Young Adults' Considerations for Whole Genome Sequencing

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I would like to dedicate this thesis to my amazing boys.
Aaron and Joshua, you are both my inspirational motivators and major distractors.
Thank you for being my personal fan club and greatest loves!

Declaration

I hereby declare that except where specific reference is made to the work of others, the contents of this dissertation are original and have not been submitted in whole or in part for consideration for any other degree or qualification in this, or any other university. This dissertation is my own work and contains nothing which is the outcome of work done in collaboration with others, except as specified in the text and Acknowledgements. This dissertation contains fewer than 100,000 words including appendices, bibliography, footnotes, tables and equations and has fewer than 150 figures.

Pepita M Barnard
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Abstract

Background: Young adults' (YAs) attitudes regarding undertaking, receiving and sharing genomic information will inform translation of genomic technologies into improvements in health and healthcare.

They have greater exposure than those before them with increasing opportunities to access whole genome sequencing (WGS). As YAs, the potential benefits from WGS, through preventative and therapeutic measures lie ahead. WGS results may offer relevant new information to them and their relatives. By nature of genomic data, the act of sharing WGS results with genomic databases or databanks has the potential to improve societal health. Yet, as a group, their preferences towards undertaking WGS and related individual characteristics are little known, requiring further examination. Theoretical models to support research about attitudes and behaviour have not been appraised to address their suitability for use in the context of WGS. Several established models for technology acceptance and health-related behaviours exist yet their appropriateness to the context of WGS remains untested. Appraisal and considered use of theoretical models for research design and analytical purposes is important to increase rigour of empirical studies. Each model reflects different characteristics, influencing the lines of research enquiry. Advancement of appropriately underpinned research facilitates development of comparable empirical research in particular fields of study, such as genomics. Continued examination of the fit between the phenomenon being explored and the theoretical underpinnings themselves is also necessary. This allows gaps to be recognised between models used and reality, furthering understanding and model development or refinement. This PhD thesis was in partnership with Nottingham University Hospitals NHS Trust.

Methods: Studies with YAs were informed by literature that related to their use of WGS and theoretical models that could reflect undertaking WGS. A quantitative survey study was undertaken with 112 YAs to identify relationships between their sharing preferences and their gender, educational attainment, STEMM background and genetic knowledge. A WGS Pathway was proposed to reflect the steps of undertaking WGS, receiving results and sharing them. The Proposed WGS Pathway was used to structure the question order for a semi-structured interview study with 11 YAs. Qualitative data were collected and analysed

using theme-based content analysis. This method simulated YAs' preferences and reasons, captured in the order they might occur if the YAs imagined undertaking WGS. An appraisal of theoretical models was undertaken using data collected in the YAs' studies to inform their relevance and fit to WGS. A WGS framework, constructed to represent YAs' consideration factors along the WGS Pathway was evaluated by domain experts, who ranked the WGS framework's factors by likelihood and importance, and shared their views about the Proposed WGS Pathway.

Results: Characteristics such as gender and genetic knowledge were statistically significant in relation to YAs' willingness to engage with and share information about WGS. Themes from interviews indicated YAs had interests related to health and self-discovery. Health professionals and trusted researchers were seen positively for sharing WGS results information with. Appraisal of theoretical models indicated the Theory of Planned Behaviour (TPB) was best placed to support a WGS framework representing findings from the YA studies. From TPB factors presented to them, the domain experts decided utility-related attitudes and perceived behavioural control (PBC) were more important than subjective norms (SN) and external factors. They also identified differences between what factors they perceived YAs would consider compared to those they thought were actually important.

Conclusion: The findings demonstrated the significant impact individual characteristics had on YAs' attitudes towards undertaking WGS, receiving results and sharing genetic information. Analysis of YAs' responses illustrated areas for further investigation including expectations of WGS and sharing preferences. Appraisal of theoretical models identified the need for a wide lens to incorporate findings about undertaking WGS. Domain experts pointed to a need for YAs to undertake some form of pre-WGS intervention so they may take a step back to make an informed decision about the undertaking.

Implications for Practice: The WGS framework offers a successful translation of WGS into services to improve health outcomes for YAs. A clearer understanding of knowledge and educational needs when choosing to undertake WGS, receive results, and make sharing decisions would better inform individuals. Further exploration of YAs' sharing preferences and attitudes regarding health professionals would contribute to a better understand of factors affecting communication related to WGS and the resulting information.
As genomics permeate more into the realms of the quantified self for self-care and healthcare, views of people who are undertaking, receiving and managing their WGS information needs further exploration so systems and services may be designed to meet their evolving needs.

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Nomenclature

Acronyms / Abbreviations

1°	1st level or Bachelor's level degree
2°	2nd level or Master's level degree
CRC	United Nations Convention for the Rights of the Child
DNA	deoxyribonucleic acid
DTC	Direct-To-Consumer
GA4GH	Global Alliance for Genomics and Health
HBM	Health Belief Model
HCP	Health Care Professional
IDT	Innovation Diffusion Theory
IT	Information Technology
MM	Motivational Model
MPCU	Model of Personal Computer Utilisation
NGS	Next Generation Sequencing
NHSB	Nottingham Health Science Biobank
NHS	National Health Service
NUHT	Nottingham University Hospitals NHS Trust

PBC Perceived Behavioural Control

PMT Protection Motivation Theory

SN Subjective Norms

STEMM Science, Technology, Engineering, Maths and Medicine

TAM Technology Acceptance Model

TBCA Theme-based Content Analysis

ToM Theory of Mind

TPB Theory of Planned Behaviour

TRA Theory of Reasoned Action

UTAUT Unified Theory of Acceptance and Use of Technology

VUS Variant of Uncertain (or Unknown) Significance

WES Whole Exome Sequencing

WGS Whole Genome Sequencing

YAs Young Adults

YA Young Adult

Chapter 1

Introduction

This chapter introduces the scope of research addressed in this thesis. The first section presents background and motivation for the thesis. The second section outlines the overarching aim and the objectives. The third section is an overview of the methodology. The fourth section describes how the thesis is organised, in chapter order. The fifth section outlines the contributions offered by the findings of the research undertaken. The sixth and final section of Chapter 1 describes the relation between the thesis and the external partner.

1.1 Background and Motivation

We are living in the midst a new genomic era where technological advances and cost savings in deoxyribonucleic acid (DNA) sequencing have allowed millions of people to have their genome sequenced and analysed. Whole genome sequencing (WGS) offers coverage of the coding region that is more accurate and complete than other options available. With prices and turnaround times tumbling, the unprecedented complete coverage offered by WGS is expected to entirely replace whole exome sequencing (WES) [204, 354].

Many countries including USA, UAE, China, Japan, Estonia, Turkey and UK are undertaking WGS projects [243]. The UK's 100,000 Genomes Project, a deliberate hybrid of clinical practice and research [77], successfully reached its target in 2018 [111]. In 2016, the UK's Chief Medical Officer, Prof Dame Sally Davies called for a "genomic revolution", stating that genomics should be available to more patients, whilst being a cost-effective service in the National Health Service (NHS) [70, 77]. Until now, WGS has primarily been undertaken within the settings of research studies or clinical care [252].

Our technological landscape is in a state of tremendous flux, as genetic sequencing capabilities become more powerful and costs continue to decline [43], and new personal

genomic applications and services are increasingly accessible including direct-to-consumer (DTC) products and services available online.

WGS is now increasingly available as DTC products and services online, removed from usual care pathways (General Practitioner to specialists), in which pre-testing genetic counselling to assess appropriateness of WGS and prepare individuals for the undertaking, are included [207]. As prices continue to drop, preventative genomic screening becomes increasingly viable as a cost-saving intervention for health systems to undertake [354]

There remain unanswered questions regarding the relationships between knowledge and attitudes towards genetics and its applications [52]. In spite of progress in the research field and increased exposure to genetics and genomics, studies indicate that scientific understanding of genetic concepts has not reached the public [41, 52]. Yet, attitudes towards undertaking genetic testing are relatively positive when answering hypothetical questions [185], with the vast majority of research participants and society at large in favour of receiving actionable secondary findings from WGS and WES [76][246]. As DTC genetic testing services become more available, it is helpful to identify knowledge and attitudinal characteristics related to their uptake [283]. Young adults may choose WGS to seek personal insights about susceptibility and diagnosis for serious diseases, including neurological disorders, cardiovascular diseases, immunological disorders and cancers, such as breast cancer and melanomas. Melanomas alone account for 11% of all cancers in 15-30 year-olds [339]. Young adults' who contribute their genomic data to support health research are hopeful that they are furthering knowledge of conditions that may affect them, relatives, and others [128].

WGS results can provide information about health risks to family members other than the person undertaking testing, and passing pertinent information onto said family members can provide them with useful information for themselves. Sharing WGS results with relatives is, however, an area of concern as the act of sharing may be complicated by the unwelcome nature of such news [335].

