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# Understanding experiences of recruiting for, and participating in, genomics research and service transformation: the 100,000 Genomes Project, 2015-17

## Final report

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## Final report

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## Acronyms and abbreviations

**BHSCT** – Belfast Health and Social Care Trust

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**BRCA1** – a human tumour suppressor gene involved in susceptibility to breast cancer

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**CT** – computed tomography

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**DH** – Department of Health

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**DoH NI** – Northern Ireland Department of Health

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**DNA** – Deoxyribonucleic Acid

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**EDS** – Ehlers Danlos syndrome

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**GeCIP** – Genomics England Clinical Interpretation Partnership

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**GMC** – Genomic Medicine Centre

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**HEE** – Health Education England

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**HERG** – Health Experiences Research Group

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**HEXI** – Health Experiences Institute

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**LSHTM** – London School of Hygiene and Tropical Medicine

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**MRC** – Medical Research Council

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**NGS** – Next generation sequencing

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**NHS** – National Health Service

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**NHSE** – NHS England

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**NIGMC** – Northern Ireland Genomic Medicine Centre

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**PHE** – Public Health England

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**PM** – personalised medicine

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**PIRU** – Policy Innovation and Evaluation Research Unit

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**WGS** – Whole Genome Sequencing

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## Executive summary

## Background

The aim of the 100,000 Genomes Project (the 'Project') announced in December 2012 was to produce new capability and capacity for genomic medicine in order eventually to be able to transform a wide range of clinical services in the NHS in England. It also aimed to produce new capability for clinical genomics research and establish infrastructure for the protection and analysis of clinical and genomic data. The principal objective of the Project was to sequence 100,000 genomes from patients with cancers, rare disorders and infectious disease, and to link the sequence data to a standardised, extensible account of diagnosis, treatment and outcomes. This goal was achieved in December 2018, marking the end of data collection.

The Policy Innovation Research Unit (PIRU) at London School of Hygiene and Tropical Medicine (LSHTM) was initially approached in 2014 by the then Department of Health to conduct a qualitative study exploring participant and health care staff experiences of taking part in, and recruiting for, the 100,000 Genomes Project, as well as the public's perceptions of genomic research generally. Data collection for the current study took place between late 2015 and late 2017.

The aims of the study were to:

- Understand the motivation of people who agreed to take part in the 100,000 Genomes Project; their experiences of receiving information, giving consent and taking part; their attitudes to data sharing, governance and confidentiality; and their views about feedback and use of their Project data for research and clinical care.
- Learn about the experiences of clinicians who asked people to take part in the Project.
- Explore the understanding and perceptions of members of the public of genomic research generally.
- To explore the understanding and perceptions of the non-specialist NHS workforce of genomic research generally and of the 100,000 Genomes Project in particular, and to identify potential training needs related to any roll-out of genomic medicine services within the NHS.
- To draw on the above, in order to make suggestions for improvement, thereby improving the likelihood of the Project achieving its goals.

## Methods

This qualitative study generated data via one-to-one interviews with 100,000 Genomes Project participants with rare diseases and common cancers (n= 32), December 2015-September 2017; one-to-one interviews with 100,000 Genomes Project health professionals (n=26), December 2015-June 2017; focus groups with members of the general public (n=9, involving 5-8 participants), October 2015-October 2017; and focus groups with non-specialist healthcare staff (n=4, involving 6-8 participants), January-October 2017.

## Findings

### Project participants

The cancer and rare disease groups were distinctly different in their prior experiences and motivation in taking part in the Project. The latter commonly had longstanding experience of, and a clear interest to discover more about, their conditions. Cancer participants were mostly at an early stage in their illness and their focus was very much on their immediate treatment rather than what the Project could potentially help identify relevant to their treatment. Cancer patients typically had little time between



being invited to take part and their surgery when the Project sample would be taken. There was general concern about the lack of communication from Genomics England once samples had been donated. Participants had not received results at the time of interview and there was frustration from some about this delay. Not surprisingly, participants did not differentiate between Genomics England and the NHS Genomic Medicine Centres (GMCs) which were responsible for all patient contact, guided by NHS England (NHSE) under the terms of their contracts with NHSE.

Despite these concerns, there was a markedly positive attitude towards taking part in the Project and some participants described the pride they felt in being part of potentially transformative work. While some direct benefits to participants were mentioned, such as additional screening or the possibility of finding out whether a rare disease was inherited, there was a strong sense of wanting to contribute to medical advances and of wanting to 'give back' to the NHS. Expressed trust in the NHS and in Genomics England was high, and meant that most participants did not feel the need to be told in great detail about the Project. They generally trusted that their personal data would remain confidential and that their samples would be appropriately used. Reasons for data sharing, including with commercial bodies, were well understood, though sharing with commercial bodies raised more concerns about privacy and exploitation than sharing with public, non-profit users. Two ethical concerns were raised: the potential for technological developments based on genomics to lead to the termination of fetuses with certain genetic abnormalities; and receiving results related to familial genetic risk and what this might mean for wider family members who had not consented to finding out this information. It has to be recognised, however, that these findings derive from interviews with people who had been approached and chosen to participate in the Project. The views of non-participants might have been very different.

### **Members of the public**

There was considerable enthusiasm for the Project among the wider public. Most focus group participants began with little or no knowledge of genomic research or the Project. They raised more concerns than were raised in the interviews with Project participants. These were largely about data protection and ownership of the data more generally. Some people, particularly from black and minority ethnic groups, expressed greater caution about privacy and control over the uses to which their data might be put. Genomics England has subsequently undertaken in-depth work to understand the views of people and patients from BAME backgrounds (see: [www.genomicsengland.co.uk/about-genomics-england/how-we-work/patient-and-public-involvement](http://www.genomicsengland.co.uk/about-genomics-england/how-we-work/patient-and-public-involvement)).

### **Health professionals involved in implementing the Project**

The Project was regarded by all as presenting significant opportunities and challenges, though these were often experienced and described differently by those in the Genetic Medicine Centres (GMCs) and those at the centre (in NHS England and Genomics England). The endeavour, which was the first attempt to transform a healthcare system using genomics, was described positively and seen to be exciting by many staff. Staff working at the centre expressed concern about the pressure to implement the Project quickly, but were in a better position than local staff to manage these pressures and remained more excited about the prospects for the Project than local staff. By contrast, local staff described more negative experiences about the implementation process, including lack of consultation, poor communication, the volume of additional work in an already overstretched NHS, unrealistic expectations in terms of meeting recruitment targets, frequently changing requirements and delays, and the challenge of setting up testing and feedback mechanisms for patients.



The balance between research and service transformation was understood but caused some tensions and concerns that the buy-in of the academic community might be lost. Local staff echoed participants' frustrations about delays in their ability to communicate results. While there was recognition of the scientific potential of genomic research, there was a sense of uncertainty among local staff at what this might mean in practice for patients.

### **Non-specialist NHS clinical staff**

These staff had very low awareness of the Project and knowledge about whole genome sequencing (WGS). There were positive views about WGS' potential but also worries that it might lead to unnecessary treatment, with uncertain benefit for individual patients. Generally, these staff were more sceptical about the potential of genomic medicine than those directly involved. The resource and training implications for an already-stretched NHS were a source of anxiety, with a fear that access to genomic services in future might be unequal, favouring those who could pay outside the NHS.

## **Conclusions**

Overall, there was support for, and trust in, the 100,000 Genomes Project from participants, members of the public, and specialist and non-specialist NHS staff. However, the roll-out of genomic medicine in the NHS in future will depend on more effective communication with, and engagement of, patients and a wide range of non-specialist NHS staff than was apparent in the period of the study (2015-17). Since the data were collected for this study, Genomics England has attempted to address these concerns by instituting a 'Track my sample' process which was launched in December 2017 after data collection in the current study had finished. This was followed by a regular participant newsletter and more information on the Project's website focused on the needs of participants. In addition, towards the end of the Project, its contribution to the clinical care of participants began to become apparent. Currently the Project reports providing a diagnosis in 20-25% of its rare diseases cases and in 50% of cancer cases, the data are judged as containing the potential for a therapy or a clinical trial ([www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project](http://www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project) accessed 3 February 2020).

In the case of non-specialist staff, there remains a need to communicate the proof of the value of genomics to a dispersed clinical community which has many other competing interests and pressures. Given the progress that the Project has made, for instance, in providing diagnoses in cases of rare diseases, it should be possible to craft more positive messages for communication to the wider NHS workforce. There are other opportunities to learn from the Project for the future, in particular, about the need for more engagement from the very start of planning with those who will be delivering genomic medicine across the NHS to ensure more realistic targets and milestones.



## Chapter 1: Introduction

### 1.1 Background

In the last decade, the development of next generation sequencing (NGS) technologies has resulted in a substantial reduction in the cost and time needed to sequence an entire human genome. Many research projects taking place across the world now incorporate whole-genome or whole-exome sequencing, and qualitative research on people's attitudes to and experiences of taking part in such studies is beginning to emerge. However, we know little about people's perceptions of large population level studies such as the English 100,000 Genomes Project ([www.genomicsengland.co.uk](http://www.genomicsengland.co.uk)) which are still comparatively rare as a patient participation opportunity.

Many of the issues discussed in the academic literature in relation to participation in genomic research are similar to those discussed in relation to participation in 'traditional' medical research. Informed consent, motivations for participation and concerns related to participant data ownership and storage dominate. These issues are accompanied by discussions of the return of secondary or 'incidental' findings to participants and their concerns and/or preferences related to these processes, discussions which are specific to genomic research.

Informed consent and ownership of donated material are habitual ethical concerns in medical research involving the provision of human samples. In the bioethics and social science literature, it is often assumed that people are suspicious of, and resistant to, using human tissue in medical research which Dixon-Woods, Wilson et al. (2008) describe as a discourse of 'social unease'. There are concerns that the exploitation of bio-samples – for research and sometimes for profit – threaten human dignity and autonomy (Andrews and Nelkin 2001; Scheper-Hughes 2001). Waldby and Mitchell (2006) suggest that voluntary donation 'has simply rendered the body an open source of free biological material for commercial use' (p.24). Some have, therefore, argued that participants in such studies might be paid royalties or a share of the profit (Laurie 2004). The long-running debate about research use of cancer cells derived without consent from the late Henrietta Lacks (the HeLa cell line) is one example; over 60 years after her death, family members have finally agreed with the US National Institutes of Health that they will have some control over how data about the family's DNA are shared, as well as acknowledgement in scientific papers (Hudson and Collins, 2013) – though they will not receive any profits.

However, Dixon-Woods et al (2008) query how far 'social unease' really represents the public's views in the UK on donating bio samples. Empirical studies of the views and reasoning of people who have contributed tissue samples for biobanking research have identified generally supportive and willing attitudes (Richards et al 2016; Barr 2006; Dixon-Woods, Cavers et al. 2008; Hoeyer 2003; Locock and Boylan 2015). It is not that donors have no concerns, but that they are much less focused on the ethics of consent than is often assumed (Hoeyer 2008). Lipworth et al's 2011 review of sociological evidence on biobanking confirms that public attitudes are generally willing and supportive of donations; people understand biobanks well and do not feel the need for detailed information; while they are aware of risks they are not particularly worried by them; they want to be asked for consent but do not generally want recurrent consent requests or to place limits on sample use; and they are willing to countenance commercial access to samples if it contributes to scientific endeavour. The centrality of trust to the decision to participate in biobanking is highlighted by Nobile et al. (2016) in the context of Germany; they suggest that the morality of this 'trustful relationship' should be investigated. Lipworth et al. (2011) argue that trust can help explain the apparent paradox of an awareness of risk alongside a general willingness to donate. People know they may be harmed, but they do not expect to be, because of their confidence and/or trust in science, researchers and institutional governance in the health system. They also tend to deal with the status of tissue and personal information differently from researchers and



ethicists in that, generally, people do not see their tissue as a special part of themselves, or something over which to assert ownership rights. On the contrary, Lipworth et al (2011, p801) argue diseased tissue may be seen as a ‘foreign and unwelcome invader’ and other samples simply as waste. Boylan and Locock (2015) in their study of biobanking experiences explored how people felt about the emphasis in policy and research discourse on donating samples as an altruistic ‘gift’. They found that the idea of describing something as mundane or distasteful as a urine, tumour or saliva sample as a ‘gift’ seemed exaggerated or even ridiculous to many people (although views on the special status of blood were more mixed). They suggest that ‘focusing on the value of participation and the information derived rather than the value of the physical sample might have more intuitive appeal to potential participants’ (p.814).

Facio (2011) found that healthy participants in a genomic research project cited reasons for taking part such as a desire to promote medical research of benefit to society as a whole, as well as a more personal desire to learn more about the genetic factors that might contribute to their own health risks. Sanderson et al. (2016) also explored the motivations of healthy people to take part in genome or whole exome sequencing and found that participants in their mixed methods study expressed a variety of health and non-health-related motivations including an interest in their ancestry.

Hallowell et al. (2010) explored why people with a family history of cancer participate in genetics research, and identified three categories of motivation: social (research participation benefits the wider society); familial (possible benefits for current or future generations of their own family); and personal (individual therapeutic or non-therapeutic benefits). They argue these motivations are interdependent and cannot be separated into neat either/or categories of benefiting oneself or benefiting others. These authors (Hallowell et al. 2009) also explore the interface between clinical practice and research in cancer genetics raising issues around the ‘boundary work’ specialist health professionals engage in partly to manage the conflicting demands associated with their roles as a clinician and as a researcher. This ‘boundary work’ potentially undermines the consent process which, arguably, lies at the heart of genomics. Berrios et al. (2018) similarly highlight that genetic counsellors need to be aware of their potential influence on participants stemming from their clinical role. This study also identified issues relating to the heightened expectations participants may have about the study process and return of personal results (Berrios et al. 2018) which is mirrored by a study exploring the moral reasoning behind parents’ decisions to participate in genetics research on autism (Singh, 2015).

Haase (2015) contends that hope of benefit plays a large part in people’s decisions as to whether to participate or not. When conducting qualitative research with participants from a whole genome sequencing study of families at high risk of cancer, she noted that although most participants did not expect immediately to benefit personally from the study in question, they were motivated to join the study in the hope that its findings could at some point in the future provide information of use to their own, or to someone else’s family. Researchers also viewed the family as immediate beneficiaries if specific diagnostic results were forthcoming, and as long-term potential beneficiaries in general as genomic knowledge increased as a result of the research. This emphasis on the impact on the family further calls into question the notion of the autonomous individuated patient/participant in genomic research, with implications for consent and return of results’ issues which are at the forefront of much debate in genomic research (e.g., Beskow and Burke, 2010; McGuire et al., 2008; Wolf, 2012). Indeed, Hylind et al. (2018) suggest that patients should be provided with resources to discuss disease risk with their families. Haase (2015) asserts that promises of genomics for personalised medicine and clinical care are far from being realised, describing potential and probable disappointment on the part of both participants and researchers as the focus in their small scale qualitative study was on finding the cause of genetic cancers, yet particular emerging technologies



have given rise to what Martin et al. (2008) term “promissory bioeconomies,” in which “hope itself is being capitalised as the basis of commodity value” (p. 127).

There is an extensive ethical and socio-legal literature on the nature of the relationship between donors and research in biobanking and what it should be (Kaye and Stranger 2009; Tutton, Kaye, & Hoeyer, 2004; Tutton and Corrigan 2004; Petersen, 2005; Hansson, 2005; Solbakk, Holm et al. 2009; Thornton, 2009; Hawkins & O’Doherty, 2010; Lenk, Sándor et al. 2011; Widdows and Cordell 2011; Johnsson, Helgesson, Hansson and Eriksson 2013). This fits within a wider debate on trust among the general public in government, public services and experts, including health professionals (Luhmann 1979; Habermas 1991; O’Neill 2002), and the feasibility (or not) of fully informed consent in the control of personal data (Manson and O’Neill 2007). Informed consent is particularly challenging in bio samples and whole genome sequencing, given the long term nature of sample storage and the difficulty of anticipating every possible future use, coupled with growing pressure from funders for publicly funded research data to be shared as a public good (OECD 2007). With respect to trust in genomic projects, there has been a small amount of research that conceptualises trust or describes it in practice. Trinidad (2010) describes participants in genomic research projects as viewing trust between the researcher and participant as central to the research process, and that informed consent as a tool is but a small part of the governing relationship between researchers and participants, especially in a context in which future recipients and downstream uses of data may be difficult to predict. The lack of certainty as to the future uses of genomic data was also highlighted by Jamal (2014), whose qualitative study with genomic research participants found that participants valued confidentiality as a form of control over information about themselves, and this control was valued as a safeguard against discrimination in a context of uncertainty about future uses of individuals’ genome data. Thus expectations of confidentiality, trust in researchers and a desire to advance science are the most common reasons why participants are willing to share identifiable data with investigators.

### **1.1.1 The 100,000 Genomes Project**

In December 2012, the Prime Minister announced a programme of whole genome sequencing (WGS) as part of the UK Government’s Life Sciences Strategy. The broad aim of the 100,000 Genomes Project (the ‘Project’) was to produce new capability and capacity for genomic medicine in order to transform clinical services in the NHS. It also aimed to produce new capability for clinical genomics research, and establish infrastructure for the protection and analysis of clinical and genomic data. The principal objective of the 100,000 Genomes Project was to sequence 100,000 genomes from patients with cancers, rare disorders, and infectious disease, and to link the sequence data to a standardised, extensible account of diagnosis, treatment and outcomes.

Specifically, the aims of the Project set out in the Project protocol (Genomics England, 2017) were:

- Patient benefit: providing clinical diagnosis and, in time, new or more effective treatments for NHS patients
- New scientific insights and discovery: with the consent of patients, creating a database of 100,000 whole genome sequences linked to continually updated, long term patient health and personal information for analysis by researchers
- Accelerating the uptake of genomic medicine in the NHS: working with NHS England (NHSE) and other partners to deliver a scaleable whole genome sequencing (WGS) and informatics platform to enable these services to be made widely available to NHS patients. In addition, through the Genomics England Clinical Interpretation Partnership (GeCIP), creating a mechanism to both continually improve the accuracy and reliability of information fed back to patients and add to knowledge of the genetic basis of disease



- Stimulating and enhancing UK industry and investment: by providing access to this unique data resource by industry for the purpose of developing new knowledge, methods of analysis, medicines, diagnostics and devices
- Increasing public knowledge and support for genomic medicine: delivering an ethical and transparent programme which has public trust and confidence, and working with a range of partners to increase knowledge of genomics

Genomics England, a company wholly owned and funded by the English Department of Health (DH), now Department of Health and Social Care (DHSC) was set up in 2013 to deliver the Project, which completed sequencing of NHS patients by the end of 2018, a year later than originally planned. Genomics England worked with NHS England (NHSE), Public Health England (PHE), Health Education England (HEE), NHS Trusts, the Northern Ireland Department of Health, Social Care and Public Safety, and a number of Health and Social Care in Northern Ireland (HSCNI) organisations to deliver the project. According to the Secretary of State for Health and Social Care, Matt Hancock, the 100,000 Genomes Project has delivered life-changing results for patients with one in four participants with rare diseases receiving a diagnosis for the first time, and providing potential actionable findings in up to half of cancer patients where there was an opportunity to take part in a clinical trial or to receive a targeted therapy .

To identify and enrol participants for the 100,000 Genomes Project, NHS England commissioned 13 NHS Genomic Medicine Centres (GMCs) to contribute to the project between 2015 and 2018. The Department of Health in Northern Ireland, in partnership with the Medical Research Council (MRC), commissioned the Belfast Health and Social Care Trust (BHSCT) to set up a Northern Ireland Genomic Medicine Centre (NIGMC), to facilitate recruitment of patients to the Project in Northern Ireland. Each centre included several NHS Trusts and hospitals. GMCs recruited and consented patients and then provided DNA samples and clinical information for analysis. Illumina, a biotechnology company, was commissioned to sequence the DNA of participants whose data were then returned to Genomics England. Genomics England also developed infrastructure to store the genome sequences and clinical data. The data were analysed within this infrastructure and any important findings, such as a new or refined diagnosis, were passed back to the patient's clinician.

The Project sequenced 100,000 genomes from 85,000 patients, and is currently the largest national sequencing project in health care in the world according to the DHSC (2018). Rare diseases, cancers and infectious diseases were selected as the focus for the 100,000 Genomes Project as it was felt that these diseases offered the strongest prospect of patient and scientific benefits, and had the ability to drive transformation of the NHS in terms of the application of genomic medicine to routine practice. It was planned that, over the five years of the Project, 50,000 genomes would be obtained from the cancer arm of the study (two per patient, therefore 25,000 patients), and 50,000 from the rare disease arm (three per patient, comprising the affected person plus two blood relatives – therefore, roughly 17,000 patients and 33,000 relatives). In all, just over 40,000 patients, and about 75,000 people were originally to be involved. The study completed a pilot phase (2014-2015) in which 2000 people from families with a rare disease, and 3000 patients with lung, breast, colon, prostate and ovarian cancer were recruited. The main programme took place between 2015 and 2018. Eventually 85,000 participants, 1,500 NHS staff and over 3,000 researchers were involved in the project.

The full protocol, which outlines project structures, processes, and information architecture in detail can be accessed at:

[https://figshare.com/articles/GenomicEnglandProtocol\\_pdf/4530893/4](https://figshare.com/articles/GenomicEnglandProtocol_pdf/4530893/4)



## 1.2 This study

### 1.2.1 Background

The DH-funded Policy Innovation Research Unit (PIRU) based at London School of Hygiene and Tropical Medicine (LSHTM), was asked in 2014 by the then DH to conduct a qualitative study exploring participant and health care staff experiences of taking part in, and recruiting for, the 100,000 Genomes Project, as well as the public's perceptions of genomic research generally. This study was undertaken from 2015 to 2017 through a collaboration between PIRU, and the Oxford University Health Experiences Research Group (HERG) and Health Experiences Institute (HEXI), in association with the DIPEX charity which publishes the acclaimed website [www.healthtalk.org](http://www.healthtalk.org).

### 1.2.2 Rationale

Genome sequencing and storage has huge potential to transform our understanding of the causes of disease, and to take the search for treatment in new, previously unexplored directions, including towards more personalised forms of medicine. But genome sequencing also raises many potentially new ethical, technical and policy issues. The success of the Project depended entirely on the willingness of relevant people to take part, which, in turn, rested on their understanding of why it was important, and their level of confidence and trust that their data would be stored safely and used responsibly. Earlier problems with the presentation of the NHS care.data programme showed how important it was to get this right; the debate around care.data may have led to some short-term erosion of trust among the general public and willingness to volunteer for similar projects (Anonymous 2014) which could affect recruitment to the 100,000 Genome Project and to similar future projects (although there were significant differences between the 100,000 Genome Project and care.data in terms of the approach to consent and referral). The Government's decision to delay the implementation of the care.data programme was suggestive of its concerns about the public's trust that its personal data would not be misused and/or disclosed in a personally harmful way. However, there has been no empirical research into whether this was in fact the case, or whether the care.data debate was another example of media, professional and policy commentators assuming a level of social unease and mistrust which does not match what the public and patients think.

The study was commissioned to provide insights into how people make sense of data sharing and whole genome sequencing not only to inform the longer term development of the 100,000 Genomes Project, but also to provide valuable resources for training staff and explaining the Project and the wider field of genomic medicine to future participants and non-specialist health care professionals.

### 1.2.3 Aims

The original aims of this study were to:

- Understand the motivation of people who agree to take part in genomic research in the form of the 100,000 Genomes Project; their experiences of receiving information, giving consent and taking part in the Project; their attitudes to data sharing, governance and confidentiality (including their level of trust in the 100,000 Genomes Project and other similar initiatives); and their views about feedback and use of their Project data for research and clinical care
- Understand why some people who are invited to take part in the 100,000 Genomes Project refuse to do so or withdraw





- Learn about the experiences of clinicians who ask people to take part in the 100,000 Genomes Project
- Explore the understanding and perceptions of members of the public of genomic research generally
- To draw on the above, in order to make suggestions on how to improve the experience of participants and clinicians involved in recruiting for the 100,000 Genomes Project; and how to engage with the general public and non-specialist workforce, thereby improving the likelihood of the Project achieving its goals.

It was also agreed that the interviews of participants in the 100,000 Genomes Project would be used, with participants' consent, to produce a new section on [healthtalk.org](http://healthtalk.org) designed to inform prospective participants in the Project, to inform future gene banking and data sharing initiatives, to inform the public about genomics and as a resource for NHS staff training in the practicalities of genomic medicine services as they are made more widely available beyond the Project. [Healthtalk.org](http://healthtalk.org) receives over 5 million visits per year and was one of the earliest websites to be awarded the Information Standard. [Healthtalk.org](http://healthtalk.org) is recommended as a source of patient experience evidence in the latest version of the National Institute for Health and Care Excellence (NICE) Guidelines Manual; a recent systematic review of qualitative evidence related to young people and obesity found that the site met the highest standards for usefulness and reliability, and was also the most comprehensive source of evidence included in the review (Rees et al, 2013). Details of the [healthtalk.org](http://healthtalk.org) resource are given at the end of this report (see section entitled 'Dissemination via [healthtalk.org](http://healthtalk.org)').

As the study developed, it became clear that it would not be possible to contact people who had been invited to take part in the 100,000 Genomes Project but had refused to do so, or who had withdrawn. GMCs were asked if they could identify people who had refused to take part in the main Project to invite them to take part in this study. However, staff were uncomfortable re-contacting these potential participants. It also became apparent that it would not be possible to interview people who had received their results within the original timescale of the research which was due to have been completed by June 2017. In order to be able to include participants who had received some feedback after providing their DNA samples, a six-month extension was agreed to take into account the revised key milestones of the 100,000 Genomes Project, which were reached later than originally intended. In particular, key milestones which affected data collection for this research included the late start date of the cancer main programme in March 2016 and participant result feedback beginning later than originally planned towards the end of 2016. In addition, only very small numbers of participants received their results during 2017. Despite an extension to the research timescale, it was not possible to obtain the views of any patients who had received their results from the 100,000 Genomes Project in the current study.

As part of the research extension, and while waiting for participants to receive their feedback from the Project, we added an additional research component comprising a series of focus groups which explored the understanding and perceptions of the non-specialist health care workforce of genomics in general and the 100,000 Genomes Project in particular, and tried to identify their potential future training needs. As genomics and genomic medicine is now moving from the domain of specialist services and professionals with a particular interest to become a reality for all clinicians, the NHS workforce will need to integrate genomic knowledge and technologies into its work. The specific objectives of the additional focus group research were to support the development of the Project itself, leading to closer integration of local delivery partners with each of the Genomic Medicine Centres (GMCs); the development of appropriate educational interventions for the wider NHS workforce; and identify what else is needed from a staff perspective to facilitate the broader rollout of genomic technologies into routine clinical practice across the NHS.

The research aims were updated accordingly to reflect this additional work and an additional aim was added:

- To explore the understanding and perceptions of the non-specialist NHS workforce of genomic research generally, of the 100,000 Genomes Project in particular, and to identify potential training needs related to any roll-out of genomic medicine services within the NHS.

#### **1.2.4 Research ethics approval**

The project as a whole received research ethics committee approval from LSHTM's research ethics committee (REC reference number 8982, 31 March 2015).

The qualitative interview methods used by HERG in this study were approved by NRES Committee South Central – Berkshire (REC reference number 12/SC/0495, 7 September 2012) for all health conditions or topics involving participants aged 10 years and over as part of the wider study 'Narratives of health and illness for [healthtalk.org](http://healthtalk.org) (formerly DIPEX) and [www.youthtalk.org.uk](http://www.youthtalk.org.uk)'.

