings.

An accompanying Annex provides detail on the methodology, processes and stimulus employed. It is set out in three sections:

1. Methodology and workshop designs
2. Stimulus materials
3. Participant welcome pack

We use terms such as 'a few', 'several', 'some' or 'many' to reflect areas of agreement and difference. These should be considered indicative rather than exact. Where views apply to one group or location only, we make this clear in the text.

It is important in any dialogue process that the report reflects the voices of participants. As such we have used quotations taken from transcripts to emphasise main points. Some quotes have been edited to remove repeat or filler words. We have made no other edits, so as not to distort speakers' meaning. Throughout we have provided discussion snapshot boxes, which highlight a longer reflection from a participant, which adds force or emphasis to the points being made in the narrative.

2. Methodology summary

The Project Team included representatives from Genomics England, the UKNSC, Sciencewise, UKRI and Hopkins Van Mil. An Oversight Group[5] of 21 specialists was established to provide challenge and guidance to the project. It included the individuals, groups and interests set out in figure 2.1.

- 100,000 Genomes Project Participant Panel members
- Charities
  - Patient support / advocacy (genetics / disabled children)
  - Public education / awareness
  - Under-represented groups
- Clinical genetics
- Consent/ confidentiality rights
- Ethics / social science
- Genetic counseling
- Health governance / social justice / research inclusivity
- Midwifery
- Governance
- Government/ DHSC policy
- Professional education and training
- Screening
  - Policy
  - Clinical
  - Laboratory

Figure 2.1: Oversight Group composition

The Oversight Group met four times between October 2020 and April 2021. They helped to shape a comprehensive approach and unpack the complex subject of WGS for newborn screening. The Group worked with the Project Team to ensure that the stimulus materials presented a range of views without privileging any one in particular, to give participants with no specialist knowledge in the subject a foundation from which to build their deliberations. Twenty nine specialists[6] spoke to public participants from policy, clinical, ethical and lived experience perspectives, giving presentations and answering questions during workshops. In addition twenty three observers attended sessions, some of whom also responded to participants' ad-hoc queries during small group discussions.

2.1 The background to the dialogue

In 2016 the then Chief Medical Officer Dame Sally Davies, in her report 'Generation Genome', made a number of recommendations for taking forward genomic medicine in the UK. One of those recommendations, was that there should be a public dialogue to explore the shared social contract between patient, public, clinicians and academics in relation to genomic medicine. This resulted in the 'social contract' dialogue co-funded by Genomics England and Sciencewise that reported in 2019[7]. That dialogue provides a clear enunciation of public support for genomic

[5] A full list of Oversight Group members is provided in Chapter 11
[6] A full list of specialist presenters is provided in Chapter 11
[7] Ipsos MORI A public dialogue on genomic medicine: time for a new social contract Genomics England/ Sciencewise April 2019

medicine and also the 'red lines' concerning the use of their genomic data, as well as affirming the principles of reciprocity, altruism, and solidarity that underpin the NHS's values.

Another recommendation from 'Generation Genome' was that the UK National Screening Committee evaluate the opportunities offered by genomics for present and potential screening practices, both individual and population-based. This should 'include evaluation…of acceptability [of such a programme]'. In its response to that report, the UKNSC highlighted that there are many societal, ethical, and logistical factors that will need consideration should genomic technologies be introduced to screening programmes.[8]

Before this public dialogue was commissioned Genomics England and the UKNSC asked Professor Felicity Boardman, Warwick Medical School, to conduct a rapid literature review which was presented to the Oversight Group in October 2020 and ensured that the HVM team built on rather than duplicated the research.

HVM followed the literature review up with 17 stakeholder interviews[9] to ensure the design of the programme was informed by existing expertise and to understand who would provide the different perspectives needed during the dialogue workshops.

The dialogue was independently evaluated by Ursus Consulting, led by Anna MacGillivray. Ursus attended all dialogue events and Project Team meetings and sought input from the Oversight Group through interviews held outside the meetings. The insights from the formative evaluation have helped to ensure the dialogue follows best practice Sciencewise principles[10].

2.2 A deliberative process

Before setting out our approach in detail it is worth reflecting on why the public dialogue approach fulfilled the needs of the project. Public dialogue is not a 'we tell you this and you tell us what you think about it' information exchange. Dialogue works when participants interact on a level playing field with specialists: academics, scientists, and those that inform and make policy. In this dialogue these included screening and genomic policy makers, clinicians, midwives, genetic counsellors, those with lived experience of the issue and charities supporting those with genetic conditions and their families. This specialist evidence is then viewed through the lens of participants' own lived experience, leading to rich and powerful insights.

In a public dialogue citizens come together, with sufficient time to reflect, to:

- Learn about the issue
- Talk with, not past, each other
- Consider diverse points of view
- Discover key tensions and values
- Spark new ideas

[8] UKNSC, Generation Genome and the Opportunities for Screening Programmes, August 2019
[9] A full list of interviewees is provided in Chapter 11
[10] Sciencewise Guiding Principles (July 2019) and Sciencewise Quality Framework (August 2018)

This leads to an understanding of what people value, what they see as benefits and harms, their trade-offs and redlines and, in this case, highlights areas to be considered in the development of a research study to pilot WGS for newborn screening.

We used a consistent group of HVM facilitators in all dialogue workshops. Each small group comprised no more than seven participants working with one facilitator. Facilitators followed workshop process plans designed in discussion with the Project Team and in consultation with the Oversight Group and other stakeholders we interviewed. The process plans and stimulus were tested and refined in pilot workshops in January 2021 with seven recruited participants.

2.3 Recruiting the public dialogue participants

A total of 133 participants were recruited to the dialogue. Eighty four people using a specification and screener to ensure that as far as possible, participants reflected the demographics of the UK population, sampling for age, ethnicity, gender, sexual orientation, life stage, disabilities and socio-economic group. These participants formed four groups from Northern England, Southern England, Wales & Northern Ireland and Scotland (twenty one participants in each location).

In addition weighting was given to four groups by recruiting forty-nine participants the project team considered might have different perspectives to the wider population on WGS for newborn screening. These groups comprised people with Black, Asian or minority ethnic heritage; new and expectant parents; people with a family history of genetic conditions; and young adults (aged eighteen to twenty four). The first three of these groups comprised fourteen participants, and the final one seven.

We excluded those who had taken part in qualitative research in the previous twelve months. Participants were given a cash honorarium/shopping voucher (according to preference) to recognise the time committed. This is standard in Sciencewise public dialogues and means people are not excluded because of their financial circumstances. Figure 2.2 illustrates the recruitment coverage.

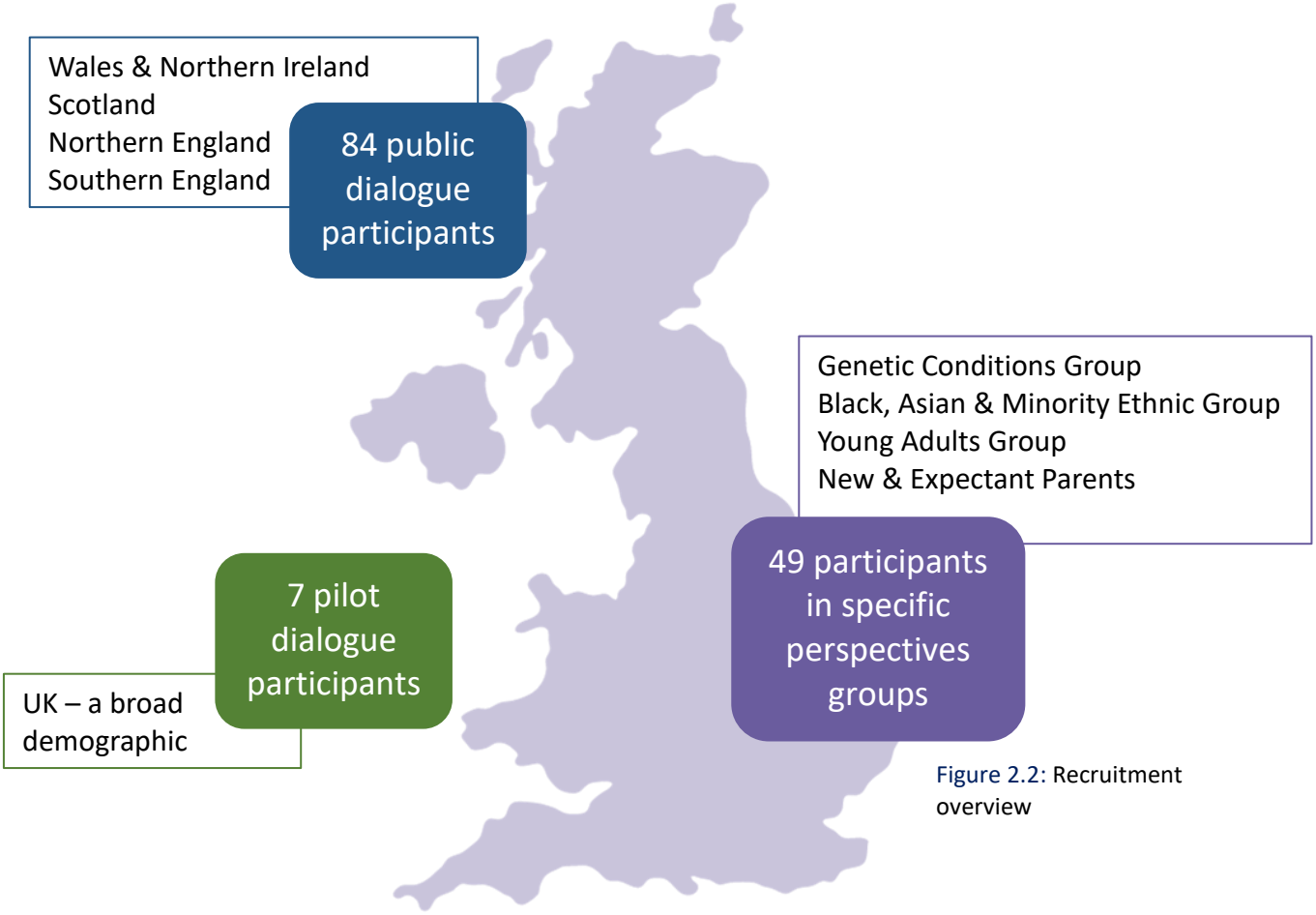


Figure 2.2: Recruitment overview

Digital inclusion is an essential part of recruitment for an online dialogue. No one who wished to participate in the dialogues was excluded because they did not have the hardware, software or technical knowledge to attend an online workshop. Before every set of workshops, HVM ran a 'tech support' session in which people could run through, in an informal way, how to use the key elements of Zoom. We opened the workshop 30 minutes before each session so that participants could check their technology was working. Each workshop also had a dedicated tech support team member to get people back online if they lost their connection and find solutions for loss of sound or visuals.

It has been key to HVM's process during the pandemic to ensure everyone in the dialogue feels safe and able to discuss matters of emotional and ethical significance in the online space. To enable this the 'Welcome pack' distributed in hard copy to all participants in advance of the first workshop included guidance on who to contact if they felt affected by any of the issues raised in the discussions. Contacts included the HVM support rep, a facilitator available at each session, and external advice organisations including charities that support children and families with genetic conditions.

2.4 What did participants do?

For all participants the dialogue involved three main elements:

- five online events – a webinar and four workshops;
- an online space to review materials, ask further questions and add additional comments in participants' own time;
- online polling during the workshops to ask for quick reactions and/ or to sum up how participants feel about an issue.

Examples of the detailed process plans and stimulus materials used throughout the dialogue are available at Annex 1-3.

Interaction with specialists is an essential element in Sciencewise dialogues, providing participants with insight into the different perspectives on a topic. In this dialogue we worked with a range of specialists who contributed to the dialogue in the following ways:

- presenting during workshops;
- answering participants' questions;
- explaining key concepts and terms.

Figure 2.3 sets out the process route map. The core information participants required was on:

- NHS health screening programmes;
- whole genome sequencing;
- case studies to help participants consider the implications of introducing WGS to the NHS newborn screening programme and potential **novel or alternative** uses of WGS

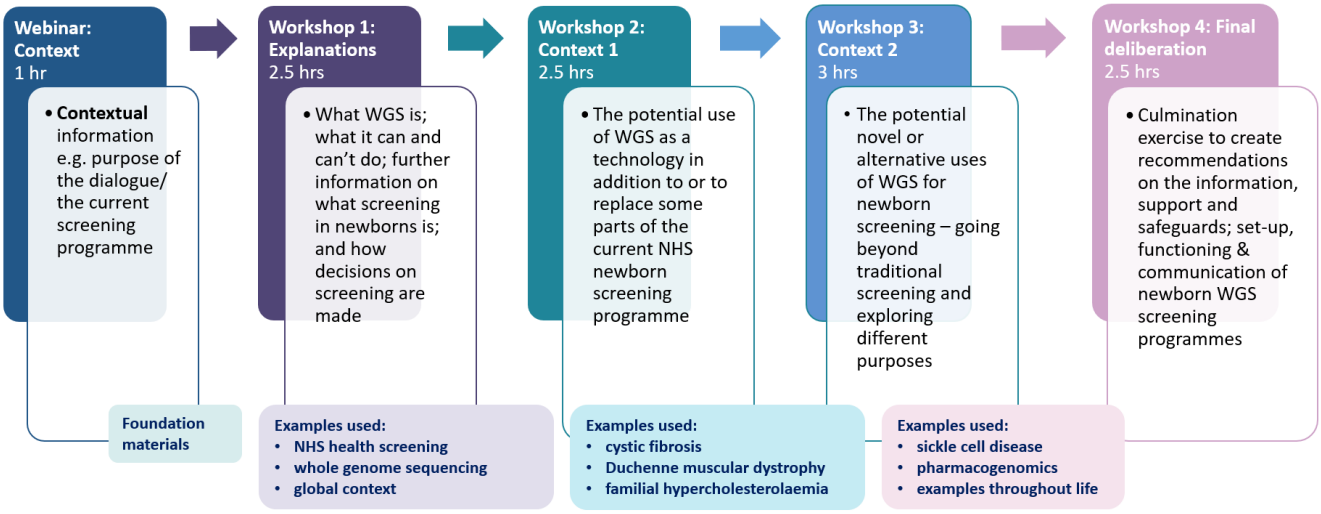


Figure 2.3: The process route map

2.5 Analysis and reporting

The Zoom dialogue workshops generated over 120 hours of audio recordings. These were transcribed for analysis using NVivo software together with:

- data from the reflective tasks that participants completed in between each workshop
- results of the online polling questions used live during workshops.

HVM applies grounded theory to our analysis of public dialogue deliberations. We build theories from what we have heard rather than having a preconceived hypothesis to test. We make use of Sciencewise Guidelines for Reporting (July 2019) and the evaluation of previous public dialogues to inform our work. Throughout the process the HVM coding, analysis and writing team have maintained a rigorous approach and held frequent sense-checking sessions to mitigate against researcher bias. Public dialogue is a qualitative methodology, findings do not demonstrate statistically representative analysis. We present the subtleties and nuances of participants' views, concerns, hopes and aspirations so that they can inform the next steps in the consideration of WGS for newborn screening.

Part B: Dialogue findings

This section of the report will be of particular interest to those wishing to delve into the analysis of the public dialogue findings.

Part B contains the following Chapters:

3. Contextual knowledge

Key findings

Participants began their dialogue experience with little knowledge of either the current NHS newborn screening programme or whole genome sequencing. However, they are aware of NHS health screening more generally, and used this knowledge to inform their discussions. Insights raised in this chapter include:

- Recurring questions throughout the dialogue were around the potential **cost of the programme** and the **ability to resource it effectively** given the pressures faced by the NHS.
- They were concerned, given some people's reaction to the COVID-19 vaccine, that **take-up of WGS for newborn screening** might be limited if people do not have enough trust in WGS as a technology.
- Participants are fascinated and interested in both the **pace of scientific and technological change** and the innovations brought about by human endeavour.

3.1 NHS Health Screening and WGS: participants' initial understanding

In this chapter we describe participants' initial understanding of WGS for newborn screening. In our first dialogue event we asked participants what came to mind when we said, 'NHS health screening'. Responses to this question revealed participants have some knowledge of screening programmes drawn from experiences of screening in their lives. Participants mentioned screening for cancers, most frequently breast and bowel cancer, to prevent disease.

Some said they knew nothing about screening at all,

> I didn't even know that national screening is available before doing this. I thought you'd only go if you had a health issue for the doctor. They would then prompt you, 'We should get you screened for-,' as opposed to just going like, 'I feel a bit like I should get screened for the health benefit purposes.' I Participant, Scotland

Out of the 133 dialogue participants only one, in the Black, Asian and Minority Ethnic group, spontaneously mentioned 'newborn' screening as coming to mind in response to this first question on NHS health screening. As the dialogue progressed we found very little knowledge of newborn screening generally, with those closest to it, the New and Expectant Parents group referencing the heel prick test most frequently. However, participants in all groups who did remember their child having the heel prick test said they had no understanding of the nine conditions currently screened for, or that they could opt-out of the screening programme should they not wish it for their child. None of the dialogue participants had heard about the prospect of whole genome sequencing being used for newborn screening before joining the dialogue.

Despite this lack of awareness of newborn screening, participants felt that screening programmes offered to everyone in the population were an important part of the NHS.

> I can only go through the testing I've had in my life. I'm so happy that the Health Service contacted me when I was 60 to have the bowel test. They found abnormalities which has improved my life. I Participant, Northern England

In the early stages of the dialogue participants were asked to note down something that they had learnt about NHS screening programmes, including if WGS was used as a technology for newborn screening in the future. Figure five summarises the points made by participants.

Main early stage dialogue learning points
Not everyone with positive results from screening will develop disease
The process of screening, and that it is not a diagnosis
It doesn't give a diagnosis, just tells you if the baby is high risk or not
This is a new idea for the advance of medicine to enable diseases to be detected early
After screening people will be fully supported by clinicians etc as required
Cystic fibrosis is one of the nine health conditions currently screened for
Screening is always a choice
This is a public dialogue for a potential future programme to screen for childhood illnesses that can be treated
There are psychological and ethical implications including false positives and effects on parents
How vast this programme will be if rolled out
There is a difference between the current newborn screening programme and one which might include WGS in the future
Impact on mental health from the trauma related to finding your propensity to develop a serious illness in later life

Figure 3.1: Early learning points on the subject

Participants spoke of being fascinated and excited by the potential for WGS for newborn screening. They saw benefits in being able to help people who have serious, life threatening and life limiting genetic conditions. For some this fascination and excitement meant that it was hard initially to see any downsides in WGS for newborn screening, particularly when considered as an addition or to replace some parts of the current NHS newborn screening programme.

> I don't have kids but it's definitely the kind of thing that if I was in that position and like you say, if you can track down these things on day dot and get that support, that information, whatever it might be. I'm a little bit hard pushed at the moment to see downsides to be honest. I Participant, Southern England

> I am just amazed how cutting edge this is. It is very exciting! As a gay man the advancement in HIV medications and prevention have been amazing to observe over the years especially as you see how this affects many of those in your own community who are often as close as family to many. **I** Participant, Young Adults Group

3.2 Views on science and technology in healthcare

Many participants' had positive views of scientific and technological developments in healthcare more broadly. They spoke about the fast pace of developments, that science is constantly pushing boundaries, and that innovations and breakthroughs are the result.

> There are many examples of science and technology in healthcare that make me feel excited for the future. From the creation of antivirals to keyhole surgery, to the most recent developments in the COVID-19 vaccines - especially the mRNA vaccines. I hope that science and technology in healthcare could one day prevent, provide a cure for, or at least provide a treatment for all diseases no matter how rare. **I** Participant, Southern England

3.2.1 Take up of WGS for newborn screening

We see throughout the report that participants are supportive of WGS for newborn screening as an addition to or to replace some parts of the current NHS newborn screening programme. They do not wish the current high take-up of newborn screening to be undermined by its introduction.

A very few participants said they were themselves sceptical of scientific developments in healthcare because of their experience of, for example, racial inequalities and/ or listening to what is shared on social media about COVID-19 vaccines. An example is given in discussion snapshot 1.

Discussion snapshot 1 – vaccine scepticism:

I'm one of those people that are sceptical about taking the vaccine, because to me, from what I've seen in the videos that have been flying about, especially in the United States, I'll be scared that maybe what they're giving me an injection for the vaccine for the COVID that is not the same thing they are giving my White colleague or my White partner. **I** Participant, Scotland

This points to a social divide that was seen as important for many in the dialogue. That fear and mistrust of science in healthcare by some can affect society's view of whether to accept a new technology or not. The example of COVID-19 was used to explain this potential divide between people who trust scientific developments in healthcare and those who do not,

> COVID has shown that there is a big divide in people that have faith in healthcare and science, and those that believe it is dangerous and unethical, e.g. the vaccine will save us versus the vaccine will put a tracker in us, and we will be killed within a year. **I** Genetic Conditions Group Online space

Combatting scepticism towards WGS for newborn screening was seen as critical. Participants in many groups said that there is a great deal of trust in science and technology, particularly in the light of the development of COVID vaccines, but no one should be complacent about the level of understanding in society required to make the pilot study or longer-term use of WGS for newborn screening effective. Participants argued for evidence of the benefits to be explained coherently

and clearly to everyone in the population and for time to be taken to build trust in the science. As one participant put it,

> I'm a teacher, I've got parents at school who think that COVID is a hoax, and that it's caused by radio waves. So, if you've got that going on that extreme, is there a level of trust? So we can't just blindly go ahead with things and expect people to accept it. **I** Participant, Genetic Conditions Group

Some participants felt that religious views could affect whether or not people would accept WGS as part of the newborn screening programme.

> I'm not a particularly religious person myself, but there might be religious views that affects people's opinions on this. I don't know if the whole genome sequencing, whether you can pick different tests that you want to know about and others that you don't, if it doesn't agree with your ethics or whatever, whether you can be selective about the whole selective process, if that makes any sense. **I** Participant, Northern England

3.3 Can we afford it?

Participants voiced the concern that the NHS is under strain. During the COVID-19 crisis they have seen daily governmental briefings on the need to reduce pressure on the NHS and have heard in the news and social media that cancer treatments and routine operations have been delayed whilst the healthcare system deals with the pandemic. All groups and many participants asked whether the NHS can afford to bring in WGS as a technology for newborn screening.