Individuals' attitudes will impact how families use WGS information together to translate results into health outcomes, yet attitudes towards receiving, managing and sharing genomic information have scarcely been explored [283]. In 2018, Godino and colleagues' found that once aware of a genetic disorder in their family, young adults (18-30 years-old), who did not understand what it really meant, sought information online, while others did not want to use the Internet as a source of research [117]. To support individuals with their decisions about undertaking WGS and use of this genomic information, including sharing results, it is important to address both their understanding of WGS and their motivations for undertaking WGS. As many new DTC services entail less regulation and more personal choice about receiving, managing and sharing results than those offered through conventional health care,

such as the UK's NHS, where health care professionals (HCPs) are involved in the testing process and decisions about what results are returned, knowledge and views held towards undertaking and sharing results from genetic and genomic testing, such as WGS, becomes increasingly relevant.

The age at which young people should be able to undergo pre-symptomatic genetic testing for adult-onset disorders remains a matter of debate [117]. Despite improving cost-effectiveness of genomic testing and recognition that young people have the most opportunity to be affected by genomic developments throughout their lives, they often are not included in empirical studies [140]. In a 1998 study, 19-24 year-old students' offered a range of responses to questions about prenatal screening and genetic therapy, including moral and social arguments about sharing information that may be used to limit diversity [219]. Participants' responses illustrated potential difficulties when seeking to come to some consensus for the application of new technologies in genetics [219].

In Godino and colleagues' study [117], the majority of young adults did not share their decision to undertake pre-symptomatic genetic testing for hereditary cancer with friends, some did share with only close friends because they felt that other people would not understand the complexities of the situation. Looking back some expressed a desire for a different experience to the one they'd had.

Young adults are at the start of their autonomous lives, with responsibility for self-care and health. Although it is likely that young adults will use genomic services [79], the benefits they could gain are limited by their genomic literacy [19]. There is little genomics literature available relating to young adults' knowledge and attitudes. McGill and colleagues' 2019 literature review addressing attitudes towards genetic testing of those aged 21 years and under, found they had open attitudes, and when adult-onset testing was delayed because of clinical judgement, they felt powerless and frustrated [199]. This tension between clinicians' judgement and young people's desire for information speaks to whether it is uncertainty or knowing one's genetic status that poses the greatest emotional burden [80]. This is a complex question and different people may offer alternative answers with subtle nuances involved in their reasoning.

Despite the range of uses for genetic technology and variety of findings that can impact diagnostic and clinical decisions, people make broad judgements about its utility and generally report positive attitudes [185]. Those who encounter genomics in the clinical setting are slightly more knowledgeable about the subject than the general population [185]. It may be that research respondents do not consider the individual differences among all the different ways genetic knowledge and testing can be used, and the various ramifications that genetic test results can have [185].

To further improve our understanding of their concerns, more research into young adults' views of genomic testing, including exploration of factors that might, in combination, affect their use of services is necessary[190]. Future studies that compare selections for different genetic tests would help in understanding how they contribute to inconsistencies in decision-making found across studies [290]. Research into gender-related attitudinal differences among young people is also needed [253, 208] to inform policy-making decisions and designs for genomic services.

In 2020, Young and colleagues published a framework indicating youth-friendly care approaches to guide adolescents and young people, defined by life-stage processes, not chronological age, their families, and healthcare professionals working with them through the genetic counselling process [350]. As people become more enabled to access genomic services without an HCP involved, individuals may increasingly make decisions about the importance of their results and whether to seek further consultation. As such, they will take on clinical decisions for themselves and would benefit from having the criteria and skills used by clinicians to guide themselves. What remains to be created is a framework for young adults and health professionals to use that will highlight important considerations for undertaking WGS and acting on the results, including sharing them with others.

1.2 Aims and Objectives

The overarching aim of this research is to explore young adults' attitudes towards undertaking, receiving and sharing information resulting from WGS, and to produce a framework to produce guidance to support professionals and YAs when considering WGS. This is broken down into the following objectives.

1. Understand the genomic landscape in relation to YAs and identify relevant theories used to frame empirical findings by undertaking a literature review related to young adults' and genomics, focused on knowledge, attitudes and relevant theoretical models.

2. Identify relationships between individual characteristics and preferences related to YAs' knowledge of and views about undertaking WGS and sharing results information with relatives, through a large scale quantitative study and statistical analysis of data.

3. Build detailed understanding of components of young adults' attitudes towards WGS, receiving results and sharing information with others, through a qualitative study and thematic analysis of data.

4. Propose a framework suitable for young adults' considerations for WGS based on the themes using a theoretical underpinning.

5. Evaluate the proposed theoretical framework with domain experts.

1.3 Overview of Research Methodology

This research began with a review of existing research literature in the field, gathering data from published work to inform empirical studies with young adults. Young adults' studies provide both quantitative and qualitative data to propose consideration factors that are developed into a theoretically grounded framework. This proposed framework was then evaluated with domain experts in fields relevant to WGS and young adults.

The literature review included studies related to young adults but also other groups. Because WGS is relatively new and genomics has developed out of genetics, it was necessary to use research literature referring to genetics. The literature review explored the variables and themes related to young adults considering undertaking, receiving and sharing WGS results. To further inform the topic it explored adult patient and public knowledge and attitudes as well as professionals' perspectives of WGS.

Studies in the form of quantitative surveys and semi-structured interviews were undertaken with a sample of young adults. Variables and themes identified from these surveys and

interviews were further analysed in relation to a theoretical framework relevant to the topic. A proposed WGS Pathway for young adults' considerations was developed by applying empirical results to a theoretical model. Using surveys and interviews, the proposed pathway was evaluated by genetic professionals to further enhance it with their informed knowledge and experience.

This thesis process identified gaps in knowledge, put questions to a sample of potential future gemonic service users, analysed results in relation to theoretical models to create a proposed framework for young adults' considerations and evaluated the proposed framework's factors with domain experts in the field.

1.4 Organisation of the Thesis

The thesis is organised as follows:

- Chapter 1 introduces the thesis, its context, aims and objectives, methodology, organisation (this section), contribution to knowledge and relation to external partner, Nottinghamshire University Hospitals NHS Trust.
- Chapter 2 presents literature from fields related to young adults undertaking WGS: Knowledge and attitudes from the perspective of professionals, patients, the general public and young adults, and theories that address health-related technology.
- Chapter 3 presents a quantitative survey study undertaken with 112 young adults that questions relationships between their individual characteristics (e.g. gender, educational level, genetics knowledge) and their views about undertaking WGS and sharing results with relatives.
- Chapter 4 presents semi-structured interviews with 11 young adults gathering both numerical data regarding their preferences and themes from qualitative data related to undertaking WGS.
- Chapter 5 presents a theoretical appraisal of existing models that address technology acceptance. A determination is made of how well the results of the young adult studies may be framed within models for planned behaviour, information technology and health-related ones.
- Chapter 6 presents a survey of domain experts to evaluate the proposed framework. Experts ranked factors identified from the earlier studies with young adults as likely and important. The study was undertaken with or without an accompanying interview.

- Chapter 7 offers concluding remarks regarding contributions, limitations, dissemination and future work.

The Thesis Structure Map in Figure 1.1 graphically represents the Aims, Objectives and Research Activities for each of the seven chapters.

