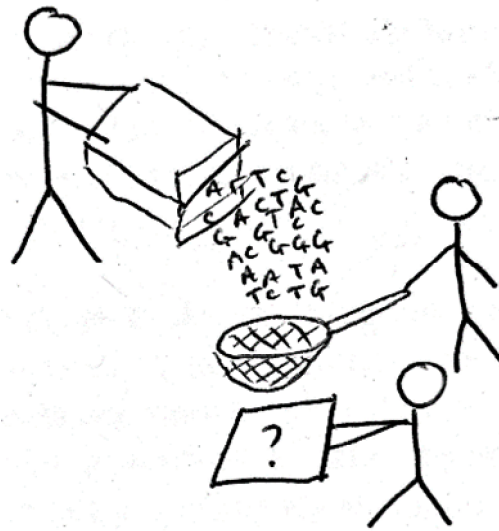


‘What is the result?’

Using facet methodology to explore the construction of results from genomic data



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Thesis submitted for the degree of Doctor of Philosophy

Michaelmas 2025

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Abstract

Genomic tests distil ‘results’ from the 4.1-5 million variants each person has in their genome. A proportion of these variants will be linked to disease, but their clinical significance will fluctuate with respect to multiple parameters. What then is the nature of a ‘genomic result’, and how should we seek to arrive at it?

I used facet methodology to analyse how genomic results were evinced in: stock images; UK news items; an archive of writing about everyday life; NHS clinical genetics appointments; interviews with people experiencing genomic tests; and through various engagement-oriented activities. My aim was to integrate how genomic results appeared in different arenas, bringing together empirical data and ethical analysis to generate ‘flashes of insight’ as to their nature and the processes by which they are determined.

I found that popular discourses tend to portray genomic results akin to ‘hidden gems’- potentially hard to find, but valuable and qualitatively different to the variants surrounding them. In clinical settings, they often seemed to have a different nature- nebulous, provisional, but animate and evolving. They grew through discussion and collaboration, and might be re-interpreted in different settings and for different purposes. The challenge was not so much ‘finding’ them, as determining what- if anything- they meant. Yet ‘hidden gem’ ideas often seemed to sculpt conversations around genomic results, limiting the ways in which we can discuss them, and representing only a fraction of what they are.

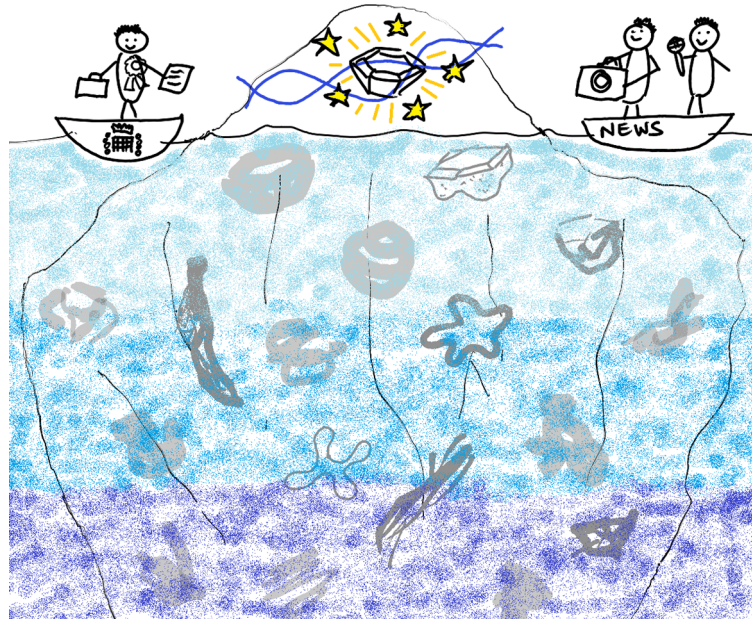
I argue we should aim for wider concepts of genomic results, positioning ‘hidden gems’ as the tip of an iceberg. Under the surface lie a variety of complex and sometimes challenging or dissatisfying experiences. The editing out of these experiences from popular discourse undermines abilities to have fruitful debates about when and how to use genomics to improve population health. It also creates an environment where consent conversations struggle to prepare people for subtle or underwhelming outcomes from genomic tests, and adds to the isolation of those who experience these in the context of rare disease diagnosis.

I conclude that a genomic result is more than a proven or likely connection between a variant and a disease. Hundreds of variants in any person’s genome could fulfil this definition- in appraising them as being a ‘result’ we are making choices to do so. If we could recognise and centre these choices, acknowledging genomic results as created, rather than simply uncovered, it might allow more constructive clinical and societal conversations around how, whether, when and why we should value particular genomic variation(s) as being ‘results’.

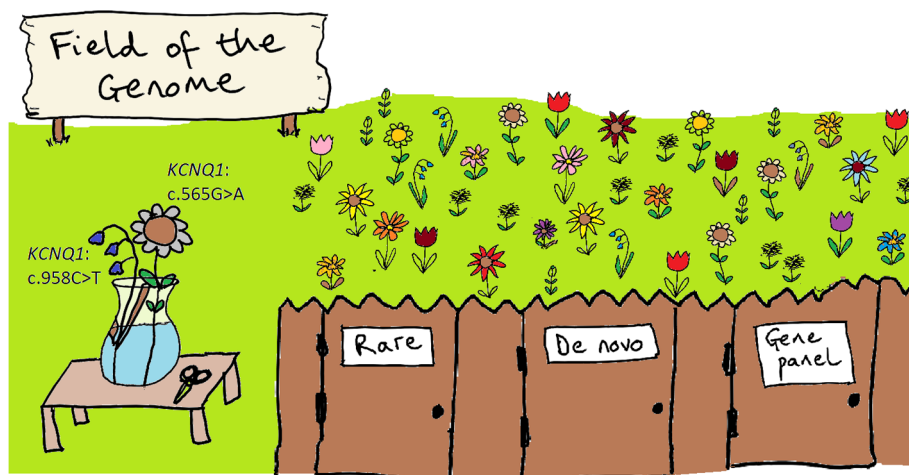
Visual abstract

How should we construct genomic results?

- a) We need wider concepts of genomic results that encompass complexity, subtlety and contingency: the powerful and transformative results given most attention in popular discourse are only the tip of a much bigger iceberg.



- b) A genomic result is more than a variant with a proven or likely link to disease. Choices made in navigating, appraising and engaging with the landscape of genomic variation all have a bearing on whether, when, why and how a genomic variation is valued as being a 'result'.



How will you approach?
Which will you choose?

Acknowledgements

I have had an amazing time doing this project and I am really grateful to lots of people for their role in making it such an interesting and enjoyable few years.

Firstly, I would like to thank my supervisors: Prof Anneke Lucassen, Dr Susie Weller, and Dr Angela Fenwick. This project would not have been possible without Anneke and I am hugely grateful to her for giving me this opportunity, for all her expertise and effort helping me improve my research, and for the constant encouragement and inspiration she has provided throughout. It has been brilliant being part of her research group. I am extremely grateful to Susie for the incredibly patient, illuminating and thoughtful support she has given me since becoming my supervisor in 2022. Her insights and guidance have added so much to my project and have really helped me grow as a researcher. I also owe huge thanks to Angela, who supervised this project from 2019-2020 and so constructively helped me think about my research question and approach in ways that were very new to me.

This project was funded by a Wellcome Trust Research Award for Health Professionals in Humanities and Social Science (218092/A/19/Z), and I am very grateful to the Wellcome Trust for giving me the opportunity to undertake this work. I have so enjoyed this chance to spend time doing research in this area and it has been a really fulfilling and inspiring experience. I would like to thank all the people who generously participated in my project and helped me learn more about the nature of genomic results, and the Trustees of the Mass Observation Archive at the University of Sussex for the opportunity to work with responses to the Mass Observation Project. I would also like to thank the team at Wessex Clinical Genetics Service who have been so understanding and supportive of my taking time out of my clinical genetics training to do this research.

I was very lucky to do this project in the context of the Clinical Ethics, Law and Society group, and from 2021 onwards within the Centre for Personalised Medicine, which gave me the chance to work with great teams of people with lots of research experience and diverse disciplinary backgrounds. The kindness and enthusiasm of the CELS team meant presenting and discussing my work was always really enjoyable as well as useful and challenging. The supportive and resourceful team at the CPM made it a very exciting place to work where it always felt very possible to turn ideas into reality. I would especially like to thank Dr Lisa Ballard, Dr Kate Lyle, Dr Julia el Mecky, Dr Gabrielle Samuel and Dr Juliette Schuurmans for the guidance and support they have each given me at many points throughout this project. I am also very grateful to Prof Michael Parker and Prof Caroline Wright, who examined this thesis, for all their encouragement and expertise in helping me improve it.

On a more personal note, I am really grateful to my incredible husband who has supported me throughout, and I would also like to thank my daughters, who slowed down this project by several years but brought me lots of joy along the way. I also want to say a huge thank you to my inspirational parents, my amazing sisters, and my extremely supportive mother-in-law.

Finally, I would like to thank Dr Ling Felce. Ling was such a massive support to me in my academic aspirations but also in my personal life. She was the most practically supportive person I have ever met, and at the time in my life I felt most lost she was pivotal in helping me find my way. She made the world a better place for me and many others. I owe her more than words can say.

Notes

Various chapters of this thesis build on or overlap with articles written and published during the course of this research project, of which I am first or joint first author.

Chapter 1 builds on arguments outlined in my commentary: *Unpacking the concept of a genomic result*. Horton R, Lucassen A, Fenwick A. The American Journal of Bioethics 2019; 19(1):70-71. <https://eprints.soton.ac.uk/429584/>.

Chapter 3 follows on from and overlaps with work reported in: *Glowing gels and pipettes aplenty: how do commercial stock image banks portray genetic tests?* Horton R, Boyle L, Weller S, Lucassen A. European Journal of Human Genetics. 2024 Apr;32(4):456-460. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10999410/>

A condensed version of Chapter 4 is forthcoming as: *'Transforming our future by unlocking the power of DNA: the representation of health-related genomic testing in UK news items'*. Horton R, Gordillo K, Lucassen A, Weller S. European Journal of Human Genetics. 2026.

A condensed version of Chapter 5 is published as: *'Everyday genetics' in the Mass Observation Project: insights on genetics from people writing for an archive of everyday life in Britain*. Horton R*, Weller S*, Ballard L, Lucassen A. European Journal of Human Genetics. 2026. <https://doi.org/10.1038/s41431-026-02113-x>

Chapter 8 discusses work published as:

- *Genomic data: building blocks for life or abstract art?* Horton R*, Lyle K*, Weller S*, Ballard L, Lucassen A. Front. Young Minds. 2024. 12:1249534. <https://kids.frontiersin.org/articles/10.3389/frym.2024.1249534>
- *Challenges of using whole genome sequencing in population newborn screening*. Horton R, Wright CF, Firth HV, Turnbull C, Lachmann R, Houlston RS, Lucassen A. British Medical Journal. 2024 Mar 5;384:e077060. <https://www.bmj.com/content/384/bmj-2023-077060.long>
- *Ethical issues raised by new genomic technologies: the case study of newborn genome screening*. Horton R, Lucassen A. Cambridge Prisms Precision Medicine. 2022 Oct 6;1:e2. <https://pubmed.ncbi.nlm.nih.gov/38550936/>
- *Making progress with newborn screening*. Lucassen A, Horton R, Weller S, Sansom S. Centre for Personalised Medicine, University of Oxford. 2025. <https://ora.ox.ac.uk/objects/uuid:74b2d861-c9c2-40af-b16a-c256ff72a558>
- *Realistic expectations are key to realising the benefits of polygenic scores*. Sud A*, Horton RH*, Hingorani AD, Tzoulaki I, Turnbull C, Houlston RS, Lucassen A. British Medical Journal. 2023 Feb 28;380:e073149. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9973128/>

Contents

1	Introduction	1
1.1	The starting point: human genomic variation	2
1.2	Navigating genomic variation in rare disease diagnosis.....	4
1.2.1	UK initiatives using genome sequencing in the context of rare disease diagnosis 7	
1.2.1.1	The Deciphering Developmental Disorders (DDD) study	7
1.2.1.2	The 100,000 Genomes Project	8
1.2.1.3	The NHS Genomic Medicine Service.....	8
1.3	Predicting future disease from genomic data	9
1.3.1	Predicting rare disease	10
1.3.1.1	The Generation Study (Newborn Genomes Programme)	12
1.3.2	Predicting common disease.....	13
1.3.2.1	Our Future Health	13
1.4	The climate in which genomic results are being constructed	14
1.4.1	Political positioning of genomics	15
1.4.2	Curricula around genomics.....	16
1.4.3	People's expectations from genomic testing	19
1.5	Why explore the construction of genomic results?	21
2	Research questions and investigative approach	24
2.1	Research questions.....	24
2.2	Research context	24
2.3	Ontological and epistemological stance	25
2.4	Facet methodology	29

2.4.1	Overview of key facets.....	32
2.4.2	Synthesis	33
2.5	Empirical bioethics.....	34
2.6	Ethical considerations in relation to this project.....	35
2.6.1	Ontological/epistemological considerations	36
2.6.2	Methodological and reporting considerations	37
2.6.3	Institutional ethics approvals	42
2.7	Summary.....	43
3	‘Genomic results’ in stock images	45
3.1	Rationale for analysing stock images.....	45
3.2	Methods.....	47
3.2.1	Critical discourse analysis orientation	47
3.2.2	Image collection.....	48
3.2.3	Specifics of image analysis.....	49
3.3	Results.....	50
3.3.1	Genetic material or data derived from it are often foregrounded in stock images 51	
3.3.1.1	The double helix	52
3.3.1.2	Slab gel electrophoresis-inspired patterns	54
3.3.1.3	ACGT	56
3.3.2	People are absent or take a secondary role in many stock images, with more emphasis given to laboratory equipment and genetic material or data.....	56
3.3.2.1	People having genomic tests	57
3.3.2.2	People delivering genomic tests.....	58

3.3.2.3	Laboratory equipment.....	59
3.4	Summary.....	60
3.5	Reflections on this facet	62
4	‘Genomic results’ in UK news	64
4.1	Rationale for analysing UK news	64
4.2	Methods.....	67
4.2.1	Collecting news items	67
4.2.2	Analysing news items	71
4.3	Results.....	74
4.3.1	Characteristics of news items included	74
4.3.2	Common frames by which genomic results are presented in UK news stories	
	78	
4.3.2.1	Genomic results are the fruit of amazing technological progress and we are lucky to live at a time where we can benefit from them	79
4.3.2.2	Genomic results are produced by ‘reading’ the entire genetic code	83
4.3.2.3	Genomic result as societal panacea	91
4.3.2.4	Virtuous people would want to share their genomic data.....	98
4.3.3	Absent voices	104
4.4	Summary.....	105
4.5	Reflections on this facet	107
5	Public perspectives around outcomes from genomic testing: analysis of responses to a Mass Observation directive on ‘ <i>Genetics and health in our everyday lives</i> ’	109
5.1	Rationale for examining how genomic results seem to be envisaged in the Mass Observation Project	109
5.1.1	The 2006 ‘ <i>Genes, genetics and cloning</i> ’ directive	111

5.2	Methods.....	112
5.2.1	Development of the 2022 ‘ <i>Genetics and health in our everyday lives</i> ’ directive	112
5.2.2	Analysis of responses to the ‘ <i>Genetics and health in our everyday lives</i> ’ directive	113
5.2.2.1	Thematic analysis.....	113
5.2.2.2	Specifics of analysing Observers’ responses.....	114
5.3	Results.....	117
5.3.1	Characteristics of Observers responding to the ‘ <i>Genetics and health in our everyday lives</i> ’ directive.....	117
5.3.2	Observers saw ethical expertise and societal involvement as essential in making decisions about genetics and its future uses	119
5.3.3	The word ‘genetics’ evoked a breadth of ideas.....	122
5.3.4	Observers drew on material across many domains and over a long time period in forming their opinions around genetics and its future uses	126
5.3.5	Genomic results tended to be written about as an amplification of genetic results rather than as potentially having a different nature	129
5.3.6	Observers wondered how ‘genetic knowledge’ might change the human experience or the nature of humanity	133
5.3.7	Observers held a range of views regarding taking part in genetic databases 137	
5.4	Summary.....	139
5.5	Reflections on this facet	141
6	Observations of clinic appointments where genomic results are discussed.....	144

6.1	Rationale for observing clinic appointments discussing genomic tests	144
6.2	Methods.....	146
6.2.1	Recruitment for observing clinic appointments.....	146
6.2.2	Generating data through observing clinic appointments.....	147
6.2.3	Analysing data generated via observation of clinic appointments	147
6.3	Results.....	149
6.3.1	Characteristics of appointments observed.....	149
6.3.2	Themes identified from observing clinic appointments.....	151
6.3.2.1	‘It’s like a jigsaw puzzle’: genomic variations do not stand alone as results 152	
6.3.2.2	‘It’s all very well saying to someone we’ll sequence all your genes, but if we don’t know what they do or what they mean...’: shared ideals versus ‘real’ results 155	
6.3.2.3	‘I’m not going to be able to answer that question for you today’: provisionality in the quest for genomic explanations	158
6.3.2.4	‘There seems a lot more on Facebook’: family members as interpreters of genomic results.....	161
6.4	Summary.....	163
6.5	Reflections on this facet	167
7	Ideas around genomic results arising in interviews with people experiencing genomic tests.....	170
7.1	Rationale for interviewing people experiencing genomic tests	170
7.2	Methods.....	172
7.2.1	Recruiting people experiencing genomic tests.....	172
7.2.2	Generating interview data relating to genomic tests.....	172
7.2.3	Analysing interview data relating to genomic results	173

7.3	Results.....	176
7.3.1	Details of interviews	176
7.3.2	Themes identified from interviews with people experiencing genomic tests 184	
7.3.2.1	“Forewarned is forearmed”: the power of results in the abstract.....	185
7.3.2.2	The heterogenous nature of genomic results	192
7.3.2.2.1	‘Nothing found’	193
7.3.2.2.2	Clear molecular diagnosis.....	193
7.3.2.2.3	Unclear outcomes.....	197
7.3.2.3	Building meaning through interaction: the role of collaboration in the construction and reconstruction of genomic results	202
7.4	Summary.....	207
7.5	Reflections on this facet	210
8	Genomic results explored via other angles	214
8.1	‘Building blocks for life or abstract art?’	215
8.2	Contributing to discourses around the use of genomics in population screening 220	
8.2.1	Newborn screening.....	220
8.2.2	Polygenic scores.....	223
8.2.3	Promotional discourses encourage uptake, but ultimately threaten the success of population screening involving genomics	227
8.3	Contributing to policy	228
9	Constructions of genomic results	230
9.1	In what ways do popular discourses invite us to imagine genomic results?.....	230
9.2	What features do people conceptualise genomic results as having?	232

9.3	What sorts of features do genomic results appear to have in clinical settings?..	234
9.4	How should we construct genomic results?.....	236
9.4.1	Results imagined.....	236
9.4.2	Results created	245
9.5	My project in context	250
9.6	Areas for future research.....	251
9.6.1	Exploring ways to introduce more rounded concepts of genomic results into curricula around genomics	252
9.6.2	Considering ways of thinking about genomic results with clinicians and scientists involved in the results construction process	252
10	References	253
11	Appendix.....	268
11.1	Publications relating to this DPhil.....	268
11.2	Other engagement-oriented outputs created during this DPhil project.....	271
11.2.1	Centre for Personalised Medicine podcast series	271
11.2.2	Centre for Personalised Medicine art competition	273
11.3	Project timeline	276
11.3.1	Timing and relationship of different facets	276
11.3.2	Diagram showing project timeline.....	281
11.4	UK news item analysis: building a frame	282
11.5	Material relating to work with the Mass Observation Project.....	283
11.5.1	The 'Genetics and health in our everyday lives' directive.....	283

11.5.2	Mass Observation Project data analysis: organising codes to develop a theme	286
11.5.3	Analysis of attitudes of Observers responding to both the 2006 and 2022 directives	287
11.6	Favourable opinion letter for ethics application relating to clinic observations and interviews with people experiencing genomic tests	293
11.7	Material relating to clinic observations	295
11.7.1	Text of participant information sheet for clinicians regarding clinic observations	295
11.7.2	Text of consent form for clinicians regarding clinic observations	298
11.7.3	Text of participant information sheet for families regarding clinic observations	299
11.7.4	Participant information sheet for young people aged 13-15 regarding clinic observations	302
11.7.5	Participant information sheet for young people aged 10-12 regarding clinic observations	303
11.7.6	Text of consent form for families regarding clinic observations	304
11.7.7	Text of permission form for young people regarding clinic observations....	305
11.7.8	Observation framework for clinical appointments.....	306
11.8	Material relating to interviews with people experiencing genomic tests	309
11.8.1	Text of participant information sheet regarding interviews	309
11.8.2	Text of consent form for interviews	312
11.8.3	Interview guide	313

11.8.4	Interview analysis: organising codes to develop a theme.....	315
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List of figures

Figure 1: A cancer-predisposing BRCA1 variant in a ‘healthy’ woman- many factors could change the path and no-one knows where it will lead	3
Figure 2: Genetics education in UK schools over the years: Mendelian inheritance of fully penetrant traits/conditions takes centre stage.....	18
Figure 3: Project overview	32
Figure 4: Genetic material and the data derived from it as represented in stock image banks	52
Figure 5: Genomic results were framed as the fruits of years of labour- a precious opportunity we are lucky to have the chance to access	83
Figure 6: A genomic test being read	87
Figure 7: A brighter future thanks to genomic results	95
Figure 8: Use your genomic data in the fight against disease	101
Figure 9: A sequence variant is one piece of the puzzle – what more is needed to make a picture? Who decides when the picture is clear enough?	155
Figure 10: How sure will we be this time?.....	159
Figure 11: Genomic result construction carries on beyond the clinic – it may go onto be interpreted in different settings and with different purposes.....	162
Figure 12: Characteristics of results experienced by interviewees	184
Figure 13: I could not get away from a shared imagination of results as lying in the genome pre-defined, there for the looking.....	189
Figure 14: Outcomes from genomic tests were very variable- some were powerfully helpful; some oppressive; some unproductive.....	201
Figure 15: Working to make others’ results more meaningful	207

Figure 16: Photos of our 'building blocks' activity at the Southampton Science and Engineering Festival.....	219
Figure 17: Unpacking a typical human genome	221
Figure 18: Choosing thresholds for declaring a 'high' polygenic score	225
Figure 19: Popular discourses tend to present genomic results as 'hidden gems'.	231
Figure 20: Constructing a result in clinical settings appears more like surveying an ecosystem.	235
Figure 21: 'What's this?' Hidden gem concepts of genomic results invite us to position societal debates around use of genomics as questions around whether to open Pandora's box. What discussions might a broader concept of genomic results make possible?	238
Figure 22: How could political discourses around genomics shift?.....	243
Figure 23: CPM art competition winner, 2022-23	274
Figure 24: CPM art competition winner, 2023-24	274
Figure 25: CPM art competition winner, group category, 2024-25	275
Figure 26: CPM art competition winner, individual category, 2024-25	275

List of tables

Table 1: Some possible understandings of the term ‘genomic result’ in a clinical context ...	28
Table 2: Experimental facets through which I examined the construction of genomic results	33
Table 3: Genetic material and derived data in stock images.....	51
Table 4: People in stock images relating to genomics.....	57
Table 5: Sources searched for news stories	68
Table 6: Search terms used to collect news items	69
Table 7: Number of results identified via Google searches as of 4/12/24	74
Table 8: Key events reported in the news items	75
Table 9: Sources referred to in responses to ‘Genetics and health in our everyday lives’ directive	127
Table 10: Details of clinic appointments observed	149
Table 11: Interviews with people experiencing genomic testing.....	177
Table 12: The Lego blocks from which a result would be constructed	216
Table 13: Episodes of the CPM podcast relevant to the construction of genomic results...	271
Table 14: Many Observers who responded to both the 2006 ‘Genes, genetics and cloning’ directive and our 2022 ‘Genetics and health in our everyday lives’ directive appeared to hold fairly stable attitudes towards the use of genetics in a healthcare context over time	287

1 Introduction

Over the past two decades, the use of genetic testing in healthcare has evolved considerably. Historically, testing tended to involve targeted analysis of single genes very carefully chosen on the basis of a patient's symptoms or family history. These tests were time-consuming, expensive, and therefore gatekept very rigorously. However, when a genetic variation was found in this context, it was quite likely to be medically relevant(1). The balance of testing has since shifted. Single gene tests still have a role, but many contemporary genetic investigations start with genome sequencing¹: trawling a person's entire genetic code (genome) to try to establish the ways in which their genome differs from a 'reference' sequence². Given that we all differ from a reference sequence in many thousands of ways, results must then be produced from this soup of genomic variation. The challenge has changed from whether relevant variation will be captured by a test, to how to determine the most pertinent amongst the clamour of variation in the genome.

This chapter starts by discussing human genomic variation: the substrate from which a genomic result might be created. I then outline how such variation might be sifted in the process of rare disease diagnosis, or the prediction of future disease, in each case describing recent UK initiatives which are seeking to generate genomic results in these different contexts. I then discuss the climate of expectation in which many genomic tests

¹ This is often called 'whole genome sequencing' (WGS) but Jarvik and Evans argue that this is misleading: *'Neither whole genome sequencing nor whole exome sequencing is "whole," with nontrivial parts of the genome eluding even high-quality sequencing at present. Dropping the "whole" would also remind us of the limits of our technology'*(2).

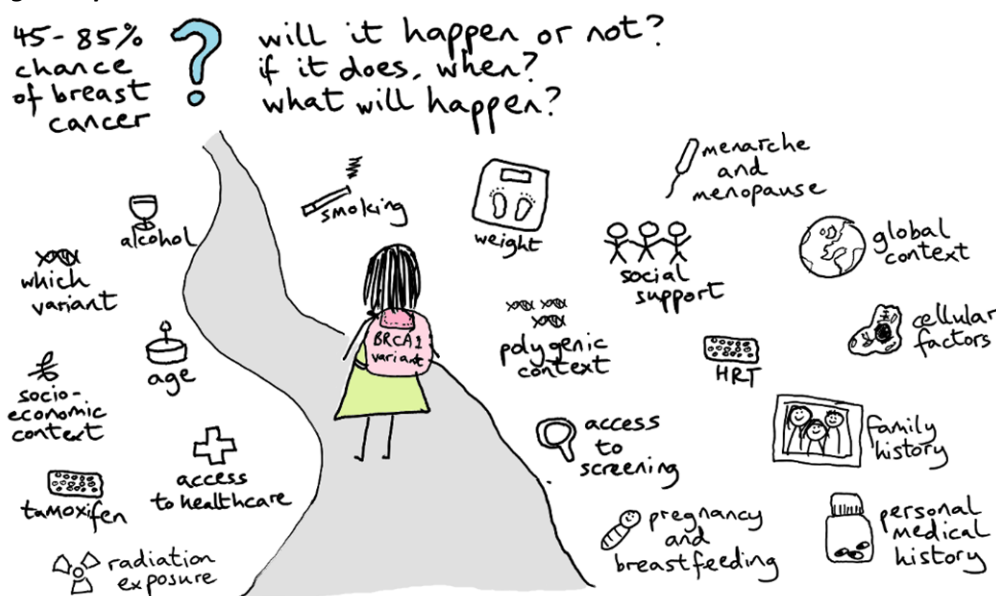
² A human genome reference sequence is *'an accepted representation of the human genome sequence that is used by researchers as a standard for comparison to DNA sequences generated in their studies'*(3). It is a composite rather than the genome of any one person: about 93% of the current reference GRCh38 is made up of sequences derived from 11 people; the remainder comes from sequences derived from over 50 people(4).

take place, before ending the chapter by reflecting on the need to explore my research question: **‘how should we construct genomic results?’**

1.1 The starting point: human genomic variation

We each have around 4.1-5 million variations in our genome(5), and genome sequencing aims (as far as possible(2)) to catalogue them all. Many genomic variations will have no known impact on health, but could be used to infer whereabouts in the world our genetic ancestors might have lived. Many others might impact health in very subtle ways, nudging disease risks up and down by tiny increments, with their effects dependent on their context amongst a palette of multiple genomic, environmental and stochastic factors. A few variants stand to impact health very significantly, but again, often, context is key. Our age, sex, position in a biological family, medical and family history, genetic background, environmental exposures and socioeconomic context might all have a part to play in determining whether and when particular genomic variations impact our health(6–8) (see Figure 1). Although our genomic variations are largely static throughout our life course, the contexts around them are continually changing, and sometimes in unpredictable ways. For example, genomic variations which now influence our risk of becoming seriously ill if we get Covid(9) have been present in us since we were conceived.

Figure 1: A cancer-predisposing BRCA1 variant in a 'healthy' woman- many factors could change the path and no-one knows where it will lead



Considerable effort has gone into delineating a wide range of 'normal' human variation, with aggregate databases such as the Genome Aggregation Database (gnomAD) playing a massively important role in the clinical interpretation of genomic data(10). However, most genomic databases are heavily biased towards people with European ancestry(11), meaning many genomic variations from across the globe are not well represented. As we start to use genomic data to predict subtle, adult-onset health risks, the phenotypic and contextual detail linked to genomic databases becomes increasingly integral to their power to help interpret the genomic data of others(12,13).

As Kingdom and Wright outline in their review discussing complexities of interpreting genomic variation, '*the same genetic variant found in different individuals can cause a range of diverse phenotypes, from no discernible clinical phenotype to severe disease, even among related individuals*'. They reflect that: '*finding low penetrance pathogenic variants in large numbers of asymptomatic individuals challenges the concept of pathogenicity, particularly in the absence of known modifiers. What does it mean to describe a genotype*

as pathogenic if it is frequently found in individuals without disease and no explanation as to why?’(14).

Everybody will have some genomic variation of this type: potentially very solidly associated with disease from a statistical perspective, but with minor impact on absolute risk for the disease in question. We will all also have multiple genomic variations that look highly concerning at face value: for example, we each have around 85 heterozygous and 35 homozygous protein-truncating variants³(15), and within a panel of 500 disease genes, most people will have at least one rare non-synonymous variant⁴. Around 200 of our variants will be very rare(10), making them particularly challenging to interpret as there will be very little data to draw on regarding their likely effects. Given this mass of seeming abnormality in the genome of every ‘healthy’ person, when, why and how should genomic variations be valued as results?

1.2 Navigating genomic variation in rare disease diagnosis

The use of genome sequencing in rare disease diagnosis is generally underpinned by the idea that there is a variant, or variants, in a single gene, causing the clinical features for which a unifying diagnosis is being sought. Initial analysis involves trying to clear aside all the other variants in a person’s genome, with the hope of being left with the causative variant(s)(16). The start of this process is automated, involving variant filtering pipelines built with a purpose of narrowing down the millions of variants identified by each genomic test, to a shortlist of variants potentially relevant to a patient’s rare disease(17). Such

³ Protein-truncating variants are predicted to shorten the protein produced by a gene, which might stop the protein being made or mean the protein does not work properly. For a homozygous protein-truncating variant, we would predict that both of our two copies of a particular gene would not work properly (i.e. we would have no working copy of the gene).

⁴ A non-synonymous variant is predicted to alter the amino acid sequence of the protein encoded by the gene: this has potential to affect the way the protein works in the body.

pipelines filter variants based on aspects like rarity; predicted effect on gene product; location within genes known to be linked to disease⁵; mutational mechanism (e.g. haploinsufficiency, dominant negative); and pattern of inheritance (e.g. comparing an affected child's genomic data to that of their unaffected parents)(18).

Once automated pipelines have produced a shortlist of potentially relevant variants, these are scrutinised by scientists and/or clinicians with the brief of determining which, if any, should constitute the 'result' of a genomic test. At this point, consequences of earlier programmed decisions may become visible. For example, decisions to include a wide variety of genes in virtual panels in an effort not to miss diagnoses, may mean that analysts are shown possible health risks unrelated to the symptoms under investigation(19).

Conversely, decisions to only examine a small number of clearly relevant genes may mean diagnoses are missed. Decisions to draw on parental genomic data to help filter an unwell child's genomic variation may increase sequencing and data storage costs (financial and environmental)(20,21), and in rare cases show that biological relationships are not as expected(22). Yet decisions not to use such data may mean that causative variation is drowned out and a child misses out on a diagnosis, or a variation that is not relevant to the child's symptoms attracts attention such that hope, time, energy and resources are used up in the process of disproving its link with the child's condition(23).

In the process of reviewing shortlisted genomic variants, scientists and/or clinicians will usually draw on variant classification guidelines. The first widely used guidelines were developed by the American College of Medical Genetics and Genomics (ACMG) in 2015(24) – these were adopted by the Association for Clinical Genomic Science (ACGS) for use in UK

⁵ This may involve creation of virtual gene panels: where the assay involves genome sequencing, but the analysis only examines selected genes.

diagnostic genetic laboratories in 2016, with various subsequent refinements and a number of disease/gene-specific guidelines added since(25). Superficially, these guidelines read like a highly technical list of instructions, with the fine detail and caveats around each element snowballing over time. Yet underpinning them is an emphasis on the importance of collaborative working and professional judgment in the process of appraising variants. Guideline developers are evidently navigating tensions of (a) trying to harmonise variant interpretation between laboratories, yet recognising that seeing guidelines as prescriptive may not get the most accurate outcome in every setting, and (b) avoiding misdiagnoses while not being so cautious that no diagnosis can be made.

Before broad genetic tests became readily available, clinical genetics consultations often involved carefully selecting one or a very few of our >20,000 genes to sequence in the hope of making a diagnosis for a person affected by a rare condition. In this scenario, the prior probability that any concerning-looking variant detected would be the explanation for the symptoms that had led to testing was high: the gene had already been flagged as one of the most likely, out of thousands, to be associated with the person's health concerns(1).

This approach left many without a genetic explanation, especially people living with conditions which could be due to variations in many hundreds of genes, like intellectual disability. In such situations, genomic testing improves the chance of making a genetic diagnosis. However, the prior probabilities associated with each variant are massively lower(1). To take the example to the extreme, given a list of 4 million variants and no further information except that they relate to a person living with a monogenic disorder, the chance that any one variant explains the disorder is 4 million to one (assuming a dominant condition). As more data are brought into the picture, for example specific detail regarding phenotype, or qualities relating to variants (like rarity or arising *de novo*), the

probabilities around each variant will shift. Filtering processes capitalise on this to sift away noise such that any variants that make it through the process have a much higher chance of being medically relevant. But in considering what they say about disease causality, we have to be conscious of their legacy of having been found via an indiscriminate assay. Writing in 2014 before genome sequencing really hit the clinic, MacArthur *et al* cautioned that *‘whole-genome sequence data sets are in some ways more prone to misinterpretation than earlier analyses because of the sheer wealth of candidate causal mutations in any human genome, many of which may provide a compelling story about how the variant may influence the trait; a problem that has been referred to as the ‘narrative potential’ of human genomes’*(1,26).

1.2.1 UK initiatives using genome sequencing in the context of rare disease diagnosis

Above I have outlined the broad-brush approach underlying the interpretation of genomic data for the purpose of rare disease diagnosis. Various UK-based initiatives have sought to apply these in practice in an effort to make diagnoses for people living with rare conditions, and as such are playing central roles in navigating and constructing genomic results. This section briefly outlines key initiatives in the context of rare disease diagnosis in the UK.

1.2.1.1 *The Deciphering Developmental Disorders (DDD) study*

The DDD study is a *‘large-scale sequencing study involving more than 13,500 families with probands with severe, probably monogenic, difficult-to-diagnose developmental disorders from 24 regional genetics services in the United Kingdom and Ireland’*(27). For participating children, the project team collected detailed phenotypic data and performed exome sequencing and microarray analyses, reporting candidate variants to clinical teams for review and potential discussion with families. Recruitment ran from 2011 until 2015, with

analysis ongoing until 2030. As of 2023, the study had made a genomic diagnosis for around 41% of probands, and identified around 60 new genetic conditions(17,27).

1.2.1.2 The 100,000 Genomes Project

The 100,000 Genomes Project was launched in the UK in 2013 *‘to apply whole-genome sequencing to the study of rare diseases, cancers, and infections in a national health care setting’*(28). ~85,000 people joined the project between 2014 and 2018. The project had a ‘rare disease’ arm, aiming to find molecular diagnoses for people and families affected by rare genetic conditions, and a ‘cancer’ arm, analysing both tumour and germline genomes for people affected by cancer (hence the project sequenced 100,000 genomes from ~85,000 participants). Participants could also opt for ‘additional findings’- analysis of a small number of genes associated with health conditions for which screening or treatment is available that are not associated with the condition that led to the person joining the project(29). In 2021, the project reported having made genomic diagnoses for 25% of probands in the rare disease pilot study (involving 4660 participants from 2183 families) and had enabled discovery of three new disease genes(28). In 2022, the project reported on cancer genome analysis leading to the discovery of 58 new mutational signatures⁶(32).

1.2.1.3 The NHS Genomic Medicine Service

The NHS Genomic Medicine Service was launched in 2018, aiming to build on infrastructure developed through the 100,000 Genomes Project to ensure equitable access to genomic and genetic testing across England(33,34). This established seven NHS Genomic Medicine

⁶ Mutational signatures are *‘characteristic patterns of somatic mutations in cancer genomes, reflecting the underlying mutational processes’*(30). Specific mutational signatures may reflect particular exposures, for example tobacco smoking(31).

Service Alliances alongside seven laboratory hubs, delivering testing as per a national genomic test directory(35).

This test directory describes eligibility criteria for genetic and genomic tests offered via the NHS, and lists which clinical specialties would be expected to request the tests. As Griffiths and Lewis explain, the test directory *'includes the provision of whole genome sequencing for many indications and in most cases, genomic testing can be requested by non-genetic medical specialists (known as 'mainstreaming'). Mainstreaming has been necessitated by the expansion of available genomic tests, increased clinical utility, the incorporation of genomic tests into standard clinical care pathways and the limited resources of clinical genetics services'*(36).

Where genomic testing is offered via the NHS, patients are usually also asked to consider contributing their data to the National Genomic Research Library(37), a *'comprehensive database that enables approved researchers to access de-identified genomic data, health data and samples. It is a partnership between NHS England and Genomics England'*(38).

1.3 Predicting future disease from genomic data

Genomic data can be explored in an effort to establish molecular diagnoses for existing symptoms. But because our genetic code is largely fixed throughout our life course, genomic data can also be analysed with the intention of predicting future disease. A whole range of susceptibilities could in theory be commented on. Dilemmas as to how we should interrogate a genome sequence become more obvious in this context: which conditions should we seek to predict, and how, when and why? What level of risk, what solidity of evidence, and what options for mitigation, are necessary to make a prediction worthwhile?

Efforts to use genetic tests to predict disease are not new: people in the UK with a high chance of developing Huntington's disease have been able to access predictive testing via direct mutation testing since 1993(39). Proband *BRCA* testing became available on the NHS in very limited circumstances from 1997(40), making predictive testing possible within a few families where many people had been affected by young-onset breast and ovarian cancers. In these settings- examining for specific variants which have already had a very significant impact on a person's family- expectations around a person's future might be very different depending on whether the variant proves to be present or absent.

But as we move to instead using genomic data to make predictions relating to a wide range of diseases, in the 'general population' rather than for people with a high prior probability of developing the condition in question, predictive power becomes increasingly dilute. The quantity of seemingly abnormal variation in every 'normal' genome (Section 1.1) challenges our ability to work out which variations really matter, and which we can safely ignore. Non-genetic factors (such as smoking) may also be much more influential than our genomic variation in determining our risks, especially in the context of common disease. While in a population screening setting, genome sequencing potentially offers opportunities to predict and avert ill health, in tandem it will sometimes divert energy, time and resources into the prevention of health risks that will never transpire.

1.3.1 Predicting rare disease

In the rare disease investigation context, some diagnostic genomic tests have for several years included opportunistic efforts aiming to seek out additional health-relevant information. For example, in 2013 the American College of Medical Genetics (ACMG) published a minimum list of genes recommended to be evaluated for '*specified categories of variants to the extent that the available data from the genome or exome sequence allow*'

in pursuit of secondary findings whenever exome or genome sequencing was undertaken(41). This list has been updated over time, most recently in 2023, and now contains 81 ‘actionable’ genes recommended for opportunistic analysis in the course of clinical genomic sequencing(42). The 100,000 Genomes Project offered participants the option of analysing a small number of genes for ‘additional findings’ (*‘looked-for known, pathogenic mutations of high clinical relevance, confined to a very limited list’*)(43) – see 1.2.1.2). Such plans position ‘secondary’ or ‘additional’ findings as being potentially valuable results, though notably these relate to a pre-specified list and are actively looked for; they are not supposed to be stumbled upon unexpectedly in the process of working through genomic data towards a result(19).

Mechanistically, the filtering process aiming to produce ‘results’ from screening for rare genetic conditions tends to work similarly to rare disease diagnostic pipelines, annotating variants based on similar criteria (rarity in population databases, presence in databases cataloguing pathogenic genomic variation⁷, predicted effect on gene product, etc)(45). However, there are key differences: usually, analysis is restricted to a pre-selected list of specific genes, with all other genomic variation being ignored, and the investigative premise is not that there *must* be something that needs to be found, but that there *might* be something though probably isn’t. Accordingly, criteria for appraising a particular genomic variation as constituting a ‘positive screen’ for a condition are usually much more stringent than for flagging its possible relevance if encountered when investigating the genome of someone already known to be affected by a rare condition(46,47). As many rare genetic

⁷ Databases such as ClinVar and the Human Gene Mutation Database aim to catalogue genomic variations known to be associated with particular rare conditions. These databases allow quick detection of variants previously thought to be pathogenic, but may include inaccurate classifications. For example, a 2020 study examining 65,896 variants from the Human Gene Mutation Database in light of the ACMG guidelines suggested that 3.47% of these variants were misclassified(44).

conditions affect children(48), efforts to predict and avert rare disease have often centred around the newborn period.

1.3.1.1 The Generation Study (Newborn Genomes Programme)

The Generation Study is a partnership between Genomics England and the NHS that aims *‘to screen 100,000 newborns born across England for treatable genetic disorders using whole genome sequencing as an initial test ... The Generation Study aims to explore the benefits, challenges and practicalities of sequencing and analysing newborns' genomes. As well as exploring the value of a genome-led approach to screening, it will also support healthcare research and explore attitudes and expectations around the longer term storage of genomic data to support healthcare’*(49). Recruitment started in October 2024 and is ongoing.

The study has several aims: to identify rare conditions in babies earlier than currently happens; to enable research; and to explore the risks and benefits of storing an individual's genome over their lifetime(50). Collection of genomic data is necessary to fulfil the latter two aims, but the screening offered by the study could in theory be provided with much more limited genetic data(51). Regarding the rare condition screening aspect of the study, the conditions screened for were chosen according to four principles: (A) *‘There is strong evidence that the genetic variant(s) causes the condition and can be reliably detected’*; (B) *‘A high proportion of individuals who have the genetic variant(s) would be expected to have symptoms that would have a debilitating impact on quality of life if left undiagnosed’*; (C) *‘Early or pre-symptomatic intervention for the condition has been shown to lead to substantially improved outcomes in children, compared to intervention after the onset of symptoms’*, and (D) *‘Conditions screened for are only those for which the interventions are equitably accessible for all’*(50).

1.3.2 Predicting common disease

Rather than working on a premise that variation(s) in a single gene are likely to be the major contributor to a person's risk, tools aiming to gauge genomic predisposition to common disease tend to work differently. Polygenic scores are designed to examine variation at thousands of sites across a person's genome – each individually common, and many having an almost negligible impact on absolute risk. The idea is that taken as a complement, all these variants when appraised together might say something meaningful about a person's risk of disease(52).

The mechanism of generating a polygenic score is therefore very different to that of establishing the molecular basis of a rare condition: instead of trying to distil out one or two currently unknown but aetiologically key variants, tests assess masses of prespecified, individually uninteresting variations to produce a composite score. The development of such scores draws on genome-wide association studies, which are heavily biased towards populations with European ancestry (88% according to the GWAS diversity monitor as of September 2025(53)). As such their (controversial(54)) predictive utility will generally be lower for people who do not have European ancestry(55). For many common conditions, genetic predisposition accounts for a relatively low proportion of a person's overall risk(52), so research efforts around polygenic scores often focus on how they might be combined with other data known to influence disease risk, in order to produce a more holistic assessment(56).

1.3.2.1 Our Future Health

Our Future Health is a *'prospective cohort study in the UK, [that] has a mission to help people live longer, healthier lives through the discovery and testing of more effective approaches to the prevention, earlier detection and treatment of diseases. Our Future*

Health is a charity supported by the UK government, industry and medical charities that aims to recruit 5 million volunteers from the UK adult population to create a unique resource that will catalyse etiological and translational research for both common diseases and rare diseases'(57).

Full study recruitment began in 2022, aspiring to involve a diverse range of people in order to build a resource that *'truly reflects the UK population'*(58). Participants are asked to complete a baseline questionnaire, have various physical measurements, donate a blood sample (which among other tests will be used to extract DNA and conduct genotyping), and consent for linkage to health-related data(59). The study team plans to *'offer participants feedback of personal health-related results (including lifestyle and genetic results) if they wish to receive them and consent to feedback'*. The details are still being thrashed out but under consideration are *'integrated risk scores that provide disease risk estimates'*, creation of which is likely to involve polygenic scores(59).

The study was announced in 2019 in the context of a green paper on *'Advancing our health: prevention in the 2020s'* as the *'Accelerating Detection of Disease'* challenge, which at that point had a specific aim of *'offer[ing] as many participants as possible their polygenic risk score'*(60). This followed on from a short-lived scheme which would have involved 'genomic volunteers' receiving personalised risk prediction for various diseases on the condition that they both paid for the report and agreed to contribute their genomic data to a research database(61).

1.4 The climate in which genomic results are being constructed

The previous sections have aimed to give a very brief overview of the mechanics of navigating from genome sequence to some sort of 'result' in the context of rare disease

diagnosis, and the prediction of future disease, together with examples of UK initiatives undertaking this work in practice. This section aims to outline the climate in which these efforts are taking place.

1.4.1 Political positioning of genomics

Genomic technology is the subject of considerable political enthusiasm. For example, it plays a starring role in the recent government report *'Fit for the future: 10 year health plan for England'*, which is illustrated throughout with pictures of sparkly double helixes. The report discusses how increased use of genomics, together with new diagnostics and predictive analytics with artificial intelligence means *'the NHS of the future will proactively maintain wellness, identifying and mitigating disease risks years – even decades – before symptoms arise'*. It also describes an intention to *'implement universal newborn genomic testing and population-based polygenic risk scoring'* (62), seemingly assuming that these will so obviously be beneficial there is no need to wait for evidence before deciding (63).

UK political discourses around genomics often position it as being likely to bring powerful benefits. For example, the 2020 policy paper *'Genome UK: the future of healthcare'* was written under a different government but also expressed how: *'Genomics is revolutionising the way we think about healthcare. It is providing us with a far more detailed understanding of what causes illness and infectious disease and is underpinning the development of new interventions that would have been unthinkable even a decade ago'* and describes a commitment to *'a future where genomics greatly improves the mental and physical wellbeing of the UK population and millions more worldwide'* (64). Similar ideas run through the 2016 Chief Medical Officer's report *'Generation Genome'*, which exhorts us to *'welcome the genomic era and deliver the genomic dream!'* (65).

Genomics England, the company delivering the 100,000 Genomes Project (1.2.1.2) and Generation Study (1.3.1.1), and that partners the NHS in administering the National Genomic Research Library (1.2.1.3), is wholly owned by the Department of Health and Social Care(66). Accounts for Genomics England Limited discuss how the UK genomics sector *‘can make a significant contribution to kickstarting economic growth. The Company [Genomics England] is a critical element in delivering this, acting as the Government's data and evidence engine for national genomic healthcare, research and innovation’*(67).

Genomic technology is therefore developing in a world where politicians have an interest in it being seen as worthy of investment and successful. Towards the end of the 2010-2024 Conservative governments, UK genomic capabilities were positioned in multiple political documents as standing to have a substantial positive impact on our health, and being directly attributable to forward-thinking government policy(60,64). For the subsequent Labour government, genomics has also been presented as part of the solution to challenging problems ranging from the cost of providing medical care to an ageing population, to faltering economic growth(62,68). Centring genomic predisposition as a key contributor to ill health may also be attractive from a political perspective as genetic propensity to illness is unlikely to be blamed on the government, whereas they might be seen as having responsibilities around many of the non-genetic factors that affect our health outcomes.

1.4.2 Curricula around genomics

In the UK, many adults will have been taught about genetics when they were at school; younger people may also have been taught about genomics(69)⁸. When people encounter

⁸ ‘Genetics’ and ‘genomics’ overlap considerably. In some contexts, people differentiate between ‘genetics’ as relating to narrow, often single gene, tests, with ‘genomics’ encompassing all of a

genomic tests in adult life, the ideas and expectations they bring to these may be somewhat influenced by the context that their genetics education gave them.

In 2005, Madden (based at the University of Reading, so likely discussing the UK context) noted that *'in the current school curriculum, the principal emphasis in genetics is on mutations in single genes, inherited in a Mendelian fashion, that give rise to serious disease in humans. Three or four conditions that exemplify the main patterns of inheritance form the basis of nearly all course specifications and probably many science teachers' knowledge of the subject, namely: Huntington's disease, cystic fibrosis and/or sickle cell disease and haemophilia ... Polygenic and multifactorial conditions, which are the major cause of ill-health and death in our society and which affect us all, are seldom addressed in schools. Rarely is the notion of environmental influences on gene expression backed up by sophisticated, concrete examples that reflect its importance. Rarely, if at all, is the probabilistic nature of screening technologies raised'* (74).

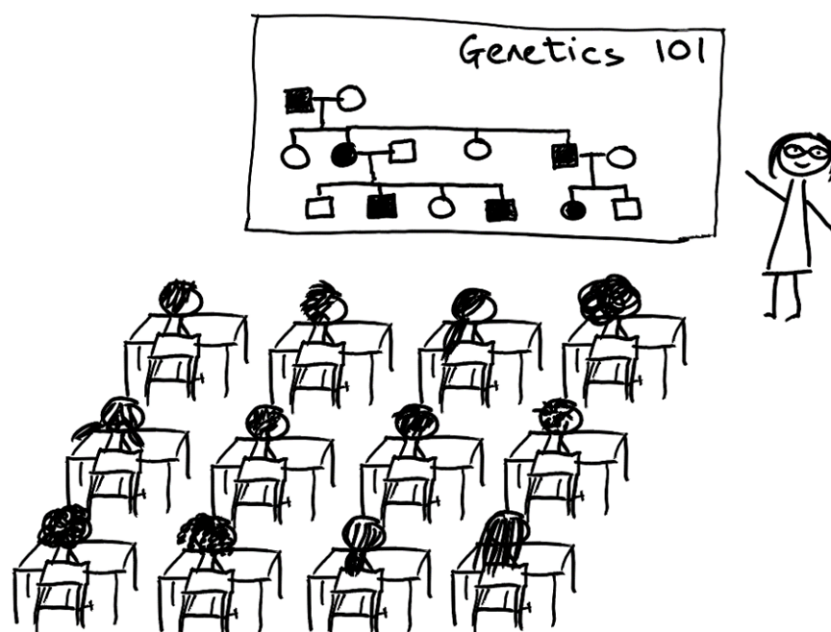
In 2008, Ashelford examined the teaching of genetics at key stages 3 and 4 (pupils aged 11-16) with reference to the science curriculum in England. She described how *'the teaching of variation and genetics can give rise to the mistaken idea that genes are the sole determinants of our characteristics'* (75). The well understood mechanics of mitosis, meiosis, and monogenic inheritance patterns received considerable focus while

person's genetic code(70,71).

In practice, many people would consider the term 'genomics' to be encompassed by 'genetics', in that all genomic tests involve determining genetic sequence, albeit across the genome. But not all 'genetic' tests are 'genomic' – for example tests that involved sequencing of a particular gene would not be 'genomic' (unless they involve genome sequencing followed by application of a virtual panel involving just one gene). Exome tests start with sequencing just the protein-coding sections of a person's genome (about 1% of their genetic material)(72) but as they involve generating data on >20,000 genes they would generally be seen as fitting under a 'genomic' umbrella, except in scenarios where people specifically want to distinguish an ability to analyse non-coding sections of the genome(73).

complexities and uncertainties around how genotype becomes phenotype, and recognition that most diseases do not follow Mendelian inheritance patterns, got little attention (see Figure 2).

Figure 2: Genetics education in UK schools over the years: Mendelian inheritance of fully penetrant traits/conditions takes centre stage



Such concerns persisted in 2017, when Jamieson and Radick undertook a study where their ‘diagnostic hypothesis [was] that the Mendelian emphases typical of introductory genetics teaching at every level promote determinist attitudes which persist long after people learn that, in fact, genes are not destiny’ (76). Drawing on the work of Weldon, a contemporary critic of Mendel, they had the idea to ‘*imagine what genetic knowledge would look like if interaction was the main message, and scenarios in which interaction can (for certain purposes) be ignored are relegated to the margins. That imagined reorganization—with flipped centre and periphery, foreground and background, grand generalization and special case—is the vision behind the curriculum taught in an exploratory study in Leeds in autumn 2013*’. They found that undergraduate students who attended this ‘Weldonian’ course were

less determinist about genes by the end of their teaching than students who attended the standard ‘Mendelian approach’ university course in introductory genetics(76).

In his 2023 book *Disputed Inheritance*, Radick reflects that ‘*Although they are only beginning, classroom experiments in “Weldonizing” introductory genetics suggest that our biology teachers are not doomed to produce students whose first thoughts about genes are of character-makers, dominance, recessiveness, and Punnett squares*’(77). Updating curricula to better reflect the messiness and contingency of genomic variation right from the start will be so important – but still leaves us with many people taught from a Mendelian starting point that might not serve them well in anticipating and navigating outcomes from contemporary genomic tests.

1.4.3 People’s expectations from genomic testing

Perhaps in part arising from high profile promotional discussion around genomics (1.4.1), and having been taught about genetics in a somewhat deterministic way (1.4.2), many people have high expectations from genomic tests. A recent scoping review of 99 articles (~60% of which were conducted with populations in Australia, Canada, UK and USA) exploring publics’ knowledge of, attitude to, and motivation towards health-related genomics concluded that ‘*Publics had high expectations of genomics and perceived that it could provide them with information for their future*’(78). In a 2018 YouGov survey of 1954 people from the UK general public exploring views around genome sequencing in healthcare, overall people had a positive view, choosing ‘*informative*’ as the most popular word, and ‘*family legacy*’ as the most popular analogy representing genome sequencing for them(79).

Exploring the intersection between expectations and experiences, Donohue *et al* undertook a study interviewing parents of 22 children having genomic testing in New York City to investigate a neurologic, immunologic or cardiac disorder, and found that *'parents reported that when the genomic test results were returned, most of their expectations were left unmet. Disappointment was the most common reaction to the genomic test result, which occurred for many parents despite the test result (positive, uncertain, or negative)'* (although they did note that expectations varied considerably and some were met)(80). In the UK, Peter *et al* undertook a mixed methods study involving surveys and interviews with families undergoing genomic testing – they reported that: *'in most cases, more negative emotions, like disappointment and sadness, were experienced by those with a no primary finding result ... Often, the source of this disappointment could be attributed to a mismatch between people's expectations of receiving a diagnosis and their actual results. Whilst some had tried to be "open-minded", it was clear that many parents had pinned their hopes on finding a genetic cause'*(81).

Examining the role of hope more deeply, Gurasashvili *et al* interviewed nine parents whose child had a rare undiagnosed condition and a 'no primary finding' result from genomic testing (in many contexts the most common outcome from diagnostic genomic testing(82)). They reported that: *'The receipt of a 'no primary finding' result saw a sharp change of direction in hope ... profound disappointment, a period of sadness, frustration, and resignation taking the place of hope ... However, hope is not entirely lost, and our findings show that it re-emerges in time ... in this new guise "hope" is more dulled, less tangible, less immediate, and one which they "put to the back of the mind" ... The nature of hope changed from somewhat naïve, optimistic hope, which metamorphosed as their journeys progressed to a version of hope which was viewed as an unwanted nuisance, tinged with sadness'*(83). It is, however, important to note that this does not necessarily mean that people had

inaccurate expectations as to the likelihood of establishing a genomic diagnosis via their test – obviously it is very possible to have an intellectual understanding that a hoped-for outcome is unlikely, yet still to hope.

Nevertheless, a climate which invites people to expect clarity and helpful outcomes from genomics is clearly likely to engender more situations where people experience a discrepancy between their expectations and their experience. Writing in 2004, Nelkin and Lindee commented on how *'In supermarket tabloids and soap operas, in television sitcoms and talk shows, in women's magazines and parenting advice books, genes appear to explain obesity, criminality, shyness, directional ability, intelligence, political leanings, and preferred styles of dressing. There are selfish genes, pleasure-seeking genes, violence genes, celebrity genes, gay genes, couch-potato genes, depression genes, genes for genius, genes for saving, and even genes for sinning. These popular images convey a striking picture of the gene as powerful, deterministic, and central to an understanding of both everyday behavior and the "secret of life"'* (84). In the decades since, many direct-to-consumer genetic testing companies have traded off the idea that genetic tests can reveal meaningful and helpful information about any person's future (85,86). Deterministic representations of genetics have threaded through popular culture- what might this mean for people making decisions around genomic testing today?

1.5 Why explore the construction of genomic results?

To summarise, the process of navigating through genomic data in the hope of making clinically meaningful inferences can be complex and subtle. This is especially so as the use of genomic sequencing strays from the diagnostic to the predictive – for example the process of developing a polygenic score is very different in nature to the construction of a pipeline designed with the aim of diagnosing symptomatic rare disease.

Yet the climate in which genomic results construction takes place fails to mirror this – frequently implicit in political promises, educational policy, and popular culture is a concept of genomic results as unambiguous and powerful. Ethical issues might be seen to abound by virtue of their intimate connection with our destiny and their scope to reveal potentially unwanted or exploitable truths about our futures, but the ways by which we might understand and value something to be a ‘result’ of a genomic test are rarely under focus. Where questions come up, they tend to centre around whether or not a ‘result’ should be communicated or hidden, which potentially invites quite different responses to the question of whether, why and how a particular genomic variant or collection of variations constitutes a result at all.

Garrison *et al* undertook a study of policy debates around genomics, introducing a concept of genomic contextualism which *‘encourages individuals to recognize a fundamental duality: Genomic tests both share characteristics with other types of medical tests and represent a combination of features that make them distinct’* (87). Using stasis theory to examine attempts to build policy around genomics – *‘questions ... used to evaluate an argument and decide at what level a disagreement is taking place, and whether disputants are even arguing about the same thing’* – they determined that key debates around issues like returning secondary genomic findings were stalling at a definitional level. Disputants were talking past each other and unable to meaningfully debate policy decisions because they had not reached consensus on a much more fundamental level: *‘How should the thing we are debating about be named and understood?’* (87).

This project aims to contribute here, not by finding answers, but by trying to highlight that the nature of a genomic result is an open question with ethical dimensions. Results are not lying pre-defined in the genome waiting for us to react around them – the choices we make

in navigating and appraising genomic data, and in taking outcomes from them forward into our lives, all contribute to whether, when and how genomic variation(s) may be valued as a 'result'. As we move to using genome sequencing for population screening, this question of 'how should we construct genomic results?' becomes increasingly pressing. In order to have helpful conversations around what to do with genomic results, we first need to recognise the choices we have as to what they should be.

2 Research questions and investigative approach

This chapter begins with the research questions I set out to explore in the course of this project and the context in which this work took place, then my reflections on the nature of genomic results and how I might generate new knowledge around this topic. I then discuss how facet methodology and empirical bioethics informed my overarching investigative approach. The subsequent five chapters present specific methods that I used to explore aspects of my key research question: ‘how should we construct genomic results?’, along with the results generated using these methods.

2.1 Research questions

My overall research question is: **‘how should we construct genomic results?’**

In order to inform this, I tried to ascertain and examine a variety of ways in which genomic results currently appear to be constructed via the following subsidiary research questions:

- In what ways do popular discourses invite us to imagine genomic results?
- What features do people conceptualise genomic results as having?
- What sorts of features do genomic results appear to have in clinical settings?

2.2 Research context

I undertook this project in the context of the Clinical Ethics, Law and Society group (CELS), an interdisciplinary research group focused on ethical, legal and social aspects of implementing new technologies in healthcare, led by Anneke Lucassen and now based at the Centre for Human Genetics in Oxford(88). This was a brilliant setting in which to explore research questions with dimensions where multiple disciplines stand to bring insights, and a really valuable opportunity to learn from colleagues with expertise in areas including social science, ethics, health psychology, political science and medicine.

From September 2021 until September 2025 I was also a Junior Research Fellow at the Centre for Personalised Medicine, a partnership between the Centre for Human Genetics and St Anne's College, Oxford which provides a focus for multidisciplinary communication, engagement and research(89). This gave me a chance to work with colleagues with diverse expertise including social science, molecular genetics, public health, data science and health economics, and provided a platform for more engagement-oriented work relevant to my project.