University of Oxford research ethics committee approval was obtained for the focus groups undertaken with patient representatives and the public (REC reference number MS-IDREC-C1-2015-175 (R42460/RE004) on 1 October 2015 and for those with non-specialist health professionals on 12 December 2016 (R47746/RE00).



## Chapter 2: Methods

This qualitative study generated data via one-to-one interviews with 100,000 Genomes Project participants; one-to-one interviews with 100,000 Genomes Project health professionals; focus groups with members of the general public; and focus groups with non-specialist healthcare staff.

### 2.1 One-to-one interviews

#### 2.1.1 100,000 Genomes Project participants

In total, 32 in-depth interviews were conducted with 34 participants from the 100,000 Genomes Project. Fifteen participants had rare diseases (including Kartagener Syndrome, Primary ciliary dyskinesia, Ehlers Danlos Syndrome, polycystic kidney disease and undiagnosed genetic conditions) or had caring responsibilities for children with rare diseases in four cases. Nineteen participants had cancers of the breast, prostate, endometrium, ovary, kidney and colon. Participants were aged between 17 and 84 years (eight were under 35 years of age, ten 36-55, 12 were 56-75 years of age and four were 76 or older). Most were White British (Welsh, Scottish and English), with one White German person. Participants were at a range of different points in their journey through the Project. Some were pilot participants who had been moved into the main sample and had donated blood samples over a year before their interview. Other participants, particularly the cancer participants, had given a tumour sample within weeks of the interview.

Interviews were conducted between December 2015 and September 2017. A senior qualitative researcher usually visited the participants in their homes and conducted in-depth semi-structured interviews which lasted between 30 minutes and 1.5 hours. One interview was carried out over the phone. A diverse sample was sought, though this was not possible despite extensive efforts to recruit interviewees from black and minority ethnic groups.

Participants were recruited through Genomic Medicine Centres, condition-specific support groups, social media and snowballing (see Table 2.1, below).

**Table 2.1: Recruitment avenues**

Recruited through	Number of participants
Social media (Facebook, netmums)	7
Support groups	8
Genomic Medicine Centres	15
Snowballing	4

During the recruitment process, 194 charitable organisations, support groups and online social media groups covering a wide range of issues were contacted by e-mail and online contact forms over a 15-month period. The following groups agreed to publicise the study through their newsletters:

- Cardiovascular disease (e.g. Down's Heart Group, Children's Heart Federation, Arrhythmia Alliance)
- Ciliopathis (e.g. Primary Ciliary Dyskinesia Family Support Group, British Lung Foundation, Genetic Disorders UK)
- Dermatological Disorders (e.g. Ectodermal Dysplasia Society, Debra, RareConnect)
- Dysmorphic and congenital abnormality syndromes (e.g. Kabuki UK, Unique – Understanding chromosome disorder)
- Endocrine disorders (e.g. Child Growth Foundation, Diabetes UK, Hypopara UK)



- Growth disorders (e.g. Swan UK, Restricted Growth Association, Beckwith Wiedemann syndrome support group)
- Haematological disorders (e.g. PID UK, Diamond Blackfan Anemia UK)
- Hearing and ear disorders (e.g. Microtia Mingle UK, Microtia UK)
- Metabolic disorders (e.g. Lily, The Children's Mitochondrial Disease Network)
- Neurology and neurodevelopmental disorders (e.g. Muscular Dystrophy UK, MD Myotonic Dystrophy Support Group, TAG – The Arthrogyposis Group)
- Epilepsy (e.g. Epilepsy Action, Young Epilepsy)
- Ophthalmological disorders (IGA – Glaucoma Association, Nystagmus network, Muscular Society, [Wonderbaby.org](http://Wonderbaby.org))
- Renal and urinary tract disorders (Kidney Research UK, British Hypertension Society)
- Respiratory disorders (e.g. Action for Pulmonary Fibrosis, Papworth Pulmonary Fibrosis Support Group)
- Rheumatological disorders (e.g. Amyloidosis local patient support groups, NRAS – National Rheumatoid Arthritis Society)
- Skeletal disorders (e.g. The Perthes Association, Stickler Syndrome Support Group)
- Tumour Predisposition disorders (e.g. The National Hereditary Breast Cancer Helpline, The Haven, Against Breast Cancer, Friends of OSCAR, Monty's corner)

In addition, information and invitation packs were sent to Genomic Medicine Centres in London, Oxford, Exeter, Nottingham, Cambridge and West Midlands for staff to distribute to participants in the 100,000 Genomes Project after their recruitment.

Potential participants were given a study recruitment pack with an information sheet, reply slip with pre-paid envelope and the contact details of the research team. The researchers spoke to or corresponded by email with participants who returned a reply slip, and organised an interview date. Before the interview began researchers demonstrated the Healthtalk website to the participant, answered any questions and gained informed consent to taking part in the interview which was video and/or audio-recorded with permission.

It was explained that names of health care staff and hospitals, and the names of family members and other identifying information, would be removed from the transcripts. Participants were asked what name (their own or an alias of their choosing), they would like to have used on the [Healthtalk.org](http://Healthtalk.org) website.

The interviews with participants covered a number of themes (see Appendix 1 for full topic guide), including:

- When and how they were invited to take part in the Project.
- Why they wanted to take part and any concerns they had
- What they knew about genomics research when they were invited, and what they thought about the information they were given by the Project
- The process of giving consent, and giving a sample
- What they knew and thought about data protection and sharing
- What they expected from the Project overall and from Genomics England.

Interviews, conducted by SR, MS and EH were audio and video recorded with the participant's consent and transcribed verbatim. The transcripts were checked by a researcher and sent back to each participant in case they wanted to remove any content. At that stage, participants were asked to sign a copyright form giving permission for their data to be used on Healthtalk.org in audio, video or text form for research, teaching, publications, the making of audio-visual resources and broadcasting.

Data were coded and analysed thematically drawing on grounded theory techniques of constant comparison and deviant case analysis (Pope et al 2000, Ziebland and McPherson 2006) with the organisational aid of specialist qualitative analysis software package (Nvivo 11). Analysis and data collection proceeded largely in parallel in

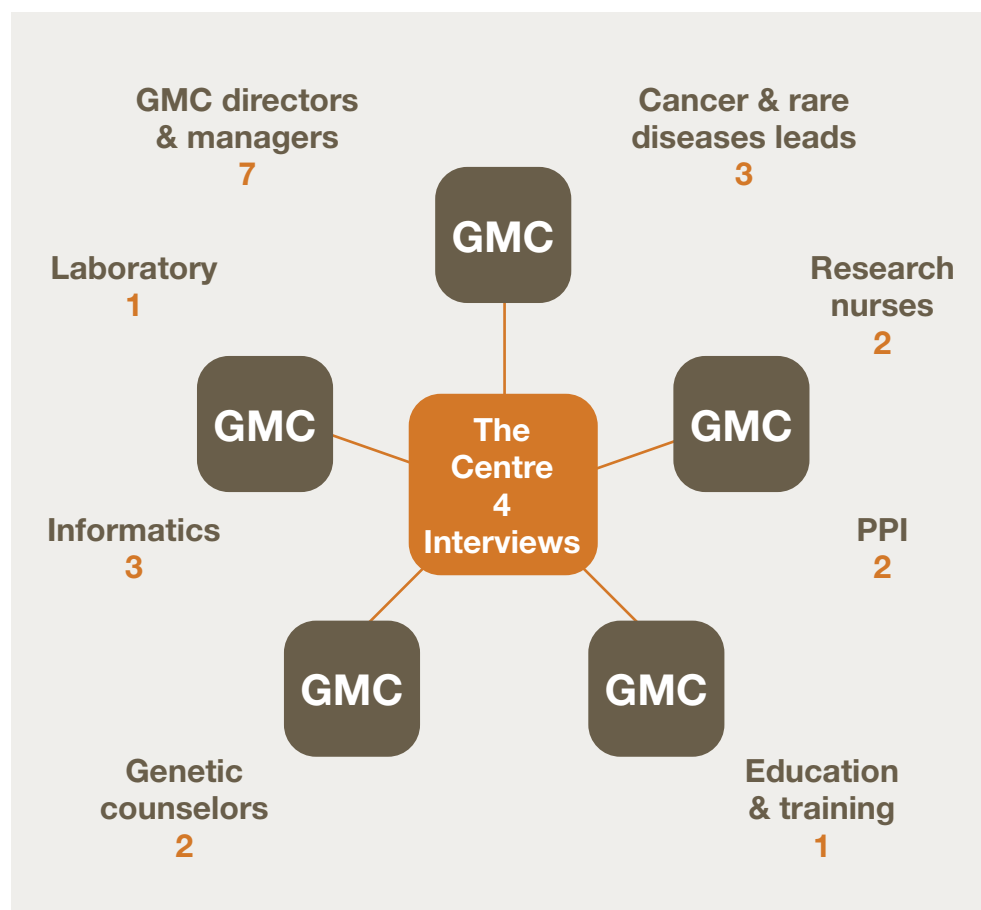


order to try to reach ‘data saturation’ to ensure that the widest practical range of experiences had been included (Patton 1990). The coding structure was developed iteratively as codes become subsumed into broader categories and new ones were added. Coding reports for each category were then analysed more conceptually using an analytic approach called ‘One sheet of paper’ (Ziebland and McPherson, 2006). This comprehensive approach enabled lay summaries to be written for publication on [Healthtalk.org](http://Healthtalk.org) which captured the full range of participants’ experiences, as well as forming the basis for academic publications.

### 2.1.2 100,000 Genomes Project healthcare professionals

Twenty-six healthcare professional interviews were carried out over a period of 18 months (December 2015 to June 2017). A wide range of professionals involved in designing and delivering the 100,000 Genomes Project were interviewed from across the health system (Figure 1). They were purposively sampled to include those with different levels of experience in setting up, managing and recruiting to the Project. This included four interviews with people working at the ‘centre’ – NHS England, Genomics England or otherwise involved in policy, advice or central oversight of delivery. Nineteen people working in GMCs or local services were interviewed, including those with experience in rare diseases, cancer, informatics or research and those working to support the involvement of patients and the public (PPI). Some people could have been counted in more than one category, for example GMC managers who were also practicing clinicians. Three GMC staff were interviewed on two occasions, approximately a year apart in order to provide some sense of how the implementation of the Project was unfolding. The professionals interviewed came from five GMCs.

**Figure 1: Range of interviewees among professionals involved in designing and delivering the 100,000 Genomes Project**





Initially, healthcare professionals were identified through discussion with NHS England and those GMC leads who responded to an initial email request. Once interviews had commenced further interviewees were identified by 'snowballing', interviewees suggesting people who might be interested in taking part. Identification of potential participants included asking for introductions to people in specific roles to ensure the range of professional groups were interviewed.

The majority of interviews were conducted face-to-face at the professionals' location of choice, for example, university campus, public space such as a café, or home. Three interviews were conducted by phone. The majority of interviews took an hour. This was the likely length of interviews indicated in the invitation to participate. Two interviews took half an hour.

Initial discussions with professionals, before interviewing commenced, identified areas of potential interest to explore in interviews (see Appendix 2). The interviews themselves were conducted with a narrative approach to allow participants to speak freely about matters of importance and interest from their perspective. Interviewees were asked initially about their role and how they became involved in the 100,000 Genomes Project and then asked what it had been like to be involved, what their experience had been. The rest of the interview followed the interest of the interviewee. Prompts for further discussion were used only if a topic was brought-up by the interviewee, such as recruitment or consent. This approach was taken given the breadth of backgrounds of professionals. Thus, for example, consent as an issue for discussion was raised by clinical staff and counsellors, but not by lab staff. Towards the end of the interview, all interviewees were asked about how they saw and felt about the future of the Project and genomics more broadly.

Interviews were audio-taped with participant consent. None were videoed as professionals' interviews were not planned to be included in the Healthtalk resource to be developed alongside the research. All interviews were transcribed verbatim and a thematic analysis (Braun & Clarke, 2014) was undertaken. Transcripts were initially reviewed by one researcher for emergent themes and concepts and then coded against these themes using qualitative data analysis software (Nvivo 11). Initial findings were then reviewed and refined in face-to-face and phone discussions with a second researcher.

## **2.2 Focus groups**

### **2.2.1 Members of the public and patients with specific conditions**

We conducted nine focus groups between October 2015 and October 2017. Each group comprised 5 – 8 participants. Discussions were facilitated by one researcher, with a second observing the sessions in order to make notes on interactions and group dynamics. A brief focus group plan was used (see Appendix 3) and short videos on genomics and the 100,000 Genomes Project (named in the topic guide) were shown to provide background information to participants and/or initiate discussion. Videos were selected as appropriate to the invited participants and lasted under five minutes. All videos are available in the public domain and sources included Genomics England and DH.

Groups included members of the 'general public' (three groups), people with rare diseases and cancer (two groups of people who were not participating in the 100,000 Genomes Project) and groups of people whose voices are seldom heard in research (four groups). Group description and recruitment methods are outlined below.



**‘General public’ Group 1** – Participants were recruited through a research team contact from an Oxfordshire primary school. The school head teacher was approached and agreed to publish a notice in a parents’ newsletter, inviting potential participants to contact the research team directly. Five people responded to the notice and three additional participants were recruited by word of mouth. The group took place in a local village hall. It consisted of five women and two men who were all white, with six identifying as British and one as Welsh, aged 20-70 years.

**‘General public’ Groups 2 and 3** – Participants for the groups were recruited via Oxfordshire patient and public involvement (PPI) networks. Adverts were placed in the Thames Valley Patients Active in Research and the Nuffield Department of Primary Care Health Sciences’ established PPI groups’ communications (advert hosted on a website notice board, and included in email alerts). Members were asked to contact the research team directly if they wished to participate. Sixteen participants were recruited in two groups. The groups were mixed gender (F=10, M=6), primarily white British/European (n=14) and aged 40-80 years.

**People with rare diseases Group 4** – Participants for the group were recruited via the Cardiomyopathy UK support group in the North West of England which circulated details of the study to its members. Members were asked to contact the research team directly if they wished to participate. The group comprised eight members (F=6, M=2), all of whom were white British/European, aged between 20 and 50 years.

**People with common cancers/cancer patient advocates Group 5** – An existing research contact introduced the research team to a cancer patient advocacy group which helped recruit members of various cancer patient advocacy groups, including Independent Cancer Patient Voices (ICPV) and Cancer 52. Members were recruited through word of mouth, and snowballing methods. The focus groups comprised seven people (F=6, M=1), all of whom were white British/European, aged between 40 and 80 years.

**Seldom heard Group 6** – Learning disabled adults – An Oxfordshire self-advocacy group was contacted and circulated details of the study to members. 5 people who were known to each other took part (F=2, M=3), all of whom were White British, aged between 40 and 60 years.

**Seldom heard Group 7** – Young people – An Oxfordshire comprehensive was contacted and the head teacher agreed to a session being run with mixed gender Sixth formers. The focus group comprised 8 young people (F=4, M=4), aged 16-18 years, all of whom were White British.

**Seldom heard Group 8** – Black and minority ethnic (BAME) women – A room was booked for an afternoon at a women’s enterprise hub in the Sparkbrook area of Birmingham which has a population which is predominantly of South Asian ethnicity. EH and MS invited women (face-to-face) using the community space and present in the wider area on that particular day to take part in a focus group. Eight women were recruited (South Asian=6, Black African/Caribbean=1, white British/European=1) aged between 16 and 60 years.

**Seldom heard Group 9** – BAME community – A research contact at an African/Caribbean community centre in Leicester facilitated recruitment and a group was convened with patrons of the centre. Eight people took part (F=6, M=2), all of whom were Black African/Caribbean, aged between 20 and 70 years.

Participants were given a £25 high street shopping voucher for volunteering their time, and travel expenses were paid for groups 1-7 and 9.



The groups were audio-recorded with participant consent and transcribed verbatim. Analysis method took the form of a listening workshop (Ryan et al 2017). EH, MS, and SR spent two days together listening to the focus group recordings. Similarities of views, differences and unexpected points in the discussion, both within the groups and across the groups, were noted and discussed. Emerging themes were identified and the data were further interrogated and transcriptions coded to further define and categorise the main themes and findings.

### **2.2.2 Non-specialist healthcare professionals**

We conducted four focus groups between January 2017 and October 2017. Each group comprised 6-8 participants. As for the public focus groups, discussions were facilitated by one researcher, with a second observing the sessions in order to make notes on interactions and group dynamics (see focus group plan, Appendix 4). Delegates attending professional events (organised by the Royal College of Physicians, Royal College of Surgeons, Royal College of Nursing and University College of London Great Ormond Street Institute of Child Health) were invited to participate. Official communication from event organisers including information about the focus groups was sent out up to 3 weeks before events, and delegates were asked to contact the research team directly to reserve a place in the groups. All group participants were physicians (non-genomics specialists), and included GPs, endocrinologists, neurologists, cardiologists, and others. The groups were audio-recorded with participant consent and transcribed verbatim.

Analysis was conducted by EH and JH. Transcripts of the focus groups were coded for emerging themes, and discussed to define the main findings.

## **2.3 Engagement with policy makers, patients and the public**

The research was supported by an advisory panel comprising staff from NHS England, Genomics England, the Department of Health, Healthwatch and the Royal College of Nursing. The panel also included clinicians and lay representatives of patient organisations (cancers and rare diseases). The panel met at appropriate intervals during the research process and provided advice to the research team, primarily on how best to recruit the various sub-groups among the research participants. Early and interim findings were reported to Genomics England primarily but not exclusively via presentations to, and discussions at, its Ethics Advisory Committee (chair: Prof Michael Parker, University of Oxford) and face-to-face meetings with the relevant policy team in DH. The Ethics Advisory Committee also reviewed the initial proposal for the research in addition to the independent reviewers appointed by the DH's Policy Research Programme. However, it was understood from the outset that, as independent research, the interpretation of the findings rested with the research team alone.





## Chapter 3: Findings of face-to-face interviews with 100,000 Genomes Project participants

At the time of interview, participants had not yet had any results from Genomics England so the findings below relate to their experiences of participating in the Project and not the outcomes of any personal genomic information they might have received as a result of taking part. For many participants, their initial engagement with the Project had taken place at least six months before their interview. There were clear differences between the experiences of participants with rare diseases and those with cancer.

### 3.1 The rare diseases group

This group included participants with a wide range of conditions. Some participants were family members of a child or partner with the condition while others had the disease themselves. The conditions are detailed in Table 3.1 and include Ehlers Danlos syndrome, Kartagener Syndrome and dilated cardiomyopathy. This group typically had done considerable research into their condition over years and many had amassed substantial medical notes about their own cases and information about their conditions in general. They had established relationships with consultants and clinic staff, had a good understanding of genetics and some had experience of taking part in medical research. The rare disease was an integral part of their lives. Participation in the 100,000 Genomes project involved donating blood samples and this was often mediated by health professionals whom they already knew and took place in settings they were familiar with.

### 3.2 The cancer group

These participants were being treated for a range of cancers including prostate, breast, womb and ovarian cancer. For this group, the disease was a very recent, often unexpected and a potentially life-threatening addition to their lives. The settings and health care professionals involved were new to them and participants were often distracted by their cancer concerns. Their engagement with, and interest in, the 100,000 Genomes Project was typically secondary to the treatment they were undergoing. The timing of involvement for this group was much tighter as participants were usually invited to take part in the Project during their pre-operation consultations a week or so before surgery. Participation involved giving permission for a sample of the tumour removed during the operation to be used in the 100,000 Genomes Project.

### 3.3 Vague knowledge of genomic research

Many participants had not been aware of the 100,000 Genomes Project, or genomic research more broadly, before being invited to take part in the Project. A few were aware because of their keen interest in medical research developments or because they had seen leaflets or a poster in a hospital waiting room. This lack of awareness was surprising to some of the rare disease participants, many of whom had a longstanding interest in genetics and genetic testing, and had assumed that they were well informed of developments. Karen, whose son and partner have polycystic kidney disease, said:

*I was a bit blown back by it all at first, bit blown away. Because I'd obviously never heard of it. So yeah, I was a bit —*

*So it's completely new to you?*

*Completely new, yeah. Yeah.*

*[...] I'd never – never seen it anywhere, never heard of it. There's a few of the people in the forums that I go onto, regarding polycystic kidney disease forums, and there's a few people that are on it. They also sent me forward to [Name] Children's*



*hospital website, and then since being on there I've found them all talking about it, like all these other adults with children that are also put forward for it.*

Karen said that once she found out about the Project and was directed to a hospital website, she found other parents talking about the Project. This gap in knowledge was a consistent theme in both the interviews and the focus groups.

Some participants worked in a healthcare profession or had family who had studied science or medicine. This could make the Project seem slightly more familiar, as Sue, whose son has an unknown rare disease, described:

*Did you know much about the 100,000 Genomes Project at that time? Had you ever?*

*No. I think I'd read little bits about it in the media. Obviously, because of my background, I tend to read more of the medical side of things [laugh], and I was aware of it. But it's certainly not something I come across in my day to day work at all. My husband had certainly never heard of it at all. And most of the family have never heard of it at all. So, we kind of thought it was interesting.*

Participants who had heard or read about it in the news or through a rare disease support group had a "vague" understanding of what the Project was about. Rebecca had heard about it on BBC News – "they were trying to look for genes or something" – but did not know what the Project was trying to achieve. Cherry said, "I'd heard whisperings about this Genome Project thing. But nothing, nothing hugely." Richard, who has primary ciliary dyskinesia (PCD) reflected:

*I think because, because my wife runs the PCD Support Group and the likely, a likely cure for PCD is genetic, then we've known about what's been going on in the worlds of genetic research all the time. So, I think we were aware of it. So, I can't exactly remember. So, it wasn't a surprise when they mentioned it at [Eye hospital] [...] So, I think we were aware of it. Because of with, you know, with the boys and myself, the likely cure is genetic, then obviously we take a very firm interest.*

These extracts illustrate a peculiarity related to asserting a definite interest in, and knowledge of, genomic research (Sue says 'obviously' and Richard states 'we take a very firm interest') with an apparent lack of understanding about it. Even to interested parties the reach of the 100,000 Genomes Project was limited.

## **3.4 Communication**

### **3.4.1 Waiting for results**

Participants were still waiting for results when we interviewed them and only a few had had any communication from Genomics England since donating their sample. Participants who had taken part in the pilot study or early on in the main part of the 100,000 Genomes Project were hopeful they would hear something soon. Initially, there had been an estimated six month waiting time for results but this had later been revised to one year. Participants had different expectations or had been given different information about these lead times; some expected to hear back within a year while others had been told it could take up to two years.

Some participants were resigned to a long wait and thought it was inevitable given the complexity of the process, while others found the waiting frustrating.



*We thought we might have got some results by Christmas but we had a letter to say it will be another nine months at least. So...*

*Right, OK.*

*You know, it's just the waiting now, really.*

*OK. So, when you got that letter how did you feel about it?*

*We were a little bit sort of disappointed. We thought maybe we'd have got, you know. But we understand. I mean the testing is very quick but it's the reading of the results that takes the time. And you know you kind of have to understand they've got lots to look at haven't they? (Andrew and Kim)*

Some of the cancer participants were not expecting results and several spoke of wanting to put the experience of the cancer diagnosis and treatment behind them. There was some confusion among some participants who described 'a lot going on' related to their treatment but were not sure whether to expect results or not. In the following extract, Ashley demonstrates some ambivalence about her involvement in the Project.

*And if you don't hear any results from Genomics England, what do you feel about that?*

*I don't mind. It might not be [sigh] – [laughing] Maybe my biopsies won't be worth anything. I don't know. I don't really know what I think, what to expect. I don't know. It's all [er] a learning curve. Like another friend of mine who's got cancer, she said, "It's a journey. And you don't know any more than the next – what the next week will bring." You don't.*

*And [um] so you mentioned there you're not so bothered if you didn't hear results, or hear anything back?*

*No. I mean, obviously they'll do a lot of people. They'll approach a lot of people for this sort of thing. [um] Some, some will help. Some won't be able to help. Some -thing, if I don't hear anything, then – you know – fine. I've done what I could do, and I can't do any more, so.*

Finding out what caused their cancer was important to some participants. As one woman said: "Well [um] if like now I just wouldn't mind going back to see [the consultant], you know, see the consultant. And him say to me, "This is what caused it and this is, you know, what you've got to avoid in the future".

### **3.4.2 More general communication**

Even if participants were not expecting results, some raised concerns about not hearing anything having taken part in the Project. A letter saying that "everything had gone as planned" or updating participants on the Project's progress would have been appreciated by some. Sally described being disappointed that she would not hear anything further.

*Well, I'd be interested to see what they'd used it for and [um] what sort of things they were doing. You know what I mean?*

*Okay.*

*You know, I think most people who, who joined it would [um] be interested to*



*see what happens to their blood and, and their, their tissue, what it went for and what they did with it and-.[...] Because sort of you do all these things and then you're just left dangling in the air sort of thing. You don't know what they've done with your blood or anything. I mean they explain that it's for research and things like that, which you understand. But we're just interested to know what they used it for.*

Alongside this, some felt there was a general responsibility for Genomics England to communicate with participants more. Participants drew on the example of organ donations in these discussions:

*I would say I think they could learn a lot of lessons from [um] the Transplant Service actually. That every gift they receive is treated exactly as that, as a gift. And you know there is thanks given, and they are made to be the absolute centre of what is going on. And I think Genomics England could learn a huge amount from the way they approach it, that every person who volunteers for this study is giving you a gift. That they are giving you access to their personal data. And they are allowing you to build medical knowledge forward. So, I think they need to be respectful of that decision that people have made. I think they need to make sure that we're being fed back the information on what's going to happen. And also kept informed. And just things made as easy as possible for people to become involved. Because it is hugely stressful. It's a really personal decision that people have to make, and I think they should – yeah, just treat people as individuals. (Sue)*

Participants also felt that the Project needed to have a public 'presence' and be more visible, whether through posters and leaflets or on the news. This was seen as having three benefits: to improve public awareness of the project and trust in it; to promote participation; and to honour the current participants and their contribution. John, who was interviewed with his mother Flo who has mitochondrial disorder, discussed the importance of increased public awareness:

*I mean, if I had to say anything, it would just be more public awareness. People trust more things they're already aware of. I, I didn't even know about it until I was asked about it. You know, I was more than happy to take part in something that would benefit research. But I think it would be good if people generally – even if they're not going to participate – knew that it existed before they were potentially asked to sign up for it ... Perhaps a little bit more presence. Even if it's just outreach to news media, or a newspaper, just so people know that it exists.*

Most participants were genuinely interested in the Project and saw their participation as important. Because of this, they wanted to understand more about how their samples were being used and what the outcomes were. In effect, they wanted to see how the Project as a piece of medical research translated findings into medical developments.

*I, I'd like it to be more known, and more known what you're finding out." So that, you know, I can say, "Oh, I, I took part in that, and they found out this." So, updates, maybe, maybe you could have more bulletins on the, the BBC News. So, you know, a little snippet of what you've found out this year. Or, or put it on the Cancer Research website. That would be a good place to put it. So we can look and sort of see, "Oh, you know, they are doing research. They are finding out these things, and it's led to this." Because otherwise we, we think, "Oh, that was just in isolation and they didn't find anything out." (Edie)*



### 3.5 Being invited to participate in the project

Participants were invited to take part in the Project in different ways. Cancer participants were usually asked by a healthcare professional while waiting for their pre-operative consultation.