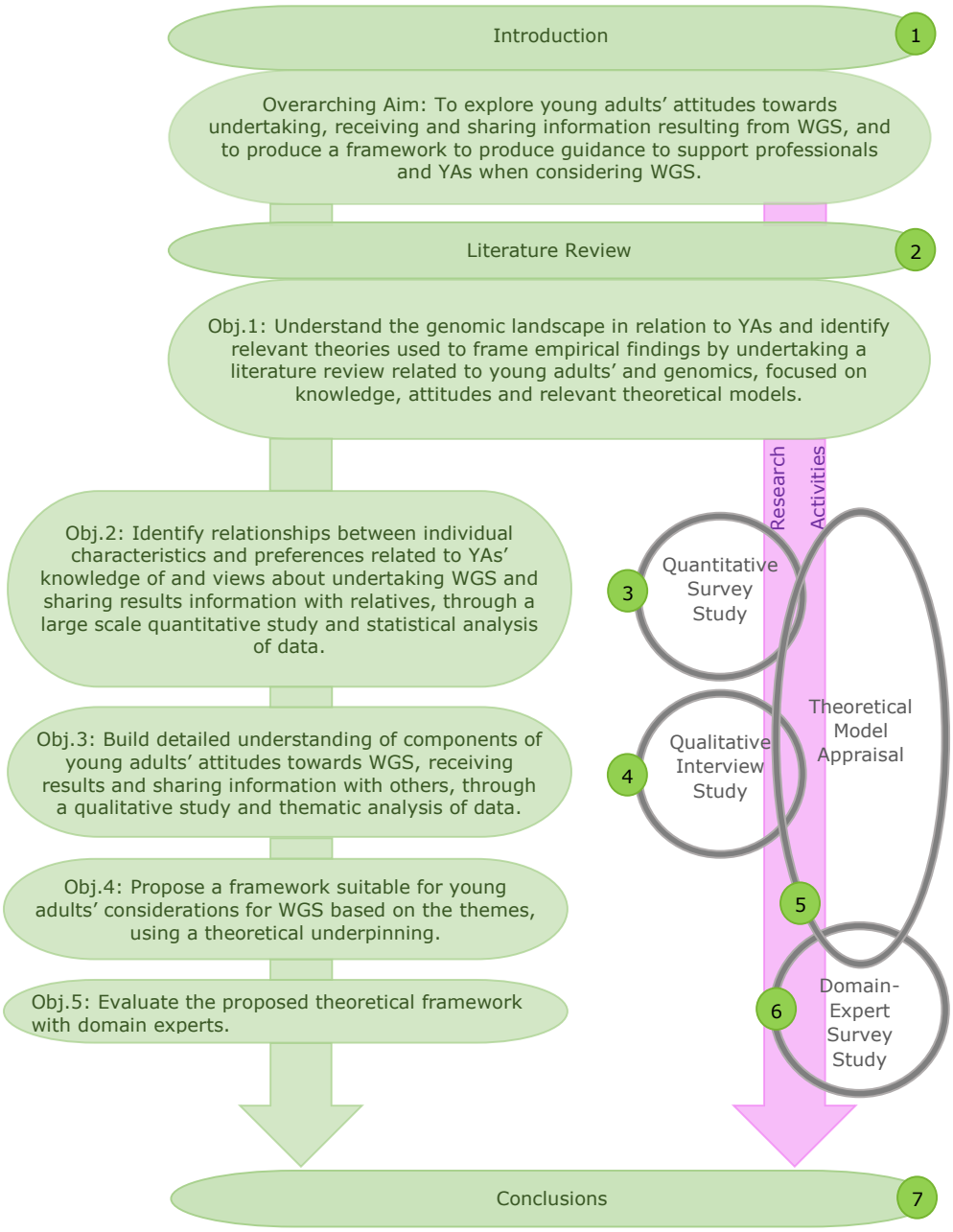


Fig. 1.1 **Thesis Structure Map**

1.5 Contribution to Knowledge

The findings offer the following contributions:

- individual characteristics of young adults that affect attitudes related to undertaking WGS and sharing results,
- a proposed WGS Pathway in the form of a process map of young adults' WGS considerations,
- themes and frequencies for young adults' considerations for WGS, utilising theme-based content analysis,
- appraisal of relevance of theoretical models related to planned behaviour, technology acceptance and use, health and fears,
- young adults' WGS considerations as factors categorised by Theory of Planned Behaviour constructs and WGS Pathway steps,
- genetic professionals' expectations of and prioritisations for young adults' considerations for WGS.

These contributions may be used to appraise the needs of young adults and inform the requirements for design of educational and healthcare programmes, research studies, commercial offerings, and related technological systems.

1.6 Relation to External Partner

Nottingham University Hospitals NHS Trust (NUHT), hosting the Nottingham Health Science Biobank (NHSB), is the external partner and part-sponsor for this thesis that is primarily funded by the Engineering and Physical Sciences Research Council. NUHT is a teaching hospital with two major campuses in the city of Nottingham. The NHSB provides a centralised, quality assured, biofluid and tissue resource to underpin translational studies and to provide added value to clinical trials. Biobanks require people to donate their data and samples to be able to have data to provide to research studies so new discoveries may be made for scientific knowledge to further advance. The University of Nottingham's Horizon Centre for Doctoral Training (CDT) focus on 'my life in data', in partnership with NUHT, enabled the PhD to be completed from this particular perspective of personal data.

As a major provider of health care, the external partner for this thesis, NUHT, has an interest in how people are likely to interact with this growing technology and why. NHSB's

specific interest is that this thesis explores young adults' attitudes towards undertaking WGS and sharing their resulting genomic data. In the future, due to their age of majority and their access to new or as-yet-unavailable DTC services, young adults may be able to choose what genomic services and technologies they use and decide what to do about their data. Individuals' choices and the reasons they make them are of interest to NUHT, NHSB and similar organisations.

Chapter 2

Literature Review

2.1 Introduction

This chapter presents the literature that relates the background context for the studies that follow and will introduce theoretical models considered as analytical tools for findings. The chapter opens with a search methodology section that includes the search strategy and terminology used. The literature is then presented, first knowledge and attitudes for different groups related to WGS followed by the theoretical models that may be used as analytical tools for such studies. Models' benefits and constraints are described and relevant studies that used them are presented. Gaps in current knowledge are indicated to support the studies planned. The summary to conclude this chapter will outline the research activities planned to address this PhD's research aims and objectives.

2.2 Search Methodology

This section describes the strategy taken for the initial literature search related to knowledge and attitudes to inform the thesis' studies. Following description of the search strategy, the terminology section will clarify terms used to indicate groups of people and technologies referred to in the literature. The terminology is established for the literature search and for further use in the thesis. What these terms mean and how they relate to terms chosen for studies will be described.

2.2.1 Search Strategy

This literature review gathers knowledge to provide familiarity with and frame the current genomics research context in terms of knowledge and attitudes towards undertaking genomic

sequencing or genetic testing. A new generation of genomic services are becoming available making the decision to engage with such health technologies increasingly relevant. This review of literature provides context for these issues and identifies gaps in current knowledge and potential research questions.

Genetic studies with families affected by a condition will be reviewed. Studies of relatives of young people will be included as family is a vital context for health research, particularly in terms of how genomic information is likely to be shared.

In addition to WGS and genomic, where the term genetic appears alongside other key terms in literature searched, they are reviewed as there are many examples from genetics that lend themselves to the burgeoning genomics field.

Articles were selected for review if they satisfied the following criteria: (i) the article was published in English language; (ii) they were returned from the search terms below related to communicating human genomic or genetic testing information, including return of results and genomic information sharing or from the reference lists of articles returned from the search terms used and further suggestions associated with the search terms; and (iii) they were freely accessible as full-text documents through electronic databases and libraries made available for research purposes. Reports of empirical research studies, literature reviews, abstracts, conference proceedings, opinion papers and articles in popular press are included.

The search terms, original search dates and sources of literature used for the initial planning of the studies can be found in Appendix A. Following the original search, this thesis' studies were designed. Searches were updated during the writing process to capture relevant new publications.

2.2.2 Terminology

Terminology for types of technologies and groups of people described in the relevant literature are presented, so that similarities and differences in meanings can be expressed and considered in relation to the terms that will be adopted for this thesis.

Whole genome sequencing and related terms

Because genomics and whole genome sequencing have evolved out of developments in the field of genetics, the definitions for the following terms offer an opportunity to clarify their meanings and relationships with each other.

- deoxyribonucleic acid (DNA): a long molecule that contains our unique genetic code to all the information needed to grow and maintain an individual [103, 101].

- gene: a segment of DNA that contain the instructions to produce one specific chain of amino acids called a polypeptide chain [105, 104, 107]. Polypeptides form proteins or components of proteins [105], which in turn control how our body grows and works, and are responsible for many of our characteristics [101].
- genetics: the study of genes and how they are inherited [105].
- genome: an organism's complete genetic material, including both genes that provide the instructions for producing proteins (2% of the genome) and the non-coding sequences (98% of the genome) [105]. The human genome contains around 20,687 protein-coding genes [101].
- genomics: the study of the body's genes, their functions, their influence on the growth, development and working of the body, and how alterations lead to changes in how proteins function or are produced by cells through the use of a variety of techniques to look at the body's DNA and associated compounds. [225, 344, 145].The main difference between genomics and genetics is that genetics scrutinises the functioning and composition of the single gene whereas genomics addresses all genes and their interrelationships in order to identify their combined influence on growth and development of the organism [345].
- omics: the collective technologies used to characterise and quantify pools of biological molecules and to explore their roles, relationships and actions in the cells of a living creature, e.g. the suffix 'omics' describes the use of these technologies to examine proteins (i.e. proteomics), the chemical processes involving metabolites (i.e. metabolomics) and ribonucleic acid (RNA) molecules (i.e. transcriptomics) in cells, as well as genomes [102].
- Next generation sequencing (NGS): an umbrella term to describe modern high-throughput DNA sequencing techniques that have emerged since Sanger sequencing was introduced in 1977 [106].
  - Whole exome sequencing (WES): sequencing only the protein-coding regions of the genome (around 2% of all bases) [108].
  - Whole genome sequencing (WGS): A type of genetic sequencing that has the potential to sequence every DNA base in a genome [109]. Whole genome sequencing is increasingly becoming a part of routine healthcare, aiding the prediction, prevention, diagnosis, and treatment of disease [109]. [105].

- Recreational genomics: recreational testing may encompass all information domains, including most kinds of predictive health risk information, as even predictive information for serious health conditions can be perceived as interesting statements about oneself rather than something that requires serious attention due to the baseline probabilities and levels of increase or decrease in risk generally being so small that their practical implications do not go beyond common-sense lifestyle improvements [88]. Because of their focus on marketing information for well-being, leisure and entertainment rather than traditional medical models, there is a lack of regulation surrounding recreational genomic tests such as those offered for uses like ancestry testing, general check-ups, nutritional testing, skincare, athletic aptitude, educational or career planning [340, 257, 191]. Companies are able to sell direct-to-consumer (DTC) products and services which may be bought by individuals for themselves or as gifts for others [191].