Some expressed the concern that using WGS for newborn screening would result in greater insight into potential future problems. They felt this could result in cost-cutting in other parts of the NHS.

> I was just wondering if we're going to be testing for more and more problems what are the cost implications and what happens if treatment for certain problems is very expensive? How are we going to get round these things? Will it come off other parts of the health service? **I** Participant, Northern England

4. Implications for the NHS & society of WGS for newborn screening

Key findings

In this Chapter we find that dialogue participants feel that WGS for newborn screening is a significant development in health care. Insights include:

- The programme could deliver a **seismic shift in current healthcare systems** moving towards a more prevention focused NHS. Attitudes to health in society could shift so that people take **more responsibility for their own health** as a result of the knowledge they may gain from their genomic sequence.
- A desire for the NHS to use **WGS data as part of forward planning** with the potential to **save money** and **resources** over time.
- However they **caution against the programme being a slippery slope towards people feeling they have no choice but to use private health care** if the NHS is not able to provide care, treatment and support for all those that might need it.
- Participants expressed **considerable excitement in the possibilities for research** to deliver earlier diagnosis and more effective treatments for genetic conditions. This includes a greater understanding of regional and national trends and patterns to, for example, understand the **relative importance of environment in relation to genes and vice versa** in relation to population health.
- **'No postcode lottery'** was the cry throughout the dialogue. Participants want WGS for newborn screening to be rolled out with due care and attention.
- A desire for **a UK wide roll out of WGS for newborn screening**: if, for example, just England introduced WGS, it would undermine population level research data and early diagnosis and treatments as well as creating social divisions.
- A genuine fear was expressed that increasing use of genetics in healthcare could lead to **designer babies** and a desire to create **a 'perfect' society with no illness or disability**.
- It was critical to many that the people involved in the pilot study, and any subsequent programme, should **reflect the ethnicity of the UK**. They fear, if not, discrimination by the back door is likely and an unwelcome two-tier system of healthcare could emerge.
- Participants called for those setting up the pilot to consider **the long-term implications of data collection, storage and use**. They want the data to be of use, but do not want anyone to experience harm as a result of data loss or misuse.

The chapter ends with reflections on dating and family planning. This begins the call from participants to take time with the planning and execution of the pilot study and any subsequent use of WGS for newborn screening, to fully consider the long-term cultural, ethical and social implications. Considering these implications and creating an understanding of when a line of acceptability could be crossed – and not stepping over it.

During the dialogue participants saw the societal implications of WGS for newborn screening as exciting and terrifying. One person summarised the views of many in saying,

> One thing that I remember from the session the other night was really the world of possibilities. I think the fear of those possibilities and what they mean for the future innovations, and the excitement if changes can be made or intervention can be had at the right stage, there are possibilities for eradicating or changing outcomes for our future health. So, equally exciting and terrifying. **I** Participant, Black, Asian & Minority Ethnic Group

The chapter begins with a consideration of the changes participants felt that WGS for newborn screening might bring about in the NHS and society.

4.1 A seismic shift in our health systems and attitudes

Participants said that introducing WGS into newborn screening has the potential to create significant changes in how the NHS operates and how society views health. For many in the dialogue this shift in emphasis presents a new, twenty first century way of thinking about the NHS to reconsider its purpose and re-boot its original 'cradle to grave' ethos,

> I think it's a good opportunity for the NHS, obviously when it was created it was cradle to grave, getting back to that with that modern twist. Obviously we could be world leaders in this and actually come up with a streamlined NHS that supports society, something that we can really be proud of. **I** Participant, Genetic Conditions Group

In the context of a refreshed, modern NHS with genomics used as a screening tool from birth, participants felt that the NHS default delivery mode would shift from treating the unwell to preventing illness in the first place. They consider this shift could be a turning point in society's attitude to health summarised in discussion snapshot 2.

Discussion snapshot 2 – a seismic shift:

In 30 years (WGS for newborn screening) could be completely normalised, and it could be that we carry around our complete profile like we might know our blood group now. We might know everything, and all that data would be stored on whatever we wear instead of a watch in 30 years' time. Just like people carry around their portable fitness devices now, it will have become so normalised that generations to come will be fully aware of the whole of their genomics. So, it could be a seismic shift equal to the Internet. It's a health shift similar in scope to, 'How did we ever live without this?' type of thing. It takes us in all the directions we've discussed, and we can't predict. We can get probabilities, but we can't predict, but every technology has had unforeseen downsides, hasn't it? There's nobody here that would say, 'I think we've done enough with the Internet. We should turn it off now', even though there are dramatic downsides to it. So, it will be the same with this. We'll uncover new downsides we never thought of, but we'll never go back. **I** Participant, Genetic Conditions Group

4.1.1 A pivot to prevention

Participants spoke, as in a previous genomics public dialogue[11], about a new contract with the NHS. In this dialogue participants felt that the contract hinges on population level take up of a newborn screening programme which includes whole genome sequencing. If take up is high, the health service could conduct more effective research into early diagnosis and new treatments. It would be able to communicate more effectively so that society pivots towards prevention as the default. In return society will contribute data and the government will align its policies and resources to the endeavour.

> I think how it can be maximised is if this progressive new way of trying to build an infrastructure, a health care, for hundreds of years that keeps people safe and healthy if that mirrors what's happening with the vision of government. If those align you maximise the whole thing. If they don't align you see a health care system that's at war with the government, at odds with the government, that's not good for anybody. It can be maximised if both of them have the same outlook and are building for the same thing. **I** Participant, Scotland

In creating a more prevention focused NHS, many, particularly in the Young Adults group felt that the population would take more responsibility for their own health and buy-in to a prevention focused approach for themselves and their families. They spoke of the potential for greater NHS use of personal monitoring drawing on, for example, the technologies people use to monitor their heart rate when exercising. So that those whose screening had led to a diagnosis of a condition could be monitored to keep them in a stable condition, manage their condition more effectively, and perhaps reduce death from unexpected health issues such as stroke and heart attack.

4.1.2 Forward planning

Many participants felt that WGS for newborn screening could bring benefits to the NHS in being able to forward plan based on the evidence provided by newborn screening genomics data. They spoke of allocating human and financial resources to areas the data might show as being of high demand, because of a condition screened for at newborn stage. Resource management as we have seen in Chapter 3 was seen as a high priority for the NHS and many thought WGS for newborn screening could be valuable in addressing this issue.

> It's just things like if we're screening for a particular condition and we know we're getting a certain number of children with that condition then we know how many doctors, nurses, clinics we're likely to need and that might free up resources for other areas that are short of facility potentially. Cost benefit rather than an actual cost. **I** Participant, Northern England

[11] Commissioned by Genomics England and Sciencewise - A public dialogue on genomic medicine: time for a new social contract?, April 2019

4.1.3 A slippery slope towards private health care

Some participants felt that there was a risk that introducing WGS for newborn screening could push some people into accessing private health care, particularly if they felt that the NHS could not provide them with:

- Treatments that would address their needs in a timely fashion
- Support for their family and child to address the psychological impacts of the discovery of a genetic variant
- Long-term care/ treatment for their condition

> I think the number one concern for most people in the British population will be the cost to the NHS, because everybody's already scared that the NHS is underfunded and it's all going to get privatised. So, some people might see this is maybe a step forward in the privatisation of stuff, maybe it's only for a certain, I guess, you could say, class, but a certain type of patient that could afford it. I Participant, Young Adults Group

4.2 A research bonanza

A view was shared that advances in medical science are important and the data resulting from WGS for newborn screening was a powerful and important benefit for everybody in society. As such many participants supported the use of genomic data for research into the causes of and treatment of genetic conditions. The areas of research set out in figure 4.1 were frequently cited by participants. There was understanding that research programmes can take time to reach meaningful conclusions.

> It might be that it's more of a long term game that in the front end you have the additional costs as I mentioned, but also it won't see as much of a benefit of what it could have ten years down the line when we've got more knowledge about different genes and what those combinations could be. So, it's not only the benefit we have right now, but it's the potential benefit we have in the future when our knowledge grows in medicine and the field. I Participant, Southern England

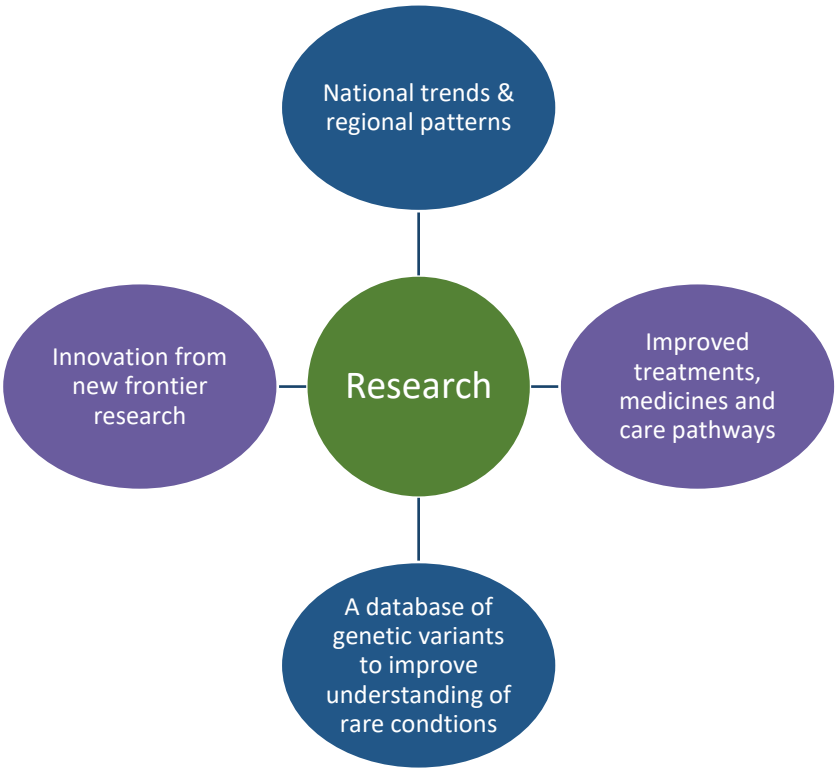


Figure 4.1: Research areas

The research that dialogue participants are calling for and are strongly supportive of is seen to feed into the shift to preventive medicine described previously.

> The benefits are pretty clear that the more data you have, the more research that can be conducted and the more breakthroughs there could potentially be in how to treat conditions which, at the moment, we aren't able to do. **I** Participant, Wales & Northern Ireland

4.2.1 Understanding patterns and trends

Participants described the future of the health service as being determined by understanding population-level trends and patterns in the data. They saw huge potential in genomic data gathered at newborn stage to develop understanding of:

- Regional trends such as clusters of disease
- The relative impacts of environment and genes in respect to health
- Genetic patterns in ethnic groups
- Global trends and disease patterns
- Those who are most at risk/ likely to display symptoms from gene variants

One reason for excitement about the potential for research in this field was to target resources effectively,

> By screening all newborns you're going to end up with this massive dataset, you would really hope that someone far better at maths than me would be able to start finding trends, you know, analysing it to some extent. If you then find that actually one mutation is super common in one area or one ethnic group then you can start directing funds and research or even specialist support. **I** Participant, Southern England

For many it was also about the potential to take preventive measures when clusters of a condition are found in a particular geographic area. Participants gave examples of high incidences of multiple sclerosis in parts of Northern Ireland and referred to the effects of pollution and climate change. There was considerable interest in understanding the relative importance of environment on health, which it might be possible to alter, compared to a person's genetic inheritance, which cannot be changed.

> How WGS can contribute to understanding more closely how ethnicity and environment influence disease clusters and propensity, compared to our genes. **I** Participant, Southern England Online space

4.2.2 No postcode lottery

Participants considered geographic disparities on current treatments and drugs available within the NHS. There was a concern that the more WGS uncovers in terms of genetic conditions, the more it might cost the NHS to develop treatments. They was a certain uneasiness that medicines might prove too expensive for the NHS to offer nationally, or the more people that were found to have a need for the medicines would push them into being too expensive to offer. Participants

reflected on their own understanding of how drugs are made available currently, for example in treating cancer or infertility. Their concerns about an over-stretched NHS played into this sense of unease.

> We all hear about the fertility postcode lottery. Is this going to become a treatment postcode lottery? The NHS resources are already strained. Is this going to become an inequality thing? A rich person, poor person. You don't know, do you? I think that would be a worry if drugs become available for things and you know you've got it, or you know you've got a disposition to get it, the accessibility of the treatment to that could depend on where you live. **I** Participant, Genetic Conditions Group

Participants in the Wales and Northern Ireland group said they perceived the health funding formula for the devolved administrations as not being equally distributed. They understood that health has been a primarily devolved matter since powers were transferred to the Scottish Parliament, Welsh Senedd and Northern Ireland Assembly in 1999; and that the responsibilities of the devolved authorities include organisational control and funding of the NHS systems. They felt this could lead to a risk that the scheme would not operate evenly throughout the UK and individual devolved administrations may decide not to allocate funding to WGS for newborn screening. They argued that this would be a risk to the whole project: undermining population level research data, and early diagnosis and treatments as well as creating social divisions.

> However, a harm could be divisions within families, divisions within society, if it's not delivered nationwide and it's just used as a tool to develop science, there could be a lot of division within society because areas of the nation might say, 'Well, it's available here but not here', or, 'Why do I have to travel 100 miles to get this treatment?' **I** Participant, Northern England

4.2.3 Ensuring the sample reflects the ethnic diversity of the population

A desire for understanding clusters of disease in the population, and a fair distribution of WGS for newborn screening across the UK, also included discussions on ethnic diversity and the risk that unintentional discrimination might occur.

> Different parts of the country have different ethnic make-ups, so again if a certain area wasn't funded in some way, there's a risk that ethnic minorities or different people from different backgrounds be accidentally forgotten, accidentally not treated fairly. **I** Participant, Northern England

Participants were disappointed to learn that current samples of data from WGS, for example in the 100,000 Genomes Project, did not have sufficient samples from people of ethnicities other than White Northern European. They were concerned that families from Black, Asian and minority ethnic backgrounds are less likely to consent to WGS for newborn screening if they feel that the programme is 'not for or about them.'

Central to these discussions was that participants in all locations and in all groups believed that without representation reflective of the UK population not enough understanding is gained to

inform the early diagnosis and treatment for genetic conditions that they prize so highly (see Chapters 5 and 6). They saw a certain degree of altruism in this, so that those who consent for their baby's genome to be sequenced would understand the value of that data as part of the big picture of the population.

> Your, or your baby's individual genome, on a grander scale, can be used then to help develop treatments for other people. What I mean by that is, if we were screened at various stages throughout our life, looking at the data, they may be able to find the reason why some people seem to be immune to various conditions, yet others are getting them. **I** Participant, Wales & Northern Ireland

For some participants this also included global collaboration and sharing of genomic data to learn from as many people's genomic data as possible. The public health benefits were seen to be significant.

> I guess the research benefits are going to be great for public health. The whole idea of having a huge database where people can learn more about your genetics and how that's going to implement and effect treatments, and stuff like that is obviously going to be beneficial for the country. Possibly other countries as well if you share that information and it's an international database. **I** Participant, New & Expectant Parents Group

Inclusion was an important part of this discussion. If WGS for newborn screening is to be integrated as a technology for newborn screening then it should be clear to parents that the programme is appropriate for all babies whatever their heritage or background.

> I think I'm getting worried that the screening will be tailored towards White people. And we saw earlier with sickle cell that people from other backgrounds are more prone to different things and if we're tailoring people's medicine, people from different backgrounds will need different things. **I** Participant, Black, Asian & Minority Ethnic Group

> That WGS works the same for everyone regardless of racial background / genetic makeup. **I** Black, Asian & Minority Ethnic Group, Online space

Discussion snapshot 3 - inclusion:

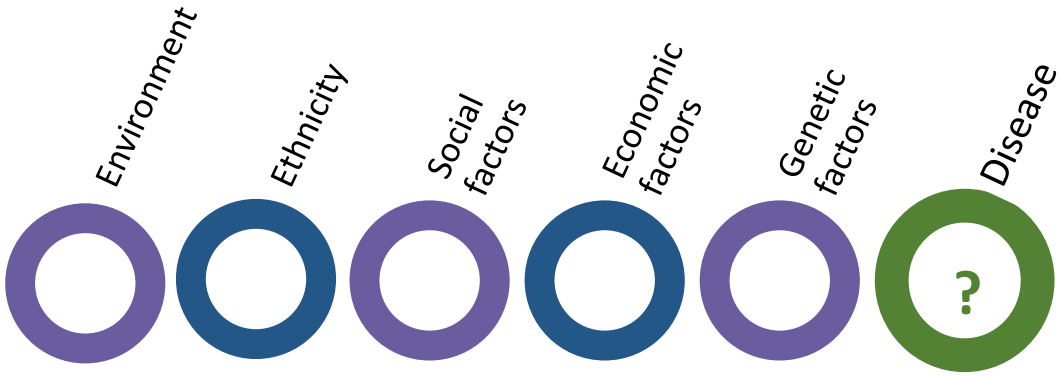
I know it's not for newborn screening, but some of my antenatal screening, I was told that I wasn't going to be screened for certain things because of my ethnicity, because I am White British. From the flip-side of that, I know that it's a bit different, but to not be included in something when we're trying to breakdown these barriers and say that it's not just, say, that it affects people who are Asian. We weren't included in something, so, on the flip-side, I think ethnicity actually is being brought into screening, at the moment, anyway, and you are almost being discounted from being screened for things, whereas if it's just automatically done with everyone, then, there's no need to say, 'Oh, you're not going to be screened for that because you're White,' or 'You are going to be screened for that because you're Black.' It's just inclusive for everybody, so, it could have quite a positive effect. **I** Participant, New & Expectant Parents

Participants' lived experience informed these discussions as we see in snapshot 3 and in the quotation below,

> It disappointed me that although people of BAME backgrounds were often more likely to develop some disorders yet there is little diversity in research. Sadly I'm not surprised. Black women are four times more likely to die during childbirth yet there seems very little research or support into why. **I** Participant, New & Expectant Parents

Participants felt a significant benefit of WGS for newborn screening would be to gain a richer understanding of the relationships between environmental, ethnic, demographic, socio-economic and genetic factors, in order to improve health outcomes and to find new treatments.

Figure 4.2: Inter-connected health factors



Whilst many participants raised this point of a reflective sample, many also saw it as a potential risk that the programme would demonstrate links between certain ethnicities and genetic conditions which they felt could lead to discrimination, or a fear of hearing the results from newborn screening, which would deter those from diverse populations from consenting for data to be collected for research purposes.

> Screening for a particular disease, even using whole genome sequencing, there may be a stigma then tied to a particular disease that's prevalent in an ethnicity, and then, it becomes a disease that's tied to that particular group of people. That could be, obviously, bad, not just for screening purposes, but it gives a bad name for the whole genome screening itself. People may see it as a negative thing rather than a positive thing with even racist implications lying within it. **I** Participant, New & Expectant Parents Group

Participants wanted those who are considering the development of the pilot study to not slip into established thinking which would potentially lead to the programme being set up with in-built racial inequalities.

> As an ethnic minority working class female, I do realise that most things are based around middle class White males, and I do think it is more difficult in medicine for ethnic minorities, just because if you think of a disease, like sickle cell disease, before today I thought that was just among people with Black backgrounds. I didn't know anybody could

> get it. So that fact just shows, I think, there are ethnic barriers just in healthcare. I Participant, Northern England

4.3 Societal awareness of genetic conditions

Participants expressed the importance of a society in which mental and physical illnesses and disability are openly discussed. If the technology is integrated into newborn screening nationally there was a view expressed by many that understanding of genetic conditions will increase as more newborns are screened using WGS.

Whilst all groups referenced awareness raising as a route to de-stigmatise illness and disability, it was particularly a focus of interest for the Young Adults group in terms of disabilities and also carrier status,

> In the future many more people will know that they also have this carrier status of diseases, it would de-stigmatise people from discriminating because it humanises that anyone can be, and you would know someone with this issue. I Participant, Young Adults Group

They spoke of breaking the stigma of genetic conditions and other diseases, linked to good communication around WGS and the newborn screening programme (see Chapter 10). They felt discrimination was of particular consideration for younger people in society.

> I think the whole thing about discrimination is a real big thing in our generation anyway. Discrimination is something we are fighting against on a daily basis, so this definitely shouldn't be another one we add to the pile. I Participant, Young Adults Group

4.3.1 Avoiding a dystopian future

Some participants felt WGS for newborn screening could offer society opportunities over time to eradicate genetic conditions which are extremely life limiting. They saw this as a benefit for future generations as more treatments are available as a result of the data provided through genomic sequencing.

> For me, I think it is amazing, and I think it's brilliant that we can get this screening done at a very early age. It may help future generations to eradicate these ghastly diseases or improve treatments to treat them. I Participant, Wales & Northern Ireland

> Over time, people might decide not to run the risk of passing that gene down on to the next generation and therefore, over time, it might be that some conditions could be wiped out completely. I Participant, Northern England

However, this view was tempered by serious ethical considerations including disability rights. Some spoke of the loss such developments could bring.

> I'm thinking, as we get better at treating certain disabilities, there could be a cultural loss. For example, if you manage to cure deaf people, there wouldn't be any more native speakers of sign language, or any deaf culture. For example, it would be a big loss if there were no more autistic people. **I** Participant, Black, Asian & Minority Ethnic Group

Going down this route in workshop discussions was uncomfortable for participants but seen as important so that society doesn't inadvertently go down a path of eradication. There was a view that these issues need to be raised and discussed in this exploratory phase before any pilot study is implemented. A genuine fear was expressed that the goal of eradicating illness could lead to a dystopian situation with a desire to create a 'perfect' society with no illness or disability. As this discussion in the group from Scotland demonstrates,

> Participant 1: There's a risk you're just trying to design a human being, design a society. We've seen it in the 1930s and 40s and millions of people died. So it's a huge topic because so many countries in the world are just totally different. And in some places it'll work perfectly and in other places it'll be the demise of millions of people.
>
> Participant 2: It'll become a weapon.
>
> Participant 1: Exactly, it will just be weaponised.