Working in CELS and CPM showed me the value of interdisciplinary working firsthand. Support from colleagues from a wide range of disciplines was hugely important in helping me begin to recognise and examine the many assumptions around genomic results that I had at the outset of my project, and played an essential role in helping me refine my ontological and epistemological perspectives as to the nature of genomic results.

2.3 Ontological and epistemological stance

At the outset of this project, my training in clinical genetics meant that I was developing experience in working with genomic tests in clinical contexts. I had gained some familiarity in trying to determine which genes might be most helpful to analyse in a particular situation; discussing possible tests and their likely outcomes with patients; and appraising and communicating the outputs of tests. I had also had the opportunity to do an MSc in Genomic Medicine where I had done modules on genomic technologies and bioinformatics, and I had spent a few months on attachment with an exome project in Southampton where I tried to find molecular diagnoses for various patients by looking through multiple variants shortlisted by large virtual panels. I had some experience of considering genomic data together with laboratory colleagues from regular participation in a local multidisciplinary

team meeting, where scientists and clinicians discussed evidence surrounding particular genomic variations.

At this point, I had not really questioned how I might define a genomic 'result', but the definition I applied in clinical practice would probably have most closely aligned to *'the variant(s) that ends up typed on the document summarising the outcome of a genomic test'*.

I saw results as arising from a very technical process, where ideally if you sent the same DNA sample to any lab with the same clinical question, the same variants with the same interpretation should end up written on the summary of the test outcome. I had a post-positivist perspective in that I thought there was a 'truth' about how genomic variants clinically impacted people, and therefore whether they should be considered results, and we would never be perfect at ascertaining this but our job was to try to get as close to perfection as possible.

I also held an ideal that a result should be a clear and useful answer to the question being asked (usually in the clinical context I was working in: why does this person have these health problems?). Sometimes this meant I ended up dealing with a result (something written on a bit of paper) that I did not feel should really be a result (because it was not clear or useful). I saw this as arising because the technical process of results production was inevitably imperfect because our understanding of genomic variation was evolving. I imagined that over time the results that ended up written on paper would increasingly match my ideals around what results should be – because results production was a technical process and the technical foundation underlying it would improve.

During this project my perspective has shifted. At the variant level my stance is still post-positivist in that I think there are objective data we can collect regarding whether and how

a particular variant might influence the health of the person in whom it is found. For example, data commonly drawn on in variant interpretation guidelines like its frequency in ostensibly 'healthy' populations; its having been observed in other people with similar conditions; the way it has been inherited through a family; its demonstrated impact on RNA production or protein function(25).

At the level of overall results from genomic testing, my perspective has become more relativist. I increasingly think there are many contextual factors that might legitimately influence how and when a genomic variant or collection of variants should be appraised as a 'result' from a genomic test. The geography of where a DNA sample from the same person seen by NHS services with the same clinical query happens to be sent should not influence result construction in and of itself. However, I can see that the different people involved in the construction process in different labs might draw different conclusions, even when working with the same guidelines, that could both be justifiable. Many contexts ranging from the age of the person, to the conditions under which they gave a DNA sample, to the current state of technical genetic knowledge, to the financial pressures under which the NHS operates, might justifiably have a bearing on the results construction process and therefore on the outcome of a given genomic test.

A challenge for clinical genetics services is that where genomic variants are separately appraised in people from the same family, differing constructions of what constitutes a result may be put in direct tension. Reaching consensus here may be necessary in order to facilitate equitable treatment of people in the family, but perhaps rather than seeing such discrepancies as aberrations or evidence that one lab has drawn the wrong conclusions, these situations provide opportunities to consider the nature of genomic results and reflect on what constructions of results are most helpful.

The Oxford English Dictionary offers various definitions of the word ‘result’(90), including:

- *The effect, consequence, or outcome of some action, process, or design, etc.*
- *A decision, a resolution; the outcome of the deliberations of a council or assembly.*
- *Chiefly Science. A finding or an item of data obtained as a result of an experiment, project, survey, etc.*

At the outset of this project I would have seen genomic results as fitting more within the first definition – the outcome of some sort of process or recipe that could be blindly followed such that the same DNA sample with the same question should always generate the same results. Progressing through the project, I started to give more weight to the second definition, seeing deliberations- i.e. people’s thoughts and choices- as playing an essential role.

Table 1 suggests some possible understandings of the term ‘genomic result’ in a clinical context. How one might anticipate a result may look could vary a lot depending on working definition. For example, if envisaging a result as *‘an answer to a specific clinical question asked of a person’s genomic data’*, one might expect it to be clear, useful and meaningful. If seeing a result as *‘any variant that could in theory contribute to or act as a marker of present or future human disease’*, one might anticipate that this would include information with varying degrees of certainty and meaningfulness, including much that is likely irrelevant or will turn out to be spurious.

Table 1: Some possible understandings of the term ‘genomic result’ in a clinical context

All variants detected in a given genome relative to a reference sequence
An answer to a specific clinical question asked of a person’s genomic data
An attempt at an answer to a specific clinical question asked of a person’s genomic data

Any variant that could in theory contribute to or act as a marker of present or future human disease
Whatever ends up typed on the document summarising the outcome of a clinical genomic test
The variant(s) that ends up typed on the document summarising the outcome of a clinical genomic test
The variant(s) that ends up typed on the document summarising the outcome of a clinical genomic test, if it seems useful in the clinical context
The interpretation of the clinical significance of the variant(s) that ends up typed on the document summarising the outcome of a clinical genomic test
The outcome of the process of analysing genomic data with a clinical question in mind
The product of the choices made in analysing and appraising how genomic data may relate to a person's health and/or the health of their present or future family

Over the course of my project, I shifted more towards seeing genomic results as a product of the choices made in analysing and appraising genomic data. They are built from elements- genetic variants- whose effects I think we can aim to appraise with a degree of objectivity. Similarly, the distillation or filtering process necessary in the journey towards a result has many aspects where I think 'objective evidence' should play an important role. But entwined throughout such filtering decisions, and certainly in the overall construction of a result and the ways it is then taken forward and used in people's wider lives, I think contingencies and choices become hugely important. I therefore chose a research approach suited to '*a multi-dimensional, entangled and connective ontology*' and designed to seek out '*contingency, entanglement and connection ... seeing these as central to the intellectual puzzle*'(91) – facet methodology.

2.4 Facet methodology

I chose a facet methodology orientation to explore my key research question: 'how should we construct genomic results?'. With this approach, which was developed collaboratively

by Katherine Davies, Carol Smart, Brian Heaphy, and Jennifer Mason, *'Research fields are seen as constructed through combinations and constellations of facets as we might see in a cut gemstone, where facets refract and intensify light, taking up the background, and creating flashes of depth and colour as well as patches of shadow. In facet methodology, the gemstone is the overall research question or problematic, and facets are conceived as different methodological-substantive planes and surfaces, which are designed to be capable of casting and refracting light in a variety of ways that help to define the overall object of concern by creating flashes of insight. Facets involve different lines of enquiry, and different ways of seeing. The approach aims to create a strategically illuminating set of facets in relation to specific research concerns and questions'*(92).

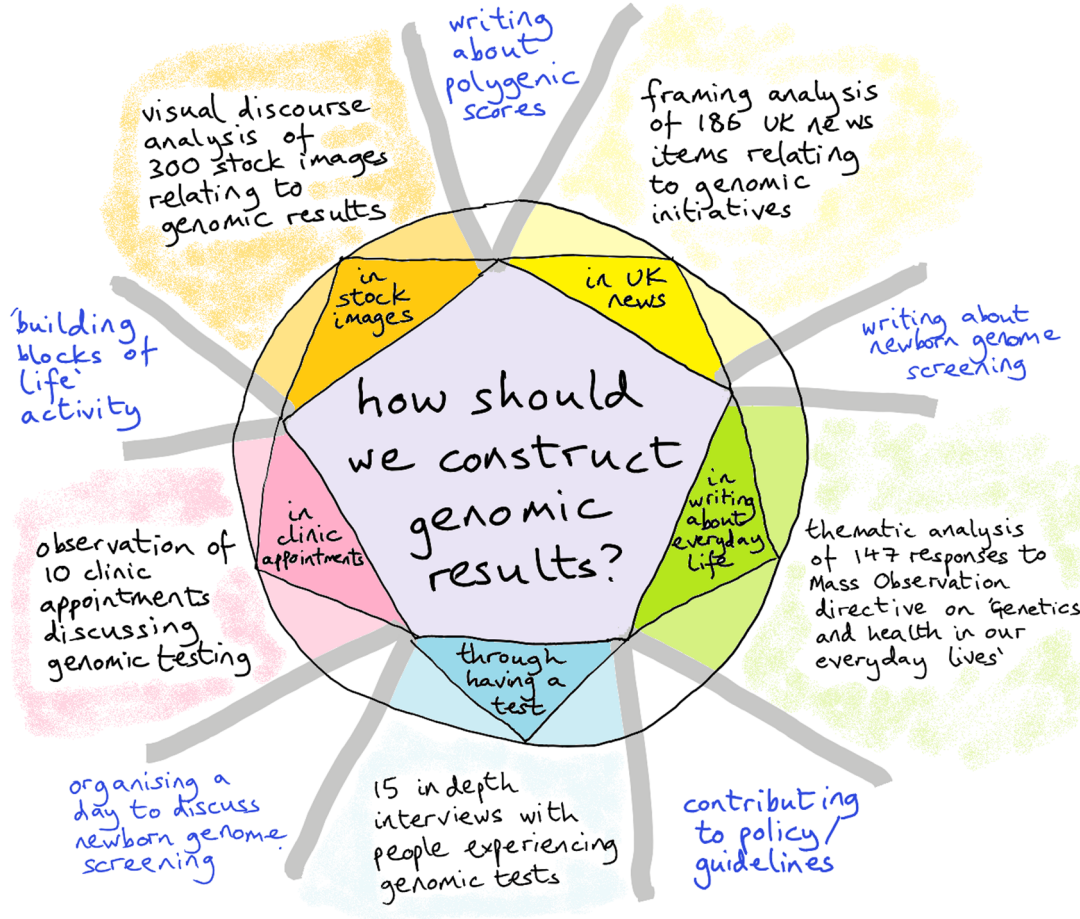
I was attracted to facet methodology partly in view of my difficulties in determining my ontological perspective as to the nature of genomic results – here was an approach where I could play with different ways of thinking about results, and try to explore them through different lenses and with different perspectives. I also thought it suited my research problem in view of the huge variety of situations in which genomic testing is now sometimes turned to – for rare disease diagnosis, for informing cancer treatment, to influence public health. Intuitively it felt appropriate that genomic results might look quite different when viewed from these different angles, but that the endeavour to construct results in particular contexts might usefully inform how it might be helpful to think of genomic results in other contexts. Facet methodology explicitly considers connections between the angles through which an object might be viewed. For example, in what ways might the ability of genomics to diagnose rare disease connect with its use as a screening tool? I also thought a facet methodology approach well suited to exploring my research question in the context of a project where I have been very lucky to have lots of interesting opportunities ranging from writing for *New Scientist*(93) to contributing to policy

documents(94,95), and I also have in a sense a personal stake in the question through my work as a clinical genetics registrar. Its purposely creative and inventive approach gives scope to draw together data and experiences gained via a wide variety of routes in the pursuit of ‘flashes of insight’.

Perhaps genomic results are often thought of through the flashiest facet – as giving clear answers that open up new and helpful options – and they sometimes do do this. But facet methodology aims to be *‘an approach that helps us to do research that can create new ways of seeing, that can “trouble” existing categories, and that can shift prior assumptions’*(92), and there are many other facets to genomic results- some potentially murky, chipped, hard to access or contested- that we should be aware of, and maybe sometimes intentionally draw on when seeking to describe what a genomic result might look like. With this in mind, I have tried to examine genomic results produced for a variety of reasons (rare disease diagnosis; cancer; screening for common and rare conditions) and seen from a variety of angles (in stock image banks; in UK news; in written responses to questions around genetics and health in our everyday lives; in observations of clinic appointments where genomic results are discussed; and in interviews with people experiencing genomic tests), as illustrated in Figure 3.

Figure 3: Project overview

Examination of how genomic results appear to be conceptualised in various contexts were intended to shed light on my central research question. Facets with text in black represent the more formal analyses I undertook (Chapters 3, 4, 5, 6, 7); text in blue reflects more engagement-oriented facets (Chapter 8) which influenced my thoughts around my central research question.



2.4.1 Overview of key facets

Table 2 gives brief details of the experimental facets I designed, and the specific research questions they were intended to explore in order to ultimately shed light on my central research question: 'how should we construct genomic results?' Specific details regarding each facet are provided in subsequent chapters.

Table 2: Experimental facets through which I examined the construction of genomic results

Facet	Key method	Related research question(s)
In stock images (Chapter 3)	Visual discourse analysis of 300 stock images relating to genomic results	In what ways do popular discourses invite us to imagine genomic results?
In UK news (Chapter 4)	Framing analysis of 186 UK news items relating to genomic initiatives	In what ways do popular discourses invite us to imagine genomic results?
In writing about everyday life (Chapter 5)	Thematic analysis of 147 responses to a Mass Observation directive on 'Genetics and health in our everyday lives'	In what ways do popular discourses invite us to imagine genomic results? What features do people conceptualise genomic results as having?
In clinic appointments (Chapter 6)	Thematic analysis based on observation of 10 clinic appointments discussing genomic testing	What features do people conceptualise genomic results as having? What sorts of features do genomic results appear to have in clinical settings?
Through having genomic testing (Chapter 7)	Thematic analysis based on 15 in depth interviews with people experiencing genomic tests	What features do people conceptualise genomic results as having? What sorts of features do genomic results appear to have in clinical settings?

2.4.2 Synthesis

I go on to describe data generation and analysis separately for each facet of my study, but this distinction is artificial – indeed in facet methodology, *'the aim is to create facets that seek out the entwinements and contingencies, instead of approaching the world as though these things are separate'*(92). I generated and analysed data from facets concurrently, so insights identified in one facet would inevitably and intentionally influence my exploration of genomic results through other facets (please see Appendix section 11.3 for a discussion of this process and a rough timeline).

As Mason describes, *'Facet methodology assumes that the world and what we seek to understand about it is not only lived and experienced, but is multi-dimensional, contingent,*

relationally implicated and entwined'(92). Accordingly, I considered whether to structure my results section by insights identified, rather than by the facets through which they were explored. However, ultimately I decided to report on each facet in turn, as the various aspects of genomic results took on different prominence in different facets and I felt that reporting by facet would retain a richer breadth of results. Chapter 9 discusses synthesis of work from different facets.

2.5 Empirical bioethics

While facet methodology provides the context for my research approach, I was also influenced by empirical bioethics. My overall research question- 'how should we construct genomic results?'- is normative, and in order to bring insights as to how genomic results are constructed in different facets to bear on this, I needed to explicitly question what ways and in what contexts they might be more helpfully conceptualised and why. This attempted integration of the descriptive and the normative is in the wheelhouse of empirical bioethics, an emerging field with a plethora of methodologies(96), connected by an intention to bring together empirical data and ethical analysis to develop normative conclusions.

Arguably this could all be considered under the umbrella of facet methodology, with ethical analysis being an interconnected 'facet' in the investigation of my research question. I am describing it separately in view of the extent to which it underpinned my approach, in that as I sought 'flashes of insight' from the different facets through which I explored how genomic results were described and conceptualised, I tried to keep normative questions of how they might usefully be conceptualised firmly in mind. As I synthesised insights gained from different facets, I sought to explicitly note and draw out ethical issues that had a bearing on how it might be useful to conceptualise genomic results.

Singh described that *'The broad remit of empirical ethics potentiates the full range of social science 'data', from interviews to texts to vignettes to participant observation'* (97), and as such, the data I generated via each facet represents a comparatively uncontroversial substrate for empirical bioethics research. She also reflected on the potential to widen our understanding of data that might be brought to bear in empirical bioethics, considering whether, for example, brain scan data could be used in such research, concluding that *'It is an open question whether the biological sites and systems should be, or can be, viewed as empirical sites on par with social sites. The importance of social contexts, power relations, embodiment and so forth that empirical ethics has acknowledged and promoted is generally not acknowledged when the notion of 'the empirical' in empirical ethics is confined to biological realms and systems. If the point of empirical ethics were to assert the importance of social context in ethics, then this branch of empirical ethics would potentially put that effort at some risk by reducing ethics and morality to the brain'* (97).

As applies to genomic results themselves, I think this issue is really interesting – in a broad sense, could genomic result construction itself be considered a form of empirical bioethics? It involves the fusion of empirical data, albeit of a more 'biological' variety, with a combination of technical, social and ethical considerations to create an output. And conceptualising efforts to construct genomic results as empirical bioethics would make more explicit the social and ethical aspects that are entwined throughout result construction but often unacknowledged or overlooked in favour of focus on the technical.

2.6 Ethical considerations in relation to this project

This section gives an overview of some of the ethical considerations relevant to my project; some aspects specific to particular facets are discussed in the relevant chapters.

2.6.1 Ontological/epistemological considerations

A key ethical question as regards any research project is whether it is worthwhile. As I argue in 1.5, I think my overall research question- 'how should we construct genomic results?'- is a pressing and important one. However, assessing the ability of my project to make a useful contribution to this question is difficult. Facet methodology does not come with specific criteria against which I could check the quality of my work. As Mason writes: *'Given that facet methodology involves "a connective ontology" and "playing with epistemologies", and given also that it does not contain a set of procedural rules to be followed, it is perhaps not surprising that it also does not contain a recipe for ensuring quality ... This requires honest and responsible thinking and practice not just in generating the insights therefore, but in working out and showing why and how they are convincing insights into that thing in particular that you are seeking to understand, and why you should be believed'* (92).

How could I ensure my analysis produced insights that were *'genuine, meaningful and incisive, rather than fictitious, fanciful, or misleading'* (92)? I aimed to achieve this throughout my project by trying to approach datasets with an open mind and being conscious of my positionality, looking carefully for counter examples whenever I was developing a theory as to what data indicated. I also tried to document how and why my ideas were evolving as my project progressed. For example, I used field notes and memos to help me trace and reflect on the process as I iterated my analysis or considered what particular encounters had taught me about genomic results. I also regularly discussed data and the conclusions I was developing from them with my supervisors and other colleagues. Given the interdisciplinary nature of our research group this was an extremely valuable way to seek new and challenging perspectives on my work.

What constitutes 'quality' in the context of qualitative research is much debated, but Timonen, Foley and Conlon argue that quality is relational, requiring attentiveness to how each stage of the research process relates to constructing credible and relevant conclusions. They describe how: *'Quality arises from formulating a research question that is relevant; sampling for (or accessing) data through a credible process pertaining to the relevant concern; engaging analysis in a credible manner and doing justice to the data while continuing to remain relevant to the studied concern'* (98). This concept of relationality links in powerfully with my facet methodology approach, which intrinsically invites focus on how insights arising in different facets around a research problematic might interrelate and intersect. I tried to strategically select facets that I thought would allow me to pursue relevant insights relating to genomic results, and to take a careful and thoughtful approach to my analysis such that the insights I gained would be credible.

2.6.2 Methodological and reporting considerations

As regards the methods used in the course of this project, roughly speaking I saw the ethical considerations as becoming more acute the closer my research became to people experiencing genomic tests. Chapter 3, which focuses on the portrayal of results in stock imagery, involved the analysis of images where any people involved were not identifiable and were likely acting/modelling a role (for example 'laboratory scientist') rather than really undergoing or delivering genomic tests. In this facet, I therefore saw the primary ethical considerations as being those I discussed in 2.6.1.

Chapter 4 focuses on the ways in which genomic results are framed in UK news items – and many of these items included stories from named people who were going through genomic testing. They (or their families) will have shared their stories for the purpose of informing news items that would clearly be going into the public domain. However, they may not

have envisaged the news items going on to be analysed in research projects, so I was worried about using their words in a way they might not feel comfortable with or approve of. As I will discuss in 4.1, I thought some (potentially critical) analysis of the treatment of genomic results in UK news could be worthwhile and illuminating, but it was also important to be fair by people and families who were featured in the news stories. I was particularly concerned (a) not to imply that they have responsibility for the way that genomic results are framed in UK news items; and (b) to reduce identifiability where possible.

Accordingly, I have tried to present the results in a way that invites scrutiny on the choices of journalists/news sources regarding what stories to feature, rather than on the people featured. I have not named or directly quoted people discussing their experience of genomic testing, except if the high-profile position they were talking from seemed very relevant context. I realise that this is imperfect in that most of the news items are freely available online and if a reader wanted to they could rapidly find the relevant article from the headline. However, this felt like an appropriate balance by which to at least slightly distance my analysis from the people whose stories were featured, while still allowing me to report what I see as useful results in a meaningful way.

Chapter 5 looks at how wider publics might envisage genomic results, by means of analysing responses to the Mass Observation Project, an archive of writing by ‘ordinary’ people about everyday life in Britain(99). This involved work with the Mass Observation Project team where ethical issues such as whether the questions we asked people to write about might cause distress will have been considered. Regarding the ethical concerns I was personally involved in navigating, the potential issue of identifiability was again a worry – Mass Observation Project respondents are all assigned a unique code under which they write, but the responses that were provided to us sometimes contained quite specific

references to locations, occupations, family structure, etc. I tried to ensure that my reporting in this chapter does not provide unnecessary identifying information, while still giving sufficient for context. For example, I have given age ranges rather than specific ages, and in some cases adjusted people's descriptions of their occupation to make them less specific. While I of course still tried to consider each person's writing with care, I was less worried here about the prospect of people feeling their words had been used against them or in ways they might not have envisaged than for Chapter 4. This was partly because I could work directly with each person's contribution, rather than just seeing what a journalist had thought relevant to include of their story, and partly because participants were writing to the project in the knowledge and expectation that they might also be addressing a range of researchers.

Chapters 6 and 7 are the ones where the ethical considerations felt most intense, as they involved working directly with people and families navigating genomic testing. As regards clinic observations, a major concern I had was whether the offer of recruitment to my project would generate anxiety or false expectations for people and families attending genetics clinics, for example that the appointment must be going to involve discussing a result. One way I tried to mitigate this was by recruiting through clinicians (see 6.2.1), so that the appropriateness of offering recruitment was reviewed by someone with insight into the person's clinical situation and the potential anxieties around it. Another way I aimed to navigate this was in the phrasing of my participant information sheet, for example including the statement: ***'Being asked to participate in this study does not mean that you will receive a genomic result or be offered a genomic test during your appointment. This will depend on what would happen anyway during the appointment as part of your standard clinical care. You are being sent this information because the clinician that you are due to see sometimes discusses genomic tests and results during their appointments'***. For

the purposes of recruitment materials, I also changed to a blander project title '*Ethical and clinical perspectives on interpreting genomic data*', rather than the original title which began '*What is my result?*' (see Appendix 11.7.3).

The prospect of participants being identified was again a concern, particularly as genomic tests are often done to investigate unusual health problems that could in themselves be potentially identifying. In my reporting, I have tried to minimise this risk, for example I have largely avoided referring to specific gene or disease names, have used age ranges rather than specific ages, and have kept symptom descriptions quite broad. Were I doing this project again, I would keep to the same principles as regards reporting but I think I would retain more potentially identifiable data in my fieldnotes (which are stored securely with restricted access). On reflection I took the data minimisation principle of GDPR a bit too much to heart, redacting quite a lot of information, for example specifics around occupations, family context and caring networks, because I was trying to keep the data collected '*limited to what is necessary*' (100) and at the time I did not see them as being clearly directly relevant to how we should construct genomic results. My ideas around this changed as my project progressed, and had I retained more specific and richer details in my fieldnotes it might have allowed a deeper analysis.

The interviews were the aspect of my study which I think raised the most ethical issues (some of which I will discuss in 7.5). One issue was that many people's experiences with genomic testing touched on sensitive topics, such as deaths or serious illness in the family, and as such, questions around how people had come to encounter genomic testing had potential to distress. Another concern was the possibility of stirring up new anxieties, or destabilising ways that people had found of slotting their experience of genomic testing into their lives. As I go on to discuss in 7.1, I thought interviews with people experiencing

genomic tests stood to be a very informative facet, but clearly if I avoided any question that could possibly cause upset there would be very little I could ask. I tried to navigate this by discussing this issue at the outset of every interview as part of the consent conversation, making it clear that participants could stop or pause the interview at any time without needing to give me any explanation. In my questioning, I also tried to take a tentative and gentle approach, and be sensitive to cues that a participant might be becoming upset or anxious. On a number of occasions, I moved on from a line of questioning sooner than I might have wanted to from an academic perspective, because I thought pursuing it risked upsetting or unsettling a participant.

An interesting ethical issue related to establishing rapport, and where the line lay between listening carefully and empathetically in a way that supported people to talk openly, versus what Duncombe and Jessop call '*faking friendship*' (101). During my clinical training, lots of communication skills teaching has included discussion of how to establish rapport- often almost giving a formula for trying to do this. I felt maybe a bit too seen by Duncombe and Jessop's comment that: '*They must seat themselves not too far away but not too near; maintain a pleasant, encouraging half-smile and a lively (but not too lively) interest. They should keep eye contact, speak in a friendly tone, never challenge, and avoid inappropriate expressions of surprise or disapproval; and practice the art of the encouraging but 'non-directive' "um"*' (101)!

In a clinical setting, helping someone to talk freely might mean they share information that allows better understanding of the situation such that better/more tailored clinical care can be provided. In a qualitative interviewing situation, a participant is asked to share information in order to facilitate research, rather than in hope of personal benefit, so establishing rapport (or the appearance thereof) is in the interests of the researcher but not

necessarily the participant. Trying to err on the side of appearing cold and uncaring does not seem optimal either, but it was an unsettling process considering whether I was '*doing rapport*'(101). I tried to ensure that I was not encouraging people to disclose more than they on reflection would have chosen to by making it clear at the outset that they had no obligation to answer or discuss anything they did not want to. On occasions when transcribing interviews, I did not transcribe sections where people had told me personal things that I wondered if on reflection they would not have wanted to be known beyond the boundaries of the interview. I realise this was somewhat of a *post hoc* fix but it felt a way to allow the development of a rapport that did feel genuine, while avoiding exploitation of the candour this sometimes prompted.

Much of my project has involved examining prevalent discourses around genomic results, and how they interface with lived experiences with genomic testing. As I will go on to describe, I think promotional discourses around genomics often do a disservice to people having or delivering genomic tests, minimising the potential complexity and contingency of genomic results, and setting people up for disappointment or misinterpretation. A key way to maximise the usefulness of my project was therefore to try to make this point more widely, highlighting aspects around genomic results that do not easily fit with promotional discourses. During my DPhil I had a number of opportunities to try this, and Chapter 8 outlines ways in which I have engaged with various audiences regarding this issue.

2.6.3 Institutional ethics approvals

As regards the institutional permissions I sought to facilitate this research, the NHS East Midlands – Nottingham 2 Research Ethics Committee granted approval for the aspects of this study which involved direct work with people (observation of clinical appointments, and interviews with people experiencing genomic tests) (REC reference: 19/EM/0024). This

was also approved under the Musketeers Memorandum (a collaboration facilitating the delivery of rare disease research projects across multiple regional genetics centres(102)). My analysis of stock images did not involve human participants or their data. My analysis of the portrayal of genomic results in UK news items was approved by the University of Oxford Medical Sciences Interdivisional Research Ethics Committee (approval reference: R80372/RE001). My analysis of Mass Observation Project responses was approved by the same committee (approval reference: R82879/RE001 – this application formed part of a wider project and was led by my supervisor Dr Susie Weller).

2.7 Summary

To summarise, I approached my overall research question: ‘how should we construct genomic results?’ via a facet methodology approach, a research orientation that aims to creatively shine light on a problem/question from different angles and using a variety of methods in the pursuit of ‘*flashes of insight*’ (92). The main facets I chose were exploration of the construction of genomic results in stock images (Chapter 3); UK news (Chapter 4); writing about genetics and health in everyday life (Chapter 5); observations of clinic appointments where genomic results were discussed (Chapter 6); and interviews with people experiencing genomic tests (Chapter 7). In the course of my project I developed more engagement-oriented facets which also informed my central research question, for example public engagement activities, writing about various initiatives relating to genomic data, and contributing to clinical guidelines (Chapter 8). In attempting to integrate results regarding the nature of genomic results as explored via various facets to draw normative conclusions as to how we should construct genomic results, I was influenced by empirical bioethics.

In the following chapters, I discuss each of my main facets in turn, starting with my rationale for selecting the facet, then describing the specific methods it involved and the insights I gained from it as to how genomic results might and/or should be constructed. I conclude with a chapter considering these insights in relation to my research questions.

3 'Genomic results' in stock images

This facet was designed to inform my research question 'In what ways do popular discourses invite us to imagine genomic results?' Here, I wanted to analyse how the concept of a genomic result might be communicated in stock images. The intention was that this might inform my overall question, 'how should we construct genomic results?', by cataloguing a variety of popular ways in which genomic results might be envisaged, that I could then compare and test against insights from other facets and other relevant data to consider when and why these might or might not be useful.

The chapter begins by outlining the reasons why I chose to examine stock images, then describes my process of image collection and analysis, before detailing key results. Parts of this chapter are based on my previously published work exploring how *genetic* tests are represented in stock image banks(103).

3.1 Rationale for analysing stock images

I got the idea for analysing imagery around genomic results from seeing a scientific journal with a cover image of a sparkly blue double helix. I had recently read a discussion on social media (Twitter) where someone had criticised the decision to illustrate a vaccine news story with a picture of a big needle and a crying child. This illustrated to me how images that might be quite casually chosen to grab a reader's attention, without necessarily intending to communicate a particular message, might have significant consequences, in this case undermining public health(104). Thinking around this issue as it related to genomic results, I realised how frequently the blue double helix featured in a range of spaces, from leaflets in the clinical genetics department, to lecture slides I saw in the course of my genomic medicine MSc, to my own teaching slides for medical students doing the

clinical genetics special study module that I was organising at the time. I then looked through some news stories relating to genetics and genomics on BBC News, and saw that several included similar images, usually obtained from a stock image bank. It made me think of the saying '*a picture is worth a thousand words*' – so what did these pictures say?

Stock images are '*existing, artificially constructed visuals used by businesses and media outlets to articulate certain values, assumptions and beliefs*'(105). Commercial stock image banks buy images that they then sell on for use by clients in an industry estimated to be worth 3.3 billion US dollars in 2020(106). The more times a stock image is used, the more lucrative it will be, meaning that successful stock images need to be both applicable to many contexts, and feel tailored to the particular context in which a client might be looking to use them(107). The most lucrative stock images conform with existing and often problematic clichés – as Machin wrote, '*will we still be able to recognise 'work' without the laptop, 'freedom' without someone jumping, and 'ethnicity' without bright and multi-coloured clothing?*'(108).

For people who at present are not that interested in genomics, stock images have potential to be a significant influence on how these interests might develop. For example, for people browsing news apps or websites, a headline and the thumbnail image selected to illustrate it may be all they see relating to stories about genomic initiatives if they do not go onto read the associated article. By the point where genomic testing becomes personally relevant to them, what messages will they have been shown regarding genomic results?

3.2 Methods

3.2.1 Critical discourse analysis orientation

My approach was influenced by Harvey and Brookes, the first to examine critically the visual discourses around a health topic (dementia) in a stock image bank(105). They performed a multimodal critical discourse analysis, an approach situated within the school of critical discourse analysis.

Critical discourse analysis considers relationships between discourse and power. Advocates of the approach see '*language as social practice*', with abilities to '*[help] sustain and reproduce the social status quo, and ... [to contribute] to transforming it. Since discourse is so socially consequential, it gives rise to important issues of power. Discursive practices ... can help produce and reproduce unequal power relations ... through the ways in which they represent things and position people*'(109). As Munro discusses in her critical discourse analysis of UK newspaper coverage of house price inflation, '*An important insight of critical discourse analysis is that in using language the writer implicitly is deciding what not to say: a significant part of conducting critical discourse analysis is to interrogate those meaningful silences and absences. These 'choices' in language will often be unconscious or unthinking, as authors may simply draw on conventional or dominant representations, without any active or deliberate intention to espouse a particular ideological position or attempt to persuade or produce propaganda. However... these conventional representations can have important insights about hegemonic power, the 'taken for granted' that can constrain the way that the contemporary order of the world is seen and the extent to which alternative orders are imagined as possible*'(110).

While critical discourse analysis has most commonly been applied to text, it can also be applied to other discursive modalities. For example, Harvey and Brookes interpret stock

images as *'visual texts culminating from a system of deliberate and motivated design choices made by their producers'*(105). In many senses, critical discourse analysis could be considered particularly appropriate to images used to illustrate text, which may often be chosen as an afterthought. I therefore thought this approach would be well suited to a facet exploring how ideas around genomic results were expressed in stock images: it would help me identify *'conventional or dominant'* visual representations of genomic testing, and to consider their influence on how we imagine and construct genomic results. It would also attend to issues of power, asking the question: what concepts and experiences of genomic results are favoured in stock image banks and so stand to be widely propagated, and which are minimised?

3.2.2 Image collection

I searched Getty Images (<https://www.gettyimages.co.uk/>) and Adobe Stock (<https://stock.adobe.com/>), image banks chosen on the basis of their large size, longevity and popularity, for images relating to genomic results.

I used the search terms: 'genomic test'; 'genomic result -crops'; and 'genome sequencing'. I chose these terms trying to reflect how a journalist seeking to illustrate a story about genomic testing and results might search for relevant images. I added the '-crops' qualifier following pilot searches which showed that 'genomic result' alone tended to generate lots of images of crops, presumably tagged under 'genomics' because of the possibility they could be used to illustrate articles on genomic modification of foods. I ran the searches on 30/7/24 and 31/7/24 using the incognito mode in Google Chrome so that results would not be affected by my previous browsing history.

I used the inbuilt filters within the image banks to rank results by relevance (Adobe Stock) and best match (Getty Images). I sorted by relevance/best match as opposed to popularity, as pilot searches indicated that my search terms when filtered by popularity tended to generate generic laboratory scenes. These were likely popular because they were potentially applicable to a very wide range of articles, rather than because they had been frequently used to illustrate stories relating to genomic results.

For each of my three search terms, for both stock image banks, I selected the first 50 images which did not obviously feature crops (e.g. close-up pictures of wheat, pictures of fields of crops) for further analysis, collecting 300 images in all. I chose to analyse just the top 50 images from each search on the premise that these higher-ranking images were most likely to be seen by people seeking images to illustrate their work. For example, for Google searches, most people follow links on the first page of results only(111).

3.2.3 Specifics of image analysis

Guided by the work of Harvey and Brookes(105), I next looked in detail at each stock image and documented its features using free text. For example, what was depicted in the image? What colours and lighting were used? Were there people in the image and if so, who were they, how much of them was visible, where was their gaze directed? What was the setting? For each image, I also made a note of my personal reaction to it – the ideas or impressions that the image evoked for me.

Having done this, I noted objects commonly present in the images (for example, the double helix, microscopes, pipettes) and went systematically through each image noting whether the objects were present or absent. I then reviewed all the images in each category (e.g. all images featuring a double helix) noting common features of the way they were presented

(e.g. was the double helix glowing? Was it presented against a black background?) before counting what proportion of the relevant images this applied to. As I looked at the grouped images, I considered what messages these objects and stylistic choices might convey regarding genomic testing and its outcomes. I also presented various of the images during meetings of our research group, asking colleagues' reactions to the images. I used this as a basis for discussion regarding what the images might communicate regarding genomic testing, and to explore alternative interpretations.

3.3 Results

Of the 300 stock images relating to genomic testing and its outcomes that I analysed, most were beautifully presented with minimal clutter. For example, laboratory spaces tended to be immaculate with any equipment pristine, containers either empty or containing uniform volumes of clear, brightly coloured liquids. This presentation choice increases their attractiveness as illustrations, but potentially also engenders an expectation of neatness and clarity from genomic testing.

Slightly over half of the images were photographs, and most of the remainder were abstract images. In many cases this binary classification was somewhat misleading, for example a 'photograph' might feature a laboratory scene with a person in a white coat looking closely at a large screen featuring an abstract image of the double helix, or an 'abstract image' might involve (apparently photographed) gloved hands handling a double helix. There were a small number of 'clip art' style images (for example collections of small icons with a scientific theme, or basic diagrams of cells or sequencing machines), a few 'screenshot' type images (where an image was filled with ACGT letters), and a few images that appeared painted or drawn but these were very much in the minority.

12 images appeared twice in the data set: four featured a scientist staring down a microscope; one showed a scientist holding up and smiling at a test tube containing colourless liquid; one focused on clipboards held by people wearing white coats and stethoscopes; three centred around a droplet dangling at the end of a pipette tip (two of these were against a background of lanes of glowing bands reminiscent of slab gel electrophoresis); one showed multiple lanes of glowing blue bands against a dark background; two images were filled with small ACGT letters.

The great majority of stock images did not feature an ‘end process’ of genomic testing, such as a scene showing a result being discussed with a patient. Instead, many images featured genetic material or ‘uninterpreted’ data derived from it, or laboratory equipment with or without scientists, with some images involving a composite of all these. Section 3.3.1 discusses how genetic material or data derived from it were foregrounded in many of the images. Section 3.3.2 discusses the representation of laboratory equipment and people in the stock images analysed.

3.3.1 Genetic material or data derived from it are often foregrounded in stock images

Table 3 shows the proportion of images featuring genetic material and derived data, and Figure 4 aims to represent how these were commonly depicted in stock image banks. I then discuss the various representations of genetic material or data in more depth: the double helix (3.3.1.1); slab gel electrophoresis-inspired patterns (3.3.1.2); and ACGT (3.3.1.3).

Table 3: Genetic material and derived data in stock images
(note some images featured objects from more than one category)

Feature	Number of images (percentage)
Double helix	93 (31%)

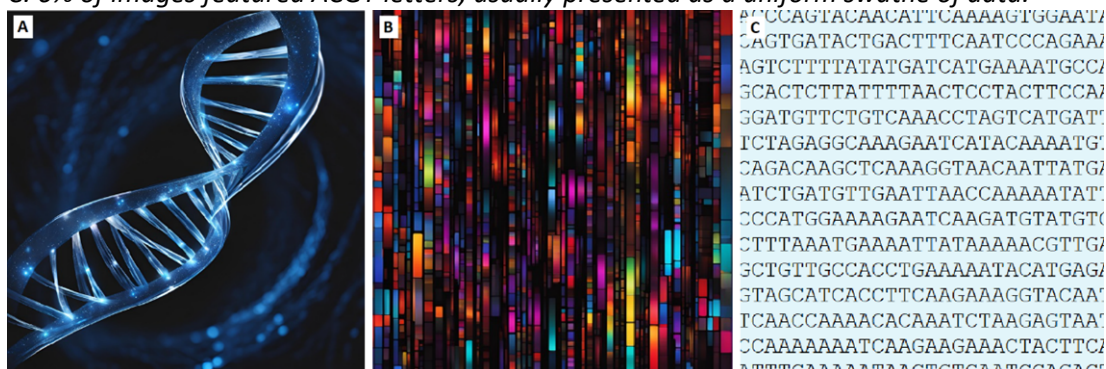
Feature	Number of images (percentage)
Slab gel electrophoresis / 'band-like' pattern	48 (16%)
ACGT letters	18 (6%)

Figure 4: Genetic material and the data derived from it as represented in stock image banks⁹

A: 31% of images featured a double helix – this was usually blue and often glowing or sparkly;

B: 16% of images featured lanes of bands reminiscent of slab gel electrophoresis, often these were heavily stylised and involved multiple lanes;

C: 6% of images featured ACGT letters, usually presented as a uniform swathe of data.



3.3.1.1 The double helix

In work published in the European Journal of Human Genetics where I used a similar approach to that described above to examine stock images relating to the search term 'genetic test', 23% of images included the double helix(103). The double helix was even more prevalent in stock images relating to genomics, featuring in 31% (93/300) of the images analysed. 37 images (12% of all images analysed; 40% of all images involving a helix) showed solely the double helix. In such images, the double helix was usually blue and often softly lit or glowing though occasionally overtly sparkly, sometimes with light emanating

⁹ To avoid infringing copyright, these are illustrative re-creations rather than actual images analysed. Figures 1A and B were created using artificial intelligence (Canva AI image generator with the prompts 'blue double helix running across dark background with light sparkling out of it' and 'dark background, narrow glowing brightly coloured rectangles arranged at irregular intervals in neat columns'). Figure 1C was created using Paint.

from it (see Figure 4A). Helices were typically presented against a dark background, sometimes with poorly defined bright spots alongside or around them, creating a similar effect to some Hubble space telescope images.

These composition choices potentially evoke an idea of genomic testing as examining something fundamental and profound, with illumination arising directly from our DNA. In *The DNA Mystique*, Nelkin and Lindee argue that *'DNA has assumed a cultural meaning similar to that of the Biblical soul. It has become a sacred entity, a way to explore fundamental questions about human life, to define the essence of human existence, and to imagine immortality. Like the Christian soul, DNA is an invisible but material entity, an "extract of the body" that has "permanence leading to immortality." And like the Christian soul, DNA seems relevant to concerns about morality, personhood, and social place'*(84).

Putting the iconic double helix centre stage invites us to remember stories of the discovery of its structure, heralded as *'the secret of life'*(112,113). As Nelkin wrote in her discussion of the *Gene as a Cultural Icon*, *'the gene has been identified with a sacred, God-given basis of essential humanity, the 'fundamental stuff of life''*(114), and the choice of stock image artists to represent the double helix as suffused with light or sparkly against a dark or outer space-like background echoes this, imbuing genetic material with a grandeur and quasi-sacred nature(115) that potentially invites a viewer to expect a lot from genomic testing.

In the other 56 images featuring a helix, the helix was often still a focal point of the image, but presented together with other objects or people. A common format involved a blue glowing double helix against a dark background displayed on a computer or occasionally smartphone screen, often with annotations such as graphs or numbers also present on the screen to the sides of the helix. Occasionally these images featured a person in a white coat gazing at the screen but more often the screen stood alone in a laboratory setting, awaiting

viewing. Another fairly common pairing was the double helix together with a magnifying glass or microscope, potentially evoking the idea of the genetic code under inspection. These composition choices convey that work is necessary to create meaning from the genetic code – either by close inspection of the double helix, or by reading the annotations alongside it, but the journey from double helix to insight is implied to be more akin to reading results directly from the code, than trying to make sense of it.

3.3.1.2 *Slab gel electrophoresis-inspired patterns*

48 (16%) of the images analysed included a pattern of bands suggestive of a slab gel electrophoresis picture¹⁰. Many pictures involving such a pattern looked they had originally been based on a restriction fragment length polymorphism assay or similar. In these pictures, the band pattern was generally very prominent though often partnered with other items, for example being the background to a pipette tip or gloved hand holding a liquid-filled vial. Composition choices potentially invited an expectation that such patterns translated to important insights, as bands were typically starkly delineated in the manner of a barcode and sometimes glowing. Sometimes images featured people reacting around these patterns, for example pointing at a particular band or holding a gel picture up to the light as they scrutinised it.

As O’Riordan notes, the *‘image of DNA bands or ladders across a surface resembling something like a photographic negative has become a distinctive and frequently used genomic icon ... this kind of image is employed as a visual aid in television crime dramas, for example, to indicate genetic testing or DNA analysis’* (116). The older technology that creates such images is now rarely used in genomic testing for health purposes, but its use in

¹⁰ Slab gel electrophoresis is a technique for separating large molecules (like proteins or DNA) on the basis of size. A ‘gel picture’ will typically involve several columns or ‘lanes’ containing bands laid out at varying intervals like the rungs of a ladder.

stock images about genomics may invite viewers to connect expectations they have around the use of genetics in investigating crime (often seen as a clincher in proving guilt or innocence – see section 5.3.3), to the use of genomics in the setting discussed in the story the stock image has been chosen to illustrate.

However, compared to the ‘band-like’ pictures I examined in my analysis of stock images relating to *genetic* testing(103), several of the genomic stock images featured many more lanes/columns of bands, and many of these were heavily stylised (see Figure 4B). For example, bands might be arranged in concentric rings rather than columns, or with lanes fading out partway across the page, with columns of different widths and the position of the bands in each column bearing little relationship to the position of bands in other columns. Some were reminiscent of gel-type patterns by having clearly delineated lanes, but these lanes looked like streaks with brightly glowing sections, rather than containing distinct barcode-like bands.

These images involving more columns or bands in a slightly less orderly arrangement conveyed the sense of a large quantity of data. Bands were often sharply delineated or glowing, occasionally both, and as such might give an impression of clarity and illumination when looking at sections of the image in isolation. However, the number of bands per image, and the less regimented arrangement meant that to me the image when viewed as a whole often gave an impression of complexity and overwhelmingness. I thought various of the images might usefully communicate that while one could in theory make sense of the data, the quantity was so huge that it was hard to know where to start. As I aim to represent in Figure 4B, while such images still presented an attractive and ‘glossy’ picture of genomics I felt they better presented the potential messiness of making sense of the genetic code than images using less stylised outputs from slab gel electrophoresis.

3.3.1.3 ACGT

Several stock images featured DNA sequence as represented by ACGT letters. Typically, these images either featured a mass of tiny black ACGT letters which appeared printed on white or cream paper, similar to text in a dictionary or telephone directory, or ACGT letters, sometimes colour-coded and sometimes black, in the type of font computers use when they are starting up or crashing, appearing as if displayed on a computer screen (though with only letters visible in the image – see Figure 4C). A couple of these images included some form of annotation: in one, approximately 3% of the ACGT letters had a blue square highlighting them, and in another, four consecutive nucleotides were written in red amidst a mass of black letters. The bulk of the images featuring ACGT showed a uniform swathe of data, though in three cases these letters were displayed above a corresponding Sanger sequencing trace.

The distinctness and unambiguous nature of the letters representing the DNA nucleotides may give an impression of theoretical readability and clarity, and images with ‘annotated’ nucleotides potentially imply they can be classified in a very binary way. Their typical presentation in a solid block of text that is implied to stretch out in every direction around the image conveys that genomic tests involve an inordinate quantity of data. ACGT images with black text printed on a white background may tap into widespread metaphors which describe the human genome as *‘the book of life’* or *‘our own instruction book’* (117,118).

3.3.2 People are absent or take a secondary role in many stock images, with more emphasis given to laboratory equipment and genetic material or data

People were absent in 54% of the stock images I analysed. My search terms aimed to reflect those that someone searching for a stock image to illustrate their work might initially use, so did not specify that I was interested in human testing, or in a healthcare context. It is

therefore unsurprising that many images did not clearly situate genomic testing as involving people. Indeed, images of crops were so commonly generated by the search terms that I specifically excluded these from further analysis, and 7 images (2%) featured one or more viral particles (as represented by spheres with well-defined spikes jutting out of them).

However, in images where people were featured, these were generally people involved in providing or undertaking genomic tests: of the photographed people where enough of the person was visible in the image to tell if they were wearing a white coat, 141 out of 156 (90%) were doing so. Table 4 shows how people featured in the stock images I analysed.

Table 4: People in stock images relating to genomics

Person/people	Number of images (percentage)
No-one	162 (54%)
Scientist(s)/clinician(s) only	127 (42%)
Person having genomic testing only	0 (0%)
Scientist/clinician and person having genomic test	5 (2%)
Other (e.g. blue figure rising out of double helix)	6 (2%)

3.3.2.1 *People having genomic tests*

People having genomic tests, or receiving outcomes from them, were largely absent from the stock images I analysed. Only five of the 300 images pictured people having genomic tests, and three of these were by the same content creator. In four of these images, a ‘clinician’ (as indicated by a stethoscope and white coat) was in sharp focus with their face visible, and the possible ‘patient’ they were talking to was in blurry focus and viewed from behind. These images likely involved actors, but the blurry focus on people in a ‘patient’ role, while it may have been intended to indicate preservation of anonymity, had the effect

of minimising or obscuring the patient from a visual perspective. The only other image that arguably depicted people having genomic testing featured hands holding a magnifying glass, in the lens of which was shown a double helix and three children in silhouette.

3.3.2.2 People delivering genomic tests

132 (44%) of the images analysed involved people delivering genomic tests. Images tended to strongly emphasise the role of technical scientific work: as previously discussed, 90% of all the people shown in stock images were wearing white coats (where enough of them was shown that it was possible to tell), and typically people were engaged in work with samples or technical equipment, for example holding up a sample tube or looking down a microscope.

Usually, people were pictured working alone – 99 of the images with people delivering genomic testing featured a sole worker (75% of images featuring a scientist/clinician). In these images, the primary focus of the image was rarely the person – the image instead centred around the equipment or sample they were working with. For example, in 24 of the images (24% of images featuring a sole scientist/clinician), only their fingertips, hand or arm was visible and the main focus of the image was the object they were holding. In images that did feature a scientist or clinician's face, their face was often in profile, often partially obscured by goggles or a facemask, and sometimes in blurry focus or poorly lit. Three images showed a scientist smiling directly at the camera but much more commonly their gaze was directed at a screen, microscope, or other lab equipment.

27 images featured more than one scientist/clinician – in 14 pictures they were independently occupied (for example staring down separate microscopes) but in the remaining 13 they were either interacting directly with each other, or interaction was

implied in that their attention was focused on the same object, usually either a screen or some kind of lab glassware containing fluid. To me, such images continued to evoke the idea of genomic testing as a technical enterprise as white coats and laboratory paraphernalia were prominent, but they also centred teamwork and the idea that collaboration, discussion or shared expertise might have a role in the generation of genomic results. I thought images showcasing this have a potentially useful role to play in presenting a vision of genomic results as constructed by people for people, in contrast to the majority of images which arguably play into visions of genomic result generation as a sterile, automated process which people merely serve or are subject to, rather than actively participate in.

3.3.2.3 *Laboratory equipment*

Many images appeared to be set in a laboratory, and scientific equipment was often prominent. 58 images (19%) included a microscope, despite microscopy not playing a prominent role in most genomic tests. 7 images (2%) featured a magnifying glass, typically focused on a double helix. Where a magnifying instrument was featured, this was often the main focus of the image, potentially evoking ideas of scrutiny and close inspection of the genetic code. This chimes with Van Dijck's observation regarding '*the ostentatious presence of... visualising instruments*' in pictures of genetic scientists in the 1990s(119)- at which time they will have played a more important and frequent role in the genetic testing process because of their use in karyotyping. As with images based on slab gel electrophoresis patterns, it is interesting that many stock images intended to represent genomic testing in the 2020s continue to lean on technologies or equipment that while far from obsolete have in many clinical situations been superseded by newer techniques.

46 images (15%) featured a pipette tip or dropper. In the majority of these, the pipette tip was the main focus of the image, and was usually pictured in the centre of the image, often with a small volume of liquid visible inside it and/or a droplet poised at the end, sometimes with the body of the pipette pictured, usually held by a gloved hand. Images featuring pipette tips potentially invite expectations of accuracy and precision from testing by visually prioritising the delicacy and exactness of techniques involved in the genomic testing process. 8 images (3% overall, 17% of images featuring a pipette tip or dropper) included multiple pipette tips. These were usually shown as an array of loaded tips poised above a multiwell plate and the mechanism by which fluid might be collected or dispensed was not shown (i.e. the instrument onto which the pipette tips were loaded, and the person involved in supervising it, were not pictured). To me, these images evoked a different sense, emphasising genomic testing as large scale, automated and impersonal.

3.4 Summary

As relates to my research question 'In what ways do popular discourses invite us to imagine genomic results?', many stock images suggested that genomic results arose from a highly technical, precise and accurate process. Scientific equipment was frequently depicted in the images, and often visually foregrounded at the expense of the people using it. Various of the images focused on genetic material or the data derived from it, and several of these showed results being read almost directly from the genetic code, with annotations around double helices, highlighted nucleotides, scientists pointing at a particular band on a barcode-like ladder. The double helix was frequently centre-stage and often glowing with light, potentially implying power and profundity to genomic results. People having genomic testing barely featured in the images, which tended to tell the story of a sample and technology being the necessary aspects of producing a genomic result – scientists read off the results the technology tells them, and the people having testing have no bearing on the

process. However, in contrast to images focused on *genetic* testing(103), various images conveyed that *genomic* tests involve huge quantities of data, and the challenge of where to start in making sense of them often came across.

Connecting to my overall research question, ‘how should we construct genomic results?’, stock images tend to prioritise a particular idea- one that emphasises the technical, and represents cleanliness, precision and accuracy as key qualities to expect from the results construction process. Various images showcase genomic results construction as involving vast quantities of data, but at the more granular level these data are often neatly delineated and just need the results reading off them, or are so packed with powerful insight that they cannot help but glow. Such representations are pervasive – as I go onto discuss in the next chapter which focuses on the portrayal of genomic results in UK news items, many news stories about genomics are illustrated with stock images. A sparkly DNA motif featured as the cover image on the recent government report ‘*Fit for the Future: the 10 year health plan for England*’(62), subliminally presenting genomics as powerful, precious and profound – the magical answer to the NHS’ current problems.

This is one version of genomic results – and this set of successful stock images rarely make it clear that there might be other versions too – where people get no [clear] answers from genomic testing, or end up living with more uncertainty or additional concerns as a result of their genomic test. The roles and importance of people in genomic result construction, both in terms of engaging with testing and incorporating results into their lives, and in working with genomic data to make meaning from it – are rarely showcased. As to how we *should* construct genomic results, I argue that these alternative possible aspects of genomic results need more attention. Using the sparkly double helix can be a useful and attractive shortcut, but if it promulgates a one-dimensional glittery view of genomic results this then needs

balancing in order to allow meaningful personal and societal conversations around whether and when to engage with genomic testing.

3.5 Reflections on this facet

This facet has sought to explore how genomic results are portrayed in stock images but has a number of limitations. I have examined these images ‘out of context’ whereas most people engaging with these images will be seeing them partnered with text such as a headline or news story, which may put a particular spin on the image. My analysis involves my personal interpretation of many of the images, drawing on my clinical experience and reading of wider literature. While I have refined these interpretations through discussions with my supervisors and in research group meetings, other people viewing the same images might of course read them differently.

There is also very little evidence regarding how images representing genomic testing or results might influence a viewer’s ideas and attitudes regarding genomic results. Even if the images themselves present a one-dimensional view of genomic results, this only matters insofar as it influences people’s expectations from genomic testing. To me, it seems very plausible that images may affect what people think – indeed much of the advertising industry is built around this premise. As Messaris explains when introducing his book *Visual Persuasion: The Role of Images in Advertising*, ‘because of the implicit nature of visual argumentation and the relative lack of social accountability which images enjoy in comparison with words, pictures can be used to make advertising claims that would be unacceptable if spelled out verbally’ (120).

I am not suggesting that stock images around genomic results would routinely be chosen as illustrations with the tactical intention of getting people to have genomic tests, but I think

there are some parallels where images may be chosen to illustrate all sorts of materials relating to genomics (websites, leaflets, news stories, scientific journals, policy documents, etc) because they look eye-catching and attractive, so might make it more likely that people would give their attention to the materials. Yet embedded within these images may be inaccurate messages around genomic tests and their results that go unchallenged because they are not explicit, and that might on some level influence the ideas and expectations that people then bring to genomic tests they might have in the future.

4 'Genomic results' in UK news

Like the work described in Chapter 3, this facet was also designed to inform my research question 'In what ways do popular discourses invite us to imagine genomic results?' Here, I wanted to analyse how the concept of a genomic result might be presented in UK news items. The intention was that this might inform my overall question, 'how should we construct genomic results?', by providing an overview of how genomic results are commonly framed and conceptualised by UK news items. I could then explore these in relation to insights from other facets and other relevant data to consider when and why these might or might not be useful.

The chapter begins by discussing why I chose to analyse genomic testing and its outcomes as presented in UK news. I then detail how I collected news items reporting on recent genomic initiatives (details of which can be found in Chapter 1 – Deciphering Developmental Disorders study (1.2.1.1); 100,000 Genomes Project (1.2.1.2); NHS Genomic Medicine Service (1.2.1.3); Generation Study (1.3.1.1); and Our Future Health (1.3.2.1)), and the process by which I analysed them, before outlining key results.

4.1 Rationale for analysing UK news

While '*the potential impact of genomics on medicine*' has been part of the Biology curriculum for UK students in Years 10 and 11 (ages 14-16) since 2014(69), many adults will not have had any formal education around the use of genomics in a healthcare context. In 2016, Parry and Middleton reported that '*the word [genomics] itself has the power to confuse*', stating that members of the public had sometimes asked them whether they had meant to say 'gnome' as opposed to 'genome'(121).

But discussion of genomics has become more mainstream. For example, when the CELS group (see 2.2) ran a survey via YouGov in 2018 asking UK adults their opinions regarding genome sequencing in healthcare, 97% of people indicated, after being advised of the topic, that they were willing to complete the survey, suggesting at least sufficient familiarity with the word 'genome' to choose to engage further(79). A recent international scoping review exploring publics' knowledge of, attitude to and motivation towards health-related genomics indicated *'general positivity about genomics, with high awareness but little familiarity or factual knowledge. Publics had high expectations of genomics and perceived that it could provide them with information for their future'*(122). However, very few of the articles included in this review explicitly asked about the source of participants' information regarding genomics although one Korean study identified the media (TV, internet) and friends as sources of awareness(123). The authors of the scoping review recommended that *'future research may benefit from a stronger focus on social influences and media'*(122).

Looking beyond genomics, Happer and Philo discussed the role of the media in the construction of public belief and social change. They argued that *'The media play a central role in informing the public about what happens in the world, particularly in those areas in which audiences do not possess direct knowledge or experience'*, giving examples of how in *'[their] work on disability [they] showed the relationship between negative media coverage of people on disability benefit and a hardening of attitudes towards them'*. They describe how this involves a *'complex process of negotiation in which audiences receive messages involving a range of factors including current and past media accounts, beliefs, knowledge and prior experience, structural barriers and values. These may lead to attitudinal and ultimately behavioural commitment and change, or may inhibit these'*(124).

While most people accept that the media can influence us, there is much debate as to how and to what extent(125). For example, do media discourses around genomics sculpt or simply mirror people's existing attitudes? Evidence regarding this is lacking, but many adults will have become aware of genomics via the media or discussions with friends and family, rather than via formal education. As such, it is plausible that the ways genomics has been described and presented in news content may have contributed significantly to their thoughts and expectations around genomic testing. Choices made as to what aspects of genomic testing to report on are also very relevant – as Conrad writes, '*what becomes news is not inherent in an event or piece of information, but is defined by interested parties*'(126).

In constructing a facet to explore media discourse around genomic testing and its outcomes, I opted to analyse how this subject has been dealt with by UK national news outlets. The 2023 Ofcom report on news consumption in the UK noted that 96% of UK adults say they consume news in some form, with 68% consuming news via online sources. Among people using websites or apps to access news, 58% used the BBC website or app and 16% used Sky News. The use of print newspapers has declined over recent years but many now access the corresponding news source digitally instead. The Daily Mail/Mail on Sunday and the Guardian/Observer are the most widely read titles(127).

Looking to the future, other aspects of media, for example social media, are likely to play a more prominent role, especially given that for 16-24 year-olds '*online sources of news dominate their news diets, social media in particular, and they have a weaker direct relationship with traditional news media*'(127). However, historical news articles provide the backdrop against which current discourses around genomic testing and its outcomes operate, and as such a facet exploring the framing of genomic results in UK news items

stood to provide useful '*flashes of insight*' on my key question as to how genomic results should be constructed.

4.2 Methods

4.2.1 Collecting news items

I sought advice from a research librarian as I developed my search strategy. As I was including a variety of online sources rather than newspapers only, I opted to use Google to run the searches as opposed to the Nexis database (<https://www.nexis.com/>). The Nexis database provides full text access to newspaper articles and current affairs publications but does not systematically catalogue BBC News and Sky News articles, which I was keen to include in view of their wide reach. Nexis also provides text only versions of articles, and where possible, I was interested to look at the images chosen to illustrate the news items that I analysed, linking in with my work on how genomics and its results are represented in stock imagery (Chapter 3). Via Google search, I could easily access the news items as presented by the relevant news outlets, including any images used to illustrate them (with the exception of Times articles which were behind a paywall – here I used Nexis to access their text).

I chose to search the BBC News and Sky News websites on the basis of their popularity with people consuming news online(127). I included five UK national newspaper titles, chosen based on their popularity and aiming to encompass a range of political views and styles, as outlined in Table 5. My selection was influenced by Barkas *et al* who undertook an analysis of how UK national newspapers had represented cancer patients and their care during the early part of the COVID-19 pandemic(128).

Table 5: Sources searched for news stories

News source	URL used for search	Political orientation	Style
BBC News	Bbc.co.uk/news	Neutral	Broadcast/online
Sky News	News.sky.com	Neutral	Broadcast/online
The Sun	Thesun.co.uk	Right of centre	Tabloid/online
The Guardian and Observer ¹¹	Theguardian.com	Left of centre	Broadsheet/online
Daily Mail and Mail on Sunday	Dailymail.co.uk	Right of centre	Midmarket/online
The Times and The Sunday Times	Thetimes.com	Right of centre	Broadsheet/online
The Mirror and The Sunday Mirror	Mirror.co.uk	Left of centre	Tabloid/online

Next, I developed search terms aiming to elicit relevant news items that discussed genomic testing in clinical contexts. This involved extensive piloting of different terms aiming to reach a set with a pragmatic balance of sensitivity and specificity.