- pharmacogenomics: the study of genetic variations that influence individual response to drugs [310].

Terms for groups of people

There are several terms for groups of people that require some definition or clarification. Terms related to the developmental stages or ages are of interest, given that young adults are the group this thesis focuses on. Terms used to indicate the various professions, working with genetics or genomics and groups of people also require description. First, groupings by developmental stage or age followed by the public and professional groups of interest.

Groups related to Young Adults In the literature, young adults is not a clearly defined group, nevermind a universally agreed term. The Cambridge Dictionary defines young adult as a person who is in his or her late teenage years or early twenties [50].

In addition, there are various other terms for groups of people that may be included in studies that are relevant to the 18-25 age range chosen for this thesis, for example, “Young people” and “adolescents” which are broad terms without clear definitions.

In the literature, young adulthood is not clearly defined, nor a universally agreed term, the World Health Organisation states: An adult is a person older than 19 years of age unless national law defines a person as being an adult at an earlier age [346]. The European Union Agency for Fundamental Rights states that the age of majority in all EU Member States is 18 years except for Scotland, where children are considered to have full legal capacity from the age of 16 years [95].

Erik Erikson developed his psychosocial theory of human development from the 40s through the 60s [60, 84]. It is an extension of Sigmund Freud's description of human phases in the early years of life; Erikson's work indicates that young adulthood extends from late adolescence till early middle age [222, 82].

An Eriksonian perspective dictates that no aspect of development is ever actually complete [292]. Erikson and his followers recognise that the ages in the adult stages are fuzzier than those in childhood stages and people may differ dramatically [203, 36]. Erikson's stages are psychosociological in nature and the age ranges appear to have elongated since Erikson's original stages were developed. Depending on the source, the young adult stage's originally started at 20 and ended at 25 [298] but in contemporary times it is quoted as starting anywhere from 18 and ending at 39-40 years old [266, 337].

The variable age ranges for the end of young adulthood in Erikson's stages may be related to the lengthening of this stage of maturity over recent generations. Intimacy and isolation are the key interpersonal constructs individuals are tasked with negotiating during this stage [82, 36]. Given today's complex world, attainment of maturity and relative independence can take a considerable time [92], however this does not preclude young people from making important life decisions, including undertaking WGS.

A YouGov poll found that the general consensus is that 'youth' lasts up to, and includes, the age of 29 and that once a person reached the age of 30, the majority of Brits no longer consider them to be 'young' [281]. Franet, the multidisciplinary research network for the European Union Agency for Fundamental Rights, states that the age ranges for various terms related to 'youth' vary from one regulatory context to another [95]. In EU Member States, 'youth' is the only term used to describe an age group that goes beyond 18 years and it is often used when States want to include young adults as well, sometimes up to the age of 30 years [95, 55]. The UN's definition on the term 'youth' includes all persons between the ages of 15 and 24 years; UNESCO uses a wider and more flexible definition depending on the context [95]. In the EU Strategy for Youth, the term 'youth' refers to teenagers and young adults aged between 13 and 30 years whereas EUROSTAT statistics consider the youth population to be aged between 15 and 29 years [95].

The UK's General Medical Council defines the term young people to mean older or more experienced children (under 18 years old) who are more likely than younger more immature children to be able to make important decisions for themselves [299]. Likewise, England's National Association of Citizens Advice Bureaux recognises young people as someone aged 14 or over but under 18.

Like young adulthood, adolescence also does not have a clear-cut age range and is often not defined in EU Member States' national legislation [95]. Definitions for adolescence may

be based on considerations of cognitive, psychological, social or physical development [180]. The definition of adolescence varies most by the the academic discipline or researcher's lens [180]. World Health Organisation defines an adolescent as a person aged 10 to 19 years inclusive [346]. Dependent on studies' definitions, adolescence can start around age 10 and complete by early 20s. The UN Convention of the Rights of the Child (CRC) committee recognises adolescence as the period of childhood, from the age of 10 till one turns 18, during which puberty occurs [95].

Late adolescence is a recognised third and final phase of adolescence, and in keeping with conventions of previous scholars some studies categorise young adults, e.g. those aged 18-20, as late or older adolescents [69, 242]. However, recognising adolescence after 18 is beyond the scope of many bodies including the UK's Royal College of Nursing's Transition Framework and the Department for Education's National Curriculum Academic Age Ranges [180]. Studies with adolescent participants are reviewed to identify whether they include young adults.

A child is usually recognised as any person under 18 however the World Health Organisation extends this to include people up to the age of 19 [346]. In medical research literature and the NHS, the term paediatric is used to refer to area of medicine that manages medical conditions affecting infants, children and young people [146], with a cut off that varies from 16 to 21 [146, 59], when the young person transfers to adult care.

There is a wealth of literature that refers to parents and children, and paediatrics is relevant to the research of young adults, especially given that parental decisions may affect a child as a young adult. However, paediatrics is a complex context with its own particular research considerations, therefore this literature review will instead focus primarily on adult participants. Studies sampling university student populations usually contain 18 to 25 year-olds but may also include other ages. Such University-based studies need to be reviewed to identify whether they pertain to students, and specifically those falling within the young adult age-range.

For the purpose of this thesis, adulthood was assumed to start at 18 years of age, and young adults (YAs) were defined as falling between 18 and 25 years old. By defining 18 to 25 as the age range for YAs, this thesis aimed to sample people who had recently reached the age of majority and were therefore newly recognised as legally autonomous adults, able to make independent decisions for themselves but not yet likely to be at the end of their maturation from young to middle adulthood. Papers referring to WGS, genomics or genetics, that address people between 18 and 25 years of age, were reviewed, as were papers about their genomic or genetic knowledge, attitudes and intentions regarding tests, receiving results and sharing genetic information with relatives. Results from studies about attitudes to genomics

and genetics related to wider adult age groups may have a bearing on the 18 to 25s, and so will be reviewed for relevant information they may contain.

Groups representing ordinary people Studies with participants who do not necessarily belong to a specialist interest group related to genetics will be important to review for the development of research questions directed at ordinary people.

Members of the public and lay persons represent consumers of advancing genomic companies that walk a fine line, promising to empower individuals to lead healthier lives by claiming genomic results information is educational material, while avoiding diagnostic claims [17].

Cambridge Dictionary defines 'public' as relating to or involving people in general, rather than being limited to a particular group of people [49]. Layperson may also be used to describe someone who is not an expert in or does not have a detailed knowledge of a particular subject [47]. These terms are often used synonymously. The term 'general population' is also used to refer to the public [338]. In epidemiology, the general population refers to all individuals without reference to any specific characteristic [336]. For current purposes, there is no need to distinguish these terms further as they may be used interchangeably.

For genomics, as is the case in other related fields, studies with diverse members of the public help inform the effective, efficient and equitable translation of scientific developments into innovative practices [38] and such studies are of interest to the design of research questions.

Patients are people who are receiving medical treatment, or who are registered to be cared for when necessary [48, 187].

Groups representing domain experts by profession There are a number of terms for professionals, from fields of genetics, genomics, both or neither, who may be considered domain experts for the purposes of this thesis' focus. Domain experts are people who have a wealth of knowledge and practical experience of working in fields that relate to genomics or genetics and are relevant to YAs.

Genetic or genomic health professionals are Health Care Professionals (HCP) and other health professionals whose work relates to genetics or genomics and YAs. Non-health care professionals include researchers, academics and developers whose work relates to fields genetics or genomics and YAs. There are multiple terms to describe the same or similar professions, these are indicated in the following list.

- genetic counsellors: genetic health professionals who help patients and their families understand and make informed decisions about a range of genetic conditions [250].

- genomic counsellor: this term reflects the increased focus on the use of genomic information and technologies in healthcare with a broader title for such counsellors [144].
- clinical or medical geneticists or genomicists: medically trained doctors specialising in genetics or genomics [144], the shift in conceptual focus from genes to genomes has added the realm of bioinformatics to the genomicists' role [186].
- medical specialists, doctors who are not geneticists nor genomicists: medical professionals who are comfortable with carrier-screening tests and have experience with related types of genomic or genetic counseling, e.g. reproductive medicine, obstetrics [53].
- doctors: this catchall term is used to describe medically trained professionals, including primary care physicians (PCP), general practitioners (GP) and other medical specialists. The term doctors is used when alternative medical specialisms are not indicated in the literature or if referring to all within the medical profession.
- academics or educators: a teacher or scholar those whose work relates to genomics and is relevant to YAs.
- health services researchers: those whose research adds to a multidisciplinary scientific endeavor that studies and generates knowledge. Health services research seeks to identify the most effective ways to organise, manage, finance, and deliver high-quality care to generate knowledge [163].
- health technology researchers: those whose work includes undertaking health technology assessment to systematically evaluate the properties and effects of a health technology, addressing the direct and intended effects of this technology, as well as its indirect and unintended consequences, and aims mainly to inform decision making regarding health technologies [160]. A health technology is an intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organise healthcare delivery [160]. The term used in this thesis includes all who research health technologies related to genomics and relevant to YAs.
- health technology developers: those creating technologies related to genomics and relevant to YAs.
- Direct-to-Consumer (DTC) providers: DTC companies that market and sell genomic products, i.e. tests, directly to the consumer e.g. via the Internet or television, and

provide the consumer with access to his or her genetic information without the involvement of a health care professional [143]. By rejecting traditional professional gatekeeping, DTC personal testing companies move individuals away from being treated as patients to cultivate them as genomics consumers [181]. Direct-to-consumer genomic testing has become a highly accessible and increasingly affordable option for consumers [143]. Most of the companies offering such services are based in the United States, but their clients may come from nearly anywhere in the world [126].