*So at what point during your stay in hospital did a nurse come and talk to you about the Genome Project?*

*Quite early on before I started the, in fact I think it was before the operation, in fact. Yes. They were doing several blood tests and things and I just thought it was very interesting altogether. I love to have new experiences, quite an adventurous person and I said, "Yes I'll go ahead with that." And she explained what it was about as far as the bits of paper were concerned. And I'm glad to help. (Elsie)*

Some of the rare disease group were asked by their consultant during a routine appointment. Others were contacted by letter, email or telephone call. One participant found out about the Project via a rare disease newsletter and contacted her consultant to ask if she could take part. She was sent sample packs in the post and asked to arrange to go to her GP and have her blood taken.

As we saw above, the contact was a surprise to some participants as they did not know about the 100,000 Genomes Project. Helen, who has an unnamed rare disease, was surprised to hear from a hospital from her childhood.

*[...] when we went to [hospital] when I was little, we let them keep our details. And then I got a phone call about twelve months back, saying "We're running this project, we've still got some of your data, and we're wondering if you would be interested?" So it was a bit of a shock, but. I was a bit like, well yeah, probably [laughing]. And then she sent me through all the information, and I spoke to my Mum about it, and she said she would be up for it as well, so.*

Receiving a letter rather than being told about the Project in person was helpful for some as it enabled time to read the information before giving an answer. The rare disease participants did not feel pressurised into participating and described having the time to digest the information, ask questions and do their own research before giving consent. Many had spent years trying to find out about their condition and the 100,000 Genomes Project was another possible route to answers.

A concern for those participating in the cancer arm of the Project was that people were invited at a time when they had recently been given a diagnosis of cancer. In depth description of the emotional turmoil that they were experiencing as they and family members made sense of the news was used to demonstrate the awkwardness of the timing. There was, furthermore, only a short time between being told about the Project and taking part. People were not able to give the invitation detailed consideration, because their minds were elsewhere. Kristina described how "You talk about your diagnosis and your future [...] this was more of an add-on [...] that wasn't such an important part of that appointment to me." Some participants said it was helpful to have a family member present because it was difficult to take in the details in such a setting.

Jenny was approached to take part straight after seeing her consultant about surgery for ovarian cancer. She described how "It's a bit of a funny time to ask, isn't it, because it's a bit of a scary time in your life, actually." Other participants described feeling "overwhelmed" or "this was more of an add-on" at the time of being asked because of their cancer diagnosis. Sally, who could remember the detail of being asked to participate, said:



*They expect you to read the leaflet and when you go back next time to either join, say yes or no. Because, as I said a lot of people just won't read the leaflet.*

*What is the problem with the leaflet?*

*There's no problem with the leaflet. But the point is, you've got to understand that when you've been diagnosed with cancer, a lot of the time you can't be, be bothering with anything else. That's your priority, the cancer that you've got. And I think a lot of people that have come home with that leaflet will just shove it on the table and think, "Well, I've got enough to be bothered with, without sitting reading that".*

The cancer participants who were asked in the waiting room before their pre-operative consultation described wondering why some people were invited to participate while others with a similar condition were not:

*I've sat with one or two in the waiting room and I, we were talking about it and one or two have said, "Well, they didn't ask me. Well, how did they choose you?" I says, "Don't ask me. I don't know nothing about that part of it." So —*

*Okay. So, so that's interesting. Because do you think they should explain a little bit, I don't know, on their website about why some people are chosen?*

*Yeah.*

*Why do you think, because —*

*Well, I've no idea. And I mean one or two said to me they were quite disappointed that they hadn't been asked, 'cos they would have probably joined it. And I, they said to me, "Well, how do they choose?" I says, "I've no idea." I said, "I just presumed that they asked everybody". (Sally)*

Some participants could not remember much about their involvement in the Project. William could not quite recall who invited him but thought it might have been the nurse who told him he had prostate cancer. Kristy was asked before she had an operation to remove a tumour in her ovaries. She was not sure if the woman who asked her was a doctor or not:

*Yeah. And what did she explain to you?*

*Well, [sigh] I can't really remember what, what she actually said. But she just did say it would help, it would help you, and more than you it will help a lot of other people – help us in our research. To you know, into the – how people get cancer. And so that, you know – I thought, "Well if I can help anyway. I will." So that was it.*

Despite these concerns about the timing of the invitation, cancer participants reported that they did not feel pressurised into agreeing and knew they could withdraw at any time. They trusted the Project, found the staff professional and were happy to take part. The process was described variously as "friendly and supportive", "there's no rush, no pressure. It's all done very well", and "professional":

*There was no pressure put on me. However, what I will say is that it was, the consent and information was given to me at a time when I was taking in a lot of other information about pre-op, about an operation, about my diagnosis. And there were times when I just thought, "Is this too much? Do I want to do it?" However, having read the information, I realised that, actually, I didn't have to do very much at all. It was very much, you know, the tissue sample was going to be there anyway. The blood tests, I was going to have a pre-op and blood.*



*It was just going to be another vial of blood. And actually there was very little input from me to be involved in this trial. I could only see benefits. And then that's why really I signed the consent and went with it. (Josie)*

*I don't think there was any pressure at all to do it ... No, she just left me to read it [the consent form]. She didn't feed me with any information, like, "This will be good for you because blah blah blah". You know, nothing like that. She didn't use any tactics to influence my decision at all. It was very – read it, you can do it, or not, doesn't matter either way. (Corinna)*

Overall, it was clear that despite the pressure on recruiting staff to invite participants to take part during their pre-operative appointments (see Section 5 below), this was handled with sensitivity and care, at least in the case of those who consented to take part in the Project. It must be remembered that we were not able to interview people who had been approached but decided not to take part.

### **3.5.1 Reasons for participating**

Participants described taking part in the Project for various reasons, including:

- to find out more about their own or a family member's health
- to find out how their children or grandchildren might be affected by their own health condition
- to help others in the wider population
- to contribute to future research and innovation in diagnosis and treatment
- to give something back to the Health Service that had looked after them.

Participants often expressed what appeared to be genuinely positive feelings about the Project. The language and tone used suggested feelings of excitement, pride and even duty in taking part, as there was a recognition that existing treatments were based on people taking part in past research projects. Some participants also wanted to give something back to the NHS. They felt they had already benefited from others being involved in medical research in the past and now it was their turn to help future generations.

*Well it sounded like a sort of big project. Sort of an ambitious one, so something that would be influential, not just a tiny thing ... to me, yeah, it sounded useful. The fact that I might get extra screenings was a plus. ... And it's almost giving something back isn't it [laughing]. In a setting where you are, well receiving free health care from the NHS basically, and yeah, returning something to it. (Corinna)*

Kristina said "I was quite keen to participate because it'll benefit wider society. It'll – and it's nice to be part of that, as well, to think well, I'm one of those hundred thousand." While Betty described participation as vital:

*In general what is your attitude to the idea of taking part in medical research?*

*Excellent because it's vital isn't it. And I appreciate that it's vital that people co-operate and, and that's why I want to do it. Yeah.*

*Ok. Vital, what do you mean by it?*

*Well, if we didn't co-operate no one would find out. I mean if we want to be helped with health conditions they need to know more and more of where things start and what it's about. So that is vital. I think it's very important. (Elsie)*



There was thus a sense of pride and satisfaction at being part of the 100,000 Genomes Project, of being ‘a pioneer’. Elsie felt that her reasons for taking part, as well as helping her daughters and family, were in part because she “would like people to know that it’s possible to get to 85 and still be interested in everything”. Some participants described feeling they were playing a special role in something bigger than themselves, and potentially ground breaking for humanity. Jenny, for example, said “my having cancer can help the process of cancer being cured”. This was reinforced by a belief in the Project’s ability to lead to real and tangible improvements in diagnosis and treatment of rare diseases and cancer for future generations.

Some participants were interested in research, biology and genetics more widely, and this motivated them to take part. A few people had taken part in medical research (trials) in the past. Ruth had taken part in a drug trial when she had first been diagnosed with lymphoma and said, “As soon as I hear the word ‘research’, I’m all for it.”

These positive general motivations for participating were often easier to articulate than other reasons more directly related to individual and family health, such as finding out if their condition was genetic; getting more information about a rare condition; assessing the likelihood of developing other diseases in future; and discovering whether other family members might be at risk.

Molly was interested in where her condition – dilated cardiomyopathy – had come from because neither her parents nor her siblings had it:

*I was six weeks old when I got diagnosed. And we just never knew where it came from. So, we’ve got no one else in the family that has got any signs of cardiomyopathy at all. ... So, yeah, it was just one of those that it’d actually be really nice to, to know where it came from, especially for my own family planning and things like that. .... So, yeah, it would be, it would be good to know not that it would put me off but I think it would be nice to know.*

Corinna, who was diagnosed with endometrial cancer, thought she might get “extra screening” by taking part. Carol, whose daughter’s genetic condition had not yet been identified, felt that it was worth taking part as a genome sequence might provide the answer her family had been looking for. Jane had spent years while her daughter was young trying to find out why her daughter’s hair would not grow. She hoped the 100,000 Genomes Project would provide the answer.

*And that’s why I used the Genome Project. It was – I have other members of my family that have dislocated joints and bendy joints, and want to go down the route of having children. And if I can find out – because I’m the only one in the family that’s got this condition. I had a Granny that had a muscular disorder, but in those days they didn’t have EDS [Ehlers Danlos syndrome], and they didn’t know about it. So, I’m the only person that’s displayed any symptoms, so we’re trying to find out if it’s me that’s started it, or if it is actually in the whole family, in which case the other members of my family need to be careful when they have children, and how they look after themselves. (Lucy)*

In this extract Lucy describes ‘using’ the Genomes Project and it was apparent that several rare disease participants had taken part in medical research in a quest for answers over the years, both for themselves and others.

*And what do you think the potential benefits are?*

*Well the potential benefits are they actually isolate one of the defects that I’ve got which is linked to mitochondrial disease. And that would almost certainly help my position from an understanding point of view. (Sheila)*





Cherry has two rare genetic conditions. She said, “the changes in the understanding of my condition over twenty years, I was diagnosed when I was four. I’m 24 now. Changes are really huge.... another ten years they could find out even more, then it’s only to everyone else’s benefit, as much as mine”.

*You know, we’ve done this 1) to get an answer, hopefully, but we accept we may never. And our main reason for doing it was so that no other family goes through what we have. We just hope that if they do find something at all – be it this year, be it ten years, be it fifty years in the future – that they can say, “This is what’s going on”. And another family won’t have to go through what we’ve been through. I think we’re resigned to the fact we may never ever get an answer for him. But we, we kind of want to help advance medical knowledge so that other people don’t go through it. (Sue, mother of son with an unnamed rare disease)*

However, while participants saw the benefits of receiving results and additional health information (i.e. secondary findings and carrier testing), this could raise challenges and difficult emotions for some. While some “wanted to know” about future health risks, they also accepted that other family members might prefer not to know. As Sue reflected, “Do we want to open this can of worms?” Participants who were parents described feeling guilty about their children having to go through more tests, and children sometimes worried about their parents feeling responsible for their health problems if results showed that their condition was inherited.

### **3.5.2 The consent process**

People were asked to give their consent before taking part in the 100,000 Genomes Project and were encouraged to discuss the risks and benefits of taking part with a member of the health care team or family members. Where possible people were given as much time as possible to look over the information and consent form before they decided to take part, although as we detailed earlier, some of the cancer group were consented and recruited on the spot at pre-operative consultations and therefore had less time.

Consent giving varied in where it took place. Many participants signed the form in hospital after a face to face discussion with a member of the health care team. Some participants were invited to an appointment with the genetics team at the hospital to sign the consent form and have samples taken while a research nurse travelled to gain consent and take blood samples from one family.

The consent form contains a series of boxes which participants were required to read and initial. Some participants found this complicated and talking through with a medical professional helped to put the information into layman’s terms. Others felt able to complete the paperwork without a health professional present.

The process of consenting to take part and having samples taken for the Project – signing a form and giving samples of blood, saliva and possibly tissue (from a cancerous tumour) – was often described as straightforward. Most participants were content to trust that the processes for taking consent and samples had been carefully thought through.

The amount of information participants wanted at the point of consent varied. Some read the information sheets thoroughly while others chose not to. A few participants felt that more or different information would have been helpful. There was a view that the written information provided to participants was not drafted with lay people sufficiently in mind.



*The actual materials that are sent out, the information sheet, it's all very jargony and it's all very, it's worded like a lawyer and it's difficult to get your head around first read and it's quite, it's quite, quite a lot to read. So, I think that could be sort of dumbed down a little bit. It's the way it's worded I think needs to be looked at because it's not for, for everyone. But they did a good job at, you know, talking us through each, each bit and so we made sure we definitely understood what they were saying. (Molly, daughter with cardiomyopathy)*

Some described re-reading the material many times. Others relied instead on face-to-face communication with health care staff who told them about the Project.

*Jane: I think we wanted more information about how they were going to do it.*

*Helen: Yeah.*

*Jane: Rather than how it would affect us, and what could happen. We were more interested in the —*

*Helen: Yeah.*

*Jane: – mechanics of what they were actually going to do. I think, and when they sent us the additional information, there was quite a lot of it. So, it was quite a big bulky document. And we all had busy lives, and sitting down and putting a lot of time and effort into reading it all. Although we did between us, I'm fairly sure we did read it all. But it was sort of was one extreme to the other. So, sort of overly basic on the, with the basic form, and then this really thick bulky form full of technical terms. (Helen and Jane, rare disease)*

*Do you remember much about what information you were given about the project?*

*Not really, I barely. I had enough paperwork to read. Once I had the operation I just put it all away anyway but it takes a lot of reading you know what I mean. Part or half day I spent what I was supposed to read through. (William, prostate cancer)*

*Participants made allowances for the density of the information and some thought it was clear, "self-explanatory" and they understood the necessity for such detail; "you have to understand what you're getting into". (Kim)*

Others were more puzzled at the amount of written information they were given and the number of consent questions in the consent form, as Helen reflected.

*I think they were very detailed, the consent forms. And I was surprised how, just how detailed they were. And that – to me, being part of the Project, some of the questions they asked 'would you be happy to share this information?', so would you be happy to share this information with the people on the Project? Well, I wouldn't be there if I wasn't happy. But then, part of the rules and regulations that the researchers had to follow, probably that you did have to sign for that. I did, so I was just quite shocked really that, how much consent that you did have to get for each individual little thing .... I think the only thing that I would've been concerned about, would've been about my personal details being in a public domain. But provided that they were only being used by people in the Project or people using it to – in furthering, serving medical research, then I was happy with that.*

The quality of face-to-face communication was key as participants reflected back on the time and attention staff had given them. Several participants recalled that the person taking the consent spent a long time talking through the form with them,



carefully explaining to check that they understood what they were consenting to, with opportunities to ask questions. Some participants recalled being given contact details in case any further questions arose. Again, participants demonstrated an understanding that it was important to take the time to gain informed consent.

*I think generally when you get [consent] forms like that, as a parent you kind of already know that you will be asked those kind of questions anyway. And if, generally if you're enrolling your child into something that's, that's going to be quite a big thing – like through hospitals, and elsewhere – you know that you're going to have to give kind of that kind of data out. So, I was quite, yeah. Once they explained it back, it was understandable. Yeah. (Karen, daughter with a rare disease)*

*And that – you know, and I was sort of getting a bit of irritated, because I do loads of ethics forms in my job. .... So, they read everything out to me, and checked my understanding all the time. And they said the same things in different ways to further check my understanding. So, it was very thorough. Yeah. They didn't just say "Sign here." [Laugh]. (Jenny, ovarian cancer)*

Again, it has to be borne in mind that the participants in the current study had agreed to take part, so others who did not agree to take part might have had poorer experiences when approached to take part in the Project.

A few participants had participated in research before, or had worked in, or had family members who worked in healthcare or scientific research. These participants tended to take more interest in the quality of the information and processes. They were more likely to want to do their own research about the Project, to fully understand their rights and choices, and to consider the possible outcomes of participating, whereas participants with little background knowledge of scientific research appeared to be happier to take things on trust. This could extend to signing the consent form without looking through the paperwork in detail. This was more common among cancer patients for whom participation coincided with operations to remove a tumour which they wished to expedite. Participation in the 100,000 Genome Project was of less importance to them in that moment than their treatment.

*Well I was just waiting to go in for my operation to have my right breast removed, and a lady popped up before me and said, "Would I agree to take in this study, take part in this study." And I said, "As long as it doesn't involve needles I'd be delighted to." She said, "There will be needles, but that'll all be done when you're having your operation. I will take samples and blood, and things." I said that would be absolutely fine, I'm very happy to take part. So I signed the form, and it all went on when I had my operation, and I knew nothing about it. (Joanne)*

Some of the consent process is mandatory while other sections are voluntary such as finding out about genomic changes that may cause an increased risk of certain genetic diseases. Some participants consented to everything. Lara, who had breast cancer, for example, talked about 'embracing' it all:

*If you are going to take on this trial you embrace it totally. You don't do a little bit of it and not the other bit of it. So, if you are going to do it you do it as a whole issue.*

*Ok. But you have no concerns with sharing the?*

*No, no, no. You again, you know, it's not going to be broadcast that it's me, is it [laugh]? So as far as I am concerned it's fine.*



*Ok. So there are no worries at all?*

*No, none.*

Others were more selective in their engagement:

*I think there was a box you could tick to it. It was either a yes/no, or I think it was – you know – that you'd consent, I think it was. And it was – some of them I, I hadn't got a problem with at all. But there was a couple of them that I wasn't a hundred percent happy with. Which I put down that I would only do if I consented separately to those. Yeah. (Cherry, Kartagener Syndrome)*

The interviews with Project participants took place between December 2015 and September 2017. During this period, the Project's consent procedure for participants changed. In early 2016, an evaluation of the consent and patient documentation was commissioned by Genomics England which reported in late 2016. This led to the consent form being shortened and simplified, with less technical language (NW Coast NHS Genomic Medicine Centre 2016). As the findings reported above show, despite some criticisms, participants were generally not too concerned by the materials or the process. There was acceptance that the process needed to be formal and detailed. Most people interviewed took large parts of the materials on trust and some scarcely read any of the detail.

### **3.5.3 Providing samples**

Participants typically gave blood samples in the hospital. Cancerous tissue samples were taken during a planned operation while the person was under anaesthetic, and did not involve a separate procedure. Blood samples were taken either during a pre-operative assessment and operation or by appointment at the genetics centre of the hospital. Liz was unclear whether she had given a blood sample in addition to a tissue sample during her cancer operation:

*They just said that some of the tissue would be taken, probably. And then maybe some blood tests. Now, I don't remember any blood tests but I think they may have been done while I was having the operation, so.*

*Right. Yeah. So you gave a sample, or you think that the sample —*

*I think that's, I think so. I think a blood test was. I think she said to me that that would probably, that would likely happen while, while I was under the anaesthetic. So – I mean you obviously don't know about it so [laughing].*

*Yeah. And in terms of the sample, you said about tissue?*

*Yes. I think that she did tell me that that would be going to the lab, you know. Some obviously goes to the lab anyway, in the hospital, but then some would go over, wherever.*

*And how do you feel about that? Sort of donating, or obviously it was tissue from the womb?*

*Yeah that's – I don't have any problem with that at all. I think that's fair enough. You know. You want to find out things then you've got to be able to have the process of being able to do it, haven't you?*

This extract again highlights the uncertainty participants expressed when talking about their experiences of taking part in the 100,000 Genomes Project. Liz was not



sure exactly what samples she had donated or where these samples would end up. 'Some would go over, wherever'. At the same time, she was unconcerned about not knowing and it was arguably an artefact of the interview process that some participants were even thinking about the precise nature of their involvement.

Kristina experienced a 'mishap' when giving her blood sample which meant she had to go to a different part of the hospital to give blood after her operation. Again, she was mild in her criticism of this, describing it as 'a bit annoying':

*That was a little bit unfortunate. Well they were supposed to take the blood sample at my pre-op, but my breast cancer nurse forgot to refer me. ... So, I then arranged – the breast cancer nurse arranged another – on the morning of my operation, that they would come to the day-case unit and I would sign it there. And that was fine. And they took tumour samples I guess, from the operation. And they – after the operation they tried to take some blood from me while I was still under the aesthetic but it didn't work because I was so dehydrated. And then they had to try again during my recovery. And I became really ill. That was a bit unfortunate. It was just a mishap, because would it have been done at the pre-op it would've been fine.*

*Yeah.*

*That was the only downside that was a bit annoying. And then having to deal with the stress – not much of a stress, but you have the operation and then you have to, have to go to nuclear medicine.*

The amount of blood taken varied (from one phial to six or seven phials) and some participants were surprised at how much was taken. Kim and Andrew had five phials of blood taken which seemed a lot at the time. Molly said, "I mean it looked like they were taking quite a lot but it was just a lot of little tubes, so it looked like a lot when you put them all together but no it, it was all right. It was just a blood test really." Other participants found the process unsettling.

*The only thing I didn't like as I said to you before was getting phial after phial of blood. I said, "Hey you've got about an armful now" and that was beginning to be a little bit stressful to me when the needle was in for a very long time but there you go. It was over and done with. And I understood that they needed the blood for different places for different reasons to check, so all in a good cause. (Elsie)*

Joe, whose tissue sample was taken during his colonoscopy felt that giving a tissue sample was very straightforward and he would happily donate more samples if needed.

The consistency with which participants excused discomfort, or the disruption the process could cause, as we saw above with Kristina, is striking. In the following extract, Sue describes her partner fainting and the struggle they had trying to get her son's sample, with only a minor admonishment to those involved about better forward planning:

*Weren't really sure of how many blood samples they were going to be taking. And actually it's a lot [laugh]. So, you actually take about six or seven bottles of blood. Which is fine from an adult, and my husband unfortunately did pass out while he was having his taken [laugh]. Because he just wasn't expecting the volume I think that they were going to take. But it was very, very difficult to get blood out of my son.*

*Mmm.*

*Who is kind of known to have venous issues as well. So, I think again, just having that understanding of a family that actually you're likely to run into*



*problems here. And it meant that we had – end up having to hold him down for about forty to fifty minutes, to get this blood. Because it was so important that we got it.*

*Mmm.*

*But you know, we just thought that with a little bit of forward planning that might have been avoided.*

That the tissue samples were taken during operations that would have taken place anyway and generally while they were unconscious meant that the cancer participants tended to be quite vague and unconcerned about the details of this additional process. Josie and Suzannah were uncertain what had happened but were unconcerned in the following extracts:

*It was very easy. Any donation I had to make of blood [sic] tissue was very easy because the tissue was taken during operations when I knew very little about it. And they were taking tissue anyway. .... The blood samples, I believe, I probably had one additional blood sample taken during my pre-op. So, whether that was for the Genome Project but I was having blood taken anyway. (Josie)*

*Then I went for the results of the biopsy and they told me that I had cancer. And then I was given the form with all the, the details, and we went through it all, and I initialled it all. And that's how it – and I said yes that I was obviously, would do it. I didn't know really – well I know I initialled everything, but you don't always take it all in do you at the time [laughing]. So I wasn't absolutely sure what it would entail, if anything. (Suzannah)*

### **3.6 Data sharing, data protection and trust**

The 100,000 Genomes Project has data protection systems in place to protect the information of people who take part. The personal details of people are removed and replaced with a unique code. These de-identified data are, in turn, kept in a secure data centre and researchers who want to access these data have to have their application approved before they can have access ([www.genomicsengland.co.uk/the-100000-genomes-project/data](http://www.genomicsengland.co.uk/the-100000-genomes-project/data)).

Participants were generally confident that their data would be kept safely. This included confidentiality and strict rules on data sharing. Trust in scientific research procedures, research ethics procedures, data protection processes and in the NHS were key factors in assessing risk. Most people trusted the health professionals who invited them to participate and trusted Genomics England to keep their data safe and this was a factor in them agreeing to take part. Cherry said she was trusting Genomics England with “my blood, my DNA, my heritage, my genes, my family tree.”

Even where people did not have a clear understanding of the data protection process, trust in the institutions of the NHS and Genomics England, seen as reputable organisations, replaced their need for detailed knowledge. Kristina, for example, said, “My information is in safe hands”. This trust was sometimes generated through personal experiences of data protection policies, but more commonly because the Project was government-commissioned research and run through the NHS.

Knowing that the data would be de-identified was particularly important for people. De-identification had multiple benefits: it assured confidentiality; and reduced the likelihood of third parties contacting them (for example, to try and sell them new treatments).



*So, somebody, somewhere has, has the secret list with names next to numbers but that, that is held securely and not shared with any research establishment or third party. And indeed the data is then, you know within a pool of data of course and but we are not separately identifiable to, you know, anybody who is using the data. That's the way it's been explained to us." (Richard, Retinitis Pigmentosa)*

For Mike, the de-identification process meant that he had no concerns about the use of his data. He referred to his own experience in explaining how commercial companies are not interested in individuals:

*In that I know that the information is there, used. It tends to be, it is used just purely for the data purposes. Looking at it from a similar perspective of how I've done it previously in work, is that all you're interested in is the results that you get from it. You don't care if it's Joe Bloggs, or whoever. You're looking for the trends to find out why. Yeah.*

However, there were some inconsistencies or ambivalence in the discussions on anonymity and data sharing. For example, Josie raised a number of issues in the following extract:

*And you hear about people, you know, being able to access information. I honestly think there is nothing in my information that, you know, that is particularly worrying to me. I wouldn't want anybody, everybody to have my information but actually, you know, I do have breast cancer. I've. [laugh]. You know there's an awful lot of people who know an awful lot about me anyway. ... And I think the fact that it is research that's you know, ethically people who do research have to jump through so many hoops to get approval that actually probably it's one of the safest methods of having your information out there anyway. So, it, it doesn't worry me particularly. I think we're at risk anyway and it doesn't put me at any more risk. I don't think.*

She considers the risk to herself of her information being shared, including the reflection that much is already known about her because of her cancer diagnosis. She then shifts to the protective layer provided by research ethics committee scrutiny, ending with the reflection that participation in the project will not increase the risk she already faces.

There were also some conflicting views among participants about data sharing with commercial companies. In the first extract, Elsie emphasises her trust in Genomics England, while clearly stating her lack of trust in commercial companies:

*And do you see any kind of potential risk or pitfall in taking part in the Genome Project?*

*I hope not. I mean I'm giving it because I trust the people who are going to look at this and say, you know, make up their mind about me and what's happening to me. I trust them not to give this information to the wrong people whoever they may be. .... I trust the NHS to keep, to keep things within the remit of, of the Project.*

*OK. So, the wrong people would be people who have other interests?*

*Yes, of say, pharmaceuticals, somebody who might want to persuade me to spend my good money on medication that really is not possibly required. I, I guess I don't trust the pharmaceutical industry.*



In contrast, Cherry demonstrated pragmatism in her consideration of the commercial use of data perhaps because she has a complex condition that may benefit from personalised medicine based on genomics. Her trust in the Project is underpinned by the resources Genomics England has to protect data and information:

*I believe that they've spent quite a few million pounds designing a building to hold the DNA. [pause 3 secs] It's being run by the government. As far as I'm concerned it's for medical benefits, and medical benefit only. I don't mind pharmaceutical companies, as far as they're developing drugs to try and cure it or to manage it, or – cure is a weird word to use, but better drugs to manage it. Because people with EDS are like completely different to normal people. We react so differently to medicines and, and even eating food. Everything normal is not normal when you have EDS. Your body acts differently. So [um], I trust them, that it's going to be used for that. And I understand that they've spent a lot of money to protect it.*

Josie was also pragmatic about data sharing and commercial companies:

*It does, it does state that results of the research will be used commercially. But again that's what this is all about. And there is no use doing some research in genetics if then the companies that can do something about the treatments don't get that information. So for me that was part of the process and part of the, part of being involved and the purpose of the study. So, I think if you consent to being part of the Genome Project, you have to realise that it will be used commercially. Your information will be used but as part of the group and anonymised and one of the 100,000 people rather than who I am, where I am.*

There was some concern related to commercial companies selling data to third parties who might use the data for the wrong reasons. This largely centred on a concern that participants would be contacted by companies trying to sell them targeted products. There were also some concerns about the effect on insurance policies and whether the guidelines adhered to in the UK would be affected if the data were shared more widely.