Others took this further and raised a concern that society could move towards the creation of designer babies.

> It's for the advancement in medical science. That's what it is, if we go too far beyond that, beyond trying to treat people and get better medicine, we go into designer baby territory, which I'd be very against. **I** Participant, Wales and Northern Ireland

Some also discussed another form of discrimination, that some people might be seen as too much of an expense for the health service due to gene variants discovered at newborn screening stage.

> This is a worst case scenario but if the cost is such a big factor, are people who are screened for disabilities, mental or physical, are they going to be seen as excess baggage in some way? Are we going to say we can't really afford to support people who are going to be a drain? That's a really ugly way of putting it, but I think the implication needs to be considered. **I** Participant, Wales and Northern Ireland

For those that discussed this, the use of language in relation to WGS for newborn screening was seen as significant as well as how research data is used, presented and published. This was borne from a desire for the programme to succeed and provide the rich understanding of genetic conditions that could result from WGS for newborn screening. They said they thought there was a need for great care in associating certain ethnicities with genetic conditions, learning from recent events and further back in time about how conditions are discussed.

> We saw it with COVID-19, it got called the Chinese virus. People associate it with a certain race as a way to attack them indirectly. Instead of coming for their race you can attach it at the side. There's another example, they did it with the AIDS crisis. They would associate it with being gay and then it was a reason for inaction. I Participant, Black, Asian & Minority Ethnic Group

And they called for sensitivity and caution so that the programme can achieve its ambitions.

4.3.2 Workplace discrimination

Another potential threat to people's acceptance of the programme was the risk that employers of the future would make racial profiling assumptions based on a potentially increased awareness of which ethnic group were predisposed to a genetic condition.

> The implications are pretty unpleasant, really, aren't they? Is all this going to lead to employers racially profiling people and saying, 'This ethnic group is more prone to this genetic disease, so let's not hire them.' It is not great, from what I was hearing.
> I Participant, Wales & Northern Ireland

Many more participants in all locations and in all groups feared that in the future there would be an obligation to disclose your newborn screening whole genome sequence results to employers and/or insurance companies. And that this obligation would extend to revealing any illness that the data showed you had a risk of contracting – even if that risk was far in the future and you currently had no symptoms.

4.4 Future data collection and use

We have shown that participants place an emphasis on the value of research using the data collected as part of WGS for newborn screening. Here, we set out what participants see as the opportunities and risks in collecting and using data from the newborn screening programme. Some participants felt there was a benefit in collecting as much data as possible at the newborn screening stage. As technologies develop at pace and new treatments are brought on-stream, data for which society didn't have a use initially may become useful over time. Their ambition is for as many people as possible throughout society to benefit from the research leaps they expect to be possible from having the data available for research purposes.

However, how data is kept secure and who gains access to the data were both significant areas for discussion on the implications for society of WGS for newborn screening. Participants were focused on the areas listed in figure 4.3 in particular:

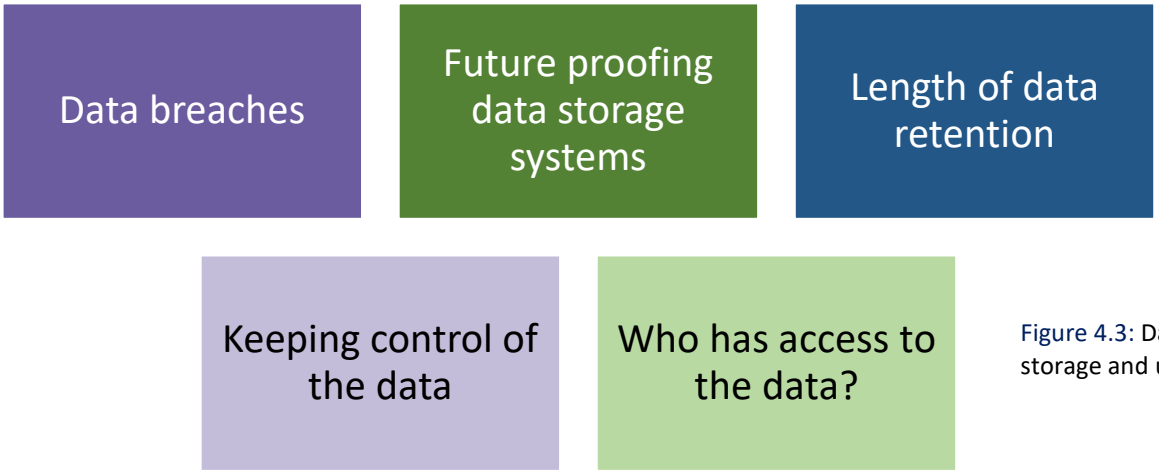


Figure 4.3: Data collection, storage and use considerations

Participants reflected on an important implication inherent in WGS for newborn screening: it is the parent not the child who consents to the storage of data. This feels to many riskier in terms of data breaches than if you are consenting for your own data to be collected, analysed, and stored. Participants referred to the 2017 WannaCry ransomware attack which affected many businesses and organisations globally, including NHS computers, and felt that despite lessons learnt[12] there remained risks in storing genomic data over time.

> What would happen if the information centre of the NHS got hacked? It has happened before, so what would happen to any of the people that had gone through this afterwards?
> I Participant, Southern England

Discussion snapshot 4 highlights the points made in the Young Adults group in relation to this issue – leading to a key question for those developing the pilot study – is it worth retaining data beyond the newborn screening stage? Would changes in technology, data storage, security and genomics mean it will be more cost-effective to analyse what's needed for the screening of a newborn, and then destroy the data? Particularly as participants were told that WGS was becoming cheaper to do all the time.

Discussion snapshot 4 – data retention:

The question of generating information that could then be tapped into over the life course of the child, raises some quite tricky issues. These include things like the technical standard of the information we generate now about a sequence, would that still be worth anything in 10 or 20 years' time? The sophistication of what is done is going to increase and whether it's worth generating whole genome sequences and hanging onto them when the IT systems, the software and even the hardware is going to be changing, not even by the decade, but more often than that. The actual cost implications are immense and if the information you're generating now is just not up to scratch for the standards that will be in place in 10, 15, 20 years' time, there is a good argument for generating the information now, analysing it in the way we need to, to use it now and then chucking it away. I Participant, Young Adults Group

For some people the risk is minimal. They questioned what value the string of un-analysed data would have for anyone other than researchers. They felt the benefits of collecting and storing genomic

[12] Smart, W, Department of Health and Social Care, Lessons learned review of the WannaCry Ransomware cyber attack, February 2018

data far outweigh the data breach risks and there is no value to the data stored unless it is analysed by a clinician who understands the complex implications of what they are looking at,

> At this moment in time I can't think of any organisation that would find it of any use to them apart from this one, the legitimate one, because what am I going to do with it? So, I've got 100,000 blobs sat on my computer and I look at it and I think, 'So, what does this prove then? There are 30 people living in South London who've got cystic fibrosis,' you know what I mean? What use is that to anybody?. I Participant, Southern England

Those that agreed with this point of view were surprised at the extent to which other participants were concerned about data storage, partly because we give away data about ourselves every day through the Internet and social media use.

The Young Adults group and the New & Expectant Parents group both discussed the impact of introducing WGS as a technology for newborn screening on the climate. They were concerned about large data storage facilities on computers and the energy that is needed to sustain them, and equally the environmental consequences of the life-span of the population increasing.

Participants wondered if control and management of the genomics data gathered would rest with Genomics England, the NHS, researchers or policy makers. They also considered to what extent citizens would have control over how long data should be retained. For some, retaining their data is not a personal question, they have an altruistic motive in sharing it for research purposes, for others it is a question of autonomy and of being in control of their own life decisions,

> I should have the control to say, 'You've told me, either now delete it, keep it, save it.'
> I Participant, Black, Asian & Minority Ethnic Group

Participants were clear that it is unacceptable for a third party to gain access to data about individuals' genetic status and use that information for targeted marketing purposes. Given knowledge of current commercial services offering to analyse a person's genome for ancestry and health research, a concern was also expressed about the potential exploitation by commercial entities offering to analyse newborn screening data.

4.5 Societal implications

Planning for families in the light of genome sequencing data at newborn stage was one example of a societal implication. Using newborn screening data when the child grows up and is considering a family came into participants' minds. Discussion snapshot 5 sets out some of the consequences of carrier status for family planning.

Discussion snapshot 5 – carrier status and family planning:

With everything, there is an advantage and a disadvantage. Coming from a sickle cell point of view, because it [occurs frequently] in African and Caribbean countries, knowing your genotype you know that there is a likelihood of you having a child with sickle cell disease if you have a child with a carrier. So, back home it is normal to be aware of that, when you date somebody who is a carrier, you will end up having a child who has sickle cell. Because of that knowledge, people plan their future better. So, I think that's a benefit to it. But the disadvantage is that you can't just date anybody you like or have a child with anybody you like. **I** Participant, Genetic Conditions Group

For many this was significant as a fundamental change in the way society views health, including for people who want to have children. They saw a possible future in which society will consider it normal to know in advance the implications of who you choose to have children with.

The implications for dating were raised in many of the dialogue groups. They considered the potential detrimental aspects of including your genetic profile on a dating app and letting the algorithm do its work. These included taking the romance, fun and unpredictability out of finding a partner and falling in love.

> It takes the fun out of life almost. Do I even want to bother dating anymore because there are then all of the complications of, forget falling in love, I want to see the list of your genomes? Having a child, I think sometimes things need to be more instinctual than asking for a CV, that could complicate that side of life really. It could sterilise life to a certain extent I think. **I** Participant, Scotland

Some participants referred to this consideration to who you date and have children as being common practice in some communities, they referred to Tay-Sachs disease, a rare genetic condition which affects people of Ashkenazi Jewish descent. Discussion snapshot 6 gives such an example.

Discussion snapshot 6 – a family planning example:

This is a little bit different, but I went to college in South Florida and it was a huge Jewish community down there. Now, this is mainstream, I'm getting it straight from the communities that it's very normal when you're dating within the Jewish community to do a DNA test, just to make sure that that's not a distant relative. It's weird and uncomfortable to talk about, but it's so normal to those communities and maybe that'll just be the new norm. It's weird to think about, but it's already happening in some ways. **I** Participant, Genetic Conditions Group

The dating dilemma led some participants to another question. Are we, through WGS for newborn screening, creating a risk averse society?

> Future generations are going to be living their lives in fear that they might be getting this, or they might be getting that, and everybody's already scared stiff at the moment. You go out and everybody's scared stiff of having medical problems and this is just going to carry on and carry on, the fear. **I** Participant, Wales & Northern Ireland

This then led groups to discuss further the ethical dimensions of WGS for newborn screening, including whether society would know whether or not it had taken the use of the technology too far.

> I don't want to put a dampener on this, but where do we stop? When you get to the stage where you can actually have designer babies? Where does the technology and the science stop? In twenty years, are we going to be able to clone people, are we going to be able to, seeing science fiction films, freeze people and bring them back in 30-odd years' time? I just think while WGS is very good, I think it has the potential to really quickly get out of hand. **I** Participant, Scotland

5. Earlier diagnosis

Key findings

- Whole genome sequencing at birth is seen by most participants as **a highly positive enhancement to the current newborn screening programme** for its potential to identify a wider range of immediate onset, treatable conditions at birth than the current blood spot test.

- Participants also gave considerable thought to the wider implications of WGS at birth: the **potential for whole genome sequencing to identify other, longer term conditions** and that this information could have an impact on the child as it grows up, its parents and other family members.

- This Chapter shows that whilst there is **strong support for the early diagnosis of immediately treatable conditions**, there are a **range of views on the early diagnosis of conditions that currently have no cure, or treatments that help prevent or manage deterioration**. This is particularly the case if there are a range of 'actionable' opportunities that could improve a child's health if they are diagnosed earlier, such as therapies and the potential for involvement in research for new treatments.

Given a genetic diagnosis has implications for other members of the newborn's family, participants discussed how this might affect their health and wellbeing. Some participants saw the **ability to identify and treat life-threatening conditions in the child's parents**, such as familial hypercholesterolaemia, as a benefit of WGS at birth. But they also discussed the distress and uncertainty this information could cause among family members who didn't wish to be made aware of genetic issues that might affect them.

5.1 Identifying genetic conditions that can be treated immediately

One of the first benefits discussed by participants at the start of the dialogue was the opportunity of using whole genome sequencing as a screening tool to diagnose and treat serious, life limiting conditions in the earliest days of a newborn's life. Many of the benefits they pointed to are true of the current newborn screening programme and include short as well as long term benefits:

Figure 5.1: Screening programme benefits

> It's treatability, being able to go straight into dealing with the situation, that is always an advantage, if it helps to have something done sooner rather than later. | Participant, Southern England

The distinction between the newborn blood spot test and WGS was seen as its ability to pick up genetic conditions that cannot be detected by the current blood test and may not be identified until health has been damaged or even a life has been lost:

> I think that this will be good to implement in a screening of the population, because this is a little bit more specific, in my understanding, whole-genome sequencing, because it clearly only reveals genetic problems. But if it's being implemented in a screening programme, it would try and help to diagnose genetic illnesses much quicker, and maybe that child or person could have much better chances, to even survival, or even to improve their health or condition. | Participant, Scotland

There was widespread support for the use of WGS to identify immediate health problems in newborns that could be treated. But as we will see in this Chapter, there is also a hope amongst some participants that WGS should pick up not just conditions that are cured or prevented by medical interventions in the early days/months of life, but also conditions that can be managed for example, through dietary changes or preparing for the onset of mobility problems by adapting/ moving home. We will see that this proactive view is balanced by concerns that early knowledge could be distressing and stressful for both the child and their families.

5.2 Preventing a distressing diagnostic journey

An early diagnosis through WGS was seen by many participants as helping to prevent a long and distressing diagnostic journey. Participants heard from dialogue speakers (from the 100,000 Genomes Project Participant Panel and parents with children with cystic fibrosis and Duchenne muscular dystrophy[13]). There was hope - and amongst some an expectation - that a genetic diagnosis early in life would dramatically reduce the time to diagnosis and also reduce or completely cut out the need for invasive, potentially painful tests such as lumbar punctures and repeated blood tests. At the very least, some expected WGS to give a more specific route to diagnosis.

> The screening, does that hopefully remove the need for interventions, if somebody is querying whether they have a condition? Does this screening mean that it's a blood test as opposed to repeated scans and biopsies and stuff like that? Is it less of a physical toll on the individual? Does it give the medical team a steer? 'The blood test says it looks like it could be X, so we'll send the testing down that route,' as opposed to trying everything and hoping to get the needle in the haystack type situation going. I Participant, Northern England

[13] See Chapter 11

> 'Avoiding horrible diagnostic journeys'. So it would mean, rather than having the whole, looking into different things, it would cut all that out, and parents of a child who had an illness would be able to cut the waiting game out and go straight to the source of getting the proper tests done that are required, rather than going through all these different tests. It would give them an indication of what was wrong at a very early stage. That to me made me think, if you had a child that was unwell, you wouldn't want to go down that journey. You would want to get the information as quick as possible. **I** Participant, Scotland

The impact of long diagnostic journeys on both the parent and child was discussed in most groups. Both in terms of stress on the parents and the disruption to children's lives, particularly their schooling. When thinking about the 'horrible diagnostic journeys', some participants questioned why genetic testing isn't used earlier in current diagnostic practice. They were surprised that in some of the experiences they heard, the genetic test that identified the child's condition came at the end of the process.

> It sounds so positive and so helpful and not particularly invasive, why would it be considered a last resort option, rather than something that comes earlier in the process of diagnosis? | Participant, Scotland

5.3 The implications of early diagnosis at birth

The birth of a child was universally recognised by participants as a time of physical, emotional and mental intensity. During the dialogue much thought and discussion was centred on the impact that WGS could have at this point in life. Participants felt it was particularly important when considering the use of a new technique to screen newborns that the context of the birth of a child and parents' emotional and practical support needs be thoroughly understood.

5.3.1 Support system in place at birth vs when child is older

Participants in the New & Expectant Parents group and in Wales & Northern Ireland talked about the period around birth as being a time when parents have regular, proactive contact with healthcare providers and when their support needs as new parents are well recognised. They compared this to later years in childhood when parents' interaction with health services tends to be reactive. They felt that learning about a diagnosis when parents are 'in the system' and support is closer to hand was preferable to getting a diagnosis when you might be seen as an 'experienced parent' and therefore less in need of support.

> It could be an advantage of the newborn screening that you might get more support because it's newborn, whether that's right or wrong, I do think that the older your child gets, the less support you get. You don't see midwives and health visitors and all that stuff as much. So, if you get some potentially bad news when they're newborn, you might be more likely to get the support that you need, than if they're older, because people think you can probably deal with it then. | Participant, New & Expectant Parents Group

5.3.2 Impact of early diagnosis on bonding with baby

Across almost all groups, and most strongly in the New & Expectant Parents group, participants

shared their concerns about the impact that an early diagnosis could have on parents as they are bonding with their child. Three main concerns were that the joy of their child could, like a rug, be pulled out from under them if:

- WGS gave an 'overload' of information that parents would find hard to process at such an intense moment in life
- WGS gave a diagnosis of a condition for which there is no immediate treatment
- WGS gave an uncertain diagnosis that led to harmful speculation and frantic 'Dr Googling' to try to understand the implications for the child:

> There's quite a lot of load on a new parent, whether it's their first child or multiple, and there's a lot of changes, there's a lot of things to be considered in getting a massive load of information about that baby, their long-term health implications when you don't even know them as a person, they don't have their own personality. That might just be a bit much for new parents or carers. I Participant, Northern England

5.4 Impact of early diagnosis of longer-term conditions

As well as diagnosing immediate onset conditions that could be prevented through special diets or treated to avoid harm in the first weeks and months of life, many participants talked about the prospect of WGS identifying longer term conditions – both those that might lead to early interventions and those that are later onset.

5.4.1 Early diagnosis with no cure, but treatment may be beneficial

Across all groups, some participants raised the prospect of WGS helping to manage conditions in young children that had no outright cure but could deliver health or mobility benefits through earlier delivery of treatments and therapies. Duchenne Muscular Dystrophy – used as a case study in the dialogue (see Annex 3) – was referred to by several participants. They felt that earlier knowledge of the condition would give more opportunities for therapies to be used that could yield positive outcomes such as slowing declining mobility or improving balance.

> With Duchennes, up to 5 years, there seem to be no specific illnesses involved, but then it all goes downhill fast. If you knew that your little boy was going to have this at 5, you might be able to have more physio. I don't know what other treatments you would do, but there might be something that would lead them to be less affected by the time it kicked in.
> I Participant, Wales & Northern Ireland

Participants in some groups referred to the speed of technological advancements in recent years and how this gave hope that treatment discoveries could happen ever more quickly in the future. In light of this, they saw the benefit of an earlier diagnosis so that a child could be signposted to research which might give earlier opportunities to take part in experimental treatments.

> If it was done at a newborn stage, with how fast technology advances nowadays, if you knew from newborn that they had something like muscular dystrophy and then, by the time a child gets to 2 years old, there's been further research and experiments to say there's actually some treatment now. Then, you can get the child in earlier for treatment,

> rather than waiting until they're a bit older to find out. I Participant, New & Expectant Parents Group

5.4.2 Early diagnosis of adult onset conditions in newborns

A small number of participants thought it would be helpful for children and parents to have an early diagnosis of a genetic risk for later onset conditions, such as breast cancer, so that the child could be more closely monitored from the start of life and offered earlier and more frequent screening to check their health status. They felt that screening could be tailored to the individual's genetic risk for the condition. More frequently if you have the variant, less frequently if you don't.

> The newborn is already screened with this variant, and, for that particular person, you can have regular mammograms. For someone who doesn't have that variant, they don't need to have the mammograms that regularly. If the person with the variant is having it every year, the one who doesn't have the variant can every once in, say, 3 years, 5 years. The regular monitoring would be much better if the variant is detected while doing the WGS. I Participant, Black, Asian & Minority Ethnic Group

However for most participants the prospect of sharing adult onset health information at birth, was seen as highly likely to cause far more harm than good.

> You don't have an answer for how to fix it if you do get it. Other than getting a mastectomy, the whole nine yards to counteract it. There's that fear factor from such an early age, being a mum, knowing you've got a little girl or a little boy that when they grow up could end up with breast cancer, they've got enough to deal with having a little baby. I Participant, Southern England

5.4.3 WGS and pharmacogenomics for newborns

Whilst a few participants were concerned about medicalisation, others identified where they thought WGS could be positive for a child's health. Having heard about the potential for WGS to enable greater use of pharmacogenomics in Workshop 3, some participants spoke about how valuable it could be to help children in their early years receive targeted, more effective treatment sooner, avoiding the waste and distress of ineffective treatment as well as adverse reactions to allergenic drugs.

> For certain elements this would be incredibly useful to know, I think particularly with the use of antibiotics, as my family all have severe anaphylactic reactions to penicillin, but my partner doesn't, so I'd like to know the likelihood of that happening to our baby, rather than finding out how my parents did by giving me medicine and watch me suffer badly. I Participant, New & Expectant Parents Group

> Pharmacogenomics could definitely prevent newborns identified with certain conditions to being subjected to consuming medications that serves as a waste and might alter their health negatively. I Participant, Genetic Conditions Group

5.4.4 Overmedicalisation of children?

In some groups, Wales & Northern Ireland in particular, a few participants expressed concern that putting young children on medications so early in life could be debilitating. They worried that the range of information that early WGS diagnosis could provide could lead to an ever increasing drive to intervene, which may not be in the interests of a child's quality of life.

> With the medications, another disadvantage would be, I know with epilepsy, some medications for children, it takes 10 years off their lifespan. It's good diagnosing young, but the medications, they need to look at different alternatives because, yes, you want to help your child and let them live as long as they can, but sometimes the medications can take a lot out of their life. I Participant, Wales & Northern Ireland

5.5 Impact on lifestyle choices and behaviour

As well as using WGS at birth to help identify conditions that could respond to medical treatment and therapies, participants talked about how an early diagnosis could affect lifestyle decisions. Participants discussed both the potential for lifestyle decisions that could be life improving for the child, but also the risk of parents becoming overly protective, 'wrapping their child in cotton wool' and so limiting their lives.