2.3 Knowledge and Attitudes to Genomics

Advances in microarray and sequencing technologies means genotyping and genome sequencing are more affordable and readily available [39]. The falling cost and time needed to undertake WGS has increased expectations that it will be increasingly used by the wider population to understand and inform their health, thereby mitigating their risk of disease [252, 205]. In Australia, Zhang and colleagues calculated the impact and cost-effectiveness of offering health system–funded preventive genomic screening for multiple conditions to all young adults [354]. They demonstrated that population screening could significantly reduce the incidence and mortality of hereditary cancers, and the burden of severe childhood-onset genetic disease, compared with targeted testing, and when more conditions are concurrently screened for, preventative genomic screening of young adults becomes increasingly cost-effective [354].

Most of the published research literature focuses on genetics and much of that addresses clinical patients with cancers, rare diseases and other specific conditions. Some address the views of the public but often research participants are patients or relatives of patients. Studies of the public, i.e. healthy individuals are not nearly as abundant, though they are increasing. Studies addressing YAs specifically, are rarer.

Attitudinal studies regarding professionals in the field have found a substantial gap between how genomic scientists and health professionals think genomics should be discussed and what the public actually understands [239]. There has been limited empirical data on attitudes, values and beliefs about receiving results from whole genome research studies [211], excepting a few notable large online studies using video-shorts to provide accessible explanations before collecting data [239, 302, 209, 214].

Generation Genome, the 2016 Annual Report of the UK's Chief Medical Officer [70], describes an automated pipeline and a useful schematic from an organisational perspective, however it does not address the process for individuals undertaking WGS without input from HCPs. The traditional approach taken assumes individuals will access WGS via an NHS

clinical service, or their usual general practitioner for their concerns about a specific condition (e.g. cancer or rare undiagnosed disease). Online DTC personal genomic services are rapidly increasing their market offerings of WGS and similar technologies to consumers as tools to help them plan for their present and future health needs [87, 91]. Genomic consumer research literature remains limited due to the relative novelty of the technologies available to the consumer market [309]. Genome sequencing is becoming more widely used in DTC genetic tests [153]. DTC consumers may bypass traditional healthcare systems [213], minimising the HCP-patient relationship prior to testing. DTC companies offering genetic testing have raised concerns about regulation, accuracy, privacy, trust, lack of counselling and expertise among Australian participants [62]. More research is needed to address management and sharing of results from WGS or similar technologies currently being marketed to the public [39, 66].

Although research about the public's knowledge and attitudes to genomics and similar technologies continues to grow, YAs are only occasionally sub-grouped in studies about the public and are rarely studied as a specific group in their own right. YAs are of particular interest because their autonomy as an adult is relatively new and simultaneously they are being increasingly exposed to a growing genomic services marketplace. Research literature related to YAs and WGS will be reviewed where available, however other groups and relevant technologies will be referred to particularly because there is very little research addressing the area of interest.

Having made a general overview about peoples knowledge and attitudes, next the following groups will be looked at in more detail:

- Health-related professionals
- Patients
- Public
- Young Adults

Their knowledge and attitudes about issues related to WGS is presented first, followed by their views about sharing WGS results. WGS-specific literature was preferred but where this was not available, relevant studies addressing other aspects of genomics or genetics are presented. The following section looks at knowledge and attitudes held by the domain experts, health-related professionals.

2.3.1 Health-related Professionals' Knowledge and Attitudes to WGS

For health professionals, clinical validity and clinical utility are the main concerns for returning genomic results [30, 212], yet there is no universally accepted definition of clinical utility. The utility of genetic testing has different dimensions (public health, clinical, personal, and social), and the term "clinical utility" may be too limiting, especially if narrowly defined [124]. Narrow definitions for the term clinical utility focus on the impact that an action has on concrete health outcomes, to prevent or ameliorate adverse health outcomes such as mortality, morbidity, or disability through the adoption of efficacious treatments [124]. Other definitions for clinical utility comprise much wider ranges of usefulness, sometimes even including societal value [309].

WGS results allow both targeted and incidental information about heritability patterns. Incidental findings, sometimes called secondary findings, describe findings not associated with the reason for testing. It is estimated that there is a strong likelihood for people undergoing WGS for a particular problem to return at least one incidental finding with substantial health implications and dozens of notable genetic variants that are likely to influence disease states [327]. Furthermore, as knowledge about relationships between variants and diseases increases, so will the probability of incidental findings [327]. Incidental findings may have medical or social implications beyond the individual, to their families or society [305].

The word 'incidental' is problematic as it has two different meanings: (i) unrelated, or (ii) unimportant [78]. It is not a term laypeople tend to use to describe a risk of systemic disease or other life-changing information, even if incidental to the original reason for the test [61]. The shift from targeted tests designed to ask specific clinical questions to a broad 'trawling' test has an effect on the interpretation of incidental [61]. To some extent there will be no WGS findings that have not been 'looked for' as part of the process, and while information may be incidental to the original reason for the test, it does not mean it is insignificant or less important to the patient [61]. Because of the large amount and types of information that can and will result from WGS, the terms "incidental findings" and "secondary findings" lose some of their meaning, particularly when the person has a desire to know whatever can be found out from having their genome sequenced. With regards to DTC test results, the Royal College of General Practitioners and the British Society for Genetic Medicine recommend that health professionals should exercise caution when asked to offer, or provide, clinical expertise about the results of DTC genomic or genetic testing due to the analytical validity, sensitivity and clinical utility of such testing may being much lower than popularly perceived [264].

Apart from specialised healthcare professionals and researchers, many people do not understand even the most fundamental information about genetics and this limitation in genomic literacy reduces their ability to attain the potential benefits that may be contained in their genomic information [19].

Studies from the USA [259, 173, 136, 265], Canada [51] and European countries [255, 240] found that even if a genetic test is potentially beneficial, doctors and pharmacists often lack the formal genetic education or knowledge necessary to understand and fully exploit the wealth of information obtainable from genetic tests to be able to relay the appropriate diagnostic information and deliver better healthcare to their patients.

To promote effective genome-scale research, genomic and clinical data for large population samples must be collected, stored, and shared [308]. Participants often provide consent for their data and samples to be stored in a biobank for use in future research, irrespective of the type of genetic testing or technology [175]. The term 'sharing' can be defined as a personal and voluntary activity of interacting with other people. Individuals may use resources such as the personal experiences of others to navigate dilemmas or simply to create a sense of community [332]. Sharing can also be illustrated as an activity organisations use to govern; imposing significant constraints on individuals' social identities, who are obligated to share in ways that support the institutional goals [332]. As healthcare professionals' understanding of interpreting the clinical relevance of results from WGS-based genetic testing advances, the long-held debate of whether to return results is becoming one about how to return, who should return, when to return and what results should we not return [175]. A survey of national and international laws and policies found four different approaches used for the return of individuals' results from WGS-based genetic testing [175]:

- Only panels of specific genes or targeted sequencing are allowed to reduce the potential for incidental findings, although this not always explicitly stated.
- Results can only be returned when they are analytically valid, clinically significant and actionable.
- an ad hoc case-by-case determination
- no return

When compared with the public, genetic health professionals and genomic researchers are much more conservative about returning genomic results[212]. Genetic health professionals are five times more likely to think that incidental findings should not be returned [212]. Both genetic health professionals and genomic researchers agree that it is not appropriate for genomic researchers to actively search for and share ancestry data [212]. These professionals'

views are in direct opposition to those of the public who are more likely to want ancestry data returned [212] and genetic health professionals were.

As researchers increasingly obtain clinically significant and actionable findings from the longitudinal studies they access, biobanks and other data controllers may need to consider communicating individual results in the future [175], a significant change to traditional biobanking practice.

The proposed International Code of Conduct for data sharing in genomic research seeks to provide common guidance on the basis of two fundamental values: (i) mutual respect and trust between scientists, stakeholders and participants; and (ii) a commitment to safeguarding public trust, participation and investment. The elaboration and eventual implementation of such a code should be the object of ongoing discussion [174].