*Actually are we going to have to say we've been involved in the study? And is that going to impact on insurance in the future? That that was one of our big questions. Because it's a concern. We've all watched the sci-fi movies and Gattaca and the like, and you think actually are we going to start making decisions based on people's DNA code? So that was one of our big concerns, I think.*

*Yes. And how do you feel they addressed those concerns? What did they sort of say about that?*

*They tried to reassure us, I think. And tell us that you know – there certainly is nothing like that in the pipeline, there's – they're not allowed to use that [for] insurance. We don't have to say that we've been involved in the study at all. (Sue)*

The long-term nature of the Project generated some concerns for participants, in particular, whether data protection laws might change in the future. A few felt reassured that they could withdraw from the Project at any time if they wanted to. Others were not too concerned about the long-term.

*John: I have to say, sort of signing up – I imagined that the data that's created or found from, you know, sequencing the genomes, I imagine that's just going to continue existing. And it will probably eventually become public property. But you sort of imagine if you're giving blood to science, then it's going to get shared around. I mean, that's the point of it, really. And you can't do very much with something if you've got it under lock and key. So.*





*Flo: Mmm.*

*And what about commercial uses? Would you be content for it to be used commercially?*

*John: Well I mean obviously it'd be nice to see some of the royalties first [laughing].*

*Flo: I take the opinion if they can find anything useful in my blood, they're welcome. [laughing] People might find a cure for the common cold in there somewhere. It, it doesn't particularly bother us.*

*John: No.*

*Flo: I think if you're sensible and you think about it, we're not really into the Frankenstein side of things here, are we? You know, that this is more common sense.*

*John: Yeah.*

*Flo: Let's just look at what you have got, kind of approach.*

*John: I mean, from my point of view, I don't really – I don't really mind in a way, if people make commercial use of genetic material, so long as it's clear what's being done with it and it's transparent. And so long as, you know, if somebody's genetic material is being used, then they are compensated, or they are informed accordingly. It makes sense, really.*

*Flo: Communication, really.*

*John: Yeah. But we've not been – we've not been kept in the dark at any stage, have we.*

*Flo: No. No concerns.*

While participants had a good deal of trust in the 100,000 Genomes Project itself, the role of genomics research in the future was something that concerned a few. Although participants appreciated that there were strict ethics requirements for genomic medicine, some talked about wider concerns they had with how genomics research in general might be developed in the future. When Sue first heard that the Project was about genomes, she thought: "you know, the two cloned sheep and things like that, do pop into your head. But I trust that it's going to be used for the right purpose".

Some participants worried that in the future genomics research might be a platform for introducing ethically questionable practices, such as pre-natal gender selection of foetuses, or to reduce the number of babies born with Down's syndrome or autism. There was conflict expressed between a desire to take part in the Project to enable treatments to be developed, for example, for common cancers, and concern about the potential uses of genomic research in the long term.

*That – I think the aim of the project is bigger than the bit that I'm interested in. Because it's looking at genes which give rise to [um] you know, disease like cancer and so on. But I think there are aspects of it about genes that give rise to things like Down's syndrome which I think is problematic. ... I think it's – it's very difficult, isn't it, because there are – there are potentially fantastic medical advances, which could eradicate things which are absolutely horrendous on any planet that you could possibly name, like your 25 year old son dying of cancer. And that would be brilliant, if – if cancer was cured, that would be brilliant. But I absolutely think there's a massive danger of this*



*sort of homogeneity of the population, where anything that's outlying from the sort mythical norm, or whatever, is deemed as undesirable, and can be eradicated. And this is happening with this Down's syndrome test, which I think is hugely disgracefully problematic. So, I think there's a big ethical [um] debate that hasn't properly been fully realised, because people mix up disability or difference with disease. And I think they're not the same thing at all. Absolutely not. So, I think it needs – I don't know, I just wish that my contribution had only been about cancer. That, that was the only conflict I had. (Jenny)*

*And if genetics start to mix with the amount of boys, the amount of girls – because somebody's got two boys and they want a girl desperately – I don't agree with that. I don't agree with that. Because I feel we're given what we should have. And I feel this also about my illness [struggling against tears]. Because I am a very, very strong person. And I believe that these things are only given to people that can cope with them. Yes, a lot of us need help along the way. But the bottom line is, it's you yourself. But as far as genetically modifying babies, or anything like that. No. I think genetics in that respect should be left alone, and leave it to nature. But as far as genetical work towards illnesses, I'm one hundred percent behind you. Yes. (Ruth)*

Much of what participants discussed was conjecture and it was clear that the reputation of the NHS was a key factor in reassuring participants about the use of their data over the long term.

*Jane: Yeah I, yeah I trust, yeah.*

*Mike: Well I think we can only trust that. I mean, I've not inspected their systems and their processes and procedures so all there is left is trust actually. And that's the balance that you have when you enter, you know, do a project of this nature is that there is a line where you can only get so far and then it is, it does become a trust barrier that you go through. But I think ...*

*Jane: I think the desire to want to do good with it for something good to come out of it is going to be far outweighs the negative thoughts which I have had so far.*

*Mike: Yeah exactly.*

### 3.7 Summary

It must be borne in mind that the findings reported in this chapter relate to participants' experiences between late 2015 and late 2017. The Project continued to evolve after that period. It is also important to recognise that these are the reported experiences and views of people who had chosen to take part in the 100,000 Genomes Project. Non-participants could have had different, potentially more negative views on a number of the issues described above.

The cancer and rare disease groups were distinctly different in their prior experiences and motivation in taking part in the Project. The latter commonly had longstanding experience of their conditions and established relationships with consultants and other health professionals. Most participants in this group had a strong desire to know more about their disease and often had considerable knowledge of genetics and their particular disease. In some respects, they had a 'vested interest' in taking part in the 100,000 Genomes Project to generate greater understanding of their own condition and the implications for other family members and future generations. Cancer participants were mostly at a very early stage in their illness experience and their focus was very much on their immediate treatment. This group did not typically



have longstanding relationships with health professionals or much engagement with, or interest in, medical knowledge. Only a few cancer participants expressed an interest in knowing why they, in particular, had developed cancer and what the Project could help them learn in this regard.

The timing of the process of taking part was also strikingly different between the two groups as the cancer patients typically had little time between being invited to take part, which often happened during a pre-operative assessment, and their surgery when the Project sample would be taken. This seems to have been mitigated by the fact that participants were asked to donate a section of tumour, diseased tissue, which was going to be removed regardless of their participation in the Project. The rare disease group were invited via different routes, for example, by email or letter or at a yearly appointment, and had time to think about whether or not to take part. It is important to again flag that we were only able to recruit participants for interview who had already agreed to take part in the Project. We do not know whether the differences between the two groups extend to those who decided not to take part in the 100,000 Genomes Project.

There was general concern about the lack of communication from Genomics England once samples had been donated. This ranged from slight pique about not being contacted soon after donating a sample to have their participation acknowledged (as would be the case, for example, with blood donation), to longer term disquiet about not hearing anything. Participants had not received results at the time of interview and there was frustration from some about this delay (the current study period was extended twice in an attempt to be able to interview participants who had received results but to no avail). Being kept informed with a brief newsletter or email was clearly important to many participants and there was some reflection on their part that they had experienced better communication in other medical research, such as biobanking, which Genomics England could learn from.

Despite these concerns, there was a markedly positive attitude towards taking part in the Project and some participants described the pride they felt in being part of potentially transformative work. While some direct benefits to participants were mentioned, such as additional screening or the possibility of finding out whether a rare disease was inherited, there was a strong sense of duty related to people's participation, of 'giving back' to the NHS.

There was also a high level of trust demonstrated in the Project which appears to relate to strong confidence in the NHS 'brand' and the fact that the Project was a publicly funded government initiative.

The strength of this trust can be demonstrated by the lack of concern or even interest some participants expressed in the consent process, and only slight concern raised about the long-term use of the data. Participants were clearly reassured that their data were in safe hands and had been anonymised effectively. There was generally, if not exclusively, pragmatism about the commercial use of their data. The casual uncertainty, even confusion, some participants expressed about the details of the Project further demonstrates their high level of trust. Participants did not know or understand aspects of the Project and appeared comfortable with not knowing which has implications for how much information is provided.

Finally, two ethical concerns were raised: the potential for technological developments based on genomics to lead to the termination of foetuses with certain genetic abnormalities; and concern about receiving results related to familial genetic risk and what this might mean for wider family members who had not consented to finding out this information.



## Chapter 4: Focus groups with members of the general public and people with specific conditions

### 4.1 Characteristics of the focus groups

In some of the groups, participants already knew each other (people with rare diseases group, people with common cancers/cancer patient advocate group, adults with learning disabilities group) which may have led to more fluid discussions at the beginning of these focus groups. The young people group took place the week after a documentary ‘A world without Down’s Syndrome’ had been shown on television which some had watched and this influenced their discussions. Knowledge of the 100,000 Genomes Project varied across groups. Participants in the cancer and rare diseases groups had an interest in genetic research, and some had been to talks specifically about the Project, so were well informed. Three family members in the rare diseases group were taking part in the 100,000 Genomes Project. The young people’s group had learnt about genomic research through biology lessons and TV documentaries but had not heard specifically about the 100,000 Genomes Project. The other groups had a vague knowledge of genomic research and the 100,000 Genomes Project derived from the media. Billbeer in the BAME women’s group said, “I think I have heard something, but I have not paid attention to it. Something on BBC channel.”

Focus groups took place over a two-year time period and so public knowledge of genomic research may have increased over this time and influenced the discussions.

### 4.2 Perceived benefits of the project

Participants were enthusiastic about the benefits that genomic technology could offer the individual and future generations, and its ability to advance medical science.

#### 4.2.1 Benefits to the individual

There was agreement across the groups that there were benefits in being able to identify people’s risk of developing a genetic disease. Improving diagnostics was seen as a key benefit across the groups, in particular, being able to diagnosis conditions when people were younger. David (learning disabled adults group) said the project could help to diagnose conditions similar to his own, in childhood and so enable treatment sooner.

*Like I said earlier, I said, I’d love to know how, because it says sometimes a lot of the conditions people get through the family. The family, when my mum and dad and I said, I said, “The only problem, I’m the only one in the family it got, I’m the only one in the family. And I got, I’m the only one in the family got Dundee Walker Syndrome. The only problem, I know what Dundee Walker Syndrome what the symptoms and not, not heard of any medical research on that. Because wondering with any medical research on that kind of stuff. What it’s about and how could it get better?”*

Emily (young persons’ group) talked about the benefits of genomics research to identify allergies in children to prevent anaphylactic attacks. Tamsin, who was born with sickle cell disease, thought it would have been useful to have known she had a risk of developing multiple sclerosis before waiting for it to progress. Participants who had family histories of cancer, heart or other conditions saw the benefit of identifying risk early to facilitate preventive action. Those with specific genetic diseases within their family explained that genomic technology would benefit them directly when deciding whether to have children.

Another benefit that participants discussed was the value in tailoring treatment to the person. Targeted cancer treatments were considered by all groups to be beneficial both to the patient and to the NHS, by reducing costs. Barbara (cancer group) explained how targeted treatment could have helped her late husband rather than a series of chemotherapy treatments which weakened him.



*Barbara: Yeah, but if I could just take up what [female participant] has said. I mean that's what happened with my husband twelve years ago. Because of a contact we had, we knew that there was a test that would tell whether you're responsive or not. But it wasn't administered so he went through three round of chemo and was the two out of three that don't respond and that weakened him.*

*I: Yeah.*

*Barbara: Now, you know, if we'd had that test, he wouldn't have needed to do all that.*

*(Common cancers/cancer patient advocates group 5)*

Participants in the BAME people group were in favour of moving away from “a one size fits all” way of treating people and hoped targeted treatment might help to tailor medicines for black and minority ethnic groups.

*RM1: My concern was about what I felt they have this sort of one size fits all situation in treating like say people from the Caribbean or sort of black people. We are different, in a good way. For me it's always why is it that I go and they say, this might be wrong with you and they are giving me this medication and it might not be for me or whatever. That has always been my concern is, why is it that it's always a Eurocentric view that is taken on board. It always concerns me. Quite often, the story goes that people being treated for that and it was the wrong medication. Oftentimes, it's too late. I think they need to gear it into the cultural differences and all of that need to be taken into consideration in meting all treatment to people. (BAME people group)*

In addition to the benefits to the individual and to medical science, participants also agreed that genomic research would benefit the NHS by reducing the cost of treatments, diagnostics and long-term support for people with chronic diseases.

#### **4.2.2 Benefits to future generations and advancing medical science**

Participants recognised that although genomic research had come a long way in the last ten years, it was likely to be future generations that would benefit the most from it and so collating research data to contribute to the advancement of medical knowledge was important. Michael (general public group) reflected this perspective when he said, “Personally, I'd be happy if I felt that it was giving some benefit for future generations. Wouldn't worry me too much.”

Participants in the BAME women's group explained why looking at the long term, bigger picture was important.

*RF1: I think it's great for future generations. At the moment, there's lots of ethical issues for us as individuals. If you look at it long term, I think that —*

*RF2: Pave the way.*

*RF1: We have got to start somewhere haven't we? If there is no starting point then there is no end point and things will go wrong in that journey from beginning to end, always.*

*RF2: There is me saying I want to map my own and things could go wrong there —*

*RF1: If you look at cancer research, the headway in cancer research has been*



*huge and treatment has changed and it's all through collation of data, isn't it?  
(BAME women group)*

There was recognition that genomic research in England was, “at the forefront of medical science” and initiatives like the 100,000 Genomes Project needed people to take part and donate their samples. Altruism was evident in both older and younger participants. Tom (young people’s group) felt he would be contributing “towards the advancement of mankind. It gives purpose to your life.” Iris (BAME people group) said, “I am not bothered. If it’s going to help other people, it’s fine by me. I am an old woman now. What else is there to do?”

*RM1: “Well, I think – I mean, there’s a sense of altruism as well, that you want to offer your bits towards medical science. In that sense, I think that’s again down to personality. Some people aren’t interested, other people are. I would be. So any tests that I’ve had and disclaimers that I’ve had to sign said yeah, you can use – you can use any information that you have, for your research. Which is something that has happened to me in the past. So, that’s fine. But [um], yeah. I think it’s just, just important to kind of know, you always tend to feel that – you know – you are contributing towards something. And – you know – gene therapy could be – you know – not far, that far off. We don’t know. And if there are ways of kind of eradicating life-limiting diseases through some kind of gene therapy, first we need to work out – I don’t know enough about it, but the genome sequencing. And so obviously – you know -they need people to help with this. (General public group 1)*

## 4.3 Positive factors about the project processes

### 4.3.1 Trust in the NHS

Participants across all groups talked positively about the fact that the NHS was leading the Project. There was trust in the NHS to safeguard people’s genomic data. Participants felt confident because the Project was a large scale project run by a non-profit organisation which had experience of looking after patient records and confidential medical data. Being at the forefront of medical science and in the public eye gave participants confidence that the project would be sufficiently controlled and regulated.

*RF1: But I think if it’s proved to be for the greater good, you know, and it’s not too intrusive on you or, you know, your loved one, I think most people are up for it if they think it’s safe and secure. And if it’s in the NHS...*

*RF2: Mmm.*

*RF1: ...whatever’s wrong with the NHS or whatever coming to on the NHS is ‘we think they know how to look after us...’*

*RF2: Yeah.*

*RF1: ...and by and large they do.*

*RF2: Yeah.*

*RF1: You know, including our data I think would be.*

*RF2: People trust the NHS.*

*RF1: Yeah, no – no, of course you do. Me and you grew up on it, didn’t you?*



*Moderator: What is it about the NHS that's so trustworthy?*

*RF1: Well I'm not so sure, actually I think generally it does keep pretty good care. When you think how many millions and millions of treatment sessions, visits there are in a year. It doesn't often lose people's information, if you put it in actual context. (Common cancers, cancer patient advocacy group)*

Some participants in the rare diseases group and learning disabled adults group said that personal experience of the individual hospitals involved also influenced their trust and confidence in the project. Where participants had positive experiences of care, they felt more confident in the project.

Participants in the rare diseases group talked about factors about the NHS which built their confidence and trust in the project:

*RF6: You can only go off your own experience and I, and I've worked in central government and local government and, you know, I know they are not perfect and things, but I do know they are under major scrutiny all the time. And if they are choosing to spend this money at the moment on such a big initiative, they are going to have to be qualifying that and they are going to have to be squeaky clean and, if they are not, then it is going to be a big problem. So, I sort of, I think that does give you comfort, but I wouldn't trust a private initiative to do it because I think they'd be doing it, they only do something for themselves.*

*R5: Saving money*

*RF: Saving money or to*

*RF6: Yeah*

*RF: Commercial. I mean, I know that in a way this is also doing that*

*RF6: But you would hope that there would be some integration and central sort of objective around it.*

*Moderator: Ok so [participant's name] just mentioned confidence and you were talking about faith in Cambridge, would you maybe say little bit about what you mean by those terms and what made you have this, not what made you have that but what do you mean by those terms?*

*RF: I think it's trust isn't it.*

*RF: Yeah it's all about trust and it's about*

*RF6: It's trust. It's what you know.*

*RF: You're not going to be completely*

*RF6: There's not many options to go with that you don't know is there really that you would trust outside of a*

*RF: About how comfortable you are trusting them with your data and obviously ultimately your money. [laugh]*

*RF6: Yeah and I don't know some of it comes from having been because I think all of us have been exposed to centres of excellence in some sort of way haven't we...*



*R: Yeah.*

*RF6: ...where you see a very. I mean I've had, you know, heart tests throughout well since, you know in the last 20 years that then when I went to, you know, the cardiomyopathy specialist unit were very different. And it was very different and you become exposed to different things when you go to what I call a centre of excellence and that I think instils massive confidence when you are dealing with specialists like Cambridge or you know the people that you would hope are involved.*

*RF: But then recruitment-wise as well that's got to be a lot more reassuring for people to sign, wanting to sign up.*

*RF6: Yeah, yeah. But you have, I think you have more trust in them, don't you?*

*R: Yeah.*

*RF6: I think it is about trust.*

*(People with rare diseases, group 4)*

Where people had had poor experiences of care, they felt strongly that they would not participate in the project if specific Trusts or hospitals were involved. Simon (learning disabled adults group) explained how trust in the hospitals taking part in the project was vital:

*LD1: I am not being nasty and I'm not being horrible, right. I know what you're saying. I know I'm not like that, right. If it was someone like who right you gotta find out who's been doing the test, right, yeah. If it was [name of hospital], I'm not being nasty, right. I would not go into it. I would not do it.*

*LD2: [name of hospital] don't exist anymore.*

*LD1: But you know what I mean. I'm talking about the Trust, right, yeah. I want something that I can trust and someone like you, you be comfortable with, right. I would not go into someone – I wouldn't go into summat if I know I ain't gonna be trusted and I know it ain't gonna work, yeah.*

Participants in the rare diseases and the BAME women's groups were aware of the smaller commercial DNA tests that are available, but they were sceptical about their reliability. The 100,000 Genomes Project was considered to be more structured and controlled, and so likely to provide more reliable results.

*RF1: And it just surprises me how you've got companies now saying, "Oh we can do this, that and the other." And you've seen deals where you can buy a box from [the pharmacy] or something and you can test your DNA to find out what you're susceptible to but how do they know? Because if, you know, they are doing this massive project*

*RF2: Even experts don't know*

*RF1: If the experts don't know there's this massive project going on to find out all this information how can these stand-alone little, relatively small clinics and companies actually give you the right information. It's just, that's what made me think about there they are saying, you know, by getting all this data you can improve drugs and that sort of thing, which is what it is there for.*





*RF: They'll compare it to a sample, like a standard sample of the population.*

*RF: Yeah*

*RF: You know what I mean? They'd compare it to an average or whatever, you know*

*RF: It just seems*

*R: They wouldn't be as. I, I don't know*

*RF: Specific*

*RF: Yeah, I mean I'm guessing that's how it works. I don't know*

*RF: I have no idea, but it just surprises me how, you know companies can get away already with saying, "This is what we can do." When, like you say, even the, the specialists and the people, the medical professionals don't really know. And, and you know you can let people have access to the data.*

*(Rare diseases group)*

## 4.4 Concerns about the Project

Although there were many perceived benefits of the project, participants also raised concerns. Prominent in each group was the issue of the security of the data and how the technology was going to be used.

### 4.4.1 Security and storage of the data

Security of the data was a key concern across all groups. Participants were aware of the media coverage of data security failings, however, despite this, they still had a tremendous amount of trust in the NHS and the government organisations involved. Some participants accounted for previous data failings by saying that it was usually random acts by individuals that caused data to be unprotected.

Participants agreed that security arrangements needed to be governed and regulated, and reviewed very carefully since there would always be a risk of hackers who could find a way to access the data, however robust the security arrangements were. Transparency was key. John (cancer group) said, "The more we know about what's going on the better really." Participants across the groups stressed that it was important that the public was informed of where and how their data would be stored and how they would be protected.

Keeping records anonymised, so that names were not attached to genomic data, was an important factor in helping participants to feel confident in the security arrangements for the data. Participants in the young people's group explained why anonymity of data was important to them:

*RM1: I think as long as you're made anonymous. Like maybe even though they know who you are, don't put the name on the file. Maybe remember a number, or something like that. And rather than having your name on all the paperwork, if it's made anonymous, I don't think people would feel too bad about it being in there, because then if somebody does find it, they won't have a clue who they were. They wouldn't be able to find them, they wouldn't be able to pinpoint what, what their problem was.*



*RM2: Because hacking has become a lot more common, hasn't it?*

*RM1: Yeah.*

*RM2: Especially, you know, "Oh look, email has been hacked from whoever."*

*RF1: Yeah, but what's someone going to do with information that might say 'oh well [female participant's name] got cancer'?*

*RM1: Well I mean*

*RF1: But if somebody hacks that, that's not going to be the most useful information.*

*RM2: It's a loss of privacy – invasion of privacy, isn't it?*

*RM1: It could be sensitive information as well.*

*RF1: But it could help someone else, like. If you've got all this data stored, and it's like x amount of people have got some form of cancer, then when somebody else finds it, or they say "Oh, I don't know what this is, but somebody else had that similar issue, and we've stored that data and we've kept it there so we can say ah, this could be —"*

*RM1: But then it's invasion of privacy of a person if the other person agreed that they want – I mean, I understand what you -*

*RM2: – sign something.*

*RM1: Yeah, I agree with – but I —*

*RM3: Yeah, if you get them to sign something, that's – that's completely different.*

*RM2: – I agree with, I agree with [female participant], that it would be useful to have it there and see oh this xxx, but I just don't think names should be put to it.*

*RM1: No.*

When data were to be shared with other organisations, participants felt strongly that there should be transparency in how the data would be kept secure. More information was needed about how researchers would access the data and keep it secure. One of the women from the BAME people group explained why she thought there should be transparency in security arrangements when the data are shared with pharmaceutical companies:

*RF4: But that's the thing though, that if there is no way around that because they are drug companies, but they can be transparent about how they use it. Just the same way, I am sure all of us at some point have been online internet shopping and you go on a website and you think that doesn't look secure and I am not going to buy anything, I am going to the shop. There is all the websites where they show you. We've got an encrypted website and all of your details are saved and they don't go past here. We can't see your card details. To me, it's no different. They can, if they tried, show you that this is the level of security that we do. (BAME people group 9)*



#### 4.4.2 Sharing the data

The sharing of data with commercial organisations, pharmaceutical companies, researchers and internationally led to differences of opinion and thought provoking debates. In the BAME people's group, some participants who were willing to share their data at the start of the group ended the group discussion with doubts.

However, for some participants in the rare diseases and BAME people's groups, sharing of genomic health data was viewed as essential to enable pharmaceutical companies to develop new medicines and for medical knowledge to progress. Participants in the rare diseases group discussed why they thought data sharing with pharmaceutical companies was necessary:

*RF1: That was explained that it would be used by people that would make money out of, you know, off of it, as well as people that are doing it for, you know, pure sort of research purposes. So, I think that was made quite clear, wasn't it.*

*RF2: Yeah.*

*RF1: I think as long as it's substantial, you know, you need these pharmaceutical companies to develop the new drugs and*

*RF2: It's a catch 22, isn't it?*

*RS: Yeah*

*RF2: There's always going to be someone trying to make a buck out of it but at least if you, if it's moving in the right direction to developing new drugs or getting some answers that you need then I suppose we're all selfish in that way. But it's like, well, you know, I give you what you need and I'll get what I need.*

*RF1: You kind of, you've got to give the data to kind of hope that it will help develop something for the future which means you can't then sort of hold them to ransom too much, can you, because you want them to have the data to try and do something. You just hope that in the long term that the government negotiates that they don't get ripped off and then the public don't get ripped off in actually trying to get at something that will prevent, because you need it, don't you, to prevent the whole knock on cost of keeping the public alive. (People with rare diseases group)*

Some participants felt that without sharing the technology or the data, genomic research could not reach its full potential, particularly where rare diseases were being researched and there would be benefit in collating more data internationally. They felt the data and the technology should be available for sale to benefit other countries and that this process might lead to reinvestment in health services in England.

*RM1: But if we've got this one package that we can sell to other countries, then I think that's, the commercial arm of that, think it's a great thing because it's going to benefit everybody and it's not like it's the pharmaceuticals are in it to make money for themselves. It's actually going to help other countries as well. I think it's good.*

*RF6: Also, it could lead to, I'm back to investment again. But it could, couldn't it because it will, our people, the scientist people will be leaders in, in that research won't they so hopefully that will generate investment in England. (Rare diseases group)*



Where concerns existed related to data sharing, they were mainly about commercial companies having access to the data which might gain financially from their use or use the data maliciously against people. There was concern from some participants that sharing the data might lead to insurance companies using the information to affect life insurance and other policies.

In the BAME group discussions, two participants felt strongly that none of the genomic data should ever be shared with private organisations and control of the data should remain with the NHS or non-profit organisations. Providing parts rather than all of the data, for a fee, was considered more favourably by some of those who had concerns.

*RM2: Personally, I would say, it shouldn't ever go into private, it shouldn't go into private concerns anywhere in the world. It should be regulated as a non-profit thing. If the companies do want, they can probably purchase or lease or license part of it to research medicines and stuff. But not, you know, it's a whole building blocks of human life that they get hold of now, aren't they? That's what it meant back in 2003, I think I was told.*

*RM2: Yes, I personally think you can't have the private side of the NHS and that and this. You can't. It's wrong. For me that would be wrong. That would be totally unacceptable. The NHS will have to control, I think, and it has to be on the State.*

*Moderator: Can you say a little bit more why though? What is your thinking behind that?*

*RM2: My thinking behind that is that it's going to be one of the biggest commodities in the world, isn't it, around the globe it's going to be the biggest thing. It has to be —*

*RM1: Just clarification. The biggest thing in the world for who?*

*RM2: Medicine. For medicine because it's also NHS —*

*RM1: It's just basically here in England.*

*RM2: Yeah, I know, but these are where they are doing the research and experiments are they not, just a research thing. The building blocks for this Project are here but it's something that is going to be expanded, of course. The whole thing is going to design new drugs and new treatments, where the pharmaceuticals now are going to want to say as to how they want to, what level of power they are going to have in all that.*

*Moderator: The data set that they are going to produce from the 100,000 Genomes Project, it is going to be commercially available.*

*RM2: That is what I heard.*

*RF4: I think that's the thing that I have a worry, but I think it's just my personal opinion, I don't think healthcare should be a privatised thing. I don't think there is one company that should benefit off someone's healthcare or human being and it affects anybody, that's NHS. There is people in other countries that can have their leg fallen off and can't get healthcare.*

*(BAME people group 9)*



Other participants were cautious on the grounds that increasingly parts of the NHS were being run by private companies and so genomic data could be passed to private companies in the future via the NHS, perhaps with people being unaware.