5.5.1 Early diagnosis helping with lifestyle choices

Some participants said that knowing about a condition could enable parents to make more informed judgements about how to help their child live well but also avoid anything that may harm them. This included not only diet, exercise and play but also planning for home adaptations.

Some participants spoke in general terms about knowledge of a condition prompting greater attention to eating a balanced diet or taking regular exercise to help maintain health. Others referred to specific conditions – sometimes drawing on case studies used in the dialogue (see Annex 3), or in the case of the Genetic Conditions group, from their own life experience.

> With us, the bone disease that we've got, we were able to adjust my son's diet and from an early age, although we couldn't do much to help him, we cut out calcium to try and cut down on excess bone growth. So, although there might not be treatments available, possibly there might be dietary changes or other things that parents could do. I Participant, Genetic Conditions Group

For Familial Hypercholesterolemia, several participants talked about the merits of parents knowing about that condition so that they could ensure their child ate healthily and kept an eye on the amount of high fat foods in their diet.

> Something like FH, a condition discussed last time, diet is extremely important, because it is cardiovascular. So, if you know that straight-away, you can really try and do something and just change your diet or just treat it and be more careful of things that maybe you wouldn't be doing. So, I think that's definitely an advantage. I Participant, Southern England

Other participants talked about Duchenne muscular dystrophy (DMD) and that whilst they had heard there was no medical treatment available from birth, they thought it could be in the child's interest for the parents to be aware of what they are capable of and to help their child live well but not in a way that risks harming them or exacerbating their condition.

> Participant: If they have that muscular dystrophy, you can then allow that child to engage in activities where they'd be at an advantage rather than a disadvantage. So, rather than allowing that child to go on a 10,000-metre sprint, for example, or a marathon, maybe short bursts of activity, 5 minutes at a time throughout the day, so it's targeted towards their ability based on what medical deficiency they have. That way, they can still get the benefit of engaging in that activity, but in a way that they can derive the most benefit.
>
> Facilitator: So, that's not so much finding treatments for them, but the way you might manage their condition?
>
> Participant: Yes. If the family's aware of it, then they can come up with a plan and a method that would allow the child to still retain some level of normalcy. **I** Participant, Northern England

Again, prompted by the DMD case study, some participants thought that an early diagnosis of a condition that would affect a child's mobility could help the family to prepare both emotionally and financially for home adaptations. They thought that a later diagnosis, when the child might be on the brink of declining mobility, might be more traumatic and financially harder to cope with.

> I think a huge advantage is giving the family time to plan. Obviously, not everyone has the financial backing or savings to adapt their house so, it'll give them that few years to get everything in place that they need, to do their research, like we've already touched upon. So, I think that's a huge advantage to knowing early and having the newborn screening.
> **I** Participant, New & Expectant Parents Group

Some participants thought that an earlier diagnosis could also give parents more time to find a support network. They talked about making connections amongst family and friends and with condition-specific networks and charities that could support them both emotionally and financially as their lives changed in light of their child's needs.

> To find routes for what you're going to have to do to your home and to get funding for all of that. Perhaps, that can even lead on to certain charities being able to focus more on areas that they can help fund, outside of the NHS. **I** Participant, Southern England
>
> Diagnosis through WGS means you can find your community of people with similar rare diseases and can mean coping with diagnosis, symptoms and treatments easier.
> **I** Participant, New & Expectant Parent Group

5.5.2 Overly-protecting children

Parents feeling that they needed to protect their child from harm if it has had an early diagnosis of a genetic condition led some participants to fear that all joy could be squeezed from a child's life. They worried that anxious parents would stop them from experiencing the pleasures of childhood: bike rides, rock climbing, drinking fizzy pop or playing football. Some feared the affect this would have on the child, including feeling marginalised from society.

> Some parents are born worriers, and so would just spend the rest of their life making their child's life unhappy. I Participant, Northern England

> If you're the parent with all that knowledge and those conditions then the younger ones, they're going to become cosseted. You're going to want to make their decisions and talk them out of doing certain things. I don't know, you just want them near you to protect them rather than, 'Yes go out there and do all this'. I Participant, Scotland

5.6 Impact on child's mental wellbeing & self-perception

As well as thinking about the impact on the parents' behaviour, participants discussed what a genetic diagnosis at birth could mean for the child as it grows up. As discussed in Chapter 4, the potential for discrimination was at the forefront of many people's minds. Participants reflected on a future where genetic science defines more conditions and this leads to more labels being applied to children. They worried that a label could become a self-fulfilling prophecy where children are limited by the name of a condition that they feel defines them.

> I am generally positive about science and technology - but - not in how we may defer to it in unintended ways when we turn people and lives into data points and labels. I see this in education when a child says 'I'm a C grade' or 'I'm dyslexic so I don't have to spell words/read things well' - they become the label. So if we uncover more labels, more conditions, more opportunities for failure, for potential disease, do we label and allow people to restrict themselves in unintended ways? I Participant, Genetic Conditions Group

A concern raised particularly strongly in the Young Adults group was that an early diagnosis that a child has a genetic variant could lead to the child feeling that the variant defines them and that then creates limits and barriers on the path the rest of their life could take, including the work they could do.

> There's a huge risk and I think this is quite likely of people growing up with their birth report, their genetic report predetermining their lives and especially in the children stage when people don't really have the maturity to deal with this information. These children are like, 'Oh my God, you are this, you are that. You can't be a dancer, you can't be a whatever, anything physical.' I think that children would loathe how their lives have been already predetermined for them due to that. I Participant, Young Adults Group

5.7 Early diagnosis: time to prepare vs ignorance is bliss

Across all of the groups, participants shared their views on whether an early diagnosis for a long term genetic condition for which there was no proven treatment available from birth was helpful or harmful to the family. We frequently heard the term 'knowledge is power'. Many participants talked about an early diagnosis giving time for the family to come to terms with and prepare for life with a child diagnosed with a condition such as DMD. They thought that being told earlier in a child's life would give them more time to adapt emotionally, financially and their lifestyles to help them and their child to live well. Some also thought that if a child is aware of their condition at an earlier stage they would see it as part of who they are and grow up with the knowledge, rather than a later diagnosis coming as a shock.

> If a little one has got some kind of a disease, or require treatment, kind of thing, if you start it early, parents mentally are prepared. So, the family is prepared mentally, so it's less of a shock reaction when they find out something later on in life. So, they expect something, we have to go to the doctors, or we're going to have to make arrangements for their lives, so you prepare for this. So, it's less of a stress on them. I Participant, Black, Asian & Minority Ethnic Group

Other participants felt they would prefer to be told a diagnosis only when symptoms started to show. They shared the same view as the father of a young boy with DMD who spoke about looking back with great affection on the first four years of their son's life where they believed he was healthy and lived life accordingly.

> I feel that the DMD side of things, knowing early, and that guy said quite heartfelt he wouldn't miss the first 4 years of his child's life, and to know at an early age, I think I'd be with him and not want to know then. Because of the way it progressed, I think, the first four years of the child's life are very, very important. I Participant, Northern England

Participants also heard from another parent who talked about an early diagnosis leading them to spend hours and days combing for information on 'Dr Google' looking at all the different scenarios that a condition – particularly a long term condition - might bring. Those participants felt that only informing a parent when the condition was manifesting itself and some form of care or therapy was available would save them from spending so much time looking at outcomes that may never be relevant to them.

5.8 Impact of early genetic diagnosis on family planning

A baby with an early diagnosis of a genetic condition through WGS which could then inform the parents' decisions about future children was discussed in all groups. We will see in this section how some participants could see this information as helpful to parents to inform decisions about future children. Others reflected more on the harms this information could cause in terms of creating a burden or leading to decisions that parents would later regret, such as not having

further children. Some participants could see how both situations held true and didn't feel in a position to make a definitive call on the rights or wrongs of parental decision making.

5.8.1 Early diagnosis and family planning

Some participants thought early diagnosis in a first child would help parents to make plans to avoid having other children with the same condition. This could be by deciding to not have any more children, by having ante-natal screening, genetic counselling, IVF or by deciding to adopt. By making these choices, they thought parents would avoid the guilt of having another child with a life limiting condition and the wider impact on the family in terms of caring for another affected child.

> It could also give parents an informed choice, so, if it was diagnosed, if something was pinpointed early, that perhaps it wouldn't be wise to have more children, for example. It could give them quite an informed decision or some food for thought at an earlier stage, in case they had more children with the same or similar conditions. **I** Participant, Southern England

Participants were aware through the dialogue and their own life experiences that many genetic conditions have patterns of inheritance with variable likelihoods of a child being born with that condition. Some were concerned that knowing about a genetic condition through the WGS of their first child could put pressure on them to not have further children to avoid any risk of passing on the condition again. One participant in the Genetic Conditions group reflected on the impact an early diagnosis of his first child at birth may have had for his family:

> The disadvantages, as I've said elsewhere, is that if my wife and I had known that she was a carrier of (this genetic condition) after my son was born, we might not have had other children. That's the strongest one that comes to mind. **I** Participant, Genetic Conditions Group

> The fear would be that once you find out, you may choose not to have any children or any more children because the risk versus reality, possibly put you off. **I** Participant, Black, Asian & Minority Ethnic Group

5.9 Impact of early genetic diagnosis on the parents' relationship

The guilt a parent could feel if at the moment of birth they were told that they had passed on a genetic condition to their child was raised by some participants in most groups. They worried that this could have a harmful impact on the parent's relationship with the child, creating tension or distance. But as well as feeling guilt, they worried that blame could be a factor and it could also be divisive for parents if one blamed or felt blamed by the other.

> Participant: I think the guilt. I think that's something that we haven't spoken about really, is the guilt that you might have if you find out that your child has got that from you. Could that lead to almost a feeling of rejecting? I don't think we've covered that really, rejecting a baby. That's already a really sad thing, isn't it? But I suppose it could possibly lead to that.

Facilitator: Is there something about discovering it through a genetic test as opposed to a blood test that changes that rejecting?

Participant: I guess from a genetic test to know that it came from you whereas with a blood test you just know that they've got it, don't you? So, say it came from mum not dad, or dad not mum, it could lead to problems within the parental relationship as well, couldn't it? Which I don't think we've really covered either. I Participant, Genetic Conditions Group

Participants in the New & Expectant Parents group worried that one parent might have known about a genetic condition, but not told the other parent and this could lead to relationship breakdowns when the diagnosis was made.

So, yes, I guess in that sense it would be around, it might lead to a relationship breakdown, for example, if one parent felt guilty or one parent blamed the other parent for potentially causing it. I guess other mental health issues could come up with that. Maybe a partner hasn't told the other partner, if they knew that they were a carrier, all of that kind of thing. I Participant, New & Expectant Parents Group

An even more life-changing outcome of WGS could be that an early diagnosis reveals the true paternity of the child. Some groups mentioned this, but it was not discussed by everyone.

It would be harm as well because what if the father wasn't your father and you never knew who the father was and the mother was pretending that her husband or partner at the time was the father, but he wasn't really? I Participant, Wales & Northern Ireland

5.10 Impact of early genetic diagnosis on the wider family

During the mid and later stages of the dialogue particularly, participants talked about how a genetic diagnosis in a newborn could impact on the wider family, parents and beyond. There was a keen understanding that, in contrast to the current blood spot test which is all about the baby's health, whole genome sequencing could lead to results that have implications for the wider family. Participants could see both the health benefits that a diagnosis could bring to other family members, but also the stress and strain on family relationships.

5.10.1 Enabling treatment for other family members

For those participants who favoured early diagnosis, many felt that enabling family members to be informed of a genetic variant that might affect them was a positive aspect of WGS. They felt that knowledge of a genetic condition could empower family members to make choices about their health, lifestyle and give them access to medical treatments and monitoring that could prevent, minimise or manage problems down the line. Participants were clear that the objective first and foremost should be for WGS to benefit the child, but if the information that stemmed from WGS could help the health of their family members, some thought it should be used to do so.

There are things in my family's genes and things that if WGS had been around when I was a youngster, things that might have been sorted and fixed. I'm extremely excited about it and

> I definitely think it's the right way to go. Not just for newborns but for the whole of society. I Participant, Scotland

> The objective for the health of our child, and added onto that, to check in our immediate family any health issues. Then it's a win-win. It's a plus. It's almost like 2 for the price of 1. I Participant, Southern England

The case study on the genetic condition Familial Hypercholesterolaemia (FH) raised the issue of whether it is appropriate and acceptable to test a baby for the condition and, if present, then test the parents and provide treatment if the test identified the gene mutation in them. Many participants felt that it was in the child's best interests to help identify a parent at risk of early onset heart disease and take steps to avoid poor health or an early death.

> I think that's one of the conditions that it would improve because, as you said, it will help a parent because they may never know that they had that and it is very easily treatable with statins and two, it would also help the child. So, it's kind of helping both the parent and the child, isn't it, as opposed to some conditions where you couldn't help the parent because it was too late, if that makes sense. So, I think for a condition like that, I would think that whole genome sequencing is a really positive step forwards. I Participant, Genetic Conditions Group

In the Young Adults and Black, Asian & Minority Ethnic groups, some participants could see benefits in using WGS at birth to identify genetic links to adult onset conditions such as cancer and Alzheimer's disease. They felt that genetic information of this sort would enable family members to access monitoring and treatments, without which their health could be at risk or their lives shortened.

> My main hope is the aspect of identifying illnesses within the parents, just from the child itself. I Participant, Black, Asian & Minority Ethnic Group

> It might have benefits for the whole family unit, we were talking earlier how the results affect everyone. I was thinking it might even have further implications for society in that if someone is diagnosed with one of these breast cancer traits then the whole family are more aware of the gene so it might mean they maybe get more smear tests or they get extra tests which mean we can detect things like cancer much earlier on. I know with Alzheimer's I think things like smoking makes it worse, so you can change the whole family unit's life or do things to make it better. I Participant, Young Adults Group

In Scotland, participants talked about the way in which knowledge of patterns of health conditions was part of a family's folklore. They talked about WGS establishing the truth behind whether some conditions could be attributed to inherited traits or not. Others talked about how introducing WGS into a family could help establish patterns of incidence, such as a condition skipping a generation.

> I think we also learn that people in our lives, in our families, get illnesses. My grandad got cancer, my grandmother got a problem with her liver. We are already finding out things that are potentially in the family and, with a little bit of research, we can find out if it's hereditary or not. So, even if we did have a better grasp of knowing, it's not that different to what we already do just through word of mouth. Just through living life, you find out if certain illnesses are in your family or not. It would probably be better to know for certain if that's true or if it's just that misinformation or a bit of a wives' tale or whatever. **I** Participant, Scotland

5.10.2 Creating anxiety and straining wider family relationships

In Scotland and in the Genetic Conditions group, participants talked about how a decision to have a child screened using WGS should be made with the wider family in mind. Some worried that this would make the consent process for WGS more complex and burdensome for the parents. They wouldn't just be consenting to something that would affect their child, but also potentially their wider family. The impact on the wider family's mental health was a particularly strong concern.

> It's not just health this is impacting. The consent question is huge. That's opening up what could be your mother, your father, your siblings, your son, your cousin. It's opening up another five or six people straight away. I think it's good for you personally, but you need to think about the later impacts of your mother or your son getting contacted and say, 'This has come up.' Are they in the mental state to deal with that, are they at the age to deal with that? I don't know. I think that's quite a big disadvantage. **I** Participant, Scotland

Participants also raised the issue of some family members not wanting to know about genetic conditions and the risk of this knowledge being forced upon them and causing distress and resentment. Participants spoke about family members who may already be contending with existing health issues or with financial difficulties and that this additional information about a genetic condition could be damaging.

> If you decide you would like to find out for your own children, you have whole genome sequencing and something is discovered, your brother or sister might not want to know for their children. And sometimes genetic conditions are very much like what my son has. They can run in families, so this is going to cause, I guess, relationship difficulties with family members. There'll be differences of opinion. **I** Participant, Genetic Conditions Group

6. Diagnose more

Key findings

Whole Genome Sequencing offers the possibility of screening for more conditions than the nine included in the current newborn blood spot test. In this Chapter we learn that **participants see clear benefits in increasing the number of conditions screened for if they are all treatable, but that for some, the leap from nine conditions to six hundred raised important questions**.

Some of these questions were around implementation:

- Are these six hundred conditions really treatable?
- How could this be afforded?
- How could the process be communicated and consented?
- Would screening so many conditions mean longer waits for diagnosis and treatment?

Other questions focused on what the six hundred conditions could include and whether that number would be overwhelming at such an intense moment in life.

Some participants were extremely positive about **significantly increasing the number of conditions screened for**. They believed that screening for more conditions using WGS **could reveal the true extent of some assumed-to-be rare conditions** and therefore attract more funding and research. Some felt that screening for nine conditions was too few and **WGS would bring newborn screening up-to-date.**

6.1 What participants heard about diagnosing more conditions

During Workshop 1 and on the online space participants heard from specialists about why WGS was being considered for newborn screening. One of the potential outcomes of bringing in WGS at birth is the identification of more conditions. Participants learned that six hundred disorders with an intervention that could reduce harm or prevent problems could be identified. The slides in Fig. 6.1 show the information shared with participants. The number of six hundred conditions was an eye-opener for participants and many of their questions and reactions stem from

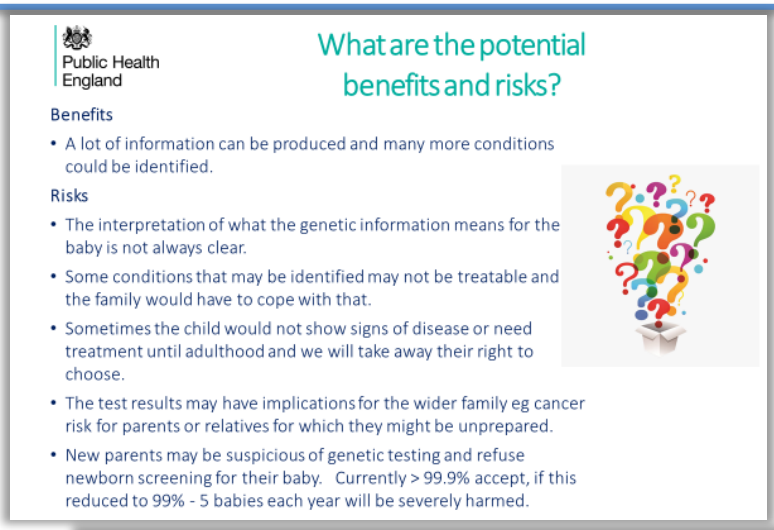


Figure 6.1: Slides showing risks/benefits of WGS

comparing it with the current number of conditions screened for: nine.

6.2 The positive aspects of diagnosing more

When discussing the most important benefits of WGS for newborn screening, two aspects featured highly for participants: the ability to identify and treat conditions earlier and the ability to diagnose more conditions in a single screening tool. In this section we look at the positive outcomes participants believed could come from diagnosing more conditions as part of newborn screening.

6.2.1 Rare conditions: more knowledge on their prevalence and treatments

By using WGS at birth, some participants, particularly in the Black, Asian & Minority Ethnic group, believed that conditions currently classified as rare could be identified more frequently. They hoped that WGS would help reveal the true extent of a condition. This was seen to have the following positive outcomes:

- Attracting more resources to research
- Enabling the government to more accurately plan and fund services for the condition and
- Creating communities of support amongst families with the condition

> To identify what we currently think are rare mutations and once you scale them up, maybe they're not as rare, because once you have the volume of numbers coming in, that allows us to do more research and focus on trying to find solutions to those things that we think are rare now. **I** Participant, Black, Asian & Minority Ethnic Group

6.2.2 The ability to diagnose and treat more conditions

For many participants, if conditions that immediately affect a baby's life could be identified and treated immediately, then they were strongly supportive of including them in the newborn screening programme. They saw the combination of the larger numbers of genomes sequenced through newborn screening and the larger number of conditions screened for leading to better health outcomes and breakthroughs in treatments.

> We only test for nine but we have the capability of testing for six hundred, and these are life changing diseases and conditions that we do have effective treatments and managements for, so why not? Why not test for them. **I** Participant, Scotland

6.2.3 Greater understanding of conditions

The diagnosis of more conditions through WGS leading to a greater understanding of their prevalence in the population was a benefit identified by most groups. This was important for understanding if some conditions were more common in certain parts of society or the UK. Information on this could inform where funding and resources are needed.

> Participant 1: I think the finding out how many people are suffering from these different diseases is incredibly important. Figuring out how many people are generally affected in

> the UK specifically, can then give the government an idea of where funding needs to go. Where their focus needs to be.
>
> Participant 2: Following on from that, if there are any disparities in different groups, like Black and Asian minority ethnics, or people of lower socioeconomic backgrounds and how we can focus our efforts to support those people. **I** Participants, Young Adults Group

6.2.4 Moving into a modern age of medicine

The thought that six hundred conditions could be screened for and treated prompted some participants to reflect that the current number of conditions in the blood spot test was too low and out of step with modern medicine. They thought that introducing WGS for newborn screening would remedy that.

> I think that the medical improvement that's going to come from newborn screening and doing WGS is just going to be an incredible step forward for the medical industry, especially in the UK, and I honestly feel like medicine is ten to fifteen years behind where it should be right now. I feel something like this is really going to pull things back, and it might only be for nine conditions right now, but hopefully, in ten to fifteen years, it'll be for more, and that just will pull everything so much further forwards and put us really into the modern day with medicine, I hope. **I** Participant, Southern England

6.3 The implications of diagnosing more

The difference between screening for nine conditions and screening for six hundred was striking for many participants. Whilst the prospect was appealing, at the same time it prompted questions, uncertainty, and concerns. Here we explore the different implications that participants drew from the prospect of screening for more conditions.