Health-related Professionals' Attitudes Towards their own WGS Results

Among the attitudinal studies available, little has been published about health professionals' preferences when choosing genomic options for themselves. Zierhut and colleagues' 2015 survey study of 38 researchers, administrators and clinicians who undertook WGS at a symposium [356] found the most dominant motivations for their domain-expert participants were professional enhancement followed by curiosity, personal health benefits and reproduction with participants stating that they wanted to receive all findings as all information had value to them and that categories used for packaging the results, such as medically actionable or not, cancer, neurological conditions, childhood onset or adult onset, were not sufficiently well defined for them.

Middleton and colleagues' 2016 study gathered views from the public, genetic health professionals, non-genetic health professionals and genetic researchers and found the majority of participants, in all groups, wanted pertinent findings returned to them if they were to partake in genomic sequencing research [212]. Differences among groups were apparent for incidental findings with 91% public, 87% non-genetic health professionals, 84% genetic researchers but only 72% genetic health professionals wanting those [212].

Lay people, HCPs and parents of children with rare diseases shared concerns regarding anxiety about genetic discrimination and the potential use of information by agencies such as employers, medicines manufacturers and insurance companies [305].

In Zierhut's study, all respondents reported sharing the news that they were undertaking WGS with their co-workers and partners [356]. They shared their experience with their partner the most, followed by co-workers, physician, mother, father, with their children (for those who were parents) and their friends [356]. Some also mentioned telling bartenders and speaking with a genetic counsellor after receiving their results [356]. From the little written

about professionals' preferences for themselves, what has been found indicates their general desire not to have pre-defined filters applied to their results; these are similar preferences to those found for lay people [305]. The following section will consider the knowledge and attitudes of patients towards WGS.

2.3.2 Patients' Knowledge and Attitudes Towards WGS

Insights from patients with experience of partaking in a genomic study are very useful when considering attitudes about WGS for YAs or others. An abundance of research has demonstrated that patients have limited knowledge of genetic principles and limited understanding of personalised medicine, current genetic and genomic tests [132]. Until recently, WGS was only for patients' who met strict criteria and were under the care of doctors who could order WGS. By December 2019, however, Veritas Genetics were offering a standard annotated WGS service from $599 (December 2019) with information on more than 200 conditions [321]. Veritas also offered their own "clinical geneticist expert advice and a fast path to physician sign-off" with optional genetic counselling sessions at $299 per hour [321]. A premium service with information about over 650 genetic conditions and over 225 carrier conditions for $1600 and a diagnostic service costing up to $3600 for those with a history was also available [321]. Meanwhile USA-based Dante Labs offered WGS that had not been clinically validated to Europe on sale for €169.00 EUR, down from their usual price of €849.00 EUR [67]. These two examples were by no means the only companies offering WGS directly to the public [227]. Marketing exposure means the public's view will contain those of individuals who may choose to access WGS and can now do so without their HCP's approval, nor their assistance in decision making.

Although public opinion data provides valuable insight into general attitudes toward genetic research, it does not necessarily reflect the views of those undertaking genomic testing. Patients anticipate health improvements from genomic medicine, but public enthusiasm is tempered by concerns including costs of and access to testing, genetic discrimination, psychological harm, loss of privacy, employment and insurance [132]. Attitudes to testing depends on type of test and how it is understood, with some patients viewing multiple levels of resulting information positively whereas others hold negative attitudes concerning fears that genomic tests will lead to 'information overload' during the course of treatment for an illness like cancer, as well as greater privacy breaches anticipated from WGS compared to testing individual genes [132].

The Implementing GeNomics In pracTicE (IGNITE) network brought together data from six genomic medicine projects, funded by the National Institutes of Health in the USA, to identify effective ways to incorporate genomic information into clinical care and develop

clinical decision-making support for providers across diverse healthcare settings [236, 230]. In 2019, IGNITE reported that younger adults (all predominantly middle aged), females and those with a university degree were significantly more likely to have a more positive attitude to genomic medicine than males, older adults and those with a high school education [236], however the younger adults also reported a greater decline in their positive attitude post-intervention.

Survey respondents answering hypothetical questions may not be as emotionally invested nor as engaged in the details as research participants undertaking WGS [233, 326], yet even when participants' emotional investment can be presumed, their hypothetical preferences differ from their actual choices [233]. Intentions are hypothetical yet remain a much utilised proxy for what someone may be willing or choose to do or to accept. For individuals to answer hypothetical questions they need to to imagine how they would feel, think and act in the hypothetical situation, creating a self-simulation [293]. If asked what someone else is likely to think about a situation, individuals need to use their self-simulation as a resource to simulate another person's mind and behaviour [293].

Most participants enrolled in a large scale genomic sequencing study were favourable towards receiving results, but preferred results for which an intervention was available, and wanted results about variants of uncertain significance (VUS) [274]. Patients and the public generally want more information than has previously been the norm through traditional approaches, leading some studies where participants were told they would not receive results at enrolment to reconsider their policy [274]. There is an urgent need to develop educational strategies that streamline and compliment genetic counselling including electronic decision aids and learning tools, electronic or not, to enhance decision making [258]. These strategies should aid patients' decision making process by helping them to forecast their short- and long-term emotional responses to their potential decisions [258].

Patients' Views Towards Sharing WGS Results

Although individuals' preferences varied by treatability or preventability of conditions, the majority of participants in a 2015 study, who had a genetic condition or an affected relative, wanted to know anything that a geneticist might accidentally discover during the analysis of their genome, regardless of the seriousness of the condition the finding relates to, or whether it is clinically actionable [142].

When deciding how best to relay information to support family decision making, efforts must be made to counteract errors that should be expected to accumulate in the process when patients communicate their test result information to relatives [324]. Like a whisper game, the original information faded out at every communication step [324]:

- from the information actually communicated by the genetic counsellor to the patient's recollection of the information
- from the patient's recollection to their interpretation
- from the patient's interpretation to their relatives' recollection
- from the relative's recollection to their interpretation

Adult patients from six genomic research studies in Houston, Texas had much more restrictive hypothetical data sharing preferences than their actual data release decisions [233]. The Genetic Alliance in the UK found patients with genetic conditions were willing to share their WGS data with other organisations for research; in particular they were comfortable with the NHS, universities and charities, but felt discomfort with private companies and government [142]. Participants appear to make a privacy-utility trade-off between the privacy protection risks inherent in DNA data and the utility associated with amassing genetic data to help advance research when they consent to public access data release [233]. Either that or they have difficulty understanding complex concepts, like data sharing or other key elements of their participation that impacted their final choices [233].

2.3.3 Public's Knowledge and Attitudes Towards WGS

WGS is likely to be increasingly considered for population-based carrier status screening yet it is virtually impossible to make a general statement about what the public thinks [19, 354]. One exception is from a USA based study of 543 healthy adults where 98.1% of participants were motivated to undergo sequencing because of curiosity about their genetic make-up [357]. The public's attitudes towards genetic testing and pharmacogenomics are generally positive and individuals' attitudes towards genetics are influenced by affects arising from perceived personal benefits and harms [56]. Attitude formation often carries an implication of finality, as if it is a stable, univocal, embedded psychological construct rather than a context dependent and goal biased one that responds to stimuli, constantly reevaluating for the matter at hand [99, 56].

A survey of 1,399 Dutch Health Care Consumer Panel members found participants with lower educational attainment were more interested in an offer of genetic testing for cancer, cardiovascular disease and dementia than those with a higher education level, also older participants were more interested in specific tests for cardiovascular disease and dementia compared to younger participants [322]. An online survey of 955 University of Sheffield students and staff found that their desire for genetic information increased with the potential to prevent the disease as well as disease seriousness [148].

The Multiplex Initiative is a study of gene panel tests for 15 individual markers [300]. An ancillary study to the Multiplex Initiative, with 294 healthy 25-40 year-old "young adults", found that increasing the number of conditions tested for increased the public's interest in genetic testing [280]. Another study ancillary to the Multiplex Initiative, this time with 286 healthy 25-40 year-olds, indicated that regardless of whether participants chose testing for multiple conditions or not they processed information about each of the types of results possible when deciding what results they would want to receive from a genetic test [325]; in addition, those who selected more results were more likely to take up testing [325].

Public enthusiasm for genomic medicine is tempered by concerns about being genetically discriminated against, including by HCPs who decide who merits testing [132]. The information needs of different age groups has implications for interventions and health policy where improved education is necessary [254]. When broken down by gender (i.e. male v female) differences in the public's knowledge of genetics present contradictory findings [151, 162].

Understanding segments of the public and the factors most commonly associated with their decisions to accept or decline testing will be essential for families who might benefit [19].

Whether they were from research or clinical findings, participants claimed personal and clinical utility as important reasons for incidental findings to be disclosed to them [64]. With regard to receiving genetic information, lay participants in a 2012 study [305], felt their 'right to choose' outweighed any anxieties they may have or doctors' reservations to disclose and they did not want professionals to apply filters to pre-packaged results on their behalf. In a 2013 study [64], participants wanted to be told about findings that were unexpected to them and viewed the management of such information as a shared responsibility between professionals and themselves. Participants in a 2016 study were more interested in learning about preventable conditions and less interested in receiving information that was uncertain or uninterpretable at the time of receipt [212]. A 2013 review of empirical studies into DTC genetic testing and personal genomics services [256] found that neither the worst fears of catastrophic psychological distress, misunderstanding of test results and undue burden on the health care system nor the health benefits of significant improvements in positive health behaviours have materialised. In 2019, Zoltick and colleagues found regret or harm from the decision to undergo sequencing was rare among healthy adults ($< 3\%$) [357].