For some participants, there was less concern about sharing genomic data if the data were anonymous and names were not attached. These participants felt their information was personal and sensitive and they would not want their name or address linked to their genomic data when data were being shared. Anonymity reassured them against the risk of hackers or cyber attackers gaining access to their information.

With these concerns being raised, participants felt it was important to ensure that data sharing was regulated and governed, and that consent literature should clearly state who would have access to the data, how data were being stored and what they were being used for. Some participants thought the public might not fully understand who would have access to the data and so it was important that informed consent took place before people gave their samples.

Some participants also felt re-consent was necessary if data were going to be used in new ways not explicit in the original consent process.

*RF: I think – I think you would want to know what that company's going to be doing with my information. And what is their – what is their purpose of having my information, and what do they want to do with it? If I've signed a consent form of one company, does that mean I have to sign another consent form with them, so that my information doesn't get released with them, or would it all stay the same? I feel like everyone's going to have loads of different questions about everything that will definitely have to be answered by that company personally, rather than the NHS, or someone saying it for them. (Young people's group)*

Intertwined with data sharing is the concept of ownership and who owns the genomic data once a consent form has been signed. Some participants felt comfortable that ownership of the data would be passed to the organisation that was running the Project and if their data were anonymous and they were no longer identifiable, then sharing with other organisations was not a concern.

However, unease existed amongst participants in the BAME people group about their personal health data being owned by a private company.

*RF2: That's where I think I have the issue with technology itself is needed. It is something that should have been a no brainer and it's brilliant that now we have the ability as a species to actually do that to go on a computer and de-code something. To have something that's running through my veins, something that creates me and then someone says, "You know what, because I have figured it out, I now own it." and that is almost a commercial way of saying, "I now own you and I know how you work and I know what will work with you and I know what won't work with you. I know what will harm you and what will heal you." How can a corporate body tell me that when it's me. It should be other way around – can we use this? Can we use this to assist you? Can we do that? Is it okay if we do this? Not we now own your sample.*

*RM1: You know nothing. You become nothing.*

*RF1: That is when you literally become a number. It's a fact that that's when you literally become a number.*

*Moderator: [RF2], you asked the question who owns the data. How do you feel it should be? —*



**RF2:** *It should be public domain. Colleagues are saying that it shouldn't be owned by the private corporate companies at all. (BAME people group 9)*

Having an option to withdraw from the project gave people reassurance that if, in the future, the data were used in ways they were not in agreement with, they could remove their data. However, some participants in the young people's group, the cancer group, the BAME women's group and the general public group felt ownership of data was a debatable issue as we live in a culture where personal data are already shared on social media. Some suggested that the general public was not aware of how much personal data are already being shared when they use social media and store cards. In several of the groups, participants believed issues of ownership of genomic data would become less of a concern with the younger generation who had grown up sharing personal data on social media, and in the future, issues of privacy might become less of a concern.

**RF2:** *I think we'd all be hypocritical if none of us could get out our purses and say we don't have a [store] card, or a – you know – [supermarket] card, or this card. That's quite – you know – because we are now in this day and age doing that constantly, giving our data out. You know, once you give that and they're swiping that, they're doing research to find out – you know – what we're buying, stuff like that.*

**RF3:** *Mmm. What we're buying.*

**RF2:** *So, I agree with you. It should be ours to own, but we are doing it the whole time. We're ticking -*

**RF1:** *What if you decide I'm not going to give any loyalty to any brand, I'm going to cut up all my cards, and -*

**RF2:** *You probably wouldn't take part in that sort of study.*

*[laughing]*

**Moderator:** *I know, but I'm just saying – change of mind?*

**RF2:** *But how many times do you click that little box when you're doing something on the internet, because you can't be bothered to read that whole list of "Do you abide by blah, blah, blah." You'd be surprised if you read it, what it's saying. You don't own your data any more.*

**RF1:** *No, I know.*

**RF2:** *If anybody uses [photo saving website], they own all your pictures.*

**RF1:** *Mmm.*

**RF2:** *So it's a bit hypocritical if you turn round and say, actually. Because we all do it constantly.*

**Moderator:** *Okay.*

**RF2:** *But I do agree, it would be good to say "Well actually, I want it back." ..*

**Moderator:** *[female participant's name], you like you're not agreeing?*

**RF3:** *Well I think, I think there should be a proviso that only if you want to, while you're still living, if you want to have it removed you should be allowed to have it removed.*



*RM: I would be surprised if there wasn't that in place, most trials you can withdraw at any time, you're allowed to withdraw from it.*

*(General public group 1)*

#### **4.4.3 Use of genomics technology in the future**

Genomics technology was generally thought to be a very positive development by participants, but it needed to be used with caution and follow strict guidelines. Some participants talked about the “power” that genomics technology had in identifying the “building blocks of human life.” It is therefore not surprising that discussions about use of genomics technology in the future provoked strong reactions. Participants in each of the groups expressed some level of concern about how the technology might be used in the future. The amount of concern varied across the groups.

Participants in the young people's group and the BAME people group talked passionately about how the technology could be used against people, either psychologically through blackmail or to eradicate differences between people or, indeed, entire groups of people. They believed there needed to be caution in sharing the technology with other countries because people might use it for malicious or unethical reasons.

Concern existed in the young people's group and the general public group that the technology could be used to create “designer babies”, or to reduce the number of babies born with Down's syndrome. There was agreement that it would be wrong to use the technology to create designer babies and there was a fine line between eradicating disease and just trying to change or improve a person for cosmetic reasons.

In other groups, participants talked of a sense of unease about the way technology was developing, and that there had to be caution and strict guidelines about how it could be used.

In the general public group, participants talked about how genome mapping might become a way of life in the future.

*RF2: I think it's not about this particular data in the study, but the way of the future going*

*RM: insurance, yeah.*

*RF2: Yeah. genomes, oh yes, you're born, you have your genome mapped, it's then sorted with everybody else. That's the future for sort of -*

*RM: Yeah.*

*RF2: – that concerns me more.*

*RF3: Yeah. And sort of, you know, everybody having their – you know – so when you decided to have children, I mean, you look at your genome —*

*RF: Look at their genomes, make a decision.*

*RF: I'll assess their genomes first.*

*RF2: It's just that, yeah, worry about – yeah. That sort of – science of – you know – it's a bit like having a barcode, isn't it? You're scanned in, you know exactly what you're about.*



*Moderator: What is it about the future, specifically, that is a concern? Is it about the storage of this data for unspecified lengths, or?*

*RF1: It doesn't bother me because I've already worked in clinical trials and storage of data won't, I have no concern about the storage of the data of the trial, I'm thinking more about the concept of being genome-mapped.*

*Moderator: Right.*

*RF2: And having a tag somewhere, where people can tap into, and -*

*RF1: Yes, and this will become a sort of way of life. When you're born and you're mapped out, and that's the way it goes. (General public group 1)*

Participants in the BAME people's and learning disabled adults' groups were concerned that in the future genomic research might be controlled by the private healthcare system and, as result, personalised medicine might not be available on the NHS and therefore not available to all patients, which could lead to marginalization of the needs of certain groups in the population.

In contrast, some participants felt comfortable with the idea of genomic technology. A few participants felt it was just about getting used to a different type of data, and future generations would not have the same concerns about the technology, just as mobile phones are now commonplace. Victor (BAME people group) reflected, "what will be will be" and participants in the rare diseases group agreed that developments like cloning of human beings would be far in the future and not something they were concerned with.

Importantly, participants described the decision to take part in genomic research as personal and individual. In the young people's group, students felt that the option to take part needed to be voluntary, so that people, "didn't feel pressurised to be involved for the greater good of medicine."

## 4.5 Feedback of results

How the results should be fed back to people was discussed in the general public group, the cancer group and the BAME people's groups. Concerns were raised that feedback needed to be handled sensitively, face-to-face by a health professional rather than a researcher, and that plenty of information about the results and possible treatments should be provided at the time the results were received.

Preparing people about what their results might show before their tests were taken was also regarded as important. Participants felt that people should understand that there might be sad news or their results might show nothing, or not be clear-cut. In the rare diseases group, participants particularly talked about preparing people for unclear results.

*RM: I think the other thing is that we, the way I think of it, I think, well, all these brain box scientists with all the analysis to do and all the rest of it, are they going to get it right and it's.....*

*Moderator: Ok.*

*RM: ...it's going to be a definitive, yes or no. And I don't think genetics is like that. It might be in some instances but certainly when we had the talk about genetics what have you, you know, sometimes it's undetermined because she said, you know, it could come back there is something in it.*





*RF1: There's lots of unknowns isn't there. They don't know.*

*RM: Yeah, yeah, yeah.*

*RF1: Unfortunately there's lots of genes or things are ...*

*RM: thought process of, you know, 'I'll get my results back and they'll be absolutely clear.' They will tell these people what we can that maybe, you know, you might consider wanting to get yourselves checked or whatever just as purely a peace of mind and stops there. And now I'm thinking, "what if it comes back it's all a bit fuzzy that actually maybe doesn't help," and you want it to be black and white.*

*Moderator: Yeah.*

*R2: It is a situation where you do, don't you, you know, you really you want, it's weird. (Rare diseases group)*

#### **4.5.1 Secondary findings and impact on participants and their families**

Views within the groups differed about the option within genome mapping to find out about the risks of other diseases that people might develop in their lifetime.

Some participants thought it would be beneficial to know their chances of developing a disease that could be treated, so that they could plan their life and take preventive action. The young people's group discussed this perspective:

*RM1: Think you would want to know.*

*RF1: I think, yeah.*

*RM1: Then you know that you've got a chance of this, disease or something, and you can – when it comes along, you're not too shocked, you already know that there was a chance. So, incidental findings – if you do find something, personally, I would want to know. Not sure what would everyone else would feel, but.*

*RF1: I feel like if they do it -*

*RM1: I would want to know. I think it depends on the person, as well.*

*RF1: Can't that happen with breast cancer, when women go get their – it all checked and everything, and if they find it, they – sometimes they'll remove part of the tissue. And I feel like if I was told that a part of my tissue could have it, I would want it removed. Because I think like a celebrity had it done, and then they were like – they had loads of abuse about it, because her breasts shrunk.*

*Moderator: Angelina Jolie?*

*RF1: Yeah, her breasts shrunk. But she then had to explain, and she's like "I shouldn't have to explain this."*

*RM1: No.*

*RF2: Yeah, I think I – I would like to be given the option. You know, "Would you like to see your data, or not?" I think – and like beforehand. If there's – if there is a problem, and there's something that you can do about it to prevent it, please tell me. But if it's something that they can't prevent, I wouldn't want to know. I wouldn't want to live my life knowing in six years I'm going to get cancer. I wouldn't*



want to know that at all. I think that – that could, you know, completely destroy somebody's life. So they need to be careful about how they tell people, you know, and I – yeah – think they should say, "Do you want to see your data or not?" Not say, you know, "Well, do you want to know whether you have this disease or not."

*Moderator:* Yeah.

*RM2:* I think it could, as you said, destroy someone's life. But I think it could also make them live their life how they want to live it. Because if they knew that this was going to happen in six years' time, then they can think right, I'm going to set myself a goal to do this before it appears and live my life as well and as happy as I wanted to.

*RF3:* Yeah.

*RM3:* However, in the same way that ignorance is bliss – if they don't know, they're not going to worry about it. (Young people's group)

However, others envisioned problems that could occur from people knowing whether they had a risk of developing a disease in their lifetime. For some people, it could cause increased health anxiety and a lot of worry which, in turn, could affect their health, lessen their quality of life and increase the resources required by the NHS to support counselling and visits to the GP. Some participants said that people might start attributing symptoms to a disease when they could be entirely unrelated. Participants in the BAME women's group talked about the downsides of knowing about secondary findings:

*RF1:* Then you have got cautionary side to that as well, haven't you? If they do discover that there is something else and so you are going to have to lead into counselling and therapy for them. It has the financial knock on effect again and I think this is a huge area. If you have got the money for, Angelina Jolie, you know, fair enough, go for it. The person on the street who is having this study, this kind of treatment done, then what happens to them, because it is and also has a knock on effect as you said with the extended family as well? Where does the research end? Where does the actual treatment continue and where does it end? It could go into, "Well, if you've got it, what about another family member and what about extended family and what about, you know?", so it is, that is like a domino effect.

*RF2:* And it can cause anxiety.

*RF1:* Absolutely. Everything, it can just, you know....

*R3:* And that information can be abused as well, you know, with the insurance companies and things like that. (BAME women group)

However, there were mixed views about knowing about secondary findings:

*R2:* I, personally would want to know, so I could modify my behaviour and my lifestyle and give myself a good enough chance. It's like going to the GP and being told you have got hypertension and that's fine. I can't modify my genetics on what I have inherited from my parents. I can change my diet. I can do exercise and stop smoking, I don't smoke, so there is no point in stopping, you know, things like this. I'd like to be able to be in control, personally. I don't see why my health should be, it's my personal view, should be a burden to the health care service or the system. That is how I think.

*Moderator:* Would everyone want to know if you, how would you go, if you could be told what the future would hold for your health?



*R3: I would want to know.*

*Moderator: You would want to know as well. Okay.*

*R2: You would?*

*R3: Yeah.*

*R2: Explain?*

*R3: It's kind of, so that what I could do to*

*R2: There is a danger that it might not happen, so you could start suing everybody. [laughs] I got so anxious. My insurance has gone up. And my life is very distressing.*

*R1: We have become very much an American culture. Let's sue.*

*R2: We do medicalise everything as well. People have a little bit of stress at work or whatever and it becomes an illness and we start treating everything, so where do you stop? Where are the boundaries, you know?*

*Moderator: How about you guys?*

*R4: I don't think I would want to know.*

*Moderator: You wouldn't want to know. Why not?*

*R4: I very much deal with things as they come along. I am very much like that and if it's going to happen, it's going happen. You know what I mean? I get about the prevention, that makes a lot of sense and I agree that when you go to the doctor and they say, "you have got this that and the next. It's like well, if you change your diet." Stuff like that when you are just going do more of these experiments to find something, I'd leave it. [laughs].*

*(BAME women group)*

If secondary findings were potentially available, there was agreement across the groups that there must be a fully informed discussion with a health professional before a decision about testing is made. People should be given counselling and plenty of information beforehand, and afterwards, and be told their results sensitively face-to-face by a health professional. The general public group talked about how secondary findings results should be given to people.

*RF2: I think it's just more about making sure that all of that kind of thing is handled really sensitively, and in partnership with the consultants that the patients are under. Because I think – you know – patients tend to be very, very trusting of their consultants when they are in a situation where they've got incurable cancer, for example.*

*Moderator: Yeah.*

*RF2: They tend to say to their consultant, you know, "I trust, I trust you'll do the right thing." But actually, you know, sometimes all those risks are given and actually people aren't able to consider them all, I suppose, that's what I mean.*

*(General public group 1)*



Secondary findings not only have an effect on the people taking the test, they also have implications for other family members. Some members of the family may not want to know the results, but others may. Participants who talked about the impact of secondary findings said, “it’s like a domino effect,” and raised concern over where the investigations would end and the added resource implications required to manage the anxiety that secondary findings could create. After the results are given, it is the responsibility of the patient to decide what to do with the information and whether to share it with other family members. Participants in the rare diseases group felt that this could be difficult and that there should be support for people to help them make these decisions.

Rachel (rare diseases group) talked about how she felt about her family being tested for secondary findings:

*RF4: Yeah. When they obviously came home from all this conversation about it and everything [um] and it seemed as if they were going to be sort of realising what they were predisposed to and all those sorts of things. It’s like, well if they’re predisposed to it, I know they’ve agreed to be tested and such but if they found out they’re pre-disposed does that mean that I am? I’ve not agreed to be tested. I don’t want to find this sort of stuff out. But by them finding things out that automatically means I really find things out. But then I think it got a bit clearer when, because that was when Mum you were saying about, “Well you know I wonder if Alzheimer’s is going to be on the list?” And this that and the other getting quite excited. [laugh] And I was sort of, “I don’t want to find that out.” [blah, blah, blah, blah] but then it came out of that that they weren’t going to be doing this long list of things that you could be predisposed to. It’s things that can be treated and possibly prevented and things like that. So, I think that’s made it more of a comfortable situation to be in from my side.*

*Moderator: You are saying you might not want to find out really, you know.*

*RF4: Yeah and I am sort of the opinion that we’re all going to die anyway. So I mean I wouldn’t personally want to be like*

*RM5: One day.*

*RF4: Oh that’s what I’m going to*

*RF5: Not too soon.*

*RF6: That’s why I’m going to do it.*

*RF: [laugh] Yeah*

*RF4: Oh I don’t want to be like, “Oh, that’s what I’m most likely going to die of.” [laugh] Like, that’s what I can look forward to. I mean it’s not really for me but it’s, it’s good for (participant’s name) that she can. I mean, I can obviously see the benefits and they outweigh the negatives of it really for me, so.*

*(Rare diseases group)*

One area where participants needed more information was how data would be used after the person involved in the Project had died. Participants in the rare diseases group, who had a more in depth knowledge of the Project, discussed how the consent form gave permission for the data to be used, ‘birth, death and beyond,’ and some questioned whether permission for data use might be left in a will and how family members might feel about this responsibility. Other participants felt that because the data would be anonymous, it would be unlikely the Project would prioritise re-contacting participants far into the future.



## 4.6 Resource implications

While there was great enthusiasm for the technology and the concept that individualised medicine could improve people's quality of life and reduce costs, some participants in the general public group, the cancer group and the BAME women's group questioned how the results would be implemented and whether there were the solutions available to offer to people based on their results. In the general public group, a health professional raised the concern about how the Project's findings would affect NHS patient services.

*RF1: But I suppose it will have an impact in a good way on the NHS. But it may have an impact, taking people away from patient services, potentially. I'm just being – you know – front line, and actually – you know – consultant time, GPs' time, is actually really valuable. And I'd like to think that it was [laugh], it was kept for the patients that really need it, than – you know – I don't know. It's just difficult, isn't it.*

*RF2: Yeah.*

*RF1: Because it's a really good idea, but actually how? How are we going to, or how is it going to be managed, that loss of time, potentially?*

*RF3: Or also, on that point, is how it will be filtered down. Like you could have all this theory....*

*RF2: Yeah.*

*RF3: That comes to nothing.....*

*RF1: ... On the wards. You know? You could have all of this, but it would therefore cost too much to put it into practice, in order to actually treat people. That, that's – you know – or, you know, how the consultants have -*

*RF2: The right machine —*

*RF1: ... whatever equipment you need, to make – whatever beds you need, for how long, in order to help this. You know, from that practical point of view.*

*(General public group 1)*

Some participants in the learning disabled adults' and BAME people's groups were concerned about the costs of maintaining the genomics research programme in the long term. Bilbeer (BAME woman group) wondered how the technology would be maintained in the long term. Some participants were curious about what would happen if the government changed its priorities and the Project's findings were not implemented.

## 4.7 Information needs of the public

Genomic research is complex and involves sensitive and personal information. While group participants recognised the benefits of genomic research, there were also concerns. For some participants, the group discussion was the first time they had heard about genomic research in any detail and at the end of the group discussion, some felt they needed to consider the complexity of data sharing and issues of data ownership in greater detail before they could say whether or not they would be willing to take part.



Participants recognised that for genomic medicine to progress it needed the public to support it and be willing to donate samples. More information for the general public was needed on data security and data sharing. Importantly, participants felt that there was a need to educate the general public on the benefits of genomic research to counteract the negative reports in the media which might prevent people from taking part.

Specific information needs expressed by group participants were:

- Clarity on the funders of the Project and the resource implications of implementing the findings generated by the Project;
- How the data would be used after a participant had died;
- How researchers were to access the dataset and keep it secure;
- How people were recruited to the research, including eligibility criteria;
- Explanation of why the target was to collect 100,000 genomes.

## 4.8 Summary

Most focus group participants began their discussions with little or no knowledge of genomic research or the 100,000 Genomes Project. They raised more concerns than were raised in the individual interviews with Project participants described earlier and these were largely about data protection and ownership. People from BAME groups, in particular, expressed more concern about data protection and ownership with strong views that the data had to remain within the control of the NHS as a trusted data custodian. Concerns were also raised about the future applicability of the technology and how it could be used to eradicate differences between people or as a form of blackmail. Both the BAME and learning disabled people's groups raised concerns about the potential for the benefits of the technology to be eventually be controlled by the private sector and so act to further marginalise the health needs of particular groups of individuals.

It is important to note that views sometimes changed during the course of the focus group discussion underlining the importance of clear information and communication around this area. There were also strong views across the groups around the importance of transparency as genomic research develops, particularly in terms of who has access to the data. There were differences between groups about the sharing of data with pharmaceutical companies. The rare diseases groups, for example, thought this was necessary in order to realise the potential of the technology while the BAME group were more resistant to this idea. There was some reflection around pervasive data-sharing happening in life more broadly and how younger people who will have grown up sharing data on social media may be less concerned about this issue in the future.

There were mixed views around secondary findings and how these should be negotiated although there was clear agreement across the groups of the importance of fully informed discussion with health professionals and the provision of clear and accessible information.

Overall, participants recognised the potential for genomics research to improve wellbeing, particularly around tailored treatment. There was a strong sense of altruism across the groups as people understood the benefits would likely be felt by future generations and there was a sense of pride in contributing to this developing technological change. Despite the concerns raised, participants ultimately exhibited trust in the NHS and government, and thus in the Project.



## Chapter 5: Interviews of health professionals involved in the 100,000 Genomes Project

### 5.1 Introduction

Interviews were conducted with staff undertaking a range of roles including: frontline research nurses and genetic counsellors responsible for consenting participants; clinicians and managers leading GMCs; those involved in education, informatics and pathology; senior staff with central roles in GEL and NHS England (described subsequently as ‘the centre’). Interviews took place between December 2015 and June 2017 with three local staff interviewed a second time after an interval. The interviews were conducted very flexibly to allow participants to speak freely about matters of importance and interest from their perspective. Participants were asked initially about their role and how they became involved in the 100,000 Genomes Project, and then asked to talk about their experience of this involvement. The rest of the interview followed the interests of the participant. Given the sensitivity of some of the issues raised, all quotations are anonymous and only identify if interviewees worked at the centre or the locally within a GMC.

Overall, participants presented the Project as an undertaking that, although within the NHS, was outside the mainstream; an unusual enterprise, with its own goals and targets unrelated to day-to-day patient care. The Participants reflected the differences between the two arms of the Project identified in Chapter 1, with the rare disease group being seen as having had a long history of engagement with genetic medicine, considerable knowledge about genomics and generally supportive of the Project, while the cancer patients posed more of a recruitment challenge. The latter were frequently only in the early stages of coming to terms with their diagnosis and had no particular reason to have prior knowledge of genetics, or, specifically, of advances in genomics.

The description of experiences relating to the design and implementation of the Project featured prominently in many interviews, more so than discussion of the overall purpose, possible outcomes, or the interface with public and patients.

The findings presented in this chapter are divided into three main themes: central versus local perspectives on the Project; implementation; and views on the research versus service transformation aims of the Project.

### 5.2 Central versus local perspectives on the Project

Perhaps inevitably, there were differences in the type of experiences and strength of feelings described by participants working in GMCs in comparison to those working at the centre. For local participants, there was a strong sense of a process imposed from above, with insufficient involvement, followed by consistent pressure to increase recruitment numbers within an overstretched and under-resourced local clinical setting.

*And I’m, I’m fairly busy and my fingers are probably in too many pies, it’s been done against the background of, you know, I’m already in a fairly busy job. As well as the health, health side of things. It’s obviously been done on the background of services which are being delivered routinely. So this is all on top of current people’s roles, practices. A lot has happened fairly quickly actually though, as you probably know. It’s all come to fruition fairly rapidly.*

*GEL dictate what’s going to be happening, and we’re supposed to nod politely and simply accept it.*

There was also frustration expressed at the perceived lack of recognition by the centre of the scale of extra work being done within the GMCs. One participant, who described the overall project as ‘really rewarding’, said that the ‘national steer [um] has been a bit challenging’.



*People are very, very hacked off ... I mean, there's just enormous frustration which is a shame. It's a tremendous shame, when you think of all the investment that's gone into this project ... And I suppose I do feel a bit ground down by it all. I signed up to it because I thought it was a fantastic opportunity for our patients.*

Some GMC participants felt there was a lack of initial involvement and that the centre continued not to listen to them or utilise their expertise sufficiently during the implementation of the Project. They felt that they were ignored and their potential input was not valued.

*Initially I was feeling uncomfortable with it, as a process. So, it's moved from a stressful kind of unknown, but also feeling like a bit imposed – if that makes sense. [...]*

*It feels like we weren't involved. It suddenly appeared. We weren't involved in the discussions about it. So, I, I wonder if we'd had a bit more input. I mean, maybe other departments were, I don't know.*

*Yeah, so, I mean, I think we are certainly being listened to more now. But it's frustrating it's taken so long, and there's, there is still more to be done around making sure that we get the right level of collaboration.*

The pressures within the Project were also experienced by those at the centre, although their ability to make changes to the Project was seen as an important way to manage these challenges. Staff at the centre often spoke about the positive aspects of working on a cutting-edge project that would transform healthcare. This engendered continued positive feelings in them such as excitement, despite the challenges.

*So, I think just being involved in something that's right at the beginning, that gets the backing of some really senior people who believe that this is really going to make a significant change to people's lives – you know – it's really exciting from that perspective.*

The shared nature of both the challenges and pressure was recognised by some in GMCs, despite others expressing more negative views and experiences.

*And actually the, the senior leadership of the project has been very open and very, you know, and been listening. So on that perspective, it's been, it's been, it's been fine. I mean, they've been given a project to deliver – you know – from DOH. And yeah. You know, they're managing it as best they can, in a, in a nice way, so.*

*I don't think the project, the people leading it, have done anything wrong. I just think it's a big project. Big processes. Big issues at stake. It involves patients, it involves their lives. It can affect their families. So these are, you know, all massive issues.*

Despite this frustration and discontent, some local participants remained excited by the potential of genomic research for better services and their role in the Project. The three GMC staff who were re-interviewed 9-12 months after their initial interviews largely felt more positive about the Project and the extent to which the concerns of the GMCs had been listened to and acted upon.

*It's the most exciting project I have ever been involved with, and the most exciting scientifically.*





## 5.3 Implementation

Many participants from GMCs, GEL and NHS England discussed the implementation difficulties associated with the 100,000 Genomes Project. All agreed that it was particularly challenging. Specific areas mentioned as problematic included resourcing, workforce, planning, governance and communications. These issues were generally mentioned without any specific questions needing to be asked by the interviewer. On the other hand, participants often had to be prompted to describe the Project's successes.

### 5.3.1 Workload and resources

Many of those interviewed recognised that many challenges related to the speed of implementation needed to achieve the target of 100,000 Genomes within a fixed period.