Initial searches such as ‘genomics’ and ‘genome’ yielded hundreds of results, most of which were not relevant to genomic testing to inform clinical care. For example, many related to Covid testing or archaeological genetics. In reading through some of the news items identified, I found that the most pertinent ones tended to discuss or at least mention recent or current clinical genomic initiatives. In view of this, I developed searches aiming to elicit news items mentioning large UK initiatives offering tests examining large amounts of genetic code: the 100,000 Genomes Project; Our Future Health; the Generation Study; the NHS Genomic Medicine Service; and the Deciphering Developmental Disorders Study.

The search terms I settled on are detailed in Table 6. As advised by the research librarian, I tested the terms for each site to ensure they were detecting relevant news items and to

¹¹ At the point the searches discussed here were undertaken, the Observer was owned by Guardian News and Media Ltd, and operated as a sister paper to the Guardian. Ownership transferred to Tortoise Media in April 2025(129).

see whether synonyms or different formats might be required. For example, Google detected the same articles whether I used ‘100000’ or ‘100,000’ in my search relating to the 100,000 Genomes Project, but using inverted commas around “100000 genomes” (or “100,000 genomes”) yielded fewer articles than using the search terms without commas, including missing a few relevant news items. However, for Our Future Health, using inverted commas were necessary to give appropriate specificity to the search as without these the search yielded hundreds of thousands of results, the vast majority of which were irrelevant.

Table 6: Search terms used to collect news items

Initiative	Search terms
100,000 Genomes Project	100000 genomes site:[relevant URL]
Our Future Health	“Our Future Health” site:[relevant URL]
Generation Study	((newborn OR baby) AND (genome OR genetic OR dna OR gene)) OR “generation study” OR "genomes programme" OR "genome programme" site:[relevant URL]
NHS genomic medicine service	NHS genomic medicine service site:[relevant URL]
Deciphering Developmental Disorders study	DDD deciphering developmental disorder site:[relevant URL]

I ran the searches with no date restrictions, allowing Google to omit results very similar to those already displayed, throughout November 2024, re-running all searches again on 4/12/24 to collect any news items that had been published in the intervening days. For each search, I collated all the results generated into an Excel spreadsheet and then visited each URL, checking the title of the news item and where relevant reading its full text in order to determine whether it should be included in further analysis. Times articles were behind a paywall so where it was not immediately clear from a headline that a news item was irrelevant, I searched for the headline in the Nexis database in order to find the full text

and assess it (I also used the Nexis database to collect the text of included Times articles for ongoing analysis).

Results were excluded where:

- The result did not lead to news content, for example, it linked to a journalist's profile with a list of stories that they had written, or a sitemap relating to the news stories featured on the day an article about genomics was published. (Content such as opinion or comment pieces, promoted content in the style of a news article, letters and obituaries were included if they discussed genomic testing for health purposes).
- The news item had only been displayed in a particular region of the UK (for example, regional BBC News articles).
- The news item did not discuss human genetic or genomic testing for the purposes of diagnosing illness or improving/maintaining health.
- The news item discussed a research finding raising the future possibility of a test, but it was not clear from the text that such a test yet existed (on a research basis or otherwise).
- The only test discussed in the news item was for the presence or absence of a single specific genetic factor (i.e. it was clearly not a genomic test), e.g. predictive tests for a cancer-predisposing *BRCA* variant.
- The initiative or the genomic aspect of it was mentioned in passing with no comment made regarding its scientific or societal value, e.g. articles mentioning stock market performance of genomics companies; articles about Our Future Health focused almost entirely on cholesterol testing.
- The item was not primarily text-based (e.g. the URL led to a video).

Once I had collated the included news items from all searches, I manually removed duplicates.

4.2.2 Analysing news items

I analysed the news items in collaboration with a Masters student in Philosophy, Bioethics and Health at Vrije Universiteit Amsterdam, Kendra Gordillo, who was undertaking an internship with the Clinical Ethics, Law and Society group¹². We undertook a framing analysis, aiming to explore which aspects of genomic results are portrayed in UK news items. As Barkas *et al* wrote in the paper that inspired us to take this approach, framing analysis '*attends to the ways that issues can be conceptualised in different ways through foregrounding some aspects and eliding others, exploring how this aligns with the strategic interests of various actors in advancing authority, power or resources*'(128). Entman explains that '*framing essentially involves selection and salience. To frame is to select some aspects of a perceived reality and make them more salient in a communicating text, in such a way as to promote a particular problem definition, causal interpretation, moral evaluation, and/or treatment recommendation for the item described*'(130) [underline reflects Entman's italics in the quoted article].

As well as drawing a reader's attention to particular aspects, frames may also divert attention from other aspects – '*most frames are defined by what they omit as well as include, and the omissions of potential problem definitions, explanations, evaluations, and recommendations may be as critical as the inclusions in guiding the audience*'(130). We

¹² Kendra and I had regular meetings throughout this section of my project where we discussed analytic approach and developed frames, guided by Dr Susie Weller. I led on planning our analysis, suggesting putative frames, and writing up our results. Kendra and I shared collection of metadata and coding of news items equally. Kendra assisted in the process of refining and iterating frames through our regular discussions, bringing a valuable alternative perspective to the analysis through her background in ethics, and context outside the UK.

analysed with the aim of identifying common ways of framing genomic results in UK news – which aspects were given prominence, and which were neglected? What ideas might these framing decisions evoke in a reader as to how genomic results should be constructed, and why?

We started by gaining familiarity with the news items, reading each one carefully and cataloguing metadata on a Google spreadsheet regarding year of publication; headline; word count; and name and role of the author. As part of this process, we collated specific instances where genomic testing of a particular person was discussed. With the exception of Times articles, where we could only access the text, we also noted which images had been used to illustrate the news items. Following this familiarization with the dataset, we moved on to closer analysis of the articles, using the qualitative analysis software NVivo v15 to manage the data, and developing inductive codes through reading and regular discussion of the news items. These codes initially focused on the very broad content of news items (for example, ‘challenges’, ‘process of testing’, ‘benefits’), and provided a starting point from which we generated themes exploring how genomic results were dealt with in the dataset.

We then went back to the articles thinking more specifically about how genomic results were *framed*: Entman cautions how in a framing analysis ‘*the major task of determining textual meaning should be to identify and describe frames; content analysis informed by a theory of framing would avoid treating all negative or positive terms or utterances as equally salient and influential. Often, coders simply tote up all messages they judge as positive and negative and draw conclusions about the dominant meanings. They neglect to measure the salience of elements in the text, and fail to gauge the relationships of the most salient clusters of messages- the frames- to the audience’s schemata*’ (130). Looking again at

our collection of news items reinforced his point that *'journalists may follow the rules for "objective" reporting and yet convey a dominant framing of the news text that prevents most audience members from making a balanced assessment of a situation'* (130). For example, often mention of the limitations of genomic testing appeared briefly right at the end of news articles, akin to a disclaimer.

Through discussion of key themes we had noted relating to the construction of genomic results across the dataset, we identified four frames which we then went back to the individual news items to test, refine and explicate. (Section 11.3.2 in the Appendix aims to give a flavour of the ways I tried shuffling and sorting the dataset in the process of building a frame). Within each news item we paid attention to which experiences relating to genomic results were foregrounded, and which ignored. We considered who was quoted, the order in which quotations were presented, what happened in stories about genomic tests (e.g. did a test have a clear outcome, did it lead to improved treatment, etc), and where we had access to images we examined which had been chosen to illustrate the news items. We also studied how genomic testing and its outcomes were described: which concepts or ideas around results were given airtime and which were not? We went on to consider who might benefit and who might be disadvantaged by the way genomic results were framed in these news items, and in what contexts these frames might be helpful or unhelpful.

The following section presents our analysis, starting with a brief overview of the articles analysed, before discussing four key ways that genomic results were framed.

4.3 Results

4.3.1 Characteristics of news items included

I ran the site-specific Google searches detailed in section 4.2 on 4/12/24, identifying 1519 results, of which 250 met inclusion criteria. After removing duplicates, 186 news items remained for further analysis: 23 from BBC News; 10 from Sky News; 12 from the Sun; 45 from the Guardian/Observer; 36 from the Mail; 47 from the Times; and 13 from the Mirror. Table 7 gives a breakdown of the number of results identified and news items included by site and by genomic initiative.

Table 7: Number of results identified via Google searches as of 4/12/24

News items were included where they discussed human genetic or genomic testing for the purposes of diagnosing illness or improving/maintaining health (please see 4.2.1 for specific details regarding exclusion criteria)

Project	100,000 Genomes Project		Our Future Health		Newborn Genomes Programme		NHS Genomic Medicine Service		DDD study	
Site	Screened	Included	Screened	Included	Screened	Included	Screened	Included	Screened	Included
BBC News	124	14	17	3	8	4	33	9	2	2
Sky News	34	6	2	0	8	3	8	5	0	0
Sun	47	5	10	1	8	5	13	4	1	1
Guardian	290	29	49	2	9	7	52	22	2	2
Mail	298	28	37	4	8	7	76	11	0	0
Times	199	31	35	5	8	5	35	17	2	2
Mirror	72	9	12	1	8	3	12	3	0	0

The earliest included news items were published in 2012 (announcements relating to the idea for the 100,000 Genomes Project). Most news items (159 items, 85%) were written by

people primarily working as journalists. Several journalists (often health or science correspondents) had written multiple articles – for example, seven journalists had written five or more. Ten articles (5%) were written by people primarily known as politicians or political appointees; three by people representing companies operating in the genomic sector; and two by people working for health-related charities. Four articles were written by people working for a group campaigning for public awareness and democratic participation in the governance of genetic technology; one was written by an independent watchdog group; five were written by doctors also working as journalists; and two were letters by clinicians with no background in journalism.

News items featured in the Sun and Sky News tended to be shorter (median length 393 and 410 words respectively), with items in the Guardian/Observer and Mail being the longest (median length 749 and 873 words respectively). Table 8 gives a timeline of key events reported in the news items, illustrated with the headlines of relevant news items.

Table 8: Key events reported in the news items

Date and event	Headlines around the event
August 2014 Announcement of 100,000 Genomes Project	DNA project 'to make UK world genetic research leader' [BBC] DNA research: this is the age of the genome. And there are exciting times ahead [Observer] PM: genome project will transform cancer care [Guardian] PM Hails £300m Project To Unlock Power Of DNA [Sky] DNA project to help target cancer care [Times]
December 2014 Launch of 100,000 Genomes Project	NHS DNA scheme to fight cancer and genetic diseases [BBC] Cancer breakthrough that could spell the end of chemotherapy within 20 years: Mapping DNA could lead to faster diagnosis and new drugs [Mail] Cancer experts believe DNA study could lead to end of chemotherapy [Mirror] DNA Study To Put UK At 'Forefront Of Science' [Sky] DNA testing promises healthcare revolution [Times]

Date and event	Headlines around the event
January 2016 First diagnoses from 100,000 Genomes Project	First children diagnosed in DNA project [BBC] First genome project diagnoses give hope to two four-year-olds [Guardian] The little girls with 'mystery' health conditions who finally have a diagnosis: Landmark £300m project reads a person's entire genetic code to detect disease [Mail] Girls' mystery illness diagnosed through ground-breaking DNA sequencing [Times]
July 2017 Publication of Generation Genome report	Chief medical officer calls for gene testing revolution [BBC] Give patients with cancer and other serious illnesses a genetic test to create tailored treatments, says chief medical officer [Mail] Keith Grimaldi: DNA testing for all would be a vital step in making our lives healthier and could revolutionise the NHS [Sun] (NB Keith Grimaldi is Chief Scientific Officer at DNAFit) Call for revolutionary DNA cancer care on NHS [Sky] Give every cancer patient a gene test, says health chief [Times] Genomic medicine is changing lives and Britain leads the field [Times]
July to September 2018 Announcement of Genomic Medicine Service	Routine DNA tests will put NHS at the 'forefront of medicine' [Guardian, 3/7/18] 'Forefront of medicine' Patients to get routine DNA tests on NHS to tailor treatment to genes in world first [Sun, 4/7/18] NHS will become the first health service to use routine genetic testing in a move that will 'transform patients' lives' [Mail, 20/9/18] DNA holy grail: NHS is to become the first health service to use routine genetic testing to make early diagnoses [Sun, 20/9/18]
January to July 2019 Announcements around scheme for 'genomic volunteers'	NHS to offer paid-for DNA tests if patients share data [BBC, 26/1/19] NHS to sell DNA tests to healthy people in push to find new treatments [Guardian, 26/1/19] NHS to offer paid-for genetic blueprints that predict health risks [Sky, 26/1/19] Gene test for sale on NHS; Healthy patients to learn risk of killer disease [Times, 26/1/19] - Controversial plan to allow healthy patients to pay to have their DNA analysed to predict their risk of cancer, dementia and Alzheimer's 'breaches a core principle of the NHS' [Mail, 29/1/19] The NHS should run a mile from the genome sequencing goldrush: David King [Guardian, 7/2/19] (NB David King is director of Human Genetics Alert) - NHS abandons plan to let healthy people pay for DNA sequencing: Amid concerns over two-tier health system, new scheme will read volunteers' DNA for free [Guardian, 25/7/19] Millions of NHS patients will receive a FREE personalised health report based on their DNA to help them live for longer, the Government announces [Mail, 25/7/19]

Date and event	Headlines around the event
November 2019 <i>Plan for newborn genome screening pilot announced</i>	Babies' DNA will be checked at birth in major NHS trial to 'save thousands of lives' by spotting genetic diseases such as epilepsy and cystic fibrosis [Mail] Brit DNA breakthrough will save thousands of kids from killer diseases [Mirror] Cot a miracle! Babies to have DNA checked at birth to identify any inherited diseases and risk of illness in later life [Sun]
June 2019 to January 2020 <i>Announcements relating to exome sequencing for unwell babies</i>	Genome sequencing 'revolution' in diagnosis of sick children [BBC, 10/6/19] Seriously-ill children with mysterious conditions in England can have their entire DNA mapped as of next year in a move hoped to revolutionise the diagnosis of rare disorders [Mail, 11/6/19] Gene test hope for critically ill babies as DNA testing on the NHS could speed up diagnosis and lead to quicker treatment [Mail, 3/1/20] World first: DNA testing for critically ill babies rolled out on NHS to speed up diagnosis and treatment [Sun, 3/1/20]
April 2022 <i>Tumour genome analysis finds new mutational signatures</i>	'Like fingerprints at a crime scene': study finds new clues about causes of cancer [Guardian] Cancer breakthrough as scientists find a 'treasure trove' of 58 new genetic clues that point to causes of the disease and raise hopes about better treatments to save more lives [Mail] 'Treasure trove' of DNA from tumours provides British researchers with hope for new cancer cures and clues that point to causes of the disease [Mail] NHS cancer patients will be told what caused disease thanks to 'world-leading' research [Mirror] Scientists find cancer 'fingerprints' that bring hope of new treatments [Times]
October 2022 <i>Launch of rapid whole genome sequencing service</i>	Life-saving gene test for seriously ill children in England [BBC] New NHS genetic testing service 'could save thousands of children' in England [Guardian] DNA revolution 'to save thousands of young lives': NHS will offer blood test which can spot 6,000 deadly genetic diseases within days, in world-first inspired by David Cameron's son Ivan [Mail] 'World-first' NHS England rapid genetic tests 'could save thousands of children' [Sky]
October 2022 <i>Invitations start for Our Future Health</i>	Millions invited to take part in UK scheme to diagnose diseases earlier [Guardian] Our health heroes! Three million Britons will join global medical study to help develop new ways to detect illnesses sooner [Mail] The Times view on Our Future Health programme: speak your weight [Times]

Date and event	Headlines around the event
December 2022 Announcement of Newborn Genomes Programme	Genome sequencing trial to test benefits of identifying genetic diseases at birth [Guardian] Babies will get blood tests to see if they have rare childhood cancers under major new screening drive being trialed on NHS [Mail] NHS to launch DNA test which predicts the risk of inherited diseases in newborn babies [Mirror] Cot a miracle! Newborns set to go through groundbreaking DNA tests that spot rare diseases [Sun] 100,000 newborn babies to have their DNA decoded in hunt for rare diseases [Sky] Trial to halt rare diseases in newborns [Times] Scottish newborns to miss out on new cancer screening trial [Times]
October 2024 First newborns recruited to Generation Study	First newborns join screening for 200 rare diseases [BBC] NHS England to screen 100,000 babies for more than 200 genetic conditions [Guardian] DNA testing of 100,000 newborn babies begins as part of major study into 200 rare conditions [Mail] Babies set to receive a pioneering genetic test on the NHS - but many newborns will still miss out [Mirror] DNA tests: NHS hospitals screening newborn babies for rare genetic illnesses in world-first DNA study [Sun] 100,000 babies to be screened for rare genetic conditions [Times]

4.3.2 Common frames by which genomic results are presented in UK news stories

Here I discuss key ways in which genomic results were framed in UK news stories. All articles I analysed are within the public domain in a setting where it is unlikely that those taking part had an expectation that their information would be kept private. However, as I discuss in 2.6.2, I have avoided using direct quotations from people talking about their personal experiences of having genomic tests, as this felt like a use of their words beyond what they might have envisaged in contributing to a news feature. I have included direct quotations from people whom I considered as speaking in a ‘public’ capacity, for example politicians and people with leadership roles in genomic initiatives, including where they discussed personal experiences relating to genomic testing, as given their high-profile roles and power to sculpt discourses around genomics it seemed fair to use their specific comments to illustrate my analysis.

4.3.2.1 *Genomic results are the fruit of amazing technological progress and we are lucky to live at a time where we can benefit from them*

Many news stories contextualised contemporary genome sequencing against initiatives such as the Human Genome Project, reminding readers of the time, effort and cost it took to sequence ‘one’ genome and then inviting them to share in the excitement that now, a person’s genome can be sequenced for a few hundred pounds in less than a day. Genomic results were implicitly presented as the culmination of decades of painstaking work – with our opportunity to access them now being something that people in the relatively recent past could only have dreamed of.

A BBC News story featuring a quotation describing the 100,000 Genomes Project as ‘*transformational in what it means to society and humanity*’ described how ‘*When the first human genome was fully sequenced in 2003, it had taken 13 years and cost £2bn. Today, a genome’s worth of DNA can be sequenced in only 30 minutes, at a cost of £600*’ [BBC News, *Faster diagnosis from ‘transformational’ gene project*, 5/12/18]. A Mail Story describing how a ‘*simple blood test which looks for genetic faults in a patient’s DNA will speed up treatment for the seriously-ill, saving thousands of young lives every year*’, included comparable context that ‘*The first decoding of a human genome - completed in 2003 as part of the Human Genome Project - took 15 years and cost £2.15 billion*’ [Mail, *DNA revolution ‘to save thousands of young lives’*, 12/10/22]. A Mirror story started with a similar drumroll:

Reading the first-ever complete genetic blueprint for a human took 13 years of painstaking research. It was a scientific breakthrough on a par with splitting the atom and putting a man on the Moon. Today, nearly 15 years on, cutting edge technology means sequencing the three billion letters of DNA that make up a human genome takes just three days [Mirror, Britain leading the way in the fight against rare diseases with cutting edge gene machine, 30/9/17]

Genomic results are accordingly framed as something we are lucky to now have access to- a precious opportunity to value and embrace. Articles discussing rapid genomic testing of unwell children frequently contrasted a past where families waited many years for answers that often did not come, with the hope that genomic testing would offer a better future. For example, former UK prime minister David Cameron wrote about the inspiration he was given by his son Ivan, who died as a child from Ohtahara syndrome, to improve things for families living with rare conditions. Reflecting on the time when Ivan was young, he described how the norm had been a '*gruelling process*' of slow, sequential genetic testing with clinicians '*left to rely on intuition and antiquated tests to determine which of the 7,000 rare diseases may be affecting the child*'. Writing in 2018, he described:

Yet we are on the brink of a huge breakthrough. We have access to the comprehensive technology of clinical whole genome sequencing. Instead of looking at individual chromosomes, we can sequence the whole genome, determining the unique ordering of three billion letters found in almost every cell in a person's body. Rather than testing one disease at a time, this process simultaneously can test for all rare diseases, 80 per cent of which are genetically based. All it takes is a blood test. It is that simple.

He went on to describe a recent situation where a young baby having seizures had potentially had her future rewritten for the better because she had had the opportunity of genomic testing: '*Analysis of her entire genome revealed that she had ... Ohtahara, enabling doctors to give her targeted medication immediately. Today she shows no signs of significant developmental harm*' [Times, David Cameron: what I learnt from our son's rare disease, 28/2/18].

This frame of our good fortune today to have access to previously unimaginable technology was particularly prominent in articles around newborn genome screening. Such articles often featured parents of children who had died or been severely disabled by genetic conditions that might now be screened for, reflecting on the benefit that this opportunity

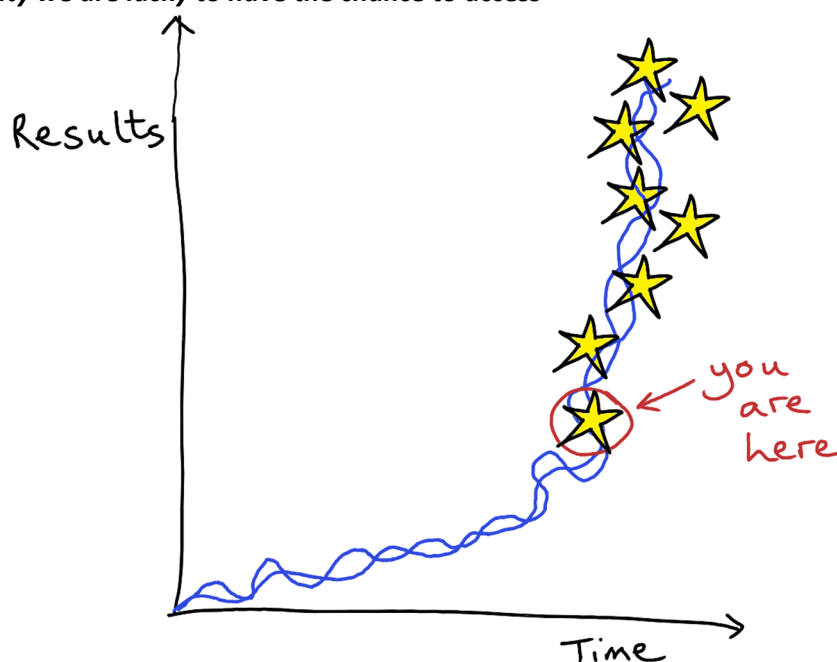
might have brought to their family and encouraging others to seize it. In this context, screening/prediction from the genetic code of a 'healthy' newborn was generally treated as synonymous with diagnostic testing in an unwell baby. For example, a Sun article discussing newborn genome screening described: *'Genomic screening works by scanning DNA from a blood sample. It compares sections of genetic code to a database of illnesses to see if the patient has any. The software can check for more than 6,000 conditions in days'* – the screening process was presented as a yes/no way to determine whether a baby has any of the illnesses screened for [Sun, *Cot a miracle! Newborns set to go through groundbreaking DNA tests that spot rare diseases*, 12/12/22].

Articles often framed newborn genome screening in a way that augmented its potential benefit, by inviting readers to conceptualise the alternative as a diagnostic odyssey of many years. For example, a Mail article discussing newborn genome screening described that *'Doctors hope the simple blood test, which looks for genetic faults in DNA, will speed up diagnosis and treatment for thousands of babies born every year'* and featured a quotation from the Generation Study describing that: *'Children with [genetic] conditions often go years without receiving a diagnosis'* [Mail, *DNA testing of 100,000 newborn babies begins as part of major study into 200 rare conditions*, 3/10/24]. A BBC article interviewing two new mothers who had felt very positive about enrolling their babies in the Generation Study included a comment that *'At present it can take years for genetic diseases to be diagnosed'*, along with a story about a child who had been severely disabled by one of the screened-for conditions, who had waited over two years for a diagnosis after becoming symptomatic [BBC News, *First newborns join screening for 200 rare diseases*, 3/10/24]. Another BBC article heralding plans for newborn genome screening asserted: *'It should spare hundreds of families in England months, or years, of anguish waiting to find out why their children are ill'* [BBC News, *Newborns to get rapid genetic disease diagnosis*, 13/12/22].

As such, articles celebrated the technological progress that gives us the possibility of trying newborn genome screening, but reinforced this by creating a false equivalence. They implicitly set the ‘future’ of newborn genome screening against the past of long diagnostic odysseys, thereby glossing over the issue that the sorts of diagnoses that would be flagged by newborn genome screening should be quickly identified by diagnostic genomic testing of a symptomatic child. There was little to no acknowledgment that children currently on long diagnostic odysseys would not have been helped by newborn genome screening. In the UK, such odysseys mostly persist because our understanding around how genomic variation impacts on health is imperfect and it is not possible to make a genomic diagnosis at this time, rather than because they have not had the opportunity of a genomic test(131).

To summarise, articles tended to present genomic results as a prize that society has gained through years of painstaking work (Figure 5) – an opportunity that cost and sequencing capability previously blocked us from accessing, but that we are lucky to now be able to realise. Many articles were written in such a way as to invite us to wonder at our present-day opportunities to have genomic testing. Often articles framed genomic testing for prediction and for diagnosis as virtually equivalent, especially in the context of newborn genome screening: the pinnacle of our abilities rather than a venture into the unknown.

Figure 5: Genomic results were framed as the fruits of years of labour- a precious opportunity we are lucky to have the chance to access



4.3.2.2 Genomic results are produced by ‘reading’ the entire genetic code

Many articles referred to genome sequencing as ‘reading’ the genetic code, potentially inviting an expectation that the sequencing process might involve understanding, not just cataloguing, of a person’s genomic variation. For example, several Mail articles featured an explainer on genome sequencing which described ‘Whole genome sequencing allows researchers to read all the little bits of code that make us who we are’ [Mail, *Babies’ DNA will be checked at birth in major NHS trial to ‘save thousands of lives’ by spotting genetic diseases such as epilepsy and cystic fibrosis*, 6/11/19; *DNA revolution ‘to save thousands of young lives*, 12/10/22; *Babies will get blood tests to see if they have rare childhood cancers under major new screening drive being trialed on NHS*, 13/12/22; and others]. A Mirror article described the 100,000 Genomes Project as ‘aim[ing] to read the genetic blueprint, or genome, of around 75,000 volunteers’ [Mirror, *Cancer experts believe DNA study could lead to end of chemotherapy*, 23/12/14], and a BBC article had a similar explainer describing the genome as ‘the blueprint for how our bodies function, written in chemical code called DNA’

[BBC News, *Newborns to get rapid genetic disease diagnosis*, 13/12/22]. These descriptions frame the genetic code as fundamentally determining ‘who we are’, and genomic testing as reading about it – genomic results as the outcome of such a process should presumably then be meaningful and clear. Such language is not invented by journalists but echoes the way genomics is discussed in many settings, for example school curricula (1.4.2), policy documents (1.4.1), and educational materials for healthcare professionals(132).

Some articles implied that a genome could almost tell you the answers itself. For example a BBC News article reporting on the completion of the 100,000 Genomes Project included a quotation from the chair of Genomics England envisaging: *‘Your health record will eventually have a genomic backbone to it; that will enable what is happening to you to be compared with what your genome is telling your doctor, and therefore a more accurate diagnosis or treatment will be available’* [BBC News, *Faster diagnosis from ‘transformational’ gene project*, 5/12/18]. Sometimes this ability of a genome to ‘tell’ things of importance was described as being related to its completeness and comprehensiveness: a Mail story about a baby with a tumour that genomic testing showed was benign featured a quotation from a paediatric oncologist: *‘Standard molecular tests only look for specific errors and don’t let the tumour tell us what it is. This is why [whole genome sequencing] is so powerful’* [Mail, *[Baby] was saved from unnecessary chemo by gene mapping technology that could revolutionise healthcare for kids*, 3/7/23].

It was rarely made clear that obtaining a comprehensive sequence dataset, and performing a comprehensive analysis, were not the same – the frequent implication was that if a gene had been sequenced it had been ‘checked’, and by extension, genome sequencing would check everything. For example, the same article which had told the story of a baby whose tumour was found to be benign by genomic testing segued to

discussion of the Newborn Genomes Programme where it asserted '*with [whole genome sequencing] a tiny sample of blood will be used to check all 20,000 genes in the baby's body for around 200 known genetic conditions that are treatable*' – implying that all 20,000 genes will be analysed in the screening process. The Times similarly described newborn genome screening as '*a simple blood test [that] will look at the entire genome of healthy newborn babies in search of genetic faults in their DNA, speeding up diagnoses and allowing earlier intervention*' [Times, *Scottish newborns to miss out on new cancer screening trial*, 15/12/22].

Exploring the images featured in the 139 news items where I could view the associated pictures, 38 news items (27% of those where images were available for analysis) were illustrated with a picture of a double helix, usually blue and often glowing (see also 3.3.1.1). 27 news items (19%) featured an image with prominent scientific equipment such as a pipette (see also 3.3.2.3), and 12 news items (9%) featured a slab gel electrophoresis-type pattern (3.3.1.2). Only 2 news items (1%) featured ACGT letters: in one case, white ACGT letters filled the background and in the foreground was a gloved hand holding a magnifying glass, in the lens of which were coloured ACGT letters surrounding the word 'Cancer' [BBC News, *Chief medical officer calls for gene testing revolution*, 4/7/17]. Quite often where a news item featured an image of this type it was the first image in the story, so likely to have been the thumbnail image, meaning that for people browsing for news who did not go on to read the associated story, this and the headline will have been all they saw. As I argue in 3.4, I think some of these images encourage an idea of results practically shouting out of the genetic code.

Where articles specifically discussed genomic analysis, they generally presented this as an enormous undertaking involving colossal volumes of data, but the context to the discussion

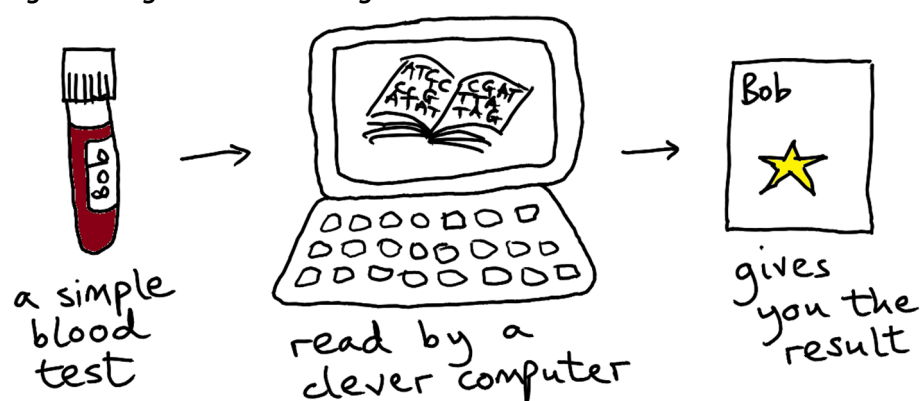
was often a story where genomic testing had successfully produced a helpful result. The scale of the data was therefore framed in such a way as to maximise the marvel of the technical achievement, rather than to make clear the corollary that people may not get clear answers from diagnostic genomic testing. For example, an Observer article discussing the 100,000 Genomes Project described in reference to a child's genomic test that *'Given that each of us has a genome made up of more than 3 billion letters of DNA, this decoding represents an enormous task, one that has required the use of some of the world's most advanced sequencing machines as well as computers capable of storing millions of gigabytes of data'*. But the next step described was the finding of a genetic diagnosis, essentially implying that the machines and computers had decoded the genome and out dropped the child's result [Observer, *The DNA database that is key to beating our rarest diseases*, 3/2/18].

A Times article- promoted content by Genomics England- started by telling the story of a child where diagnostic genomic testing had made a treatable diagnosis, and explained *'His DNA was extracted from a spoonful of blood and his genome – his entire genetic blueprint – read. It is a mind-bogglingly huge task – just one person's genetic sequence consists of enough data to almost fill an average laptop. But thanks to developments in AI and data reading, it can now be done relatively quickly and rolled out on a large scale. The results can be life-changing'* [Times, *Code read: The science of genomics is just a few decades old, but recent breakthroughs have meant that many children with rare diseases can now live normal lives*, promoted content with Genomics England]. Again, amazing technology had read the child's genome and out popped his result.

The simplicity of obtaining a sample for testing was frequently highlighted, with multiple articles across several news sources describing genomic tests as *'a simple blood test'* (see

Figure 6). 15 news items (11% of those where I had access to the images) featured images portraying the act of taking a sample for testing – a combination of blood tests, cheek swabs, and heel pricks. This tallies better with my previously published analysis of how *genetic* tests are portrayed in stock image banks, where 9% of images showed a sample being taken(103), than with the analysis presented in Chapter 3 relating to *genomic* tests.

Figure 6: A genomic test being read



Detective metaphors were common throughout the articles – headlines made reference to ‘*solving the genome puzzle*’ [Guardian, 21/9/18] and ‘*uncover[ing] new clues*’ [BBC News, 21/4/22]. ‘*Spotting*’ and ‘*pinpointing*’ were also common ways to refer to making a genomic diagnosis or asserting a future health risk, and the importance of comparison to other genomes was sometimes discussed in this process. For example, a couple of BBC articles described genomic analysis as ‘*a giant game of spot the difference*’ – once between tumour and germline genomes in people with cancer [BBC News, *NHS DNA scheme to fight cancer and genetic diseases*, 22/12/14]; once between healthy parents and their unwell child [BBC News, *First children diagnosed in DNA project*, 12/1/16].

The role of genomic databases was also sometimes described, though often with a finality that implied that if something was logged in a database as causing disease there was no

need for further debate. For example, describing a newly available genomic test for seriously ill babies, the Mail explained: *'the new test will be able to determine if a child has any of 6,000 genetic disorders by checking their DNA for faults. Scientists use a process, known as whole genome sequencing, which involves extracting patient DNA from a sample of blood and running it through a machine for analysis. They examine the DNA for genetic mutations, which are then checked against a database of thousands of genetic conditions – with results returned to local doctors within a week'* [Mail, *DNA revolution 'to save thousands of young lives'*, 12/10/22]. A BBC article covering the same story described: *'Using a single blood test, scientists can spot gene mutations, run them through a giant database and identify the cause within days'* [BBC News, *Life-saving gene test for seriously ill children in England*, 12/10/22]. Descriptions tended to frame genomic results as elusive but inarguable – you might have to search carefully but when you spot them they will be unambiguous.

Some longer articles (mostly in the Guardian/Observer) discussed genomic testing in a way that made clear to readers that technology plus genomes might not always equal useful results. For example, one article featured stories from several families living with rare conditions that were undiagnosed despite extensive testing [Guardian, *'Nobody knows what's wrong with me' – life with an undiagnosed condition*, 6/12/22]. Sometimes articles included detail in tempering an otherwise simplistic description of genomic analysis. For example, an article that started by describing how *'reading the full genetic code of childhood cancers'* could improve outcomes included a comment deeper into the article that *'while the process gives in-depth information, it is complex work and requires careful interpretation, typically taking two to three months, as opposed to the few days to weeks required for more targeted cancer tests'* [Guardian, *Whole-genome sequencing can improve childhood cancer outcomes – study*, 8/11/21].

Reporting around direct-to-consumer tests was a key area where limitations were frequently raised. Occasionally such tests were presented as being as on the crest of a wave set to transform healthcare, one notable example being a Guardian article written by Anne Wojcicki, at the time CEO of 23andMe, which ran with the tagline *'Discovering your DNA sequence is cheap and easy, and that genetic knowledge could change – even save – your life'* [Guardian, *Know your genome: what we can all gain from personal genetics*, 13/3/13]. However quite often the choice to undergo direct-to-consumer genetic testing was implied to be indulgent and poorly thought through, with potential results presented almost simultaneously as terrifying and trivial. For example, a journalist writing about her personal experience of direct-to-consumer genetic testing described how:

*The home-testing kits could be said to fit in with our increasingly health-conscious and, if you wish to be cynical, narcissistic times. What says you're "special" more than finding out everything about yourself, right down to the nitty-gritty of genetics? In this way, these kits could be viewed as the latest plaything of the "worried well" ... Another key customer type could be people like myself, hurtling through middle age, perhaps just starting to feel the cold bony hand of mortality clamp down on their shoulder. People, who, in the past, may not have exactly prioritised their health, who are starting to wonder what may be in store for them and who are in the ("Hypochondriacs R Us") market for some hard-core insight and advice [Observer, *What I learned from home DNA testing*, 23/7/17]*

Where articles discussed limitations of genomic testing, they often anchored their criticism with reference to direct-to-consumer or 'paid for' tests. For example, a Guardian article discussed that *'Polygenic risk scores are so unreliable that they also wrongly tell one in 20 people who receive them they will develop a major illness, even though they do not go on to do so'*, describing this as being important in reference to *'a boom in the number of companies offering polygenic risk score tests'*. Towards the end of the article it mentioned that Our Future Health will also use polygenic scores, but somewhat detached it from the criticism in the body of the article, featuring its Chief Medical Officer emphasising that here the polygenic scores would be part of *'integrated scores that will take in all the important*

risk factors'. The article ended by quoting him that *'its 5 million volunteers will help it "discover whether these risk scores have a role to play in giving thousands of people the chance of a longer and healthier life"'* [Guardian, *Over the counter genetic tests in UK 'fail to identify 89%' of those at serious risk*, 17/10/23].

Several articles written in early 2019, when the idea was floated of *'genomic volunteering, offering people the chance to pay to have their DNA mapped in return for voluntarily donating their anonymised data to help researchers develop treatments that will benefit everyone in the future'* [Sky News, *NHS to offer paid-for genetic blueprints that predict health risks*, 26/1/19], discussed that making predictions from the genetic code could be difficult, though often as comment to balance political assertions that such a scheme would be beneficial. For example, a Times article regarding this reported former health secretary Matt Hancock saying that *'Genomics has the potential to transform healthcare'*, but also included a comment from Anneke Lucassen that *'there is still a lot of misunderstanding of what whole genome sequencing can deliver. There is a view that it will give you clear clinical predictions. And most of the time it will not ... People tend to think the test finds a high risk or not, but without a family history of breast cancer the predictions might be very uncertain'* [Times, *Gene test for sale on NHS: healthy patients to learn risk of killer diseases*, 26/1/19].

However when the 'paid for' nature of the scheme fell by the wayside, so too did the column inches given to this issue – it seemed that uncertainties that might arise from genomic testing are only considered an issue if you are paying for it. The murky, controversial and somewhat unsavoury nature often attributed to direct-to-consumer or paid-for tests tended to be kept very distinct from freely provided NHS or university-led genomic tests. These were more typically presented as heroic efforts to use our new abilities to read the entire genetic code in order to save lives. Aspirations to identify people

at high risk of future illness often seemed to be regarded as synonymous with making diagnoses early.

4.3.2.3 *Genomic result as societal panacea*

Connected to the presentation of genomic results as the fruit of our amazing technological progress in ‘reading’ our genetic code, they were often framed as enormously beneficial. At a personal level, the opportunity of genomic testing was often connected to a healthier and more fulfilling life. A former Chief Medical Officer, writing in the Times, described how:

The diagnostic odyssey of being sent from medical expert to medical expert is something we all fear if we are sick. It is stressful, frustrating and most of all worrying ... Unfortunately, the stress of a long testing process, diagnostic red herrings and multiple opinions is a reality for too many. But imagine a world where that does not happen. One where with one blood or saliva sample a doctor could diagnose you and make sure you get the targeted treatment you need [Times, Genomic medicine is changing lives and Britain leads the field, 4/7/17]

This expectation of personal benefit from genomic testing was echoed by a former health secretary who wrote: ‘Whole genome sequencing is life-changing because it is a diagnostic test of absolute certainty that can help diagnose rare diseases in weeks, not years, and can help treat cancer’ and then described how he had taken a genomic test ‘to see its power for myself’ [Times, *My life may have been saved this week*, 20/3/19]. Several articles connected the chance of genomic testing with increased longevity – a Mail article reporting on early plans for Our Future Health described how ‘Millions of NHS patients will get a free personalised health report based on their DNA to help them live longer, the Government has announced. The Department of Health and Social Care said the move will flag which conditions people are at risk of getting before any symptoms appear’ [Mail, *Millions of NHS patients will receive a free personalised health report based on their DNA to help them live for longer*, 25/7/19].

Where articles featured examples of genomic testing aiming to find a diagnosis for a specific symptomatic person, the chances of achieving a molecular diagnosis were unusually high. The diagnostic rate quoted in clinic would be around 40%(82), whereas from 85 specific instances across the news items where diagnostic genomic testing of a specific symptomatic person was discussed, 75 made a genomic diagnosis – a diagnostic rate of 88%. The small ‘undiagnosed’ proportion (10 instances) included several people interviewed right at the outset of testing before any results would be expected, so a reader might be left with the hope/expectation of results to come, and 4 instances where it was clear that testing had not achieved diagnosis despite some time having passed were all in the same article [Guardian, *‘Nobody knows what’s wrong with me’ – life with an undiagnosed condition*, 6/12/22]. Where diagnoses had been made, an unusually high proportion had substantially changed the person’s medical care – though perhaps because several of the instances were the same story repeated across multiple news items. Seven specific stories featured in three or more news items. All had a genomic diagnosis and for four this had made a substantial difference to day-to-day medical care for themselves or their surviving family. For two, having a diagnosis had not significantly altered their treatment but had been useful for family medical care or reproductive planning, and for one (featured in several articles discussing newborn screening) different treatments might have been possible had the diagnosis been made earlier.

42 articles (30% of those where images were available for analysis) featured images involving people or families who had been affected by genomic testing – for example children who had had genomic testing aiming to diagnose a rare condition, or adults who had signed up to participate in Our Future Health (in this category I am not counting stock images, for example stock ‘newborn baby’ photos which illustrated several articles on newborn genome screening). Images of ‘real people’ were most common for BBC News

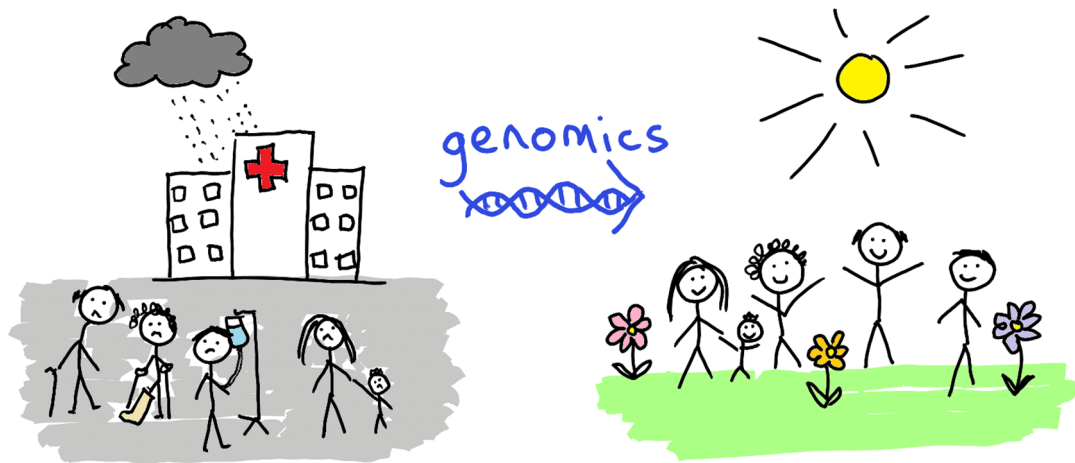
articles, where 65% featured at least one photo of a 'real' person who had been in some way affected by genomic testing, and least common for Guardian/Observer articles where this applied to only 9%. The Mail and Mirror featured photos of 'real' people in 36% and 38% of news items respectively, but where they did so they tended to show multiple photos. For example one Mail news item featured 11 photographs of 'real' families who would likely have had better outcomes if genetic diagnoses had been made earlier [Mail, *Our children were handed a death sentence when a simple blood test at birth could have saved their lives - by the time doctors took us seriously, it was too late for treatment*, 5/11/24] – the other image on the page showed a newborn baby with an annotated glowing double helix hovering over their cot (the thumbnail image for the linked article: Mail, *DNA testing of 100,000 newborn babies begins as part of major study into 200 rare conditions*, 3/10/24).

Where articles showed only one or a few pictures of a 'real' person or family affected by genomic tests, these tended to look either like smiley family photos or would show the people involved with a relatively neutral but thoughtful expression. Sometimes these photos appeared to be taken at home, for example a family might be sitting together on the sofa and smiling at the camera, and sometimes they looked like holiday snaps, for example a child with their parents at the beach. Where articles featured multiple photos, these tended to be a selection that on the one hand symbolised 'everyday family life', for example parents playing with their child in their living room, siblings smiling together in a garden, together with a few separate images that emphasised severe illness and vulnerability, for example a small child sleeping in a big hospital bed, surrounded by drips and tubes. Looking at them as a set, they gave me the impression of a family ricocheting between terrible stress and happy family life – with the implication being that genomic

results were key in shifting them from the overwhelming illness made evident in certain of the photos, to the smiling family whose photo was at the top of the news item in question.

When discussing the impact of genomic testing on individuals, it seemed that the more beneficial a genomic test had proved to be, the more likely it was to be featured in news items discussing genomic initiatives. Stories were often framed in such a way as to invite readers to either share in the joy of successes relating to genomic testing, or empathise with the sadness that such testing had not happened sooner. But while the potential of genomic results was celebrated at the level of the individual, at a societal level genomics was presented almost as a panacea (Figure 7). For example, the BBC described the 100,000 Genomes Project as *'aiming to revolutionise medicine by unlocking the secrets of DNA'*, including a quotation from then prime minister David Cameron that *'I believe we will be able to transform how devastating diseases are diagnosed and treated in the NHS and across the world'* [BBC News, *DNA project 'to make UK world genetic research leader'*, 1/8/14]. A Sun article reporting on the development of the NHS Genomic Medicine Service included a quotation from the chief scientist at Genomics England that: *'We are ushering in a new era of genomic health. This is a big step and it grows over the new two years. It's a total transformation'* [Sun, *Forefront of medicine: Patients to get routine DNA tests on NHS to tailor treatment to genes in world first*, 4/7/18]. A Mirror article introducing Our Future Health stated that *'Everyone living in the UK has been invited to sign up for a world-leading research project which could give unprecedented insights into your health ... Health leaders say it will help transform global understanding of health and how we should live'* [Mirror, *Brits urged to sign-up for world's biggest research project into health and disease*, 16/10/24].

Figure 7: A brighter future thanks to genomic results



Genomic results were framed as the catalyst for our transformation into a healthier society, where illnesses are prevented rather than cured. A Times article discussing the 100,000 Genomes Project included a comment from the then life sciences minister that *‘without genetic data doctors were practising “blind medicine”’* [Times, *DNA testing promises healthcare revolution*, 22/12/14]. A Mail article reporting on the new Genomic Medicine Service included a comment from Chief Scientific Officer Sue Hill that *‘The holy grail of the health system for the future is that we take a more prognostic and preventative healthcare approach, and [the establishment of the Genomic Medicine Service] will enable us to do that, by understanding some of the genetic make-up of individuals that might predispose them to developing certain conditions’*. It also included a quotation from the then Health Secretary Matt Hancock that *‘The power of genomics plus AI to use the NHS’ data to save lives is literally greater than anywhere else on the planet’* [Mail, *NHS will become the first health service to use routine genetic testing in a move that will ‘transform patients’ lives’*, 20/9/18]. A Guardian article written by current prime minister Keir Starmer when he was leader of the opposition envisaged that: *‘With the power of genomics, we could help every one of us live a healthier life, prevent more illness and take more care of our lifestyle*

choices' [Guardian, *No more missing records or letters lost in the post – I will bring in a totally digital NHS*, 22/5/23].

More specifically, the hope that genomic testing would vastly improve cancer treatment came up throughout the articles. Reporting in 2014 at the outset of the 100,000 Genomes Project, BBC News, the Guardian, the Mail, Sky News and the Times all featured a quotation from the director of the Wellcome Trust that: *'We will look back in 20 years' time and the blockbuster chemotherapy drugs that gave you all those nasty side effects will be a thing of the past'* [Sky News, *PM hails £300m project to unlock power of DNA*, 1/8/14; and others].

Reporting in 2022 on the analysis of 16,000 tumour genomes, the Mirror quoted the chief scientific officer at Genomics England as saying: *'Lives will be saved. We will see patients being directed to treatments which will benefit them that otherwise might not have happened'* [Mirror, *NHS cancer patients will be told what caused disease thanks to 'world-leading' research*, 21/4/22].

Many news items presented genomic progress as a source of national pride, with British science working to benefit the world. For example, a BBC News article reporting on the 100,000 Genomes Project quoted the NHS England medical director as saying that *'the impact of genomic medicine will be on the same scale as other British successes including the smallpox vaccine and IVF. He said: "Our NHS is better equipped for the emerging science that will determine the future practice of medicine than any other Western healthcare system. [It] puts us in a position to unlock a series of secrets about devastating diseases, that have remained hidden for centuries, for the whole of human kind"'* [BBC News, *NHS DNA scheme to fight cancer and genetic diseases*, 22/12/14]. This framing was particularly prominent in Mirror articles, with headlines such as *'Britain leading the way in the fight*

against rare diseases with cutting edge gene machine' [30/9/17] and *'Brit DNA breakthrough will save thousands of kids from killer diseases'* [5/11/19].

More recently, this shifted somewhat from presenting British genomic capabilities as the envy of the world, to framing these as being essential to the viability of the NHS. A Times article reported on Our Future Health with the headline *'Inside the medical trial that could save us — and the NHS'*. This discussed how the trial is built around an idea *'so simple it sounds like a platitude. How about not waiting until people are ill to treat them? How about catching them early?'*, featuring a quotation from the trial's chief medical officer that *'What we really have in this country is a National Sickness Service. What we need is a National Health Service'* [28/1/23]. A Guardian article reporting on the Generation Study ended with the comment that: *'Wes Streeting, the health secretary, said the future of healthcare must be "more predictive, more preventative and more personalised" to help fix the "broken" NHS. "This kind of advance in genomics will help us achieve just that," he added'* [Guardian, *NHS England to screen 100,000 babies for more than 200 genetic conditions*, 3/10/24]. Various articles included financial information that presented genomic testing as a 'no brainer' from a taxpayer's perspective. For example, a Guardian article reporting on the 100,000 Genomes Project included the example that:

*As well as improving patients' lives, WGS can also free up NHS services, saving hundreds of thousands of pounds in some cases. For instance, a 10-year-old girl who endured multiple hospital visits and intensive care admissions during her seven-year diagnostic odyssey is estimated to have cost the NHS £356,571. Once genome sequencing identified her underlying problem, the bone marrow transplant that cured her cost £70,000 [Guardian, *Whole genome sequencing could save NHS millions of pounds, study suggests*, 10/11/21]*

The exception to this framing was articles discussing 'direct-to-consumer' genomic tests – as discussed in 4.3.2.2, these were generally treated very differently to freely available NHS or university-led tests. Their results were often represented as burdening the NHS, which

had to pick up the pieces of tests it had not asked for. Similar criticisms arose relating to the 2019 ‘genomic volunteering’ scheme where people would have paid for health reports based on their genome – when the scheme was reborn as Our Future Health concerns around this issue seemingly became detached.

To summarise, the framing of genomic tests across the news items tended to present them as being quite likely to deliver substantial benefits to individuals. Yet even if these were not forthcoming, readers were given the sense that by participating in the genomic enterprise, benefits would no doubt arise for others in the future. It was quite common for news items to wander between specific examples of genomic testing leading to personal benefit, and much broader assertions as to how the overall result of genomic projects would be a healthier future for everyone.

4.3.2.4 Virtuous people would want to share their genomic data

Several stories alluded to the importance of big datasets in improving our understanding of genomics. Many stories connected participation in genomic testing with improving health care for everyone- for example through discovery of new treatments- though the ways in which this would happen tended to be loosely articulated. For example, a Guardian article discussing the Generation Study described how: *‘Researchers are also hoping the study will help them learn more about the link between genes and health, which could lead to new treatments’* [Guardian, *NHS England to screen 100,000 babies for more than 200 genetic conditions*, 3/10/24]. Reporting on the short-lived 2019 ‘genomic volunteering’ scheme, various news outlets featured a quotation from then Health Secretary Matt Hancock that: *‘Every genome sequenced moves us a step closer to unlocking life-saving treatments’* [BBC News, *NHS to offer paid-for DNA tests if patients share data*; Guardian, *NHS to sell DNA tests to healthy people in push to find new treatments*; Times, *Gene test for sale on NHS*:

healthy patients to learn risk of killer diseases; Sky News, NHS to offer paid-for genetic blueprints that predict health risks; all 26/1/19]. Several articles written in 2022 around research into mutational signatures based on tumour samples from the 100,000 Genomes Project described the data as a ‘treasure trove’ that stood to profoundly influence the future treatment of cancer [Guardian, ‘Like fingerprints at a crime scene’: study finds new clues about causes of cancer; Mirror, NHS cancer patients will be told what caused disease thanks to ‘world-leading’ research; Times, Scientists find cancer ‘fingerprints’ that bring hope of new treatments; all 21-22/4/22].

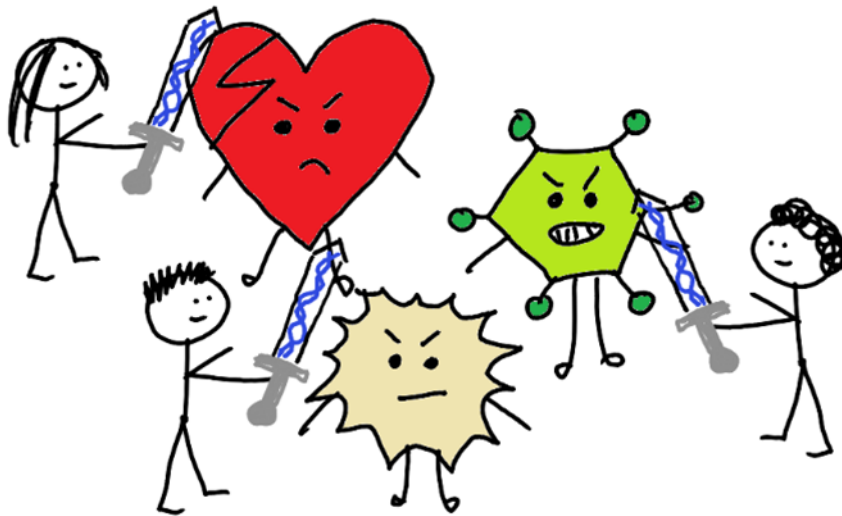
The contribution of a genome to a database was therefore framed as facilitating progress for everyone, in order to allow ‘groundbreaking discoveries about how diseases work, who could be susceptible to them, how we can treat them, and what treatments might work’ [Observer, *What I learned from home DNA testing*, 23/7/17 (the comment was made in reference to the 100,000 Genomes Project, not ‘home DNA testing’)]. This also tended to be the case for the relatively few articles which were more sceptical about the benefits of genomic testing of healthy populations. For example, an Observer article discussing genomic screening, mainly in the context of direct-to-consumer tests, ended:

*But in terms of personalised or precision medicine, it’s all rather vague and hopeful. That, however, is where the science of genome sequencing mostly is right now – vague and hopeful. It promises a great deal and, in time, will probably deliver on many of those promises. As [Caroline Wright, then senior lecturer in genomics at Exeter] says: ‘For some people genome sequencing is very predictive and hugely useful. For most people, at this point in time, it is neither.’ But the greater the number of genomes sequenced, the more that balance will shift. And when that happens, genetic medicine is going to become much more precise and, ultimately, far more personalised [Observer, *Will genome sequencing bring precision medicine for all?*, 28/9/19]*

Given the frequently highlighted connection between amassing genomic data and achieving societal benefit, many articles framed a decision to share genomic data as virtuous and

prosocial. People who contributed to genomic datasets were soldiers in the fight against disease (Figure 8), and playing their part in ensuring the health of future generations. For example, the Mail and the Times both ran quite directive articles essentially telling their readers to take part in Our Future Health. The Times article started: *'Check your weight. Monitor your diet. Take your blood pressure and note how many pints you drink a week. And then report all the details to the Our Future Health programme, the world's biggest and most ambitious attempt at mass observation of the way people age. It could save your life, and the lives of millions of other seemingly fit men and women who will go on to develop diseases that could easily be halted if caught early'* [Times, *The Times view on Our Future Health programme*, 24/10/22]. The Mail article was written by a journalist participating in the programme, who described being *'about to have what is perhaps the most important blood test I've ever had'* and explained that *'This ambitious project could change the way the NHS treats disease for ever. But it needs the volunteers first'*, together with details of how to sign up [Mail, *Why I've signed up for the UK's largest medical study to help firefighters such as Kieran and Miriam's grandchildren*, 29/7/23]. Another Mail article described participants as *'Our health heroes!'* in its headline [Mail, *Our health heroes! Three million Britons will join global medical study to help develop new ways to detect illnesses sooner*, 24/10/22].

Figure 8: Use your genomic data in the fight against disease



Such framing implies that good people would share their genomic data – and perhaps people who do not are selfish or afraid of progress. As regards newborn genome screening, in most articles covering this there was little focus on the complexities of parents making decisions around participation on behalf of their seemingly healthy babies. For example, a BBC article discussing the start of the Generation Study included comments from parents who had decided to enrol their babies in the study, where both mentioned part of their motivation for doing so being the prospect of helping others in the future. The article included strong encouragement for new parents to participate, and the only potential downside mentioned, deep into the article, was *‘But it might also raise ethical questions about what health information is appropriate to share with individuals about their future health risks’*. It ended with a quotation from the then NHS chief executive that newborn genome screening *‘had the potential to give thousands of children the chance to access the right treatment at the right time, giving them the best possible start to life’* [BBC News, *First newborns join screening for 200 rare diseases*, 3/10/24].

However, several articles did portray the decision to participate in a genomic database as not one to be taken lightly. Two articles on newborn genome screening, both written by

doctors also working as journalists, discussed potential pitfalls of contributing data. Max Pemberton described feeling conflicted about the possibility, writing in the Mail that:

We are now facing the prospect of being able to analyse a child's entire genetic code to understand their future risks of developing diseases, and even much more about what is to come in their lives. However, while this might sound like an invaluable tool in the fight against human suffering, it has the potential to be used for much more — and this is what has some ethicists worried. For WGS opens the prospect for more sinister and intrusive things, giving an insight into our children's future lives that could shape the way we and society view them. And if this information were to fall into the wrong hands, it could be used for even more chilling purposes [Mail, Would you want to know your child's risk of diseases before they were born? 9/8/21]

Miriam Stoppard was more critical, writing in the Mirror that:

A person's genome is a huge amount of personal data, and acquiring this from everyone before they're old enough to give permission is morally questionable ... One of my major concerns is the privacy and freedom of an adult being ransomed when they're only a baby. Would that adult agree to having their genome sequenced? And do we trust our government? ... I'm highly sceptical about genome sequencing of babies who have no say in the matter. We haven't even agreed that all adults should be subject to this surveillance [Mirror, Harvesting baby DNA to uncover potential diseases is an invasion of our privacy, 4/4/22]

The possibility of a 'middle ground' where newborn screening might be extended without requiring the contribution of whole genomes was very rarely mentioned – most articles implied that the possibilities were all or nothing.

Regarding genomic testing more broadly, the Guardian/Observer ran four articles and the Mail ran one written by or heavily featuring Edward Hockings, a bioethicist with an interest in privacy and transparency, which were highly cautionary around genomic data sharing.

For example, the Mail article described:

[Hockings] says genomic data is 'the oil of the digital era' and there is nothing stopping it from be [sic] captured, bought and sold in the future ... When it comes to genetics, the implications are particularly frightening, says Edward Hockings. For example, there is evidence of a link between genes and criminality. Scientists say 40 per cent of sexual offending risk is down to genetic factors. A 'single national knowledge base' as the one the UK government is aiming to create might therefore

be used for broad genetic profiling [Mail, Google could soon get access to hundreds of thousands of patients' genetic data: An expert explains why we should be concerned, 5/7/17]

As shown above, concerns often centred around who might have access to data, what inferences they might draw from it, and whether these might be used against people participating in genomic databases. Very occasionally, news items reflected on the timeframe over which data might be held, and to what extent participants could rely on the principles by which their data were currently governed to hold over many years.

However, for most articles, if privacy/security concerns were mentioned this was in the context of a brief comment towards the end of the article, often followed by an assertion that in the genomics initiative featured in the article this risk was being carefully managed. For example, a Mail story on the Generation Genome report started: *'Genetic tests should be offered to millions of patients with cancer and other rare diseases, according to the chief medical officer. Dame Sally Davies said these would enable doctors to diagnose illnesses more quickly and prescribe a bespoke treatment'*. In the middle of the article was the comment: *'But the ambition for a central database will prompt concerns that medical information will fall into the hands of hackers or be used by insurance firms to boost premiums. Only two months ago the NHS was crippled by a huge cyber attack which was thought to have been carried out by hackers in North Korea. Dame Sally insisted the database would be extremely secure and that the risks of a hack were outweighed by the huge benefits of holding the information'*. The article ended with quotations from the head of genetics at Wellcome, and the then health secretary respectively, celebrating the idea of more genomic testing as a *'bold and forward-thinking vision'* and a way for *'the NHS to continue its relentless drive to push the boundaries of modern science to benefit even more people'* [Mail, *Give patients with cancer and other serious illnesses a genetic test to create tailored treatments, says chief medical officer, 4/7/17*].