6.3.1 The credibility of six hundred conditions being treatable

When discussing the number of six hundred conditions to be screened for, some participants did not believe that all could really be treatable. The leap from nine to six hundred diagnosable and treatable conditions seemed too large to be credible. Some participants were concerned that the six hundred might include less serious conditions or conditions with no treatments:

> I keep hearing there are six hundred plus or whatever it is, but there can't possibly be treatments for all those six hundred plus conditions at the moment. **I** Participant, Southern England

6.3.2 How to communicate more conditions: too much information at birth?

A concern expressed, particularly in the New & Expectant Parents group, was that the information associated with screening for six hundred conditions could be overwhelming for parents, particularly mothers, when they might not be physically or mentally at full strength.

> It might be a little bit overwhelming because it might be a bit too much information all at once when you're dealing with your own, from a woman's point of view, you're dealing with your own physical recovery and your own health and healing. So, to deal with a new diagnosis or potential issue I think could be quite a lot, too much information all at once. I Participant, New & Expectant Parents

Questions were asked about how that quantity of conditions could be communicated in a way that consent could be meaningfully given. Participants also raised the expectation that all conditions screened for need to be explained on the NHS website to prevent incomplete or misleading information on less reliable websites causing harm.

6.3.3 The infrastructure and funding needed to screen for more conditions

Screening for this increased number of conditions led some participants to raise questions about cost. Can the NHS afford this? They talked about the enlarged infrastructure needed to process tests and the capacity to deliver follow up care. Some participants were concerned, post-COVID, that such an increase in the number of conditions screened might be unaffordable and unmanageable. This led to questions about what other parts of the health service might have funding cut to pay for this expanded screening service or whether funding might come from 'multinational pharma companies'.

> Does the NHS have the help, the counselling, the money, the resource, the development of technology once they find these six hundred new variants that they may all be carrying? What are they going to do with it if they don't have the money? We've just been through this current pandemic, we know what strain the NHS has been under, we could just be adding more and more onto a very, very shaky ship | Participant, Black, Asian & Minority Ethnic Group

> I'm not saying this isn't important because it is very important that we are able to find out six hundred conditions that a child may have or may carry then that's great but it did make me think when they guy said, 'Are we taking the money from somewhere else?' I Participant, Scotland

7. Consent

Key findings

Participants recognised the complexity of the consent process when parents are consenting for a newborn baby. In this Chapter we explore participants views of consent and find that:

- The **impact on families and parent/ child relationships** is important in this context – the decision to consent or not **could cause family divisions** if not handled sensitively.
- Twenty first century families do not come in a standard format: children are born into wide-ranging scenarios e.g. adoption, sperm donor, parental break up, so it is necessary to think about how consent works in practice in all situations. Participants thought it was **beneficial for individuals who do not have contact with their biological parents to have WGS findings from birth** so that they can learn about their medical and genetic background.
- **Consent for research** can initially be sought from the parents, but children as they become adults could confirm that they are happy with this.
- Participants felt that it was **essential to share WGS information with parents at the newborn screening stage if a condition could be treated**. The issue of when to share becomes more complex when the findings affect conditions in later life or carrier status. Many participants felt this information should be shared when the child reaches adult-hood rather than earlier.

7.1 Consenting on behalf of the newborn child

Participants thought the implications around consent for WGS for newborn screening can be more complex than at any other point throughout life. Participants thoroughly considered the impact on the child of having their genome sequenced at birth, when they were unable to give their own consent for something so important and potentially life-altering. There was a spectrum of opinions on whether consent given by parents on behalf of their child was acceptable. Some felt it was the right of the child to decide to be tested, not the choice of the parents. Others thought that parents were entitled to make decisions for their newborn child based on what they think is in their child's best interest.

> I think it's seen as a disadvantage, but as parents they need to make decisions all of the time about say piercing their child's ear, or circumcision, or something. This is them doing what they think is best. I Participant, Black, Asian & Minority Ethnic Group

Participants considered what the impacts may be for families should the child grow up to have their own views and potentially have opposing opinions to their parents on WGS, suggesting that they may not want to know about their findings or may take unwelcome or distressing news badly.

> What's the emotional impact of telling your child about the data that you found out about? How much do you tell them? When do you tell them? Could it cause some separation within a family, animosity between parent and child from what's been discussed, and at what age? **I** Participant, New & Expectant Parents

Participants also deliberated on the impact it would have on a child and their family unit should parents not consent to WGS for newborn screening. They thought that the child may grow up to feel disappointed that their parents chose not to get them tested and may feel that they are missing out on finding out valuable information about themselves.

> What happens if a parent says that they don't want to know from the test? That could cause major problems when a child turns 16 or 18 and they could say, 'Well actually I want to know.' That could cause massive issues later on in life, especially if they have then presented something and the parents had the opportunity to find that out but chose not to? **I** Participant, Genetic Conditions Group

Participants considered the complexities around consent when other factors beyond just the health of the child impacts parents' decision to take up WGS at newborn screening. They discussed the influence of religion and the pressure parents would feel to make the right decision for the health of their newborn child.

> When it's a newborn, that whole responsibility is on you, as a parent, and if that goes against your religious beliefs, it might make you feel like you've got to make a choice. **I** Participant, New & Expectant Parents Group

7.2 Consent and the family

Participants understand that twenty first century families do not come in a standard form and felt that could give the consenting process at newborn screening another layer of complexity. Given that children are born into wide-ranging scenarios, it is necessary to think about how consent works in practice in all situations, especially due to the sensitivity of the genetic data from WGS. Examples of where participants felt consent for WGS may become more difficult includes where:

- Children are being adopted, from within or outside the UK
- A surrogate mother or sperm donor is used
- Biological parents are separated
- The parents are still children themselves and under the age of consent
- The parents have learning disabilities or mental illnesses that impact their ability to consent on behalf of their child
- If one parent refuses to consent
- The biological parents did not consent but the adoptive parents, shortly after birth, do want to get their child screened using WGS

Participants in the Young Adults group discussed the difficulties for women who give birth in prison and how that might impact on the consent process:

> Would that mother still be in charge of the data of that baby because it's not her choice to be giving up her baby in the first place because she's in prison. Does she still have a say over what data is used, how her baby's data is used? I Participant, Young Adults Group

When discussing the relative value of WGS findings, participants thought it was especially beneficial to have WGS findings from birth for individuals who do not have contact with their biological parents. This would allow children to learn more about their medical and genetic background than they would otherwise have been aware of.

> If a child is adopted, or they lose their parents and you don't know about medical history, it has just struck me that having that information captured is going to be incredibly useful in the longer term. I Participant, Black, Asian & Minority Ethnic Group

A few participants questioned whether infidelity would play a role in whether a parent gives consent to WGS for newborn screening. They felt that some parents would opt to hide their infidelity over choosing to get their newborn screened, despite believing WGS to be an advantage for the health of the child.

> It's a bit negative, but what if it's infidelity that has caused the child to have carrier status? That could be a whole minefield if it's one of the things where the baby is sequenced and the information is given to the family, but then the family are found potentially not to have that genomic difference and so that's a way of finding out that there's been some infidelity. That could open up huge, huge issues within a family. I Participant, Northern England

7.3 Consent and research

Some participants recognised a distinction between consenting for WGS for the purposes of providing medical care to the child and using their information for research purposes. Where results are used in research, some participants felt consent should be left for the individual to provide when they reach the age of consent rather than seeking confirmation for the use of data from parents.

> Consent to store the WGS in a research database should come from the child when an adult. If the idea is to build a research database quickly ask the parents for their WGS. I Participant, Genetic Conditions Group

However, this wasn't felt unanimously by all participants. Many recognised the value in research (as described in Chapter 4 and Chapter 8) and stressed the importance of consenting from birth for both health and research purposes if society is to strive for medical and technological advancements. For some this led to a compromise approach whereby consent is initially given by the parents, and then later consent is re-sought from the child as they become an adult.

7.4 When to share information

Although screening a newborn using WGS would provide families with their baby's genetic findings from only weeks or months into their child's life, participants debated whether the information should be made immediately available and shared with families. Participants explored issues of consent in assessing whether it's morally and ethically correct to disclose this information to parents. Some felt it was necessary, and the whole point in performing WGS at birth:

> If you've given your consent for your child to be screened then surely you're doing that because you want to know if there's something wrong, so if there is potential help out there you could get it? I'm not sure why you would give your consent for the data just to disappear and that be job done. I Participant, Genetic Conditions Group

Others felt information should be shared with the individual later in life, most likely when they reach teenage or early adult years:

> I think if they're tested when they're newborn, it has to be looked at again when they're 16, 18, whatever age, when they can make decisions for themselves whether they still want to know what the future may hold for them. I Participant, Genetic Conditions Group

One participant in Scotland described it as holding a 'ticking time bomb' and discussed the concerns about being given this information too early in life in discussion snapshot 7.

Discussion snapshot 7 – sharing information:

I was speaking to one of my friends yesterday about this, and he's a twin. And his brother developed symptoms, because his mum is a carrier, and his brother developed symptoms, and he didn't, and he feels guilty for it. And I didn't really take that into consideration until I was speaking to him yesterday about this. Because what I said to him was, the disadvantages of this. If you knew what date you were going to die, would you want to know? And he said, yes, if I knew I was going to die at 70, I would like to know when I'm 69. But I wouldn't like to know that when I'm 5, because it's a time bomb going off. So, I think too much information can be a bad thing, but also a good thing, and it all depends on the person and how they deal with this information that is their data package. I Participant, Scotland

Participants also explored the implications if individuals feel that they are the last to know about their genetic information. Participants were concerned about the impact this would have on children growing up who were discovering very sensitive and personal information about their genes from family members or other people who have far greater understanding of the genetic make-up of the child than the person themselves.

> I think first thing that needs to be considered is the initial landing of the bomb. The initial, 'This is all of your information, it's all of yours. We've told your parents about it, we've told everyone about it, everyone knows, but it's actually you.' It's you getting told about the digital version of you. I think that really has to be

> looked into and the impact on how that's going to affect the person. I Participant, Scotland

There was a shared worry that disclosing findings to teenagers when they become young adults or reach the age of consent might add stress to an already hectic time in their lives. Participants were apprehensive that it may have devastating repercussions if the teen is unable to deal with the information.

> What if they don't tell me until I'm a 16-year-old girl, now I'm 16 and I have a chance that I could die from breast cancer. 16-year-old girls have enough stuff on their plate, so then you've got the mental thing that comes into it, if you're not mentally able to handle that. Is that now going to bring in suicide rates for children because they're now given another extreme bit of information about their life at a time when they're going through god knows what. I Participant, Southern England

Participants in Wales & Northern Ireland even considered what the legal implications would be, should parents not disclose all WGS findings to the child who was screened.

> When you become an adult, if you're diagnosed with a condition and you find out that your parents knew this at birth, are there any legal implications there? Are we going to have scenarios where children may want to sue their parents for having not disclosed private information? I Participant, Wales & Northern Ireland

7.4.1 Consent and carrier status

Many participants felt that the correct time to be informed about carrier status is when individuals are thinking about starting a family rather than from childhood as that information will largely only impact that person when deciding to start a family. However, they did identify a benefit for parents in identifying carrier status at newborn stage, as it could inform the parent's decision to have more children. Some felt it was more apt for potential parents to have WGS prior to starting a family rather than screening the newborn using WGS, so they could make an informed decision on their reproductive choices considering the findings.

> If it turns out they could potentially be a carrier for cystic fibrosis, you don't need to know that when you're a child at primary school. Later on, if they get screened at 16, 18, then that's valuable information. I Participant, Wales & Northern Ireland

7.5 Eligibility

Participants had questions and concerns about how WGS for newborn screening would work in practice and explored some of the potential grey areas around inclusion of newborns and their families in screening using WGS. Questions on eligibility included:

- Will parents whose baby was born just before the roll out of the programme be invited back for screening if the parents are interested?
- Can you choose not to have your child screened but change your mind down the line? If so, what age is the cut off?

- If a genetic variant is discovered, would you perform WGS on siblings or other family members?

- What if parents don't consent but when the child grows up they would like WGS?
- What if a child is born in the UK but lives elsewhere? Would they still be eligible for WGS? What are the implications if they discover something which is not treated in their home country?

8. (Un)certainty of WGS findings

Key findings

The **uncertainty of WGS results was a main concern** shared by many participants across the dialogue. There were two schools of thought: those who felt **knowledge is power** and those who consider **ignorance to be bliss**. There was understanding that provision of uncertain results has different impacts, for some the information would be useful and for others it may cause anxiety and be detrimental to their health and wellbeing.

The primary concerns around uncertainty of WGS findings, whether it be false positives/negatives, unknown penetrance or uncertainty over whether a condition would develop later in life were:

- The mental health impact on the individual and their families as they grapple with uncertain results.
- An unnecessary journey of testing for the child and the impact this would have on their wellbeing as well as NHS resources.
- The impact this would have on major life choices, such as choosing whether to start a family or having surgery to reduce the risk of developing cancer.
- That it may be detrimental to physical health as uncertain results become a self-fulfilling prophecy.
- Whether uncertainty would negatively impact the uptake of newborn screening.

However, many participants acknowledged that for certainty of results to improve, increased research into WGS is required. Therefore there may be a period of necessary uncertainty in the initial roll out of WGS for newborn screening before **enough data is gathered and understanding and certainty of results progresses.**

Discussions also explored **how data accuracy affects the certainty of results**: participants cited large gaps in health care professionals' understanding of complex genomic data and a lack of joined up data as sources of uncertainty leading to unclear results.

Participants were **generally optimistic about the use of precision medicines** through WGS to reduce the risk of uncertainty around treatments, particularly in relation to cystic fibrosis. Yet some questioned whether as a society we truly know enough about the genome to take on WGS for newborn screening or if uncertainties are just too high.

8.1 Accuracy and uncertainty: attitudes towards the use of WGS for newborn screening

Participants were positive that the use of WGS for newborn screening could result in improved accuracy and less uncertainty for some conditions. There was an expectation shared by some that accuracy using WGS should exceed that of current newborn screening methods. In the Black, Asian & Minority Ethnic group, participants stated that whether screening results are accurate or not is more important during newborn screening than screening at other life stages. They discussed the impact it would have on an individual throughout the course of their entire life, rather than just as an older adult when other population health screening – such as for breast cancer - takes place.

> Accuracy is very important for public screening but here, I think it's even more important. It's very, very important because it's a newborn baby… I think if you make a wrong diagnosis here, it might affect the whole future of the child.
> **I** Participant, Black, Asian & Minority Ethnic Group

8.1.1 Nothing in life is certain

Broadly, there was agreement across the dialogue groups that absolute certainty is an often unachievable feat. Participants recognised that WGS would not be a miracle tool in diagnosing and predicting genetic conditions. A few participants talked about not expecting certainty in other aspects of life, so why would we expect any different when it comes to using WGS for newborn screening.

> There have been a lot of the speakers that have said that scientifically, it is ground-breaking but sometimes with the accuracy of the results, nothing's 100% accurate. **I** Participant, Wales & Northern Ireland

But if WGS is to be implemented as a newborn screening tool, participants felt that it must be made clear that it cannot tell all and there should be clarity on what it can and cannot do.

> You need to be open and honest with people. If the likelihood of you getting this is 60%, it's about relating that onto the person, not about saying, 'We think you may have this.' It's about saying, 'Our test results show you have a 60% likelihood of having this,' so being open and honest about it. **I** Participant, Scotland

8.1.2 The increase of research and decline of uncertainty

When exploring the degree of uncertainty in WGS results which was acceptable to them, participants described the sense that it was a 'chicken and egg' scenario. Many acknowledged that there is only scope for uncertainty to decline as research into the genome improves. For this to be achieved there will be a period where some people will receive results which are not as certain as hoped, to allow for future generations to have improved certainty and understanding when it comes to genetic conditions and their treatments. Some participants suggested that where there remains uncertainty in results, the information is not disclosed to individuals or families, but retained only for research purposes to achieve the long-term aim of improving accuracy and certainty.

> Maybe that's the information that can be used for a research purpose rather than something which is just portrayed back to people because, again, of the mental health implications it can have knowing that you've got a higher chance of having something but they could use that for research to get better treatments and then when you've got enough information on that go from there and bring new things out but that would be quite a while in the future. **I** Participant, New & Expectant Parents Group

8.1.3 Data accuracy affecting uncertainty of WGS findings

Participants voiced their concerns around how data is understood and interpreted. They worried that an inadequate understanding of the findings by healthcare professionals, human error or a lack of joined up data, might affect the certainty of WGS results. Participants reflected on their own experiences of the healthcare system to conceptualise how this may play out with WGS findings from newborn screening, which were perceived to be even more complex than other forms of medical data.

> The misdiagnosis and interpreting data wrong, not joined up thinking and all those sort of problems and I had a similar problem with my family… It doesn't necessarily fix how the data is used and joined up thinking of different professionals using it appropriately and proficiently. We tend to think with technology, 'Oh, isn't that brilliant?' but there's still humans involved who cock it up. How do we know that this data is interpreted and joined up properly across different NHS trusts or across different administrations? **I** Participant, Genetic Conditions Group

8.2 Attitudes towards receiving uncertain WGS results

In this section we see that participants make two distinctions when considering WGS results:

1. Uncertainty of early/ immediate onset conditions such as cystic fibrosis
2. Uncertainty around conditions for which the baby might have a genetic predisposition such as breast cancer.

8.2.1 Knowledge is power/ ignorance is bliss

As explored in Chapter 5, some participants shared their view that knowledge is power, that the more that can be known, the better. For many participants, this remained true even when probed about the uncertainty of results: the certainty of whether a condition would develop; when it would develop; the unknown severity of an illness; and the risk of false positives.

> I would prefer to know something, and we actually have that in a family that we had the same thing, just to know something it can give such a peace of mind to people. Then even if it's not 100% and then you can do your research after that, so I think it's much better than not to know anything. **I** Participant, Scotland

Within the context of uncertainty, others felt more comfortable with an 'ignorance is bliss' viewpoint than knowledge is power. One participant in Scotland described it as the fear of the unknown (discussion snapshot 8). These participants thought that where the results of the WGS were uncertain, it was preferable not to disclose all.

> If I'd have been told when I was born, I was 68 before I was told I've got cancer, which I'm told is now gone, we'll see. I wouldn't have wanted to know for the last 60 odd years that I may or may not get cancer. I think in the end you would just become a gibbering wreck. It's too early to know for that length of time.
> I Participant, Southern England

Discussion snapshot 8 – fear of the unknown:

Some people end up living in fear, I have a lineage where there's breast cancer but it's so helped that most times whenever I stand at the mirror, almost daily, I always check for lumps, check myself to see. We do have it in my family, nobody has had it but I still check for lumps. When you have an idea that you have it, it's going to live with you, you're going to live with that fear. You know how you lie in bed and wake up it goes numb, maybe you've been lying on your side, you get up and you're, 'This is cancer coming'. I Participant, Scotland

There was agreement by participants that information provision of uncertain results from WGS for newborn screening is not a one size fits all. Some people will want to know and others won't. They discussed how some people would use the information in a positive way to motivate them in life, whereas for others an uncertain result hanging over them could cause severe detrimental harm to their lives.

> And it probably wouldn't affect everybody the same, there will be different variants, some people will be motivated by it, others will be demotivated by it. I just don't think there is one size fits all type thing. I Participant, Genetic Conditions Group

8.3 Uncertainty about whether a condition will develop

Participants frequently explored their views on uncertainty of older adult-onset conditions and untreatable illnesses using the example of Alzheimer's disease. Most dialogue participants agreed that conditions such as Alzheimer's – which often develops only in late adulthood and has no cure – should not be shared at newborn screening because it is no more than an uncertain prediction of when and to what degree it will develop, if at all. Participants reflected not only on the impact this would have on the individual receiving the result, but also family members' concern that a condition might develop over time in their loved one.

> With Alzheimer's there isn't currently a cure, and unfortunately it does tend to affect those around you more significantly, would you want to know that you would be putting that burden on your family at some point in your life? The stress that would cause would really take a toll on mental health, as would as a parent knowing what was going to happen to your newborn baby. I Participant, New & Expectant Parents Group

8.3.1 A self-fulfilling prophecy?

Across the groups participants discussed the impact that knowing that you have a risk factor for developing a condition at some point in your life would have on your physical health. Participants

discussed whether being armed with this uncertain information would lead to a self-fulfilling prophecy. They considered whether living with the knowledge that you are at high risk of developing an illness would cause so much stress that you become physically ill with worry.

> I think the words 'self-fulfilling prophecy' come to mind. If you think you might have earlier heart disease then that's going to cause you stress, so you're more likely to get it. In that case, ignorance would be bliss. **I** Participant, Wales & Northern Ireland

8.3.2 When uncertain results influence major life choices

When faced with results – even if uncertain – individuals may choose to make significant life choices based on their WGS findings. Participants often used the example of the risk of developing cancer with the BRCA gene to explore their views on making decisions that may not be necessary, based on the chance that a condition will develop. Participants thought that people might make drastic decisions relating to their uncertain WGS results, such as making different choices about family planning than would have otherwise been made, or even having surgery to reduce the risk of illness.

> Yes, it has occurred to me, back with the BRCA gene again, that if you knew that when you were 18 that you might arrange or have your children earlier. Rather than scanning for breast cancer or whatever, you might have some surgical option. I would choose to do that. I know one of my cousins has. **I** Participant, Genetic Conditions Group

Another concern expressed by participants was that it may cause people to live their lives differently to how they ordinarily would, resulting in missed opportunities that people may live to regret.

> You might be living your life overly cautiously and then if you didn't get something, even if you've got an increased chance of having it because you've got this gene variant you might think as you get older, 'I've wasted my whole life,' because of information that didn't go into anything. **I** Participant, New & Expectant Parents

8.3.4 Focusing on what's expected rather than reality

Participants considered the possibility that society would become overly focused on the condition expected to present itself from WGS results, rather than taking into account other factors which may be the true cause of an illness. There was fear from some that health care professionals and individuals would become too dependent on WGS results from newborn screening and fail to consider whether symptoms may be indicative of other illnesses influenced by other environmental factors such as diet or where you live.

> The benefit I mentioned before was all about saving time, relieving pressure, and getting that treatment as soon as possible. If it turned out that it wasn't the illness that was expected, but you start treating that illness anyway, it's going to have the adverse effect. It's going to cause even more delays. Treatment being given unnecessarily. That would be quite harmful to the patient. **I** Participant, New & Expectant Parents Group

8.3.5 Putting additional pressure on the NHS

Raised by participants in Scotland, there were concerns that sharing results of WGS from newborn screening that lacked certainty would result in increased long-term pressure on the NHS sparked by a person's insecurity and anxieties over developing conditions identified at newborn screening.