*And there's been incredible pressure, and obviously partly political, partly financial, economic, partly kind of logistical; about trying to get things done in time.*

At a local level, work on the Project was often an addition to participants' usual NHS work, often added to existing workloads without additional resources.

*So it was a case of 'can you please do this clinic?' Or 'we need people to volunteer to do this'. But it was actually sort of voluntary paid overtime that wasn't voluntary [laughing], in the sense that it was like, you know, there's an extra pot of funding, we need you all to do some extra work.*

*We've not had any time taken off our diaries, or been seconded away from other roles to do this. It's been basically done on the background of delivering clinical care and research across the piece.*

Concern was also expressed about how focusing on the Project had a knock on effect which could adversely affect the other services provided.

*But even that is, with it comes with its challenges, because everyone's very busy, and so, you know, it's releasing people to go and spend time to help design the national programme. It's, you know, it's going to distract from what we're doing locally.*

*But it gets forgotten a lot, the impact it has on main services. Because there's a lot of time and effort that's put in, of many people. That just doesn't get factored into the project.*

The resources needs and impact on services was not always predicted in planning, for example the need for laboratory staff to stay late to process samples to ensure they did not degrade.

*So we have had occasions where staff have stayed until eleven o'clock at night, for example, processing samples.*

Similarly, smooth recruitment of participants in clinic sometimes needed two members of staff: one for data entry, alongside someone to counsel and consent.

In addition to the significant work involved in recruiting participants and taking samples, some local participants described the burden of communications from the centre for example the volume of emails and calls.

*Constantly being sent papers. We had a telephone conference on – was it sometime towards the end of last week? And an email with five attachments*



*came out sixteen hours before the teleconference. I mean, it just, it, it ... I think it's rude.*

Whilst it was acknowledged that targets were a valid way of monitoring progress and that the Project's success depended on recruiting a certain number of participants, it was generally felt that the primacy of reporting numbers recruited did not adequately reflect the complexity, scale and effort required locally to achieve them. For example, setting up new IT and pathology systems, approaching large numbers of potential participants, etc., all within very tight time scales. Given this, the weekly publication of progress against target across the GMCs did not appear to be a motivator for local staff.

*It is of no relevance to us how many samples other centres have got, and how many they think they're going to get this week. We can't influence it.*

Some commented that the extra funding of £200 per sample did not cover all the costs associated with collecting samples. For example, it did not include the cost of the time and personnel needed to get a fresh sample from theatres to the laboratory in the short time frame necessary, especially where facilities were spread across more than one site.

There was a feeling expressed by some GMC staff that there was a shortage of professionals across the country who were trained in genomics, for example pathologists, trained to integrate histopathology and genomic data. Some thought that this then created tension when staff with genomics expertise were seconded to the centre making local delivery of the Project harder.

The focus on recruitment, coupled with perceptions of not being listened to, created in some local staff significantly negative feelings.

### **5.3.2 Moving the 'goal posts'**

Other Project pressures identified were perceived to be an outcome of the speed of implementation and weaknesses in the original plans for the Project. The pace of implementation was further complicated by the ways in which changes were implemented.

*It's a very challenging project, I think it's fair to say. Challenging, mainly, because the, the sand shifts significantly. And it's very difficult to plan.*

*So we're already asking for money from organisations in a very challenging financial environment. And then when you're seeing wasted effort because you're having to redo things because of the changes that should've really been thought through earlier on, that's quite frustrating.*

For example, changes in laboratory procedures required for processing samples were not fully understood at the outset of the Project, so were not adequately costed into plans and budgets. Similarly, locally built IT architecture had to be changed with shifts in national requirements. The IT challenges, in particular, seemed to cause negative local experiences (see below for more detail).

Changes to the eligibility criteria were also commented on:

*... rather against our advice, Genomics England developed over-specific eligibility criteria. And I suppose for non-geneticists, maybe there was need for some guidance, to make sure you weren't recruiting people who were very unlikely to benefit. And ironically, they're now talking about lifting most of those eligibility criteria.*



The overall impact of the way in which changes were managed was commented on, for example:

*But the thing that has been totally and utterly missing from all of this, is – well, the two things, are – the planning around how they're going to manage the change and the governance around actually managing the changes.*

These factors added to both the resource and work pressure on GMCs and were summed up in this comment:

*There's not going to be a magic trick that just suddenly recruits everyone into the project and gets us up to whatever the original two year target was. That's, that's not going to happen. I think we need a bit, we need resources if possible to kind of scale up delivery. And we need a stable set of requirements, stable data sets. We need the time and space to deliver. And we need results to come back in an effective way. And Genomics England to listen to GMCs and, you know, especially around those key factors. Around stabilising things, how results are coming back, and how what is realistic, in terms of delivering. [...] I think ultimately we need the resource to deliver and we need a stable set of requirements, and I think that's going to get a long way in moving towards the second half of the project.*

### 5.3.3 Complexity and delay

There were a number of significant delays during the Project, notably in IT, pathology and sequencing which led to further delays in starting the main cancer programme and obtaining results to feed back to participants. This appeared to erode confidence in the Project at local level and was felt by some also to have eroded the willingness of clinicians to buy in to it.

*We were trying to push this into their day to day – we spent a lot of time – and I didn't, but I know the people who did spend a lot of time trying to get in with the cancer teams to get them to support this – to then tell them "Oh okay, guys. We've pushed you forward and forward and forward, now you're going to have to sit and wait for three and a half months while the techies go and write the new computer system". Really didn't do a very good for the PR point of view of selling the project.*

The sustained delays in the return of patient results was seen by many to be at odds with initial promises from Genomics England.

*It's been a huge problem. Because Mark Caulfield [GEL's Chief Scientist] stood up originally and gave lots of talks saying, you know, "In seventeen days we'll be able to turn round results", and so on. And you know, once seventeen months have passed and we still hadn't had a single result, people began to get a bit sceptical. So we're being chased all the time, to recruit more patients and yet there's no corollary of that. There's no reciprocal way of chasing them for results.*

*And of course the other thing around engagement is the return of results. And that's been, because that's been slower to come through, as you know. That's been difficult to get people enthused about recruiting their patients to the Project because they have no clarity on when they may get results back for them.*

Very few results had been received by GMCs during the data collection period of this study. Frustration was expressed that those returned required local validation before being communicated to patients, which further contributed to delays.



### 5.3.4 Informatics

Defining the dataset and developing the means to capture data generated commentary which included, again, comments on lack of consultation and not listening to local views and experiences.

More specific comments related to the Project's data platform, *Open Clinica*, described by one interviewee as “*about as friendly as a cornered rat when it comes to usage*” and another as “*fairly hideous*”. In some clinics, two people were found to be necessary to make recruitment work smoothly – one talking to the patient and the other entering data.

The fact that the dataset took a long-time to finalise and consequently changed caused local difficulty.

*... enormous challenge, because the data sets particularly have changed so much that, and we've almost scrapped half of what we've done halfway through the project.*

Some of the specifics of the dataset also seemed to have caused difficulties, such as the requirement to collect participants' head circumference at birth, a variable that was not easily available for older potential participants.

### 5.3.5 The Project's successes

Despite the challenges described above participants talked about a set of project successes.

Participants outlined several positive changes that have been made to procedures or services resulting directly from the implementation of the Project even if some of these caused delays early on. During the pilot and initiation phases of the Project, experimental work had been undertaken to adapt the DNA extraction process from cancer patient tissue samples to minimise DNA damage. This work concluded that fresh tissue was required for optimal whole gene sequencing and that the implementation of new processes was required across the GMCs. This work was viewed positively by participants, for their own work, for patients and also for the wider scientific community.

*... laboratory transformation, in addition to a clinical transformation, that I think is equally important. Because it's, you know, it's the way NHS labs or diagnostic labs are working, has already changed a lot. I mean, we had to – in the last couple of years – in order to get the cancer programme off the pilot, get this off the ground, we had to break down boundaries between pathology and the genetic labs.*

*I'm really impressed by the way how they've [NHS England] managed to engage with genetic labs, that really, you know, weren't, to a large extent up for it, I think, at the time. And so they've turned round.*

*They've had to kind of reconfigure the whole approach to pathology. Which is I think potentially, you know, hugely important. I think it's made people think about genomics, and not just genomics, but the sort of innovative science as being really more at the heart of medicine.*

Despite the difficulties described, IT services were also felt to have improved as a result of the Project, as were relationships and communication between different professionals and services, particularly between genetics services and local non-specialists.



*So, I suppose just in terms of getting our faces known, I would hope that that's helped. And we've had probably slightly more referrals from each of those areas after we've been out to them, of patients – not for the 100,000 Genome Project – but patients for whom we in genetics hopefully having something to offer.*

Similarly, being part of a high profile project was perceived to be positive:

*I think, I think the idea of the Project has been a very positive thing. I think being part of it was a very positive move for the department. And there were all sorts of challenges that come with it. But the idea of being part of that national project, you know, an international leading project has been good.*

*So the exciting bit because it really is; there's always something new coming up. And when you stop and think about actually what we're doing, it's a huge shift for healthcare, and on a grand scale.*

The review and simplification of the consent literature was seen to be a very positive step in the Projects development.

An early focus on dialogue with patients and the public was also commented on as being beneficial.

*I do think taking public concerns seriously and trying to find at least some way of addressing some of those is a step in the right direction.*

## **5.4 Research versus service transformation**

The 100,000 Genomes Project was the first to be processed through the Health Research Authority as a NHS transformation project. As such, it had hybrid status; requiring research governance, but also intending to transform clinical practice. The Project was often referred to as a research (rather than transformation) project by local participants, however, there was recognition that the combination was what made the Project exciting for some.

*This is bigger than just a research project, if you like. It's really – because we're trying to build for the future, and it's got a big transformational element to it – it's not just about collecting the samples. And that really starts to hit home as you get, you know, it started off with just trying to collect some samples. Now it's a much bigger agenda, so. But, you know, that makes it exciting as well.*

However, it was not always clear that the transformation aim of the Project was understood by all staff involved in its delivery.

*So, that's difficult to see, because I think it's – you know. I think a lot of people see where this is – what this is trying to, to do. Where does it go once it finishes in a year or two years' time? So, some people don't necessarily see that. The lab people or, you know, the senior technicians seeing the blood processing might not see that. You know, they're just told they've got to deliver this project and understand it, being across it. So, the bigger picture may be lost, depending on the level of understanding and also people involved. And also interest in the Project. Some people may just do it because they have to do it, because, you know, it's a DoH project and we're, you know, being very closely monitored. So, I think there's a, you know, a sort of a, a spectrum of people's interest and understanding of what the Project's about.*



Delays in the Project also seemed to make it harder for some staff at local level to envisage how research and transformation goals could be implemented in tandem.

*And even though we've been recruiting for eleven and a bit months, we haven't had a single result back yet. And we've moaned, obviously. And that would be a, particularly a result that transformed someone's care, then we could use that as a beacon, exemplar example, and I'm sure that would be, you know, a major help, actually. Because at the moment there is a sense of well, it's research, isn't it? Why are we doing this, it won't make any difference will it? Particularly for cancer, I think.*

Some questioned whether it was actually possible for both clinical and research staff to see benefits, given the time scales involved.

*This programme is losing the support of the academic community, show patient benefit within three years, on the other hand you have to have xxx publications and there's no way you can do that, one single person can have both.*

Others commented that, it should be publicly acknowledged that, in line with other R&D projects, as opposed to service development ones, some investment would not pay off.

*[It] should be accepted on leading edge projects like that, that actually there is a degree of you have to pour a certain amount of money into a project like this, where there is a very high risk that it will just disappear, and actually nothing will be delivered for it.*

The tensions between a research project and work that could be embedded in every day practice were exemplified by the debates around informed consent. Whilst there was recognition of the appropriate attention paid to the consent processes, and the challenges involved in getting these right, concerns were raised about how the emphasis on reaching targets might impact on gaining informed consent in practice.

*And that's what the top leaders are bothered about. They don't care how it happens, they just, they don't care how they get the numbers, they just need the numbers.*

This was seen to be particularly challenging given the complexity of the consent process and the complexity of what potential participants in Project were being asked to understand and sign-up to.

*So it would be nice to know what the patients, because I think that maybe we – my concern is actually how much – when we get to the consent process, is how much the patients are really absorbing? And how much do they understand that they're actually consenting to?*

*But I also think that you can't give true voluntary non-coerced consent to something when you're being asked to do lots of things at the same time. So, parents consenting their children, to getting a diagnosis is all very well, but then having to also at the same time also consent to their own and their child's DNA being stored indefinitely, and researched indefinitely, and used for all sorts of purposes is not necessarily a bad thing. But I don't think they can take that on board at the time.*

One genetic counsellor described the inherent tension in providing the 'right' clinical care against the (research) needs of the Project for recruitment. This resulted in, for a particular family, making a second appointment as they were unsure whether to participate (they didn't after the second appointment). This resulted in cancelling sample couriers and incurring costs. The counsellor described the dilemma of doing



what was right for the patient/family against knowing that their department had been given additional funding to achieve target numbers of samples.

*I was focusing on what was important for them, but the department had a clashing set of needs.*

A further research/practice tension was described: the fact that an individual's genome can be sequenced (and provide a wide range of potentially useful research data) set against whether the information generated is actually useful to this particular patient at this particular time.

*So that we can make sure that, you know, like I said, that we're offering tests that we know how to manage the results of, rather than because we can offer a test.*

*And I think it took quite a long time for us to explain to them that actually if you've had a child who's been seriously ill from birth, got worse and worse, is now a few years old, is clearly dying, actually there are other things on your mind. And that maybe, discovering that your child's illness was genetic and potentially inherited from both of you might be the last thing you'd want to be told at this moment.*

An alternative view of these ethical concerns was offered by a GMC participant who viewed the 'forcing' of further discussion about these ethical concerns as a positive development:

*And that was the situation at the beginning of this Project. But over time, the kind of public debate and expectations have changed. And now we've moved to a place where there's a kind of expectation that you will at least offer the opportunity, in the context of whole genome sequencing, of other kinds of information that someone might be interested in. There's a kind of responsibility in some ways, to do that kind of thing. And that raises then a question, well what is that responsibility? You know, what kind of responsibility is it? What should be offered? What shouldn't be offered? How do we go about deciding, you know, whether the information is, is useful or whether it's something a person would want? Whether there's anything that could be done. And I think that debate has shifted, partly because of the wider international debate, and public debate, but partly because of project. I think the 100,000 Genome project has kind of forced that discussion.*

This extended discussion involved moving beyond thinking about clinical responsibilities as being the sole responsibility of clinicians, to thinking about the responsibilities of those managing data and research activities.

Finally, there was discussion by many participants about the future use of genomic sequencing in routine practice. Some expressed the view that in order for transformation in clinical practice to take place there was a very significant workforce training and development agenda that needed greater focus. Similarly, there needed to be greater public information and debate. These transformation needs may have been overshadowed by the research needs and focus on achieving a given number of samples in a short time.

## 5.5 Summary

The 100,000 Genomes Project presented significant opportunities and challenges, often experienced and described differently by those in GMCs and those at the centre. The endeavour, which was the first attempt to transform a healthcare system using genomics, was described positively and seen to be exciting by many staff involved.



However, the volume of additional work, within a stretched NHS, driven by an overriding focus on recruitment targets, with frequently changing requirements and delays led to negative experiences for a substantial number of staff, at least in the period covered by this research. The Project continued to evolve in the ensuing period. Challenges reported in the current study included poor communication, limited resources, moving the 'goalposts', role definitions and responsibilities, considerations of what results might mean for patients and the uncertainty inherent in fast moving technological developments.

Overall, ambivalence was identifiable through the analysis. While there was recognition of the scientific potential of genomic research, at the same time, there was a sense of uncertainty at what this might mean in practice for patients.





## Chapter 6: Focus groups with non- specialist workforce

The majority of non-specialist healthcare professionals who took part in focus groups had little knowledge of the 100,000 Genomes Project, and their familiarity with whole genome sequencing (WGS) generally was limited. Whilst the researcher facilitating the focus groups gave participants some background information on the Project, discussion primarily covered speculation on the potential of WGS, the concerns it raises and the role it could play in the future of the NHS.

### 6.1 Knowledge about genomics and the Project

#### 6.1.1 Knowledge about genomic medicine and whole genome sequencing

There was some confusion amongst the non-specialist healthcare professionals about what WGS involves, what is already possible in this field and what could become possible in the future. At times, respondents conflated knowledge and concerns about WGS with other therapies and technologies, such as gene therapy and genetic testing.

These health care professionals showed varying knowledge of WGS, with a majority of participants admitting that they had very little personal experience of this domain. Two participants in focus group 3 spoke of having used WGS as part of research. One described looking at patients' genetic risk scores, but clarified that this was not standard practice:

*It's not a recognised investigation at the moment. It's for validation, I think.  
(M, group 3)*

Other professionals discussed their experiences of genetic screening. Some described having screened patients for a specific gene, including for the diagnosis and treatment of arthritis and diabetes, but this had not extended to WGS.

Genomic medicine was a more familiar term than WGS for most. Some spoke of working in this field, and others knew of it from colleagues in other departments, although discrepancies arose over exactly what was covered by this term. A range of terms were used to describe genomic medicine. "Personalised medicine", "precision medicine", and "genomic medicine" were used interchangeably, with some participants showing confusion over similarities and differences between genomic medicine and other terms:

*... what is precision medicine, and what is personalised medicine? Do they get like individual medicine? (M, group 1)*

One participant spoke of having received some teaching about genomic medicine, but, nonetheless, remained unclear on what it was precisely:

*We did certainly touch on the concept of genomic medicine, er, in my core medical training....But, that again, I'm not entirely clear when it becomes genomic and when it's personalized. (F, group 1)*

Some participants felt that medicine is already "personalised" especially in treating conditions such as breast cancer, cystic fibrosis and diabetes. For example, one participant described how diabetes treatment already takes into account factors including the patient's renal function, their hepatic function and other co-morbidities. Similarly, another participant illustrated her experience of personalised medicine by recalling culturing a patient's tumour and treating it with medication that was against standard guidelines:



*This lady would have never been treated with this medication though if we hadn't checked it...And her tumour has responded. And this is a properly personalised medicine. (F, group 1)*

For some participants, there was a feeling of scepticism about the extent of novelty of “personalised medicine”, and that the distinction between personalised and genomic medicine needed to be clarified:

*... the way we practise medicine is, in a way personalised anyway, because we give the patient options. I would like, you know, it to be more precise and say personalised based on gene, or based on genetics. (M, group 1)*

Some health care professionals spoke of having received very little formal training on genomics in their education or career, but understood this field through its coverage in celebrity and popular culture:

*... I don't know, we don't get much education about this I have to say, but 14 years ago, I presume Angelina Jolie would not have had a double mastectomy. (M, group 4)*

It was suggested by some older participants that the younger and emerging generation of health care professionals might have had more training in genomic medicine. In contrast to the majority of health care professionals in the focus group, one participant was more confident in her knowledge of this subject, and the others' limited understanding of genomic medicine was a source of surprise to her:

*... I am quite surprised with what I heard. Er, because I have never come across to my head that people may not really feel it and understand this. For me it was so obvious, that I just kind of really shocked myself. (F, group 1)*

### **6.1.2 Knowledge about the 100,000 Genomes Project**

Knowledge of the 100,000 Genomes Project was also limited. Focus group participants had little understanding of how it was run, by whom and with what aim. Some knew basic details of the project such as the following:

*It's mapping cancer genetics and rare conditions genetics. It's also mapping, isn't it about 30,000 people who have no apparent disease, is mapping their genomes as well? (M, group 2)*

Whilst some health care professionals viewed the Project's aim as creating a database for use by researchers, and not extending to offering individual patients any feedback, the potential of secondary findings was also mentioned:

*There also seems to be an element of possible genetic prediction, of a predisposition to a whole host of illnesses. (M, group 2)*

Other health care professionals had heard about the 100,000 Genomes Project from a research point of view, but not within clinical practice. One participant claimed to recall two of his colleagues using data from the Project in their PhDs on diagnostics in arthritis and diabetes, respectively, though it was not entirely clear whether this was a correct recollection. Personal interest was a reason others knew of the Project. For example, one participant spoke of reading about it in the newspaper.

Beyond the Project itself, discussions also emerged on related sequencing initiatives such as the over-the-counter '23andMe'. There was confusion over the differences between commercial ancestry testing and the 100,000 Genomes Project, which was reflected in the lively questioning that arose in focus groups:



*Is this the same kind of tests that you can send off and it tells you whether you're an... You're always seeing articles like that, about I am 50% Viking ... is it the same test? (M, group 3)*

Although the level of knowledge reflected in these questions is quite basic, commercial services do frequently offer to provide information on genetically related disease risks.

## **6.2 Speculation about the future and the potential of genomic medicine and whole genome sequencing**

In spite of the limited knowledge many had about WGS, there was a general tendency to view it as representing “a huge achievement” in science and in medicine (*F, group 1*). Several spoke of WGS as enabling a huge increase in knowledge, and some saw this knowledge as the future of health care. Focus group participants speculated on the positive implications the increasing use of genomic medicine and the 100,000 Genomes Project might have on clinical practice and patient care in the future. Several felt that WGS could aid patient diagnosis and focus treatment, leading to improved patient outcomes, and also potentially offer a way of predicting disease so that it could be prevented in the first place. Some spoke about its theoretical ability to provide more precise probabilities about an individual's chances of contracting a range of conditions. This could lead to more targeted monitoring of individuals over time, so that any changes identified could be acted upon early or even pre-symptomatically. The benefits of this were mentioned particularly in the context of hereditary diseases, as the relatives of those with a genetic condition could be tested to ascertain their chances of contracting the disease in the future. Knowledge on the BRCA1 gene was used as an example of progress in this area:

*Catching things early, especially if you find someone, like you find someone with the breast cancer gene, and you know that this is a particular gene that's probably replicated in many females or males in the family. And then we will liaise with the GPs, to get them talking about these things, send the patients back to the specialist for more testing. (F, group 1)*

However, one participant pointed out that the level of knowledge about the role of BRCA genes had yet to be replicated in other areas:

*... with the predictive aspects of this, we are very early stage. Obviously, some genes like BRCA, we know a lot about. But all the other stuff, it's the risk, it's very vague, the information you get back is vague. We don't really know how to use this. My feeling is this is going to carry on and it's going to get better.*

Nonetheless, the development of WGS was seen to go hand in hand with a move from treating to preventing cancers and other diseases:

*... genomics is to be welcomed. It really will help us to do preventive medicine, really from the beginning and provide people with genetic counselling about what the future holds. (M, group 2)*

Both cervical and breast cancer screening programmes were cited as existing and successful screening measures that were in place to identify diseases at a treatable stage. However, the financial implications of further testing and follow up treatment for individuals deemed at risk of disease were a worry for some, with one participant suggesting that this would pose a “massive cost” to the NHS (*F, group 1*). By contrast, it was also suggested that early diagnosis could be cost-effective, enabling early treatment at lower overall cost:



*... you're not catching someone way into breast cancer and spending money on surgeries, and chemo and radiotherapy, but because you know this person is likely to carry the gene, or you've detected it, then you know, treatment has started a lot earlier. (F, group 1)*

Whilst early diagnosis was seen as having the potential to improve outcomes in terms of length and quality of life, it was pointed out that this still might not translate into a cure for patients:

*... finding out about it causes the problem to be dealt with from an earlier stage, which may not actually lead to the change in the outcome, potentially. (M, group 2)*

Similarly, there was a concern that having one's genome sequenced could cause "unjustified confidence" in some people (M, group 3), who might feel that their future health was more certain than it is. Nonetheless, WGS was mentioned to hold benefits for the field of oncology more generally, as it "gives huge amount of data on the biology of cancer itself" (F, group 1). One participant felt that in the future, predicting disease might be taken one step further, leading to certain conditions being eradicated before they present:

*... but next thing will be to probably prevent the disease from developing in somebody who it's likely to, but you know that they've got the cystic fibrosis gene, maybe you can give them something, so that it doesn't become a disease. (M, group 4)*

In line with the aims of the 100,000 Genomes Project, focus group participants suggested that WGS might advance knowledge and diagnosis relating to rare, non-specific, or difficult to diagnose conditions:

*I think that would be the first step, to diagnose those rare conditions which are difficult to diagnose from the start. Pre-symptomatic and ... other conditions which are relatively and non-specific in presentation that you have a diagnosis of... (M, group 4)*

Whilst the cost of such technology could pose a challenge, as well as the time that might be needed before receiving results, this could still potentially enable more rapid diagnosis than currently available:

*... you'll immediately have an answer, you don't have to go searching through the haystack looking for the particular condition that may or may not be the cause... it's got to be better than the piecemeal search for this particular gene, for this particular condition. (M, group 4)*

Some felt that NHS genetics infrastructure would have to be scaled-up for genomic medicine to be cost-effective compared with the status quo, but, nonetheless, genomics was anticipated to offer huge potential to neurological and wider medical fields. It was also suggested that improving the accuracy of diagnosis would prevent the cost and harm of unnecessary and inappropriate treatment. Discussions arose on how genetic testing is already leading to more accurate diagnosis, with one healthcare professional working with cystic fibrosis patients describing how this had benefits in his field. In cases of incurable disease, the benefit of better estimates of prognosis, was mentioned by one participant:

*At least you can tell them they are likely to live three months or will likely to live five years or this might happen to you and they have prepared for that. (M, group 4)*



The potential of WGS being used to target therapy, leading to better patient outcomes, arose in the focus groups. The current existence of targeted therapy in oncology was raised in discussions on personalised medicine:

*... you go for the chemotherapy. But then it's a question of which one. And then it starts the question you know, have you got those receptor or those receptors? And then... the mosaic appears. (F, group 1)*

Some were sceptical about how far WGS would advance this, questioning whether it would readily translate into better treatment options, and how long it would take to develop the expertise to act upon personalised results (see below for more on these concerns):

*I suppose my concern is now we have found where genes are, and the conditions associated with it, how are you going to deliver targeted therapy to those genes in a particular individual. I feel that's where the challenge will come, and how many years are we looking into the future, 15, 20 years? (M, group 4)*

The possibility of WGS enabling targeted therapy for common conditions such as heart failure was also mentioned, as individualised treatment could be provided based on how individual patients were likely to metabolise particular drugs and thus how they might respond to certain treatments. Related to this, it was suggested that screening could be used to predict complications that could arise from infections, from pneumonia to urinary tract infections, including how patients may react to particular antibiotics. The benefits genomics could have if implemented in more diverse contexts were also mentioned. One participant felt that it could be useful to look for susceptibilities to, and target treatment for, diseases like malaria.

Targeted therapy was also expected to have positive financial implications for the NHS. Understanding which drugs were likely to work for individual patients before they were treated could inform drug provision, reducing the need for multiple or ineffective treatments, therefore using NHS money more efficiently. One participant expressed hope for developments in this area in the future:

*What we could do with is a test that tells us this expensive drug is going to work for you rather than wasting years trying the wrong drugs and wasting vast amounts of money on expensive drugs. (M, group 3)*

Indeed, a trial-and-error approach to prescribing treatments was mentioned by one participant as a difficulty he faced in his work with diabetes patients:

*We try one after another after another or some multiple ones altogether without any great knowledge of actually who is going to be best, most effective for. (M, group 3)*

WGS was something he felt might improve his practice.

The potential use of WGS in drug discovery and development was raised in focus group 2. One participant spoke of her/his previous experience working in the pharmaceutical industry, and finding that certain drugs had a positive effect on some patients, yet not on others. This meant that they did not perform well in clinical trials, and consequently were not marketed for wider use, although "clearly there are sub-sets for patients that might benefit" (M, group 2). WGS might thus enable more targeted clinical trials of particular drugs in specific patient sub-populations based on their genomic profiles, thereby aiding the provision of specialised drugs.