To summarise, many news items subscribed to a narrative that the more genomic testing we do the better results will get. They tended to focus on the benefits of large datasets in making sense of a person's genomic data, with little mention of the issue that diluting the reasons for accessing testing will affect the quality of the inferences that can be made from a person's data as regards their own personal health. Some articles did explore privacy concerns relating to genomic database participation in some depth, but for the most part, people who contributed genomic data to research databases were framed as 'health heroes', generously sharing their health information in order to reach a place where as a society we can all realise the many benefits of genomic testing.

4.3.3 Absent voices

Above I have discussed common ways in which genomic results were framed in UK news items – here I discuss elements relating to genomics that were given little attention in the articles analysed. No news items made mention of the environmental impact of genomic data collection and storage. The variable performance of genomic tests depending on genetic ancestry was also given little attention – most news items did not discuss this at all; a few mentioned it in one to two sentences deep within or towards the end of the article. The 'need' for genomes in the provision of genetic screening was also very rarely questioned. For example, hardly any articles relating to the Generation Study alluded to the issue that the newborn screening aspect of the study will only involve a tiny proportion of the baby's genome.

As discussed in 4.3.2.3, people's experiences of genomic testing appeared to be more likely to be featured if they had a clear-cut and helpful result. Few news items featured people with rare conditions who had had 'nothing found' from genomic tests, and only two included personal stories where the outcome of a diagnostic genomic test had been

confusing or had not matched the medical issues the person was experiencing. This exclusion potentially adds to the isolation of people and families who have not had clear-cut, transformative results from genomic testing.

Regarding genomic screening, several news items did make it explicit that some people might choose not to do this. For example a Mail article discussing newborn genome screening had the headline '*Would you want to know your child's risk of diseases before they were born?*' [9/8/21] and discussed both pros and cons that might come into a decision. However, 'real' people who had made an active choice not to take part in genome screening were not represented in the news items. In many senses this is very understandable – for example new parents in this situation might not have wanted to talk to journalists about why they declined the offer to participate in the Generation Study, or it may not have felt relevant to a journalist covering such a study to seek perspectives from people who chose not to engage with it. But the consequence is that the experience of thoughtfully deciding not to have genomic testing in particular contexts is not represented – the impression from the news items is that anyone given the chance to have testing would seize it.

4.4 Summary

As relates to my research question 'In what ways do popular discourses invite us to imagine genomic results?', UK news items discussing recent genomic initiatives tended to present genomic results as the pinnacle of our technological prowess – a valuable and precious opportunity that we are lucky to now be able to access. While the scale of the data involved was often highlighted, this was usually in such a way as to heighten our appreciation for the amazing machines and computers that can 'read' our blueprint and tell us about our health, rather than helpfully representing the many people who do not gain obviously useful

outcomes from genomic testing. Where news items discussed specific instances of genomic testing, these tended to be experiences that either showed genomic testing at its best, or that made us wish it had happened earlier in a child's life course. It was rare to hear of experiences where genomic testing had had uncertain, confusing or underwhelming results. In the context of NHS or university-led genomic testing, these were presented as laudable, almost heroic, efforts that stand to give us all a better and healthier future. People contributing their data to such efforts were 'our health heroes', forward-thinking and virtuous people playing their part in our great fight against disease. That said, the articles were not uniform in their conception of genomic results – many discussed or alluded to concerns around data privacy, and a few reflected that constructing a genomic result in a healthy person might be somewhat different to explaining disease in a person who is obviously sick. But akin to the stock images I analysed (Chapter 3), the prevalent idea was of genomic results as standing to be powerful and transformative, in whatever context you are lucky enough to encounter them.

As relates to my research question 'how *should* we construct genomic results?', my thoughts on this issue overlap considerably with my opinions around the representation of genomic results in stock images (3.4). News items celebrate the best of genomic results, but in doing so, they potentially imply that useful and sometimes life-changing outcomes from genomic testing come as standard, rather than being a precious outcome realised for relatively few. This presentation may contribute to societal support for funding genomic initiatives, and might in some ways be helpful to families who currently have no diagnosis from genomic testing in allowing hope that this may change. However, it risks contributing to a climate where people have high expectations of benefit from genomic testing, increasing the intensity of disappointment and disillusion arising where these are not met. The frequent tendency to frame predictions from the genome as being almost synonymous

with diagnoses may also impede meaningful societal discussions around what role genomics should play in population screening. If you can read actionable, unambiguous diagnoses directly off the genetic code and then act to indisputably improve or save a person's life, why wouldn't you?

4.5 Reflections on this facet

This facet has sought to explore the portrayal of genomic results in UK news items. I developed a pragmatic search strategy focused on eliciting news items relating to large UK genomic initiatives as I felt these were most likely to influence people's expectations around the sorts of results they might experience were they to participate in similar genomic testing here in the UK. However, genomic testing is discussed in many other contexts, for example as playing a role in forensic testing, archaeology, and tracing the evolution and spread of Covid. The framing of genomic results in these contexts might also have an influence on how people construct genomic results, and this work has not explored these.

Similarly to stock images, clear evidence is lacking as to what extent the portrayal of genomic results in UK news items might impact people's expectations from their own genomic tests. However, there is evidence that people tend to have high expectations from genomic testing in clinical contexts(79,122), and as many UK adults will not have encountered genomics in the context of formal education, it is plausible that less formal sources of information around genomics, for example news articles, play a part in sculpting these expectations.

When people come to have genomic tests, formal information provision and sometimes consent conversations aim to set expectations appropriately. Yet they are not always

successful in doing so. For example, in surveys of families who had received a variant of uncertain significance from genetic testing of an unwell child, less than 20% had been aware of this possibility in advance of receiving the result, although this would routinely be mentioned as part of consent conversations for such testing(131). Part of the reason such information may not land effectively may be that some people electing to have genomic testing have essentially already made the decision to do so in advance of their ostensible ‘consent conversation’ (see 7.3.2.2.3) – and the ways genomic results tend to be constructed in popular discourses might influence their expectations more than a disclaimer-laden consent process they need to sit through in order to get the test.

A final point to note here is that young people are less likely to access traditional news media, instead tending to source their news via social media(127). By the time babies enrolled in the Generation Study reach an age where they start to engage with news, the landscape of news consumption may be quite different, with social media playing an increasingly influential role. However, narratives dominant in UK news items today may yet shape people’s ideas around genomic results many years down the line, as the work described in Chapter 5 will indicate.

5 Public perspectives around outcomes from genomic testing: analysis of responses to a Mass Observation directive on *'Genetics and health in our everyday lives'*

This facet was designed to inform my research questions 'What features do people conceptualise genomic results as having?' and 'In what ways do popular discourses invite us to imagine genomic results?' I was interested in how wider publics might envisage genomic results, and what experiences and sources of information might contribute to people's ideas around this topic. As a route into this, I sought to explore how the topics of genetics and genomics were considered in the Mass Observation Project, an archive of writing by 'ordinary' people about everyday life in Britain(99). I intended that this would inform my overall question, 'how should we construct genomic results?' by providing insight into some of the ways in which people who often did not have personal experience of clinical genomic testing appeared to conceptualise results. Another aim was to consider which influences might be important as people develop their ideas around what genomic results could and should look like.

The chapter begins by describing the context of the Mass Observation Project before discussing how we worked with the project to explore wider publics' views around genomic results. I then outline my approach to analysing the responses, before detailing key results.

5.1 Rationale for examining how genomic results seem to be envisaged in the Mass Observation Project

Mass Observation is a social research organisation founded in 1937, aiming to create '*an anthropology of ourselves*'(99) by curating perspectives and experiences of everyday life in

Britain. In 1981 it set up the Mass Observation Project, creating a panel of Observers from across Britain, who are asked to write responses to prompts ('Directives') three times a year. These Directives are open-ended questionnaires, developed by the project directors in conjunction with researchers, which cover a whole variety of topics (two or three per directive). Some Observers contribute to the project over many years, and there is no deadline for sending in responses to each Directive. Observers may choose to respond to all questions or may be more selective – there is no minimum or maximum word limit and Observers may also respond by means other than writing, for example by drawing or sending pictures. Physical responses are housed at The Keep on behalf of the University of Sussex, though many Observers now contribute electronic responses, and researchers can apply to work with the project in commissioning Directives and analysing responses.

The nature of the Mass Observation project, engaging with Observers over long periods of time to '*develop an archive of everyday life, thought and feeling in Britain*' (99), may engender a feeling of responsibility towards the project, which asks Observers to reflect on and write with regards to a whole range of subjects. As Haran and O'Riordan discuss, '*to write to the archive is to address the future and to carve out a place in the making of knowledge*' (133). Over time, Observers may gain considerable experience of reflecting on and writing about topics outside their everyday experience, though '*ordinariness*' and '*ordinary lives*' remain central to the project (134). Their responses are intended to remain anonymous – each Observer uses a unique identifier and they are encouraged to use initials or made-up names for people they mention in their responses. The Mass Observation team also redact information that they consider has potential to make a participant identifiable.

The open-ended nature of responses, and the opportunity to hear from a wide range of people (though not intended to be statistically representative of the UK population) made

the Mass Observation project an attractive option to explore conceptions and expectations around genomic results. The longitudinal nature of the project is an additional benefit, as questions around genetics were also asked in 2006, and this offered an opportunity to see how some Observers had engaged with genetics and the issues that it might raise over time. I was curious to see how a group of people not selected on the basis of their relationship with genetic testing appeared to conceptualise genetic and genomic results in response to questions around genetics and its future. I was also interested to explore to what extent this paralleled common constructions of genetic and genomic results in stock imagery, newspaper articles and interviews with people with personal experience of genomic testing.

5.1.1 The 2006 '*Genes, genetics and cloning*' directive

In Spring 2006, Haran and O'Riordan commissioned a Mass Observation directive asking Observers to respond to prompts about '*Genes, Genetics and Cloning*'. This contextualised questions for Observers with reference to the recent completion of the Human Genome Project, and the cloning of Dolly the sheep, and asked Observers their thoughts and experiences regarding: genetic testing for inherited conditions; paternity testing; forensic testing and criminal investigations; and research purposes. The directive also explored where Observers got their information from on these issues, and asked what they thought about the regulation of scientific research. Haran and O'Riordan analysed responses over the following decade, reporting on the work in 2018, with a key focus on '*how media cultures resource public knowledge-making over time*'. They noted how responses indicated '*a pro-science and engaged public culture in relation to genetics in the UK*' and reflected on how multiple media genres, accessed by Observers over many years, played into this(133). This influenced my decision in Chapter 4 to explore how UK news items have tended to frame genomic results over the years, rather than focusing solely on very recent stories.

5.2 Methods

5.2.1 Development of the 2022 '*Genetics and health in our everyday lives*' directive

As part of the CELS team (see 2.2), I was involved in developing a directive which was sent to Observers in September 2022, entitled '*Genetics and health in our everyday lives*'. The work was led by Dr Susie Weller. In developing the directive, we wanted to explore Observers' ideas and experiences around what constitutes personalised care, and to gain a sense of what Observers thought about genetics and genomics, particularly in light of major technical developments since the 2006 directive. Over the course of several meetings we came up with a range of questions and prompts encouraging Observers to draw on their own experiences and those of their friends and family to explore: experiences of healthcare; genetics in our everyday lives; the issues genetic testing can raise; and future uses of genetics.

These questions were then shared with the Mass Observation team, and refined via an iterative process with reference to their expertise in how to write engaging and accessible directives. In September 2022, the completed directive was sent to their panel of Observers, together with other directives on '*Grudging Acts*' and '*The Royal Family*'.

Questions particularly relevant to my work were:

- Please share what comes to mind when you think of 'genetics'. You are welcome to write down words, phrases, or to include images or sketches.
- Please tell us about **any experience you have had of genetic testing** including the experiences of those around you – family, friends, neighbours, colleagues, and others. You could include any test that has looked at your DNA (genetic code) either via the NHS or those bought direct from shops/online (e.g. Ancestry tests or 23andMe).

- Are there any news reports, films, television programmes or books about genetics that have been of interest to you? If so, please share how or why.
- What do you think might be the consequences (positive or negative) of being part of a DNA database?
- How do you imagine genetics might feature in our lives in the future?
- We would be interested in hearing **your views** on [the UK Newborn Genomes Programme pilot study]¹³. What might be the potential benefits and drawbacks?
- Do you have any particular hopes or worries about the future uses of genetics?

Please see 11.5 for the full '*Genetics and health in our everyday lives*' directive¹⁴.

5.2.2 Analysis of responses to the '*Genetics and health in our everyday lives*' directive

I undertook a thematic analysis of the responses to our directive, seeking to identify key ways in which Observers conceptualised genomic results, and sources that had been important in developing their ideas.

5.2.2.1 Thematic analysis

Thematic analysis '*aims to identify patterns and meanings within data*' (135). This is the analytic approach I took here and in the next two chapters, which focus on genomic results in the context of clinic observations (Chapter 6) and interviews with people experiencing genomic tests (Chapter 7). However, as thematic analysis is a family of methods rather than

¹³ Text in brackets read 'this initiative' in the directive, but was contextualised by a paragraph reading: '*How do you imagine genetics might feature in our lives in the future? One potential future use is the UK Newborn Genomes Programme pilot study, which will examine the benefits and drawbacks of sequencing a baby's entire genetic code then analysing parts of it to look for various genetic conditions. It could detect more conditions than the current newborn 'heel prick' test. However, the programme might also cause more uncertainty (for example, where a possible genetic risk is found but no-one is sure if it will make the baby ill or it is unclear what the best treatment option is)*'.

¹⁴ Questions around what comes to mind when you think of 'genetics', and asking about media that had interested Observers relating to genetics, were particularly shaped by my research interests.

a method *per se*, and for different facets I opted for somewhat different approaches, here I aim to give a very broad overview of some the options.

Finlay writes that: *'Loosely speaking, thematic analysis can be divided into two (overlapping) camps: 'Scientifically descriptive' versus 'Artfully interpretive'* (135). Regarding the scientifically descriptive camp, Finlay explains that *'the goal [is] to use an objective approach to analysis in order to provide explanations or make predictions, while working to minimize human subjectivity/biases'*. For an artfully interpretive analysis, *'meanings are understood as contingent upon the specific context and the particular interpretive/theoretical lens through which they are viewed'* – a researcher would not seek (or necessarily think it possible) to objectively represent the data they analyse, but would instead aim to creatively and evocatively share their interpretation of those data.

Finlay describes that *'In practice, most qualitative researchers probably have at least a foot in each camp, and some locate themselves firmly in the middle. As these qualitative researchers pragmatically craft their analysis, they tend to take a critical realist or constructivist epistemological position which recognises that any knowing is produced by the researcher who is actively (co)constructing meanings with participants. They consider meanings to be fluid while accepting that participants' stories reflect something of their subjective perceptions of their experience (if not their actual experience). Both science and art may therefore be embraced'* (135).

5.2.2.2 *Specifics of analysing Observers' responses*

As I analysed responses to the *'Genetics and health in our everyday lives directive'*, I aimed to take a position between the scientifically descriptive and artfully interpretive camps. I thought elements of a scientifically descriptive orientation would be valuable in seeking to

give some idea as to the experiences Observers wrote about relative to genetics and genomics (for example, what proportion had personal experience of genetic testing), and the influences they described as being important (for example, were particular sources referred to by multiple Observers?). However, I also thought an artfully interpretive approach would be useful in allowing me to go beyond describing what Observers said, to explore aspects like what ideas around genomic results might be implicit in what they said. My analysis therefore aimed to encompass elements of both. Where I wanted to make a more scientifically descriptive point, for example commenting on frequencies, I ensured that as regards this aspect I had coded responses in a systematic and reproducible way. Where the point I was making was more artfully interpretive, I again aimed to analyse comprehensively but here my emphasis was more on re-reading responses looking for examples and counter-examples to iterate and refine my ideas, rather than to ensure that every occurrence in the dataset had been catalogued in a systematic way.

Regarding the mechanics of my approach, in the first instance, I read through Observers' full responses, using NVivo v15 to tag sections where people spoke of their ideas and experiences around genetics and genomics (as some of our directive focused on personalised care, and fairly often responses to this element would not refer to genetics or genomics). Where the responses collated by the Mass Observation project had been scanned in handwritten, I typed up relevant excerpts for ongoing analysis. I wondered about continuing to work with the scanned handwritten responses as they were, as it felt like I was then working more directly with the Observer's contribution and I found it easier to retain a sense of the context in which it had been created. However, when I started to use NVivo to code sections of scanned handwritten pages I found it unreliable so I decided to type up the extracts, losing something of the essence of the archive in doing so, but meaning I felt more confident that each response would be accounted for in my analysis.

Next, I carefully read through all tagged material, trying to get a very broad sense of common themes and ideas coming up in relation to the sorts of results people might expect from genetics and genomics, and some feel for the sources they might draw on in developing these ideas. As I read, I developed questions around how people were engaging with genetics and the issues it raises, and went back through the material to look more specifically for how Observers spoke around these issues. On re-readings, I tried to stay open to new ideas and if these came up I would go back to the responses and look at them again with these in mind. Over time I developed more specific codes that I used to manage the data, for example 'had an ancestry test', 'genetics interacting with human experience', 'changes in tests over time', 'assertive lack of interest in genetics'. Some codes were developed inductively based on themes I had identified in the data, some were influenced by Haran and O'Riordan's 2018 report on their analysis of the 2006 '*Genes, genetics and cloning*' directive(133), and others were influenced by insights developing in other facets and wider reading relating to these.

Building from these codes, I developed themes around how people were engaging with genetics and genomics and the issues they raise, and went back through the material to test and refine these themes further. (Please see 11.5.2 for an example of how codes contributed to build a theme). Following this, I started to focus more on who had written which responses (for example age and occupation), and applied for access to responses to the 2006 directive. Where participants had responded to both directives, I collated their responses and for each Observer, read their 2006 response then their 2022 response immediately following, aiming to gain a sense of whether and how things might have changed in the intervening years. This activity really brought home the enduring nature of the Mass Observation Project, being able to work directly with evidence that confirmed

how an Observer had engaged with the project consistently over so many years while potentially living through huge changes in their personal life.

As I analysed Observers' responses, I sought to gain a sense of how people thought about and responded to questions around genomic results, and why they thought as they did. I considered to what extent their views might overlap with conceptions of genomic results in other facets – for example genomic results as conceptualised in interviews with people having genomic tests, or genomic results as framed in UK news items. I looked at what Observers considered important in ensuring that genetics and genomics were used well, and reflected on what this should mean for the process of constructing genomic results.

5.3 Results

5.3.1 Characteristics of Observers responding to the '*Genetics and health in our everyday lives*' directive

The '*Genetics and health in our everyday lives*' directive was sent out to over 400 Observers of whom 147 responded, in keeping with the usual response rate to Mass Observation directives of 30-35%. The style of responses was very variable: some were typed and some handwritten; some were very brief and others lengthy; some addressed the prompts in the directive point by point whereas others dealt with the topic more holistically. 22 Observers (15%) had previously responded to a similar 2006 Directive on '*Genes, Genetics and Cloning*'. 68% of the Observers were women and 64% were 60 or older, with many employed or previously employed in roles typically requiring higher education¹⁵. This sample does not aim to be statistically representative of the UK population, but the nature of the Mass Observation Archive, with Observers discussing a very wide range of topics and

¹⁵ These statistics were collated by Dr Lisa Ballard.

contributing over many years, offers an opportunity *‘to develop an understanding of what a small, socially engaged fraction of the UK population knew, believed and felt about contemporary developments in genomics, and perhaps of how they had come to form those knowledges, beliefs and feelings’*(133).

35 Observers (24%) responding to our 2022 Directive reported having had direct personal experience of genetic testing, with a further 45 (31%) reporting that a family member or friend had had genetic testing. In both cases, most tests had been to explore ancestry rather than for health reasons. In terms of medical tests, several Observers had had experience directly or indirectly with *BRCA* testing or some form of prenatal genetic testing. Two Observers wrote about a close family member having had genome sequencing to investigate health issues, and several others discussed experiences with tests that probably involved genome or exome sequencing. 67 Observers (45%) did not describe having had a genetic test or knowing someone who had. However, several people in this category had evidently engaged in depth with decisions around whether to have testing, so lack of direct experience by no means equated to lack of engagement with the issues raised by genomic testing. For example, one Observer who had elected not to have testing wrote:

We’ve been offered DNA testing as part of my son’s autism diagnosis ... but with [named research] project haunting autistic spheres, this isn’t something I’m keen to embark on. I had been curious to investigate my own DNA from an ancestry perspective, but having read ‘How to Argue with a Racist’ by Adam Rutherford, which states that after a certain amount of time you’re not actually related to your own ancestors, I sort of wrote the whole thing off as an exercise in vanity [M6759, woman in 30s, archaeology student]

In contrast, in the 2006 Mass Observation directive on *‘Genes, genetics and cloning’*, *‘respondents reported limited direct experience of issues connected to genes, genetics and cloning’* – just under 20% of respondents reported any kind of experience with genetic testing for inherited conditions, and *‘the frequency of reports of direct experience of genetic*

testing for research purposes and paternity was very low' (133). For the 22 Observers who responded to both directives (2006 and 2022), 10 (45%) reported having new direct or indirect experiences with genetic testing in the 16 years between the directives: all were ancestry tests. The responses as a whole indicated increasing familiarity with genetic testing, and there were a couple of cases where an Observer had made a brief response in 2006 along the lines of *'doesn't inspire me'* or *'only a passing interest'*, and had then gone on to write a lengthy and detailed response in 2022.

5.3.2 Observers saw ethical expertise and societal involvement as essential in making decisions about genetics and its future uses

Although many more Observers have now directly engaged with genetic testing and the issues around it, many parallels remain with Haran and O'Riordan's findings from their 2006 directive on *'Genes, Genetics and Cloning'*. In terms of attitudes towards their directive, they noted that *'some accounts included what could be characterised as an assertive lack of interest – what Mike Michaels (1996) has called a “discourse of ignorance” – in the topics of genes, genetics and cloning'* (133,136). The excerpt they used to illustrate this point started *'I am totally bored by this subject so that the amount I shall write will be very little'* [W3176].

In 2022, some Observers showed a similarly *'assertive lack of interest'* and resisted engaging with the directive. For example, one Observer's complete response was:

*Why are we bothering to talk about genetics? Who will receive any benefit from it?
The very rich who can afford expensive health care – maybe 5% of our population
[B4273, in 70s, yoga teacher]*

However, as above, where questions regarding the value of focusing on genetics and genomics were raised, this was often clearly because of concerns about inequities in

benefit, rather than because an Observer felt the topic was boring (although a couple did say they had very little interest in the subject). This aspect of disparate benefit is not prominent in Haran and O’Riordan’s report on responses to the (pre-austerity) 2006 Directive, but in 2022 the perception of genetics as a vanity project that might distract from addressing more basic issues was also brought up in a number of fuller responses (despite having received little attention in UK news items):

If it had to be a choice between a Genome Programme and additional programmes in schools geared towards resilience building, ethical dilemmas, the moral maze, compassion and resource sharing I would prioritise the latter [S6892, woman in 60s, retired psychotherapist]

Oh this is so expensive and luxurious and first world. The rich will have the test and worry and the poor won’t have the test and will worry more and the many parents in poor countries will continue to count themselves lucky if their babies survive malaria and malnutrition and the upcoming horrors of climate change [S7592, woman in 60s, tech sales]

Another factor that I noted across several of the responses was people discussing feeling ill-equipped to answer questions around genetics as they felt they did not have sufficient knowledge of the subject. For a few people, this meant they did not feel it worthwhile to engage with the directive, for example one Observer wrote:

As so often, in Part 2 [the ‘Genetics and health in our everyday lives’ part of the directive] you raise and ask questions that very few people will have the necessary knowledge of genetic research to be able to answer meaningfully [B2710, man in 90s, minister of religion]

Many Observers who did respond to various of the prompts in the directive expressed reticence about their ability to give a helpful opinion because they perceived they had insufficient technical knowledge on the subject, with comments such as:

Sorry, I am not really up on this subject, medical things go over my head ... Feel free to bin my comments [A2, woman in 80s, retired accountant]

However for most Observers, the key concerns they raised around genetics and genomics were not primarily technical but instead related to potential ethical/societal ramifications.

Various Observers stipulated that careful engagement with ethical issues was of central importance to using genetics well:

In general, genetic testing can provide insightful information but that information should be used wisely and be regulated by a panel of experts that has several experts in ethics [W6724, woman in 60s, researcher]

I think recent developments in genetic knowledge are remarkable. I think knowledge is still partial but the possibilities are wonderful. But it needs a strong ethical framework [B6659, woman in 60s, retired lecturer]

I think with all experiments and developments around genetics into the future it is essential that each department and research time is also linked to an ethical team or seriously consider the ethical implications of any steps forward. While ethics can be individual I think there is a collective duty that genetics must positively assist society as a whole and not marginalise any group. Genetics and eugenics have a real danger to become one and the same [F7710, in 20s, not in paid work]

In responses to the 2006 Directive, Haran and O’Riordan noted ‘*considerable evidence of deference to expert knowledge*’ but also found that ‘*even respondents positively disposed to scientists and research drew attention to risk and the need for regulation*’. In the responses to our directive, I found that where the importance of expert governance was referred to it was frequently stipulated that ethical expertise must be central (as opposed to technical scientific expertise). Many Observers, while broadly supporting efforts to use genetics to improve health, discussed that technological developments needed scrutiny which technical scientific experts were not well placed to provide. For example, one Observer wrote:

I think that we should work hard to find cures and treatments for genetic conditions but I do not wish to see ethical decisions left in the hands of scientists and AI experts. There should be democratic control of such important research [C7297, woman in 60s, teacher]

While in responses to our Directive, ‘*deference to expert knowledge*’ was still often implied in that Observers would disclaim the value of their own opinion on the basis of insufficient expertise, it seemed that trust in technical scientific experts was very much contingent on demonstrable efforts to engage with ethical issues and listen to societal concerns. I got the

impression that several Observers experienced a tension, on the one hand feeling that genomics had the potential to open up big ethical and societal issues about which they often had strong opinions, but on the other hand feeling uncertain about to what extent they were qualified to comment on questions involving genomics because of the perception that they needed a high degree of technical knowledge in order to do so.

5.3.3 The word ‘genetics’ evoked a breadth of ideas

One prompt in the directive was *‘Please share what comes to mind when you think of ‘genetics’*”. I was curious to see how people responded to this and wondered to what extent it might overlap with how genomic results are presented in stock images (Chapter 3) and UK news items (Chapter 4). The question was asked in the context of a directive focusing primarily on the use of genetics to inform healthcare, but I was interested to see that use in healthcare seemed to form a relatively small aspect of the images that were conjured up for Observers by the word ‘genetics’. Several Observers recounted school biology lessons and remembered Mendel’s peas. There were various overlaps with common stock images relating to genomics (3.3): many described thinking of the double helix, often mentioning Watson and Crick and sometimes Franklin. Several people thought of laboratories and scientists.

I think of long strings of codes and molecules, of lab technicians in white coats and microscopes [A7000, woman in 60s, solicitor]

An image of a hospital laboratory, glass bottles, researchers in white [W6667, woman in 70s, retired teacher]

Years ago I saw a documentary about the discovery of DNA so I remember a scene in that where the scientists were marvelling at a 3D model of DNA [W6757, woman in 50s, accountant]

However perhaps more commonly, Observers framed genetics in terms of the passing on of familial traits, sometimes health-relevant but often not:

*...having my father's green eyes, mother's amazing bone structure and porcelain skin
[A2, woman in 80s, retired accountant]*

*...having my Nana's build, and my dad's nose and my Grandma's dimples. It makes
me feel so connected to my family and see that we're all such a unique blend of
people. The people who came before us are all that we are now [G7708, woman in
20s, coordinator for a charity]*

*I think of recently watching my husband, son and grandson from behind, walking
together three abreast, and seeing their heredity in their body proportions and the
inimitable gait that they share [I6609, woman in 70s, retired teacher]*

Our Directive did not contain explicit references to forensic genetics, archaeological genetics, eugenics, designer babies or cloning (in contrast to the 2006 directive which started '*Dolly the sheep, a human ear grown on a mouse, designer babies...*'). However, these topics were clearly prominent in many Observers' minds when thinking about genetics (including for many who had not responded to the 2006 directive, so this is not explained by people looking back at earlier responses in the course of researching their 2022 response). Many people mentioned genetic testing as a potential 'clincher' in solving crime, sometimes in the context of TV dramas and sometimes in real life cases:

*There is something quite fascinating about being able to prove a person's guilt from
the tiniest amounts of human matter when there is no other evidence [F7368,
woman in 40s, administrator]*

Genetic testing here appeared to be generally thought of as 'solving the case', finally allowing justice and closure. This echoes Lynch's observation in *The Truth Machine: The Contentious History of DNA Fingerprinting*, as to how forensic genetics has been presented in popular discourse: '*it is common to read that DNA fingerprinting is the "gold standard" in forensics; that it is a "truth machine"; that it represents "God's signature"; and that it produces "unassailable" or "infallible evidence"*', achieving such a status that it is now used '*as an unquestioned model for challenging the epistemic status of other previously settled forms of evidence*'(137). However, a few Observers discussed that the presence of DNA

might not equate to guilt, usually where they were describing potential concerns about participating in a DNA database:

Being on a DNA database comes with its own risks if you happen to have left DNA at what subsequently becomes a crime scene. DNA evidence has uncovered many miscarriages of justice but it is a blunt tool on its own. Contextual evidence is still just as important [B4290, in 50s, works for a university]

Various Observers also described 'detective work' with genetic testing in the context of tracing their family history. Several people referred to paternity tests on daytime TV, or programmes such as Long Lost Family. A number of people described situations where they or someone they knew had found distant relatives via ancestry testing. Observers were often scathing about attempts to quantify ancestry:

I'm aware that it is nowadays possible to take a swab of saliva or similar body fluid and send it off for analysis ... the company testing it can then inform you of your "ethnic origins", something along the lines of 25% English, 42% Viking, 21% Icelandic, 9% Nigerian and 3% Klingon. And to my mind this is nothing other than a parlour game [P6988, man in 60s, retired prison officer]

I have never had genetic testing. It makes me laugh hearing about it sometimes as I do just think a lot of the time it's just white people trying to claim onto an interesting heritage and make themselves seem a bit more exotic! And then saying they're 1/12 Moroccan as if they have absolutely any connection to that [G7708, woman in 20s, coordinator for a charity]

However, although quantification of ancestry was often seen as borderline spurious, Observers recognised such tests as able to provide convincing proof of relatedness:

I've been slightly mystified by the TV adverts for companies offering to sequence one's DNA, for a fee. What would you do with the information – assuming you weren't attempting to ascertain paternity of a child or some such thing? [M3190, man in 60s, librarian]

Genetic testing in a family tracing context was generally written about as being able to prove biological relationships, potentially uncovering family secrets, or confirming or disproving family histories drawn up based on historical records.

Various Observers discussed the use of genetic testing in an archaeological context. Here, genetics was seen as providing useful clues allowing us to trace the movements of our ancestors and make some guesses about what they were like. Genetic testing in this context was not generally represented as providing 'proof', but as something that could provoke new theories or generate new questions around how our distant ancestors lived:

I am also fascinated by the fact that modern progressions in DNA research is enabling archaeologists and anthropologists to learn so much more from the remains found, even those of our most ancient ancestors and that is an absolutely amazing and fascinating area of genetics [M6807, woman in 60s, manager]

Archaeologists have been able to obtain DNA samples from extremely old bones and can tell quite a lot about the person's life from the results [L6048, man in 70s, occupation unknown]

A few Observers referenced the use of DNA testing in identifying the remains of Richard III, and here genetic testing was considered as providing indisputable evidence:

I was fascinated in the work around the skeleton recovered which was thought to be that of Richard III. I have a clear memory of the news conference where the genetic research was unveiled and where it was clear that the known descendant of Richard III had a DNA which matched that of the recovered remains. I found that really exciting and credible evidence [K7522, woman in 60s, manager]

A high-profile use of DNA testing was when the remains of Richard III were discovered and they managed to find someone sharing some of the same DNA through a common maternal ancestor and to prove that it was him. That still blows my mind! [S6976, woman in 40s, stage manager]

As Nelkin and Lindee write in *The DNA Mystique*, '[in stories built around exhumations], DNA resolves conclusively historical questions that were once dependent for their resolution on records and testimonies from those alive at the time ... DNA is itself a historical text sometimes upstaging archaeological remains' (84).

To summarise, in many situations where Observers were asked to imagine genetics in a relatively undirected way, the images that arose for them relating to genetic testing occurred outside of healthcare but often in settings where genetics was expected to

provide clear answers: inheritance patterns as shown by Mendel's peas; analysis of DNA left at crime scenes; determining relatedness. For some Observers, archaeological testing was brought to mind – here, genetic testing was credited with deepening our understanding of our past, though often by complementing other sources of information rather than providing decisive answers.

In terms of broader issues arising when Observers thought about genetics, eugenics, 'designer babies' and cloning were frequent concerns (see 5.3.6). For the 15% of Observers who had responded to both the 2006 and 2022 Directives, I was quite struck by how stable attitudes towards genetics generally appeared to be. Observers who had felt that they were undecided and easily swayed in 2006 felt the same in 2022; Observers who had been reticent continued to express reservations; those who had been broadly positive had retained their optimism about the future and potential of genetics (please see Table 14, section 11.5.3 for details). Given the nature of the Mass Observation Project it is possible that Observers may have referred to and potentially been influenced by their previous responses in writing responses to our directive, but we did not make direct reference to the 2006 Directive in our prompt so this would rely on them remembering or looking back to see that they had answered similar questions 16 years previously.

5.3.4 Observers drew on material across many domains and over a long time period in forming their opinions around genetics and its future uses

Reporting on their 2006 directive, Haran and O'Riordan noted that *'those epochs marked as different – the new genetics of the 1950s, the genome project of the 1980s and 1990s, and the genomics of the 21st century – are not marked as distinct in respondents' personal media cultures of genomics. People connect cultural production through the 20th and 21st centuries in ways that make sense to them'*. Similarly, in responding to our directive,

Observers brought in experiences and exposures to genetics in different settings when discussing their thoughts and feelings around topics such as future uses of genetics or the merits of contributing to a DNA database. Concerns raised in ‘older’ stories were evidently still seen as very pertinent: many of the media discussed in response to the 2006 directive on *Genes, Genetics and Cloning* were again brought up in responses to our directive. Table 9 lists media which Observers referred to.

Table 9: Sources¹⁶ referred to in responses to ‘Genetics and health in our everyday lives’ directive

Items in bold were referenced at least three times.

Book	Film	TV	News story/ event
1818: Frankenstein (Mary Shelley) 1932: Brave New World (Aldous Huxley) 1947: The Diary of a Young Girl (Anne Frank) 1949: 1984 (George Orwell) 1968: The Double Helix (James Watson) 1988: The House of Stairs (Barbara Vine) 2001: Seven Daughters of Eve (Bryan Sykes) 1987-2012: ‘Culture’ series (Iain M Banks) 1976-2021: Richard Dawkins’ books 2004: Life (Gwyneth Jones) 2005: Never Let Me Go (Kazuo Ishiguro)	1978: The Boys from Brazil 1993: Jurassic Park 1997: Gattaca 2005: The Island 2018: Three Identical Strangers	1993-1999: Star Trek: Deep Space Nine 1996-present: Silent Witness (genetic testing featured from 1998) 2004-present: Who Do You Think You Are? (genetic testing featured from 2006) 2009: The Incredible Human Journey 2010-present: Digging for Britain 2011: Botany: A Blooming History 2014: Tutankhamun: The Truth Uncovered 2015: Code of a Killer 2016: A World Without Down’s Syndrome? 2011-present: Long Lost Family (genetic testing featured from 2019)	1933-1945: Nazi Germany 1996: Dolly the sheep 2013: Angelina Jolie’s BRCA result 2013: discovery of remains of Richard III 2018: report that Barbara Streisand has cloned dogs 2021: Genetic testing of Tarim mummies 2022: news reports about treatments for motor neuron disease

¹⁶ Sometimes Observers did not name the content listed here directly but described it such that I was fairly confident what they were referring to. For example, when an Observer wrote ‘*I know cancer cells from a Black American woman were used for research for years, while her family continued to live in poverty and faced barriers to healthcare, and that doesn’t seem right*’ [M5645] I thought it was likely that the Observer was referring either directly to the book ‘The Immortal Life of Henrietta Lacks’, or to material that had discussed or commented on it. Sometimes Observers made a clear reference to a story but I could not be sure exactly which version of a story they were referring to (for example whether they meant the book or the film for ‘Jurassic Park’) so the classifications reflect what I thought of first when seeing the reference.

Book	Film	TV	News story/ event
2010: Immortal Life of Henrietta Lacks (Rebecca Skloot) 2014-2022: Adam Rutherford's books 2016: The Industries of the Future (Alec Ross) 2019: The Age-Well Project (Susan Saunders) 2021: Klara and the Sun (Kazuo Ishiguro) 2021: Ancestors (Alice Roberts)		2019-present: Forensics: The Real CSIs 2018-2020: A House Through Time 2021-2022: DNA Family Secrets	

I was interested to note that none of the Observers referred by name to the 100,000 Genomes Project, except those who knew someone taking part in it, and while lots of Observers discussed the Newborn Genomes Programme which we referred to in the directive prompt, many commented that they had not previously heard of it. The Mass Observation Project is not intended to be statistically representative of the UK population and this cannot be taken as a proxy for how people 'in general' might interact with genetics and genomics. But for the group of Observers who responded to our Directive I got the impression that the beliefs, thoughts and feelings they have around genetics and genomics have been developed in engagement with a wide-ranging variety of materials and experiences over a long time, with multiple sources and experiences combining to inform their current opinions and attitudes around genetics and health in our everyday lives.

However, although Observers referred to a wealth of material in their responses to our Directive, this is not to suggest that they were blindly influenced by all materials in developing opinions regarding genetic testing in a healthcare context. Observers were clearly critically evaluating the sources of information they referred to and to what extent these might be sufficient to inform an opinion. For example, one Observer wrote:

I have no personal experience and little understanding of the use of genetics in healthcare so my response to this is very limited and based only on listening to evidence and opinions gleaned from reading or documentaries on radio and TV
[C7720, woman in 70s]

Several Observers described how different sources discussing genetics had different roles to play – for example one Observer described how they saw dystopian stories about genetics as having an important protective function:

I guess a potential drawback to [programmes like the Newborn Genomes Programme] could be similar to that presented in media like Gattaca and Klara and the Sun, whereby society becomes less tolerant of difference. Again, perhaps naively, I think such drawbacks will not be realised perhaps for the very fact of the prevalence of cultural depictions warning us of them and we, as a society, will not readily accept things like widespread genetic editing or engineering a new meritocracy based on it [O7365, man in 20s, business development lead]

Observers appeared to weigh up discussions and representations of genetics in many different real and imagined settings encountered over a prolonged time period. They connected these with their personal experiences with engaging with- or considering- genetic testing, in developing their current thoughts about genetics and its future uses.

5.3.5 Genomic results tended to be written about as an amplification of genetic results rather than as potentially having a different nature

Our directive included a section framing our questions in the context of a shift in technologies underlying genetic testing (*'20 years ago, genetic tests could only examine small portions of the genetic code, and this was technically difficult. Now tests can sequence a person's entire genetic code (genome) quickly and cheaply. Sometimes this helps to diagnose a condition, or determine a treatment, but other times we don't know what to do with the information found through such tests'*).

In responses to our directive, some Observers reflected on changes in genetic testing over time. Often this involved close personal experience of appropriate genetic testing becoming available, or recent testing making a previously elusive diagnosis for someone they knew. Occasionally this formed part of a wider reflection that medical science is improving and advancing albeit still imperfect:

In 2000 testing for the defective genes implicated in ovarian cancer was possible but not widely available in the UK ... By the time my sister died testing was available ... I feel profoundly grateful that I was able to have the test [D7734, woman, retired vicar]

New science is always controversial and genetics are no exception. It will raise difficult questions but that's how we further advance our understanding of health issues. There are health issues we didn't know about 50 or 100 years ago or even have names for, which are now common knowledge, and some are now preventable, treatable or curable; some we are still looking for answers to [W3163, in 60s, retired office administrator]

A shift from genetics to genomics was rarely formally discussed but many Observers reflected on the potential for broader testing to generate more information. Generally speaking, the sorts of results expected from genomic tests (such as the Newborn Genomes Programme) were often discussed in similar ways to the results of narrower tests, with an implicit expectation of similar clarity. For example, reflecting on the possibilities of newborn genome screening, Observers wrote:

I think knowledge is power and if you know there is a possibility of some illness or disease attacking your child, you are forewarned. Parents imagine enough terrors in any event, so I don't think it would be adding to the burden, rather it would be giving positive news that they will definitely not suffer from X, but be on the watch out for Y [A7000, woman in 60s, solicitor]

Whilst it could be devastating to discover, and at such a young age, that there could be the potential for a genetic disease, ultimately it can only be a good thing to learn this as soon as possible. We all hear constantly of how early diagnosis can be a life saver, and that would seem to fit in this context [D6836, woman in 70s, retired teacher]

I don't think I'd want to know the death day of my newborn baby [A1706, woman in 70s, artist]

A few Observers explicitly referred to evolving abilities to interpret genomic variation. This was usually either in the context of close experience with medical genetic testing, or commenting on fluctuations they saw in results attempting to define their genetic ancestry:

Genetic testing has, four years ago, enabled a diagnosis to be made about a friend's son, who was about 22 then. He has [syndrome], a rare condition that explains the developmental delay that became apparent in infancy, and his profound learning difficulties. It must have been a huge deal for them to have an explanation after all this time [C6574, woman in 50s, writer]

The [genetic] test identified that my father had a couple of suspect gene mutations possibly linked to other cancers but there is too little known about these mutations at present. His results are being kept in a database and they requested that they be informed if he or his relatives developed any other dreadful condition (so that's not depressing) [E7722, woman in 60s, officer manager]

A year ago my results said I had 2% Māori DNA and now its Tibetan DNA so as last year's result was wrong by quite a bit and so now how accurate can I assume the correction to be as it's being refined as we speak [P7688, man in 50s, museum assistant]

At the instigation of my daughter and granddaughter, who are interested in family history I did take a DNA test through the Ancestry organisation ... The fact that Ancestry have amended the original findings indicate to me that this is not an exact science and the results may not be completely accurate [S3035, man in 70s, retired banker]

One Observer discussed in depth how the reliance of genomic testing on databases which were not representative of the world population meant that the usefulness of genomic tests might vary according to a person's ancestry:

Genomics has a real potential to help us understand what's "normal", target screening where it can be of most use – and this is particularly a concern when our genomic databases are so dominated by those of White European ancestry – meaning the majority of citizens of the world are getting information that won't work for them – or which is based on much smaller numbers [I6794, woman in 30s, social researcher]

A small number of Observers directly discussed how their expectations of certainty from genetic testing had shifted over the years, and often in these cases described that a particular article or book had influenced this change:

A couple of years ago I read an article in the American 'Atlantic' magazine regarding the increased use of genetic testing with respect to medical care in the USA and the thing that struck me about the article was that it asserted that reading a DNA sample was incredibly difficult and that the vast majority of tests were 'inconclusive' and the fear was that people who expected a definitive good or bad answer regarding their future health were left with lingering fears of uncertainty
[W5965, man in 50s, retired police officer]

[referring to a book by Adam Rutherford] Apparently our current understanding of genetics is too limited to say with any certainty that X gene does Y. X gene might be a factor in Y, but we can't really say much beyond that
[M6759, woman in 30s, archaeology student]

I have read articles which do claim on seeming good ground that some health issues have a genetic basis but now such articles tend to take a more cautious approach, not claiming that because someone has a particular variant of a gene that they will become ill, but that it increases the risk that they will [M3231, man in 70s, retired physicist]

Many more Observers implicitly positioned knowledge around genomic variation as evolving when writing about the benefits of participation in genomic databases. Although the mechanisms by which this would improve interpretation of genomic variation were not commonly spelt out it was very widely recognised that a decision to contribute to a research database might help others in the future.

In summary, genomic results often seemed to be thought of as an amplification of genetic results, with results of a similar nature expected, but on a grander scale. Where Observers discussed changes relating to genetics in healthcare over time, this was usually in a context of acknowledging improvements in test availability and interpretation which had led to new diagnoses or new options for them or people they knew, i.e. as part of an upward trajectory in the usefulness and power of genetics. However, several Observers referred explicitly to shortcomings in our current understandings around the significance of genomic variation, and many Observers showed implicit awareness of this issue in their support for those contributing to genomic databases.

5.3.6 Observers wondered how ‘genetic knowledge’ might change the human experience
or the nature of humanity

A common question raised by Observers was to what extent increasing use of genetic testing might change the human experience. In responses to a prompt asking about ‘*future uses of genetics*’, many Observers saw genetics as on a course to take an increasing role in people’s lives:

I think we can be certain that our quest to understand and fight disease will mean that our use of genetic testing and treatment will only become more and more normal for future generations [F7368, woman in 40s, administrator]

I would guess that as science evolves and more research is done, people will know a lot more about their genetic makeup and it might become a more normal part of our lives and growing up [R6956, man in 20s, student]

Observers often associated increased genetic testing with increased longevity, but several wondered whether this would ultimately benefit humanity:

The other question that comes up for me is how much should we just accept our fate. If we eradicate all genetic conditions, won’t we all just live till we’re 120? That has implications on the economy and society [C3210, woman in 40s, IT consultant]

If we kept everyone alive because we prevented early death via genetic testing, the world would very quickly become too over populated [T6740, woman in 40s, manager]

We’ll all be so well looked after individually and with such knowledge about why various bits aren’t working that there’ll be no need to die. I believe some scientists think there is not necessarily a ‘need’ for dying, which leads to a whole lot of other ifs and buts. Getting a bit full on planet Earth? [A1706, woman in 70s, artist]

Many Observers, when asked to comment on newborn genome screening, reflected on what it might be like to grow up with awareness of genetic predispositions from an early stage. These were often couched in quite fatalistic language but the concern that efforts to extend our longevity might simultaneously curtail our experience of living was very evident:

Perhaps we should become more accepting as humans that something, probably passed through our genes, is going to kill us. I don’t necessarily want to know which particular disease is going to kill me. Maybe if we’re so focused on our own demise

we forget to live life [C3210, woman in 40s, IT consultant]

What people know from the time they are born will have an effect on how they live their lives depending on how seriously their parents and they take those warnings. It could shape what they do and limit what they do, sometimes without need [M7490, woman in 40s, civil servant]

I've sometimes wondered, particularly as I've got older, what it would be like to have an idea of at what age you will die and of what ... Aside from things like health insurance and financial planning, would you live differently if you knew, at say age 16, that you had a 90% chance of developing a life-changing disease at about 40 than being in ignorance [R7467, woman in 70s, retired academic]

Insurance companies are rubbing their hands together already seeing huge payments from various illnesses being highlighted in your genetic make-up, meaning anything you want to do in life will exact a heavy premium JUST IN CASE. You just might contract MND when on holiday, you may just get a terrible attack of arthritis when playing football. (though it hasn't happened yet – BUT IT COULD [A1706, woman in 70s, artist]

However, many Observers also discussed that early awareness of health risks might allow preventative treatment or result in better outcomes for some of the babies being screened. Various Observers also reflected that while it might be challenging where uncertainty is raised around a baby's future health, ultimately people would adapt to and cope with this. The risk of raising potentially groundless concerns about a baby's health was something to take seriously, with ongoing research to try to mitigate this. But this was something to balance against the potential benefits of earlier knowledge of genetic predispositions, rather than a reason to avoid genetic testing:

You mention that it might cause more uncertainty, for example where a possible genetic risk is found but no-one is sure if it will make the baby ill or it's unclear what the best treatment option is. That's difficult, but perhaps this is offset by the potential benefits of this programme. In healthcare more generally, we need to help people navigate uncertainty [C6574, woman in 50s, writer]

I think people can cope with uncertainty if it is explained to them in an adult manner – for example, a potential possibility of a condition could be to monitor for it, eg., annually after a certain age (assuming parameters can be established in that way). No doubt possibilities will be thrown up that can't be checked in this way but the very fact that they are thrown up will lead to further research [H6949, nonbinary person in 50s, academic]

‘Knowledge’ of genetic predispositions was fairly often construed as a burden, and for many Observers, a key consideration was whether a person could take useful action in light of that knowledge. Some raised concerns about whether relevant treatments would in practice be accessible, and several were sceptical regarding the extent to which genetic findings would provoke meaningful lifestyle changes:

Doing [genetic testing] for health reasons feels a little deterministic. I mean, maybe I’m predisposed to some sort of illness, but I’m going to die of something – my drinking predisposes me to liver failure, my smoking to lung and heart failure, my genes will be predisposing me to something else. What am I meant to do, pick one? ‘I’ll lay off the smoking because I fancy giving my genes a chance to kill me with testicular cancer instead’? The whole thing feels a little pointless [J5734, man in 30s, charity worker]

[Discussing a survey of 23andMe health customers looking at changes people had made in response to their results] In exchange for the existential dread of identifying what’s most likely to finish them off, people seem to be doing... not very much at all [B3227, man in 50s, not in paid work]

It would be useful to know if eating copious amounts of broccoli would prevent you getting cancer but not very comforting to be told that you’ll get some awful disease but there’s nothing that can be done about it. And I’m not sure that people would actually eat the broccoli even if they thought it would save their life [E7722, woman in 50s, office manager]

In summary, at an individual level, many Observers recognised potential benefits in being made aware of genetic predispositions to disease, but were sceptical about the extent to which these benefits might be realised, and concerned that the price would be too high in terms of the constraints such awareness might place around life.

More broadly, the potential for increased use of genetics to be a pathway to eroding and distorting what humanity values was a common concern. As one Observer wrote, ‘*genetic information has the very real possibility to become not about the information but about how we can manipulate society and who and what we place worth, marginalisation, othering and importance on within humanity*’ [F7710, in 20s, not in paid work]. The potential connection between genetics and eugenics was brought up by many Observers:

33 (22%) made explicit reference to eugenics and/or the Nazis despite the directive being primarily couched around genetic testing in the context of moves towards personalisation of healthcare. These concerns were most often raised in the context of prenatal screening (which many people spontaneously raised in response to prompts around newborn screening):

I feel that DNA testing is positive for discovering diseases and conditions but if a child is aborted because of this it would change the rich diversity of our society, which would be such a loss [P7689, woman in 30s, analyst]

Checking everybody routinely for imperfections has echoes of eugenics, especially if these codes can be sequenced before birth which might result in lots of abortions [D826, in 70s, retired social worker]

Where Observers were supportive of use of genetic testing in ‘medical’ situations, they were often careful to stipulate that this support did not extend to the use of genetics for ‘non-medical’ ends (*‘none of this making sure they have blue eyes, etc’ [G7708, woman in 20s, coordinator for a charity]*). Various Observers making this point discussed that while they adhered to this distinction on principle, some situations were hard to classify in this way, with deafness and Down syndrome cited by more than one Observer as challenging ideas around what constitutes disability.

Although our directive focused around genetic testing rather than editing, genetic modification and cloning were brought to mind for a number of Observers when they thought about ‘genetics’. Again, gene editing to ‘fix disease’ had some support but gene editing for enhancement or to determine ‘non-medical’ characteristics was largely resisted, although some Observers imagined this would be a likely part of our future, whatever they might think about it in the present.

5.3.7 Observers held a range of views regarding taking part in genetic databases

As part of our Directive, Observers were asked to consider the positives and negatives of participating in a DNA database (by means of a scenario where a woman with breast cancer who had had genetic testing was asked to contribute her genetic data to a database used for research purposes). I was interested to see what roles Observers viewed DNA databases as playing in the construction of genomic results.

In common with the treatment of genomic databases in many UK news items (4.3.2.4), contribution to such a database was often seen as a laudable and altruistic decision, but the path to benefit was usually loosely articulated. Many Observers made comments like:

I would be happy for my genetic data to be stored in a DNA database to be used for research purposes. It might help other people in the future [B5725, woman in 60s, retired lecturer]

If the information about my own genetic problem helps anyone else that is great so I am happy for the information to be stored in a database [D7734, woman, retired vicar]

DNA stored in a Research database may help someone else further down the line [H2418, woman in 70s, retired library worker]

Storing genetic data on a database would be a positive move as it might help others in the future [P1009, age and occupation unknown]

A few Observers commented in greater depth on the mechanisms by which genomic databases might lead to societal benefit. This was still some distance from the great detail in which some people who had experienced genomic testing described results growing out of comparison of their genomic data with that of others (7.3.2.3), and usually involved describing how the more data there were, the easier it might be to spot patterns. For example, one Observer wrote:

[People with cancer contributing DNA to] a database could be very useful if you are looking at patterns of genes associated with particular cancers. The more data there are then the more likely you can predict whether someone will get that cancer [P5366, man in 40s, teacher]

My overall impression was that many Observers tended to position participation in a DNA database as connecting in an important and meaningful way to improving health for others, and for many the potential benefit for other people would be a key motivating factor in deciding to contribute their own genomic data. However, encouragement of a decision to participate in a genomic database was often contingent on an assumption that the data could be reliably anonymised:

I would expect such a database to inform all contributors that their data would be anonymised and therefore would be irretrievable, in which case there would be no consequences either positive or negative, just a global positive effect by advancing medical science [I6609, woman in 70s, retired teacher]

For me, the main consequence is that her data contributes to medical science. This might of course mean that her data is anonymised. That being so, the consequences to her are none [L6048, man in 70s, occupation unknown]

Various Observers wrote explicitly that their support for participation in genomic databases depended on access to such databases being carefully governed:

Anything that responsibly helps to deal with inherited diseases has to be good news. It is however essential that this information is protected [W6667, woman in 70s, retired teacher]

The positive consequence would be an altruistic one - the opportunity to help others by being part of research that might lead to new cures or diagnostic tests for cancer. I can't think of any negative consequences (assuming [the participant's] data is anonymised and the research is managed and governed well) [T7345, woman in 30s, civil servant]

Many other Observers were reticent about the prospect of taking part in a DNA database, usually citing concerns about privacy and security, for example questioning whether law enforcement or insurance companies might be able to access the database. Various Observers also clearly considered a decision to contribute genomic data as one where new consequences could evolve over time – and while under current circumstances they might be willing to contribute data, they were very aware that these might change:

For all its faults the NHS is one of the few institutions that I would completely trust with my genetic information, and would provide it if requested. At the same time, I am not convinced that the NHS will exist in any meaningful sense (other than a brand name) in 10 or 20 years' time [A7709, age and occupation unknown]

I would be worried that it all seems fine and dandy while you have a benign liberal government, but times change and that is never a given. It seems like a slippery slope towards healthcare insurers being able to access said database and hiking people's premia accordingly [C5847, woman in 40s, charity worker]

A couple of Observers reflected that they could see that a decision to participate in a DNA database might go 'under the radar' and at face value be thought of as not very significant, while actually deserving considerable scrutiny:

[A person who contributes to a genomic database] is behaving rather like a naive internet user who gives away personal data. Even if the person you gave it to uses it responsibly, you gave away for free something which could earn millions of pounds for someone else. When you give data for one study, it may be sold or subsequently used by other organisations [M4859, woman in 40s, software architect]

I had my DNA tested before I considered the implications of being on a database. It's like social media, most of us signed on without considering what was happening to all our data [P7688, man in 50s, museum assistant]

As one Observer put it, '*In the end, what we all need is reliable advocacy to ensure that the small print is writ large, because somewhere along the line we will have rights and responsibilities – not only to ourselves but to future generations*' [C7720, woman in 70s].

5.4 Summary

As relates to my research questions, 'what features do people conceptualise genomic results as having?', responses to our directive on '*Genetics and health in our everyday lives*' often gave the sense of genetic testing as a powerful tool in healthcare with results that were fairly definitive. Genomic testing was typically written about as an amplification of genetic testing, generating information of similar solidity, where results had potential to change the nature of the human experience but were not themselves different in nature to

results generated via narrower tests. While often positioning genetics and genomics as outside their remit, respondents engaged in great depth with the opportunities and challenges raised, advocating for ethical and societal considerations to form a key part of any decision-making regarding future genomic initiatives.

Connecting to my research question, ‘in what ways do popular discourses invite us to imagine genomic results?’, writers threaded together personal experiences with insights drawn from a wide variety of media, often quite old, in outlining their ideas. Observers also drew on and referred to uses of genetics in settings outside healthcare in their responses, for example in exploring ancestry, or for forensic or archaeological purposes.

This indicates that many people without prior experience of clinical genomic testing may yet have a wealth of experiences and exposures sculpting their expectations as to what such testing stands to bring. It also strengthens the justification for not restricting the news items I analysed in my facet exploring UK news items to recent years— people’s beliefs about genomic results in the present day may be influenced by experiences and exposures from many years ago. (This perhaps in part connects to the demographic of the Observers and the nature of the Mass Observation Project: 64% of respondents were 60 or older. By virtue of their participation in the project, many will have expertise in drawing on experiences that may have happened at various time points over the course of their life to reflect on a very wide variety of topics).

Concepts of genomic results common in stock image banks and UK news items (3.4 and 4.4)- as profound, clear-cut, and potentially life-changing- were to some extent echoed in responses to our directive, particularly where Observers were asked to envisage future uses of genomics. Yet for many Observers these qualities were potentially double-edged, with

concerns about eugenics or potential stiling of the human experience coming out far more prominently from this facet than from my exploration of genomic results in UK news items. Overall, responses tended to present more complex and nuanced versions of genomic results than those prominent in stock images and UK news items. Sometimes a powerfully deterministic expectation of genomic results appeared implicit in some aspects of an Observer's comments and yet seemed to be consciously resisted in other areas of their response – one Observer beautifully encapsulated the issue that many appeared to experience:

There's something quasi-magical – alchemical might be a better word – about the instinctive popular attitude to DNA testing and the research into its practical uses. It's hard not to think of it in very literal terms: that pulling a gene from one position to another (if such a thing is possible), or excising it, can immediately change physical appearance or personality traits, or directly influence the course of a disease or chronic medical condition. I'm sure that's all fantasy, but it's a creepy feeling nonetheless to feel oneself, in all one's human complexity, reduced to...well, whatever a genome sequence looks like. I'm imagining it as a Manhattan Yellow Pages-thick tome filled with variations on ATGC [M3190, man in 60s, librarian]

This 'quasi-magical' working concept of genomic results, together with an intellectual acknowledgement that 'I'm sure that's all fantasy', recurred in the facets of my project where my exploration of genomic results moved closer to the clinic (Chapters 6 and 7).

5.5 Reflections on this facet

This facet sought to explore how people writing for '*an archive of everyday life, thought and feeling in Britain*' (99) appeared to conceptualise genomic results, and to learn about the experiences and influences that may have shaped their ideas. Arguably, a major limitation here is that many of the questions in our directive asked people their opinions about *genetics*, rather than specifically asking about *genomics*. However, the introduction to our directive made it clear that in this context, our questions around 'genetics' also encompassed genomic testing: '*20 years ago, genetic tests could only examine small*

portions of the genetic code, and this was technically difficult. Now tests can sequence a person's entire genetic code (genome) quickly and cheaply' (see 11.5 for full directive). We also asked specifically about the UK Newborn Genomes Programme in our questions around the future uses of genetics.

If we had asked people to 'share what comes to mind when you think of genomics', I think it is quite likely their answers might have been slightly different (and I wonder if the response rate to our directive might have been lower). As regards to what extent a person's ideas around *genetics* might influence their expectations from clinical *genomic* testing, I cannot find clear evidence, but I think it is very likely that people would not compartmentalise genetics and genomics to the extent that their ideas around genetics bear no relation to their ideas around genomics. I would argue it is much more likely that their views around genomics might be very much anchored in their views around genetics. As I outline in 5.3.5, when Observers wrote about 'genomic' tests, most seemed to think of these as amplified 'genetic' tests, rather than having a different nature.

The mode of data generation in this facet offers an interesting angle in that respondents to the Mass Observation Project have the opportunity to think about questions and prompts over time, and could potentially research relevant issues or discuss them with others in the process of crafting a very considered response. Free text responses also allow people to give an account of uncertainties and contingencies in their answers. It would be interesting to know what Observers might have said in on-the-spot verbal discussion of our questions and how closely that would have mirrored what they ended up writing: time and the opportunity for in-depth reflection might shape responses significantly. For example, a public dialogue relating to the use of genetic testing in newborn screening for cystic fibrosis found that with time, information, discussion and reflection, a number of participants

changed their view. At the outset they favoured a sensitive approach that would detect more babies with cystic fibrosis but would also leave more families living with uncertainty as to whether their child would develop it. Over the course of the dialogue they shifted to preferring a more specific approach that would miss some babies with cystic fibrosis, but leave fewer families in limbo as to whether their child would develop it(138).

The Mass Observation Project does not seek to be statistically representative of the UK population and we should not infer from it how ‘most’ people might think about genomic results. Observers are not chosen on the basis of having had genomic testing, so they do not stand to inform the question by virtue of personal experience. However, I think this facet is very revealing for exploring where and how promotional popular discourses around genomics interface with people used to deeply engaging with topics that may be new to them. It indicates that concepts of genomic results as inarguable, powerful and clear-cut are implicit in many of the hopes and concerns people describe around the use of genetics in the future. But it also shows areas where complexities and limitations of genetic testing are widely recognised, for example attempts to quantify ancestry, which could provide a useful route into concepts of clinical genomic results that encompass more noise and uncertainty.