A Canadian University-Government collaborative research study claimed that continued efforts to deliberate with the public were warranted to inform effective and equitable translation of personalised medicine [38], but also warned against using values elicitation exercises with the public to determine policy decisions because public participants managed their fear that personalised medicine tests will be used to ration care by reasoning that access

to treatment should not be determined by results of tests, this leads to the view that if the patient wants a treatment then the treatment should be made available, irrespective of the results from a genomic test [38].

The public often have little content knowledge about new technologies to mediate their attitudes and therefore frequently rely on heuristics or cognitive shortcuts such as their beliefs, ideological predispositions and media portrayals to form judgements about issues that they know little or nothing about [99, 275]. Participants expressed a strong desire to receive proper explanation prior to undertaking genetic testing [355]. Discrepancies between consent form content and patient comprehension illustrated the importance of promoting understanding, patient autonomy and shared decision making [258]. These studies strengthen support to calls for continued effort to improve the public's literacy in terms of knowledge about genomics and personalised medicine so they may make informed decisions [38, 19]. If genomic sequencing becomes integrated into clinical care then patients' preferences may assume a longitudinal nature where decisions to query information will be made over the course of life and not at the single moment of consent for sequencing [258]. Because genetics survey research participants tend to be older than 40, more educated, female and white, Middleton and colleagues claimed it necessary for future research to use selective sampling frames to target participants from under-represented groups such as young people, those of lower affluence and educational attainment, male and non-white, so useful conclusions can be drawn about attitudes towards the use of genomic technologies [208].

Public's Knowledge and Attitudes Towards Sharing WGS Results

There are many issues for online genetic service users, including which results to share with family members and how to do so, as well as potential lack of interest from HCPs if there is no cure available for a specific genetic disorder discovered [190]. People use and make sense of online DTC genomic information alone, with friends, family members, or even with their physicians [188]. Individuals are increasingly drawing upon sharing resources including support groups, community members, colleagues, friends, celebrities and even strangers [332]. One study found those who received results for a genetic test online were less likely to share their results with others and more likely to look for more health information afterwards compared to those who received results in person with genetic counselling intervention [217]. The IGNITE network reported that their younger participants were more likely to share their genomic results [236]; unfortunately it did not report details regarding who they would share their results with. One year after receiving results, one third of DTC customers [33] had shared their results with their own doctor and this sharing was associated with further screening tests being undertaken. Studies have found that the public

and patients were willing to share their genetic results information with family members [37, 270, 356, 135, 83], with females being more likely to do so [335, 221]. Irrespective of the nature of the information, students and staff at a UK University appeared generally happy to give up their own confidentiality so that at-risk relatives could be informed about their risk [148]. Participants who were in relationships as well as those who were not religious were more willing to forgo their confidentiality if results from their genetic test were relevant to a relative [148]. A minority were reluctant to share with relatives who would benefit; yet those same few wanted to be told if their relatives had genetic test results that were pertinent to them [148]. The desire to possess personal and familial information or a lack of understanding of quantitative genetic risk information are possible reasons why the actual risk of disease development only had a small effect on participants' decision making regarding wanting to know their relatives' results [148]. A cultural shift where sharing becomes the norm will influence behaviours so that the minority, who oppose sharing, find their position difficult to maintain and justify within a culture of sharing [148].

Attitudes towards sharing personal data with researchers are complex and influenced by contextual factors, trust in the researchers and the research institutions involved [164]. Despite it not necessarily making a difference to their decision to participate, study participants were generally interested in knowing accurate financial information and transparency about who benefits [195]. Many research participants did not mind contributing identifiable personal data to multiple research projects so long as they are kept informed, to some extent, about the nature of the research they were contributing to, and were more willing to share if they believed the research would yield concrete benefits, either for themselves, society or both [164].

Many genetic studies have found high levels of insurance concerns amongst their participants [170, 305, 85, 142]. Given the complexity of attitudes towards data sharing and the emergence of adaptive, flexible approaches to data governance, in order to balance the benefits and risks of genomic testing, new communication strategies should be investigated to explore "dynamic consent" and user-friendly websites designed to help participants develop and refresh their understanding of genomics as the field evolves [164].

Laypeople in a 2012 study expressed the view that patients were responsible for tracking scientific developments, monitoring their original test results and re-contacting clinicians about their original sequencing as new genomic knowledge emerged using an annual reminder to check-up on genomic developments [305].

2.3.4 Young Adults' Knowledge and Attitudes Towards WGS

It is now possible for YAs to access genomic services without health professionals' direct involvement. The availability of genomic results outside of traditional doctor-patient and researcher-participant relationships raises questions about preparedness of YAs for receiving results from WGS [334] and yet YAs' attitudes towards receiving, managing and sharing genomic information have scarcely been explored.

WGS results are much more extensive than those that come from single gene and panel testing. The availability of WGS is growing and there are a number of roles YAs may have when undertaking WGS or related technologies dependent on the context under which they participate. They may be consumers, patients, research participants or a combination of these. They may use a DTC genomic service or one mediated by a HCP. In many instances patients and consumers contribute to research data. Research participants may themselves gain clinically relevant information from participating. Some YAs may seek further services to gain more information. Calls for future research include identifying which media outlets are raising awareness of genetic testing and the credibility they engender as reliable sources [190].

Key challenges that typically face those in transition from adolescence to adulthood may include completing education, beginning full-time employment, cohabitation, marriage and becoming a parent: the impact of testing may affect, and be affected by any of these events [117].

Advances in genetic testing technology look likely to outpace research into attitudes towards such testing [253]. Although there is a substantial literature that investigates ethical issues concerned with genetic testing, this is in almost complete isolation from empirical research concerning the knowledge and attitudes of those confronting these issues. [253].

In the USA, an exploratory qualitative study of 14-17 year-olds, 18-21 year-olds and parents of 14-17 year-olds, found 18-21 year-olds have more complete information and take a broader range of points into consideration when making decisions about hypothetical situations involving genetic testing when compared to 14-17 year-olds and the parent group, who both needed much more information to enhance their ability to make decisions about using genetic services [254].

Very little has been published about genetic knowledge and attitudes in relation to multiple-gene testing [253], and in most cases it is impossible to glean any particular age group's specific knowledge and attitudes from publications. A study of 111 advertising undergraduates at The University of Texas found a discrepancy between actual genetic knowledge and perceived self-efficacy where participants were unlikely to recognise their inability to make informed decisions in this area [190]. Undergraduates who had previously

experienced genetic testing or who expressed a strong interest in or intention to have testing identified having more control over their lives as benefits of testing, however those who perceived themselves as carriers of genetic conditions were less likely to express an interest in DTC genetic testing [190].

Young Adults Knowledge and Attitudes Towards Sharing WGS Results

In 2020, Hassan and colleagues deliberately over-sampled young people for focus groups in their NHS-based deliberative study of public attitudes towards sharing genomic data [140], recognising young people as often not included in such attitudinal studies yet have the most opportunity to be affected by developments in their lifetimes [140]. 18 year-old participants could choose whether to participate in the 16-18 age-group focus group or the 18+ focus group [140]. In 2020, the younger age-group (16-18 year-olds) participating in Hassan and colleagues' NHS-based deliberative study saw clear benefits to having data on parents and other family members to help understand familial risk factors and inform their own life choices, including treatment options [140].

YAs tend to have a positive concept of themselves in the future [331]. This positive orientation motivates YAs towards risk taking for immediate or proximal reward and desired future states, contrasting with older adults who reflect more on future states they wish to avoid [331]. Webster concludes YAs are therefore more likely to be motivated to undertake WGS to gain positive rewards, i.e. results to support their desired future states rather ones to inform them of states they they would wish to avoid [331].

In 2010, it was reported that YAs expressed greater privacy concerns and desire to control their data than older participants [307]. Although the need for genomic data to be stored securely was accepted, those in the 16 to 18 year-old groups in Hassan and colleague's 2020 study did not always comprehend how their genomic data could be valuable, i.e. of interest or use to others who did not personally know them, including hackers [140]. Concerns about the potential longer term risks of creating genomic resources, including commercial access and genetic discrimination, were largely absent from focus group discussions with the 16-18 year-olds' [140]. Younger people appear to express more concern about protecting information against unauthorised disclosures to third parties such as parents, future or current employers and law enforcement services [140]. 16-18 year-olds appeared to place particular value on exercising control and choice over who has access to their data, however, their awareness of the implications for misuse and discrimination through uses of data, whether anonymised or not, may be less well developed [140]. The study's strict focus on NHS data use may have also led to concerns about commercial access, held by young people to remain undisclosed [140]. Participants in the 18+ groups were concerned with limiting access to

third parties, including commercial companies, such as marketing companies and insurers [140].