## 6.3 Concerns and scepticism about genomic medicine

### 6.3.1 Over-medicating and unnecessary treatment

Alongside its potential benefits, focus group participants raised several concerns about the negative impacts that genomic medicine might have on clinical practice. One focus group participant worried that WGS could worsen what he saw as an existing problem, the medicalisation of everyday life. There was a concern that receiving uncertain results could drive patients to seek further information, pushing health care professionals to carry out a multitude of tests, often unnecessarily:

*You end up investigating till the cows come home because you need to know what it [a particular gene] does and a vast majority of times, it's of no significance but it's impossible to ignore. (M, group 3)*

Participants were aware that excessive monitoring could have negative physical consequences. One healthcare professional raised the potential harm that repeated ultrasound and CT scans could cause for patients' health in the long-term.

Health care professionals questioned whether patients might undergo unnecessary treatment for diseases for which they were at some level of risk, but might never develop. The point at which a risk becomes severe enough to intervene was a source of debate in focus groups, and raised both clinical and ethical concerns. The difficulty of knowing when to act upon the results of genomic screening was mused upon by this participant:

*You going to start treating them, which may not become a disease? ... as serious as cancer, you might seem clearer because you might feel that okay, you must do it because it's cancer. But there are some milder diseases. (M, group 1)*

Some worried about the medico-legal implications of having to make decisions in uncertain cases:

*And then the issue then is that, okay, so I know that this person has predisposition to breast cancer. What am I supposed to do about it? And what happens if things aren't clear cut and there is some question and you choose to do, not to do something about it. It can have a real impact on regulation. (M, group 2)*

The physical impact of overmedication was also a worry. One professional mentioned the United States as an example where this had fatal consequences:

*In the States, one in six people dies of an iatrogenic death. That means that basically they were over-medicated to death. (M, group 2)*

It was suggested that facing treatment decisions on the basis of risk scores may deter some people from WGS in the first place:

*... you will find within families that ... the desire to be screened is quite variable and some people won't want to have the screening, because they know it means a radical mastectomy and so on. (M, group 2)*

### 6.3.2 Access to, and misuse of, genomic data

How data from the 100,000 Genomes Project could potentially be misused was discussed in the focus groups. The privacy regulations relating to genomic data were raised by participants in group 3, and ownership was a cause for concern.



Understandings of the ownership of genomic profiles in the 100,000 Genomes Project varied:

*I have ownership, you can't sell it or copy it or tell everybody right, left and centre. (M, group 3)*

*You would hope it would be something that's only available to yourself and health care professionals. (M, group 3)*

*Someone else could patent that, your gene, and it would no longer belong to you. It was a patent now belonging to the company. (M, group 3)*

When discussion turned to anonymity, whether Project data would be individually identifiable and who would have access to which data on which terms, focus group participants were unsure of the basis of the Projects.

For example, apprehensions arose concerning the implications of private companies having access to individuals' genomic data, or of individuals being forced to disclose the results of their sequencing, yet without much firm knowledge. Participants questioned how the existence of genomic information could affect an individual's ability to obtain insurance, employment and a mortgage. One health care professional suggested that this was likely to be the main source of concern for patients:

*I think the patient's big worry is, 'will I get a mortgage'? That is the kind of thing. Is this genetic information going to actually impact on what I can and cannot do, job wise potentially, day to day life. How it will affect them, daily. (F, group 2)*

Some felt that these concerns may dissuade certain patients from undergoing WGS. However, knowledge of data protection law in the context of WGS was limited amongst participants. It was acknowledged that public concern about access to medical insurance was virtually removed by the availability of universal coverage through the NHS. Nonetheless, there was a worry that people could still be disadvantaged by other private insurers on the basis of their results:

*People like life insurance companies are maybe going to prey on vulnerabilities of people and use this knowledge inappropriately. (M, group 2)*

It was suggested that individuals' rights needed to be legally protected:

*I think there needs to be some kind of legislation in place that prevents insurance companies misusing this great knowledge that we have. (M, group 2)*

Another participant raised a different ethical question around disclosing results to insurance companies, "Should they know?" (F, group 1).

### **6.3.3 Secondary results and predictive screening**

In the 100,000 Genomes Project, patient participants could choose whether to be told the secondary findings from their sequencing. Although Genomics England would only share with patients results related to diseases that were treatable, this remained a cause of concern for health care professionals, who questioned the ethical and psychological implications for patients of receiving secondary results. Several noted the competing benefits and harms of WGS from this perspective:

*So, it has great potential, it has great anxiety ... as well. Having the knowledge of that information on your genes could be very powerful. (M, group 3)*



Indeed, the morbidity induced by anxiety was widely mentioned by professionals as a potential outcome of receiving secondary results, after which the patient may have to live with potentially distressing knowledge of what the future may hold, even though there is no guarantee that they will ever contract the disease in question. One participant pointed out that this anxiety may begin even before individuals learn their results:

*... that limbo period where they don't know if they have got something wrong with them or not is one of the most difficult and unsettling and high anxiety time for them. (F, group 2)*

Another saw anxiety as something that individuals should prepare for, before undergoing WGS:

*I think it probably is the future but one needs to start equipping one's self in some ways of anticipating the existential angst it may cause. (M, group 3)*

It was acknowledged in the focus groups that not all patients would necessarily want to know their medical future, rather they might wish to be treated when this became necessary:

*They would rather find out at the last possible moment and they may be lucky or they may not, sort of thing. (M, group 2)*

Participants emphasised that the results of WGS could have implications, not only for individuals, but where patients were found to be at risk of hereditary diseases, also their families,

*If they've got something that's genetic, do they then get their family tested as well? It's very scary. (F, group 3)*

One participant had personal experience of the dilemma that could arise where there was a family history of disease. His sister-in-law had died from breast cancer, and he was unsure whether or not to encourage his niece to undergo WGS to see whether she had a genetic predisposition towards breast cancer, given the anxiety it could cause her. Participants also worried that knowledge of a patient's risk of contracting a hereditary disease could lead to further ethical dilemmas for the healthcare professionals charged with responding to their results:

*Do you ask the families not to have any children? (M, group 4)*

The impact of religious and cultural factors in hereditary disease also arose in focus group 4. A participant recalled that in the area where he worked, there was a significant Muslim population where first cousin marriage was common, which had led to a rise in certain metabolic conditions. He questioned whether individuals should be offered WGS before they made decisions about marriage:

*British-born Asians they are slowly changing, but that's going to take another few years as well, so are you going to convince that to have screen, and whether they want to marry the first cousin or not? (M, group 4)*

Although the 100,000 Genomes Project did not offer patients results related to diseases that could not currently be treated, debates arose over whether patients should still have the option of knowing their risk of developing such conditions. One participant pointed out that conditions that were not treatable in previous decades might be so now, which should be kept in mind when planning genomic services in future. Another participant raised a similar point:





*Are you going to tell that person, or not, because you might decide not to because you have not looked for that, but maybe in 10, 20 years' time there will be treatment to prevent Huntington's and then what to do? I mean, if that person was told, they could have claimed that they could have taken something and did it then. (M, group 4)*

This also highlights the tensions that health care professionals may have to navigate when deciding what information to disclose to patients. Another participant argued that such tests should be used in instances where there is a family history of disease, as knowledge on a patient's future can inform how they are monitored:

*... sometimes it's not all about treatment. Because there are some things that we cannot treat today, but the awareness helps us to manage [um] the patients on the long term. (F, group 1)*

In line with the 100,000 Genomes Project, others felt that the secondary findings from WGS should include only treatable conditions:

*There's no point in knowing about a slightly high risk of something if you can't act on it. (F, group 3)*

The ethics of using WGS to provide a genetic risk profile as the primary aim was discussed by participants. Some emphasised that the objectives of screening needed to be defined before it was carried out:

*You need to do it for a particular purpose, a question in mind and want a particular response rather than a broad spectrum. (M, group 3)*

Thus, off-the-shelf screening tests such as '23AndMe' caused considerable concern amongst participants. Unlike in the 100,000 Genomes Project, such tests may reveal potentially distressing results related to diseases that may not be treatable, yet without genetic counselling, or other medical services, as follow up. The lack of regulation was criticized:

*So, I would have thought the application needs regulating, to be just suddenly you've got this technology and you could buy it off the street, would be very bad. (M, group 3)*

Indeed, one participant suggested that suicide rates could increase amongst individuals who discovered they were at-risk of incurable and debilitating disease:

*... a bunch of people kill themselves, just because they find out they've got the gene of Huntington's. (M, group 4)*

The possibility of pre-natal screening arose in discussions on WGS. Genomic medicine leading to genetic manipulation in utero, or even encouraging the abortion of foetuses with particular conditions was raised in focus groups. This was a subject which divided participants, who held a range of moral positions. One participant suggested that using genomic technology to identify and correct certain genes was "the next step", but was not without its complexities (M, group 4). Another health care professional saw clear benefits in this:

*... it will help in creating a healthy population, and the future healthcare costs will come down. (M, group 1)*

By contrast, other participants were wary of pre-natal screening, referring to regimes of eugenics, both past and in fiction:



*... historically, there has been negative horrible things done in the name of gene medicine. (F, group 1)*

*This was previously science fiction-y type stuff... And now, we are going to, we are bringing it into our current realm. (M, group 2)*

There was a concern that genomics could give rise to a similar regime:

*What if someone starts saying, "Well, actually obesity, we've found a few genes, let's start weeding out the next generation". You were talking about making a healthy population, it's a slippery slope. (F, group 1)*

One health care professional pointed out that having certain conditions may not be negative, using the example of Albert Einstein to illustrate this point:

*... he may have been prenatally diagnosed 100 years later as possibly may suffer from Asperger's and let's terminate this child rather than the wonderful creative genius he became. (M, group 2)*

The wider impacts of in utero screening on society were also mentioned:

*... you might be tempted to eliminate somebody with muscular dystrophy from the start, I don't know how good this is for society as a whole. (M, group 4)*

Indeed, concerns were raised around the implications of creating a "designer population" not only for ethical but also evolutionary reasons:

*If we rule out the variation by having a very rigid policy and screening out everybody or terminating all pregnancies that were abnormal, we would sort of naturally select, we wouldn't provide the variability we need to evolve. (M, group 2)*

One participant suggested careful regulation of WGS was needed before such issues arose:

*... I think before we have it as a science for that kind of prediction and designer babies, we have to, like I said, legislate against it being misused. (M, group 2)*

### **6.3.4 Scientific limitations of whole genome sequencing**

Some health care professionals questioned the value of WGS, both in general and specifically in relation to its use of NHS resources. For example, one participant, whilst arguing that genomic medicine was a 'promising' field, emphasised that it would not necessarily help all patients:

*On one hand, extreme, pure genetic, on the other hand, pure environment, and in the middle, [um] there are interactions between genetics and environment. So, when you say personalised, or even say personalised, based on genetics, it won't be for everyone. (M, group 1)*

Indeed, its application to common conditions such as diabetes and high blood pressure was questioned by another participant. It was suggested that the role of the environment in disease cannot be ignored:

*... there is a large part of these diseases that are not genetically mappable. (M, group 2)*



Others were more forceful in this argument, and felt that the importance of genomic medicine for general health had been overstated:

*You are right ... not smoking and exercising and having good diet is always going to trump your genetics as we proved with increasing length of life over the last 200 years. (M, group 3)*

Indeed, it was suggested that focusing on general measures to prevent common conditions would be more beneficial:

*... you will get probably more out by focussing on some basic, you know, preventive measures. Rather than, you know, this individualized. (M, group 1)*

Given that relatively few people would stand to benefit from the rare diseases strand of the 100,000 Genomes Project, there was some debate as to whether this element should be a priority. Although some argued that rare diseases are significant, others suggested that this did not justify this focus in the Project:

*I'm not saying it isn't significant. What I'm saying is you see, if you're looking at impact of the NHS and planning ahead, this is going to be a side issue, because we've got bigger fish to fry. (M, group 1)*

Some focus group participants had wider concerns about the repercussions of the 100,000 Genomes Project, and felt that it would only open "a can of worms" (F, group 1). Some suggested that there was a considerable lack of planning related to the wider implications of the Project:

*I understand that this is a positive step. In some targeted area it gives a lot of [um] good results. But still I think it's at experimental stage, we don't know what we're getting into. (M, group 1)*

*It sounds like the project has been triggered without any parameters, understanding or knowledge about where it's going to end up. They're doing it because they can do it. They're not doing it because they know what the outcomes are going to be or what they're looking for. It's just a shotgun approach, like DNA sequencing, and they're hoping something useful might come out of it. (M, group 3)*

Another participant felt that, rather than coming to dominate medicine in the future, genomics would lose popularity after the initial hype:

*But when it is then introduced everyone says, "That's brilliant, let's use lots of that". And then they find out the pitfalls and problems, and they say, "Oh! My goodness! Let's not use that any more". And then it reaches a satisfactory medium. (M, group 2)*

## **6.4 Implications for developing genomic medicine in the NHS**

### **6.4.1 Organisation and oversight**

Focus groups participants considered how genomic medicine may become integrated into the UK health care system in the future, and rolled out at scale. The current political climate was expected by some to influence the future of genomic medicine and the development of policy in this area. Brexit was raised as potentially inhibiting scientific and clinical collaboration between countries:



*I think we should be working with our European partners and putting our heads together. It should be global as well. (M, group 2)*

Nonetheless, some suggested that the development of the genomics industry would follow previous developmental trajectories:

*When we get new areas of medicine, it always starts, like with general practice, so usually in secondary or tertiary care and there are champions who introduce that and lead often with the pharmaceutical industry and in partnership with researchers... And then it becomes broad, basic, general practice and I don't see that genomics is going to be any different to that, really. (M, group 2)*

Others envisioned that far greater complexities would arise with the advancement of this field, and felt that new, extensive collaborative networks of healthcare professionals and other stakeholders from a range of disciplines would be needed in order to develop a stable and successful genomics sector.

Creating committees to oversee the genomics industry was one suggestion that participants felt could facilitate the development of genomic medicine. Participants held various ideas on the form these could take. Using cancer as an example, one participant suggested:

*... what would need to happen is there would have to be committees set up, multidisciplinary committees who [um] – stakeholders. You have your oncologist, your haematologist, your [um] lung cancer specialist, breast cancer specialist, prostate cancer. (F, group 1)*

Another participant emphasised the need for transparency amongst such committees, who should ensure that patients can give informed consent to undergo WGS. The role of patients in such committees was also discussed in the focus groups:

*The people who have the gene ought to make a decision as to how best to manage it. (M, group 2)*

*It would be worth talking to these groups, because they have direct experience of the consequences of the anxieties and tailoring it to individual patients and counselling. (M, group 2)*

It was also suggested that charities have an important role to play in understanding particular diseases that could be managed with genomic medicine:

*... the charities for specific diseases will be incredibly important in helping us to navigate through the new world. (M, group 2)*

The need for ethical regulation of genomic medicine also became apparent in focus groups:

*You have to have very strong ethical bodies on this concept of genomics. (M, group 4)*

The responsibilities of health care professionals in the future of genomic medicine arose in discussions. Participants emphasised that following WGS, genomic information would need to be carefully interpreted, and the results relayed by a trained health care professional. However, they had differing ideas on the roles different health care professionals should take. Some felt nurses would be best suited to dealing with patients:



*You'll have to have a cohort of specialist nurses, [um] you know, working with that, who would be able to sit down with patients, talk through things. Because you tell someone, "Oh, you've got a breast cancer gene which killed your Grandma," and they're going to burst into tears. And the acute physician does not have time...to sit down to you know, comfort a patient. (F, group 1)*

Others suggested that GPs should liaise with patients in relation to WGS. One participant felt that their role should be to build trusting and supportive relationships with patients:

*It is more about the nurture bit of things. I think that's how we interact and it isn't academic and scientific in that sense. It's interpretation and giving people comfort in this rather frightening world. (M, group 2)*

Participants also considered the part GPs might play in interpreting results and deciding whether treatment is needed and justified:

*Our role will be to attempt to be the voice of reason in discussing it and that will, our voice of reason, will improve as more knowledge becomes available to us. (M, group 2)*

There was a worry by some that this could increase workloads for GPs:

*GPs will get asked a lot of questions about a lot of percentage chance of things that just isn't in their field to explain. It will be a huge burden on them. (F, group 3)*

Concerns also arose over the negative impact that WGS could have on doctor-patient relationships. One participant suggested that it could pose a barrier to effective face-to-face interactions:

*People get used to the idea of I can solve this just by ordering a test rather than talking to the patient. (M, group 4)*

Another participant feared that WGS might change the role of healthcare professionals:

*We don't want to lose the essence of what being a doctor is. (M, group 4)*

Whilst participants had limited knowledge of the 100,000 Genomes Project, and of the regulations on WGS, there was an acknowledgement that logistical issues would also need to be carefully considered. One concern was how to have samples processed quickly enough. Similarly, cross-matching samples and information with complete accuracy was mentioned as something that could pose a challenge if genomic medicine was rolled out in the NHS. One participant summarised the logistical challenge as follows:

*So, problems of confidentiality, of security of information, of veracity of information, as well as you mentioned, going to the laboratory, but actually making sure that data does actually apply to the right person. There's lots of logistical issues associated with it, I think, as well as ethical issues. (M, group 3)*

#### **6.4.2 Financial implications**

Focus group participants considered the feasibility of rolling out genomic medicine in the context of the financial situation of the NHS. Not all were optimistic about the future of genomic medicine:



*I can't see us having that money in the UK. So, at risk of being the most pessimistic person around this room, I think a lot of this is just talk. (F, group 1)*

Where WGS was considered to be a possibility, several retained concerns over the implications of limited funding, and the impact this could have on the distribution of any genomic medicine service. In focus group 1, in particular, discussions centred on patient selection, and where the line would be drawn in terms of who should be offered WGS. Whilst some felt that prioritising certain patient groups, “might not be fair” (F, group 1), others felt that clear guidelines were necessary to, “stretch our limited resources” (F, group 1). It was suggested that funding must be directed towards the diseases which would see most patient benefit. Similarly, the age of the patient, prevalence of disease and likely success of treatment were all factors that were seen as important to take into account when developing guidelines. Concerns were raised over how patients might respond to patient selection:

*... not everybody is going to be happy because there's also going to be the ethical consideration of why is it my disease that doesn't get funded? Why is it your disease that gets funded? (F, group 1)*

Discussions in focus groups also centred on alternative means of funding WGS. The UK was contrasted with the US, which was cited as an example where private funding offered the opportunity for progress:

*This is a system that's trying to cater for all of us, and our patients, within a limited budget... Otherwise, you know, in the US, you'd have pharmaceutical companies sponsoring all this research... (F, group 1)*

It was suggested that genomic medicine would operate in the private sector in the future:

*I wouldn't be surprised if there was a sort of move towards saying, “Well, you can't get it on the NHS, but I'm going to pay. I'm going to pay to get my children tested for this. (F, group 1)*

Others also predicted that WGS might be funded privately, and taken up by “...the rich who think they can buy their long life and their health because they have got the money to do it” (M, group 3). The ethics of offering sequencing technologies outside the NHS divided participants. One health care professional felt that this was acceptable, as it would advance knowledge:

*... if we do not study it, they will not have the opportunity even to know. (F, group 1)*

Another participant argued that this could widen existing inequalities:

*What about the other population which will be left behind? Because it will be another class thing. (M, group 1)*

His peer, however, saw this as inevitable:

*Unfortunately that is just going to be the way humanity is. (F, group 1)*

### **6.4.3 Knowledge gaps and training needs**

The training needs of health care professionals related to WGS were a subject of discussion in focus groups. Some felt that, in comparison to North America in particular, personalised medicine in the NHS “lagged behind” (F, group 1); education



was seen as central to the development of successful genomic medicine in the UK. It was suggested that genomic medicine should be taught to medical professionals as early as medical school. Aspects that should be covered in training included when to use WGS, how to conduct the tests, interpreting the results, counselling patients and deciding treatment plans. For those healthcare professionals already in practice, some felt that specialised training would have to be provided. It was suggested that the pattern of training and spreading of expertise would have to be designed to be realistic, for example:

*... expertise needs to be developed carefully and in a focused way to be used as a resource by those of us who don't have the time or energy to learn yet another field of medicine before we stop. (M, group 2)*

One participant felt that GPs, in particular, may need guidance on genomic medicine:

*Perhaps the Royal College of GPs does actually need a department of genomics to advise and guide those GPs on each new test that is coming up. (M, group 2)*

## 6.5 Summary

Many of this set of focus group participants did not have much knowledge of genomic research and genomic medicine and had very mixed views about it. There was recognition of the scientific potential of this development among some professionals, while others remained sceptical about what it would actually mean in practice and raised various ethical and practical concerns, such as the cost to the NHS of implementation of a genomics service, equality of access to this new technology and risks related to potential 'genetic engineering'. Concern was also raised about what was seen to be unnecessary over-medicalisation within NHS practices as a result of the application of genomic testing. For example, non-specialist staff had concerns that receiving uncertain results could drive patients to seek further information, pushing health care professionals to carry out a multitude of further tests, often unnecessarily. They also questioned the impact on their own workload of the widespread roll out of genomic medicine.

In general, non-specialist health care staff were more reserved and sceptical about the potential of genomic medicine than those who worked in the field and did not necessarily believe that WGS in itself would necessarily offer additional value to society without concomitant major advances in disease-specific cures.



## Chapter 7: Discussion

### 7.1 Summary of findings

This report presents the results of a qualitative study, which explored expert professional and lay experiences of recruiting for, and participating in, the 100,000 Genomes Project, as well as the perceptions of the wider public and non-specialist NHS workforce of the Project and genomic medicine more generally. The purpose of the study was to inform Genomics England and NHS England of any issues that might reduce the odds of ‘success’ of the 100,000 Genomes Project, and to help facilitate future participation by as wide a range of people as possible within the two groups of interest – those with rare diseases and a number of relatively common cancers. From late in 2015 to the end of 2017, we conducted in depth, one-to-one interviews with people who had consented to participate in the 100,000 Genomes Project, as well as interviews with specialised health care professionals involved in its implementation. We also conducted focus groups with the non-specialist NHS workforce and the general public including sub-groups of the public seldom heard in research. As such, this report utilises a unique dataset and has captured a wide range of perspectives on a rapidly emerging area of health service activity relevant not only to the 100,000 Genomes Project but also to the NHS Genomic Medicine Service announced in March 2017 ([www.england.nhs.uk/genomics/nhs-genomic-med-service](http://www.england.nhs.uk/genomics/nhs-genomic-med-service)). On the other hand, it can only reflect the situation as it was in 2015-17. The Project has evolved since then and has also begun to be able to provide feedback to participants at scale (see below).

We found that genomics as a quickly advancing area of medical science is little understood in the public sphere and by the non-specialist (i.e. not involved directly in genomics) NHS workforce. Knowledge of this area is limited to those working in the area and to some patients/families with a strong, longstanding vested interest in the area, predominantly those with rare genetic conditions. Most people, most of the time, think little if at all about most of the issues raised by genomics unless they are prompted by personal or familial experience.

Nonetheless, we found that support for the Project and what it is trying to achieve is widespread. However, there were some concerns about genomics in general, and the Project’s implementation, specifically, but which differed between different groups. The balance between enthusiasm and caution varied. Discussions with those who had little knowledge of genomics, or of the Project, were characterised by seeking more information through questioning, and drawing on their prior knowledge of other areas of health care or what they had learned from mainstream media to discuss the topic at hand. These groups included the general public, and, perhaps more surprisingly, non-specialist health care staff. These groups primarily speculated on the potential benefits of genomic medicine, the concerns it raises and the role it could play in the future of the NHS. The general public was generally optimistic about the benefits that genomic medicine might bring to society, and speculated that future generations might not have as great a disease burden as the present population as a result of the application of genomic technology.

Non-specialist health care staff were more reserved and sceptical about the potential of genomic medicine than those who worked in the field, and did not necessarily believe that WGS in itself would necessarily offer additional value to society without concomitant major advances in disease-specific cures. Non-specialist staff also had concerns that receiving uncertain results could drive patients to seek further information, pushing health care professionals to carry out a multitude of further tests, often unnecessarily. They also questioned the impact on their own workload of the widespread roll out of genomic medicine.

There were some concerns in the public focus groups related to data protection and ownership of the data but also a recognition that the members of these groups willingly gave their consumer data to supermarkets and other retailers via loyalty





cards every day, with relatively little anxiety. Non-specialist staff also raised these issues in discussion, on behalf of the public and patients. It was telling that the BAME group expressed more serious concerns about data protection and ownership than the other public focus groups. This group held strong views that the data had to remain within the control of the NHS as a trusted data custodian. Genomics England has subsequently undertaken in-depth work to understand the views of people and patients from BAME backgrounds (see: [www.genomicsengland.co.uk/about-genomics-england/how-we-work/patient-and-public-involvement](http://www.genomicsengland.co.uk/about-genomics-england/how-we-work/patient-and-public-involvement)).

Interviews and discussions with groups of people more familiar with genomic medicine, and the 100,000 Genomes Project, specifically, were characterised by more in-depth knowledge of the potential risks and benefits of the technology, such as the potential impact of secondary findings on the patients themselves and their family members. These groups included the focus groups with a rare disease support group (Cardiomyopathy UK) and a cancer activist group (Independent Cancer Patient Voices (ICPV)), as well as interviews with health care staff involved in the Project's implementation. The two focus groups expressed strong views about the sensitivity of feeding back secondary results and the potential harm this might cause patients and their families in particular circumstances.

Key themes emerging from the analysis of data from Project participant interviews were trust in the NHS and, by extension, the Project itself, the importance of the quality of their communication with the GMCs and Genomics England, and the strong emotions generated by genomics and/or the Project. There was a striking lack of knowledge and understanding on the part of participants about how the Project was organised and run. They did not seem to feel any discomfort about this lack of knowledge. Participants did not know and did not appear to care because of their trust in the processes and the NHS. The analysis revealed trust (in health professionals, in data protection processes, in the NHS as an institution and in public good scientific research more generally) as well as excellent communication with individual health professionals (as against the Project corporately) as key strands in promoting their positive views of the Project. However, it has to be borne in mind that the study was not able to interview those who had been approached but had chosen not to participate in the Project. It is certainly plausible that they might have had more negative and/or critical views both about the Project and genomic medicine more widely.

Participants were very differently 'invested' in the Project and its processes, depending on their particular circumstances. The rare diseases group tended to be more reflective about taking part in the Project and what it might mean in the longer term, while the cancer group was more typically distracted by their disease and treatment. Across both groups, there was a sense of pride in taking part in a bigger, pioneering project. It is striking that the focus group participants expressed more concern about different aspects of the Project. It may be that the Project participants were generally more trusting and comfortable with the Project because of the thorough consent processes implemented by Genomics England and the GMCs. While some participants mentioned the onerous consent process, there was acceptance that this level of detail and care was necessary. The differences between Project participants, especially those with rare diseases, and those in the focus groups (who were mostly not Project participants) may also simply be a reflection of the fact that the former group had much higher and more specific expectations that WGS might provide them with answers to longstanding questions about their and their families' unusual conditions.

Amongst professional staff directly involved in the 100,000 Genomes Project, concerns were specifically related to their experiences of implementing the Project to date, particularly the difficulties of having to implement the Project within a resource-poor NHS setting (if participants were situated in a GMC or other patient-facing roles) and their perceptions of the Project's implementation as highly target-driven. Relationships



between the 'centre' and the 'periphery' were important and appeared to be somewhat strained in the period 2015-17. Staff close to the 'centre' of the Project (those who worked for Genomics England or NHS England) were seen by local actors as being very much in control of the Project from the outset, and 'peripheral' staff felt insufficient attention had been given to their expertise or experience in the planning and evolution of the Project. This perception was accentuated by the strong performance management of the GMCs by NHS England and Genomics England.