This facet also illustrates how people reading a participant information sheet, or attending an appointment to discuss consenting to a genomic test, are unlikely to be starting with a ‘blank slate’ as regards their expectations from the test. While provision of information might shift their views, they likely already have ideas regarding what results the test might provide, potentially developed over many years and drawing on a very diverse range of experiences and sources.

6 Observations of clinic appointments where genomic results are discussed

This facet was designed to address my research questions ‘What features do people imagine genomic results as having?’ and ‘What sorts of features do genomic results appear to have in clinical settings?’ In order to consider these, I sought to observe instances where the notion of a genomic result was discussed between clinicians and patients, both in the offer of a genomic test, and in communicating outcomes from such tests. This offered insight on my overall question, ‘how should we construct genomic results?’, by providing a route into exploring results in the clinical setting. Along with relevant ‘technical’ data, and drawing on personal experiences of trying to find meaning in genomic data in a clinical setting, this could feed into my analysis of ways of conceptualising genomic results.

The chapter begins by discussing why I chose clinic observations as a facet. I then outline practicalities of observing, and my analytic approach, before discussing my results.

6.1 Rationale for observing clinic appointments discussing genomic tests

I intended that this facet would give me an opportunity to explore how the notion of genomic results appeared to be conceptualised in clinical conversations, and how issues relevant to the production of results were discussed in clinic. This could give valuable insights as to the construction, negotiation and experience of clinical ‘genomic results’, with potential to explore overlaps and differences between how these appeared in clinical conversations, with how these appeared in other aspects of my project, for example in UK news items or stock image banks.

As outlined by Busetto *et al*, '*observations are particularly useful to gain insights into a certain setting and actual behaviour – as opposed to reported behaviour or opinions*'(139). Many of my other facets explored hypothetical genomic results, for example ideas relating to them that are evinced in stock images, or reflections around them from Mass Observation Project Observers who did not necessarily have personal experience of clinical genomic testing. Others examined both hypothetical and 'showcased' genomic results, for example those promoted in UK news stories around genomic initiatives. Even my interviews, although undertaken with people experiencing genomic tests, often explored genomic results in the abstract, with people's expectations from- and hopes for- their genomic results in the future forming as big a part of the discussion as their experiences of genomic results in the present. This facet gave me an opportunity to explore the nature of 'real' genomic results under discussion in clinic.

Mason writes that '*observation allows the generation of multidimensional data on social interaction in specific contexts as it occurs, rather than relying on people's retrospective accounts, and on their ability to verbalise and reconstruct a version of interactions or settings*'(91). While I could (and did) ask people having genomic tests about their experiences of discussing them and receiving outcomes from them (see Chapter 7), this facet was valuable in allowing me to experience the discussion of genomic tests and results 'in the moment'. Clearly, people would routinely expect clinic appointments to be confidential, so an overt strategy where I very explicitly sought people's consent to observe their appointments was necessary in view of ethical considerations.

6.2 Methods

6.2.1 Recruitment for observing clinic appointments

I recruited healthcare professionals who discussed genomic tests and results in their routine clinical practice, and patients and families attending appointments where genomic tests and results might be discussed. I aimed to observe discussion of results in various contexts – for example theoretical (from a test offered but not yet done) and actual.

I recruited healthcare professionals via a regional clinical genetics service. Participating healthcare professionals nominated clinics that they thought would be suitable for me to observe. Their NHS clinic coordinator then sent out information about my research to the patients and families due to attend these clinics (see Appendix 11.7 for recruitment materials). When patients and families arrived at the clinic, a member of the NHS team checked whether they would potentially be interested in participating. If so, I met them to discuss what this would involve, and to seek their consent for the observation¹⁷. I introduced myself to patients and families as ‘a PhD student doing a research project’, but in discussing my project and asking their consent I gave context that I was taking time out of training in clinical genetics, and fairly often at the start of appointments clinicians would reintroduce me as ‘a genetics registrar doing some research’.

¹⁷ I asked consent from people over the age of 16 years. Where appointments were attended by a young person aged 10-15 years, I asked for consent for their participation from a person with parental responsibility, but I also gave the young person age-appropriate information about the research, and only observed appointments where both the parent/guardian had consented, and the young person had assented. For children under 10 years I sought consent only from their parent/guardian, but tried to be alert to signs that the child was upset or unhappy at being observed (if that had been the case I would have left their appointment).

6.2.2 Generating data through observing clinic appointments

I used an observation framework to guide data generation. In developing this, I was influenced by Mason's guidance in *Qualitative Researching*(91), frameworks from other projects undertaken by the Clinical Ethics, Law and Society research group(140), and my previous clinical experience. I also had a very helpful conversation with Dr Sarah Wynn from Unique (an organisation providing information, support, and networking to families affected by rare chromosome and gene disorders). This really helped me consider which aspects of a clinic appointment might be most important to families experiencing or considering having genomic tests, and the ways in which a 'result' might affect a family beyond the clinic. The framework I developed was part structured and part unstructured, covering anticipated areas to observe, alongside space to record unexpected/interesting areas of consultations (see Appendix 11.7.8). I further refined the framework based on my previous observations as my project progressed.

I observed clinic appointments where both the healthcare professional and the patient/family attending consented to my doing so. I aimed to sit in an unobtrusive position in the room, as guided by the healthcare professional running the appointment. During each appointment, I took occasional handwritten notes guided by my observation framework. As soon as possible after each appointment, I wrote detailed field notes, aiming to summarise key discussions around genomic results that had occurred during the appointment, and noting my initial reactions as to what the observation was teaching me about genomic results(141).

6.2.3 Analysing data generated via observation of clinic appointments

I thematically analysed the data I generated from observing clinic appointments (see 5.2.2.1 for more discussion of thematic analysis).

Within this facet of my study, my analytic approach aimed to align closer to an artfully interpretive analysis than a scientifically descriptive analysis. This related to the strategic purpose by which this facet stood to give me ‘flashes of insight’ regarding the nature of genomic results – by being embedded in a context where I saw them as being constructed/negotiated in real-time, and trying to be open to noticing this process and factors that seemed to have a bearing on it. The data generated, the ongoing data generation process, and the issues I wanted to explore were more suited to an approach underpinned by a constructivist epistemological position, than an approach that sought to quantify or objectively represent what happened in the clinical appointments I observed.

From a practical perspective, my analysis involved listening carefully throughout clinic appointments for any discussions that had a bearing on how genomic results might be constructed, thinking about what these communicated regarding the nature of genomic results, and documenting these after each appointment. Prior to each new appointment, I would read through my notes aiming to identify themes relevant to how genomic results were being discussed that I could be attentive to in my next set of observations. As I identified differing concepts of genomic results in other facets of my study, I repeatedly came back to my observation notes, considering whether these concepts were echoed or absent in the appointments that I had observed. I also took insights from this facet of my study, for example seeing how recognition of clinical features could transform an uncertain variant to a diagnostic result in the course of an appointment, to test in other areas where I had generated data. For example, I considered to what extent experiences such as these were reflected in the facets of my study that explore discourses around genomic results in stock image banks or UK news items. As I did this I tried to consider how and when common ways of imagining genomic results might be helpful or unhelpful to people being cared for by or working within clinical genetics services.

6.3 Results

6.3.1 Characteristics of appointments observed

I observed ten clinic appointments where tests drawing on genomic technology and/or their outcomes were discussed. Each appointment lasted roughly 40 minutes. Table 10 gives an overview of the types of appointments observed. All appointments were focused around a child/young person with symptoms suggestive of a rare condition. Various outcomes of genomic testing were discussed, including: ‘nothing found’; variants of uncertain significance in genes associated with particular genetic conditions; and variants thought to explain a child’s rare condition. In a number of appointments, further testing was offered or discussed, which also gave me the opportunity to observe theoretical discussion as to what *could* result from a genomic test.

Table 10: Details of clinic appointments observed

Reference number	Context of genomic testing	Reflections on dynamic of the observation
Obs_01	Secondary school age boy with developmental delay, deafness and large head size. Taking part in the 100,000 Genomes Project as a trio – preliminary analysis found no clear answer for health concerns.	Small clinic room. Young person and mother sat facing the clinician across the corner of a desk. I sat slightly behind the clinician but the family clearly were aware of my presence throughout the appointment, e.g. they smiled and made eye contact with me when making jokes. The appointment overall felt friendly and low-key.
Obs_02	Primary school age boy with developmental delay. Taking part in DDD and the 100,000 Genomes Project as a trio – both identified a variant of uncertain significance in a very recently described disease gene.	Medium-sized clinic room. Child brought by both parents. I sat in an unobtrusive position. The appointment felt serious and the parents appeared frustrated at times (with their experience of genomic testing, not with the clinician with whom they appeared to have a strong rapport).

Reference number	Context of genomic testing	Reflections on dynamic of the observation
Obs_03	Primary school aged boy with muscular problems. Taking part in the DDD project – variant of uncertain significance found, not present in mother, father not tested.	Small clinic room. Child and mother attended. The mother sat facing the clinician across the corner of the desk, with the child to her side. My seat was slightly screened from view by the clinician and for most of the appointment I felt I was in an unobtrusive position. The discussion between the mother and clinician felt very focused.
Obs_04	Preschool aged boy with developmental delay. Had an exome test which found a likely causative variant in a newly discovered developmental gene, parents not yet tested.	Small clinic room. Child and mother attended. The child was very excited by climbing on the examination couch and playing with the sink and a lot of the appointment I was trying to keep him entertained and make sure he didn't hurt himself, so my presence in the room was very obvious but while the child and I were quite loud and active it felt incidental to the discussion between the mother and clinician. The atmosphere initially felt anxious (the mother was concerned to have been sent an urgent appointment) but fairly quickly became more relaxed.
Obs_05	Primary school aged girl with developmental delay and unusual structural brain development, having singleton exome, test still in progress, no outcomes yet available.	Medium-sized clinic room. Child seen with both parents and her baby sibling. I sat slightly behind the clinician but I felt the family included me throughout the appointment, e.g. smiling and making eye contact with me as well as the clinician when answering questions.
Obs_06	Primary school aged girl with symptoms suggestive of genetic condition. Broad panel test found a variant of uncertain significance in a known disease gene, which was reclassified as causative during the appointment.	Quite a spacious clinic room. Child was brought by her mother and an older family member who came to support the mother. The mother generally seemed to be focused entirely on the clinician while the older family member seemed more aware of my presence.
Obs_07	[details not reported as per participants' wishes]	

Reference number	Context of genomic testing	Reflections on dynamic of the observation
Obs_08	Secondary school aged boy with developmental delay, seen with father. Had a relatively clear-cut clinical diagnosis, the DDD project had identified a variant that had been communicated to the family some years ago as potentially causative, and that was increasingly thought to be the cause of his delay.	Small clinic room and a very hot day. Young person and father sat across the edge of the desk from the clinician. I was at the back of the room. The appointment felt quite relaxed, the father seemed very engaged and interested in the discussion but it didn't seem emotionally 'charged'. I felt included throughout the appointment with smiles and eye contact.
Obs_09	Preschool aged boy with congenital anomalies, seen with parents. Taking part in 100,000 Genomes Project as a trio, project had identified a possible causative variant in a known disease gene, but the child's clinical features were somewhat different to the health issues typically experienced by people with the disease associated with the gene.	Fairly spacious clinic room. Child and parents sitting to side of clinician's desk, I was sitting in a chair at the back of the room. The parents seemed entirely focused on the clinician throughout almost the whole appointment and the child was very quiet. For much of the appointment they seemed barely aware I was there.
Obs_10	Secondary school aged boy with learning difficulties, seen with parents. Taking part in the 100,000 Genomes Project as a trio, project had identified a variant of uncertain significance in a gene associated with a developmental disease, but this was thought unlikely to be relevant to the child's health issues.	Medium-sized clinic room. Young person and parents sitting to side of clinician's desk. I was sitting slightly behind and to the side of the clinician. The parents seemed very interested in the discussion and the father asked lots of questions clarifying how their son's data had been analysed. The atmosphere felt calm and purposeful.

6.3.2 Themes identified from observing clinic appointments

Here I discuss key themes relating to ways in which genomic results appeared in the context of clinic observations.

6.3.2.1 *'It's like a jigsaw puzzle': genomic variations do not stand alone as results*

During many appointments it was clear from the discussions that genomic variations need situating within a clinical context. Clinicians frequently conveyed an impression that it is often hard to know what to make of a genomic variant in isolation, but by considering how a patient's clinical features and medical history might relate to it, and in exploring how and whether the variant tracks through a family, some idea might be reached as to its medical importance.

In one appointment that I observed, a variant's status changed from being of uncertain significance, to being likely pathogenic, within the course of the appointment. In explaining this to the family, the clinician discussed that *'it's like a jigsaw puzzle – does everything fit together well enough?'* She explained the reasons why she thought this variant was responsible for the child's health problems, in turn transforming the family's view of the variant. At the start, the mother had asked *'I don't think she's got [syndrome], has she?'*. By the end, she commented that *'it pretty much links everything'* and another family member said that *'it's not nice to know that she's got it, but it's nice to know that it's all one thing'*.

Clinicians often took opportunities to prepare patients and families that additional information, over and above variations found in the genetic code, might be necessary to create meaningful results. In one appointment with a family who had been waiting several months for a result, the clinician explained that it was still helpful to have had the appointment because *'if testing gives us a result that is useful I can interpret it having met [the child] recently'*. She also suggested collecting samples from the parents because *'we may need blood samples from you and from mum because I think that might help us understand the results when they come back'*. In another appointment, a clinician said to a family that *'we suspect this muscle protein genetic change might be what's causing [child]'s*

difficulties but we can't be sure', with the child's mother then acknowledging that 'we need the muscle biopsy and dad's sample to add it all together'.

The role of parental samples in the result construction process seemed a potential source of confusion. For example, on a few occasions, when clinicians mentioned that parental samples might help in interpreting a genomic variation, parents would make comments like *'so we can see where the condition has come from'*. Clinicians usually went on to clarify that parental samples were often most helpful in demonstrating the absence of a variation in either parent:

Clinician: *Before we start moving on with this, let's get your check and dad's check back as if either of you have it then we're wrong.*

Mother: *Why?*

Clinician: *If this genetic change is present in either of you, and you don't have the condition, then it can't be causing the condition.*

Mother: *And then it's kind of starting again.*

Clinician: *Exactly.*

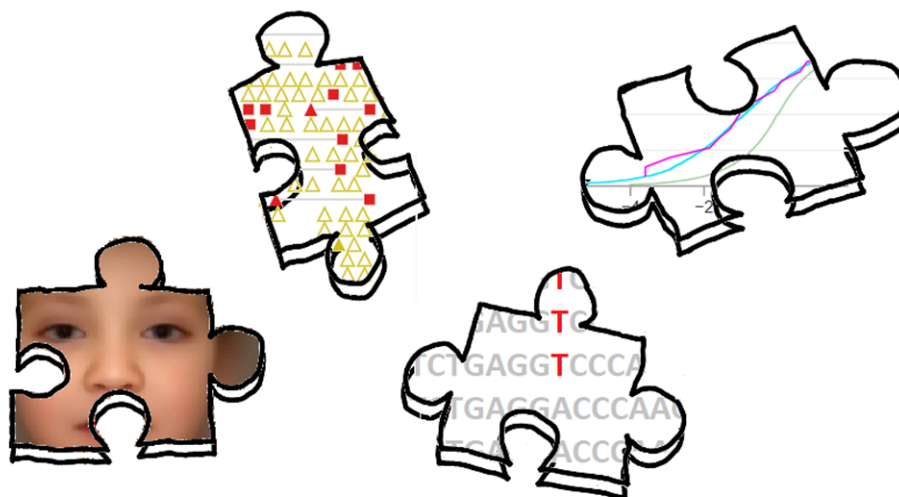
In one appointment I observed, the mother, attending clinic, had already provided a blood sample to facilitate interpretation of a variant in her child, but the father, who was not present, had not agreed to provide a sample. The mother explained that *'I told him it's to try and find out where [child's] condition has come from'*. I was curious as to whether the father had perhaps interpreted this as meaning that samples might be used to blame a particular parent for a condition arising in a child, rather than to dismiss a genomic variation as a likely cause of symptoms.

In another appointment, a misunderstanding as to how and why parental samples were needed had meant that the process of genomic result construction had so far been ineffective for the family. This came to light when the mother asked, partway through an appointment discussing a genomic test with a 'nothing found' outcome, *'when the genome was looked at, do they look at mine and his dad's too?'* The clinician explored why she had asked this question and it turned out that this was because the father had similar developmental issues to the child, which had not been mentioned at the time of the consent appointment for genomic testing. The clinician explained that *'we do analyse your and your partner's DNA at the same time, but it wasn't registered that issues were present in dad too – filtering won't have worked here, we need to re-jig that'*. They went on to clarify that *'[variants] from dad will have been filtered out. We need to re-run it'*.

Clinic appointments were a setting where a variety of strands of evidence were brought together to appraise genomic variation in the context of a person's life. Genomic results might occasionally be constructed in the moment with the addition of important new 'pieces of the puzzle', beyond the mere identification of a plausible variant (see Figure 9). But for the most part, genomic results were discussed in a way that made them appear more nebulous, elusive and uncertain.

Figure 9: A sequence variant is one piece of the puzzle – what more is needed to make a picture? Who decides when the picture is clear enough?

Puzzle pieces from left to right show: composite facies of child with Kabuki syndrome from <https://fdna.com/health/resource-center/kabuki-syndrome/>; ClinVar sequence variants in KMT2D screenshots from Decipher; fictitious KMT2D variant based on Ensembl sequence; growth chart of children with KMT2D variants screenshots from Decipher.



6.3.2.2 *'It's all very well saying to someone we'll sequence all your genes, but if we don't know what they do or what they mean...': shared ideals versus 'real' results*

In several of the appointments I observed, clinicians and families appeared to implicitly share a vision of genomic results as being 'supposed' to be clearer, more helpful, more definitive, than they had in practice proved to be. Frequently, appointments involved explanations as to why a family's experience of genomic testing had fallen short of their hopes: why a child remained undiagnosed despite 'whole' genome testing; why no-one knew whether a variant identified through testing was medically important or not; why a probable genomic diagnosis added very little to our understanding of a child's likely future.

Clinicians often went into significant depth with families to explain why interpreting genomic variation was so challenging. I got the impression that while many families were very experienced in living with uncertainty, it was often really important to them to understand why things remained uncertain. They needed to be sure that uncertainty

persisted because current knowledge around genetics meant that clear answers were not possible, rather than because they had not asked the right questions or seen the right people.

Clinicians often contextualised this for families by discussing the wide range of natural variation in the genetic code. For example, one clinician explained that *'if you look at anyone's DNA in detail, you will find around 20,000 variants that don't match a standard pattern'*. Another clinician described that *'we're looking for an alteration that's a bit different to what we usually see, and that's quite hard, because our DNA is all a bit different and that's why we're different to each other, so we're looking for something that's so different that it will cause a problem'*. The complexity was further emphasised by reference to the potential difficulty of identifying relevant variants: *'you can think of genes as being a bit like encyclopaedias, and genetic changes can be as subtle as one change in an encyclopaedia – it's quite an undertaking to read them all through'*.

Clinicians also explained that as well as variants being uncertain, the role of genes themselves might also be uncertain: *'we each have around 23,000 genes, but only 8,000 that we're fairly sure of, so lots where we don't really understand yet what they do'*.

Conversations sometimes reflected how research was changing our ability to understand genomic variation. For example, one clinician described how whilst the Deciphering Developmental Disorders project and the 100,000 Genomes Project were ongoing, *'this [gene] came up as a developmental gene'*.

Clinicians sometimes reflected the frustrations of being limited by current knowledge when trying to construct results from the genetic code. To one family seen with a variant of uncertain significance in a newly-identified developmental gene, a clinician acknowledged

that *'it's all very well saying to someone we'll sequence all your genes, but if we don't know what they do or what they mean...'*. They reassured the family that efforts were ongoing to reach clarity: *'we trawl as much as we can, in any site that we can'*. They went into great depth with the parents regarding efforts to become clearer on the clinical relevance of the variant, for example showing them a diagram of the protein the gene coded for and marking where their child's variant was relative to other variants that were thought to cause health problems. My impression was that the family found this really valuable – in knowing why clinicians could not give them certainty as to whether the variant was medically relevant for their child, the ongoing question mark over its meaning appeared easier for them to accept.

Sometimes conversations reflected a learning process for both clinicians and patients as to how results might be identified in the course of genomic testing. For example, in one appointment a clinician asked *'are you one of the families who joined the [100,000 Genomes] project early?'* They went on to explain that they had asked this because *'in the early phase, when we were first consenting people, we told people that their whole genome would be looked at, so all of the genes and the DNA in your body'*. They went on to say that actually *'though the project reads the sequence of all of the genes and DNA, when it comes to analysing results, it pulls down data on known genes'*. In one appointment, parents expressed anger that the 100,000 Genomes Project *'didn't do what they said they'd do'* – they had thought that the testing offered via the project would be a lot more thorough than it was and had been frustrated from seeing via Facebook that several project participants had received diagnoses via a clinical exome, which they felt was able to *'outdo'* the project.

Clinic appointments seemed a site where ‘real’ outcomes from genomic testing clashed against expectations of what ‘proper’ results should look like. Implicit in many discussions was a hope that as on a worldwide basis we learnt more about how to interpret genomic variation, a family’s outcome from genomic testing would grow to more clearly match what a genomic result ‘should’ look like.

6.3.2.3 *‘I’m not going to be able to answer that question for you today’: provisionality in the quest for genomic explanations*

Many appointments involved discussion of uncertain information, and it was notable how often discussions were prefaced by *‘if this is right...’*. It created a strange provisionality where clinicians and family members were engaging around genomic variation that could, if actually the cause of the symptoms that had led them to clinic, in time be the answer to a lot of questions, but could also turn out to be nothing. Where explanations were prefaced with ‘if’ by a clinician, this was not necessarily mirrored in the family’s responses. Several appointments involved in-depth discussion around the hypothetical implications of a genetic diagnosis should it turn out to be correct, with clinicians going into considerable detail while continually reintroducing the idea that it may all prove to be irrelevant.

While as discussed in 6.3.2.1, multiple pieces of information might be important in appraising a genomic variation as a ‘result’, the role of time in maturing genomic results was very evident (see Figure 10). In a couple of appointments, clinicians reflected to families that they were aware they might appear cautious in making a firm genomic diagnosis, but they really did not want to get it wrong: *‘I realise it can be really frustrating for families that we seem so cautious in making a firm diagnosis, but we want to be sure it’s right. I don’t want someone to be seeing [child] in ten years’ time and saying “Really?”’*

Figure 10: How sure will we be this time?

Clinic observations often gave the sense of genomic results as quite nebulous, where variants might drift just below and around the surface. Over time they might drift back down into insignificance, or perhaps spend more time floating at the top, becoming more secure as a 'result'



In other appointments where a variant's status as medically relevant was more secure, there were sometimes still significant elements of provisionality as a 'result' might offer little more than a name, and sometimes even that fell short (echoing findings from some of my interviews – see 7.3.2.2.3):

Clinician: I should warn you that the gene name is not catchy – genes often start being named with letters and numbers and then get catchier names later. The variant we found in [child] is in a gene called [gene].

Mother: That sounds like a robot... it would be nice if they could make a short-handed name for this.

Clinicians referred to a global learning process in understanding more about new disease genes, both explaining current shortfalls in why a new diagnosis might provide little new guidance about a child's future, and offering hope that this situation would change as time went by.

In another appointment, making a secure genomic diagnosis of a comparatively well-recognised syndrome, almost the opposite issue arose. The clinician explained to the family how while the child now had a diagnosis, there were uncertainties as to how it might affect her in the future: *'there's a very long list of things that can go with [syndrome]. But we have to think carefully because the list started to be made before we knew what caused it, so some of the people it was based on might not really have had [syndrome]. The list of things that happen with [syndrome] is a bit like when you read the leaflet in a packet of paracetamol and it tells you everything that could possibly happen'*.

Occasionally, both families and clinicians expressed that outcomes from genomic tests did not, or should not, change things. Where information from genomic tests was expressed as having value, this was often in the hope that this might allow better, more informed care for a child in the future. For example, in an appointment discussing efforts to resolve a variant of uncertain significance, a clinician said that *'I think having an answer might be helpful for [the child] in the long run'*. The mother agreed: *'to know all the stuff we need to watch, just trying to find the best way to help [child]'*. In another appointment a clinician expressed that whilst in theory, having a genomic explanation for a child's difficulties should not always matter, for practical purposes it could be helpful. They commented that *'this may sound funny because of my job, but I don't think it should matter if you've got a diagnosis, I think what should matter are your needs, and you should get help depending on what your needs are. But sometimes if you've got a diagnosis that you can put at the top of your list of needs, it helps to get the support you need'*.

6.3.2.4 *'There seems a lot more on Facebook': family members as interpreters of genomic results*

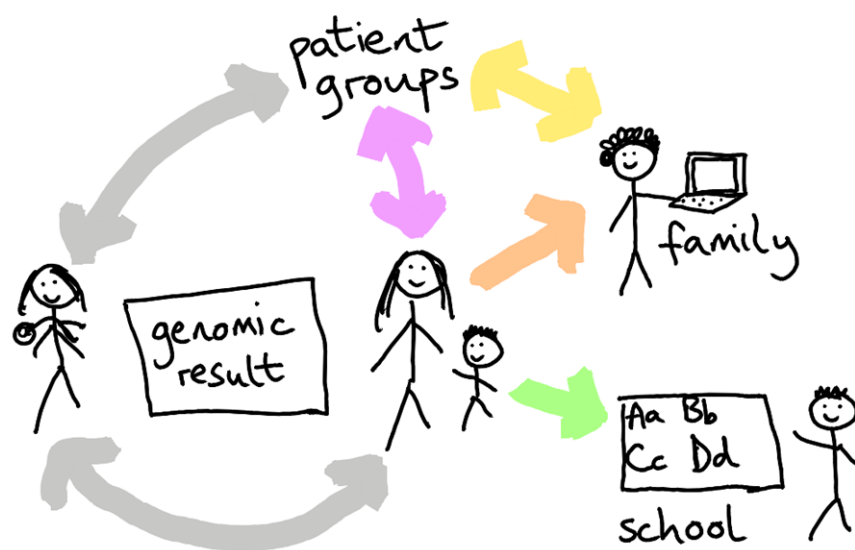
Families attending clinic often expressed a sense of confusion about genetics, with remarks like *'it's very complicated your job, isn't it?'* and *'I think they did tell me about this but I didn't really understand it'*, reminiscent of comments frequently made by Mass Observation Project respondents in relation to genetics and genomics (see 5.3.2). These same people often appeared to me to have a very good understanding of the information that had likely been discussed in previous appointments, based on the questions they went on to ask, and the comments that they made. For example, one father made several comments throughout the appointment about not understanding genetics, but in discussing an uncertain genomic finding asked questions which touched on the need to compare to a reference sequence; the relevance of a variant being *de novo*; the possibility of a causative variant being in a gene that had not yet been analysed; and whether his child's symptoms could represent an extension of the phenotype associated with the gene. This made me wonder whether people expressing a sense of confusion about genetics might have grasped pertinent information from previous appointments, but as this information was often inherently uncertain, they perhaps interpreted the uncertainty as at least in part reflecting their inability to absorb relevant knowledge, rather than as reflecting worldwide uncertainty as to what particular variations in the genetic code meant.

It was often apparent that beyond the appointment I was witnessing, patients and families would go on to share the outcomes of their genomic tests with others (see Figure 11).

Whilst a genomic result might to some extent be constructed within the appointment between a family and a clinician, going forward the family's perception might influence or determine how other people engaged with it. For example, in one appointment where a mother was receiving information about a variation in a newly described disease gene that

was probably responsible for her child's developmental delay, the mother said to the clinician: 'so that's the gene that you found abnormalities in in [child]... and it's a developmental gene. I just want to make sure I've got it so I can tell other people because they'll have lots of questions'. She then mentioned that 'I'm not a massive Googler but [my family] are', implying that in turn her family might construct their own interpretations around the information that she passed onto them from the appointment. In another appointment for a child with developmental delay, a family member had attended specifically so that she could later support the mother by going over any information that the mother had found it difficult to take in during the clinic.

Figure 11: Genomic result construction carries on beyond the clinic – it may go onto be interpreted in different settings and with different purposes



A few appointments positioned family members as having potential interpretative roles in a wider sense – clinicians sometimes spoke to families about the power of patients collaborating to improve broader understanding relating to variations in new disease genes. This was usually in response to questions from parents as to how understandings about their child's genomic result were likely to advance over time. In one appointment, a

clinician explained how *'things sometimes happen very quickly when parents get together'*, and gave the example of a very recently described genetic condition where some of the first families to be diagnosed had set up a foundation connecting families, clinicians and researchers across the world and catalysing research into the condition.

Families were clearly weighing up information from a variety of sources as they built 'results', such as they were, into the context of their lives. In one appointment for a boy with a variant in a recently described disease gene, the clinician described how there were 50-100 people in the medical literature with variants in the gene and the father commented *'there seems a lot more on Facebook'*. The clinician reflected on the benefits of such groups, commenting that *'the data that we've got are from the published [papers reporting on] patients – you may be able to get more on the Facebook group'*. The father discussed how his child had a health problem not described in the medical literature as associated with the disease gene, but that other children in the Facebook group had been affected by, and the clinician commented *'it might be that that's something that's still to come as time moves on'*. However, it was clear that while there were great benefits to families sharing information it could also be challenging to navigate, with the father describing that *'sometimes when we read on Facebook it can be hard to know if that is [gene] or something different'*.

6.4 Summary

As regards my research question 'What sorts of features do genomic results appear to have in clinical settings?', from observing clinic appointments, I got the sense that result construction within the clinic appeared to work differently to processes often prominent in popular discourses (3.4 and 4.4). Rather than shouting out from the genome sequence, outcomes of testing were sometimes uncertain and their description as [positive or

negative] 'results' seemed perhaps too binary. Evidence might be being cobbled together around particular genomic variations in an attempt to nudge understandings of their significance up or down, and sometimes this process was fast and powerful, but often, ideas around the medical importance of variations appeared to be slowly evolving over time.

Bowker and Star discuss that classification schemes can be Aristotelian or prototypical. Aristotelian classification works according to a set of binary characteristics that the object being classified either presents or does not present (for example 'does it bark? Does it have fur?'). Prototypical classification works by the classifier having a broad idea in their mind as to what something is, and extending this picture when trying to decide if a given object counts as that thing (for example 'does it look like my idea of a dog?'). Bowker and Star argued that *'medical classification systems are 'naturally' prototypical... they nevertheless have to appear Aristotelian to bear the bureaucratic burden that is put on them. This burden is to act as a gateway between the worlds of the laboratory and the hospital (with precisely defined, closed environments) and the workaday world'* (142).

I think that this concept applies to genomic result construction: many of the guidelines used in classifying genomic variations are expressions of an expectation that genetic variations should be classifiable according to a set of precisely-specified questions (i.e. they should be amenable to Aristotelian classification). Currently, many variations fall between the gaps (for example, variants of uncertain significance), but this is perceived as a technical problem that could in theory be fixed by developing an ever-better list of classifying questions, and by improved technical genetics knowledge (for example, larger databases of genetic variation). In contrast, many of my clinic observations indicated that prototypical methods of classification were important in construction of results. For example, a clinician might

draw on their expertise and experience to consider questions like ‘does this child remind me of other children I have met with this particular syndrome?’, or ‘does this genetic variation tie in with the patient’s symptoms, family history, and other investigations, such that overall I think it explains what has happened?’

From experiences of attending national genetics meetings, it seems that clinical impressions regarding the significance of genomic variations are often highly valued by scientists, and seen as proxy to the ‘truth’ of a link between variation and diagnosis. For example, at a Deciphering Developmental Disorders project annual collaborators’ meeting, DDD researchers discussed the importance of annotation of genomic variations by clinicians regarding pathogenicity and contribution to phenotype, explaining that they used these to further refine their filtering algorithms and results construction processes. The researchers aim for the variations they report to align as closely as possible with those that clinicians are labelling as medically relevant, reflecting a belief that clinical opinion is a closer proxy to a ‘reality’ of whether a variant is medically important, than the flagging of a variant as potentially relevant by a research algorithm.

Variant classification criteria are shifting in recognition of this. For example, in 2015, the ACMG guidelines included ‘Patient’s phenotype or family history is highly specific for a disease with a single genetic aetiology (PP4)’ as ‘supporting evidence’ for pathogenicity(24) – a weak tier of evidence that would need to be combined with multiple other ‘stronger’ sources of evidence to be able to assign a variant the status of ‘likely pathogenic’. In contrast, the 2024 ACGS guidelines allow use of the PP4 evidence criterion at a moderate or strong level in some circumstances, after MDT discussion(25). These guidelines include a supplementary table giving examples of scenarios that might provide supporting,

moderate, or strong evidence, still subsuming clinical opinion within a wider Aristotelian classification framework but giving it more weight.

Clinic appointments appear as a site where prototypical classification takes place, clashing with expectations that Aristotelian classification systems are sufficient to neatly produce robust genomic results. The 'genomic results' encountered in clinic sometimes seemed murky and tentative, to the point where I was often unsure whether to describe them as results in writing about them. It was also clear that results continue to be interpreted and reinterpreted well beyond the confines of a clinic appointment- they might be shared through a family, with school, with many health or education professionals, and perhaps with communities of people living with similar results. Yet as regards my research question, 'What features do people imagine genomic results as having?', there was often a sense that results should be more than this – an implicit shared idea that clinicians and families both appeared to hold that in the fullness of time, genomic results would give clear and impactful answers, which tallied more with prevalent representations of genomic results in stock image banks and UK news items.

Connecting to my overall research question, 'how should we construct genomic results?', my clinic observations indicate a frequent mismatch between ideas around genomic results prevalent in popular discourses, and genomic results as they appear in a clinical context (if we define a result as being the outcome of a genomic test). This reinforces why setting expectations around genomic results should be a central aspect of consent conversations relating to genomic tests, potentially with particular focus on the possibility of uncertain or non-diagnostic outcomes, as these aspects of genomic results may not be well represented elsewhere. It also indicates potential benefits of widening our concepts around genomic results to encompass those with a provisional or tentative nature. If we stick with a concept

of genomic results as being powerful, illuminating and highly deterministic, many of the results encountered in my clinic observations are positioned as relative failures. A more rounded concept of genomic results that embeds these possibilities from the start could bolster the robustness of consent for genomic testing, and might allow easier and more positive discussions around inherently uncertain outcomes.

6.5 Reflections on this facet

Prior to this project, I had observed many clinic appointments with the purpose of learning how to deliver clinical care: this facet offered a really interesting and helpful opportunity to examine clinical consultations from a perspective that was very new and different to me. It was challenging but also very eye-opening to shift from focusing on improving my clinical skills in interpreting, contextualising and communicating genomic information, to instead questioning its nature. My positionality as a clinical genetics registrar meant that in some senses I was an ‘insider’ - well used to being part of clinical consultations involving genomic tests and their outcomes- but I was an ‘outsider’ too⁽¹⁴³⁾: I have never myself been a patient in a genetics clinic or had a genomic test.

I was physically present in the room throughout appointments where people had agreed to take part, and all participants knew I was interested in how genomic tests and their outcomes were discussed, so this had scope to influence the conversations that happened during some appointments. However, I do not think this undermines these observations as an investigative facet- I was not seeking to gain quantitatively representative information on how genomic results might currently be discussed, but to generate ‘flashes of insight’ that might inform my ideas as to their nature and how they might be thought of⁽⁹²⁾.

'Facets can ... be very different shapes and sizes, and some might be very small – there is no predefined minimum size for a facet, because it is always dependent on the particularities of its line of investigation and hence its methodological-substantive plane'(91). Observations offered a different lens to the other facets of my study in allowing the opportunity to see constructions around genomic results in 'real time'. Families and clinicians explored technical genomic data in light of the symptoms a child had experienced to determine what meaning a particular genomic variant might have in that context, and this constituted a very rich opportunity to generate and analyse data. This allowed me to crystallise some of the issues around genomic results that had bothered me in clinical practice, and helped me to shake some of my assumptions around them to try to see them in a new way.

As regards the breadth of this facet, all the appointments I observed had a child/young person at their heart. This was not my initial aim, partly because at the outset of this project I had a much more quantitative perspective and aspirations to observe a 'representative' sample – an epistemological perspective which I have since moved away from. Observation of appointments involving adult patients might have given me different insights, but in many ways I think observations focused around children and young people having diagnostic genomic testing are strategically very useful in bringing the facets of my project together to emphasise the extent of the clash between genomic results as portrayed in popular discourse, and genomic results as encountered in the clinic. Diagnostic testing of an unwell child has historically been the paradigm for use of genome sequencing in healthcare- the quintessential setting in which you might expect to find powerful, transformative results. But as my observations show, even here, genomic results often appear to have a more complex, subtle and evolving nature.

More broadly, this facet helped me re-orient myself as a 'researcher', and the experience of sitting in clinic trying to notice and question my (many) previous assumptions around the nature of genomic results, while also attempting to be open to thinking of genomic results in new ways, was unsettling but very useful. The frustration I had previously experienced as a clinician with brokering genomic results that seemed to offer very little will almost certainly have made me readier to notice and put weight on situations where genomic results seemed unclear or provisional during the appointments I observed. However, I think situations where genomic tests fall short rarely get the attention they deserve in public narratives around genomics (Chapters 3 and 4) and as such I was keen to explore them here.

7 Ideas around genomic results arising in interviews with people experiencing genomic tests

This facet was designed to inform my research questions ‘What features do people imagine genomic results as having?’ and ‘What sorts of features do genomic results appear to have in clinical settings?’ Through interviewing people who were experiencing genomic tests, I hoped this facet might serve to show how different concepts of genomic results coalesce. I sought to explore people’s ideas around the potential of genomic results in general and their expectations regarding the test they were having in particular, the parameters that others (project staff, clinicians) might have set as to what sorts of outcomes to expect, and sometimes what it had really been like to receive findings. My aim was that this would offer insight on my overall question, ‘how should we construct genomic results?’, by showing intersections between abstract ideas of and lived experiences regarding genomic results. This could provide an opportunity to consider which ideas had resonated with the results people might be grappling with (or still waiting for) in practice.

The chapter begins by discussing my rationale for including interviews with people experiencing genomic tests as a facet. I then outline practicalities of data generation and my analytic approach, before discussing my results.

7.1 Rationale for interviewing people experiencing genomic tests

Mason writes that *‘you may choose qualitative interviews if your view of the ways in which social explanations and arguments can be constructed lays emphasis on depth, roundedness, nuance, contingency, complexity, ambivalence, and even discordance in data and argument, rather than seeking an understanding of supposedly coherent surface*

patterns and trends'(91). I thought that talking to people who had considered genomic testing and navigated its outcomes would be a useful strategy, allowing me to generate *'flashes of insight'* and *'trouble existing categories'* in line with my overall facet methodology strategy(92). Conducting qualitative interviews provided the opportunity to take a flexible approach to exploring lived experiences of genomic results and test how they appeared against prevalent ways of thinking about genomic results that I had encountered in the other facets of my project.

Kvale discusses epistemological issues of interviewing, contrasting metaphors of the interviewer as a miner or a traveller. With the former, *'knowledge is understood as buried metal and the interviewer is a miner who unearths the valuable metal. The knowledge is waiting in the subject's interior to be uncovered, uncontaminated by the miner'*. With the latter, *'the interviewer is a traveller on a journey to a distant country that leads to a tale to be told upon returning home ... The interviewer-traveler, in line with the original Latin meaning of conversation as "wandering together with," walks along with the local inhabitants, asking questions and encouraging them to tell their own stories of their lived world ... The potentialities of meanings in the original stories are differentiated and unfolded through the traveler's interpretations'*(144). The 'traveller' metaphor more closely matches my epistemological position as regards this facet of my study, positioning interviews as *'a production site of knowledge. Interview knowledge is socially constructed in the interaction of interviewer and interviewee. The knowledge is not merely found, mined, or given, but is actively created through questions and answers, and the product is co-authored by interviewer and interviewee'*(144).

7.2 Methods

7.2.1 Recruiting people experiencing genomic tests

I aimed to recruit people over 16 years old who had been offered genome testing in a healthcare context or who were supporting someone who had. I asked collaborating healthcare professionals in UK Genome Medicine Centres to help identify potential participants and provide them with participant information sheets about my research and an expression of interest form (see Appendix 11.8 for recruitment materials). I adopted a purposeful sampling strategy aiming to ensure that the cohort interviewed covered a range of age groups, gender, and reasons for having a genomic test (including people having testing to help interpret a family member's test).

7.2.2 Generating interview data relating to genomic tests

I undertook a mixture of face-to-face and virtual interviews. At the outset of my project I offered both options so participants could choose whichever suited them best. In practice prior to the Covid-19 pandemic everyone opted for face-to-face interviews, which I did at participants' homes or their local NIHR Clinical Research Facility, depending on participant preference. For a while during the Covid-19 pandemic I only offered virtual interviews via an online platform as there were legal restrictions around face-to-face meetings. As restrictions lifted, participants continued to choose virtual interviews: this may reflect that I had shifted to presenting them as the default option, partly as I was aware some participants might be particularly vulnerable to becoming seriously ill with Covid. Provided participants were happy for me to do so, I digitally recorded the interview.

I used an interview guide (see 11.8.3) to aid discussion, which I initially developed based on my previous clinical experience and in discussion with my supervisors. Regarding qualitative interviews, Mason writes that '*you may want to give maximum opportunity for the*

construction of contextual knowledge by focusing on relevant specifics in each interview.

One way to do this is to ask people to talk through specific experiences in their lives rather than, for example, asking them what they “would do” ... under certain circumstances’ (91). I

tried to follow this advice where possible though in practice, my interviews often involved a fusion of the two. Project participants had all been involved in decisions around having a genomic test, and many had received results of sorts (though sometimes ‘nothing found’), and on these experiences they were clearly in a position to provide very specific insight. However, my interviews also involved talking through more abstract issues such as what *could* be sought from genomic testing, and while I learnt a lot from our discussions, I think people’s direct experience of genomic tests turned out to be less relevant to these questions. It was interesting how much these more abstract concepts of results turned out to overlap with those showcased in other areas of my project – see Chapters 3, 4 and 5.

During my interviews, I followed up on unexpected or interesting answers that related to genomic results as they arose, rather than adhering strictly to my interview guide. I continued to develop the guide over time as preliminary analysis or other conversations around my project led to new questions. Following each interview, I made notes describing the context of the interview (e.g. where it was, who else was present in the background), my initial reaction to the interview, and the key points that I felt had arisen from it regarding how genomic results might be conceptualised.

7.2.3 Analysing interview data relating to genomic results

I thematically analysed the interview data (see 5.2.2.1 for a very brief overview of thematic analysis). As my interviews primarily sought to shed light on the issue of how, why and when variants might be valued as being results, on which I have a constructivist epistemological position, I was attracted to an artfully interpretive approach to thematic

analysis particularly in view of its suitability to '*disrupt and critique taken-for-granted certainties*'(135). However, I also aimed to give a flavour of the diversity of possibilities people encountered from their genomic tests, which on some level aligns closer with a scientifically descriptive orientation in assuming a reality that I can try to accurately represent (though this will still be inherently interpretative as my ideas and feelings on this issue will have influenced the questions I asked, the ways in which I asked them, and the aspects of participants' responses I was most inclined to notice).

As with my analysis of Mass Observation Project responses (5.2.2.2), my analytic strategy therefore aimed to sit somewhere between the two camps: for the most part a bit closer to the artfully interpretive approach, but for the section where I describe outcomes participants experienced (7.3.2.2) aiming to draw on aspects of a scientifically descriptive approach in going back and forth between my write-up and my interview transcripts to try to ensure that my descriptions closely reflected what I understood people's 'real experiences' to be.

From a practical perspective, following each interview I listened to the audio recording and transcribed it. I created 'thin' transcripts(145) (i.e. I tended not to describe aspects of speech like tone of voice, pauses, gestures, unless I thought noting them was necessary in order for my transcript to convey the sentiment of what the participant was saying (e.g. something being said in a sarcastic tone of voice)). This process helped me to become very familiar with the data. Once I finished transcribing a particular interview, I listened again to the audio recording whilst reading through the transcript to ensure it was representative of my interview such that it was suitable for ongoing analysis.

I then uploaded transcripts into NVivo v15 and read through them repeatedly, developing (primarily descriptive) codes to bracket together relevant data (for example, 'having additional findings'). As I coded more interviews I thought about how to organise the data into themes- for me this process was enmeshed with the process of writing up, as I would have an idea for a theme, try to write it out, and find that it did not quite fit. When this happened, I would reconsider the theme, discarding it or adjusting it depending on the extent of the disparity. As I honed in on themes I felt convinced by, I looked again across the dataset in light of these, trying to decide whether the theme did the data justice, and seeking counter-examples to challenge or elaborate the theme. (11.8.4 aims to show how I organised some of my codes into a theme).

As I got further into my project, I also examined the interview transcripts in light of insights I was gaining in other areas regarding, for example, how genomic results were being discussed in UK news items, or how genomic results appeared to be thought of by respondents to the Mass Observation Project (see 11.3.2 for timeline). I went through the transcripts noting where participants had expressed similar expectations or experiences regarding genomic tests to those developing in other facets of my project, and looking for areas of difference. I also noted where people were speaking to theoretical expectations from genomic testing, and where they were discussing the outcomes that they had experienced, considering how these aligned. In exploring the lived experiences of people navigating genomic tests, in combination with constructions of genomic results identified in other areas of my research, I aimed to reflect on how and why common ways of thinking about genomic results might be helpful or unhelpful to people considering or embarking on the process of having a genomic test.

7.3 Results

7.3.1 Details of interviews

I undertook 15 interviews with 18 people going through genomic testing (12 were with sole participants, 3 were joint interviews with couples). 7 were in-person at participants' homes; 2 were in-person at a Clinical Research Facility; and 6 were virtual over Microsoft Teams. In terms of the depth and quality of the data I ultimately generated that related to genomic tests and their outcomes, I did not feel there was much difference between the settings. However, for me the experience of interviewing felt very different.

My intention in offering to travel to participants' homes was to make it as easy as possible for them to take part in my research if they wanted to, and everyone I interviewed was extremely welcoming and hospitable, but when it came to it, going into people's homes and asking them questions felt surprisingly intrusive. I did not have this sense for the in-person interviews I did in the Clinical Research Facility though I think I asked comparable questions, and I wonder whether this discomfort related to going outside of clinical spaces and seeing context around people's lives that I would not ordinarily be aware of.

In contrast, my virtual interviews felt like less of an imposition on participants, but the interviews tended to feel more 'business-like' and while usually at the start and end of interviews we would have some general discussion around how our days were going etc, there was a superficiality and brevity to this that felt different to my in-person interviews. Weller analysed 'greetings and leavings' between face-to-face and online interviews and described how: *'[for face-to-face interviews], reflection documented in field notes did log in relative detail the nature of pleasantries, small talk, and the exchange of hospitality. These notes served to highlight their absence during the remote interviews. Rather, the initial focus in the internet video calls was on ensuring a good quality video connection'*(146). My

experience very much echoed this. The sense that an interviewee could end the call or step away from the screen made the process of asking questions feel less ‘charged’ for me.

My interviews typically lasted around an hour, with two being much shorter as participants had to leave for other commitments. I recorded and transcribed all except one, where the participant was happy to talk to me for the purposes of informing my project, but preferred not to be directly quoted or recorded. Table 11 gives brief details regarding why participants were having genomic tests and some context around my interviews. In the table, I have also included a quotation from each interview regarding experiences or ideas around genomic results and their generation. These are not intended to represent a participant’s overall view regarding how to construct genomic results, but to give a flavour of some of the more strongly felt ideas, concerns and experiences they brought to the question. Figure 12 aims to give an idea of the sorts of results interviewees had experienced.

Table 11: Interviews with people experiencing genomic testing

Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Ashley	<i>‘I didn’t mind it was going to take a while if it was going to look for every possible spelling mistake. I felt like we couldn’t do any better, when in reality that wasn’t true... We kind of felt that someone would go in with a metal detector and look for them.’</i> Ashley was taking part in the 100,000 Genomes Project and DDD to investigate her young child’s severe developmental delay. She had recently heard that the project had identified a variant of uncertain significance for her child in a newly described disease gene. Ashley was connecting with others going through genomic testing via social media. I interviewed Ashley in her local Clinical Research Facility following a medical appointment- we only had 20 minutes as the appointment had run late and she was going to an event. Ashley was very open in sharing her experiences and her frustrations around how genomic testing had served her family.

Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Thomas and Linda	<i>'...they've now identified [a possible genomic diagnosis for our child] not because there <u>is</u> a change in the marker, but because they found children who have a common thread of that marker being changed.'</i> Thomas and Linda had joined DDD around ten years ago to investigate their (then preschool-aged) child's moderate learning difficulties. The project had recently reported that their (now teenage) child had a possibly disease-causing variant in a newly described disease gene. Linda had had some professional involvement with medical research before having children. I interviewed them at home in their living room for around 65 minutes. Their child joined us briefly on a couple of occasions as her school was unexpectedly closed on the day. Thomas and Linda felt engaged in the discussion and it didn't feel like any aspects were particularly emotionally charged for them.
Richard and Barbara	<i>'It's a no-brainer, really. What's the point in <u>not</u> knowing?'</i> Richard was taking part in the 100,000 Genomes Project as a singleton, to explore progressive muscle problems that had started to affect him as an older adult. Preliminary analysis was 'nothing found'. Richard was a retired emergency services worker whose main motivation for having testing was helping his children and others in the future. I interviewed Richard, joined by his wife Barbara, in their living room at home for around 45 minutes. For lots of the interview I felt like I was trying to generate controversy when there wasn't any. Later I discussed the transcript with colleagues and we wondered whether at points where I was intending to discuss the interpretation of genomic data, Richard was understanding my questions as pertaining to the act of having a blood test (this issue formed an aspect of a paper I contributed to discussing the immortality of genomic data(147)).
Carol	<i>'I was <u>amazed</u> because I just have visions of these <u>thousands</u> of genes being sifted through, you know, and to think they've <u>found</u> one!'</i> Carol had taken part in the 100,000 Genomes Project aiming to find a diagnosis for her adult child, who has learning difficulties and problems understanding social boundaries. The project had identified a syndromic cause. Carol was retired but had professional as well as personal experience of supporting children with special educational needs. I interviewed Carol at home in her living room for about 70 minutes. She seemed very interested in the questions and was very happy to share her experiences and reflections.

Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Diane	<i>'If you say <u>genome</u>, then... the world's your oyster, kind of thing. Because somebody else could come along in ten years' time and say, "Gosh there's all this data here, let me go through it and let me have a look at it" and find something completely different. Another <u>mind</u> on it might do anything.'</i> Diane was taking part in the 100,000 Genomes Project to explore her (independent adult) child's health problems. Diane thought a genetic cause might have been found for her child's health problems but no results had been directly communicated to her. Diane had formerly worked in healthcare and been involved in a charity supporting families experiencing similar health problems. I spoke to Diane at home in her living room for around 65 minutes. She was very interested in my project and talking about her experiences, though I found it quite complex deciding in the moment what questions it was appropriate to ask her given that she was primarily having a test on behalf of her child who was an independent adult.
Jason and Steph	<i>'Be prepared for all possible outcomes, because... you may get nothing, you may get something confirmed, but you <u>might</u> get something, that's hidden in your genes or in your child's genes, that is <u>significant</u> and on top of what you already are dealing with. So I guess that would be my advice, is, just be prepared for all possible outcomes from genetic testing, because there's 21,000 genes and... they code for stuff.'</i> Jason and Steph were taking part in the 100,000 Genomes Project to investigate why their child had hearing loss. The project had identified variation of uncertain significance which if pathogenic, would explain their child's deafness but would also predict future sight loss. Jason had a scientific background; Steph described herself as a '<i>total non-sciencey person</i>'. I interviewed them in their living room for around 75 minutes. Their preschool-aged children were present but mostly occupied colouring and playing with toys. Jason and Steph seemed really engaged with my research although I was quite cautious when asking questions around the specific results of their test as I was worried about opening up more uncertainties.

Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Harry	<i>'I think that's what the future will be. I think people will go in and get... just get a blood test. And it'll go through the machine and then the doctor will go, "Well, you've got this this this this coming your way. So, you know, that's it. You deal with it how you want, but this is where it's at".'</i> Harry was taking part in the 100,000 Genomes Project to investigate a personal history of cancer on the background of a strong family history of a different type of cancer. He had had a letter saying nothing had been found as yet. Harry worked in the entertainment industry and was very motivated by a hope of helping others. I interviewed Harry for about 65 minutes in his local Clinical Research Facility. He seemed very interested in questions around how to make sense of genomic data, hugely supportive of research in general, and very happy to share his perspectives and experiences.
Eric	<i>'I didn't think they'd find it. You know, I thought it would go on for years and you wouldn't find what it was ... And when they come back and they said they'd found it, I was sort of, well, I was stunned, really. I was like "bloody hell, can't believe they've done that". It's brilliant that they would do that and know exactly what it is, what's been causing the problem.'</i> Eric was taking part in the 100,000 Genomes Project to investigate his personal history of prostate cancer on the background of a very strong family history of multiple other cancers. The project had found a variant linked to a cancer predisposition syndrome. Eric was retired and had previously worked in sales. He was in poor health and undergoing cancer treatment. I spoke to Eric for around 70 minutes in his living room at home. A few moments of the interview touched on some very sad experiences Eric and his family had been through, and throughout our discussion the drive Eric felt to protect his family was very evident. Towards the end of the interview we were interrupted several times by phone calls and for the last couple of minutes Eric's young grandchild was in the room watching TV.

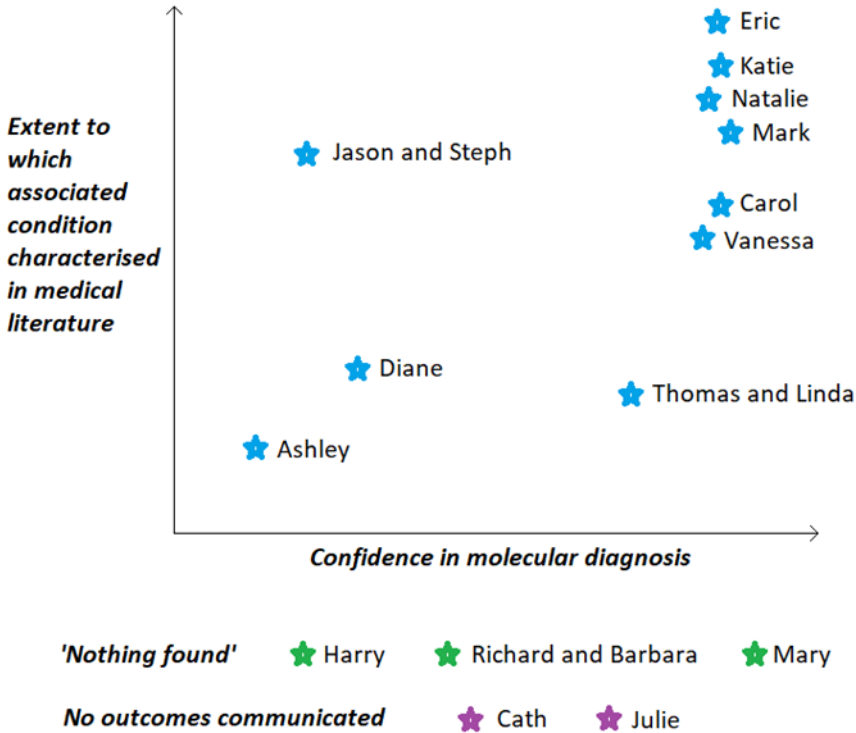
Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Mary	<i>'It is what it is. It's black or it's white, isn't it? I think. You know, it tells you... well, it tells you what it is, doesn't it? So how can that be a grey area? That's black or white. You know, like with the X and the Y, it tells you what it is, doesn't it?'</i> Mary was taking part in the 100,000 Genomes Project to investigate her young child's multiple medical problems. She had received a letter to say nothing had been found as yet. Mary was juggling full time work alongside caring for her child, and also had health problems of her own. She had agreed to genomic testing in the hope it might help her child or someone else, but saw it as peripheral to her child's care. I interviewed Mary for around 45 minutes in her kitchen at home. Her young child was there throughout but distracted by watching her tablet. Mary seemed generally relaxed and happy to discuss her experiences.
Julie	<i>'Anybody who's sort of learning, and pushing the boundaries, and trying to find out more about how we can treat some horrible things with genetics, is, you know, it's quite... quite mind-blowing to us non-medics. Yeah, just to be able to look at a piece of code and to be able to, you know, stop certain diseases or certain physical traits and things like that happening, I mean it is mind-blowing. So yes, I'm very happy for my data to be involved in that.'</i> Julie had joined the 100,000 Genomes Project around the time she had surgery for breast cancer. She had not received any 'results' from the project. Julie saw medical research as having played a part in saving her life, and felt a strong responsibility around contributing her data to it. Another motivation was the possibility of finding information useful to her children. I interviewed Julie for around 50 minutes over Microsoft Teams – my first interview since having a baby and the start of the Covid-19 pandemic. Julie seemed very open to discussing and reflecting on her experiences. Perhaps because of the virtual setting, the character of the interview felt a bit more focused and business-like than some of my previous interviews.

Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Cath	<i>'Well, it's like, would you like to know that you're going to die tomorrow? Would you want to know today, that actually you're going to get run over and killed by a car tomorrow? Would you want to know? You know, I mean... that's just an analogy. And, alright, your genetic map, I'm not saying it's quite as final as death. But it's just an idea of... it's telling you stuff, that you don't need to know. You need to breathe and eat and sleep, but you don't need to know your genetic map.'</i> Cath was taking part in the 100,000 Genomes Project as she had had bowel cancer. She had not received any 'results' from the project. Cath had adult children and over the years had worked in a variety of sectors. She had been interested in 'nature nurture' debates throughout her life. I spoke to Cath for around 55 minutes over Microsoft Teams. I enjoyed the interview and I think Cath did too but it made me reflect on my technique as when I was trying to explore ethical issues I got the sense Cath maybe felt quite personally challenged, or that there was a 'right' answer I wanted from her.
Katie	<i>'I looked at it from one perspective, "OK, fine it helps somebody else". Not once did I think that filling out [a form to permit additional research] would mean that they would come back to me and say "<u>oh</u>, you know, you're misdiagnosed" ... I felt like my medical world was turning upside down at this point, <u>again</u>.'</i> Several years ago, Katie had taken part in a diabetes research study which had involved broad genetic testing, and this had led to her being diagnosed with a mitochondrial form of diabetes (which has a wide range of health consequences beyond diabetes). Katie worked in healthcare and a major motivation was helping others. I interviewed Katie for around 75 minutes over Microsoft Teams. Katie was very candid about the challenges and frustrations she had experienced around her diagnosis and beyond. A couple of times I checked she was ok to carry on as I was conscious it involved reflecting on a time that had been very difficult for her but I got the sense it was important to her to share her experiences in the hope of improving things for others in the future.

Pseudonym	Reflection around experienced or envisaged genomic results, reason for genomic test, and brief notes on practical aspects of the interview
Vanessa	<i>'Rather than giving them a bunch of symptoms, I can now tell them the condition itself. Not many people have heard of it, but I can say "that's what's wrong with me", and they look it up, rather than <u>me</u> having to do anything about it ... It's nice to be able to say "that's because of that".'</i> Vanessa had taken part in the 100,000 Genomes Project to investigate unexplained neurological symptoms, and this had led to a diagnosis of a genetic condition which explained the symptoms but also predicted future health problems. Vanessa had two young children and worked in a caring profession. I spoke to Vanessa for around 50 minutes via Microsoft Teams- her preschool-aged child was having a nap for most of the interview but was in the room with Vanessa having a snack for the last 5 minutes. Vanessa shared during the interview that she was dealing with her diagnosis partly by being cautious about how much she wants to know, and avoiding looking further than she feels ready to. I was therefore quite conservative in some of my questions around the significance of her result and its potential consequences for her wider family as I did not want her to feel she had to dwell on issues she evidently preferred not to engage with.
Natalie	<i>'I showed the information, the [clinician] was aware of it, but she made a comment similar to "well, you're only 1% of the nation and a very small percent of my caseload". Which made me feel that my health needs didn't have any value, attention or acknowledgement.'</i> Natalie had broad genetic testing several years ago to investigate her personal and family history of diabetes. This identified a genetic cause with wider health ramifications. Natalie was from a big family and had felt a lot of responsibility sharing this information and helping others in her family make sense of it. I spoke to Natalie for just over 60 minutes via Zoom. She seemed very engaged and interested in my questions, and while we discussed some experiences that had been painful for Natalie at the time she seemed relaxed and comfortable throughout the interview.
Mark	[no direct quotation as per Mark's wishes] Mark had symptoms suggestive of a specific rare condition and had broad genetic testing some years ago to try to find a molecular cause. This confirmed a syndromic diagnosis with wider health consequences and implications for his family. We had a 20 minute interview via Microsoft Teams in the evening as Mark works full-time and has lots of commitments.