> So, they would be constantly back and forth to their GP, to their health clinic saying, 'Oh, I want testing for this because I got told thirty years ago that I might have that,' and it's like, let them come to you rather than us, constantly, saying, 'I've got a cough so it might be this,' or, 'I've done this so it might be that,' and it becomes a wee bit crazy. **I** Participant, Scotland

Participants also suggested that there may be a significant increase in cost to the NHS in having to provide far more tests than necessary in attempting to discover the truth behind false positive results.

> Well, it's use of resources, so I think it's stated the fact that if you carry out the diagnosis process on a false positive which got picked up in the screening, then if the diagnosis comes up as a false positive then you've wasted that diagnosis treatment, the doctor's hours, the resources which went into it. Even there, there were the reagents which actually went into it. **I** Participant, Northern England

8.3.6 Is uncertainty breeding a culture of fear?

There was a mutual concern amongst several participants that sharing uncertain results of WGS from newborn screening would add to what they perceived as a 'culture of fear' which has been steadily increasing in society over the past 18 months. They felt that the effects of the COVID-19 pandemic have spurred a wave of fear and anxiety about developing illnesses, even those which are common such as the cold and flu.

> It's just breeding a culture of fear, because there's going to be a lot more mights and a lot more carriers, a lot more possibilities than actually people being diagnosed. The next generation, their parents and society as a whole is just going to be a load of people going around nervous that they're going to get an illness, which is quite similar to what's been happening this last year. **I** Participant, Wales & Northern Ireland

And Scottish participants called for rationalisation around uncertainty and the probability that a condition will develop, and the need for good education across the population (explored further in Chapter 10).

> We don't know at the end of the day, no-one's going to be able to tell us yes or no so it's about being rational about there's maybe a 10-30% chance, but that doesn't mean you've got to permanently freak out about it. If you can rationally understand that it's explained to you and you're educated properly, then we can use the information much more effectively. It's like you're hearing adverts, people say as soon as you hear words like cancer, screening, it can set off alarm bells for you. **I** Participant, Scotland

8.3.7 The implications of inconclusive and uncertain results

Throughout discussions, participants voiced their concerns mental and physical impacts on families following WGS at newborn screening. Including:

- Living with the fear that you are going to develop an illness later in life and how this may affect your child's life decisions and the anxiety and distress it would cause.
- It's effect on parents' ability to enjoy their child's youngest years as they anticipate an illness or are subjected to a gruelling course of testing, which may prove unnecessary.
- The use of preventative measures, medications, or treatments against an illness which may cause more additional harm, and again may prove unnecessary.

> The emotional trauma behind that. I refer specifically to breast cancer. Sadly, I suffer from that and I went through a barrage of tests, most of which were inconclusive before I was finally diagnosed with the cancer, and the emotional trauma behind that was actually soul-destroying. So, you're going to be given an (unclear screening result) again that's a moral and ethical consideration, I think. **I** Participant, Northern England

When considering more broadly the impact of uncertain results, questions were raised about how the NHS would fare should there be an increase in testing and resources needed to achieve a more conclusive result. Participants also debated who would be accountable for incorrect diagnoses. Would this lead to a financial burden for the NHS who may have to pay compensation in years to come for those who have struggled with a diagnosis which later turns out to have been incorrect?

> I'm just wondering, I guess, what would be the long-term implications if a child was misdiagnosed and they carry this burden, I guess, perhaps for the first few years of their lives? How would they be… compensated for any misinformation or misdiagnoses that they have received, and what would be the extent of being misdiagnosed? **I** Participant, Black, Asian & Minority Ethnic Group

8.3.8 Receiving a false negative result

There were altogether different concerns from participants when exploring the impact of receiving a false negative. Using the case study of implementing WGS for newborn screening to diagnose cystic fibrosis (see Annex 3), participants were concerned about the risk of an increase in false negative results. Some participants had higher expectations of genetic testing than the current blood test which they also know to be less than 100% accurate. A few participants were cautious about the implementation of WGS if it would mean that some people may slip through the net and are told they don't have a genetic condition which may go on to cause them harm throughout their life.

> If we find out later down the line that, let's say, two percent of all these tests, they were carried out in a way which actually makes them false, then that's two percent of all births extrapolated down the line, you've got a lot of cases of people which could have unnecessary shocks or anything, or maybe they actually were false negatives in this case where they should have been picked up by screening and it hasn't been done. **I** Participant, Northern England

8.3.9 Incorrect diagnoses leading to reduced trust in the NHS

Despite acknowledging that certainty would only improve as research increases, participants were wary that uncertainty of WGS findings may negatively impact the uptake of newborn screening. As generations of screened children grow up to have their own families, participants feared that knowledge and experience of uncertainty of WGS results would deter parents from getting their own children screened. Without a high degree of certainty, there was concern that people would fail to take up screening as the potential harms of misdiagnosis, for the individual and family could cause a lack of trust in the screening programme.

> If there's greater uncertainty over screening, data storage and stuff like that, that could really impact the amount of people getting screenings, which means more potential to miss out on people who would have benefited... All the benefits of whole genome sequencing for screening would have been lost by the fact that people are not getting screened anymore. **I** Participant, Southern England

Participants suggested that uncertain or inaccurate results from WGS at newborn screening may not only affect confidence in newborn screening, but also undermine public confidence and trust in the NHS. Participants referred to the experience of the COVID-19 pandemic when articulating the importance of having trust in the NHS and health care professionals.

> I think what's going to be really important in this is accuracy, because if people feel like, 'Oh, we got told that our son or daughter doesn't have this and then, they do,' or, vice-versa, then people do talk. We were talking last week about how things spread around and if people don't trust the system, they're not going to buy into it or be reassured by it. **I** Participant, Genetic Conditions Group

9. A resource throughout life

Key findings

Whole genome sequencing at newborn screening was felt to be **a useful resource throughout life** by dialogue participants. Participants described WGS results from screening at birth as producing a library or bank of genetic information which could be tapped into throughout life when:

- Your age means you are more likely to develop a condition
- You present with symptoms
- Medical knowledge and technology develops resulting in new tests and treatments for conditions previously little understood

Participants discussed the **practicalities of accessing this information**: where would it be held, how would people be able to access it throughout their lifetime and how much would it cost.

Participants also thought about the **potential use throughout life as a pharmacogenomic tool**, preventing unpredictable reactions to medications with better tailored treatments for the individual throughout their life which would be a) most effective in treating the illness and b) have the least amount of adverse side effects. Participants regularly reflected on their own experiences of being wrongly medicated to articulate the use that WGS would have in their own lives. They also considered more unconventional uses of pharmacogenomics throughout life, such as its use in determining how individuals will react to cannabis use: dividing participants into two camps of those who thought it may be an interesting and useful finding, such as those in the young adults group, and those who feared it may lead to substance misuse.

Most participants thought that **knowing** your **carrier status** was a useful resource to access when thinking of starting a family. They explored how having knowledge of your own carrier status could help people make more informed choices during family planning and may result in people turning towards less traditional ways of starting families, such as IVF, sperm donors and adoption.

9.1 Dipping into your results when relevant

Most participants across the dialogue groups thought that whole genome sequencing for newborn screening would be a useful resource to refer to throughout the life course. They described the sequence as a tool which individuals could dip into or interpret should health problems arise throughout life, or at key ages from which we understand the risk of certain illnesses increase, such as at age 50 for breast cancer and 60 for bowel cancer.

> And all this potentially negative barrage of information, instead it's 'we need to know about cystic fibrosis right now, we need to know about this right now', whatever condition it might be. But later on, 'we don't need to know about BRCA genes, we don't need to know about risk of Alzheimer's, because it's not relevant

> at this very point in time'. And I think that probably is the best way to treat this information, is for it to be held, essentially, to prevent the risk of harm… So maybe withholding some of the information from the people themselves, until it is relevant, might be the best way to deal with this information. I Participant, Scotland

Participants conceptualised the WGS findings as a bank or library from which health care professionals can extract information throughout life. Only accessing the information when it becomes relevant was deemed as being more appropriate than disclosing all the WGS findings at birth. Participants suggested that this would allow for the influence of other factors such as environmental conditions to be accounted for, giving greater understanding of the reality of the illness rather than solely focusing on the genetic trait.

> I think it's not a case of withholding that information from people, it's just that, over the course of your lifespan, not so much your genetic makeup, but the more environmental factors and things like that might then influence how the genetic data could be read and how that could be interpreted in terms of what disease may be more likely at a certain point in life. I Participant, Scotland

9.1.1 Dipping into 'age-appropriate' WGS findings

Most participants agreed that some conditions are more useful to find out later in life than from birth. Many said that they would prefer not to find out about an illness at birth that would only affect them much later into adulthood. Alzheimer's disease was commonly drawn on by participants as an example of an illness that they would rather their predisposition to was not disclosed until well into their adult life – if at all – due to the uncertainty, stress and anxiety of wondering if and when symptoms would present and because there is currently no known cure.

> Screen a newborn. Screen them for four hundred different potential conditions, but maybe it's possible that the information that is gleaned from that screening is parcelled out. You would go back to the parents and let them know about stuff that has an immediate impact… Like you said, there's no point in a six-month-old getting a marker for potential future Alzheimer's. That might be more useful when they are, maybe, 30, and you can start making lifestyle change that decrease the likelihood that you do then develop the condition. I Participant, Northern England

To counter this viewpoint, some participants believed that the earlier you are told about a condition the better as it would allow treatment, if available, to begin earlier and give the individual and family time to plan (as discussed in Chapter 5). The morality of keeping the detail of WGS results from individuals, only to be released at certain points throughout life, was questioned by some participants who felt it was ethically correct to disclose all findings upfront after screening.

There were practical questions raised about how the process of dipping into your results throughout life would work. Considerations included:

- The **costs** involved in continually dipping into data throughout life.
- **Who would be involved**: who would individuals contact if they wanted to look into this information and who would be accountable for delivering the findings correctly to

individuals?

- **How the data would be stored**: where would it be stored safely and securely, yet be easily accessible throughout life for the individual and health care professionals.

> It's something that should be tapped into at various points throughout a lifetime and that comes down to how it's all stored. I suppose maximising the organisation of the data so that it can be accessed if and when it is required throughout peoples' lives and not just in the period they're born. **I** Participant, Wales & Northern Ireland

9.2 Raising awareness of illnesses and recognising the symptoms

Some participants had high expectations of the benefits of WGS data from newborn screening being analysed and used as a source of knowledge throughout their lives. Some spoke positively of this reserve of genetic information stating that it would leave people feeling better prepared should symptoms appear as they would already be knowledgeable of the cause, and it would prevent a mass of unnecessary tests. Additionally, they thought it gave an opportunity for individuals to do their own research into conditions, leaving them better equipped to know what symptoms to look out for.

> I think if your screening came up with something like that, for example, or it popped up with some disease or condition that you had never heard of or didn't know much about, as you approach maybe your teenage years and you start to maybe have a bit of interest into what all that data showed, you would do your own research and say, 'Right, what is coeliac disease? What do I need to be looking out for?' **I** Participant, New & Expectant Parents

9.3 A resource used as medical knowledge and research improves

Participants deemed WGS data from newborn screening to be a valuable resource as medical knowledge and research improves. They thought that having this library of information from birth means the results can be used as a research resource to scope out new treatments, conduct further research on conditions as technology and knowledge improves and be ready and prepared to get treatment should new ones emerge. Participants believed the potential for this data as a health resource would be a key reason why parents would choose to have their newborn screened using WGS at birth.

> It could make all the difference in a few years' time. If they have that information that you're going to develop this in a few years, they could maybe stop it developing because science has moved on so quick and it keeps moving on so quick. **I** Participant, Wales & Northern Ireland

Participants discussed the use of WGS at birth in reducing the risk of having to undergo repeat testing throughout life. They felt it would minimise the number of times individuals would have to go back and forth to hospital to be tested for illnesses should symptoms arise, be less invasive and reduce the time it takes to be diagnosed. The WGS results from birth could act as a resource kept throughout life that doctors can refer to and give them guidance should symptoms appear. Some

felt that it could potentially mean that everyone's genetic data could be continually analysed as new tests are developed and understanding of conditions improves.

> It might not even be something which you know about but you go along to the doctors and say I have this problem, I've got this lump, this feeling and rather than trying to diagnose something, which is guess work, having something to work off. So the doctor could look at your notes and say, 'Right okay I can see that you've got this gene mutation so I can focus my diagnostics on these 3 things,' which would obviously speed up the process. **I** Participant, Northern England

Participants thought that continual testing of the data from WGS at birth would be a comfort to individuals and families who may have received positive results for a condition, which at the time of diagnosis had invasive or no treatments and felt it may provide some hope in the future as more research is conducted.

> Well, that's the problem and I think people should be given an example of what could happen and say, 'Right, this is the test today in 2021. In 2026, we will retest you to make sure that what we have diagnosed then is still the same, because it may not be the same anymore.' … It gives them something to possibly, think, maybe, in 5 years', science will have got better, medical science will have got better and we will have found something to cure whatever it was that they may have been given the results for. **I** Participant, Southern England

Participants shared some concerns around consent when discussing the results of WGS from birth being analysed as medical knowledge develops. They felt that perhaps not everyone who had had this screening as a newborn would consent to having this resource examined throughout their adult life, articulating the need for strong consent mechanisms that are regularly called on as the screened child moves into adulthood (discussed further in Chapter 10).

> You've given consent in 2021. Obviously you've signed up for the study, you've been screened, and your data's available. Does that then give the researchers, the doctors, the health professionals access to your personal details, to then contact you, saying, 'We may need to bring you in for a diagnostic test, because we've found a link with this disease'? **I** Participant, New & Expectant Parents Group

9.4 WGS and pharmacogenomics throughout life

The ability to refer to a person's WGS from birth and throughout a person's life to inform healthcare was seen as a crucial benefit by all participants. They were excited by the prospect of having access to more tailored medication and therapies.

> Wow! The concept of personalised treatments/therapies is amazing! To be able to offer to someone a drug that would treat their specific presentation of a condition, rather than the average presentation of that condition is just mind blowing. Not only is there the potential for better, more efficacious treatment, but perhaps also fewer unwanted side effects, and fewer unnecessary drugs. **I** Participant, Northern England

Participants thought favourably of pharmacogenomics being used throughout life, not solely to avoid having adverse reactions to medicines but also to discover which medications function best for individuals (participants explored this scenario using a case study on aspirin used as a medication for cardiovascular disease in older adults – Annex 3).

> I agree it would be ideal to find out any adverse reactions early on, however it is just as important to find out what is also not effective such as those who do not benefit from aspirin who suffer from cardiovascular disease. I Participant, New & Expectant Parents Group

Participants shared their own experiences of having arduous and distressing journeys in finding the correct medication and described how valuable having this resource would be in their own lives in saving them often lengthy and invasive struggles of suffering through multiple ineffective treatments or medications (as described in discussion snapshot 9).

Discussion snapshot 9 – the benefits of pharmacogenomics:

I found out probably seven years ago now that I'm allergic to codeine and that's after I had a very horrible allergic reaction to it, luckily I was in the hospital at the time but none of my family have any kind of allergy to codeine. I don't know if that specific example is genetic related, but it would be good to know if whatever my allergy is that maybe it was just related to the amount of codeine that I was given at the time and that perhaps if I was given a different dose based on my genetic makeup that I would still have access to that kind of painkiller but just at a different level to what my body can cope with. I Participant, New & Expectant Parents Group

Participants discussed the improvements this would also bring to the lives of friends and families, who would no longer have to witness their loved ones suffering on their journey to find a medication that's right for them.

> There's a benefit to the family, because it's less stressful than for them to watch somebody going through a series of medications that aren't working. I Participant, Southern England

Participants were hopeful about the use of WGS for newborn screening in developing new treatments through research using WGS data. In workshop 2, participants explored the case study of cystic fibrosis (Annex 3) and the potential for personalised treatment based on the specific genetic variant that causes the individual cystic fibrosis. Participants were very optimistic that personalised treatments could be developed and so improve confidence in treatment plans.

> A key message that came across to me about WGS and cystic fibrosis was the potential to treat the person specifically and their specific aspects of the condition, not just a blanket treatment given to everyone. I assume this means that treatments could potentially be less invasive or have fewer side effects if only the dose really required, or the elements of the treatment that would make a difference are given, rather than the whole generalised treatment plan. This has the potential to make living with the condition easier as you only deal with your

> specific symptoms and issues, rather than potential side effects from unnecessary treatments for your specific requirements. **I** Participant, Southern England

Dialogue participants described the use of pharmacogenomics throughout life as helping to build trust in the health care system. They thought that where patients have certainty in the treatment they receive for illness, it would increase confidence in their care, reduce stress and anxiety and result in patients feeling better looked after and possibly improve health outcomes.

> As somebody who takes a regimen of pills for a heart condition, I've only got my doctors say so that the aspirin that I take is effective. And I would like to think that somewhere down the line there is a bespoke drug regimen for me. And I think that that would be fabulous. And I know fine well that the treatment that I'm being given by my GP is backed up by research into me as individual that says this is what you need and no more. I think that is great. **I** Participant, Scotland

The Young Adults groups thought about how this would pan out in the future. They shared a concern that pharmacogenomics might override a doctor's role in prescribing medication based on their own knowledge and experience. This in turn could lead to pressuring future generations to choose to have their children's genome sequenced at newborn screening, because it is seen as integral to healthcare.

> Maybe doctors might not feel comfortable prescribing things unless patients have had their whole genome sequenced. Things like the pharmacogenetics and then the breast cancer, and could that put patients under pressure to undergo genome sequencing if they're not getting treatment? **I** Participant, Young Adults Group

9.4.1 Using pharmacogenomics to test against the risk of unprescribed drugs in early adulthood

During workshop 3, dialogue participants were presented with a case study on the use of pharmacogenomics from WGS results at newborn screening to determine how an individual may react to using cannabis (see Annex 3). Most participants believed this was an interesting use of WGS data. Some felt it could be a valuable tool in understanding reactions to unprescribed drugs and regulating behaviours based on a person's propensity to have an adverse reaction (such as an increased likelihood of experiencing psychotic-like episodes).

> They were talking about the smoking of the cannabis when it came to teenagers and stuff it would maybe warn them about psychotic experiences or their mental health. Maybe if they knew that it would stop them, maybe prevent them from trying it and going on to a lifetime of mental health problems because of it.
> **I** Participant, Scotland

In a contrasting view, some participants feared that this use of pharmacogenomics may be 'opening a can of worms'. They argued that it could lead to an increase in substance abuse if individuals believe they are immune from negative side-effects, failing to account for other environmental factors.

> It's almost like giving free reign for those who aren't going to be harmed by exposure to cannabis that, 'You know what, go ahead, you're in your teens.' It

could be couldn't it? And perhaps like a parent you'd be like, 'Well, I don't really like that.' I Participant, Northern England

9.5 Determining carrier status through WGS at newborn screening and its use throughout life

WGS for newborn screening could enable individuals to determine not only which genetic conditions could – or will – affect them, but also whether they are carriers of conditions which could be passed down to future generations. Participants explored the benefits and challenges of understanding carrier status as a resource throughout life primarily through the examples of sickle cell disease and cystic fibrosis (Annex 3).

Most participants considered being informed of your carrier status as an adult as being beneficial when making reproductive choices. Understanding whether you are a carrier of a condition such as sickle cell or cystic fibrosis, was described by most as valuable in helping individuals make an informed decision on family planning if both biological parents are aware that they have the carrier gene. For these participants, the benefits of having this knowledge upfront included:

- Making reproductive decisions informed by the correct information
- Being able to take the time to consider it over the long-term
- Seeking advice from genetic counsellors
- Getting their partner tested for carrier status
- Planning for the future

> The benefit would be having the opportunity to be prepared, to have that conversation with your partner, and giving them information about sickle cell disease, and how it might affect their future planning. I Participant, Southern England

Time and again, participants returned to the point about making 'informed decisions'. They explored how having this information from WGS at newborn stage would mean potential parents could explore other avenues of starting a family when faced with this uncertainty, such as having IVF or using a sperm donor (who is not a carrier), or perhaps prompting people to adopt a child.

> A benefit for adoption is that if adults were to get their whole genome sequences screened but they would then decide that they don't want to impose that on their kids, so let's adopt, which makes more families looking to adopt kids that might end up in foster care. We all know the foster care system isn't the best, so it gives them a different option to give a home to a kid that needs it. I Participant, Young Adults Group

Concerns raised by dialogue participants about carrier status determined by WGS at newborn screening as a resource throughout life include:

- It may impact people's ability to find a partner, or cause more anxiety when choosing a partner, if they have been diagnosed with carrying a genetic condition.

- Where individuals aren't told until adulthood, they may feel it has been kept from them and would have preferred to have been told earlier in their life.

9.6 WGS results and the impact on career choice

As explored in Chapter 4, participants discussed the implications of WGS results at newborn screening being used throughout life by employers to govern recruitment based on susceptibility to develop an illness later in life. In a counter argument to the concerns raised, some participants from the Young Adults group put a positive spin on this future possibility. They thought it may be useful to use WGS results to inform career paths based on what their bodies are best suited to.

> For example, if you had the genes for very good lungs, for example, you might possibly have a better chance of being a scuba diver. I know this is weird but just telling people to avoid the kinds of careers that would treat their bodies badly.
> I Participant, Young Adults Group

10. Considerations for the introduction of WGS

Key findings

In this chapter, we explore participants' considerations and expectations for both the pilot study for WGS for newborn screening and for any subsequent integration of the technology into NHS newborn screening. Participants' expectations centred on 5 key points for the pilot study , that it:

- involves a representative sample;
- takes place across the country in a range of health settings;
- is thoroughly planned;
- provides evidence of how it improves newborn screening and that it doesn't undermine the current high uptake of newborn screening;
- uses a transparent process and makes public the study's findings.