## 7.2 Relationship with previous research

Our findings support the argument that the 'social unease' concerning the collection, storage and use of human tissue in medical research widely discussed in the existing literature may be overstated. It has been argued that it is largely based on theoretical debate among experts or single case analyses (Dixon-Woods et al, 2008). The current qualitative study of participants in the 100,000 Genomes Project and of members of the public reveals a generally supportive attitude towards genomics research and a willingness to participate, together with a strong trust in science, researchers and institutional governance, especially in the NHS (Lipworth et al (2011). Indeed, our analysis revealed a remarkable acceptance by participants of lengthy timescales, waiting for results and even some discomfort. For example, while recounting problematic experiences during the process of giving samples, participants offered only mild rebukes or suggestions for change rather than expressing serious concern with the Project. On the other hand, it needs to be recognised that the study was not able to interview those who had been approached but chose not to participate in the Project who might have been expected to have more negative or critical views.

There was also evidence within the focus groups with members of the public that unease could be generated in the minds of participants as a result of research processes. As Hoeyer (2003) found;

"The very act of questioning people or involving them in a hypothetical deliberative process may plant a seed of doubt that their judgements have been under-informed and they 'ought' to think differently as responsible citizens."

## 7.3 The 100,000 Genomes Project and the implementation of public sector projects

The 100,000 Genomes Project was as its name suggests a 'project'. This meant that it was managed separately from the routine activity of the NHS with its own structure and system of accountability. It was also time-limited and, as its title indicated, there were clear, ambitious, centrally set targets related to the number of genomes that were to be collected within the life of the Project. The Project was initiated by, and strongly associated with, central government and had a deliberately high public and political profile. The then Prime Minister, David Cameron, was closely associated with it and led the launch. While the Project was implemented through a new special purpose vehicle – Genomics England, a company owned by DH – and a network of regional GMCs, there was relatively little additional funding for the GMCs in relation to the tasks and responsibilities given to them. Also, much of the work fell to NHS staff who had to accommodate the Project in addition to their existing commitments. This was partly because the Project was initiated during the lengthy period of public sector financial austerity instituted after the 2008 financial crisis but also because there was a relative dearth of staff with sufficient training in genomics capable of implementing the Project locally. As a result, specialist staff reported that they were being stretched between their existing work and the additional requirements of Genomics England.



The work itself was novel in that nothing on this scale had been undertaken before in the relatively new field of genomic medicine in the UK and planning it involved inevitable and considerable uncertainty. The Project was also a hybrid in that it was neither a very large-scale research project nor a health service but had characteristics of both. Its task was to build a large genomic databank with potential for long-term research as well as providing an opportunity to learn how a new genomic medicine service might be provided more routinely across the NHS after the end of the Project period. The Project was officially described as an NHS ‘transformation service’ by Genomics England.

Research-related aspects of the Project meant an intense focus on participant informed consent, data anonymity and data security. The Project recruited ‘participants’ rather than ‘patients’ and participants might be past or current patients or never patients. While the Project asked participants to give consent for their data to be used in the Project over the long term, it was not set up in such a way as to be able to engage with them as participants over the long term (unlike, for example, in biobanking projects which return at intervals to their participants to collect further data and to report on the findings emerging from the research that has come about as a result of the biobank). Some participants were told by their recruiting consultant, appropriately as it happens, that they might never be contacted by the Project again. Our analysis suggests that the rare disease participants would have welcomed more communication after donating a sample but cancer patients possibly not.

This combination of high expectations from central government, novelty (with related technical and logistical challenges), multiple goals and very constrained additional funding produced a stressful environment for national and local implementers. This appeared to be felt especially at GMC level where staff reported a lack of involvement in the planning of the Project and a sense that their expertise was not being listened to. This meant that any initial enthusiasm had to compete over time with some disillusionment. The initial highly publicised targets were not met because it took considerably longer to undertake each stage in the process; identifying potential participants, analysing samples and making them ready for research and/ or feedback to participants. Returning ‘results’ to participants was perceived by GMC staff as particularly stressful. Our analysis suggests that the Project could have been implemented more effectively and there may be value in learning from the Project to inform similar initiatives in future.

Evidence suggests that successful implementation of a service transformation depends on a range of interdependent processes. The report of a recent WHO expert meeting on health system transformation (WHO, 2018) highlighted the following as potentially critical:

- reconciling and managing tensions between ‘bottom-up’ and ‘top-down’ approaches to policy implementation;
- developing a coherent vision of the desired end-state;
- ensuring ongoing political support;
- appropriate leadership across all the agencies involved;
- adequate resources; and
- supportive information and other technology.

To what extent did the Project demonstrate these features in the period 2015-17 and what can be learned from the experience? It appears that the Project largely succeeded in developing a coherent vision of the desired end-state, ensuring ongoing political support and had appropriate leadership. However, it is less clear whether support from Ministers and the top-down imperatives to deliver the 100,000 genomes were effectively informed by, and reconciled with, bottom-up feedback to the centre on the practical realities of implementing the Project. The speed of



planned implementation was not realistic and the Project could have benefitted from more effective interaction between officials at the centre and the GMCs. The central government culture of 'can do' and emphasis on 'delivery' means that there is a tendency for officials to avoid raising awkward details of implementation for fear of being seen as obstructive of activist ministers (King and Crewe, 2014). For example, necessary changes in laboratory processes had not been identified fully before the Project started. During the pilot and initiation phases of the Project, experimental work was still having to be undertaken to adapt the DNA extraction process from cancer patient tissue samples to minimise DNA damage. This work concluded that fresh tissue was required for optimal WGS ([www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project/information-for-gmc-staff/cancer-programme](http://www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project/information-for-gmc-staff/cancer-programme)) and a new process had to be implemented at short notice across the GMCs.

Staff at GMC level were not encouraged to question the aims of the Project or the means of implementation. The high level of ambition announced at the start of the Project was not informed by a thorough feasibility assessment of what could be done within a particular period of time. Staff at all levels had to locate and solve implementation problems as they arose.

Our analysis of the data from the interviews with specialist professionals revealed concerns specifically related to experiences of implementing the Project within a resource-poor NHS setting (if staff were situated in a GMC or other patient-facing roles). Participants perceived the implementation of the Project as highly and possibly excessively target-driven. The high level political support and level of ambition was a two edged sword; it both maintained the profile of the Project and a sense of urgency to generate 100,000 genomes while demanding unrealistic recruitment targets.

Participants further reported feeling that insufficient attention had been given to their expertise or experience in the planning and evolution of the Project which meant that the Project plan was insufficiently grounded in the realities of local health care systems, at least from their perspective. Communication was experienced as largely uni-directional, with staff close to the 'centre' of the Project (those who worked for Genomics England or NHS England) seen as being in control of the Project at the outset while GMC staff were 'peripheral'. These are issues around effective leadership and communication and provide further evidence of unmanaged tensions between 'top down' and 'bottom up' approaches.

Information technology systems played a major role in the implementation process but were highly problematic. The speed of initial planning and setting of ambitious milestones, perhaps understandable in the context of high priority politically led policy developments, did not fit with the practicalities of implementing a new system of data collection and storage. This is exemplified by the need to change the basis of sample collection to fresh frozen during the Project. This had not been identified as a risk at the outset and there was no contingency built into the Project for such unexpected eventualities. Given the novelty and scale of what was being attempted, this was risky and speaks to a lack of adequate resources and supportive technology.

These findings resonate with those of a more detailed evaluation of the implementation of the West Midlands GMC undertaken entirely separately but over approximately the same period as the current study, between December 2015 and January 2017 (Brown and Exworthy, 2017). The West Midlands study, which included interviews with national level stakeholders, core GMC staff and recruiters, but also staff in Local Delivery Partner (LDP) organisations in the West Midlands, identified a similar tension between the Project as a research enterprise and a service transformation initiative designed to lay the foundations for the introduction of genomic medicine into the mainstream of the NHS in England. Similarly, participants grappled with the dissonance between having a strong vision of how the Project



might benefit patients and the NHS in the future, and the current reality of practical challenges, delays in processes and in results reaching participants, and the length of time before findings would be likely to benefit patients. Interviewee staff in the West Midlands reported how delays were de-motivating staff in LDPs and beyond which was reflected in the findings of the current study. LDP staff similarly complained that the GMC did not understand or take adequately into account the constraints under which they were operating in just the same way as GMC staff in the current study complained about the way in which staff at 'the centre' failed to appreciate the environment and capacity of the GMCs. In the West Midlands, there were similar concerns about the capacity within the GMC and the LDPs of already busy staff to cope with the extra work demanded by the Project within the timescales required to meet centrally determined targets. Similarly, GMC and LDP staff reported that work on the Project was having negative consequences for other pre-existing areas of their work and particular groups of staff (e.g. phlebotomists) due to insufficient additional resources being available. As with the participants in the current study, informants in the West Midlands were also able to identify positive effects of involvement in the Project, for example, when it was possible to recruit more staff (e.g. from charitable sources as well as from Project funds) and when front-line staff became more knowledgeable and confident in approaching patients to recruit them to the Project. Although relationship building took longer than Project timescales allowed, staff did report how the GMC's activities had initiated the development of a network of relationships across the Region. Although only a narrow range of clinicians and other staff were actively engaged with the Project in 2016 and early 2017, the network had the potential to provide a basis for the future.

One aspect of the Project which appears to have been particularly effective was obtaining participants' consent. There was upfront commitment to evaluate consent materials and process at an early stage on the grounds that this was a crucial part of the Project, particularly given the demanding time-related targets for participant recruitment. The evaluation led to prompt action to simplify the materials given to potential participants (NW Coast NHS Genomic Medicine Centre, 2016). In this case, experience of similar research programmes did appear to have been used in the planning process.

The evidence of past successes and failures of UK Governments indicates that setting up the Project as a 'project' with dedicated central management rather than as part of the routine work of government or the NHS was also a definite advantage. A number of past failures of innovative centrally led initiatives have been associated with inadequate attention to the complexity and ambition of innovations and the resultant need for dedicated expert management (King and Crewe, 2014). By contrast, the 100,000 Genomes Project had strong scientific leadership in place at the national level. In this regard, it conformed to the third of the ten 'lessons' or principles of effective policy implementation in the UK context contained in the Institute for Government's report, *Doing them justice: lessons from four cases of policy implementation* (Norris et al., 2014) (see below).

Where the Project was perhaps on less secure ground relates to the points made above on time pressures and the extent to which the perspectives of those at local level on whom implementation to time ultimately depended were taken into account in the planning. The full list of the Institute for Government's ten 'lessons' for effective policy implementation which cover these aspects, among others, is given below. The Project exhibited some of these principles much more strongly than others, as follows:

- 1. Be clear about the problem and the outcomes that matter most** – this was a strong point of the Project and was conveyed consistently to all parties in terms of the long-term vision for genomics in the UK;



2. **Think about implementation while still developing the policy** – the Project worked hard to integrate policy design and implementation, though not always entirely successfully, at least from the perspective of local implementers who felt that more could have been done to take their perspectives and experience into account (see above);
3. **Get the right capability** – already mentioned above and a strong point of the Project, particularly in relation to its research and scientific aspects;
4. **Be aware of, and ready to respond to, the wider system** – while the assets in the NHS were clearly built upon, it is less clear that the constraints of a health care system under immense pressure were fully taken into account in the implementation planning. In this sense, the timing of the Project during a period of unprecedented slowdown in the growth of NHS resources was a limitation;
5. **Stay close to the implementers** – this principle encourages creation of short feedback loops between implementers and the policy ‘centre’ which was certainly a feature of the Project enabling information about progress to flow easily upwards. However, GMC staff perceived that this led to increased pressure to deliver against overly demanding performance targets (see ‘lesson 2, above);
6. **Be clear about where and how decisions are made** – the use of project terminology, organization and management made decision making responsibilities very clear;
7. **Invest in routines to keep implementation on track** – this relates to regular scrutiny of progress both by officials and Ministers which was strongly evident in the Project;
8. **Use junior Ministers to drive progress** – this is the lesson that policy areas where junior ministers are closely involved tend to have the best prospects for being successfully implemented. Since Genomics England was set up as a company with its own board, outside the DH, specifically to deliver the Project, this aspect of the implementation process was much less apparent;
9. **Allow for and learn from variation** – GMC staff tended to report that the target setting and reporting process on a very regular basis allowed little space for this lesson to be applied;
10. **Build in long-term focus** – this was an explicit aspect of the Project. The website states that the Project will ‘create a new genomic medicine service for the NHS – transforming the way people are cared for and bringing advanced diagnosis and personalised treatments to all those who need them.’ [www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project](http://www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project)

One question to ask of the 100,000 Genomes Project is whether some of the implementation problems could have been identified in advance with greater deliberation (King and Crewe, 2014) which is not traditionally an activity associated with fast-moving central government policy-making in the UK. There is inevitable uncertainty in putting in place a novel system for the collection, storage and use of genomic samples on a large scale. However, a longer planning period and better engagement with GMC staff may have led to the earlier identification of technical stumbling blocks and the resolution of these problems more efficiently and at less cost. It might also have been advantageous from the outset to have adopted the approach taken in related types of enterprise such as biobanking where participants enter into a long-term relationship with the research team in which typically they are continuously kept informed about the ways in which their data are being used and



with what results. The interviews with the rare diseases Project participants suggested that these people would have welcomed more communication with Genomics England after having donated their samples.

## **7.4 Strengths and limitations of the study**

### **7.4.1 Limitations**

This study provides a unique insight into a unique project, albeit over a limited period in its life from late 2015 to late 2017 and before many participants had received their findings. The 100,000 Genomes Project was remarkably ambitious in scale, timings and implementation. This led to some delays and setbacks which affected the current study. Firstly, delays in the initiation of the cancer arm of the main Project delayed our data collection and limited the pool of people available to speak to since we were asked not to interview cancer patient participants from the pilot stage of the Project. Secondly, the very significant delays in setting up the sequencing of genomes, and consequent delays in results being processed, fed back to GMCs for checking and thence to participants, meant that we were unable to interview any people who had received their results. This remains an important focus for future research in order to understand whether, and, if so, how, the findings of WGS contribute to their health care.

A limitation we foresaw was the recruitment of people who had declined to take part in, or who had withdrawn from, the Project and while steps were taken to discuss ways to recruit this group our efforts were unsuccessful. GMCs either did not keep records for people who had declined or were reluctant to contact people who had declined participation, for ethical reasons. Despite a concerted effort to recruit people via social media and patient support groups, we were not able to recruit anyone within this category. The current study found little unease among participants about genomics or the security of their sensitive personal data within the Project. However, it is possible that people who declined to take part in the Project might have been more concerned on both counts. It is important that research focusing on participants and non-participants is conducted in future to generate a more complete understanding of attitudes to genomics and genomic research. This would be helped by seeking permission at the time that people decline to take part in genomics for researchers to contact them to explore their reasons.

This latter issue about re-contact raises an interesting ethical point. We were interviewing participants, some of whom were patients and some of whom were not. Their consent, or not, to be involved in the 100,000 Genomes Project was not relevant to the ethics of our research and their consent to participate in our study. In retrospect we might have used this argument to try to allay fears about the unethical nature of re-contact for research and to encourage GMCs to allow us to contact those who had chosen not to take part.

The scale and time pressure of the Project also had an impact on the willingness, or ability, of GMCs to help with the recruitment for our research. Five of the 13 GMCs in England were able to offer us support in recruiting participants. We do not know if the experiences of the other eight GMCs' staff are the same, although informal discussions would suggest that they are unlikely to have differed considerably.

### **7.4.2 Strengths**

A major strength of the current study lies in the range of different types of people interviewed, such as from BAME communities, learning disabled people and younger people. In particular, the recruitment of a diverse sample of focus group participants,



including people typically seldom heard in such research (e.g. members of BAME communities and younger people), generated a comprehensive and in-depth understanding of attitudes to and understandings of genomic research. Although it was extremely hard work to identify, contact, recruit and convene such focus groups, sometimes requiring creative methods such as organizing ‘pop up’ focus groups in shopping centres, we think it was worth the effort.

## 7.5 Implications

1. It is clear that non-specialist clinicians’ knowledge about genomic medicine and its potential is limited and, in general, such clinicians are wary of claims that genomics will transform their work and patient care. This suggests that professional bodies and Health Education England have a considerable task ahead to inform the wider NHS clinical workforce about genomics and how they should engage with the evolving ability of the NHS to provide genomic medicine services to support a range of different specialties and services. It also suggests that the pace of any roll-out of genomic medicine in the wider NHS will depend on successfully communicating the proof of the potential and actual value of genomics to a dispersed clinical community which has many other competing interests and pressures. Currently, Genomics England reports that the Project is providing a diagnosis in 20-25% of its rare diseases cases and in 50% of cancer cases the data are judged as containing the potential for a therapy or a clinical trial ([www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project](http://www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project) accessed 3 February 2020). This was not the case during most of the period of this research but indicates that more positive messages can now be communicated to the wider NHS workforce.
2. Participants in the 100,000 Genomes Project expressed strong support for its goals and demonstrated a high level of trust in the NHS to implement the Project in a way that would protect their interests. However, there was a desire for more information from the Project after the initial DNA samples had been collected, even among those who had been clearly told that they might not hear anything again from the Project. Participants appeared to appreciate being updated periodically as to what the Project was achieving so that they could see what they had contributed to and as a marker of appreciation for their involvement. Subsequently, Genomics England has attempted to address these concerns by instituting a ‘Track my sample’ process which was launched in December 2017 after data collection in the current study had finished. This was followed by a regular participant newsletter and more information on the Project’s website focused on the needs of participants. This sort of communication would also be likely to benefit the NHS workforce, highlighting the utility of whole genome sequencing as the evidence of benefit accumulates and so increasing the likelihood of staff embedding genomics in their future practice.
3. The 100,000 Genomes Project was a very challenging venture for the NHS, in part because it straddled the worlds of basic biomedical and clinical research, biobanking and management of large scale databases of human samples, testing and reporting of findings at the individual and family level, and service for a wide range of different actual and potential patients from extremely rare conditions through to common cancers. The implementation of this hybrid was not helped by its timing during a period of major austerity and restraint in NHS funding. There were also very ambitious timescales set at every stage in the Project with stretching targets in terms of collection and preservation of samples as well as delivery of findings to participants and relevant clinicians. Furthermore, the Project had a high political profile as it was a priority of the then Prime Minister, David Cameron. Those involved in implementing the Project at GMC level reported feeling pressurised to





deliver, sometimes they felt unfairly so, and commented on the extent to which the Project's management revolved around targets and league tables of the samples collected by each GMC. This was reflected in the title of the Project which was expressed as a target. While none of the implications of the experience of implementing the 100,000 Genomes Project are especially new, they show that there are opportunities to learn for future similar ventures. In particular, our analysis demonstrates a need for more engagement from the very start of planning with those who would be delivering the project. Given that Project milestones were routinely missed, it is possible that more realistic plans might have resulted from such a process. In turn, this might have reduced the odds of local implementers feeling disillusioned with the process. There is a fine balance between setting ambitious, collective targets and encouraging healthy competition between sites to deliver these targets, and onerous performance management which can be perceived at local level as bullying.

4. Given that this research was not able to interview people who had declined to take part in the 100,000 Genomes Project and given that such people had presumably thought carefully about this, it would seem useful to be able to find out from this group why they had made this decision with a view to improving the way the NHS approaches potential participants and/or other aspects of its management or reputation. Though declining to participate is not necessarily the result of any weakness in the consent process, it might help improve the way that the NHS approaches patients in the future to maximise their engagement with genomics services and/or related research to know more about non-participants' attitudes, preferences and views about genomic medicine. One way of making this more straightforward would be to include in any consent form an option for a non-participant to be followed up either by interview or questionnaire to provide the reasons for not engaging with genomic medicine.



## Dissemination via [healthtalk.org](https://healthtalk.org)

A new resource is ready for dissemination on the widely acclaimed website [healthtalk.org/experiences-participating-100000-genomes-project](https://healthtalk.org/experiences-participating-100000-genomes-project).

This is a key dissemination route for participants in the study as well as for a wider audience of the public, professionals and policy-makers.

Eight educational films on the following themes have been produced from the qualitative research featuring video material from the new resource:

1. Experiences of being invited to take part in the 100,000 Genomes Project
2. Concerns with taking part in the 100,000 Genomes Project
3. Reasons for wanting to take part in the 100,000 Genomes Project
4. Deciding to take part in the 100,000 Genomes Project
5. Thoughts on medical research and genomic medicine
6. Data protection and sharing in the 100,000 Genomes Project
7. Sample Storage in the 100,000 Genomes Project
8. Messages to Health Professionals and Genomics England

The films range between 2½ minutes and 10½ minutes long.



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## Appendices

### Appendix 1: Interviews with 100,000 Genomes Project participants: interview guide

#### Part 1: Project involvement narrative

- a. In this interview we want to focus on your experience of taking part (or choosing not to take part) in the 100,000 Genomes Project but could you start by briefly summarising your illness/condition experience?
- b. Could you now tell me about taking part in the Project from when you first heard about it? (Aim for participant to speak freely about their project journey with minimal prompting.)

Tell me about how you came to be involved in the 100,000 Genomes Project

Tell me what your involvement has consisted of so far.

#### Part 2: Specific topic questions

Explore areas brought up by patient in first section, may include:

##### General taking part

- What are your general attitudes to the idea of taking part in medical research?
- Why do you think you have these attitudes?
- Had you heard of the 100,000 Genomes Project before you were invited to take part?
- What is your understanding of the aim of the 100,000 Genome Project?
- What do you see as the potential risks/pitfalls of taking part in the 100,000 Genomes Project? (To yourself? To your family? To society?)
- What do you see as the potential benefits of taking part? (To yourself? To your family? To society?)

##### Invitation to take part/information

- How were you approached to take part?
- How did you feel about being invited to take part?
- Why did you decide/decide not to take part?
- What information were you given about the Project?
- Did you find the information helpful? How could it be improved?[what sort of format, online or paper form, read or spoken information, etc]
- What information did you need?
- Have you been on the GEL website? How did you find navigating the site? Anything particularly good or negative about it?

##### Decision making

- Was it a difficult decision to make?
- Did you discuss the decision with anyone?
- What were your hopes about taking part? [Or what made you decide not to take part]
- Do you feel you made the right decision?

##### Giving consent

- Tell me about giving your consent to take part in the Project
- What did you understand about what would happen if you took part?
- Do you feel you were fully informed about what taking part involved?



- The consent forms contain several tick boxes about the use of health data, confidentiality and so on. Did you understand these sections fully?
- What were your feelings around the two layers of findings you can consent to? The genetic findings and the health related additional findings?
- How did you feel about the process? What about the process made you feel this way?
- Could the process be improved? How?

### **Donating samples**

- Can you tell me what happened about donating your blood/tissue samples
- What did donating blood/tissue samples mean to you?
- How did you feel about the process?
- What was it about the process that made you feel this way?
- Did anything happen that you didn't expect or that surprised you?
- Could the process be improved? How?

### **Receiving results/feedback**

- Tell me about receiving any results/feedback (you don't have to share results with me if you don't want to, but rather tell me about the process)
- What did this diagnosis/result mean to you?
- How did you feel about the process? What about the process made you feel this way?
- Could the process be improved? How?

### **If no results**

- In what form would you like to receive your results?
- When do you anticipate receiving results?

### **Data storage/sharing**

- Tell me about what you understand about how your data will be stored/shared.
- How do you feel about this?
- Was anything said about possible commercial uses of the sample, use by private companies, drug companies, etc?
- Do you have any worries about this?

### **Messages to others**

- Do you have any messages for Genomics England about your experiences of taking part in the Project?
- Do you have any messages/thoughts for other people who may be asked to take part?

### **Finally...**

- Can you summarise now how you feel about taking part in the Project?
- Is there anything else you would like to say?



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## **Appendix 2: Interviews with 100,000 Genomes Project health care professionals: topic guide**

### **1: Background to the research**

- Who we are and what we are doing – collaboration University of Oxford and LSHTM, Healthtalk
- Funding – Department of Health, responsive policy stream
- Process – audio recording and transcription, included in analysis, but not attributable to individuals, they can check the transcription, consent form.

### **2: Their background**

- Their involvement – how and when did they become involved?

### **3: Their experience of being involved**

- What has it been like?

### **4: 100,000 Genomes Project – specific issues**

- Process issues
- Recruitment, consent (decliners and those not eligible), secondary findings, results and feedback, management – local and national
- Outcomes and success
- What do they feel has worked and what hasn't
- Learning and the future
- For the Project and for the wider NHS

### **5: Are there any other things you would like to bring-up?**

### **6: Other people they could suggest might be interested in participating?**





## **Appendix 3: Public and patient focus group agenda**

### **Introductions and ice breaker (15 mins)**

#### **Group discussion 1: Taking part in medical research) (20 mins)**

- Have you, or any of your family, taken part in medical research before?
- If yes, what motivated you to take part?
- If no, have you ever been asked to take part?
- Do any of you have any concerns about medical research?

#### **Brief overview/explanation of genomic research (show short film if available)**

[Videos, shown as needed – <https://youtu.be/gK1UKhDgc-c>; <https://youtu.be/nneWFaJ6Hfc>; <https://www.youtube.com/watch?v=P6a4N5dnxXU>]

#### **Practical section**

In pairs, think of three main concerns you would have about taking part in genomic research and three benefits of taking part. (20 mins) [These can be written on flip chart paper and stuck on the wall]

#### **Group discussion 2: Genomic research, trust and regulation (30 mins)**

- What do you think about genomic research?
- Does anything concern you about this project?
- Would you take part if you were invited?
- What would encourage you to take part?
- Who do you think should be able to use your samples?
- Questions around trust and confidentiality

#### **Concluding thoughts and summing up (10 mins)**



## **Appendix 4: Non-specialist health care professional focus group agenda**

### **Introductions (10 mins)**

- Researcher Introduction, purpose of group, agenda
- Confidentiality assurances
- Participant introductions
- Any questions?

### **Warm-up group discussion: What do you know about personalised medicine/genomics generally? (10 mins)**

- What do you know about personalised medicine (generally)?
- Do you have professional experience in this area? Does your role currently incorporate any genomics/WGS tests/research projects, etc?

### **Main group discussion 1: Perceptions of personalised medicine/genomics (20 mins)**

- What do you think the benefits of personalised medicine are? For individuals, for wider society?
- Do you have any concerns about personalised medicine? (Prompts: ethical issues, e.g. pre-diagnosing people with illness, over treating; feasibility for the NHS; hype versus reality; data; commercialisation; security; insurance)
- (What sort of impact do you think it might have on outcomes for patients in the future?)

### **Main group discussion: Perceptions of how personalised medicine/genomics will affect YOU/YOUR role/NHS in the future? (25 mins)**

- (Will personalised medicine/genomics change the NHS in the future (if at all)? In what ways?)
- Will your role change? In what ways?
- How do you feel about this? (Prepared? Excited? Training needs?)
- (Partner work: create wishlist for how NHS should integrate personalised medicine (10 mins))

### **Concluding thoughts and thank you (5 mins)**

Video – backup in case discussion is slow.

Genomics and personalised medicine – NHS Alliance (5 mins)

[www.youtube.com/watch?v=X8eNFa6fpLs](https://www.youtube.com/watch?v=X8eNFa6fpLs)

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