Figure 12: Characteristics of results experienced by interviewees

This aims to give an idea of how secure the molecular diagnoses under discussion were, and how much was known about the associated medical conditions. The ‘ratings’ I have given are very rough and informal. I based ‘confidence in molecular diagnosis’ on participants’ answers to my questions as to the certainty of their result. I rated ‘extent to which associated condition characterised in medical literature’ in relation to what material would be available to a clinical geneticist preparing for an appointment to discuss the condition. (For many well characterised genetic conditions there will still be considerable uncertainty as to how/whether a particular person might be affected).



7.3.2 Themes identified from interviews with people experiencing genomic tests

Here I discuss key themes relating to ways in which genomic results appeared in the context of interviews with people experiencing genomic tests for a variety of reasons. Throughout this section, I write about various outputs from tests as being ‘results’, which arguably makes reflections on what they tell us about how results should be constructed a bit circular. I experimented avoiding using the word ‘result’ but I thought using surrogates like ‘finding’ and ‘outcome’ disguised but did not actually address the problem. My aim was that in working through this in order to explore qualities of experienced and envisaged

results, this might lead to ‘*flashes of insight*’ regarding the nature of genomic results, and helpful and unhelpful influences in their construction.

7.3.2.1 “Forewarned is forearmed”: the power of results in the abstract

When discussing genomic results in the abstract, I struggled to get away from a concept of their being powerful, valuable, and clear, even where this did not seem to chime with a participant’s experience from genomic testing to date. Imagined results had all the qualities brought to the fore in popular discourse (Chapters 3 and 4) – they were powerful and they brought certainty, though they might be ‘*dynamite, in a lot of ways*’¹⁸.

Diane was taking part in a genomic test aiming to find an explanation for her adult child’s health problems. Her data had likely contributed to the construction of a result that sounded like at present it would not alter her son’s medical care or have clear consequences for his family: ‘*They found out that [my son has] got the same mutation as, I think it’s five other people or something. Which is slightly bizarre, but... there hasn’t been a great deal from it*’. Yet discussing in theory why having a precise genetic explanation for her son’s health problems would be important, Diane explained: ‘*It just clinches it somehow. Makes it... solid. “Right, ok, we know what it is. We can now do something about it”. Whereas otherwise, you’re thinking “oh, well, I suppose this is going to work”... but, you know, will it? ... It’s the clarity you want. It’s the absolute knowledge*’.

In many senses, Diane saw the construction of a result as contingent on the choices that might be made by people analysing a genome sequence: ‘*if you say genome, then... the world’s your oyster. But if you’re saying it’s a genetic test for, then... it limits you a bit,*

¹⁸ Quotation from Diane.

doesn't it really? Because somebody else could come along in another ten years' time or something and say, "Gosh there's all this data here, let me go through it and let me have a look at it" and find something completely different. Another mind on it might do anything'.

But together with this, she also seemed to conceptualise results as knowledge embedded in the genome- inarguable and inherently defined 'things' where the real questions were what to do with them, rather than whether to understand them as being results. Regarding the wider possibilities of analysing a genome, beyond finding a diagnosis for current clinical problems, Diane told me:

If there was something, I really wanted to know about it. I'd much rather know, than not know. And it's a kind of privilege ... to be tested in some ways, because... well, not everybody is, and... I don't know, I just like the idea of knowing. Of being... abreast of the situation, if you like. I don't like being in the dark.

This idea of 'knowledge' embedded in the genome came up many times during my interviews, with several participants discussing variations on a theme that 'forewarned is forearmed'. Mary had so far had 'nothing found' from a genomic test attempting to provide a molecular diagnosis for her child's medical problems. In our conversation she clearly placed high value on the potential for genomic testing to accurately forecast the future:

Interviewer: Is there any kind of information you can imagine you wouldn't want from a genetic test?

Mary: No I don't think so. I'm quite... yeah, I kind of deal with everything as it comes, you know. How do you say it, "full knowledge is fully armed" kind of thing, you know what I mean?

Interviewer: So you're thinking from a preparation perspective...

Mary: Yeah. I am very much a... you know, I like to know what's going on, and I like to plan, and I like to deal with things.

Perhaps this partly reflected the way I phrased the questions, positioning potential findings from genomic tests as 'information' and thereby potentially leaning into the shared theory

of genomic results as powerful and definitive that I found it so hard to avoid. Thinking about this further with Mary, we discussed:

Mary: I don't see many grey areas with genetics ... it's black or it's white, isn't it? I think. You know, it tells you... well, it tells you what it is, doesn't it? So how can that be a grey area? That's black or white. You know, like with the X and the Y, it tells you what it is, doesn't it?

Interviewer: No that's really interesting. I suppose, I'm just thinking, there are some genetic things that might be a bit less certain. Like you might say, you've got this type of risk factor, so maybe you have... like, maybe your risk is a bit higher than the next person's but it still might never happen...

Mary: Yeah, yeah.

Interviewer: Yeah and I just wondered, I suppose people have different thresholds for that sort of...

Mary: Yeah but for something like that, that's something you shouldn't worry about, because, it might not happen.

Interviewer: So does that mean you wouldn't see that information as being useful to you, if a test found "oh you've got a higher risk of this particular condition"?

Mary: I'd probably want to know. But, I don't think it would play on my mind and that I'd worry about it. Because if it's going to happen, it's going to happen. My life is mapped out now until the day I die. If I'm going to get something, I'm going to get it.

A somewhat fatalistic way of conceptualising genomic information was common, with people having different attitudes as to whether they might want the 'knowledge' but seemingly envisaging that knowledge as theoretically there. Eric, diagnosed with a cancer predisposition syndrome, and reflecting on whether there was any information he might not want from a genomic test, explained:

If there is something going to be looming up, and going to hit you, you want to know all about it. And I'd say, be really open, to whatever it is, because there's nothing worse than saying "where'd that come from?" ... But if you know about it, you prepare for it, don't you? You know, it could well be horror things, like "you've only got about six months left to live, and this is what you've got to do", but, you want to know that. I want to know that.

Cath, having genomic testing in the context of a personal history of bowel cancer, seemed to think along similar lines to Eric as to the sort of knowledge that could be gained from genomic testing, though interestingly she drew on the concept while simultaneously criticising it as inaccurate, reminding me of the way many Mass Observation Project respondents had engaged with questions around future uses of genomics (5.3.5):

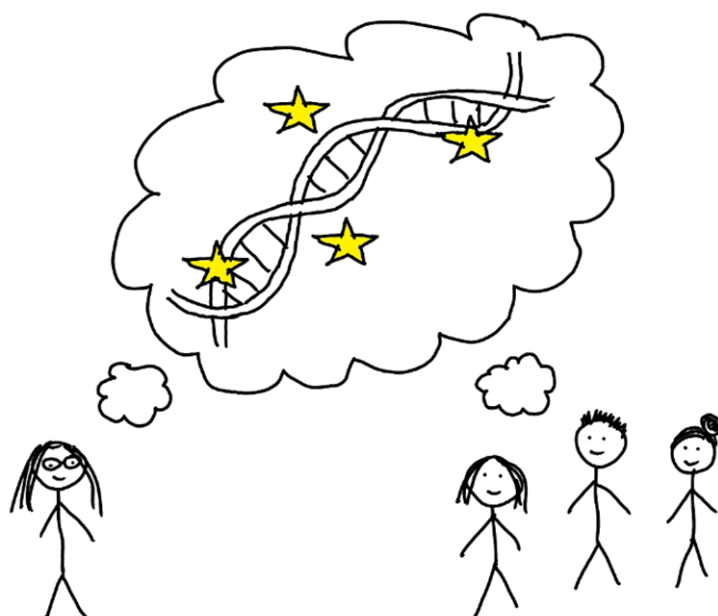
Cath: Well, it's like, would you like to know that you're going to die tomorrow? Would you want to know today, that actually you're going to get run over and killed by a car tomorrow? Would you want to know? You know, I mean... I'm not, that's just an analogy. It's an analogy. And, alright, your genetic map, I'm not saying it's quite as final as death. But it's just an idea of... it's telling you stuff, that you don't need to know. You need to breathe and eat and sleep, but you don't need to know your genetic map.

Harry, having had so far fruitless genomic testing to explore an unusual personal and family history of cancers, explained how genetic information might land differently to other risk factors: *'If a doctor just says "Oh, you know, you're overweight, and blah blah blah", it's like "Oh, that's not serious". But, if someone says "well, your genetics are going down this path, you've got, going to get this, and it's a done deal" then it's like "Ah. OK"'. Perhaps relating to this, he felt: 'if they say "Oh, you know, you've got a predisposition to some sort of cancer, or... or heart condition", or whatever... I do, I kind of want to know it? If they can give me a heads up, whether even, at the stage when they're saying "Oh, you know, there's nothing we can do, but... this this this", that's cool, I think it's good to know, I think it's good to... you know... to embrace the knowledge, really'.*

I found it really difficult picking at ideas around what 'knowledge' might mean in my interviews, and I think this tells me something about constructions of genomic results in itself. With a research agenda of problematising genomic results, and talking to people who had often themselves experienced outcomes from genomic tests that did not tally with prevailing narratives, I still could not get away from an idea that 'results' were lying in the

genome, pre-defined but waiting to be unveiled (see Figure 13). Carol, who had had genomic testing in a (successful) effort to explain her son's lifelong challenges, described having been asked whether she would want to know *'if a particular gene reared its ugly head which would have an impact on me, and perhaps my family, such as a cancer, something like that'* and I thought that beautifully encapsulated the way broader genomic findings were often implicitly positioned in my interviews both by me and by participants – inarguable, powerful, and leaping directly from the genetic code.

Figure 13: I could not get away from a shared imagination of results as lying in the genome pre-defined, there for the looking



In outlining this I do not mean to imply that this was the only way in which participants envisaged genomic results in the abstract – throughout our discussions participants frequently provided caveats around their expectations of a genomic result. For example, Thomas discussed *'if it was an easy thing to do and you could say "well you have a genetic test, and it'll map your genome and tell you any issues you've got or whatever", I'd be interested in that'* [underline is my emphasis]. Explaining what sort of information from a genomic test he might value, he explained:

Thomas: You'd want a percentage probability of likelihood or something... something that puts it in context.

Linda: Yeah, I mean I don't always trust statistics, but sometimes you have to use statistics.

Thomas: No, but you can make your own mind up can't you, you know when you've got "70% that you've got this, or 30% that it's this" ...then, you can make your own mind up about how you weigh those figures.

Interviewer: Yeah... so you'd want enough data that you could make your own mind up about it.

Thomas: Yes, I think so.

Linda: Yeah, I think so.

Thomas: Unless it was black and white, if someone said, "you know, this is, what it is, that means this, and we've got 99% certainty that we know that's going to happen", then I think you need to have that judgement, because it is subjective, and... who knows?

Harry similarly expressed 'you could upset someone by saying "Oh, you know, maybe" or whatever. You've got to have certain... points where you go, "OK, this has got legs. We maybe, we can let this out and say 'well there's a possibility on this, with this'" ... You have to get to a point where you say, "well, you can't give that information out because we don't know, we're not entirely sure", it's got to be kind of proven to a degree. When the news breaks about some cure for something they always say "Well, we'll know more in ten years' time", you know? We do the clinical trials, and blah blah. And this'll kind of be the same, really'.

For Jason and Steph, who had experienced challenging, uncertain and very unexpected information from genomic testing, this had shaken their ideas as to what they might consider valuable as a result:

Steph: I guess that's what you could ask people, isn't it? Is, do they just want to know things that cause X, Y and Z, or do they want to know every little minute... thing that is found, that is different to someone else?

Jason: Yeah.

*Steph: Yeah, see, but we'd probably have said "yes" to ours. *laughs**

Jason: It's a hard, it's a hard one to comment on, because... it's whether you're talking about a condition... whether it's one of those conditions where just, these people in the population, with these genes, are slightly more likely to get this condition, we don't know why, but it's just based on the data, that's what this says... Would you want to know every single one of those for you, probably not? But...

Steph: See, but I think we would have picked "yes".

For them, actionability had now become a key consideration – what could they do in response? While on the one hand they felt *'you'd always be better to find something early, and be able to treat it, or at least do something early ... we were both on the same page [deciding to sign up for 'additional findings' from their genomic test] instead of like "Hey, let's find down the line I've got a massive tumour and we've missed the boat on it"'*. However this decision was contingent on an expectation of responsible curation: *'I do think, I do think you shouldn't be just throwing out every single genetic abnormality because some of them in some people have caused this and some haven't, like, I guess that's the line... that's the line where either... whoever, whichever committee or whether it's ethics, or whether it's clinicians, have to decide for each condition, I imagine, what level of certainty they are about the genetic causes of these things before they input'*.

While in my interview discussions a strongly predictive power of genomic results was often implicit, this concept was undermined at points where we discussed issues like current uncertainty as to how genomic variations might relate to health and illness. But thinking about the use of genomics in the future, people sometimes imagined the potential of a time where these uncertainties were resolved. Harry envisaged *'I think that's what the future will be. I think people will go in and get... just get a blood test. And it'll go through the machine and then the doctor will go, "well, you've got this this this this coming your way.*

So, you know, that's it. You deal with it how you want, but this is where it's at". Eric expressed his hope that:

I think there should be a general genetic test for everyone. I know you have millions and millions to one chance of finding it, but I think everyone should at least have that chance ... I'd do it from when they were youngsters, because they might find something else. You can get so much from the blood now, can't you? So you might pick up something else. And it... in the end, what is it? You just go like "doop doop", blood out, arm out, and you go like "Blimey! There's something happening there", it could be like that, cos it's found like that.

To summarise, when discussing genomic results in the abstract, the working concept of results (for both me and participants) largely seemed to be that prevalent in popular discourse: the idea of results as powerful and unambiguous, 'found' rather than determined. In our conversations we shook and challenged this idea, but by and large this was implicitly our default notion and it felt like during interviews we sometimes dialled back from this in various ways but could not get away from using it as the starting point when thinking about genomic results.

7.3.2.2 The heterogenous nature of genomic results

In contrast to theoretical discussions around what *could* be constructed as a genomic result, people responded to questions around outcomes from their genomic tests with a variety of complex experiences. Elements of some of the results participants experienced certainly overlapped with common ways that genomic results tend to be presented in popular discourse – i.e. they did have a clarity and impact that made a significant difference to people's lives. But for various participants their result had left them in a different territory: some opened up new uncertainties; some gave no answers; some seemed quite peripheral to the day-to-day issues families were navigating. The following section is quite descriptive but my aim is to demonstrate that where we take a *post hoc* definition of genomic results as 'outcomes from genomic tests that have been communicated to

patients', the clarity and power often attributed to genomic results in theory are frequently either lacking or impacting people in complex ways.

7.3.2.2.1 'Nothing found'

Some participants had so far had 'nothing found' from their genomic test, and were making sense of this in a variety of ways. Richard, having a test to investigate progressive neurological symptoms, explained *'I was a bit disappointed. But if they haven't found anything, they haven't found anything. I know it's like trying to find a needle in about ten thousand haystacks'*. Harry, having testing to investigate a personal and family history of cancer, was managing his expectations carefully, focusing on the potential benefit of his genomic data to society rather than the possibility of personal benefit to himself: *'I'm not expecting anything ... But I never did in the beginning. I never really... there was no kind of like "you're going to get a lollipop at the end of this" or whatever, it was like "that's it, I'm in, do what I need to do" and that was that'*. Mary, having genomic testing to investigate her child's multiple medical problems, reflected several times during our interview that getting a molecular diagnosis was not essential: *'at the end of the day, it doesn't change anything. Because you've still got that little person, suddenly by being told they've got x y and z, it doesn't change who they are. It doesn't change them as a person. Come back and tell me she's got, I don't know, whatever. It's not actually going to change her'*.

7.3.2.2.2 Clear molecular diagnosis

Several participants had received a clear molecular diagnosis from their genomic test, and where this was the case people generally expressed high value for the result. For one participant, Vanessa, who had had testing to explore a lifelong history of unexplained neurological symptoms, her result had directly led to her being prescribed medication that she referred to as *'[her] miracle tablets'* which meant her legs were *'better than they have*

been in years'. While most others described that their day-to-day medical care was largely unaffected, clear diagnostic results had often been very powerful in other ways. For example, Carol, whose sample had contributed to the genomic test that diagnosed her son Timothy with a genetic condition, was delighted that he was now allowed more freedom because of the result:

The evidence was so uncanny, it was amazing ... people that have that particular syndrome are very sociable. And this is where Timothy's problem lay, you see, he is very very sociable. So, it has helped [people working in assisted living accommodation] because what they've done is they've written out some cards, and they've written on there, and it's just, if a member of the public objects to Timothy going up and talking to them and so on, he can just hand them this card, and it will give a description of the problems that Timothy has, and telephone numbers to contact if they're not satisfied with just reading that information. So Timothy now is able to be supervised from a distance.

A genomic result had evidently transformed Timothy's day-to-day life in a very positive way, though there was a circularity to this power in that it relied on an expectation that a genomic explanation would be capable of exonerating a behaviour to others in a way that a history of lifelong difficulty understanding social boundaries could not. Carol described that *'[the people working in Timothy's assisted living accommodation] were very very excited. Because they just wanted to know whether Timothy... could not help being so over-sociable ... if it was known that he had this particular syndrome where that was one of the characteristics, it would help them to know that Timothy couldn't help it, and it wasn't deliberate'*.

For Eric also, his result, which confirmed a cancer predisposition syndrome, had power in giving him answers as to why his family had been so devastatingly affected by cancer, but more importantly, he saw it as giving him an opportunity to change that. Eric himself had metastatic prostate cancer and he told me *'one after another was going down with it, you know, we were sort of dying from cancer, and we wondered what on earth was going on'*.

He was extremely grateful to have an explanation for this through his genomic result, and he clearly felt an enormous responsibility not only to share this information with his family, but to ensure that they acted on it, seeing the result as having power to rewrite their future for the better. For example, describing a discussion with a family member who could, because of Eric's result, have a predictive test to see if they would have a higher risk of developing various cancers, Eric told me: *'After I seen him a couple of times, I say "you ought to do it" I said, "because it would've saved me an awful lot of grief if I'd got in early"'*. The power of Eric's result to protect his family made it hugely valuable to him, but this power was contingent on his family engaging with the result and acting in response to it.

While participants who had received clear diagnostic information from their tests generally valued having it, incorporating the knowledge of their result into their lives had often been, and continued to be, a painful process. For example, Vanessa, while overall glad to have her result, described how after first hearing about it: *'I didn't sleep for a couple of days, in the end ... I just kept crying. Because it was something that was... well, come from, above me, and it was genetic? So, yeah, that made me feel a bit more... guilty, I suppose'*. She explained how she continues to deal with her result by being very judicious about what she asks about its implications, trying to find a path where she can access the potential medical benefits of having a diagnosis, without being trapped with worries about the future that she would rather avoid: *'Me and my mum we went to [city], drove down and got [public transport] to the hospital, and took another couple of hours, as well, to go through everything. But they didn't tell me about what's going to happen, cos I refused, I was like "No don't tell me, I don't want to know"'*. Again, this less helpful power of Vanessa's result derives in part from expectations around it – in this case, that it might be capable of accurately forecasting or determining her future.

For Katie, who was unexpectedly diagnosed with a mitochondrial form of diabetes through a diabetes research project involving genomic testing, her result had similarly felt powerful but not always empowering. She told me how when she heard the outcome of her test, having just about got her head around a fairly new diagnosis of presumed type 1 diabetes, *'I felt like my medical world was turning upside down at this point, again'*. In the appointment where she learnt of her result for the first time, she described: *'I said "Oh, does that mean that I will either die of this then, like either having a stroke or... something like [a stroke]"*. *"Yeah, more or less" and I was like "OK. Interesting"*. Despite the new worries for the future that arose from her diagnosis, Katie was glad to have her genomic result – and the possibility of not having it clearly played on her mind:

What if I didn't take part in that study? Because it was just some random me sitting there waiting for a monitor from the diabetic nurse, that somebody's approached me, like "oh yeah yeah yeah yeah". What if I'd turned around and said "no I'm not interested" – how long would it have taken, for them to, you know, figure out, "OK, well this is not just type 1. It's actually something else".

However, it sounded like her early experiences around the result had been extremely difficult, and Katie had felt very alone in making sense of this new information and trying to integrate it into her clinical care: *'I'd gotten used to like, when people just say "OK, you know what, you're a type 1 diabetic", I've gotten used to just leaving it at that. Because the frustration that comes with trying to explain what it is, and the difference between the two, I'm frustrated with it all, so actually like, I can't be arsed?'* Talking to a specialist mitochondrial clinic had been transformational for Katie – the genomic result itself was already powerfully influencing Katie's life, but the specialist support around it which came several years later was key in helping Katie actually benefit:

It's almost like finding out you're a mitochondrial diabetic for the first time. That was the information. I was so grateful to her, cos I said to her, I feel like I'm just having to redo this, or that this is the first time I've actually been told about it, because my journey from the minute I found out until now, it pretty much feels like

it's pointless, because there hasn't been... this is the first time anyone's actually sat down with me and gone through what I should look for. Or actually shows an interest in the fact that, OK, it's not just random type 1 diabetes.

Clear diagnostic results that participants had experienced tended to be talked about as having powerful impacts, though not always in comfortable ways. Access to expert clinical support had often been important in helping participants contextualise and derive benefit from their genomic result.

7.3.2.2.3 Unclear outcomes

Various participants were living with less clear outcomes from their genomic tests. These were affecting people's lives to a variety of degrees, sometimes in helpful ways, but sometimes in ways that made people (and probably their clinicians too) feel more trapped than empowered.

Jason and Steph told me how the genomic test seeking to explain their daughter's deafness had left them '*in limbo*', finding a genetic variant of uncertain significance that could, if pathogenic, explain her hearing loss, but that would also predict future sight loss. Their daughter was too young for clinical tests to provide reassurance (as degenerative changes in the eye that would usually be seen with the condition might not have occurred yet). They described how it had come as '*a shock out the blue, with the finding out about the results of the testing ... it was a result we weren't aware could be a result*'. Although they found this difficult to deal with, Jason and Steph still felt that '*100 times out of 100*' they would make the choice to have testing, and they were very complimentary about the care they had received following their genomic test. But they highly valued clinical tests that sought to reduce the uncertainty, and explained that from their perspective they would rather '*the timeline [had been] falsified to be shorter ... from the nature of what we're dealing with,*

you're going to be on an emotional rollercoaster regardless, so I guess... the most important thing for me is that timescale that you're on it'.

Jason and Steph had had to wait several months before their daughter could have the relevant eye tests to try to gain more clarity on the significance of the genomic variation identified. As they faced uncertain genomic information, 'next step' tests or the ability to actively do something in response were key in their constructing that information as being worthwhile to share:

Interviewer: I guess there would be a school of thought that if genetic information is quite uncertain, sometimes you might sit on that, I guess, until it becomes more certain, and not share it with a family, until there's a bit more clarity around it? What's your view on that, as people who've kind of received that sort of uncertain...

Steph: I would be fine with that.

Jason: Yeah, I think... I think in this case, the genetic information... I don't... it wasn't just genetic information that was... err... I don't think the genetic information was that uncertain, because the genetic information was, but it was linked to a condition that they know one of the signs is moderate deafness from birth, so when you feed in that, this becomes less... of an uncertainty, and definitely worth pursuing to get in contact with, with us, about. I don't think I would have rather them... I think if the data and the symptomatic input would have logically gone "this is the next test", so we need to get in contact with that, but it's...

Steph: Yeah, yeah, no in that situation I think we had to be told, and we had to have the further testing and all of that, that's fine, because the earlier it's diagnosed, the better intervention can be and all of that, that's totally right. But if it was a thing that was completely... "Dunno, we found XY3, and it might do this, it might not do this, but there's nothing we can test for that", I'd rather... not know. Cos that... has no... what would be the point in telling, particularly me, a complete layperson, like what would be the point in telling me that? I'd just be like, "alright".

In some senses, Ashley was in just the situation Steph described – she had recently become aware of a variant of uncertain significance in a very recently described disease gene in her child, who has severe developmental delay. This was not her first time dealing with uncertain genetic information as her child had also had a different variant of uncertain

significance identified via a research project some years ago. Recounting that experience, Ashley told me:

Obviously I was manically going out and googling that, but the children that had that, they tended to have this [organ malformation], so they thought [child] could potentially have it but just had a mild case of it that wasn't visually showing its face, so then that meant we then had [a scan] which we hadn't previously had reason to do yet ... That then showed that there was nothing there, so therefore... [child] didn't have what this technically caused... but then they still thought it might have caused something. It's quite hard because it's all sort of very scientific and to think that OK he hasn't had what it can cause but it can still cause something... it's kind of like an answer but not an answer at the same time, we kind of wanted eventually just to get an appointment where we go "Right, this is what he's got, and it's called this".

Ashley's frustration with the limitations of genomic testing was palpable throughout our interview – again, it had not found a clear explanation for the challenges she helped her child face every day. Part of her disillusionment seemed potentially linked to the concepts she had previously had around how genomic results might be constructed. Referring to her genomic test, she explained:

I didn't mind it was going to take a while if it was going to look for every possible spelling mistake... I felt like we couldn't do any better, when in reality that wasn't true. I think there could have been a lot more transparency about the panels ... how would they ever spot it... if there could be a thousand children like [child] but if they're only looking in the places that they looked, that they've looked previously or that they know to look in, how can you ever link those hundreds of children that actually had something completely obscure? It's like looking for your car keys in the top five places you lose them all the time, and never looking on top of the mantelpiece because you haven't lost them there before.

Discourses that present genomic testing as 'reading the entire genetic code', with results leaping directly from the data (Chapters 3 and 4) had done an Ashley a disservice. While on the one hand she still valued the chance to have genomic testing and was hopeful of clearer outcomes over time, she also felt that she had been 'sold, sort of sold something that then developed, and actually it was like they started to kind of retract once they realised what capabilities were going to be'. The interrogation of her child's genome sequence had been

much more limited than she had imagined, and the consequent result had so far been a powerful disappointment.

But reflecting on the consent process for the genomic test, Ashley told me *'I feel like the NHS already will have had quite robust ethical procedures that I could trust in them without having to have it explained in an hour and a half appointment ... I think it was excessive. We'd already had a DVD, we had... it just seemed ridiculous'*. She explained that *'as soon as it was offered to us'* she had decided she wanted to take part in the genomic testing project. The consent conversation relating to the project, essentially occurring after Ashley had already decided to take part, had either not highlighted to Ashley the difference between acquiring a genome sequence and understanding it, or perhaps had not been able to do this effectively in a context where popular discourse invites us to expect value and clarity as par for the course from genomic tests. Various other participants described, like Ashley, that they also made the decision to have genomic testing as soon as they were made aware it was an option. It seemed to me that the formal consent process had sometimes been experienced as the hoops that had to be jumped through in order to get the test, rather than an opportunity for participants to consider the range of possible outcomes and what they might mean for their lives.

Thomas and Linda had very recently learnt about a possibly disease-causing variant in a newly described disease gene in their child, around a decade after enrolling her in a project involving broad genetic testing. They were very clearly deeply invested in their daughter and her future and I got the impression that the genomic information they had recently received seemed somewhat irrelevant to this. For example, Thomas struggled to remember the gene name, despite evidently being extremely proactive in advocating for his daughter throughout her life. He explained to me *'If I could put a letter on the table that went "Jess*

has this genetic defect. Which means this” then I’d get that written into her EHCP. Because that gives you good, concrete reasons why she needs things or doesn’t need things, and explains things. Whereas, you talk about, you know, moderate learning difficulty, as I say, that’s a wide range’. The information they had recently received did not have these qualities and as such seemed more a peripheral curiosity than deeply impactful.

To summarise, as indicated in Figure 14, the genomic results experienced by people I interviewed appeared heterogeneous, with awareness of a ‘result’ affecting people in very variable ways. Access to specialist support, and willingness of others (family, clinicians) to engage with a result, often seemed to have been important in making results valuable rather than oppressive. In interviews discussing uncertain genomic information, there was often an implicit sense that a result should be better than this – a real-world outcome from genomic testing was clashing against expectations of results perhaps more in line with those invited by popular discourses. But does this mean that these real-world outcomes should not be constructed as results, or is it concepts around results that need to change?

Figure 14: Outcomes from genomic tests were very variable- some were powerfully helpful; some oppressive; some unproductive.
Which section of the picture would look nicest for your newspaper story?



7.3.2.3 *Building meaning through interaction: the role of collaboration in the construction and reconstruction of genomic results*

Some of the people I spoke to were living with considerable uncertainty, and really valued the potential of medical research to change that. People who had personal experience of uncertain outcomes from genomic testing seemed particularly aware of the role of shared data in generating meaning from their genomic tests. Thomas and Linda explained:

Linda: I guess my long-term view of it is that, because some of the things they do know so much about genetically, like Downs and [specific condition], all the other things that are identified and that they can intervene or help, based on that knowledge, and feel that, allowing... you know, her material to be analysed... just... see, 20, 30, 40 years' time, there may be something that's well-known, that she's part of, that... can be addressed in a better way, it's just...

Thomas: Well, if we, if we were to take 2006, and put all the data we know about genetics back into 2006, we'd be in a position which said, "Yes, we understand Jess' condition, and we think it's this gene". And it would have been a very straightforward...

Linda: discovery, which...

Thomas: ...but, we weren't in that position, because no-one knew about it at that point. But, the next child that comes along, with that, displaying those features and those symptoms, they would be able to test. So, in some way, we probably helped contribute.

Ashley, also navigating uncertain genomic information for the second time, described 'I think I felt some sense of duty as well, to make sure [child] was into everything he could be for the sake of other children, because I think, if everybody was, is willing to put their report out there then it means we can all get to a much better place'. This somewhat echoed Thomas' comments to me later in our interview that 'If I had my way everybody in the world would get genetically tested. And put in a database'. Thomas and Ashley both really wanted to reach a point where when people in the future had genomic tests, the results of those tests were more meaningful than theirs had been, and they saw how valuable their data and experiences could be in working towards that.

Jason, living with considerable uncertainty around his daughter's future as a consequence of genomic testing, told me *'in my head, the way a lot of these genetic... discoveries may be made, is to look at as many different genomes as you can, and then look at symptoms of those populations and then start joining up "these people with these genes seem to have symptomatic of this, and this... we might get a causal link between this gene and that". So the amount of data you need is... phenomenal*'. Reflecting on what this meant for 'his' data and to what extent he regarded that as personal to him, he said *'I think it's kind of contradictory... to want to have personalised... your genome to kind of be just looked at individually for you, when the way they actually... can get all of this information is by looking at loads of it ... the data is by its nature and by its necessity needs to be shared. Like it can't not be shared, for the progress to be made, to help find the diagnosis that you originally went into the project for ... that's a contradiction'*.

While my most detailed conversations around the value of large datasets in strengthening and contributing to genomic results were with people living with uncertain genomic information, most people who had had genomic testing expressed being glad about the potential of their genomic data to help others, although the mechanisms by which this might happen were more loosely articulated (somewhat reminiscent of UK news items – 4.3.2.4). Harry was hugely supportive of medical research in general, and told me *'I just knew that I was a small cog in a big machine, and I've done something that's positive, and that was it'*. Julie, having genomic testing in the context of breast cancer, had felt a big responsibility to contribute her data: *'I know it wasn't genetic research necessarily, but if research hadn't been done into breast cancer, then, you know, in six months' time I might not have been there. So I think I felt very positive that it's... almost a responsibility? For women that... and, for people in general, that come after me, that I can help in any tiny way possible, because, you know, twenty, thirty years ago, people with my diagnosis might not*

have survived'. She had been eligible for a number of research projects and explained that [the genomics testing project was] the one I chose, because I thought that it would have the greatest effect ongoing'.

Participants saw sharing genomic data as key to making progress with genomic tests in future. For some participants- 'healthy' parents- this power to facilitate interpretation was particularly relevant because the rationale for their own genomic test was the potential value of their data in interpreting that of their child. Everyone in this situation that I spoke to had been happy to have testing, although like with my clinic observations (6.3.2.1) people sometimes had a hazy view as to why their samples might be important:

Interviewer: What was your understanding of why you and [husband] needed to give a blood sample?

Mary: Erm...

Interviewer: Was that explained to you?

Mary: Do you know what, it probably was, and in all honesty, I've probably forgotten ... I'm sure if my husband was here, he'd probably be able to tell you, but I honestly can't remember.

Interviewer: No please don't worry. But you felt happy to provide a blood test?

*Mary: Oh yeah, otherwise I wouldn't have done it. *laughs**

Carol had similarly been very happy to give a sample to facilitate interpretation of her son's test, though potentially understood her sample as having been requested to help trace the condition through the family, rather than more likely being used to help rule out particular variations as a potential cause of health problems:

Interviewer: And when [geneticist] called you up about the test and explained that it would be helpful to have a sample from you, how did that feel?

Carol: Oh! Well I just, I was thrilled. Because I could just see the benefits of that. And I just felt sorry that my husband wasn't alive because of course, it could well be that Timothy's problem has stemmed from my husband's family ... So, when [geneticist] suggested, I could just see the benefits of my being involved. Because then perhaps

they could find out that the problem actually lay with me. But as it happens, it's a one-off. There's nothing that I could have done that could have prevented Timothy having this particular syndrome.

Sometimes in the focus on what a genomic test might mean for a child, the potential to generate results with personal medical relevance for a 'healthy' parent became obscured:

Interviewer: Did you see yourselves as having testing, or do you see it more as your daughter being the one having the...?

Jason: Not really.

Steph: No, no. I know they took like, loads of blood from us, and I know we're getting tested for all of the... whatever it is, I can't remember, massive list. But I did more focus on the outcome for her.

Jason: Yeah, it's more like, we were a by-product of... what was happening...

Steph: Yeah. Like we had to do that, to help her and get her answers and stuff. So it wasn't really... no. But I suppose we could get a bad result, couldn't we? But you don't really think about it.

The offer of a genomic test where a participant primarily saw the purpose of the test as helping others creates the potential for a person to be blindsided by their result. Indeed, this had happened to Katie, who had been diagnosed with mitochondrial diabetes in the course of a research study that she had not realised involved genetic testing:

I filled out the form, cos I was like "OK, there's no harm in, you know, filling out some additional data, it's research" ... you know, the majority of the work, you hear, that has been, like medical discoveries and stuff ... it's part in being part of that, just so they could have the additional research, so it would help anybody else. So I looked at it from that perspective, I was like "OK, fine, I'll fill out the form". And even then it didn't seem like such a big thing for me? ... I looked at it from one perspective, "OK, fine it helps somebody else". Not once did I think, OK, that filling out that form would mean that they would come back to me and say "oh, you know, you're misdiagnosed", kind of thing like that, you don't expect these things, I looked at it from the perspective of helping somebody else.

Katie had been faced with a very unexpected and challenging outcome and described having to fight to get her new diagnosis recognised and incorporated into her clinical care

(see 7.3.2.2.2). It seemed to me that her experience of a 'genomic result' was not passively receiving it, but wanting to engage and work with it very actively, and struggling to find support with that process. As with my clinic observations, participants were not just sitting back hearing information from genomic tests then filing it away somewhere, they were trying to use it to improve things for themselves or others, but reliant on the people around them being willing to engage with their result too. For example, Eric, trying to get his family to take up the option of predictive testing for the cancer predisposition syndrome his genomic test had diagnosed, described 'you've got to sort of gee them up, and I keep geeing them up' – he felt his responsibility ended only once they had been tested and started any recommended screening.

Various participants were similarly taking a driving seat in eking what they could out of their result for the benefit of others. For example, Carol explained to me regarding her son's recent genetic diagnosis:

The amazing thing in the [leaflet about the condition her son was diagnosed with] is, there's a young lady – she's 30, and whilst that book was being published, she was the oldest person known to have that syndrome. But Timothy is [in his 40s]. But [my other child] ... has been in contact with them ... They do so want me to get in touch with them, because they said they are still learning about that syndrome, and there's lots of things about Timothy that hasn't appeared in that booklet ... so those sort of symptoms will be of great interest to them. So my New Year's resolution is that I will get in touch with these support groups, and I've written down lots of things about Timothy that perhaps will be of interest to them.

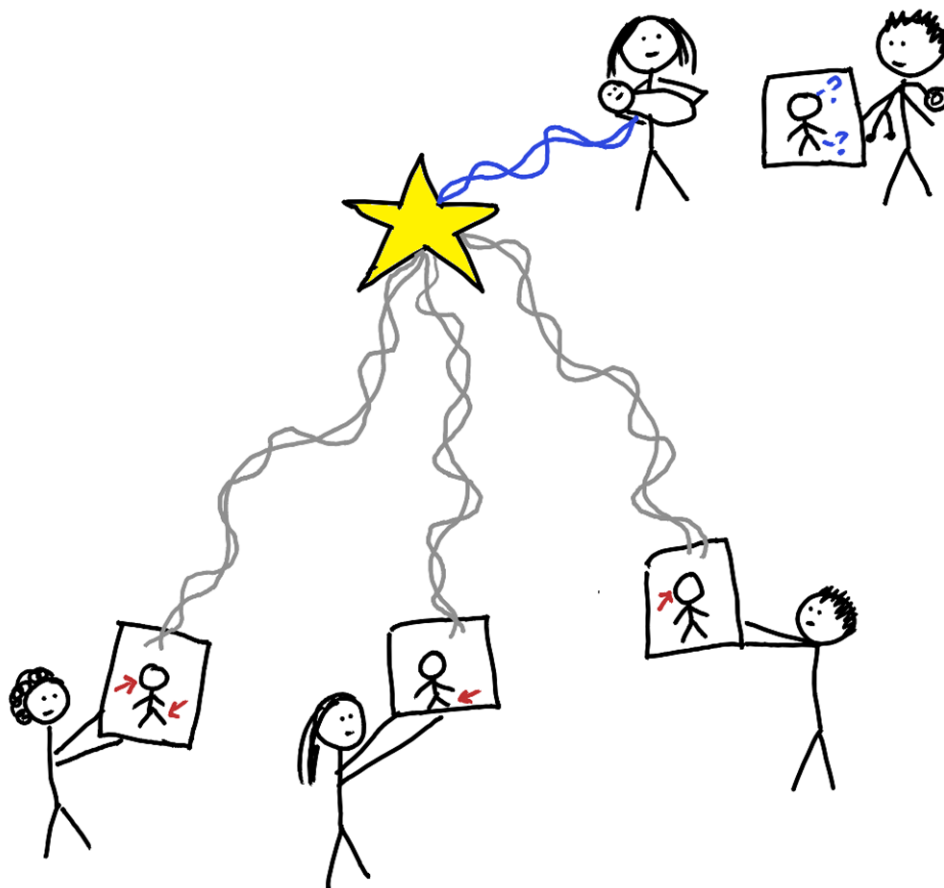
Thomas also planned to share his family's experiences with others with similar genetic variants in an attempt to generate a fuller practical understanding around what the variants might mean:

[Clinician] was saying that quite often Facebook groups spring up around these subjects before the medical profession gets themselves together, so I did have a quick look at the time; I need to look again, because that would be interesting, to

join up with other parents through social media and share experience and what does and doesn't work.

Through their plan to share details around their children's lives with families in similar situations, Carol and Thomas were going far beyond passive receipt of medical information: they were drawing on their own genomic results, such as they were, to generate new and deeper meaning around the genomic results of other people (see Figure 15).

Figure 15: Working to make others' results more meaningful



7.4 Summary

As regards my research questions 'What features do people imagine genomic results as having?' and 'What sorts of features do genomic results appear to have in clinical settings?', time and again my interviews brought up the clash between what we hope and expect from

genomic results, and how results (when defined as ‘outcomes from genomic tests that have been communicated to patients’) seem to be experienced in practice.

The results participants had experienced had a hugely variable nature – from underwhelming to powerfully helpful to disruptive to virtually irrelevant. Yet when envisaging results, the default concept was almost always of something profound, powerful, and irrefutable, though various of my interviews seemed to draw on and deprecate the concept almost simultaneously. Where there was a mismatch between the result a person had experienced and this stock concept people responded in various ways: they felt disappointed or disillusioned; they worked to generate as much meaning as they could from their result for themselves and for future generations; they looked forward to an unspecified future time when they too might have a powerful, meaningful result – and sometimes all these together. But rarely did their experience seem to rattle the theoretical idea of a genomic result being insightful, powerful, and clear.

Regarding my overall question, ‘how should we construct genomic results?’, this creates a quandary. Up against this standard, many of the outcomes that participants experienced from their genomic tests did not pass muster. Yet participants often valued them, and cataloguing the relationship between more uncertain genomic variations and health is essential to generating clearer results in the future. So perhaps the issue is not so much with outcomes from genomic tests such as they are, as with a seemingly inescapable one-dimensional concept of genomic results where our predetermined future shines directly out of the double helix.

Borup *et al* reflect that *‘Expectations circulate in various forms and shapes. This raises searching problems for us in thinking about expectations as essentially rhetorical or*

material in character. That is, to what extent are expectations the enunciated views and ideas of people (utterances), and in what way do they become 'inscribed' in texts, actions, bodies, materials, objects and machines (embedded)? What is the relationship between imagination and materiality?'(148). Chapters 3 and 4 evidence the material 'inscription' of an expectation of genomic results as powerful, profound and clear – and in this facet, the rhetorical palette accessible to participants and myself during these interviews seemed to be coloured and bounded by a similar expectation.

However, Borup *et al* write that '*rational expectations assume a realist distinction between people's expectations on the one hand and the 'real' underlying fundamentals or worth of something on the other*' and challenge this that '*if we accept that anticipation is actually constitutive of value, then we logically cannot differentiate between our expectations of things ... and what those things in fact are*'(148). Our expectations are not operating independently of a 'real' situation in relation to which we should adjust them, they potentially fashion the future we walk into.

This idea underpins the concept of sociotechnical imaginaries first developed by Jasanoff and Kim: Hendriks *et al* outline these as describing how '*a society's shared visions of the future shape its scientific and technological developments. These developments in turn influence how that society imagines its future*'(149). Appraised through this lens, today's expectations of genomic results will determine what we value as being the genomic results of the future. From this position, the prevalence of expectations of powerful, meaningful genomic results is not primarily problematic by virtue of their 'inaccuracy', but because they potentially foreclose futures that embrace nuance and contingency in genomic results.

Notions around results as lying in the genome pre-defined, and sparkling out when we look hard enough or use sufficiently fancy technology, potentially contribute to the isolation of families navigating uncertain or underwhelming outcomes from genomic testing, as discussed in 4.3.3. They also minimise the hugely significant role played by people going through genomic tests, and the scientists and clinicians delivering them, in creating, honing, and deepening meaning around genomic results. Perhaps in some senses, a vision of genomic results as powerful, profound and clear is helpful in spurring on the efforts people make to realise this future for others. But a concept of genomic results that also recognises that many – perhaps most – people have (and will continue to have) a different experience, may leave fewer people in unforeseen or lonely territory as they navigate outcomes from their genomic test.

7.5 Reflections on this facet

In many ways this was the facet of my project that I found most challenging – I felt a big responsibility to learn from people who had agreed to talk to me about their experiences of genomic testing, but it was so hard deciding in the moment of interviews how far to question. I wanted to do justice to my research agenda but I was really anxious that questions might stir up new uncertainties for people or make them ruminate on difficult past experiences that they might have preferred to put behind them. This was also the facet in which I had to make the most ‘on-the-spot’ decisions: for example, whether to continue an interview when it turned out a primary school-age child would also be present in the room (in this case, it was near the end of the interview and the participant was clear they wanted to continue, so I did but ensured that I kept to fairly benign or abstract questions where I thought a child would be unlikely to engage with or be upset by the question or its probable answers).

I also found this facet presented the most challenges in terms of navigating my clinical background. During my consent conversations I always started by introducing myself as a 'PhD student doing a research project', but for my first few interviews I gave the context that I had become interested in the issues I wanted to discuss with them because I was training to be a clinical geneticist but was taking time out to do research. However, in the way that early participants talked about their genomic tests I was sometimes worried that they might think I was involved in the provision of their test. In such cases I clarified that this was not the case as soon as I became aware of the potential misconception, and in later consent conversations I gave less emphasis to my clinical genetics background, but occasionally this issue still arose and I wondered whether my saying I was interested in researching people's experiences of genomic tests meant people thought my research was part of the genomics project that had provided their testing.

Another aspect that was challenging to navigate was when participants described things in ways that did not tally with what I thought from a clinical perspective. For example, a couple of times people referred to the additional findings the 100,000 Genomes Project was planning to look at as 'a very fixed list' or similar. In a research setting, where my overarching intention was to learn from talking to the participant, it felt inappropriate to take a position that assumed I had more knowledge, but I felt uncomfortable leaving this unchallenged as it felt a bit disingenuous to ask people's insights around things like the consent process for genomic testing, and not make any effort to support the robustness of their ongoing consent where I thought they might have a misconception. In these cases, I usually said something along the lines of 'my understanding is that the actual things they check for might change, but they should all be things where you could do something about it' and people seemed accepting of that.

With regards to the 'quality' of this facet, interviews gave me the opportunity to deeply explore some varied experiences, stories and ideas relating to genomic results. My purposive sampling approach enabled me to work with people who had encountered genomic tests through different routes, and who were navigating a variety of experiences from their tests(150). Qualitative interviewing allowed in-depth exploration of participants' expectations, understandings and experiences, generating rich data(151) with which I could pursue '*flashes of insight*' around the nature of genomic results. On reflection, a narrative analysis rather than a thematic analysis might have offered a route to different insights, through specifically exploring the meanings given to genomic results and the ways they are brought to bear in people's stories(152). My thematic analysis tended to prioritise looking across stories relative to looking within them- this fitted well strategically with my facet methodology approach as I could more readily refract themes across datasets. But a narrative analysis could probably have better captured ways in which a genomic result might reverberate through people's lives, and so perhaps contributed to a deeper understanding of the nature of genomic results.

Reflecting on what I learnt from this facet of my project more broadly, Weller writes that '*qualitative material is often regarded as co-constructed; the product of the interaction between the participant(s) and researcher(s) ... The identities of researchers and what they reflexively reveal of themselves, how they interact with participants, their techniques and approaches and the messiness of qualitative work are laid bare within the artefacts of qualitative data*'(153). The experience of using qualitative interviews as a method really brought this home for me. At the outset of my project I saw the 'job' of interviews as eliciting people's ideas, expectations and experiences around their genomic results, with minimal influence from me, in order to inform my analysis of how we should construct genomic results. As I progressed through this project I shifted to seeing myself as a

participant in the interview too. This chimes with Edwards and Holland's writing on interpretive approaches and interviews that *'as human interaction and negotiation is seen as the basis for the creation and understanding of social life in interpretive approaches, it is the interaction of the participants in the interview situation – the researcher and the researched – that creates knowledge. The data in the form of talk that comprises the interview is regarded as a co-construction – what Kvale [see 7.1] calls a literal inter-view'* (154).

8 Genomic results explored via other angles

Throughout my DPhil, I have had a number of opportunities outside of my more planned experimental facets that have helped me think about aspects of my overall research question: ‘how should we construct genomic results?’ Unlike the research I discuss in preceding chapters, these activities were not strategically designed with the primary purpose of shedding light on my research questions. However, they involved engaging with various audiences around issues highly relevant to these questions, and working on them developed my thinking. As such they became helpful additional facets through which I explored the nature of genomic results.

As the Wellcome Trust describes in their discussion of engaged research approaches, ‘*We believe using an engaged research approach improves research and makes it more impactful ... Engagement should not be a stand-alone activity but an integrated part of your research. An engaged research approach can involve a variety of methodologies, frameworks, and skills to appropriately engage relevant stakeholders at key points*’(155).

This section describes some of the ways I engaged with various groups around the question of how we should construct ‘results’ from the starting point of the genome.

This chapter starts by describing a public engagement activity I was involved in developing, then outlines debates I contributed to around the use of genomics in population screening, before reflecting on highlighting the complexity of genomic result construction in the policy sphere. (11.2 in the Appendix describes other engagement activities undertaken during my DPhil which were more tangential to this project; 11.3.2 shows when the activities discussed here took place in relation to other aspects of my project).

8.1 ‘Building blocks for life or abstract art?’¹⁹

‘Building blocks for life or abstract art?’ was a public engagement activity that the Clinical Ethics, Law and Society group undertook at the University of Southampton Science and Engineering Festival (SOTSEF) on 18th March 2023. Following on from this, we went on to write up the idea behind the activity for a journal for young people(156).

The concept we developed was to represent a person’s rare genomic variants as annotated Lego blocks. Using the same set of Lego blocks and the same clinical situation (an adult man, Bob, with progressively weaker muscles), we involved visitors to our stand in some of the decisions necessary in constructing a ‘genomic result’. We talked through different ways they could filter the Lego blocks. For example, they could start by focusing on genes linked to particular body systems (represented by the colour of stickers on the blocks: yellow for muscle, orange for breast, etc). They could also filter the blocks relating to the state of knowledge around the genetic variant in question (from red: linked to disease, to blue: not linked to disease, with various gradations in between). Table 12 shows the Lego blocks and the genomic variants they represented.

¹⁹ Aspects of this work were published in *Frontiers for Young Minds*, a journal aiming to make scientific discoveries available to younger audiences(156). Though I include it here this was very much a team activity where I worked together with several colleagues. My key contributions were the idea of creating something where people ‘built’ a genomic result through various filtering decisions, and developing the supporting clinical information (for example, suggesting ways in which the blocks could be analysed (such as starting by looking at ‘muscle genes’) and developing the menu of Lego/variants from which people could select).

Table 12: The Lego blocks from which a result would be constructed

Block and filters	Accompanying text	Additional details for event team
 Muscle (yellow sticker) Linked to disease (red block)	A person with this variant is a carrier for a condition that causes severe muscle weakness from infancy.	1 in 50 of the people in this building will also be a carrier for this condition. Bob DOES NOT have this condition and it is NOT the cause of his muscle weakness. If Bob has a baby with someone else who is also a carrier, there is a 1 in 4 chance the baby would have the condition. If Bob's partner is not a carrier, their babies won't have the condition.
 Muscle (yellow sticker) Unsure (yellow block)	We don't know what this means. Some variants in this gene cause muscle weakness, but usually when this happens people are very severely affected from birth onwards.	Variants in this gene that are known to cause disease completely stop the gene from working. Bob's variant looks like the gene 'recipe' is slightly changed but would probably still work ok (like a cake recipe which usually has 4 eggs but is changed to have 5).
 Muscle (yellow sticker) Not linked to disease (blue block)	10% of the people in the world have this variant. As far as we know, it doesn't affect health in any way.	-
 Breast (orange sticker) Probably linked to disease (orange block)	This is probably a cancer-predisposing BRCA variant (90% certain that the variant really does predispose to cancer).	Men with this sort of variant have a higher chance of developing breast cancer during their life (though their chance is still low – about 1 in 100), and a higher chance of developing prostate cancer (they could have a blood test to screen for this but the screening test isn't as good as we would like it to be and some people feel the drawbacks of screening outweigh the benefits). Women with this sort of variant have a much higher chance of developing breast and ovarian cancer as adults, and would be offered extra screening and surgery to reduce this risk. Close family of people with a cancer-predisposing BRCA variant might have the variant too.

Block and filters	Accompanying text	Additional details for event team
 Breast (orange sticker) Probably linked to disease (orange block)	This variant probably does increase the chance of a person developing breast cancer, but by a really small amount.	We all have loads of variants like this – some nudge our risk up and some nudge our risk down by tiny amounts. If we discussed every variant with this sort of impact on cancer risk with people, we'd be discussing thousands of variants every time we did a test. But if you have lots and lots of variants like this, together they might have a bigger effect. Like if the risk from this variant is like smoking one pack of cigarettes a year, but you have 300-400 variants like this, that might be like smoking one pack of cigarettes a day.
 Immune system (green sticker) Linked to disease (red block)	A person with this variant might be really ill if they take a particular medicine (which is used for treating HIV).	If Bob doesn't take the medicine, this variant will never make him ill.
 Heart (red sticker) Unsure (yellow block)	We don't know what this means. The variant is in a gene where some variants cause people to develop thickening of the heart muscle, which can stop it pumping properly.	This variant isn't known to stop the gene working properly, but it's very rare and computer programmes predict it might change how the gene works in the body. A recent UK Biobank study found that when you look at more than 500 genes, most people will have a rare variant where computer programmes predict it might change how the gene works in the body (and actually, probably the gene will work fine, or serious genetic conditions would be much more common than they seem to be).
 Heart (red sticker) Probably not linked to disease (green block)	Twenty years ago we used to think this variant increased the chance of people having dangerous heart rhythms. We now think this is a normal variant but we're not yet totally sure.	There are lots of variants we once thought were bad for health, that we now think are probably fine. This is partly because as we've done more and more genetic tests we've seen that there's a very wide range of genetic variation, and everyone has loads and loads of genetic variants.

Block and filters	Accompanying text	Additional details for event team
 Lungs (blue sticker) Linked to disease (red block)	A person with this variant is a carrier for cystic fibrosis.	This means Bob is a carrier for cystic fibrosis (like 1 in 20 of the people in this building). Bob DOES NOT have cystic fibrosis (a condition that affects breathing and digestion) and having this variant WILL NOT make Bob ill. If Bob has a baby with someone else who is also a carrier, there is a 1 in 4 chance the baby would have cystic fibrosis. If Bob's partner is not a carrier, their babies won't have cystic fibrosis.

Our activity was designed to bring up a number of principles in relation to genomic result construction:

- Many people do not get clear answers from genomic testing (there was no Lego block that would clearly explain Bob's progressive muscle weakness in adulthood).
- The wider you look, the more dilemmas you might create. For example, some participants chose to filter to look at 'muscle genes' first, and finding no clear answer, looked wider. They then saw things like cancer-predisposing *BRCA* variants and were faced with whether to include these in their 'result' for Bob or not.
- Genomic variations might be valued differently by different people, and might be more relevant in some situations than others. For example, most people doing the activity chose to look at 'muscle genes' and so were faced with a variant meaning that Bob was a carrier for a condition causing severe muscle weakness in babies. Would knowing Bob was hoping to have children influence their decision whether to include this in the 'result'?

Once each person visiting our stand had finished constructing their 'result' we asked them to add it to a Lego base board (see right hand image of Figure 16). As you can see, working with the same clinical scenario and the same menu of variants, people made a range of different choices as to what they would consider the 'result' of Bob's test. Reflecting on the

activity, some participants thought that they must have done it wrong because they had not found a clear reason for Bob's weak muscles. Some people thought none of the variants should count as a result (which we did not have a way to represent in the Lego towers!), and some felt they should include nearly all the variants they had examined – having 'seen' them and their possible relevance to Bob, they felt uncomfortable not including them in his result. Various people noted how Bob had just wanted an answer for his muscle problems, and his genomic test had not given him that but instead had generated a lot of other things to worry about.

Figure 16: Photos of our 'building blocks' activity at the Southampton Science and Engineering Festival

The left photo shows our stand; the right shows the board where we collected the Lego representing the choices people had made in constructing a 'result'



For me, this activity showed that when challenges in genomic result construction were made explicit, many people were really interested in engaging with the dilemmas that might be faced when trying to generate meaningful results from the genetic code. It also reinforced my conclusions from other facets of my project that the process and complexities of genomic result construction tend to be glossed over in prevalent discourses around genomics: for an audience of people choosing to stop by a genetics stand at a

science festival, the extent of the analytic decisions and associated ethical consequences encountered in constructing a result often came as a surprise.

Regarding my overall research question, ‘how should we construct genomic results?’, the ‘building blocks’ experience showed how much we stand to learn if we could bring this question more into the open in wider discourse. In developing ideas as to how we should construct genomic results, we first need to recognise their nature as things that must be constructed rather than simply unveiled. This activity, in making that explicit, made possible some really interesting conversations.

8.2 Contributing to discourses around the use of genomics in population screening

The more clinically-focused of my experimental facets primarily explored ‘genomic results’ in the context of diagnosing overt rare conditions. For example, all my clinic observations (Chapter 6) and most of my interviews (Chapter 7) involved people having genomic tests in an effort to explain unusual health problems (though sometimes for a family member rather than for themselves). However, genomic results are no longer the sole purview of tests aiming at diagnosis of the already unwell – increasingly, genomic technology is being brought to bear in population screening contexts. What do these new settings mean for how we should construct genomic results?

8.2.1 Newborn screening

As I discuss in 4.3.2.1, popular discourses do not necessarily distinguish between the results one might expect in a predictive context versus a diagnostic context, and as outlined in 1.4.3, 5.3.5 and 7.3.2.1, expectations around the potential of genomics to accurately

predict a person's future are often high. However, as I discuss in 1.1, genome sequencing in 'healthy' population cohort studies shows that we all have multiple hypothetically concerning genomic variations: once we start using panels involving over 500 disease genes, most people will have at least one rare non-synonymous variant(157). Figure 17 tries to give an idea of the number of theoretically worrying variations in a 'typical' human genome.

Figure 17: Unpacking a typical human genome

Based on data from (10,14,15,158). Some variants will be present in more than one category. A differently formatted version of this figure was published in (51)

4.1-5 million variations from reference genome

200 very rare coding variants (in the parts of genes that code for proteins)

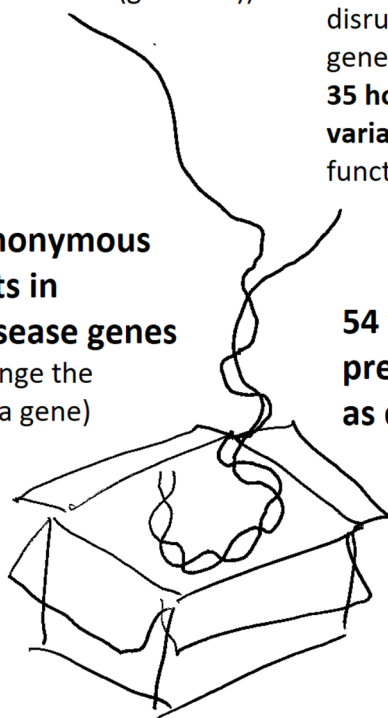
27 novel coding variants (not in the Genome Aggregation Database (gnomAD))

85 heterozygous protein-truncating variants (variants predicted to disrupt and potentially inactivate genes)

35 homozygous protein-truncating variants (so a person might have no functional copy of the gene)

7 rare non-synonymous coding variants in monogenic disease genes (predicted to change the protein made by a gene)

54 variants previously reported as disease-causing



During the course of this project, I led the development of two papers about what this might mean when trying to construct results in the context of newborn genome screening(51,159). Following this, I co-organised a day of discussions around this topic via

my role as a 'Junior Research Fellow' at the Centre for Personalised Medicine (2.2), which was held at St Anne's College, Oxford, on 25th February 2025(131). This event brought together a range of people with expertise on different aspects of newborn screening, including representation from clinical genetics, metabolic medicine, obstetrics, neonatology, primary care, health economics, ethics, sociology, the National Screening Committee, the Generation Study, and the Oxford BRC patient and public involvement group. The aim was to find areas of common ground, and consider potential strategies to mitigate or navigate some of the challenges arising around the use of genomics in newborn screening²⁰. We had lots of very positive feedback on the day, and given the contentious nature of various of the topics under discussion I was especially pleased to receive several comments on how constructive it had been.

One key issue we considered that impinges on what we should understand results to be relates to uncertainties in predicting phenotype from genotype. With a starting point of a seriously unwell baby, it would be uncontroversial to construct concerning variants in genes associated with relevant conditions as being 'results', or at least to explore their likely effects as deeply as possible with a view to determining whether or not they should be considered a result. With a starting point of a 'healthy newborn', this decision becomes much more complex. As discussed above, we all have numerous hypothetically concerning genomic variants in developmental genes where it is often mainly the time in our life course at which they are found (adulthood) that reassures us that they will not go on to cause a severe developmental disorder. We do not have solid evidence on which to estimate the penetrance of each specific genomic variation, so may have to make decisions

²⁰ This section has some overlap with the report that I drafted summarising the day(131). This was reviewed and edited by Anneke Lucassen with support from Susie Weller and Sally Sansom.

in the face of considerable uncertainty as to when and why to value a concerning looking genomic variation as a potentially helpful result.

Another interesting aspect raised by newborn genome screening initiatives is to what extent the collection of a genome should be relevant to what is then constructed as a result. For example, the Generation Study (1.3.1.1) is asking to collect the genomic data of participating babies, but the 'screening' aspect of the study is examining only a tiny proportion of those data – less than 0.01%(51). The genome is requested by virtue of its value to future research, rather than because of an intention to explore the full range of it in the process of screening the baby. Arguably, a 'result' from such screening should not be considered genomic – the test could in theory be divorced from the genomic assay, and provided using much more limited genetic data as a substrate. Though if we accept genomic results as having societal dimensions as well as personal (4.3.2.3; 5.3.7; 6.3.2.4; 7.3.2.3), perhaps this is a case where the genomic result under construction is exclusively societal – with a few babies standing to receive personal results from a more limited genetic test.