To lay strong foundations for a full roll out, **a long term, multifaceted communication, education and involvement programme is seen as essential**. This is to anticipate and respond to genetic-inspired conspiracy theories and to build trust.
For the national integration of WGS into newborn screening ten factors were emphasised:

- A comprehensive genetic database so that people from ethnic minority backgrounds are not disadvantaged by receiving more uncertain or less accurate diagnoses than the rest of the population and the certainty-level of diagnosis is improved.
- Public involvement in the governance, development and delivery of the programme.
- Legislation, regulation and other measures preventing WGS data use by insurance companies, marketing companies and employers.
- Data security is of the highest possible standard.
- NHS staff throughout the service are educated and trained on whole genome sequencing and genetics.
- There is sufficient funding and resources to deliver the programme across the country, avoiding a 'postcode lottery' and not compromising other health services.
- Practical and emotional support is available for those who receive a positive diagnosis.
- The conditions screened for at birth are treatable with medication or other therapies and interventions that will save lives or improve the child's health and wellbeing.
- The consent process recognises the nature of WGS data: its implications for the wider family and that the screening test may involve many more conditions than the current blood spot test.
- WGS data use beyond individual care is anonymised and used to improve understanding and treatment of conditions.

Participants see the introduction of whole genome sequencing into newborn screening as a major shift in the fundamental nature of healthcare, which needs to be planned and delivered with significant investment and care.

> Making this a successful screening programme will have a lot of different pieces working together as a well-oiled machine - ethical concerns, data privacy, cost, accuracy of tests and effect on the patient/parents. I Participant, Black & Minority Ethnic Group

10.1 Expectations for the pilot research study

Participants expressed their desire for a pilot research study on using WGS for newborn screening to be thoroughly planned and well executed. They want to avoid an unthought through pilot research study that could damage the existing high level of uptake of newborn screening and the potential benefits that could be realised through WGS. They expressed the expectation that the pilot study will:

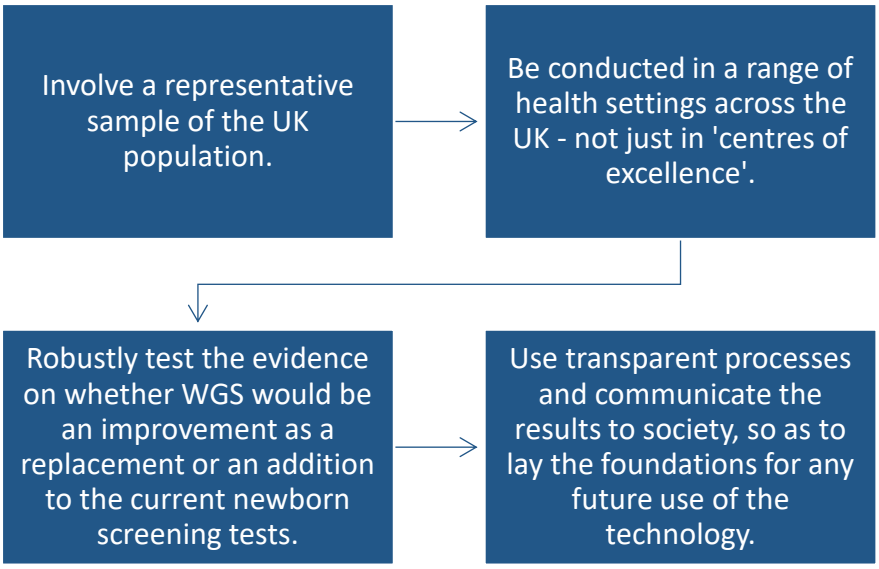


Figure 10.1: Expectations of the pilot research study

Participants in most groups talked about the lack of trust in mainstream medicine felt by some people from ethnic minority backgrounds. COVID-19 vaccine hesitancy was brought up and discussed as a legacy of historic ethnic minority mistreatment in the development of medical treatments. Again and again, participants underlined the importance of ensuring that the WGS pilot study involves a representative sample of the UK population. This would lead to a better understanding of how different people in society: ethnicity, age, sexuality etc respond to the screening process and how it is communicated and delivered. This learning, they expected, would be used to refine the national use of WGS.

> We would first have to see if there was a difference in uptake between different ethnicities, and make sure that any people who had concerns, especially if they were from minority groups, they had someone to talk to about it, but if we got whole genome sequencing data from newborns across a range of ethnicities, it could help fill in some of the data gaps that we have. I Participant, Northern England

When participants envisaged the pilot study, some talked about their fear that it would take place in a centre of excellence: an 'ivory tower' of health research, convenient for the great and the good of the health science world. But to truly test this new screening process, participants wanted to see the pilot take place in a range of health settings across the UK, including rural communities. For both the pilot and the roll out, participants hoped to see the whole of the UK involved, whilst recognising that health is a devolved matter. They thought this unified approach would help to

build trust and avoid arousing suspicions around why one part of the UK was 'going it alone.'

> If England agreed to this, what about Wales, Scotland, Ireland and if somebody in England wants to go to Scotland because they do have this and England doesn't, would it be a national programme? That would make a difference, wouldn't it? I Participant, Northern England

Participants believed the pilot is a vitally important step in the journey towards a future national roll out of WGS for newborn screening. They didn't want to see it rushed into. They feared that if the pilot was badly planned and an error in communication or delivery caused an outcry of some kind, that it would derail any prospect of a national introduction of WGS.

> My concern is that maybe because it's not been tried on such a wide scale, it's not been rolled out to the whole country, and no other country's ever done this, we don't know how efficient it's going to be when it's put into the NHS structure. Are they going to be able to keep up with demand? Is it going to be as quick as it needs to be to have a positive impact? I Participant, New & Expectant Parents Group

Concerns were also expressed, particularly in the Southern England group, that if WGS for newborns is introduced poorly, then it risks reducing the uptake of the current screening programme – and potentially causing significant health harms.

> I would think it would be a great shame if the trust that we currently have in the newborn screening is degraded by something that's not fully invested in and I think that one of the earlier presenters said something like 99% uptake in new born screening currently. This is such a great way in which we can start identifying diseases that have long term impacts that it would be a shame if that does degrade that current rate that we have. I Participant, Southern England

Participants thought the pilot study is important in building trust in WGS as part of screening. Participants expected that the pilot should have transparency designed into its delivery. They felt that clearly communicating the health benefits it has brought to families, such as early diagnosis and treatment that would not have been possible with the current screening programme, was vital in building faith in the roll out. There were also calls for any adverse learnings to be shared. Participants thought this was important to help in dispelling conspiracy theories that could sow suspicion around WGS.

> Making sure that there are clear review points and clear statistics that are coming out of it once it does get up and running that you can then use almost as marketing to people to show how successful it is or how successful it could be, what the trajectory should look like. I Participant, Young Adults Group

10.2 Foundations of knowledge

As much emphasis was given to preparing how to communicate WGS for newborn screening as to how to deliver the programme. Many participants thought that initial public reaction to whole genome sequencing at birth would be defined by suspicion. They expected people, as some of them did, to immediately think of 'designer babies', cloning or a government/commercial scheme for mass-DNA capture for population surveillance or control. They thought that if a health intervention such as the COVID-19 vaccination programme could face resistance from some parts of the population, whole genome sequencing would be a conspiracy theorist's dream.

> 'Oh, the government is trying to collect all of our DNA together, what are they going to do with it?' So I think that there'd have to be strategies for making sure that everything was very transparent, so that people could see every step of the process in regards to any legal changes, data protection, and the setup of the programme, as well. **I** Participant, Northern England

With this in mind, participants in all groups talked about the importance of laying several years' worth of strong foundations of knowledge about genetics and whole genome sequencing before considering a national roll out. The complexity of the issue of genetics merited much more than a few leaflets and posters. Participants thought it needs layers of information, built up over time in education, in the health service, in society as a whole.

10.2.1 Educating the parents of tomorrow

Given the expected timescale before a national roll out, many participants thought that education of school children – as potential parents of tomorrow - should start now. Participants believed that genetics will likely play a significant role in shaping the future of healthcare. Almost all talked about the importance of giving the upcoming generation information on whole genome sequencing – the science and the ethics. Participants said it was important that young people growing up into 'Generation Genome' are clear on both the benefits and limits of whole genome sequencing and to reduce the risk of negative associations with genetic differences. Participants were also hopeful that as children learn about WGS, they will share some of their knowledge with their parents and wider family.

> Education for children starts really young in primary schools, where we have science national curriculum, and the PSHE curriculum. Children learn about all kinds of genetics through Key Stage 2…So, I think further developing that would be useful if the programme was to go ahead, because there's no reason why children in Key Stage 3 can't learn about the whole genome sequencing and further information about genetics in school.
> **I** Participant, New & Expectant Parents Group

10.2.2 Building understanding throughout society

As we have seen in Chapter 3, most participants were aware of the national health screening programme in some form or another. However none of the participants had heard about the prospect of whole genome sequencing being used for newborn screening before joining the dialogue. Few said they had much or any knowledge of genetics or what whole genome

sequencing was. This led to many participants to call for a societal approach to building understanding of genetics, whole genome sequencing and its potential in NHS screening at newborn stage and for wider health benefits. This understanding was seen as important to build trust in WGS for newborn screening and to counter the suspicion that many thought its use might cause.

> Until I joined this group, I had absolutely no idea about this proposal or what it would mean. Which says to me there's not very much information in the public domain at the moment. I read several newspapers, I watch programmes on the television, but I really didn't know about all the detail that we've covered in just the few hours that we've been together. So, I think there needs to be an awful lot more information out there to help people to understand this and what it could mean. **I** Participant, Southern England

Participants put forward ideas on the key messages they thought would be important to communicate in the lead up to its use. These included messages on **how the introduction of WGS to newborn screening will work** and **the benefits of its introduction**:

Figure 10.2: Key messages to communicate

> I think they need to include that they will use the technology to help look for future cures and preventative treatments, and things like that. So, I think that should be included, that the research they do should have a wider use, that you're not just doing it for the sake of the fact that you can do it. You're actually doing it with the purpose of in the longer term finding treatments for incurable diseases, and trying to do it with purpose, that if you're

> going to have this database and this resource, the resource needs to be put to good use rather than stored in the system. I Participant, Wales & Northern Ireland

> It's that thing of not in a nationalistic, patriotic, ridiculous way, but in a way to say, 'We can be proud of this and we should be.' Promote it to everyone as a positive thing, not tuck it away on the back page of news. I Participants, Genetic Conditions Group

In terms of how society grows its understanding of genetics, participants saw this as a multi-year, multi-faceted endeavour, with government, media, industry, academia and civil society all playing a role. Participants talked about television programmes, from documentaries to EastEnders, media coverage and public information campaigns of the sort used to build awareness of measures to reduce the spread of COVID-19.

Many talked about the importance of transparency in helping to reduce the risk of media scepticism. There were fears that if the development of WGS for newborn screening was hidden from public view, this would lead to the media challenging it and so lead to public mistrust, particularly among people from ethnic minority backgrounds. This in turn could lead to lower uptake and therefore compromise the credibility and representativeness of the genetic data being used for diagnosis.

Some participants in the Genetic Conditions group talked about their hope that WGS for newborn screening would have support from all political parties to put to rest fears that it could be underfunded or stopped in the future.

As well as communicating and educating around the purpose and benefits of WGS for newborn screening, participants also wanted to see the opportunity taken to build a greater understanding in society about genetics. This greater understanding was focused on two aspects:

1. Genetics and the role it plays in our health alongside other factors such as the environment, behaviour, social and economic factors.
2. Genetic conditions: that they are not characterised as ‘diseases’ to be eradicated, but as conditions that can be managed with life-improving treatments.

> The language used when finding these conditions. It may be, to a clinician, officially it's called a problem or a disease, but to a parent it might not be. And yesterday there was a speaker who said autism is a disease. It's not, is it? It's a condition. I Participant, Genetic Conditions Group

The argument presented by many participants was, that if genetics is going to play a significant role in the way the National Health Service is delivered, then society should have a stronger understanding of it. This would help to reduce the risk of society overemphasising the role of genetics in health and the risk of discrimination towards those with genetic conditions.

10.3 Expectations for the development and delivery of WGS into NHS newborn screening programme

To give a newborn screening programme that introduces the technology of WGS the best chance of success, participants believed that the following aspects were essential. We explore each in more detail in the pages that follow:

- A comprehensive genetic database so that people from ethnic minority backgrounds are not disadvantaged by receiving more uncertain or less accurate diagnoses than the rest of the population and the accuracy of diagnosis as a whole is improved.
- Public involvement in governance around the development and delivery of the programme.
- Future-proofed legislation and regulation and other measures that prevent WGS data being used by insurance companies, marketing companies and employers.
- Data security is of the highest possible standard.
- NHS staff throughout the service are educated and trained on whole genome sequencing and genetics in health.
- There is sufficient funding and resources to deliver the programme across the country, no 'postcode lottery' and no compromise on other important health services.
- Genetic counselling and mental health assistance are available for those who receive a confirmed diagnosis to help with both an understanding of the health condition and to provide emotional and psychological support.
- The conditions screened for at birth are treatable with medication or other therapies and there are interventions available that will save lives or improve the child's health and wellbeing.
- The consent process recognises the nature of WGS, including its implications for the wider family and that the screening test may involve many more conditions than the current blood spot test.
- WGS data use for research: the data is anonymised and used in research to deliver improved treatment and care and accuracy of diagnosis.

10.3.1 Comprehensive genetic database

During the dialogue, participants heard about how for some conditions and for some populations, diagnosis from genetic tests can be uncertain. They heard that people from ethnic minority backgrounds received less certain diagnosis than those of Northern European backgrounds for conditions such as breast cancer. They also heard about the thousands of genetic variants related to cystic fibrosis and that whilst there has been recent breakthroughs in developing treatments for the most common variants, much uncertainty still exists around those that are less prevalent.

> If White children are being diagnosed with conditions and getting earlier treatment, but children who are not White are not being diagnosed, then they might be at a disadvantage because they're not getting access to these, maybe more novel, or earlier interventions. | Participant, Scotland

With this in mind, participants talked about the importance of building a comprehensive genetic database to help improve scientific knowledge and diagnosis. To do this, participants felt it was vital to build trust in the programme among ethnic minorities so that take up will be at the same level as the general population. Some also wanted to see global collaboration on the use of WGS to create a more diverse data pool.

> Participant 1: Asking other countries to join us. Asking other countries to contribute financially. Look what we've achieved with the COVID vaccines. We've been amazing as a world. I think that if we could get other countries involved.
>
> Participant 2: That would also help with diversity because at the beginning they were talking about the fact that at the moment you can't get enough of a varied population, but this means if you are going out to different countries, at least you are trying to get as much information as you can. | Participants, Wales & Northern Ireland

Participants compared such global collaboration with the efforts to develop COVID-19 vaccines. They had seen how pharmaceutical companies, scientists, academia and international organisations had worked together and drew inspiration from this. Within these discussions, some participants raised concerns about certain countries, notably China and Russia, and from a commercial perspective, the USA, having access to genetic data.

10.3.2 Public involvement in governance and design

Involving the public in the design, delivery and oversight of the programme was seen as essential by many participants. They saw this dialogue as the starting point for much wider and systemic involvement of UK citizens. During the workshops, participants met members of the 100,000 Genomes Project Participant Panel. Some discussed how this model should be considered as one of the ways to involve the public in the governance of the WGS newborn programme. Participants also talked about running ongoing research, both through qualitative discussion and surveys, to understand public attitudes to the programme and how its introduced.

> What's important to keep in mind is listening. Which is what you guys are doing now, which I think is really valuable and I think that everyone wants to feel recognised and respected by their doctors and medical professionals and so just to keep listening. | Participant, Black, Asian & Minority Ethnic Group

In the preparations for the pilot study participants believed that citizens could be involved in discussions on issues such as:

- What conditions are screened for and how the decisions on that are communicated

- Who should be involved in the pilot process to ensure the programme tests for equity, a reflective sample and for the potential for discrimination
- Where the pilot study will be conducted

10.3.3 Future-proofed legislation, regulation and other measures to guard against use by insurers, employers, marketers and police

As discussed in Chapter 4, participants across all dialogue groups were strongly opposed to WGS data being used by insurance companies, employers, marketing companies and the police. There were calls for proactive legislation and regulation to prevent harm, rather than only bringing in measures reactively, following a scandal and public outcry.

> I was just thinking about how often stuff happens, like developments of technology happens and then, there's some harm caused and then, there's a scramble to, or people advocate for new policies and regulations to be put in place. But I feel like, for this, there should try and be that beforehand, so that it's not like a scramble. | Participant, Black, Asian & Minority Ethnic Group

Many participants made a distinction between data use by commercial companies of this sort vs data use for health research by pharmaceutical companies, health technologies etc. They expected WGS data to be kept as private as possible and only used to generate benefits to health.

Some participants were worried about the potential for a future privatisation of their WGS data. They talked about possible changes in government policy in years to come and the increasing use of private companies in the delivery of NHS service services. They felt these could lead to commercial uses of the data that could benefit industry but be detrimental to the public. To guard against this, participants wanted to see legislation, regulation and other measures such as politically independent governance introduced or updated to factor in WGS data.

> There would have to be a question of whether we make laws or regulations to really control the spread of that data, and whether we would put in laws that would prevent future governments or administrations from changing those privacy laws or data protections. It's all good and well saying now it would never be shared with this person or that person, but 10 years down the line, are there protections to prevent that from being changed?
> | Participant, Northern England

10.3.4 Data security is of the highest possible standard

Whole genome sequence data was seen by participants as 'the essence of you'. They thought its protection was of the highest importance: to prevent data loss through hacking or human error and to build trust in the programme. Some participants talked about data breaches, such as the 2017 ransomware attack on the NHS, drawing the public's attention to the potential vulnerability of health data. Others raised the fact that data on individuals is being collected in numerous ways and that this could be combined with WGS data to create an unprecedented profile that could be used in dystopian ways.

> People have little identities everywhere, and I guess this just adds to your profile or your data being available elsewhere now, along with the hundreds of thousands of apps and websites that may have your data. This just adds to that. **|** Participant, New & Expectant Parents Group

Reassurance was sought that government would invest the funds and resource to protect this most personal of data using world-leading data security measures.

> It has to be assured that it is secure, especially when it's young children, as well, it comes back to that consent thing. If you haven't given your consent, as a child, you don't have the capacity to, then it's even more important that that is stored securely. **|** Participant, New & Expectant Parents Group

10.3.5 Sufficient funding and resource to deliver the programme in the context of the wider NHS

> It's got to be taken seriously, it's got to be funded properly. If we're going to do it, I think we don't want to…half arse it. I think it's got to be properly driven forward and really invested in to maximise it. **|** Participant, Southern England

This participant succinctly summarised a sentiment raised in all the dialogue groups. That the introduction of WGS for newborn screening is not to be done half-heartedly. Proper funding would mean having health and care staff trained in genetics and WGS, having sufficient resource and high quality technology to cope with demand in a timely fashion and investing in world class data security.

> Just as long as we have technology, it needs to be where it needs to be to get that information out efficiently and give people the information they need as and when they need it. **|** Participant, Southern England

But we heard that participants also thought it was important for the public to understand how a programme of this nature is being funded, without risking downgrading other much needed parts of the health service.

> It must be cost-effective for the NHS. We can't just put everything into that one, knowing or not knowing if it's going to work or not and forget about all the other research, like cancer, heart disease, Alzheimer's, things like that. We've still got to keep other things running in the country. **|** Participant, Black, Asian & Minority Ethnic Group

10.3.6 NHS staff are trained and educated in genetics and WGS

In the same way that participants took a long term view on how society needs to understand the use of genetics in healthcare, many also thought this long term approach was essential to the National Health Service. Some characterised this as a ten or more year effort to ensure that all staff across the patient pathway are knowledgeable and consistent in talking to patients about the nature of genetic data: what it can and what it can't tell us about human health.

A participant in the Black, Asian & Minority Ethnic group spoke of her experience of ante-natal screening to illustrate how doubt could be seeded in the value of WGS for newborn screening (discussion snapshot 10):

Discussion snapshot 10 – it's easy to sow seeds of doubt:

You're always going to get some that will toe the company line and tell you very clearly 'I wouldn't do it, but I've got to tell you.' I remember this just in my own pregnancy around Down's Syndrome screening, my midwife was very, rightly or wrongly, very negative around it and that shaped my negative view around 'do I want to get it done or do I not'. So, I think they are the key people and a lot of midwives are maybe of that older generation, that really don't understand. I mean, I'm not being disrespectful because they do an amazing job, but I think there is, maybe, a generational or education gap. They're amazing midwives, but do they understand genome sequencing and will they have the time to be trained on it?
I Participant, Black, Asian & Minority Ethnic Group

As well as ensuring health service staff such as GPs and particularly midwives and health visitors are trained and enabled to integrate genetic knowledge and experience into their practice, participants wanted to see preparation for introducing a new generation of skills into the NHS. Participants were concerned that a lack of data analysis skills could lead to delays in receiving a diagnosis, so causing a vicious circle of anxiety and triggering lower uptake in the programme. The training and recruitment of data scientists was seen as vital to ensuring that diagnoses are accurate and delivered to families quickly. Participants in Scotland talked about working with universities to ensure that courses are available in data analytics and that the NHS has a plan for attracting these analysts to work in the public health sector.

10.3.7 Counselling is available: addressing both mental and physical health and the wider family

Support and genetic counselling being available when a positive diagnosis is made was, alongside data security, consent and adequate funding, of the highest priority for participants. Given the intense emotions around childbirth, its life changing nature and all the hopes and dreams invested in a newborn, there was a strong desire to see counselling that not only explained the condition and its treatments but that also gave emotional support. The mental health of parents whose child is given a genetic diagnosis, particularly those who might be vulnerable, such as younger mothers or parents with disabilities, was important to address in the counselling support provided.

> I think young mums, people who get postnatal depression, and people who have mental illnesses, depression, anxiety, I think however this comes out, they need to make sure that all of those people are looked after, taken care of, they have something in place to support them, because if those people fall down as a result of this that will be very widely publicised and that could be a knock-on negative effect to the scheme in itself.
> | Participant, Southern England

Participants talked about the importance of how counselling is delivered. What they didn't want to see was a diagnosis given by a doctor, followed by being handed a leaflet with a helpline number.