8.2.2 Polygenic scores

At the other end of the scale to trying to forecast extremely rare conditions, genomic data are also being turned to in an effort to predict and improve outcomes for common conditions, such as heart disease and various cancers. Polygenic scores (often called 'polygenic risk scores') examine thousands of variants across a person's genome in order to predict their risk of specific diseases. I had the opportunity to write about these with colleagues who had lots of experience of trying to develop and use polygenic scores(52), and the experience helped me look at genomic result construction where the intended

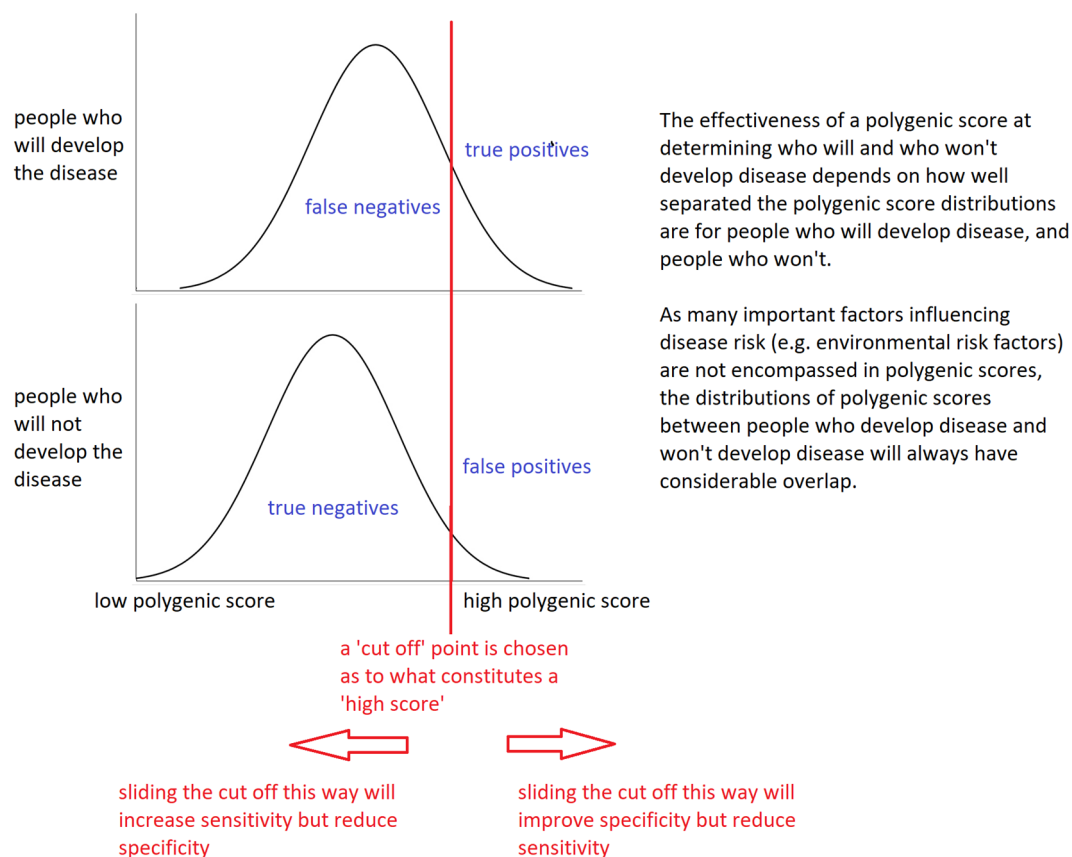
results are of a very different type to the sorts of results typically encountered in clinical genetics.

As I outlined in 1.2, constructing a result in a rare disease diagnostic context essentially starts with a filtering exercise, choosing various automated filters to sift thousands of genomic variants with the aim of being left with at most a handful of potentially meaningful ones. These can then be explored and appraised in more depth with an aim of determining whether they should, at this point and in a given context, constitute a result. Implicit within this is the idea of ‘something to find’ – the strategic purpose of the filtering process is to clear aside the noise around a putative ‘real’ result, sometimes successfully and sometimes not.

In contrast, as discussed in 1.3.2, polygenic scores bracket people into groups – for example, ‘high risk’ or ‘low risk’ – there is no ‘didn’t find it/don’t know’ option. In creating a polygenic score, design elements are very overt – scientists essentially specify the parameters they want for their score, with the caveat that some are in tension and adjusting one may intrinsically adjust another, as shown in Figure 18.

Figure 18: Choosing thresholds for declaring a 'high' polygenic score

A differently formatted version of this figure was published in (52). The figure was developed in collaboration with Dr Amit Sud.



Because non-genetic factors have such a large impact on our risk for most common diseases, most people who develop diseases like heart disease or common cancers will not have a high polygenic score(54). Many people who have high polygenic scores will not go on to develop the associated disease – in a population screening context with a false positive rate set at 5%, secondary analysis of data in the Polygenic Score Catalog as of April 2022 found that the median detection rate for all polygenic scores and all diseases studied was 11% (i.e. 89% of those with a high polygenic score did not develop the associated disease)(160).

Developing ideas around polygenic scores, I co-chaired two meetings of a patient and public involvement group run by the NIHR Southampton Biomedical Research Centre where we

discussed some of the issues around their use in population screening. Each meeting had different participants – one involved mainly older adults who were currently eligible for several population screening programmes, and one involved younger men who were not currently taking part in screening. Participants often initially spoke of polygenic scores in a similar way to how popular discourses present genomic results in general (Chapters 3 and 4), for example expressing concerns that a high risk score might feel like a ‘ticking bomb’, with potential to negatively impact mental health.

When we discussed statistics around what a ‘high risk’ result might actually mean, participants advised that there was a strong likelihood that many people would read more into such a result than was warranted, and any communications around polygenic scores should take care to make their limited contribution to a person’s overall risk really explicit. They suggested that the often-used phrase ‘polygenic risk score’ should be reconsidered as ‘it makes it seem more than it is’. This concern that polygenic scores are very vulnerable to overinterpretation is evidenced by Matt Hancock, the former UK Health Secretary, who gave a speech to the Royal Society in 2019 about how having a polygenic score for prostate cancer ‘may have saved [his life]’, after finding that his risk of developing prostate cancer by age 75 was 15% (where population risk is 13%)(161).

In terms of my overall research question, ‘how should we construct genomic results?’, this work was useful in showing me a context in which models of thinking about genomic results as powerfully predictive and highly impactful were clearly inappropriate. We might gain subtle benefits if we could find ways to use polygenic scores, combined with other risk data, to adapt aspects of population screening programmes (for example the age from which screening is offered). Yet these benefits will be outweighed by the costs if widespread overinterpretation of polygenic scores leads to unevidenced use of healthcare

resources, or large numbers of clinical appointments are required to help people navigate them.

8.2.3 Promotional discourses encourage uptake, but ultimately threaten the success of population screening involving genomics

Newborn genome screening and polygenic scores illustrate tensions in developing concepts around genomic results. In a sense, they profit from promissory discourses around genomic results as this creates a climate for their enthusiastic uptake. But their ability to lead to overall benefit for society will be reliant on their limitations being widely understood. Leaning into an idea of genomic results as powerful and transformational is therefore in the short-term interests of these initiatives but potentially undermines them in the longer term.

As Brown and Michael discuss in *A Sociology of Expectations*, ‘*Contemporary images of the future overwhelmingly and erroneously emphasize the pivotal role of technology and gadgetry. The social, on the other hand, is the domain where policy deals with ‘impacts’ and manages ‘demand’ or removes ‘barriers’ to the inevitable momentum of technology. Ironically, when futures fail, it is often because this very discourse of technologically-driven innovation change has prevailed. The lesson then lies in developing a more sophisticated appreciation of the co-evolution of the social and the technical. But such an appreciation will always hover between the requirement of innovation actors to inflate the promise of a field, and the need to intervene at key junctures where future rhetoric becomes damaging to reputations and capital investment*’ (162).

As regards my overall research question, ‘how should we construct genomic results?’, discussions on the newborn screening day illustrated how helpful it might be if we could

shift popular discourses around ‘genomic results’ to encompass possibilities of long-term uncertainty. Learning more about polygenic scores also showed me the necessity of working the potential subtlety of genomic findings into popular discourse. Ultimately, if the success of programmes like newborn genome screening and polygenic scores are to be measured in improved patient outcomes and more efficient use of healthcare resources, rather than extent of uptake in the short term, it is in everyone’s interests to bring more rounded, nuanced, and comprehensive ideas around genomic results into popular discourse.

8.3 Contributing to policy

During the course of this project, I had the opportunity to contribute to a report of the Joint Committee on Genomics in Medicine: *Ethical issues in prenatal genetic diagnosis – guidance for clinical practice*(95). My involvement was working on the 14 illustrative case studies included in the report, some of which I adapted from existing case studies and some of which I drafted. This was a great opportunity to illustrate some of the particular challenges of constructing genomic results in the context of pregnancy – a setting where binary choices (for example, whether or not to continue a pregnancy) need to be made under time pressure in the face of information that is often uncertain(163).

Case 7 in the report specifically explored the question of ‘what counts as information?’, using a vignette of a *de novo* microdeletion encompassing 14 genes, none of which are known to cause specific health problems when deleted, shown via prenatal testing at 21 weeks to investigate why a fetus has a heart defect and cleft lip. The case made the point that ‘*Our ability to generate genetic data is far greater than our ability to understand them. There are many genes for which impact on health is unknown*’. It also highlighted the importance of ongoing multidisciplinary discussion, involving expert colleagues, and

drawing on professional guidelines (where available) in attempts to arrive at a consensus as to whether it is appropriate to conceptualise this as a 'result'. The case reflected that where uncertain genetic data are discussed with prospective parents, careful communication and ongoing support will be essential as they navigate what it means for them and their pregnancy(95).

Other cases also aimed to open up different angles to result construction. For example, Case 8 explored how people might appraise the same genomic variant very differently – from being so meaningful that it might inform a decision as to whether to continue a pregnancy, to being a potential red herring for which it would be inappropriate to offer a prenatal test. Here, I developed a vignette of a woman requesting prenatal testing for an inherited microduplication thought to be possibly contributory to her 6-year-old's moderate developmental delay, but that had also been found in many people with 'normal' development. Case 2 reflected on how expectations around the accuracy of genetic testing may affect the way people engage with the results of a test, using a vignette of a woman requesting a termination of pregnancy based on a non-invasive prenatal test screening positive for trisomy 13²¹(95).

This was a useful opportunity to try to bring challenging aspects of results construction that I was exploring in this project closer to a clinical setting, where the question of 'what should constitute a result?' must sometimes be confronted very acutely.

²¹ Such tests often have a high negative predictive value, but the chance that a fetus screening positive for trisomy 13 actually has it will probably be around 1 in 2 (though this will vary depending on the test)(164).

9 Constructions of genomic results

In this final chapter, I start by discussing my findings relating to my subsidiary research questions:

- In what ways do popular discourses invite us to imagine genomic results?
- What features do people conceptualise genomic results as having?
- What sorts of features do genomic results appear to have in clinical settings?

I then consider what these mean as regards my overall research question: ‘**how should we construct genomic results?**’ I end with some general reflections on my project, highlighting areas where further research is needed.

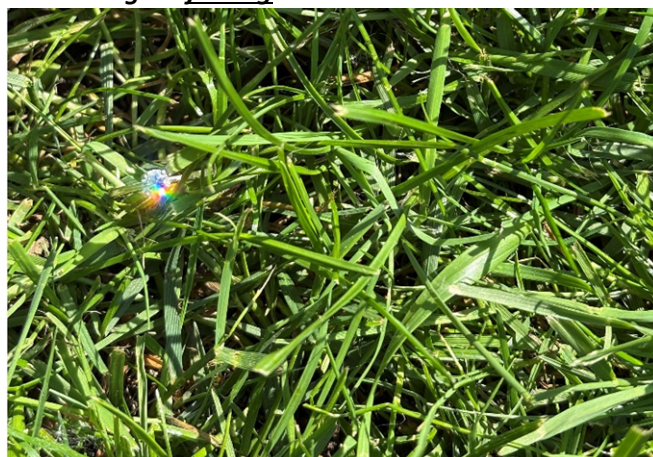
9.1 In what ways do popular discourses invite us to imagine genomic results?

As I evidence in Chapters 3 and 4, popular discourses around genomic results are often highly promotional, presenting an idea of genomic results as providing clarity, insight, and the opportunity to change one’s life for the better. Many stock images suggest results virtually beaming out of the genetic code. News items frequently present genomics as almost a panacea at a societal level – with genomic tests feeding into an ultimate result of transforming healthcare for the better for everyone. Such imagery and rhetoric around genomics can insidiously undermine efforts to emphasise subtlety and nuance. For example, a Genomics Education Programme module that aims to teach NHS health professionals about ‘*the intricate field of fetal genomics, focusing on the challenges, limitations and applications in prenatal care*’, has a course title of ‘*Fetal Genomics: Decoding the Blueprint of Human Development*’. The illustrative picture is a glowing baby/fetus that has a shining golden double helix in lieu of an umbilical cord(132).

Drawing together insights from across the facets of this project, I argue that popular discourses often invite us to imagine genomic results as ‘hidden gems’ (Figure 19). Similar to the situation in the era of narrower genetic testing (see Chapter 1), the challenge is presented as *finding* the result. Scientists may have to look very hard, and fancy technology can really help, but once a result is found there will be no debate. It will be glowing, precious, radiating out of the genome ready to improve the lives of everyone around it – if only we are forward-thinking enough to do a genomic test. There is little acknowledgement that explaining current illness, and predicting future illness, are different.

In demonstrating such discourse, my work echoes the much earlier findings of Nelkin and Lindee, who (as I discussed in 3.3.1.1) argued that ‘*DNA has assumed a cultural meaning similar to that of the Biblical soul*’ (84). Nelkin and Lindee criticised this idea back in 1995: my research adds by showing that thirty years later, popular discourse still continues to elevate genomic results as having an almost sacred power to explain our past and predict our future. News items tell the story of society on a journey to more and more incredible genomic insights, and look forward to the healthier and happier future that genomic testing will give us all.

Figure 19: Popular discourses tend to present genomic results as ‘hidden gems’.
A result is qualitatively different to the genomic variation that surrounds it, though it may be hard to spot. The challenge is finding it – we will know what it is when we see it.



9.2 What features do people conceptualise genomic results as having?

As discussed in Chapters 5, 6 and 7, concepts prevalent in popular discourse are often implicit in the way people discuss genomic results. In thinking through issues like newborn genome screening, people writing to the Mass Observation Project (who mostly did not have personal experience of clinical genomic testing) often positioned it as having potential to generate fairly definitive knowledge about a baby's future (5.3.5). In clinic appointments to discuss outcomes from genomic testing, conversations often seemed underpinned by an idea that genomic results 'should' be informative, helpful and unambiguous (6.3.2.2). In interviews that I undertook with people having genomic tests, I struggled to get away from a notion of results as 'knowledge' lying in the genome pre-defined, waiting to be uncovered (7.3.2.1).

Yet while a 'hidden gem'-type notion of genomic results often appears to be our stock concept, people recognise and criticise its shortcomings. For example, many people writing to the Mass Observation Project acknowledged the potential for newborn genome screening to leave families worrying about outcomes that might never happen. In interviews, people having genomic testing often challenged ideas around genomic results as being pre-defined or definitive – but these concepts kept popping up as conversations progressed. Clinic observations were perhaps the setting where the clash between 'hidden gem' discourses and experiences of outcomes from genomic testing was most evident. Many appointments involved explanations of why, in this case, genomic results did not fit a 'hidden gem'-type model.

So 'hidden gem'-type ideas seem prominent for many people when thinking about genomic results, and Chapter 5 includes some reflections as to how popular discourses may feed into this. But although people often implicitly draw on this sort of concept, they also

recognise far broader ideas around genomic results. When specifically engaging with questions around potential uncertainty arising from genomic tests (5.3.5 and 7.3.2.1); personal experience from genomic testing (7.3.2.2); or discussions as to what and when to value as being ‘results’ from a test (8.1 and 8.2.2), concepts of results seemed to shift to encompass subtlety and contingency. However, it seemed that particular conditions were necessary to unlock these concepts – i.e. specific invitation to reflect on limitations relating to genomic testing – and outside of these conditions we were back to a working concept of ‘hidden gems’.

My findings broadly link in with existing research which shows that people often have high expectations from genomic tests intended to inform healthcare (1.4.3). They build on this by indicating the breadth of experiences and exposures that may feed into a person’s ideas around genomic results, illustrating how these may have roots going back many years (for example to being taught about genetics in school), and connecting to uses of genetics well outside medical contexts (for example to investigate crime) (Chapter 5). My research also suggests that people often consider ‘hidden gem’ concepts to be unsatisfactory but at the same time continue to draw on them. I think this reflects both the dominance and allure of the ‘hidden gem’ concept, and the lack of compelling alternatives.

As quoted in 5.4, but repeated here because this Mass Observation Project respondent has summarised it so much better than I can:

There’s something quasi-magical – alchemical might be a better word – about the instinctive popular attitude to DNA testing and the research into its practical uses. It’s hard not to think of it in very literal terms: that pulling a gene from one position to another (if such a thing is possible), or excising it, can immediately change physical appearance or personality traits, or directly influence the course of a disease or chronic medical condition. I’m sure that’s all fantasy, but it’s a creepy feeling nonetheless to feel oneself, in all one’s human complexity, reduced to...well, whatever a genome sequence looks like. I’m imagining it as a Manhattan Yellow Pages-thick tome filled with variations on ATGC [M3190, man in 60s, librarian]

9.3 What sorts of features do genomic results appear to have in clinical settings?

Turning to clinical settings, as I describe in Chapters 6 and 7, genomic results (as defined as ‘outcomes communicated from genomic tests’) become much broader. Some people had experienced results that seemed to chime with aspects of a ‘hidden gem’ model, but many were occupying quite different territory. A number of people were living with a ‘result’ that seemed suspended between relevance and nothingness, waiting for it to drift in one direction or the other. Some were living with a ‘result’ that offered little more than a name. Rather than a family learning something new themselves from their result, clinicians were learning from the family about the potential effects of variation in a particular gene: clinical encounters were sitting in a hybrid space between research and clinical care(165).

Some sort of growing process seemed integral to many of the outcomes of genomic testing encountered in clinic. The value of drawing together and comparing information in the construction of results was frequently highlighted. It was also clear that results often travelled far beyond the person they pertained to. They were interpreted and reinterpreted in many different contexts around the person and for a variety of purposes: for school, for family and friends, for others navigating similar results (6.3.2.4 and 7.3.2.3). As such, genomic results seemed unlike ‘hidden gems’ – they were animate, evolving, and the challenge was less around finding them, than around determining them and understanding what- if anything- they meant.

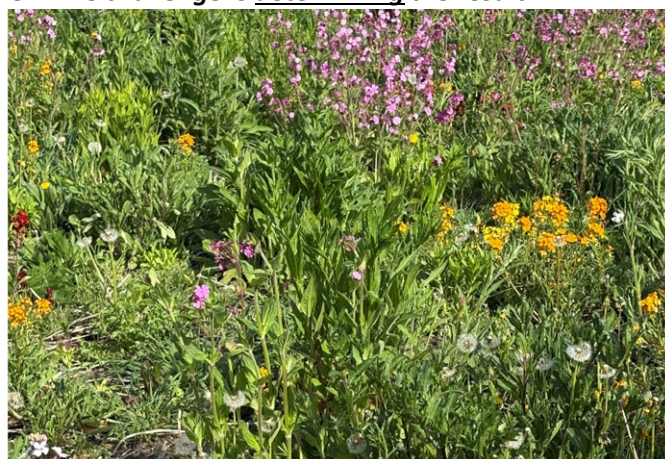
Moving to population screening contexts, a ‘hidden gem’ idea of genomic results becomes even less representative. As I explore in 8.2, everyone has multiple hypothetically concerning variations in their genome, so working out which might actually matter and when is a very difficult task. Similarly, everyone has a whole host of genetic factors that

subtly nudge their risk of common diseases up and down, and it is possible to make comment on these – but such tests have a poor predictive value and their contribution to a person's overall risk will often be overshadowed by more impactful socioenvironmental factors.

In 2005, Mauricio introduced the analogy of '*the genome as ecosystem*'(166). In this paper, he described how '*Gene networks connect genes as complex as the 'webs' that connect the species in an ecosystem. In fact, genes exist in an ecosystem we call the genome*'. Building on this, I argue that constructing genomic results in the context of informing healthcare has more parallels to surveying an ecosystem than searching for a hidden gem (Figure 20). Amidst all the potentially interesting variation in a person's genome, what should be valued as being a useful result, and when?

Figure 20: Constructing a result in clinical settings appears more like surveying an ecosystem.

The landscape of genomic variation is noisy and varied, and it is hard to know what is important and when. The challenge is determining the result.



My findings build on existing research, for example the work of Wright and colleagues delineating the volume of potentially concerning variation we each have in our genome(14,157). They also link in with guidelines around interpretation of sequence

variants in the context of clinical genomic testing(24,25), but add by approaching the issue from a different angle. My project starts with the idea of a 'result', and works backwards to consider what this means for genomic test interpretation; guidelines tend to start with sequence variants and work forward to the idea of a result. In post-positivist appraisal of the 'truths' around how a particular variant links to disease, the different- constructed- nature of the genomic results they stand to contribute to may be forgotten.

9.4 How should we construct genomic results?

Drawing together insights relating to the above subsidiary research questions, I now consider my overall research question: **how should we construct genomic results?** Firstly, I discuss this question from the angle of results imagined – how should we seek to think about and picture genomic results in the abstract? Secondly, I consider it from the perspective of results created – how should we position the navigation process from genomic data to results?

9.4.1 Results imagined

My research demonstrates a frequent and severe mismatch between the portrayal of genomic results in popular discourse, and the experience of genomic results in clinical practice. 'Hidden gem'-type concepts dominate our discourses and frame our thinking and conversations around genomic results. These powerful concepts are attractive, easy to grasp, and tie in neatly with a genetics education which takes Mendelian inheritance of highly penetrant traits/conditions as its starting point. There are also strong incentives to propagate them: to recruit to or gain money for genomic initiatives; to generate excitement around policy and get re-elected; to offer hope to people and families facing a difficult or uncertain future. But many people do not have a 'hidden gem'-type outcome from genomic testing, and their experiences are rarely represented in popular discourse.

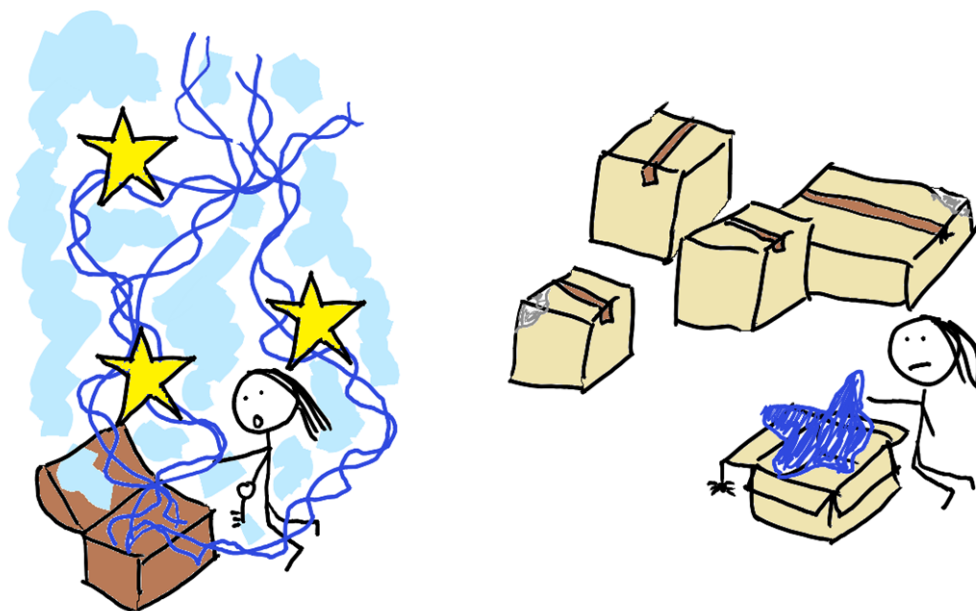
In their introduction to *The DNA Mystique*, Nelkin and Lindee reflected how '*Propaganda is a powerful historical force ... People act on the basis of images, sometimes without necessarily making the connection themselves between the image and the action ... In a practical sense, images of the gene in popular culture have consequences for both consumers and scientists*' (84). Various issues are created by the clash between outcomes from clinical genomic tests, and the propaganda-esque 'hidden gem' concept of genomic results.

A key problem is that highly promissory discourses around genomic results create a climate which sets consent conversations up to fail. As I discuss in 7.3.2.2.3, some people will be coming to consent discussions with high expectations of the potential power of genomic testing, and in little doubt that they would like to have a test. Their decision may effectively have been made already, and as such the usual patter about the benefits and risks of genomic testing may make little impression. But if this decision was based around 'hidden gem' concepts of genomic results, this may leave them vulnerable to subsequently feeling disillusioned, cheated or blindsided by their experience of genomic testing. They are also left on fertile ground for overinterpretation of results. When the frame of reference is that genomic tests stand to give powerful, definitive, life-saving knowledge, it is easy to see how something like a 'high risk' polygenic score for pancreatic cancer- constituting a less than 1% increase in lifetime risk(167)- could cause considerable anxiety. Similarly, a lower risk score could lead to false reassurance and people not seeking timely medical advice for concerning symptoms.

In framing genomic results as likely to give profound and definitive answers, with identification of a suspicious variant(s) and diagnosis of a disease being treated as almost synonymous, 'hidden gem' concepts stilt opportunities for progress. Societal conversations

that might fruitfully explore the use of genomics in contexts such as population screening struggle as issues are seen through the lens of the very dominant 'hidden gem' concept. One reaction is to jettison outcomes from genomic testing which do not fit this concept – but as a long-term strategy we cannot then make progress from engaging with and learning around tentative or provisional outcomes. Another reaction is to try to squish genomic results of a subtler nature into the 'hidden gem' frame, as exemplified by then Health Secretary Matt Hancock and his 'life-saving' polygenic score(161) (8.2.2). But these dominant concepts seriously hamper nuanced debate by essentially inviting us to frame all discussions around a theme of whether or not to lift the lid on the Pandora's box of the genome. In many cases a better metaphor might be how, whether and when to go through all the boxes in the loft (Figure 21).

Figure 21: 'What's this?' Hidden gem concepts of genomic results invite us to position societal debates around use of genomics as questions around whether to open Pandora's box. What discussions might a broader concept of genomic results make possible?



So far I have outlined why I think we *should not* routinely aim to think of- or encourage others to think of- genomic results as 'hidden gems'. But how *should* we construct them? It

is so much easier to criticise than to suggest a good alternative, but I think there is a strong case for trying to widen our concepts around genomic results, positioning 'hidden gems' as only the tip of the iceberg. These are the most amenable to being seen, photographed, talked about, and the picture of genomic results that most readily comes to mind. The majority of experiences do not match this narrative, but lie below the surface and so receive little attention.

If we could see the whole iceberg, what would we see? Looking at experiences around genomic results across the facets of my study gives a picture of them as capricious and unpredictable. They may lie on different places along a 'hidden gem' to 'ecosystem survey' axis. Some results may stand to generate personal benefit. For other results their benefit may be exclusively societal and, in some cases, arguably detrimental on a personal level. In order to create an environment which supports conversations around the integration of genomics into our healthcare, we need more rounded concepts of genomic results. We should aim to highlight their highly varied nature and potential to sometimes amplify or create uncertainty rather than resolve it. In order to have meaningful debates around whether genomic data collection is justified, we also need concepts that separate the delineation of a genome sequence from the efforts to analyse or understand it.

One could argue that the mismatch between prevalent discourses around genomic results, and how they appear in clinical settings and feature in people's experiences, is simply a practical issue that we could seek to address through better consent conversations prior to genomic testing. I argue it goes deeper than that: in positioning this as a problem we could fix by finessing participant information sheets or consent conversations, we are closing the gate after the horse has bolted.

Popular discourses tend to present such a selective and promotional view of genomic results that in effect they verge on being deceptive: they overpromise and they largely omit to mention experiences that do not dovetail with a 'hidden gem' narrative. In considering how we should construct genomic results in the abstract, we need to address this- we need a more truthful account. Kaldjian and Pilkington describe truthfulness as the first of the virtues. Critiquing a paper '*[defending] the deception of patients (or families) when the purported harms of truthful disclosure outweigh its benefit*' (168,169), they suggest that this perhaps arises from '*the practice of balancing that is integral to the perhaps most commonly discussed approach to medical ethical reasoning, principlism*'. They comment '*we have noted a different approach to medical ethical reasoning, one rooted in the tradition of virtue ethics going back to Aquinas and Aristotle, which holds practical wisdom (prudence) as preeminent among the cardinal virtues, the others of which are courage, temperance, and justice. One might ask why truthfulness is not mentioned. We suggest that truthfulness is not included as one of the cardinal virtues because it is presupposed by them all*' (168).

I realise in view of my relativist/constructivist perspective regarding the nature of genomic results, it may seem odd that I am now trying to critique 'hidden gem' concepts in relation to the virtue of truthfulness. If there is not 'a truth' regarding genomic results how can one be truthful about them? However, although I do not think there is one truth as to what should be constructed as a genomic result, I think there are a range of truths as to what experiences people are likely to have relating to outcomes from their genomic tests. I therefore think a 'truthful' account of genomic results would over time make mention of this range, rather than constantly cherry-picking the best possible version of a genomic result and implying that sort of outcome comes as standard.

O'Neill discusses the relationship between truthfulness and trustworthiness, arguing that *'to place and refuse trust intelligently we must link trust to trustworthiness, and must focus on evidence of honesty, competence and reliability'*. She describes how one aspect of trust relates to honesty: *'In trusting or mistrusting others' truth claims we aim to judge whether those claims fit or do not fit the world as it is'*, with other aspects of trustworthiness relating to commitment and competence. She goes on to reflect that *'it is often hard and time consuming to find a basis for trusting specific claims, commitments and competence, particularly when complex technologies and institutions influence, shape (and sometimes distort or falsify) the evidence we can obtain'* (170).

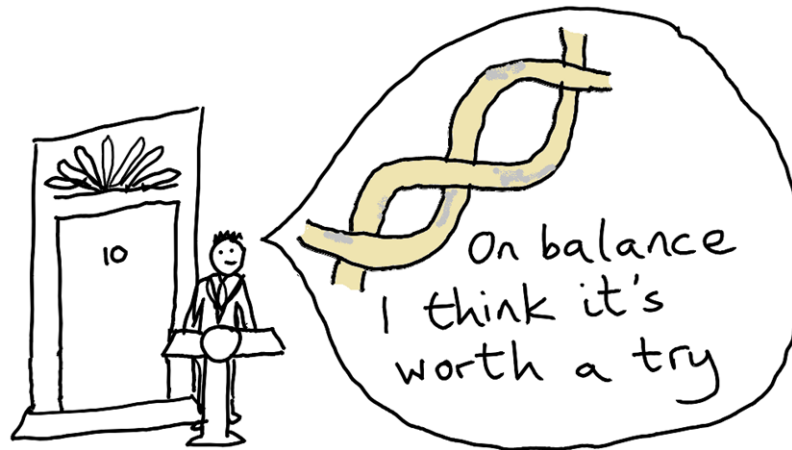
I argue that the evidence most readily attainable from prevalent discourses engenders a distorted view of the nature of genomic results. Balancing 'hidden gem' ideas around results with more comprehensive concepts is necessary in order to support the trustworthiness of enterprises involving genomic testing. 'Truth claims' relating to the nature of results that might be experienced should include and potentially emphasise the chance of subtle, underwhelming, provisional, or confusing outcomes. The possibility of amazing, life-improving outcomes will likely have been very well covered by popular discourse already.

But can we as individuals have responsibilities relating to how we invite others to picture genomic results? Discourses around genomic results have so many contributors, and as I indicate in 4.3.2.2 they often echo each other in the language they use around genomic tests – for example, the idea of 'reading' genomes pops up in news items, policy documents, patient leaflets, and educational courses. The sparkly double helix pops up everywhere. 'Hidden gem'-type results do occasionally arise from genomic testing, and it is not the occasional showcasing of this sort of result that compromises truthfulness, but the

constant unopposed portrayal of ‘hidden gem’-type results as par for the course. Who then has responsibility to change the discourse? At what point, if any, does it stop being ok to share another ‘hidden gem’-style story, or use another picture with a sparkly double helix? Another difficulty is that many discourses around genomics focus on the future, for example reporting on aspirations at the outset of genomic initiatives – and in reporting on this hoped-for future they tend to overlook what the present indicates about the likelihood of these hopes being met.

At the level of individual clinical conversations, people offering genomic tests can try to emphasise the wide range of possible outcomes, but as I discussed earlier I think this often comes too late. At the level of introducing genomics projects, the opportunity for impact is higher, but offering a comprehensive account becomes much harder. Balanced and rounded communication may still be filtered through the journalistic lens of ‘hidden gem’ concepts, with qualifiers and disclaimers cleared away to leave one punchy quote carrying all the weight of representing a very complex study. Unavoidably, people in leadership positions in genomic initiatives will also have an interest in presenting them as exciting, worthwhile and successful. If they try to present a comprehensive picture from which journalists select and showcase the ‘hidden gems’, it seems a bit much to expect them to proactively challenge this. Similarly, it seems unrealistic to expect politicians to introduce flagship initiatives in population screening with a disclaimer that most people are giving their data to get nothing useful back, and that lots of the results might be pretty shaky (Figure 22).

Figure 22: How could political discourses around genomics shift?



Journalists are another candidate for having responsibility to change the discourse: principles 2 and 3 of the National Union of Journalists' *Code of Conduct* are that a journalist 'strives to ensure that information disseminated is honestly conveyed, accurate and fair' and 'does her/his utmost to correct harmful inaccuracies'(171). But it is not at the level of individual stories that reporting around genomic results is not 'accurate and fair', it is the overall skew towards only acknowledging or focusing on 'hidden gem'-type experiences that is the problem. Drawing on their own genetics education and other stories around genomic initiatives for their research, journalists who do not work day to day with genomic data or families going through genomic tests may also be unaware that a 'hidden gem' model of results ignores and overlooks many people's experiences.

This may all sound very defeatist, but there are ways we can seek to change this. One thing that might help would be to try to share the stories of people going through challenging or underwhelming experiences from genomic tests, alongside the celebration stories of great outcomes. For example, genomics project websites could consider adding material such that along with the videos prospective participants can watch about the transformational experience of a few families, they can also see something of the disappointing or unsettling

experiences others have had. This could go some way both to balance the discourse, and to validate the common experience of a genomic test not being all it was cracked up to be.

But ultimately, if we want to escape having the ‘hidden gem’ concept as the default sculptor of our conversations around genomic results, I think we need to lay different groundwork from the very start, and reimagine school curricula to invite our next generation to think of genetics and genomics in a different way. Heavy emphasis on Mendelian inheritance guides us towards unhelpfully deterministic attitudes towards genomics⁽⁷⁷⁾ and traps us ever after in Pandora’s box debates.

In summary, in thinking about genomic results we should try to look beyond the flashy ‘hidden gems’ at the tip of the iceberg. A huge variety of complex, challenging and often unsettling or disappointing experiences lie under the surface. In shining light on these, we could open up more fruitful societal conversations about whether and how to use genomics in efforts to improve health. We might also do something to improve the isolation faced by many families living with rare conditions for whom genomic testing has not provided a ‘hidden gem’-type result⁽¹⁷²⁾.

In terms of implications for clinical practice, where offering genomic tests, we should be mindful that many people will be coming to the question with a starting point sculpted by propaganda around genomic results. Whether at the level of individual consent conversations, or at the more global level of introducing projects offering genomic tests, we should aim to offer more rounded and comprehensive ideas about what results might look like. Genomic results might offer no answers, they might introduce new uncertainties, they might represent having a genome’s worth of data collected with no benefit to you. These should form at least as big a part of the conversation as the possibility of gain.

9.4.2 Results created

Having reflected on how we should construct genomic results in the abstract, I now turn to how we might seek to build results from the genetic code in practice. During the day to discuss newborn genome screening that I discussed in 8.2.1, Caroline Wright reminded us that a genome sequence is an assay – it is not in itself a test⁽¹³¹⁾. We create the test, and its results depend on the questions we ask and the limits we set around what constitutes an acceptable answer. Building on this idea, I argue that it is through the asking of these questions and the setting of these limits that results are defined and constructed – without this process, genomic variations would still be present in people and exerting effects, but they would not be results. As I discuss in 2.3, I now think of genomic results as a created phenomenon- a product of choices made in analysing and appraising genomic data- although the process of their creation is largely ignored in popular discourse.

As we construct genomic results, we should therefore actively keep in mind that a genomic result is more than a proven or very likely connection between a genomic variant and a present health problem or future health risk. Hundreds of variants in any one genome could fulfil this definition: in giving one or a few the status of a ‘result’, we are making choices as to what we want genomic results to be. Currently, we often ignore or minimise our role in making these choices because there is not an easy space for them within the Aristotelian classification frameworks often associated with ‘good science’ (see 6.4). We have recipes for appraising genomic variants – and we treat these as a proxy for genomic results.

But I argue that we should aim for more elastic concepts of genomic results, where conversations around them, and the framing with which they are delivered, are seen as playing a part in how that result is constructed. Perhaps this could position subtle and nuanced outcomes from genomic tests more helpfully, rather than pinning all the weight of

a result on the technicalities surrounding a particular variant. It might also be quite freeing to acknowledge and accept choices present in the construction of a genomic result. When tensions or uncertainties arise as to whether to value something as a result, this would not automatically be posited as a technical issue which we need to fix in the 'right' way, with burial or broadcast of the variant in question being the only options. Instead, it could be appraised as a genuine choice rather than a procedural problem with a right or wrong answer, and this might invite a less charged and more thoughtful debate as to how it might be valuable, and whether and how it should be constructed as a result.

Recognising genomic results as being constructed rather than simply unearthed also better acknowledges the effort and expertise that many people bring to the process. In the context of rare disease diagnosis, people having genomic tests often build new meaning in others' results through sharing their own experiences (6.3.2.4 and 7.3.2.3). Clinicians and scientists develop and share opinions as to which genes may be relevant to explore, identifying potentially relevant variation and brokering its journey towards being given the status of a result (6.3.2.1). In designing population screens involving genomics, clinicians and scientists need to make explicit (and sometimes controversial) choices as to what constitutes a valuable result (8.2.1 and 8.2.2). People opting for tests will be working to incorporate results into their lives, and by sharing information as to their health outcomes and experiences, will influence how others' results are constructed in the future.

In asserting that we should recognise and value the role our choices play in the construction of genomic results, I do not mean to imply that it is not worthwhile to aim for some consensus in how we appraise genomic variations as having the status of results. We can aim to evaluate the links between genomic variants and clinical effects with a degree of objectivity, and a sound understanding of the evidence connecting a particular variant with

disease forms an important aspect of its journey towards being valued as a result. I can also see that when members of the same family are having genomic testing with the same clinical question in mind, it is important to have some consistency as to what we might regard as a result. However, we need to be careful what price we pay in our efforts to be consistent. If it means undertaking similar post-positivist assessment of the links between particular genomic variations and disease, great. If it means couching ethical questions as to what we should understand to be genomic results as being purely technical questions with one right answer, perhaps our fetishisation of consistency is holding us back.

A further interesting aspect to consider is the role that ‘seeing’ a variant plays in its construction as a result. In the building blocks public engagement activity I described in 8.1, given a scenario starting with muscle weakness, many people were happy to filter variants such that those in ‘non-muscle genes’ were filtered out. But not finding a clear explanation for the muscle weakness, lots chose to look wider and saw a cancer-predisposing *BRCA* variant. Many people described feeling that they had to include it in the test result. Yet if they had found a clear explanation in the ‘muscle genes’ and stopped looking, they would never have seen the *BRCA* variant and it would not have been included in the result they constructed.

Parallel situations occur daily in genomic laboratories in the context of rare disease diagnosis – automated variant filtering pathways aim to clear away variants not related to the symptoms under investigation, regardless of whether they are medically impactful. While there is extensive debate as to whether to then opportunistically seek out such variants in particular genes(173), the idea of clearing them aside in the process of diagnostic testing is not generally seen as controversial. Yet if they slip through the filters and become visible to clinicians and/or scientists, this creates a question as to whether they

should be constructed as a result of the test. We seem comfortable with building theoretical decisions to ignore medically relevant variants into analysis from the offset – but *seeing* them seems to change things.

Further to that, the background and experience of the person ‘seeing’ may play into whether a genomic variation ultimately becomes constructed as a genomic result. In collaboration with colleagues from UCL Queen Square Institute of Neurology, I wrote a case report for the *Journal of Medical Ethics* where this issue had come into play(19). Here, a single *FH* variant had been flagged by a genomic test investigating muscle weakness – and if the person reviewing the data had purely specialised in muscle disorders they would likely have disregarded the variant as irrelevant (because variants in *both* copies of a person’s *FH* gene are required to lead to a muscle disorder). As it happened, the person reviewing the data had an awareness of cancer predisposition syndromes and recognised that a single *FH* variant might predispose to kidney cancer(19). With a tighter filtering pipeline or a more narrowly specialised analyst this variant would have fallen by the wayside and that would likely not have been perceived as an ethical problem. If a ‘good pipeline’ would have cleared the noise away, should a ‘good scientist/clinician’ just ignore it?

I think many people would feel uncomfortable with this – that having ‘seen’ something potentially relevant confers a responsibility to consider whether it should be constructed as a result that would not exist if we just know that it *could* be there in theory. But a responsibility to *consider whether* something should be constructed as a result should not be equated to its necessarily *being* a result: litigious climates may steer clinicians and scientists towards the view that if they have ‘seen’ something they must treat it as a result. Yet the result construction process involves a whole host of inbuilt choices *not to see*. These are necessary decisions – a choice to see ‘everything’- the 4.1-5 million ways a person’s

genome differs from the 'reference' - would be overwhelming and counterproductive. However, the consequence is that technical choices around filtering are intertwined with ethical choices around what should constitute a result. It is when filters fail, and we are confronted with something that we did not expect to see, that ethical questions loom large. When filters work as expected they do not remove ethical elements from the results construction process- they hide them.

In summary, if we could recognise and centre the choices we have in appraising particular genomic variants as having the status of results, it might open up new ways in which we can usefully engage with genomic results. We should not have a starting point that there will always be a single right answer, or that in cases of discrepancy someone must have done it wrong and the other person did it right. This attitude to genomic results stifles debate around the choices that we have in their construction: it suggests there should be no choice. Where it becomes clear that there potentially was, this is seen as an embarrassment rather than an opportunity to consider whether, when, how and why we should value a particular genomic variation as being a result.

What if instead, we could lean into these choices, and value the opportunities they create to learn more about the nature of genomic results? The results construction process is threaded through with questions which tangle together the technical and the ethical. As I argued in 2.5, I think genomic result construction could usefully be positioned as a form of empirical bioethics. Technical science is massively important to the results construction process but it will never have all the answers. It can inform ideas around the solidity of a link between a variant and a disease – but whether, when and how that variant should go on to be constructed as a result is a different sort of question. Genomic variants do not equate to results – they are given that status by the ways we engage with them and build

meaning around them. We have choices as to how we do that, and we should recognise and value those choices.

9.5 My project in context

As I discussed in 2.6.1, facet methodology does not contain '*a recipe for ensuring quality*'(92), and as such there is not an easy framework for appraising the quality of my project. Some aspects of my project are double-edged. For example, its interdisciplinary nature allowed me to draw together insights and experiences from various different fields to provide new perspectives on my research question, and I feel this was very valuable in allowing me to build hopefully credible arguments that are relevant across a number of disciplines(98). However, it also means my project sits between the gaps, and I have drawn on literature from a range of disciplines rather than deeply engaging with the literature in a single disciplinary 'home'.

I think my facet methodology approach has been really valuable in allowing a creative, strategic and novel approach to my research question. Facet methodology has not been used before in this context, but as I discuss in 2.4 I think it is very well suited to exploring genomic result construction, seeking out and welcoming insights as to how genomic results appear in a wide variety of contexts in order to better understand a central research question of how we *should* construct genomic results. However, taking this approach has also meant using a variety of methods from a background of very little experience of qualitative research. This has been mitigated by the extremely patient, responsive and supportive supervision I have had throughout this project which has given me every opportunity to better my research skills.

As I discussed in 9.4, my project has various implications for how we should construct genomic results. However, one determinant of the quality of this sort of research is its power to convince others, and that remains an open question. As I discussed in Chapter 8, I have had the opportunity to raise questions around the nature of genomic results in a variety of contexts, but some of these efforts have been contentious. For example, aspects of my *BMJ* article about newborn genome screening(51) were very unconvincing to the Generation Study team(174,175). I was grateful that despite our differences on paper, various people from the Generation Study team made the effort to go to, and make significant contributions to, the day to discuss newborn genome screening that I outlined in 8.2.1. It was interesting and reassuring how much closer our ideas around constructing genomic results in a population screening setting seemed in this forum than in correspondence around a published paper.

Looking at what my project ‘adds’, arguably much of it echoes work that has been done already. For example, the idea that popular discourse presents an overly deterministic view of genetics is far from new. My project contributes by showing how such ideas persist throughout the upheavals of new genomic technology and in the context of much laxer reasons for genomic testing. The integrative approach I took also adds by tracing how such discourses interact with on-the-ground experiences of outcomes from genomic tests, shaping how we think and talk about them, yet representing only a small fraction of what they are.

9.6 Areas for future research

I have enjoyed undertaking this project and I think there is more to explore relating to the question of how we should construct genomic results. Key aspects I think need research attention in the future are:

9.6.1 Exploring ways to introduce more rounded concepts of genomic results into curricula around genomics

Jamieson and Radick's work (1.4.2) shows the potential for reimagining curricula in a way that does not centre Mendelian inheritance. Their research with university students showed how teaching using a 'Weldonian' approach led to less deterministic attitudes towards genetics (in this approach *'students encountered genetics as fundamentally tied to development and environment. Genes were not presented to them as what inheritance is 'really about', with everything else relegated to ignorable supporting roles'*(76,176)). I think this research is so exciting but change needs to start earlier – by examining and challenging how genetics and genomics are taught in schools.

9.6.2 Considering ways of thinking about genomic results with clinicians and scientists involved in the results construction process

I have found it fascinating exploring the notion of a genomic result, and over the course of my research my thinking around this has really changed. In the future, I hope to explore concepts around genomic results with clinicians and scientists involved in the results construction process, seeing to what extent my ideas around the prevalence and unhelpfulness of the 'hidden gem' concept resonate, and considering what broader ways of conceptualising genomic results might be possible.

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11 Appendix

11.1 Publications relating to this DPhil

Promises under pressure: the modest predictive power of polygenic risk scores

Horton R, Dunlop M, McCartney M, Sud A, Sullivan R, Tomlinson I, Turnbull C, Houlston R, Lucassen A. Eur J Hum Genet. 2026

<https://doi.org/10.1038/s41431-025-01996-6>

Balancing the rights of the pre-symptomatic child to be found with the risk of harm to others from the screening process.

Lucassen A, Horton R. Eur J Hum Genet. 2024

<https://doi.org/10.1038/s41431-024-01689-6>

Glowing gels and pipettes aplenty: how do commercial stock image banks portray genetic tests?

Horton R, Boyle L, Weller S, Lucassen A. Eur J Hum Genet. 2024 Apr;32(4):456-460.

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Challenges of using whole genome sequencing in population newborn screening.

Horton R, Wright CF, Firth HV, Turnbull C, Lachmann R, Houlston RS, Lucassen A. BMJ. 2024 Mar 5;384:e077060.

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Genomics and insurance in the United Kingdom: increasing complexity and emerging challenges.

Dixon P, Horton RH, Newman WG, McDermott JH, Lucassen A. Health Econ Policy Law. 2024 May 16:1-13.

<https://www.cambridge.org/core/journals/health-economics-policy-and-law/article/genomics-and-insurance-in-the-united-kingdom-increasing-complexity-and-emerging-challenges/7A668761B13E16D91CE0A352E589683E>

Ancestry, race and ethnicity: the role and relevance of language in clinical genetics practice.

Redman MG, Horton RH, Carley H, Lucassen A. J Med Genet. 2024 Mar 21;61(4):313-318.

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The ethical challenges of diversifying genomic data: A qualitative evidence synthesis.

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Genomic data: building blocks for life or abstract art?

Horton R*, Lyle K*, Weller S*, Ballard L, Lucassen A. Front. Young Minds. 2024. 12:1249534.

<https://kids.frontiersin.org/articles/10.3389/frym.2024.1249534>

Immortal data: a qualitative exploration of patients' understandings of genomic data.

Lyle K, Weller S, Horton R, Lucassen A. Eur J Hum Genet. 2023 Jun;31(6):681-686.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10250296/>

Discussion of off-target and tentative genomic findings may sometimes be necessary to allow evaluation of their clinical significance.

Horton RH*, Macken WL*, Pitceathly RDS, Lucassen AM. J Med Ethics. 2024 May 9;50(5):295-298.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC11103297/>

Realistic expectations are key to realising the benefits of polygenic scores.

Sud A*, Horton RH*, Hingorani AD, Tzoulaki I, Turnbull C, Houlston RS, Lucassen A. BMJ. 2023 Feb 28;380:e073149.

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Chapter 18: Genome sequencing: challenges for equity and sustainability in an age of big data.

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<https://uk.sagepub.com/en-gb/eur/the-sage-handbook-of-data-and-society/book281091>

Genetic risk scores may compound rather than solve the issue of prostate cancer overdiagnosis.

Horton RH, Dunlop MG, Houlston RS, Lucassen A, McCartney M, McNeill A, Sud A. Br J Cancer. 2023 Jan;128(1):1-2.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9814235/>

Ethical issues raised by new genomic technologies: the case study of newborn genome screening.

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Ethical Considerations in Research with Genomic Data.

Horton R, Lucassen A. New Bioeth. 2023 Mar;29(1):37-51.

<https://www.tandfonline.com/doi/full/10.1080/20502877.2022.2060590>

Care of men with cancer-predisposing BRCA variants.

Horton R, Pharoah P, Hayward J, Lucassen A. BMJ. 2021 Oct 14;375:n2376.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7612259/>

What is the meaning of a 'genomic result' in the context of pregnancy?

Shkedi-Rafid S*, Horton R*, Lucassen A. Eur J Hum Genet. 2021 Feb;29(2):225-230.

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Exploring broad consent in the context of the 100,000 Genomes Project: a mixed methods study.

Ballard LM, Horton RH, Dheensa S, Fenwick A, Lucassen AM. Eur J Hum Genet. 2020 Jun;28(6):732-741.

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Old consent and new developments: health professionals should ask and not presume.

Horton R, Fenwick A, Lucassen A. Journal of Medical Ethics 2019. Online 29/10/2019.

<https://jme.bmj.com/content/early/2019/10/29/medethics-2019-105868>

Direct-to-consumer genetic testing with third party interpretation: beware of spurious results.

Horton R, Crawford G, Freeman L, Fenwick A, Lucassen A. Emerging Topics in Life Sciences 2019. Online 28/10/2019.

<https://doi.org/10.1042/ETLS20190059>

Practice Pointer: Direct-to-consumer genetic testing.

Horton R, Crawford C, Freeman L, Fenwick A, Wright C, Lucassen A. BMJ 2019: 367:l5688.

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Genomic testing in healthcare: a hybrid space where clinical practice and research need to co-exist.

Horton R, Lucassen A. Expert Review of Molecular Diagnostics 2019. Online 11/10/2019.

<https://www.tandfonline.com/doi/full/10.1080/14737159.2019.1672540>

Genome sequencing in healthcare: understanding the UK general public's views and implications for clinical practice.

Ballard L, Horton R, Fenwick A, Lucassen A. European Journal of Human Genetics 2019. Online 16/9/2019.

<https://www.nature.com/articles/s41431-019-0504-4>

Consent and Autonomy in the Genomics Era.

Horton R, Lucassen A. Current Genetic Medicine Reports 2019: 7(2):85-91.

<https://link.springer.com/article/10.1007/s40142-019-00164-9>

Is it acceptable to contact an anonymous egg donor to facilitate diagnostic genetic testing for the donor-conceived child?

Horton R*, Bell B*, Fenwick A, Lucassen A. Journal of Medical Ethics 2019: 45:357-360.

<https://jme.bmj.com/content/45/6/357>

Recent developments in genetic/genomic medicine.

Horton R, Lucassen A. Clinical Science 2019: 133(5):697-708.

<http://www.clinsci.org/content/133/5/697>

The moral argument for heritable genome editing requires an inappropriately deterministic view of genetics.

Horton R, Lucassen A. Journal of Medical Ethics 2019: 45:526-527.

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Unpacking the concept of a genomic result.

Horton R, Lucassen A, Fenwick A. The American Journal of Bioethics 2019: 19(1):70-71.

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11.2 Other engagement-oriented outputs created during this DPhil project

11.2.1 Centre for Personalised Medicine podcast series

As part of my Junior Research Fellowship at the CPM (see 2.2) I had the opportunity to develop two podcast series (<https://cpm.ox.ac.uk/podcasts/>). Series 1 of the CPM podcast had been previously created by Dr Anika Knuppel, a former CPM Junior Research Fellow.

The second series I developed throughout 2022-23, working closely with Dr Gabrielle Samuel (now a Lecturer in Environmental Justice and Health at King’s College London). The eight episodes we created involved interviews with people working in or with the CELS group, discussing various ethical and societal issues relating to personalised medicine (on reflection the double helix featured on the cover art was overly sparkly!). For the third series, which I developed 2024-2025, I moved to a format of group conversations over six episodes, aiming to gather people from the CPM and various experts to discuss some of the themes in the CPM’s strategy(177).

While neither series related directly to my project, various episodes allowed an opportunity to have discussions relevant to the construction of genomic results. Table 13 describes the episodes most relevant to my research.

Table 13: Episodes of the CPM podcast relevant to the construction of genomic results

Title (Series, Episode)	Episode details
Why context matters in genetic testing (S2 E2)	For this episode, we interviewed Anneke Lucassen about how the same genomic variant can mean different things in different people (as discussed in 1.1). This links into my project in emphasising how context should be key in determining whether and when to value a particular genomic variant as the ‘result’ of a test.

Title (Series, Episode)	Episode details
Newborn genome screening (S2 E4)	For this episode, I discussed newborn genome screening with Gabby Samuel and Lisa Ballard, drawing on the papers(51,159) discussed in 8.2.1. This links into my project in that it describes the challenge of deciding what to construct as a ‘result’ for a seemingly healthy newborn baby given the variety of seemingly worrying variation we each have in our genomes. At the time I recorded this, my interest was very much around uncertainties that might arise; if I were re-recording it now I would potentially focus more on the issue of collecting whole genomes where the intention as regards screening is to examine only a tiny fraction of the genome.
Who’s ‘the patient’ in genomic medicine? (S2 E5)	In this episode, we interviewed Susie Weller about her paper on ‘linked lives’(178). We live our lives alongside others, and our decisions have consequences for those close to us – what does this mean for how we define ‘the patient’ in genomic medicine? This has parallels with my findings in 6.3.2.4 and 7.3.2.3, where ‘results’ travel far beyond the person tested.
Diversifying genomics (S2 E6)	Here, we interviewed Faranak Hardcastle about her work exploring ethical challenges with diversifying genomic data(179). This links in with my work as access to rich datasets linking genomic variation and health outcomes are so vital to the construction of genomic results (see 1.1) – and where such datasets are unavailable this can profoundly weaken the results construction process.
Risk and prevention in personalised medicine (S3 E2)	In this episode, I discussed the benefits and challenges of personalised prevention with Anneke Lucassen, Sally Sansom (CPM JRF), Louisa Chenciner (CPM JRF), and Malte Gerhold (Director of Innovation and Improvement at the Health Foundation). This linked to my project in that much of the episode dwelt on the complexities of making predictions from genomic data (see 1.3 and 8.2), and the challenges this presents in knowing what sorts of inferences based on genomics might be helpful, and when.

11.2.2 Centre for Personalised Medicine art competition

During my Junior Research Fellowship at the CPM I developed and led an art competition for young people in Years 7 to 9 (aged approx. 11-13) in the UK (<https://cpm.ox.ac.uk/art-and-science-connection/>). The aim was to engage young people with the opportunities and challenges of personalised medicine.

The first round of the competition opened September 2022 to January 2023, with a theme of ‘measurements in health and disease’. The second round ran September 2023 to January 2024, asking for art around the topic of ‘screening newborn babies for disease’. The third round, from September 2024 to January 2025, had a theme of ‘how personalised medicine affects our planet’. The fourth round opened in September 2025, looking at ‘the meaning of “personalised medicine”’.

Each year, we received really amazing entries from schools across the UK. Figure 23, Figure 24, Figure 25 and Figure 26 show the winners from the first three years of the competition²². To be honest, these are a bit tangential to my project, but the art competition is one of the things I’ve enjoyed the most and been proudest of during my DPhil, so I wanted to include it here! I hope to develop another round of the competition in the future, linked to the construction of genomic results.

²²I have largely copied the artwork descriptions from the CPM blog posts which announced the winners and finalists(180–182): many of these were based on descriptions the artists included in their competition entry form. I wrote the blog posts for 2022-23 and 2024-25, Thea Perry very kindly wrote the post for 2023-24 (I was on maternity leave).

Aneesa, 12, Oxford High School, Oxfordshire

Laranya, 13, from Worksop College, Nottinghamshire

A high-contrast, black and white portrait of a man, likely a historical figure, rendered in a halftone or dithered style. The image is framed by a thick black border. The man has dark hair, a high forehead, and is wearing a dark suit jacket over a light-colored shirt and a dark tie. His expression is serious, and he is looking slightly to the right of the camera. The background is a uniform, light gray. The overall quality is grainy, characteristic of a halftone reproduction.

Figure 25: CPM art competition winner, group category, 2024-25

Charlotte, 12, and Tommy, 11, from Mountbatten School, Hampshire

Charlotte and Tommy's artwork, entitled 'What we carry', explores how personalised medicine impacts the environment by showing medical waste painted on a human body. It highlights the amount of single-use plastics, chemicals, and packaging that one person might create through personalised healthcare. By combining the human form with hand-drawn waste, the piece raises important questions about how we can enjoy the benefits of personalised medicine while reducing harm to the planet.

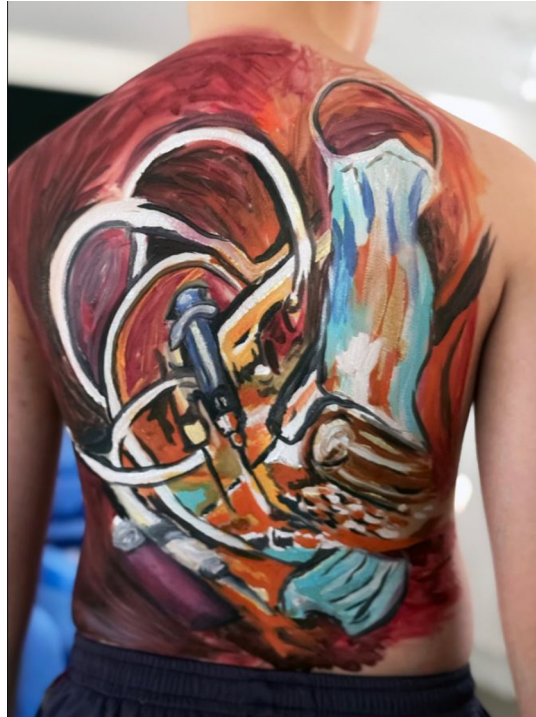


Figure 26: CPM art competition winner, individual category, 2024-25

Owen, 12, Heckmondwike Grammar School, West Yorkshire

Owen's sculpture shows scales with a medicine bottle, tablets and ointment in one bowl being weighed against our planet and plants in the other bowl, inventively demonstrating tensions between producing medication with the aim of improving human health, and environmental sustainability considerations.



11.3 Project timeline

11.3.1 Timing and relationship of different facets

In using facet methodology, I aspired to explore my key research question- ‘how should we construct genomic results?’- through a variety of different but interconnected approaches. My intention was that while each facet had potential to give me insights regarding genomic results in its own right, it also had scope to inform my analysis in other facets, and so to contribute to a more rounded and multifaceted picture regarding genomic results.

The start of my project was heavily weighted towards data generation regarding the more clinical aspects of my study. Applying for ethical approval for clinic observations and interviews with people experiencing genomic tests, then starting to undertake them, was my main focus early on. Alongside this, I was also undertaking very preliminary work as to the treatment of genomic results in news items (with much broader search terms than for the analysis I report in Chapter 4 – browsing through hundreds of articles covering topics as broad as direct-to-consumer genetic testing attempting to report on wine preferences, and DNA analysis of Cheddar Man).

During this time, my analysis of clinic observations was a strong influence on the questions I asked in my interviews with people experiencing genomic tests. For example, the confusion I noted around the role of parental samples in diagnostic genomic testing during my clinic observations (6.3.2.1) meant that the use of parental samples became a topic I specifically sought to explore in various of my interviews (7.3.2.3). Similarly, the interpretation and sharing of genomic results that I could see would continue beyond the clinic (6.3.2.4) was another aspect I started discussing with interview participants (7.3.2.3).

As I approached my first maternity leave, my focus on data generation intensified. This meant that at the point I paused the project in February 2020, I had collected and analysed a dataset relating to clinic appointments where genomic tests and their results were discussed. I had undertaken nine interviews with people experiencing genomic tests, and gained some familiarity with each by transcribing them and starting some provisional coding.

Returning to the project in March 2021, the research landscape had changed considerably in view of the Covid-19 pandemic. Clinic observations were not possible, and interviews had to be virtual rather than face-to-face. As part of reorienting myself into the project, I focussed on reading and re-reading my observation fieldnotes and interview transcripts. As I did this, I was struck by the tensions I saw between expectations and experiences around genomic results (6.3.2.2 and 7.3.2.1).

Wanting to explore this tension between experienced and envisaged genomic results further, I became interested in the role that popular discourses might be playing and started reading around these (particularly influenced by *The DNA Mystique*(84)). I was also lucky to become involved in writing a couple of analysis pieces relating to the use of genomics in population screening(51,52), a very different setting to that of rare disease diagnosis that I had been exploring through my clinic observations and interviews. This increased my curiosity as to how genomic results might be conceptualised and depicted across different settings.

As I started to consider how popular discourses might contribute to the construction of genomic results, I spent some time analysing stock images- initially relating to genetic testing(103). This connected with the very preliminary work I had started relating to news

items: probably many more people would have seen the headline and associated image, than read the text of the news items I was analysing. My clinical background also alerted me to potential connections between the representation of genomic results in stock imagery, and ways in which genomic results might go on to be implicitly represented in clinical consultations and to people considering genomic tests. Many of the information leaflets I used to hand out in clinic had a glossy blue double helix on the front cover, or directed people to websites which featured various of the sorts of images I discuss in 3.3.

Around this time, I was also very fortunate to gain an opportunity to seek data around publics' perceptions of genetics and genomics, because my supervisors were collaborating with the Mass Observation Project to develop a directive to explore '*Genetics and health in our everyday lives*'. I was really pleased that ultimately the directive included lots of questions that explored areas I had become interested in the course of earlier work on this project. We asked about people's ideas and expectations around genomics; the sources and experiences that might contribute to these; their views around use of genomics in a population screening setting (newborn screening); and their perceptions of genetic databases. I started some very early analysis of responses before starting my second maternity leave. This mainly involved tagging sections that related to an aspect I do not discuss in this thesis (experiences of care that did not feel personalised) as part of a broader project within the CELS group, but it gave me an opportunity to read all responses and get a sense of how rich they might be as a source of insights regarding the construction of genomic results.

At the point I paused the project in June 2023, I had completed data collection relating to the observations and interviews aspects of my project, and developed plans and undertaken preliminary work to explore popular discourses relating to genomic results. In

the last few months before maternity leave I had also worked on a public engagement activity around the construction of genomic results (8.1). This was a great opportunity to try to crystallise and communicate some of the issues I was exploring in my project, and I had a really interesting day at a science festival discussing this. Many conversations echoed those I had had with people experiencing genomic tests, and through working on analysis papers relating to use of genomics in population screening. Often implicit was an expectation of genomic results as having value, helpfulness and clarity. For people ‘building’ results at our stand, the aspiration to build a result of this nature was in tension with concerns about missing or not including something that might perhaps one day be helpful, but dependent on evolving scientific knowledge, or events and contexts in the person’s life that they could not predict.

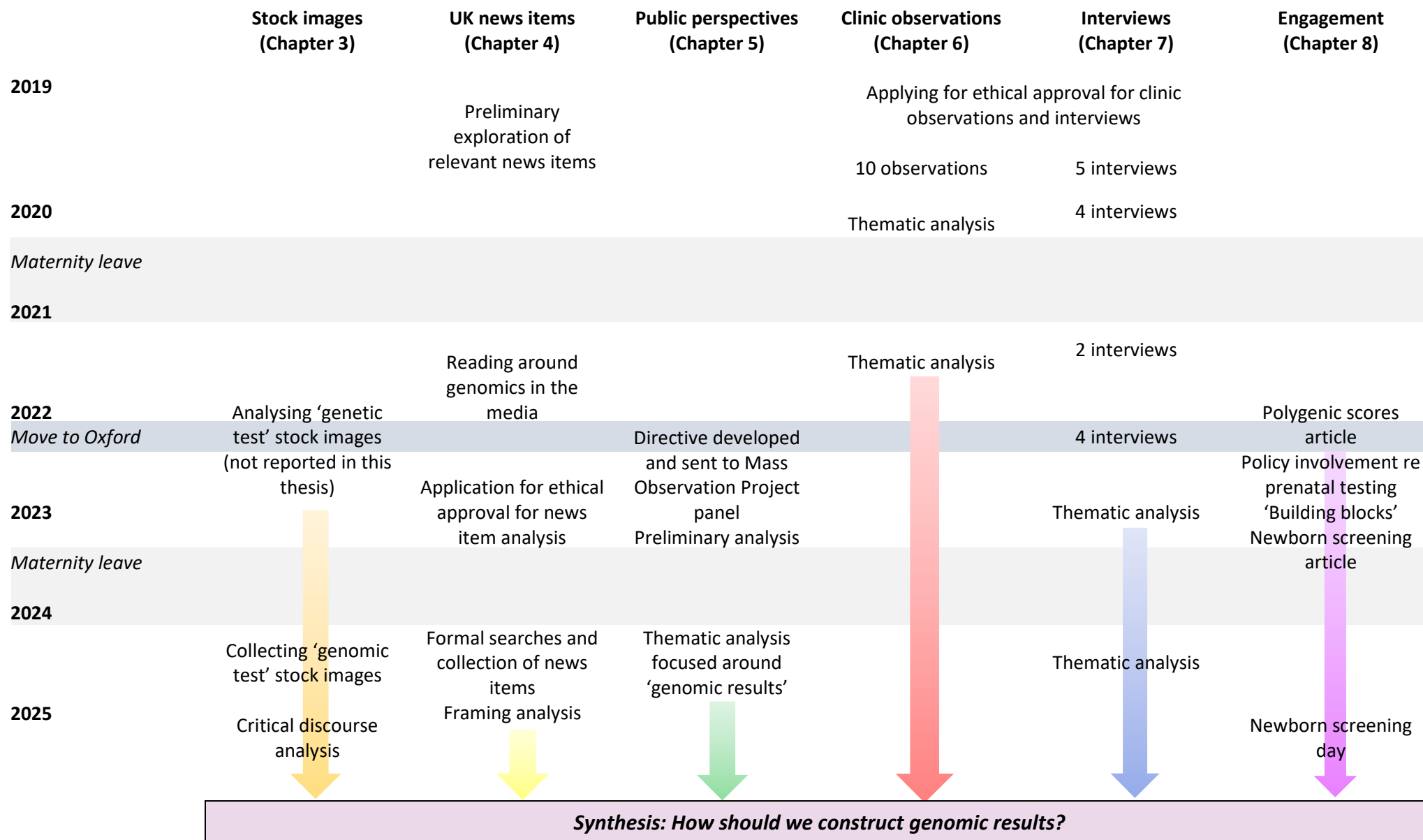
Returning to the project in May 2024, I started by taking stock of my datasets and mapping out how I would use the rest of my time out of clinical training. I began by collecting and analysing images related to genomic results (3.2), and analysing how results were written about within the Mass Observation Project (5.2.2). The facets were explicitly connected where Observers wrote of the images that came to mind when they thought about genetics (5.3.3). I thought that some ideas around the power of genomic testing and its connection to our fundamental nature also seemed prominent across both facets. For example, to me, the way the double helix was visually presented aligned with Nelkin and Lindee’s comments on the parallels between DNA and the human soul (3.3.1.1). A potentially profound and fundamental quality to genomic testing also seemed implicit in responses to the Mass Observation Project which wrote of genetics as having scope to influence the human experience and the nature of humanity (5.3.5 and 5.3.6).

As I completed my analysis of these datasets, I focused again on UK news items, refining my search strategy (4.2.1) to generate the final set of items that I would go on formally analyse. My plan to focus on news items discussing recent initiatives involving broad genetic testing was influenced partly by my interviews, trying to think in which news items the people I had spoken to might have most expected to see experiences parallel to their own. It was also influenced by the opportunities I had had to consider the use of genomics in a screening setting. Reading through the news items, I felt that many of them connected and potentially fed into the ideas implicit in various other facets as to how genomic results 'should' look. Many of these news items featured genomic results which had the transformative and powerfully helpful nature which was often hoped for and looked forward to in interviews and during clinic appointments, but lacking in practice (4.3.2.1 and 4.3.2.3 vs 6.3.2.2 and 7.3.2.2).

Having completed this analysis, I then thought specifically about each of my research questions (2.1) in light of each of the facets, aiming to bring together insights that might have a bearing on my central research question: how should we construct genomic results? This final analysis involved revisiting all my datasets, moving between them as I tested ideas across all the data I had worked with in the course of my project.

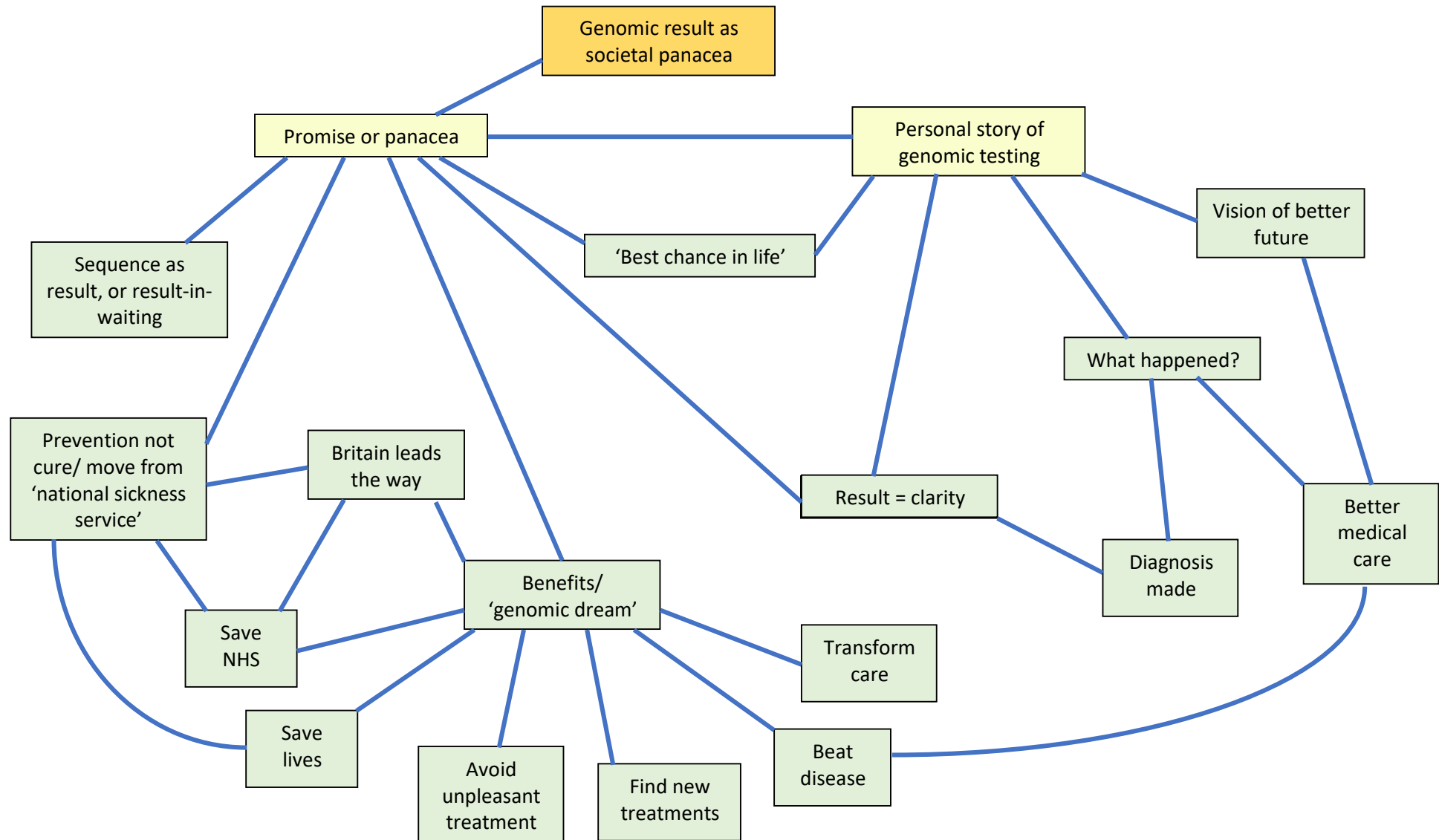
11.3.2 Diagram showing project timeline

Analysis for each workflow is presented separately for clarity, but in practice I sought out connections between facets



11.4 UK news item analysis: building a frame

This draws on some of my NVivo coding to try to give a sense of how I shuffled and sorted data in the process of developing the frame 'Genomic result as societal panacea', discussed in 4.3.2.3 (orange = final frame; yellow = relevant intermediate themes; green = early codes).



11.5 Material relating to work with the Mass Observation Project

11.5.1 The 'Genetics and health in our everyday lives' directive

For this Directive we are interested in your views and experiences of genetics and health.

Genetic tests are being used more and more ... from ancestry genetic tests that link long-lost relatives to plans to screen new-born babies with DNA tests.

20 years ago, genetic tests could only examine small portions of the genetic code, and this was technically difficult. Now tests can sequence a person's entire genetic code (genome) quickly and cheaply. Sometimes this helps to diagnose a condition, or determine a treatment, but other times we don't know what to do with the information found through such tests.

Developments in genetics mean that medicine can sometimes be made more personalised to an individual, rather than a whole population.

Your experiences of healthcare

Thinking about your own experiences of healthcare (this does not need to include genetic testing):

- Can you describe a time when you felt you experienced care that was personalised or tailored to your own specific situation?
- We would also like to hear about experiences of care that did not feel personalised to your own circumstances.
- Have you ever felt that any aspects of your identity or background have affected your experience of healthcare?

- On what basis do you think medical care should (or should not) be tailored to you?

Please share your feelings on this.

Genetics in our everyday lives

Please share what comes to mind when you think of 'genetics'. You are welcome to write down words, phrases, or to include images or sketches.

Please tell us about **any experience you have had of genetic testing** including the experiences of those around you – family, friends, neighbours, colleagues, and others. You could include any test that has looked at your DNA (genetic code) either via the NHS or those bought direct from shops/online (e.g. Ancestry tests or 23andMe).

Are there any news reports, films, television programmes or books about genetics that have been of interest to you? If so, please share how or why.

The issues genetic testing can raise

We would like to hear your thoughts on the following fictional scenario:

M has genetic testing after developing breast cancer. Her test finds she had a strong chance of developing breast cancer. M's doctor says that her sister could be tested for this inherited tendency (and if she has it, she could have extra screening or surgery to reduce her risks). M has not told her sister about her breast cancer and does not want to tell her sister about the genetic result. Her sister has a 50:50 (1 in 2) chance of having a strong genetic tendency to breast cancer.

- What do you think about this?
- Do you think M's sister should be told? If so, who should tell her?
- Should M's doctor communicate the potential risks to her sister if she doesn't?

- M has agreed for her genetic data to be stored in a DNA database and used for research purposes. What do you think might be the consequences (positive or negative) of being part of a DNA database?

Future uses of genetics

How do you imagine genetics might feature in our lives in the future?

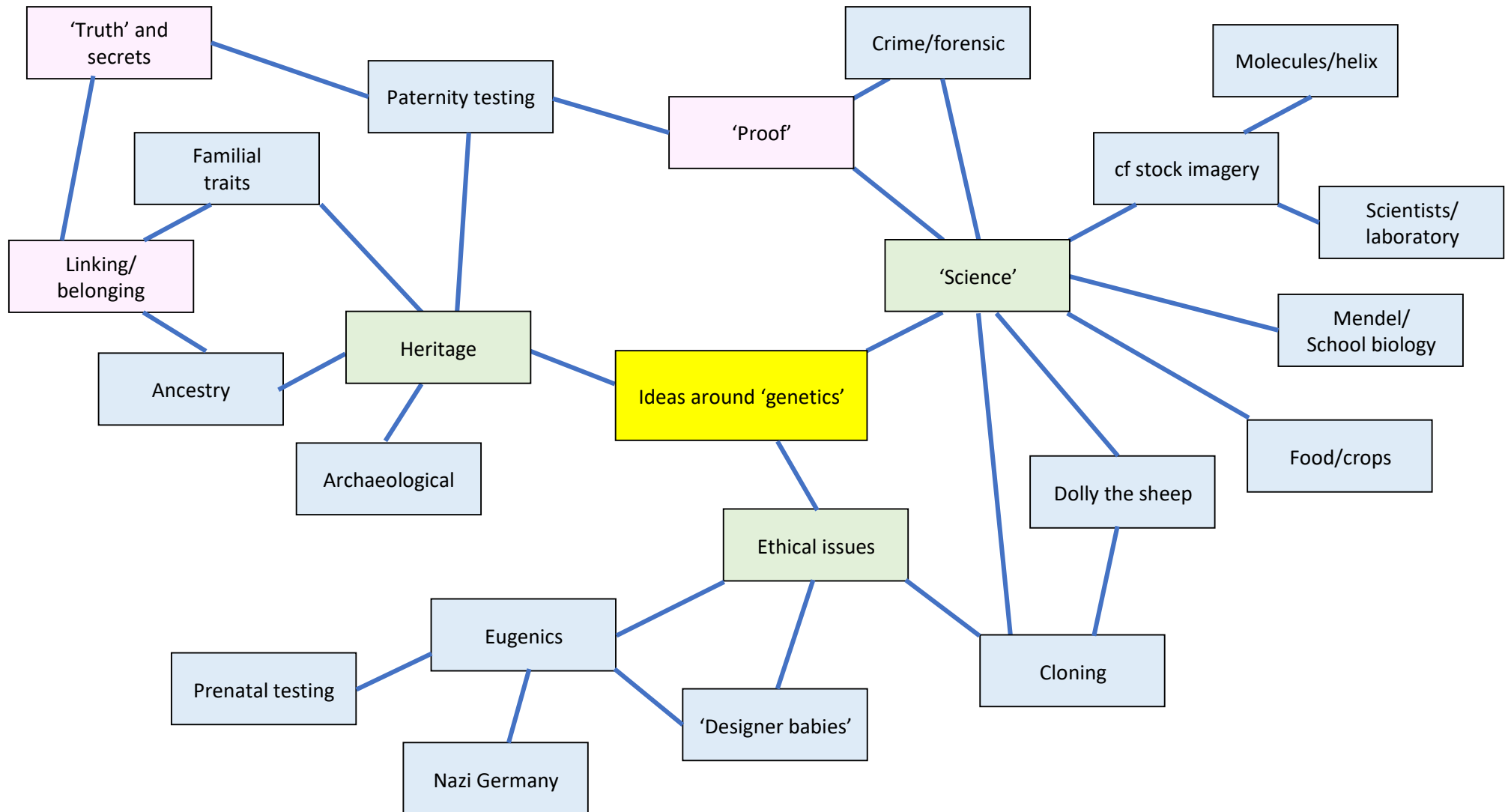
One potential future use is the **UK Newborn Genomes Programme** pilot study, which will examine the benefits and drawbacks of sequencing a baby's entire genetic code then analysing parts of it to look for various genetic conditions. It could detect more conditions than the current newborn 'heel prick' test. However, the programme might also cause more uncertainty (for example, where a possible genetic risk is found but no-one is sure if it will make the baby ill or it is unclear what the best treatment option is).

We would be interested in hearing **your views** on this initiative. What might be the potential benefits and drawbacks?

Do you have any particular hopes or worries about the future uses of genetics?

11.5.2 Mass Observation Project data analysis: organising codes to develop a theme

This aims to show the process of building the theme discussed in 5.3.3: *'The word 'genetics' evoked a breadth of ideas'*, from responses to our Mass Observation Project directive on *'Genetics and health in our everyday lives'*. Blue and green boxes show more descriptive codes; pink boxes show more interpretive codes.



11.5.3 Analysis of attitudes of Observers responding to both the 2006 and 2022 directives

I formed an opinion as to what Observers' attitudes might be by reading each response in its entirety and aiming to judge as a whole how the Observer appeared to feel about genetics in the context of healthcare. I considered what they expressed around the use of genetics in the future as being particularly relevant. For example, if Observers generally looked forward to and were hopeful about the benefits of increasing use of genetic technology I considered this as indicating a positive attitude. If they tended to be sceptical about the benefits of current use and caution against increasing future use I considered this as indicating a negative attitude. In constructing Table 14 I tried to select quotations that I thought seemed illustrative of key aspects of their attitude.

Table 14: Many Observers who responded to both the 2006 'Genes, genetics and cloning' directive and our 2022 'Genetics and health in our everyday lives' directive appeared to hold fairly stable attitudes towards the use of genetics in a healthcare context over time

Observer	Remarks around genetics
A1706	This Observer appeared to feel uncertain around the use of genetics, for example writing in 2006 <i>'Oh, big sigh – not another of those big subjects for which there is no right answer. I hear and read information on both sides of the argument but I still can't decide how far research or usage should go'</i> . This attitude still seemed evident in their 2022 response: <i>'As you say [in the directive]- "what might be the potential benefits and drawbacks". The question that arises around any new invention and can be debated endlessly with no definitive answer'</i> .
B3227	This Observer felt genetics was uninteresting and uninspiring in 2006: <i>'I'm sorry, I've tried to write on this topic, and I just can't. It doesn't inspire me, and I find I have no strong opinions on genetic testing or the boundaries of scientific research, or any of the other topics mentioned. I don't seem to care, and I can't make myself care'</i> . In 2022 they did not express disinterest but tended to question the value of genetic testing: <i>'So much of life is about uncertainty. Would parents who have their baby's genetic code analyzed for future genetic conditions really be better off for knowing what might lie ahead? I can only imagine the agonizing anxiety involved. There is surely an argument to be made for living in ignorance, and attempting to be as blissful about that ignorance as possible'</i> .

Observer	Remarks around genetics
G226	This Observer recognised positives about genetic testing in their wider responses but emphasised the importance of a cautious approach both in 2006 and 2022. In 2006 they wrote <i>'although science has progressed and some amazing things can be done, I personally would hesitate to interfere with nature to a large extent. My message would be to scientists to tread cautiously and respect nature'</i> . In 2022, they discussed <i>'I would worry about the future of some uses of genetics ... overall, genetics should be used wisely, with reference perhaps to something like the Hippocratic Oath'</i> .
H1705	In 2006, this Observer expressed personal interest in having genetic testing: <i>'[I] certainly think genetic testing for inherited conditions would be the sort of thing I would like to have done'</i> . Writing again in 2022, they retained this interest though described more apprehension about the potential for worrying outcomes: <i>'I haven't had any genetic testing but I think it would be interesting ... The slight worrying aspect of discovering possible genetic conditions is a psychological one'</i> .
H2418	For this Observer, only a small section of their 2006 response is available but what there is indicates at least some positivity towards genetics: <i>'Genetic testing for inherited conditions would be a good idea'</i> . Based on their 2022 response they continued to feel hopeful about the potential of genetics: <i>'We will be more able to see what causes disease and find more cures for more... Genetic developments are capable of making very positive advances for humanity'</i> . However, they also emphasised that: <i>'This has to be matched to a provision of healthcare for all'</i> – they were concerned about the potential for genetic screening to raise concerns which the NHS was not resourced to respond to.
I1610	This Observer seemed to retain a broadly positive attitude to genetics, writing in 2006 that <i>'This subject hasn't really touched my life but I am sure it is helping other people as the doctors discover more about our genes'</i> , and in 2022 that <i>'I know that a lot of research has been going on to alleviate sufferers and to help people decide what to do in the future with their medical conditions'</i> .
M3190	In 2006, this Observer discussed concerns around the potential for unrealistic expectations relating to genetics and the pressure this might create for scientists to ignore ethical issues: <i>'I'm concerned partly that unrealistic expectations might cause pressure to be placed on scientists to carry out work they privately acknowledge can't possibly deliver the desired outcomes'</i> . In 2022, their response indicated that they thought we should continue to temper our expectations that genetics will improve human health: <i>'I suspect genetics will be less practically useful than we hope when it comes to directly improving ordinary human lives'</i> .

Observer	Remarks around genetics
M3476	This Observer was uninterested in this topic in 2006: <i>'I can't write much about this subject because despite being a nurse I know little about the subject and am not that interested'</i> . In 2022, they recognised potential value in the use of genetics but were also attentive to its risks: <i>'Sharing genetic data recorded on a UK database may be valuable for research purposes but requires careful monitoring. The consequences of data leaks or sharing with third parties could have dire consequences. For example if data was shared with participants' employers, insurance companies'</i> .
P1796	In 2006 this Observer described feeling unsure and uninformed about genetics: <i>'I find this a particularly difficult subject and one that I really do not know very much about'</i> . Writing in 2022, they seemed to feel more comfortable engaging with the topic and perhaps overall tended towards a positive view, though they were also attentive to possible negatives: <i>'I had not heard of the Newborn Genomes Programme pilot study and can appreciate the for and against proceeding with this. Surely though the more we know the better we are at spotting things early and in so many diseases this is essential. You do though have to consider how you would feel if confronted by a genetic risk when a baby was born and how you would cope with the options'</i> .
P3209	This Observer acknowledged that people might have concerns around genetics but overall seemed to feel very positive about its potential. In 2006, they wrote <i>'There are so many ... inherited diseases that not only destroy lives but bring tragedy to those who love ... Can there be any criticism of those scientists who wish to make new discoveries that could transform lives and give hope? Even to this question to which my reply would be an obvious "no" I can appreciate the argument against'</i> . Similarly in 2022, they reflected <i>'DNA and genetic testing can also highlight the chances of serious illness in later life – Alzheimer's and Parkinson's diseases etc. For many people ignorance is bliss, they would not wish to know, but I think that testing early for such possibilities can prepare for any eventuality – planning for treatment and care at the onset. Testing does not guarantee a person will inherit these diseases but knowing the risks must be of great help'</i> .
P3373	This Observer appeared to feel consistently positive towards genetic testing. Their thoughts in 2006 were <i>'As for genetic testing for various inherited conditions, fine ... At least the parents have prior warning of what they may be facing ... These tests help'</i> . In their 2022 response, they explained <i>'I think it's important to know our family genetics such as in those families with a tendency to have cancer i.e. BRCA gene ... Surely it's better to know about possible illnesses / disorders you may carry or already have so that if you have a child, you know they may also carry that gene ... It can help'</i> .

Observer	Remarks around genetics
R1025	In 2006, this Observer described understanding the allure of genetic testing but worrying it could lead to eugenics: <i>'I understand the desire of people to identify certain genes that they have in their make up and so avoid children being born with some awful illness. But we've already seen that people are taking that too far ... Terrible as it is sometimes I think we must let things be'</i> . In 2022 they continued to feel concerned about future uses of genetics, though emphasising its potential to create anxiety as opposed to concerns around eugenics: <i>'I find it quite a scary prospect ... As for sequencing newborns genetic code I don't really see the point. All it will do is create anguish and fear in parents'</i> .
R860	In 2006, this Observer wrote <i>'I'm generally in favour [of genetic testing for inherited conditions] if it prevents pain and suffering but perhaps this has overtones of the Second World War – Hitler was said to want perfect citizens – blonde and blue eyed'</i> . From their 2022 response I found it hard to gauge their attitude as they tended to describe what they saw as the situation, rather than discuss their opinion about it.
S1399	I got the impression that in 2006, this Observer's attitude towards genetics would be quite dependent on what might happen downstream of a genetic test: <i>'Human genetics – most important issues are testing – who's got access to the results, can you get insurance after a test, treatment for conditions – the cost of it all is prohibitive'</i> . In 2022 it seemed that their attitude was similarly contingent: <i>'don't know– genetic data on DNA database/ research etc'</i> and <i>'newborns +&- conditions not treatable'</i> .
S3035	In both responses, this Observer appeared to feel reticent about use of genetic testing in view of ethical considerations. In 2006 they described <i>'The problems today stem from [the] introduction [of genetics] to the human field, where moral judgements become an issue'</i> . In 2022 they expressed their concerns around this more strongly: <i>'Whilst the Newborn Genomes Programme sounds like a good idea, it smacks of eugenics, and would result in many pregnancies being terminated on the possibility of a less than perfect baby being born ... If this programme were allowed to continue, I can see gene manipulation being undertaken to try and produce superior beings, a la the Nazis during the last war'</i> .
T1843	In both 2006 and 2022, this Observer described the use of genetics as <i>'an ethical minefield'</i> . In both responses they outlined various pros and cons of genetics, in 2006 appearing to feel conflicted about its increasing use: <i>'In general I welcome all new discoveries and advances, but it seems increasingly as though we are able to achieve so much without necessarily having the maturity and wisdom as societies to deal with any risks and consequences morally and environmentally of what we can now do'</i> . In 2022 they continued to describe having <i>'mixed feelings'</i> about issues such as participation in a DNA database, and reflected <i>'Be careful what you wish for and love and be kind to all living things. Use science for good; legislate against undesirable outcomes'</i> .

Observer	Remarks around genetics
T1961	Writing in 2006, this Observer described having <i>‘somewhat mixed feelings about genetic testing’</i>. They wrote about the concern that <i>‘Sometimes it can seem as if medical science has taken things too far and only “perfect” babies are to be born; and people are to be kept alive at all costs, even when they are old and their quality of life is very very poor’</i>. Their 2022 response implied that they saw genetics as potentially generating very distressing information but having an important role in facilitating personal decision-making: <i>‘finding out as my friend did that she had inherited the dreadful Huntingtons disease must be devastating and since it appears as yet no cure has been found that appears to be quite different from say, a mother being told she is carrying a child who has a big chance of being born Downs syndrome. I feel very strongly that a woman’s body is entirely her own and decisions in this respect are hers to make; with appropriate counselling’</i>.
T3155	From this Observer’s 2006 response I found it hard to gauge an overall attitude towards genetics as I was unsure how much weight to give to the first sentence of this excerpt: <i>‘Now the genetic testing for inherited conditions seem to me to be one of the finest advances in medical science. Imagine a world where many diseases diabetes, and heart conditions, could be prevented from occurring or diagnosed early. Great, but then big business takes a look, insurance for instance, try getting a mortgage etc. if your outlook is bleak, hmm not so sure! As with all advances in Science, there is the darker side as Mr (dynamite) Nobel could have told us!’</i>. Their 2022 response again left me uncertain- on the one hand they described <i>‘I have no qualms about [someone] having her DNA stored in a database’</i> but they also expressed: <i>‘I am sceptic about the scientific developments in the world, judging by the past history of nuclear energy and Dynamite, ironic how the Nobel prizes are given to scientists that develop these great gifts to mankind and are misused to kill him’</i>.
W1835	Writing in 2006, this Observer reflected on finding genetic testing personally helpful: <i>‘as a young mother I had a Down’s Syndrome baby. Because it was not typical – because of my age – I had my DNA investigated. This was helpful as I do not believe in abortion and ten years later I had a normal baby’</i>. Her 2022 response tended to be more descriptive rather than expressing an opinion and I did not get a sense as to what her overall feelings towards genetics might have been at that time.

Observer	Remarks around genetics
W2322	In 2006, this Observer wrote a short response including <i>'I have to admit I am not very well informed on these issues. I would rely on television to inform me'</i>, and I did not get an impression as to how they might have felt about genetic testing in healthcare. In 2022 they engaged with the topic more deeply and emphasised the importance of caution: <i>'For me the great potential danger of the Newborn Genomes Programme is that it opens the door to Designer Babies; so that those with the power and resources could ensure that "their" offspring had exactly the characteristics which they desired. This is morally unsound, and also shows an arrogance that suggests man is always right and would not make the sorts of mistakes which nature does through genetic variation ... We should be very wary of wanting to play God, and should stick to the sort of genetic studies which seeks to tackle diseases'</i>.
W3163	In both responses, the Observer described the topic as controversial, but their attitude towards genetic testing had perhaps become more positive with time. Their 2006 response included excitement around the potential of stem cells, alongside reticence around the merits of genetic testing: <i>'As far as genetic testing – I'm a bit more wary about what this will be used for. Testing for inherited diseases could cause as many problems as it might solve'</i>. In 2022 they wrote <i>'New science is always controversial and genetics are no exception. It will raise difficult questions but that's how we further advance our understanding of health issues. There are health issues we didn't know about 50 or 100 years ago or even have names for, which are now common knowledge, and some are now preventable, treatable or curable; some we are still looking for answers to'</i>.
W729	In 2006, this Observer appeared broadly positive about genetics, writing <i>'I think when a woman is pregnant it is good, if she wants it, to be able to get tested for possible inherited conditions before her baby is born, or to consider a termination if the baby is going to be too handicapped ... In the future I think genetics and cloning will play a much bigger part in our lives than they do now, and will help lots of ill people, despite some reservations about it'</i>. This positivity regarding its potential still seemed evident in 2022 though this response reflected in more detail on potential misuse: <i>'I think genetics is the way forward. Anything that is tailored to the individual, rather than the masses, has got to be good ... I think genetics is the best way to help people but it's scary too if it got out of hand. I think genetics will play an increasing role in healthcare in the future, good or bad. I hope it is well regulated though'</i>.

11.6 Favourable opinion letter for ethics application relating to clinic

observations and interviews with people experiencing genomic tests



Ymchwil Iechyd
a Gofal Cymru
Health and Care
Research Wales



NHS
Health Research
Authority

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16 April 2019 reissued 26 April 2019

Dear Dr Horton

**HRA and Health and Care
Research Wales (HCRW)
Approval Letter**

Study title: But what is my result? Bioethical and clinical perspectives on the concept of what constitutes a result from genome sequencing.

IRAS project ID: 249060

REC reference: 19/EM/0024

Sponsor: University of Southampton

I am pleased to confirm that [HRA and Health and Care Research Wales \(HCRW\) Approval](#) has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, [in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.](#)

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see [IRAS Help](#) for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?

HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to [obtain local agreement](#) in accordance with their procedures.

What are my notification responsibilities during the study?

The document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The [HRA website](#) also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?

Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is 249060. Please quote this on all correspondence.

Yours sincerely,

Michael Higgs
Approvals Specialist
hra.approval@nhs.net

(For brevity I have not included the appended table of approved documents and versions here)

11.7 Material relating to clinic observations

11.7.1 Text of participant information sheet for clinicians regarding clinic observations

(The information sheets used in practice included university branding, header and footer with version details, and a data protection privacy statement).

Ethical and clinical perspectives on interpreting genomic data

Observation of clinic appointments (for health professionals)

Participant Information Sheet

Research team: Rachel Horton, Prof Anneke Lucassen, Dr Angela Fenwick

Ethics reference numbers: IRAS project ID 249060; REC reference 19/EM/0024

You are being invited to take part in the above research study. To help you decide whether you would like to take part or not, it is important that you understand why the research is being done and what it will involve. Please read the information below carefully and ask questions if anything is not clear, or if you would like more information before you decide to take part. You may like to discuss it with others, but it is up to you to decide whether or not to take part.

What is the research about?

I am doing a PhD project looking at how patients, clinicians and scientists think about genomic results. Genetic testing previously tended to work by looking at tiny parts of the genetic code (single genes) that might explain a patient's health problems. Genomic tests look at huge amounts of genetic code in one go, finding around four million differences (variants) in the genetic code per person. Scientists and clinicians then need to sort through these variants to identify the important ones. It can be hard to know what would be relevant and helpful to communicate. I hope my research will help by looking at what patients, families, clinicians and scientists think should form the 'result' from genomic tests.

Why am I asking you to participate?

For part of my research, I would like to see how clinicians and patients talk about genomic tests and results. I am asking you to consider taking part because you may be involved in talking about genomic tests and results with patients and families.

What will happen to you if you take part?

If you decide that you would like to take part, I would ask you to identify a clinic session where you think that you may be discussing genomic tests or genomic results with patients and families. I would then liaise with your clinic coordinator to send out information about my research to patients that you are due to see during that clinic where you think that you may be discussing genomic tests or results. On the day of the clinic, I would observe any appointments where both you and the patient/family attending were happy for me to do this. I would not actively take part in the appointments but I might quietly take some notes if you and your patients talk about genomic tests or results.

Will you benefit from taking part?

You will not personally benefit from taking part in this research, but you may help us develop useful ways of thinking and talking about genomic results, and deciding what information should be included. I hope that this will lead to ways of thinking about genomic results that will be practically useful in the clinic.

Are there any risks involved?

You may feel uneasy about the clinic being observed, and you may feel that this affects your initial interactions with patients and families. This feeling usually passes quite quickly. However, if you do decide that you no longer wish me to observe the discussions, you can ask me to leave at any point. You would not have to give a reason.

What data will be collected?

If you and your patients discuss genomic tests or results during your appointments, I will quietly take some notes about the discussion that you have, and any questions that might come up, to help me understand how genomic results seem to be realised in practice. After your clinic, I would type up and securely save my notes about the discussions around genomic results, then I would shred my written notes about the discussions.

With projects like this, it is good practice to make data collected during the research available to other researchers, so that we can continue to learn from the data that the patients, families and clinicians who allow us to observe their appointments have kindly provided. I would do this by putting some of my data into the UKDA Qualibank (an archive of data for research). I would not put in any identifying data so it would not be possible for other researchers to know who had participated in my research. Future studies that wished to draw on this data would need ethics approval in order to do so.

Will your participation be confidential?

Your participation and the information we collect about you during the course of the research will be kept strictly confidential. Only members of the research team and responsible members of the University of Southampton may be given access to data about you for monitoring purposes and/or to carry out an audit of the study to ensure that the research is complying with applicable regulations. Individuals from regulatory authorities (people who check that we are carrying out the study correctly) may require access to your data. All of these people have a duty to keep your information, as a research participant, strictly confidential.

I will store my observations about what is discussed about genomic tests or results using a code number, separate from any identifiable details. Data will be stored securely on the University of Southampton network. I might quote some words or phrases that people say during appointments in reports and publications about this research. The quotations would be anonymous (i.e. it would not be possible for people reading the reports to tell who said them). If you were to read reports of this research there is a small chance that you might recognise short phrases that you or your patients said when you talked about genomic tests or results.

Do you have to take part?

No, it is entirely up to you to decide whether or not to take part. If you decide that you want to take part, you will need to sign a consent form to show that you have agreed to take part.

What happens if you change your mind?

If you agree to take part but change your mind during the clinic, just let me know and I will leave. You do not have to give a reason.

What will happen to the results of the research?

I plan to publish the results of this research in academic journals, and present them at

conferences and clinical meetings. I will also share results via my project website (<https://whatismyresult.wordpress.com/>) and other social media, and at patient support days. I will upload progress reports to my project website while the research is ongoing, and will upload a full study report when this research is completed.

Where can you get more information?

You can find out more about this research by visiting my project website at <https://whatismyresult.wordpress.com/>. If you have any questions, please contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082.

What happens if there is a problem?

If you have a concern about any aspect of this research, please contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082. If you continue to have concerns, please speak to a senior member of the research team (Dr Angela Fenwick or Professor Anneke Lucassen on 023 8120 4489). If you wish to speak to someone independent of the research team, please contact the University of Southampton Research Integrity and Governance Manager (023 8059 5058, rgoinfo@soton.ac.uk).

If you would be interested in taking part, please email me at r.h.horton@soton.ac.uk or fill in an 'expression of interest' form and post it back to the Clinical Ethics and Law group in the envelope provided. I will then contact you to talk through this research in more depth.

Thank you very much for taking the time to read this and for considering taking part in my research.

11.7.2 Text of consent form for clinicians regarding clinic observations

Observation of clinic appointments (for healthcare professionals)

Consent form

Project: Ethical and clinical perspectives on interpreting genomic data

Research team: Rachel Horton, Prof Anneke Lucassen, Dr Angela Fenwick

Ethics reference numbers: IRAS project ID 249060; REC reference 19/EM/0024

1. I confirm that I have read the information sheet provided to me about this research (version _____ date _____). I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and I am free to stop the observations at any time without giving any reason. ☐
3. I understand that direct quotations may be used in reporting the results of this research but that these will be anonymised (there will be no link to my name). ☐
4. I understand that de-identified data from the observations may be made available to other researchers when this research project finishes. ☐
5. **I agree to take part in the clinic observation.** ☐

Name of participant

Date

Signature

Researcher

Date

Signature

11.7.3 Text of participant information sheet for families regarding clinic observations

(The information sheets used in practice included university branding, header and footer with version details, and a data protection privacy statement).

Ethical and clinical perspectives on interpreting genomic data

Observation of clinic appointments (for parents/guardians on behalf of their family)

Participant Information Sheet

Research team: Rachel Horton, Prof Anneke Lucassen, Dr Angela Fenwick

Ethics reference numbers: IRAS project ID 249060; REC reference 19/EM/0024

You are being invited to take part in the above research study. To help you decide whether you would like to take part or not, it is important that you understand why the research is being done and what it will involve. Please read the information below carefully and ask questions if anything is not clear, or if you would like more information before you decide to take part. You may like to discuss it with others, but it is up to you to decide whether or not to take part.

What is the research about?

I am doing a PhD project looking at how patients, clinicians and scientists think about genomic results. Genetic testing previously tended to work by looking at tiny parts of the genetic code (single genes) that might explain a patient's health problems. Genomic tests look at huge amounts of genetic code in one go, finding around four million differences (variants) in the genetic code per person. Scientists and clinicians then need to sort through these variants to identify the important ones. It can be hard to know what would be relevant and helpful to communicate. I hope my research will help by looking at what patients, families, clinicians and scientists think should form the 'result' from genomic tests.

Why am I asking you to participate?

For part of my research, I would like to see how patients and clinicians talk about genomic tests and results. I am asking you to consider taking part as it is possible that your clinician will talk to you about genomic tests or results during your child's appointment, though they may not do. **Being asked to participate in this study does not mean that you will receive a genomic result or be offered a genomic test during your child's appointment.** This will depend on what would happen anyway during the appointment as part of standard clinical care for your family. You are being sent this information because the clinician that you are due to see sometimes discusses genomic tests and results during their appointments.

What will happen to you if you take part?

When you arrive for your child's appointment, the clinic receptionist or another member of the NHS team will check whether you might be interested in taking part in my research. If you think you might be, I would meet you to talk this through in more depth and to answer any questions that you have. If you do decide to take part, I would sit in during your child's appointment and listen to what you, your family, and your clinician say about genomic tests and results (if anything). I would not actively take part in your appointment but I might quietly take some notes if you talk about genomic tests or results.

Will you benefit from taking part?

You will not personally benefit from taking part in this research, but you may help us develop useful ways of thinking and talking about genomic results, and deciding what

information should be included. I hope that this will be helpful to other patients, families, clinicians and scientists in the future.

Are there any risks involved?

You may feel uneasy at being observed during the appointment, and you may feel more self-conscious about talking to your clinician. This feeling usually passes quite quickly. However, if you do decide that you no longer wish me to observe the discussions, you can ask me to leave at any point. You would not have to give a reason.

What data will be collected?

If you and your clinician talk about genomic tests or results during your appointment, I will quietly take some notes about the discussion that you have, and any questions that might come up. After your appointment, I would type up and securely save my notes about your discussion around genomic results, then I would shred my written notes about your discussion.

With projects like this, it is good practice to make data collected during the research available to other researchers, so that we can continue to learn from the data that the patients, families and clinicians who allow us to observe their appointments have kindly provided. I would do this by putting some of my data into the UKDA Qualibank (an archive of data for research). I would not put in any identifying data so it would not be possible for other researchers to know who had participated in my research. Future studies that wished to draw on this data would need ethics approval in order to do so.

Will your participation be confidential?

Your participation and the information we collect about you during the course of the research will be kept strictly confidential. Only members of the research team and responsible members of the University of Southampton may be given access to data about you for monitoring purposes and/or to carry out an audit of the study to ensure that the research is complying with applicable regulations. Individuals from regulatory authorities (people who check that we are carrying out the study correctly) may require access to your data. All of these people have a duty to keep your information, as a research participant, strictly confidential.

I will store my observations about the discussion around genomic tests or results using a code number, separate from any identifiable details. Data will be stored securely on the University of Southampton network. I might quote some words or phrases that people say during appointments in reports and publications about this research. The quotations would be anonymous (i.e. it would not be possible for people reading the reports to tell who said them). If you were to read reports of this research there is a small chance that you might recognise short phrases that were said during your appointment if you and your family talked about genomic tests or results with your clinician.

Do you have to take part?

No, it is entirely up to you to decide whether or not to take part. If you decide that you want to take part, you will need to sign a consent form to show that you have agreed to take part.

What happens if you change your mind?

If you agree to take part but change your mind during the appointment, just let me know and I will leave. You do not have to give a reason.

What will happen to the results of the research?

I plan to publish the results of this research in academic journals, and present them at conferences and clinical meetings. I will also share results via my project website (<https://whatismyresult.wordpress.com/>) and other social media, and at patient support days. I will upload progress reports to my project website while the research is ongoing, and will upload a full study report when this research is completed.

Where can you get more information?

You can find out more about this research by visiting my project website at <https://whatismyresult.wordpress.com/>. If you have any questions, please contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082.

What happens if there is a problem?

If you have a concern about any aspect of this research, please contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082. If you continue to have concerns, please speak to a senior member of the research team (Dr Angela Fenwick or Professor Anneke Lucassen on 023 8120 4489). If you wish to speak to someone independent of the research team, please contact the University of Southampton Research Integrity and Governance Manager (023 8059 5058, rgoinfo@soton.ac.uk), or the [local] Patient Advice and Liaison Services (PALS) on [this number].

Please consider if you would be happy to take part in my research. When you arrive for your child's clinic appointment, the receptionist or another member of the NHS care team will check whether you would be interested in taking part. If you have any questions about this research in advance of your appointment, please feel free to contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082.

Thank you very much for taking the time to read this and for considering taking part in my research.

11.7.4 Participant information sheet for young people aged 13-15 regarding clinic observations

Medicine	UNIVERSITY OF Southampton University Hospital Southampton NHS NHS Foundation Trust
Ethical and clinical perspectives on interpreting genomic data Clinic observation (for young people aged 13-15 years) Information sheet	
I'm doing research looking at how patients and clinicians talk about genomic tests. These are new sorts of genetic test that look at lots of genetic code in one go. For my research, I would like to see how patients and clinicians talk about genomic tests and results.	
I am inviting you to take part as your clinician might talk to you and the adult with you about genomic tests (though they might not). I would like to sit in during your clinic appointment and listen to what everyone says, as this will help my research.	
What are the pros and cons? This research will help me think about ways that clinicians and patients can talk about genomic tests. It won't affect your or your family's medical care. Sometimes people feel uneasy having someone else listen to them and their clinician but usually they get used to it quickly.	
What are the next steps? I will ask the adult you are going to clinic with to decide whether they would be happy for me to sit in on your appointment. I would like to know if you are happy for me to be there too. If you are not then I won't sit in on the appointment.	
Do I have to take part? No, it is up to you. If you agree to take part and then change your mind, you can let me know at any time and I will leave the room.	
Thank you very much for thinking about this. Please do ask for the adult study information sheet if you would like more information about this research.	
Version 1.6 [May 2019]; IRAS project ID 249060; REC reference 19/EM/0024 CELS (Clinical Ethics and Law at Southampton), Wessex Clinical Genetics Service, Level G, Mailpoint 627, The Princess Anne Hospital, Coxford Road, Southampton, SO16 5YA	

11.7.5 Participant information sheet for young people aged 10-12 regarding clinic observations

Medicine	UNIVERSITY OF Southampton University Hospital Southampton NHS NHS Foundation Trust
Ethical and clinical perspectives on interpreting genomic data Clinic observation (for young people aged 10-12 years) Information sheet	
I'm doing research looking at how patients and clinicians talk about new sorts of genetic tests. Your clinician might talk to you and the adult with you about genetic tests (though they might not). I would like to listen to what everyone talks about, as this will help my research. I would like to sit in the room with you and listen while you see your clinician.	
What are the pros and cons? This research will help me think about ways that clinicians and patients can talk about genetic tests. It won't affect your or your family's medical care. Sometimes people feel uneasy having someone else listen to them and their clinician but usually they get used to it quickly.	
What are the next steps? I will ask the adult with you to decide whether they would be happy for me to sit in on your appointment. I would like to know if you are happy for me to be there too. If you are not then I won't sit in on the appointment.	
Do I have to take part? No, it is up to you. If you agree to take part and then change your mind, you can let me know at any time and I will leave the room.	
Thank you very much for thinking about this.	
Version 1.6 [May 2019]; IRAS project ID 249060; REC reference 19/EM/0024 CELS (Clinical Ethics and Law at Southampton), Wessex Clinical Genetics Service, Level G, Mailpoint 627, The Princess Anne Hospital, Coxford Road, Southampton, SO16 5YA	

11.7.6 Text of consent form for families regarding clinic observations

Observation of clinic appointments (for patients and families)

Consent form (for parent/guardian on behalf of their family)

Project: Ethical and clinical perspectives on interpreting genomic data

Research team: Rachel Horton, Prof Anneke Lucassen, Dr Angela Fenwick

Ethics reference numbers: IRAS project ID 249060; REC reference 19/EM/0024

- | | | |
|----|--|--------------------------|
| 1. | I confirm that I have read the information sheet provided to me about this research (version _____ date _____). I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. | ☐ |
| 2. | I understand that my family's participation is voluntary, and that we are free to stop the observations at any time without giving any reason. | ☐ |
| 3. | I understand that direct quotations may be used in reporting the results of this research but that these will be anonymised (there will be no link to our names). | ☐ |
| 4. | I understand that de-identified data from the observations may be made available to other researchers when this research project finishes. | ☐ |
| 5. | I agree for my family to take part in the clinic observation. | |
| 6. | I am happy to be contacted by the Clinical Ethics and Law group at Southampton regarding taking part in future research. | ☐ |

_____	_____	_____
Name	Date	Signature

Names of any young people at the appointment

_____	_____	_____
Researcher	Date	Signature

11.7.7 Text of permission form for young people regarding clinic observations

Observation of clinic appointments (for patients and families)

Permission form (for young people aged 10-15 years)

Project: Ethical and clinical perspectives on interpreting genomic data

Your parent or guardian has agreed that I can sit in on your clinic appointment if you are happy with this. If you are not happy then I won't.

If you are happy for me to sit in your appointment, please could you write your name and sign below?

Name

Date

Signature

Researcher

Date

Signature

11.7.8 Observation framework for clinical appointments

Context of clinic appointment:

- ☐ Discussing whether to have a genomic test
- ☐ Discussing the outcome of a genomic test (i.e. a 'result')
- ☐ Other (give details): _____

Who was or who will be tested?:

- ☐ Proband only
- ☐ Trio
- ☐ Other (give details): _____

Type of result(s) discussed:

- ☐ Diagnostic
- ☐ VUS
- ☐ Nothing found
- ☐ Unexpected
- ☐ Future relevance/predictive
- ☐ Other (give details): _____

What result(s) discussed? (what kind of 'result' was actually fed back as the outcome of a genomic test, or what examples were given of possible results to someone thinking about having a test?)

How is the genomic test described (if relevant)? e.g. any distinction made between genetic and genomic? Reference to research or technology? Any analogies used for test or results?

Couched as clinical, research, hybrid?

How is the test/result contextualised? Any comparisons/analogies used? Any reference to public discourse around genomic tests or results?

How is time-frame for future results delivery communicated? Iterative?

Use of terms (circle and add comments if these or synonymous terms used):

- New / novel...
- Detailed
- Unfocused / broad
- Unexpected / incidental...
- Uncertain
- Reference to wider family / other relatives...
- Technology
- Routine / doing this more and more...
- Normalising? / we've all got things like this...

Words/phrases used to describe the molecular aspect of the 'result' (circle and/or write free text):

mutation	variant	change	spelling mistake	glitch
DNA	difference	alteration		

Words/phrases used to describe the value of the 'result' (circle and/or write free text):

answer	reason	explanation
--------	--------	-------------

If a 'result' is discussed, what sense is given about its value? If it appears to 'fall short' in some way to patient, family or clinician, is a sense given of what a 'true result' would look like?

Patient/family response to results – what is their reaction? Do they have any questions?

Any things difficult conceptually? (areas of disconnect, initial misconception and clarification, etc)

Any other striking things not covered by other questions?

What wasn't discussed?

Summary of observation thoughts/key messages (to complete after the observation) – what did this tell me about the nature of genomic results? How does it help me think about how genomic results should be conceptualised?

11.8 Material relating to interviews with people experiencing genomic tests

11.8.1 Text of participant information sheet regarding interviews

(The information sheets used in practice included university branding, header and footer with version details, and a data protection privacy statement).

Ethical and clinical perspectives on interpreting genomic data Interviews (for patients and families)

Participant Information Sheet

Research team: Rachel Horton, Prof Anneke Lucassen, Dr Angela Fenwick

Ethics reference numbers: IRAS project ID 249060; REC reference 19/EM/0024

You are being invited to take part in the above research study. To help you decide whether you would like to take part or not, it is important that you understand why the research is being done and what it will involve. Please read the information below carefully and ask questions if anything is not clear, or if you would like more information before you decide to take part. You may like to discuss it with others, but it is up to you to decide whether or not to take part.

What is the research about?

I am doing a PhD project looking at how patients, clinicians and scientists think about genomic results. Genetic testing previously tended to work by looking at tiny parts of the genetic code (single genes) that might explain a patient's health problems. Genomic tests look at huge amounts of genetic code in one go, finding around four million differences (variants) in the genetic code per person. Scientists and clinicians then need to sort through these variants to identify the important ones. It can be hard to know what would be relevant and helpful to communicate. I hope my research will help by looking at what patients, families, clinicians and scientists think should form the 'result' from genomic tests.

Why am I asking you to participate?

For part of my research, I would like to talk to patients and families who have considered having a genomic test, or who have experienced a result from a genomic test. I am asking you to consider taking part as you have been offered a genomic test.

What will happen to you if you take part?

I would like to interview you for around an hour to talk about your experiences of having genomic testing. I hope to talk through what sort of feedback you might find useful from a genomic test, and what sort of feedback you might not want. I would also like to hear about your experiences of making the decision to have a genomic test – what helped you think about what a genomic result might be like for you? If you think that you might like to take part in my research, I will contact you to discuss this in more depth, and to answer any questions that you have.

Will you benefit from taking part?

You will not personally benefit from taking part in this research, but you may help us develop useful ways of thinking and talking about genomic results, and deciding what information should be included. I hope that this will be helpful to other patients, families, clinicians and scientists in the future.

Are there any risks involved?

Sometimes conversations about genomic tests and results can touch on sensitive or difficult issues. You can decide what questions you are happy to discuss. If I ask about anything that you would rather not think about, you can let me know and we can move on to other topics. You can also stop or pause the interview, or ask me to turn off the voice-recorder at any time without having to give a reason.

What data will be collected?

If you decide that you would like to take part, we would agree a convenient time for an interview. I would set up our interview over Teams, Zoom, Skype, FaceTime or over the phone depending on your preference. If you give permission, I would record the interview with a voice-recorder. This would be typed up, and I would delete the voice-recording after checking that the write-up was accurate. I would use the write-up of your interview to help me work out factors that might help scientists, clinicians and patients think and talk about genomic results in the future.

If you haven't yet had feedback from your genomic test at the time of our interview, I might ask if I can contact you again once you have received a result. This would be to see whether you would be happy to have a shorter follow-up interview talking about your experience of receiving a result, and whether this has changed what you think about genomic results.

With projects like this, it is good practice to make data collected during the research available to other researchers, so that we can continue to learn from the data that the patients and families who allow us to interview them have kindly provided. I would do this by putting some of my data into the UKDA Qualibank (an archive of data for research). I would not put in any identifying data so it would not be possible for other researchers to know who had participated in my research. Future studies that wished to draw on this data would need ethics approval in order to do so.

Will your participation be confidential?

Your participation and the information we collect about you during the course of the research will be kept strictly confidential. Only members of the research team and responsible members of the University of Southampton may be given access to data about you for monitoring purposes and/or to carry out an audit of the study to ensure that the research is complying with applicable regulations. Individuals from regulatory authorities (people who check that we are carrying out the study correctly) may require access to your data. All of these people have a duty to keep your information, as a research participant, strictly confidential.

The write-up of your interview will not include identifiable details (it would use a pseudonym (false name) rather than your real name). The write-up would be stored securely under a code number on the University of Southampton network. I might use some words or phrases that people say during interviews in reports and publications about this research. These would be anonymous (i.e. it would not be possible for people reading the reports to tell who said them). If you were to read reports of this research there is a small chance that you might recognise short phrases that you said during your interview.

Do you have to take part?

No, it is entirely up to you to decide whether or not to take part. If you decide that you want to take part, you will need to sign a consent form to show that you have agreed to take part (this could be over email).

What happens if you change your mind?

If you agree to take part but then change your mind, you can stop the interview at any time without giving a reason. If you decide to withdraw at a later date, I could delete the write-up of your interview. I would not be able to withdraw data that had already been published, but from that data it would not be possible for people to identify you as having taken part in this research.

What will happen to the results of the research?

I plan to publish the results of this research in academic journals, and present them at conferences and clinical meetings. I will also share results via my project website (<https://whatismyresult.wordpress.com/>) and other social media, and at patient support days. I will upload progress reports to my project website while the research is ongoing, and will upload a full study report when this research is completed.

Where can you get more information?

You can find out more about this research by visiting my project website at <https://whatismyresult.wordpress.com/>. If you have any questions, please contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082.

What happens if there is a problem?

If you have a concern about any aspect of this research, please contact me by email at r.h.horton@soton.ac.uk, or by phone on 023 8120 5082. If you continue to have concerns, please speak to a senior member of the research team (Dr Angela Fenwick or Professor Anneke Lucassen on 023 8120 4489). If you wish to speak to someone independent of the research team, please contact the University of Southampton Research Integrity and Governance Manager (023 8059 5058, rgoinfo@soton.ac.uk), or the [local] Patient Advice and Liaison Services (PALS) on [this number].

If you think you might be willing to have an interview for my research, please email me (Rachel Horton) at r.h.horton@soton.ac.uk or fill in an 'expression of interest' form and post it back to the Clinical Ethics and Law group in the envelope provided. I will then contact you to talk through my research in more depth, and to arrange an interview if you decide that you would like to take part.

Thank you very much for taking the time to read this and for considering taking part in my research.

11.8.2 Text of consent form for interviews

Interviews (for patients and families)

Consent form

Project: Ethical and clinical perspectives on interpreting genomic data

Research team: Rachel Horton, Prof Anneke Lucassen, Dr Angela Fenwick

Ethics reference numbers: IRAS project ID 249060; REC reference 19/EM/0024

1. I confirm that I have read the information sheet provided to me about this research (version _____ date _____). I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and I am free to stop the interview at any time without giving any reason. ☐
3. I understand that direct quotations may be used in reporting the results of this research but that these will be anonymised (there will be no link to my name). ☐
4. I understand that voice-recording will be used to help the researcher remember my interview, and that I can ask for the voice-recorder to be switched off at any time during the interview. (The voice-recording will be typed up then deleted). ☐
5. I understand that de-identified data from my interview may be made available to other researchers when this research finishes. ☐
6. **I agree to have an interview for this research project.** ☐
7. I am happy to be contacted by the Clinical Ethics and Law group at Southampton for a follow-up interview. ☐

Name of participant

Date

Signature

Researcher

Date

Signature

11.8.3 Interview guide

How did you come to have genetic and genomic testing?

What did you expect from your test?

Where did your ideas about that come from?

How and why did you decide to go ahead? When did you make the decision? Was it a difficult decision?

(If relevant: what do you make of it that different tests get different results?)

Have you been given any results from your test?

What were they like? What was it like hearing about them? Were they what you expected?

Has your result changed things?

(If relevant: what if your clinician had waited until they were more sure? What was it like when things were a bit unsure to start with? How did you find that?)

(If relevant: if it turned out X wasn't related to the health problems in your family, would that stop it being a result for you?)

Have you talked about the result with anyone else? What was that like? Do you think they got it? What questions did they ask you?

What do you remember of how you received your result?

Do you see the result as belonging to anyone? What do you think about family samples being used to find results?

How long did you wait for results? Are you expecting any more results?

Do you see the results from your genomic test as being different to other sorts of medical results you've had over the years?

What sort of information do you think should and shouldn't be looked for in a genome test?

Are additional findings on your mind much?

Do you think the consent process should vary depending on what's going on in your life?

If a family can't seem to take everything in, do you think it's ok to start the test if they seem generally ok with that, and cover some of the consent later?

What choices would you want about what sort of information you might get back from your test?

Do you think your views have changed over the years?

If a scientist or clinician found some information from your test but they weren't sure whether you would want to know it or not, what do you think should happen? Why?

Would you have any advice for families thinking about having genomic tests today? Was there anything that surprised you, or that you think should have been different about the process?

Is there anything you would want clinicians who are offering these tests to know or to think about? Is there anything that could have made things easier for you?

Anything you thought I might ask but didn't?

11.8.4 Interview analysis: organising codes to develop a theme

This aims to give a flavour of how I developed the theme *“forewarned is forearmed”: the power of results in the abstract* (7.3.2.1) from my interviews with people having genomic testing. The process was messier but this shows some of the NVivo codes under which I sorted the data over various iterations of my analysis. (Orange = final theme; yellow = key subthemes that contributed to the final theme; green = some relevant early codes).