They hoped that parents would be given the time they needed, both during individual sessions and as an open ended service, rather than just a set number of appointments.

> You're speaking to a doctor and at that particular moment in time, it shouldn't just be a doctor. You should have therapists, there should be the whole support system that should follow it immediately. Because your life has changed in the blinking of an eye and you need all of that support. | Participant, Scotland

Participants envisaged counselling as a holistic service, provided not just by the NHS. In the Genetic Conditions group particularly, participants thought that health condition charities and parent networks could be co-providers of such support. This could also help to manage the cost and resources to deliver this service.

> I am a firm believer that counselling and emotional support are most effective from an empathetic standpoint from someone who actually has experienced the very feelings and emotional turmoil that a patient's family is feeling. On completion of the genetic counselling ongoing support and follow-up could be carried out by that particular group. e.g. cystic fibrosis group. This could also ideally relieve some pressure or financial burdens the extra counselling would entail. | Participant, Genetic Conditions Group

> It's not just the NHS doing it and this is what we've found, to try and bring counselling, charities, to try and bring everybody together on this so that everybody works together, and what the NHS can't offer, somebody else might be able to. But if everyone's brought into it, it will be easier for a family to get access to that. Participant, Black, Asian & Minority Ethnic Group

Recognising that parents would have different needs for the type of information and support after a diagnosis meant that several participants thought that a tailored approach to counselling was an important consideration. Counselling was also seen as helpful in reducing the risk of parents labelling their child and being overly cautious in ways that limited its quality of life – even if with the best of intentions.

Because a genetic diagnosis in a newborn could have implications for the wider family, beyond the parents, many groups raised the need for counselling and information support services being available to them. They thought this level of demand should be factored into planning the resources available.

10.3.8 Conditions screened for at birth are treatable/actionable

Other chapters in this report have explored the views expressed by participants about the kinds of conditions and information that WGS screening at birth should include and how WGS could be used as a resource throughout life.

In the Genetic Conditions and Black, Asian & Minority Ethnic group we heard a wider debate than in other groups about which conditions to screen for. Some participants in those groups wanted to see a wider range of conditions screened for, beyond those that are immediately treatable. This

was often driven by the fear that limiting what's screened for could hinder people taking preventative measures or being aware of innovative treatments.

> I'm just wary of picking on certain illnesses when they are doing this test. If it can find out as many illnesses as it can, I feel like this should just record all that and not just pick on certain things just because the NHS can't fund it or because it doesn't have a treatment. Hopefully with innovation there could be a treatment for illness and what happens to the person who doesn't know that she or he has this illness and I feel like they shouldn't just pick and choose popular illnesses. **|** Participant, Genetic Conditions Group

> I think you should still test for a condition you can't treat immediately to monitor the condition and to plan for the future. **|** Participant, Black, Asian & Minority Ethnic Group

However most participants believed there should be a definitive list of conditions and that they should all be conditions that impact the infant from early childhood and for which there are treatments or therapies. Many participants also wished to see screening for conditions such as familial hypercholesterolaemia where the earliest medical intervention may not be for several years for the child. They saw the diagnosis and treatment of a parent, so preventing a potential early death, as a direct benefit for the infant.

> One thing that we keep picking up on in not just this group, the whole wider group is that we're only testing for things that are treatable I think because the concern could be, I mean lots of people I'm sure have very little understanding of how your DNA information all works. So, the idea that you might be being told everything you could ever possibly get in life would be a terrifying concept. Just making it really clear that it's only what's treatable. **|** Participant, Southern England

Related to this, participants talked about 'Dr Google' searches on a health condition often yielding worst case scenarios and information of dubious quality. Ensuring that NHS websites provided clear and easy to access information on the conditions covered by the programme was brought up by several participants.

> With regards to information, maybe also making sure all the conditions that we are testing for are adequately signposted and have the correct level of information on the NHS website. That way those that do get found to have certain conditions or have a higher likelihood of having the conditions have strong information on procedures and treatments going forward, so that they can research that straight from the NHS. **|** Participant, Southern England

10.3.9 A consent process in keeping with the nature of WGS

Those participants who were parents talked about their experience of the heel prick blood spot test. For those who could remember anything about it, most felt they were told very little and that it was just part of a newborn health check process. Many participants felt that the nature of WGS was far more complex than the blood spot test and therefore merited a different approach to consent.

Building on the call for societal understanding of genetics in healthcare, participants thought it was essential for parents to be informed of WGS during the early stages of their pregnancy. From the moment they spoke to their GP about their pregnancy, through screening and scan appointments with midwives there was a desire to see information shared with parents about what WGS is, the kinds of conditions that are screened for and the kinds of diagnosis and level of certainty that could be returned. This early and repeated sharing of information and opportunities to discuss would avoid the situation of the WGS test being performed in the blurry, early days of parenthood without parents knowing what the test was and what it was for.

> Participant 1: Your initial scan check-ups, why don't you give the information then? As you're doing it, the nurse can be talking away, telling you about this new thing.
>
> Participant 2: It's probably a bit less scary if you give people a little bit information at a time as you're going through your scans or whatever you've got, your however many week scans and you get a little bit of information at the time, like you say, rather than being bombarded when you've also just had a baby. **I** Participants, Southern England

Participants in the new and expectant parents group were the closest to the newborn screening process amongst dialogue participants. They gave detailed and considered views on what should be included in the consent process vs what is part of the diagnostic information sharing. They wanted the consent process to focus on what is tested for, when results would come back and that clinicians would share detailed information on the conditions if a diagnosis is made.

> I think it would be useful to know what's being tested for. What the test involves, the timeline of how long it will take to take the test and get the results. I don't know if it's as important initially to tell them what could go wrong. I don't think it's necessary to say, 'If your child gets this then this is what's going to happen.' I think it's just important at the beginning to know what you're getting involved in, being really clear, understanding what is being tested for and ensuring that if something did come back saying that you had a chance of developing a condition or already having something, then being given that information about what the next steps are. **I** Participant, New and Expectant Parents

Because a diagnosis through the WGS newborn screening could deliver information of interest to wider family members, participants wanted the consent process to consider how to respect family wishes to be informed or not about a genetic condition and to enable anonymity. A participant in the Black, Asian & Minority Ethnic group suggested that a COVID-19 style track and trace approach could be used.

> Just carrying on with the idea of anonymity, maybe something that would be good to be included is a way to share a carrier status, or a result anonymously. Because sometimes that can cause rifts within families, with maybe a stigma about a certain disorder, or something. If there's a way to share that anonymously. It would maybe not cause as many possible rifts in families…in the same way we get alerts about COVID, it's like, 'Oh, you've been near someone.' It's not specific. **I** Participant, New & Expectant Parents Group

The potential to use WGS data as a resource throughout life was welcomed by most participants, on the proviso that it is underpinned by a dynamic consent process. There were no fixed views on the age at which a young person should be given the right to make a decision on whether to keep their WGS on record for their own health benefit or for wider research. However participants wanted to see the right to reaffirm consent or opt out designed into an ongoing consent process and that assurance could be given that the individual's request would be respected.

> I think what I was trying to say was if you had said yes for research and then later on in life you were like, 'No, I don't want to be part of this anymore.' How can you be 100% certain that any data that they may have about you, isn't used? How can you be sure that it's destroyed, or maybe they don't destroy it, I don't know. | Participant, Wales & Northern Ireland

Some participants thought that this right to remove your data from the system would also be helpful in combating conspiracy theorists.

> I think there could be a very good argument against the people who are saying the government just want our data, they're just looking for information on us, they just want to track us, blah, blah, blah. All of these conspiracy things. If you can just tell them, 'You can withdraw your consent for the government to have your data, you can just tell them that here is X, Y, Z way to do it,' that will put those people to bed hopefully. I Participant, Young Adults Group

10.3.10 WGS data use for research: for the public benefit

Throughout the dialogue many participants talked about the importance of making good and appropriate use of WGS in research. This is to enable greater understanding of health conditions, particularly those currently seen as rare and under-explored and to deliver improved opportunities for treatment and care. The use of data in this way, needs to be accompanied by effective and dynamic consent processes, allowing the child to consent when of age. Participants said it also needs to be supported by a more transparent approach to the use of health data for research. Some said they wanted to be able to find out easily how their data had been used in research.

10.4 Given the considerations – what should WGS for newborn screening look like?

Participants throughout the dialogue gave clear indications of what a programme of WGS for newborn screening might look like once carefully and thoughtfully prepared for, including in the pilot study. These are summarised in figure 10.3.

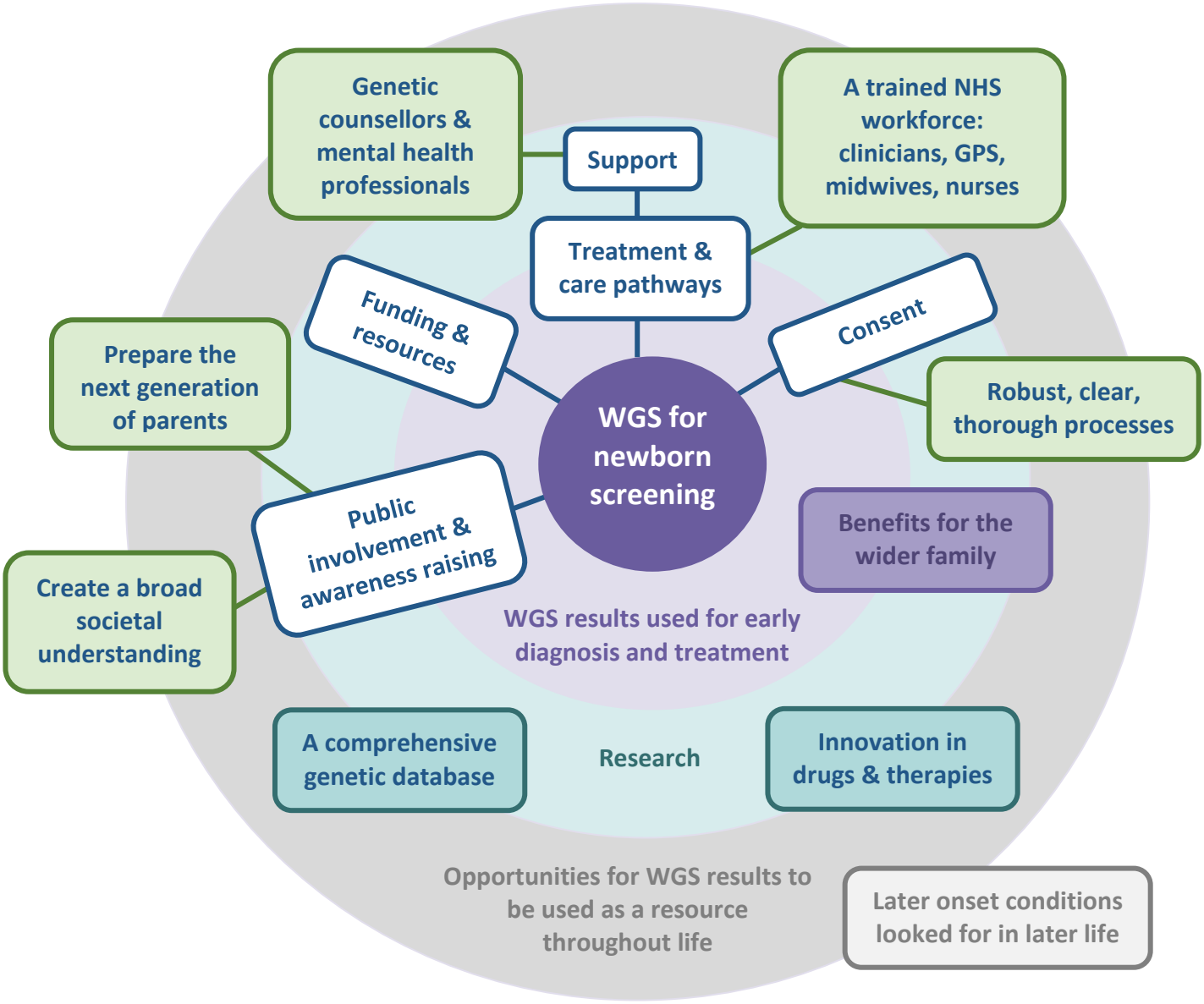


Figure 10.3: What WGS for newborn screening could look like

11. Acknowledgements

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Many thanks too to the specialist stakeholders who agreed to be interviewed in the design phase of the project. The full list of interviewees who contributed to the shaping of this public dialogue are:

Name	Role	Organisation
Vivienne Parry	Head of Engagement	Genomics England
Fiona Maleady-Crowe	Head of Ethics	Genomics England
Carmel Lloyd	Head of Education and Learning	Royal College of Midwives
Helen Mactier	President	BAPM
Sarah Coupland	Vice President for Communications	RCPath
Helen Firth	Consultant Clinical Geneticist	Joint Committee on Genomics in Medicine
Lorna Allen	PPI Lead	Cystic Fibrosis Trust
Will Pender	Senior Policy Manager	Duchenne UK
Alex Johnson	CEO	Duchenne UK
Tom Shakespeare	Professor of Disability Research	LSHTM
Dena Davis	Presidential Endowed Chair in Health	Lehigh University, US
Anne Mackie	Director of Screening for Public Health England	UK National Screening Committee
Christine Patch	Clinical Lead for Genetic Counselling	Genomics England
Martin Murphy	CEO	Syncona
Ron Zimmern	Chairman of the Foundation's Board of Trustees	PHG Foundation
Mavis Machirori	Senior Researcher; previously Research Associate, Policy, Ethics and Life Sciences (PEALS) Research Centre	Ada Lovelace Institute; previously University of Newcastle
Anneke Lucassen	Professor of Clinical Genetics, Honorary Consultant in Clinical Genetics	Wessex Clinical Genetics Service, Clinical Ethics and Law Unit, Faculty of Medicine, University of Southampton

The Oversight Group, chaired by Anne Slowther, were exceptionally generous with their time and in applying their expertise, giving guidance, challenge and support at each step in the process.

Name	Role	Organisation
Anne Slowther	Chair of the Oversight Group Professor of Clinical Ethics	Warwick Medical School, University of Warwick
Felicity Boardman	Assistant Professor, Medicine, Ethics and Society	University of Warwick
Jim Bonham	Laboratory Lead, Newborn Blood Spot Programme	Public Health England
Phil Booth	Coordinator	medConfidential
David Elliman	Clinical Lead for NHS Newborn Infant Physical Examination Programme and NHS Newborn Blood Spot Screening Programme	Public Health England
Olga Ferguson	Programme Clinical Advisor, Sickle Cell and Thalassaemia Screening Programme	Public Health England
Kerry Leeson-Beevers	Project Lead	Breaking Down Barriers
Mavis Machirori	Senior Researcher; previously Research Associate, Policy, Ethics and Life Sciences (PEALS) Research Centre	Ada Lovelace Institute; previously University of Newcastle
Fiona Maleady-Crowe	Head of Ethics	Genomics England
Rebecca Middleton	Vice-chair	Genomics England Participant Panel
Christine Patch	Clinical Lead for Genetic Counselling	Genomics England
Sandy Starr	Deputy Director	Progress Educational Trust
Bob Steele	Chair	UK National Screening Committee
Jayne Spink	CEO	Genetic Alliance
Stuart Moat	Consultant Clinical Biochemist; Director	Wales Newborn Screening Laboratory
Anne Mackie	Head of Screening	Public Health England
Mark Bale	Head of Science Partnerships	Genomics England
Joanne Harcombe	National Lead for Stakeholder Information and Professional Education and Training	NHS Screening Programmes
Anneke Lucassen	Professor of Clinical Genetics, Honorary Consultant in Clinical Genetics	Wessex Clinical Genetics Service, Clinical Ethics and Law Unit, Faculty of Medicine, University of Southampton

Alexandra Pickard	Policy and Strategy Lead, Genomics Unit	NHS England
Gail Walshe	Director of Participation and Regional Development	Contact

Throughout the dialogue evidence and information was given to participants in case studies and presentations. This range of perspectives, and the opportunity for participants to discuss them, is an essential part of a Sciencewise dialogue. We are very grateful to the specialists listed who gave their time and expertise to the process.

Name	Role	Organisation
Bob Steele	Chair	UK National Screening Committee
Simon Wilde	Engagement Director	Genomics England
Catherine Joynson	Ethics & Stakeholder Engagement Consultant	Public Health England Screening
Vivienne Parry	Head of Engagement	Genomics England
Angus Clarke	Clinical Geneticist: Professor in the Division of Cancer & Genetics	All Wales Medical Genomics Service
Mark Caulfield	Chief Scientist	Genomics England
Jillian Hastings Ward	Panel Chair	100,000 Genomes Project Participant Panel
Rebecca Middleton	Vice Chair	100,000 Genomes Project Participant Panel
Mark Bale	Head of Science Partnerships	Genomics England
Frances Flinter	Emeritus Professor of Clinical Genetics	Guy's & St Thomas' NHS Foundation Trust
Dave McCormick	Participant Panel Member	100,000 Genomes Project Participant Panel
Jim Bonham	Laboratory Lead, Newborn Blood Spot Programme	Public Health England
Alison Fox	Participant Panel Member	100,000 Genomes Project Participant Panel
Kevin Southern	Professor of Child Health	University of Liverpool
Alex Clarke	Member of Patient Advisory Board	Duchenne UK
Sean James	Genomics Ambassador	West Midlands Genomic Medicine Centre
Paula Sommer	Head of Research	Cystic Fibrosis Trust
Stuart Moat	Consultant Clinical Biochemist; Director	Wales Newborn Screening Laboratory
Lorna Allen	PPI Lead	Cystic Fibrosis Trust
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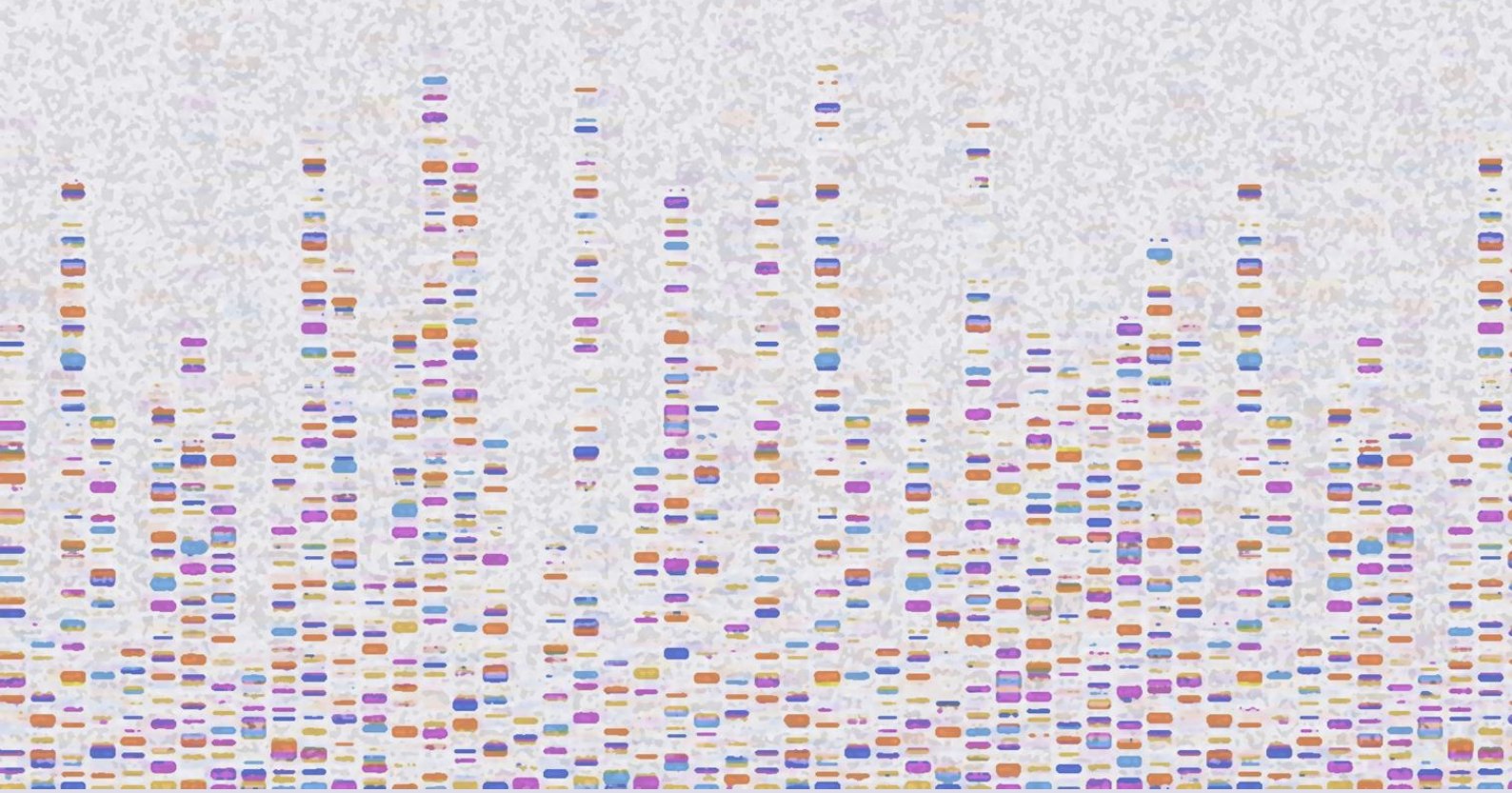
Phil Booth	Coordinator	medConfidential
Mavis Machirori	Senior Researcher; previously Research Associate, Policy, Ethics and Life Sciences (PEALS) Research Centre	Ada Lovelace Institute; previously University of Newcastle

HVM actively seeks to work on projects where close co-design with the commissioning partners and project funders is possible. This project was a delight to work on with the Project Team's expertise, guidance and calm approach in such an extraordinary year. As such we are grateful to have had the opportunity to work in close collaboration with Catherine Joynson, UK National Screening Committee; Simon Wilde, Genomics England; Suzannah Lansdell and Diane Beddoes, Sciencewise; Philippa Lang, UK Research and Innovation; and Anna MacGillivray from Ursus Consulting who has provided invaluable independent evaluation to the process.



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