2.4 Theoretical Models for Consideration

There are a number of theories and models relevant to explanations for health-related technology acceptance [125]. This section introduces theoretical models considered particularly relevant to supporting the design of studies and the analysis of attitudes towards WGS. Given that WGS is a technology, which may be used as an informative, educational or health tool, a range of models are considered.

The following sections present theoretical models found to be particularly relevant to decision-making and therefore of interest to attitudes and behaviours for WGS. They include the the Theory of Mind (ToM), Theory of Planned Behaviour (TPB), the Health Belief model (HBM), the Protection Motivation Theory (PMT), the Technology Acceptance Models (TAM), and the Unified Theory of Acceptance and Use of Technology (UTAUT).

Each of these value-expectancy theory based models deals with the influence of individual values and expectations on behaviour, and/or the development of these values and expectations [296, 141]. These models are recognised as useful to researchers; HBM addresses questions about health-related behaviours, TAM and UTAUT address technology, whereas others such as ToM, PMT and TPB may be used for either context and others [296]. The first model presented is the most generic of them all, ToM.

2.4.1 Theory of Mind

Virtually all languages have words or phrases to describe mental states, including perceptions, bodily feelings, emotional states, and propositional attitudes (beliefs, desires, hopes, and intentions). People have many thoughts and beliefs about others' (and their own) mental states [118]. Implicit in some studies is the request for participants to imagine what people might think and to respond accordingly. As theory of mind (ToM), by definition, refers to the cognitive capacity to attribute mental states to self and others, empirical studies that ask hypothetical questions, or require participants answer on behalf of another, utilise ToM concepts [118].

Simulation ToM is so named because it claims that our ability to understand other people is not based on theoretical inferences but on self-simulation. This process-driven simulation ToM exploits one's own motivational and emotional resources and capacity for practical reasoning [118]. According to simulation theory, we use introspection of our own mind in

order to simulate the other person's mind [293]. The simulation in this ToM refers to the mental operation of 'putting oneself in the other's shoes', that is, placing oneself into the other's situation with the aid of imagination [293]. Such simulation is described by Alvin Goldman as projecting into someone else's situation, appreciating what it is like to be in that situation, applying available psychological concepts to categorise feelings, desires, beliefs and other evaluations and attributing them to the simulate [118]. In such simulations, the final state of the simulation is representational to that being targeted, without the help of theorising [118].

In contrast, theory-driven ToM understands another person's mind is a theoretical and inferential process, analogous to the natural sciences in applying theory and predicting natural phenomena [293]. Where theory-driven ToM takes an observational third-person point of view, simulation-driven ToM takes as introspective, first-person one [293]. It is not necessary to ask which ToM is true as we use both to achieve the same purpose dependent on the relationships, social contexts, or the situations within which we interact with the others [293].

It is upon this premise that ToM is accepted as a function of responses to hypothetical questions and to those asking about third persons' views, considerations and decisions. Studies in this thesis will ask hypothetical questions, where participants need to use their imagination to undertake a simulation or access theoretical knowledge to obtain ToM in order to respond.

2.4.2 The Theory of Planned Behaviour

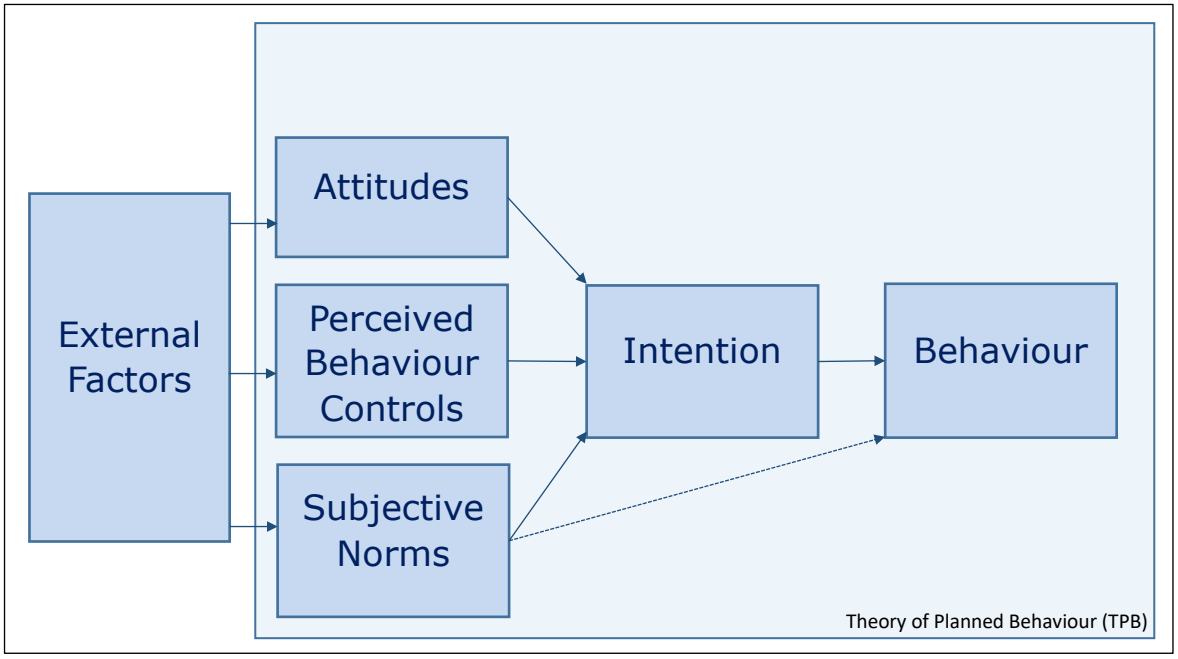
Ajzen's Theory of Planned Behaviour (TPB), [159, 116], extends Fishbein and Ajzen's Theory of Reasoned Action (TRA) [90] by adding the construct 'perceived control over performance of the behaviour' or PBC [10, 9]. TPB [159, 10, 9] has been extensively used in both health research and initiatives related to genetic information [198, 335, 221].

TPB, as illustrated in Figure 2.1, asserts that a person's intention to perform a behaviour is based on their attitude towards the behaviour, the social influence to perform or not perform the behaviour (subjective norms), and their control over performing such a behaviour (perceived behavioural control) [5]. TPB [10, 9] has been used extensively to study health behaviours [198]; it has been used in both health research and initiatives specifically related to genetic information [335, 221, 190, 87]. Attitudes, subjective norms, perceived behavioural control, intentions, along with the actual behaviour make up the five aspects to TPB.

A person's intentions towards behaviours are the product of three constructs:

- attitudes
- perceived behavioural controls

Fig. 2.1 **Theory of Planned Behaviour**



- subjective norms

Attitudes are formed from an overall positive or negative evaluation of one's beliefs about the outcomes of a given behaviour [335, 16]. Perceived behavioural control (PBC) is a construct similar to the highly predictive 'perceived barriers' from the Health Belief Model (HBM). PBC addresses the belief that one is capable of engaging in a particular behaviour [8]. PBC unifies two control concepts, perceived self-efficacy and perceived controllability. Measures of perceived self-efficacy address the perceived ease or difficulty of performing a behaviour and confidence in one's ability to perform it. Perceived controllability measures beliefs one has about the extent to which performing the behaviour is up to the actor [6]. PBC can be predicted from beliefs held regarding factors that facilitate or inhibit the behaviour and an evaluation of the power each factor has to affect the behaviour [335]. Subjective norm (SN) is a function of one's beliefs about the expectations of important others and groups (i.e. normative beliefs) weighed by one's motivation to comply with them and can also be described as perceived social pressure to perform the behaviour [83].

External variables are individual influences on behaviour, such as demographics, personality and environment, that have their impact upon behaviour via influencing components of TPB [10, 57] [9]. Individuals' evaluations interact to influence their behavioural intentions and behaviours [125]. The results of hundreds of studies summarised in several meta-analyses

and reviews provide evidence to support TPB's constructs' of attitude, perceived control and subjective norm as being highly predictive of several behaviours, including health behaviours and able to explain a large proportion of the variance in behavioural intention [116].

2.4.3 The Health Belief Model

The Health Belief Model (HBM), illustrated in Figure 2.2 has been one of the most widely used conceptual frameworks in health behaviour research to explain change and maintenance of health-related behaviours, and as a guiding framework for interventions [116].

HBM originated in the U.S. Public Health Service by social psychologists in the 1950s who sought to understand why people did not participate in disease detection and prevention programmes. It was later extended to study people's responses to symptoms, diagnoses and adherence to treatment [116, 248]. A behaviour intention is determined by the perceived importance of its goal, and the perceived feasibility of attaining this goal through the behaviour. If the goal is to avoid a health problem, the potential susceptibility to and severity of the problem must be perceived before an action is taken. In addition, the health goal must be achievable through the reduction of threat (perceived benefits), with little obstruction (perceived barriers) in the problem-solving process [155].

HBM is a value-expectancy theory-based model, focused on health behaviour, containing two values:

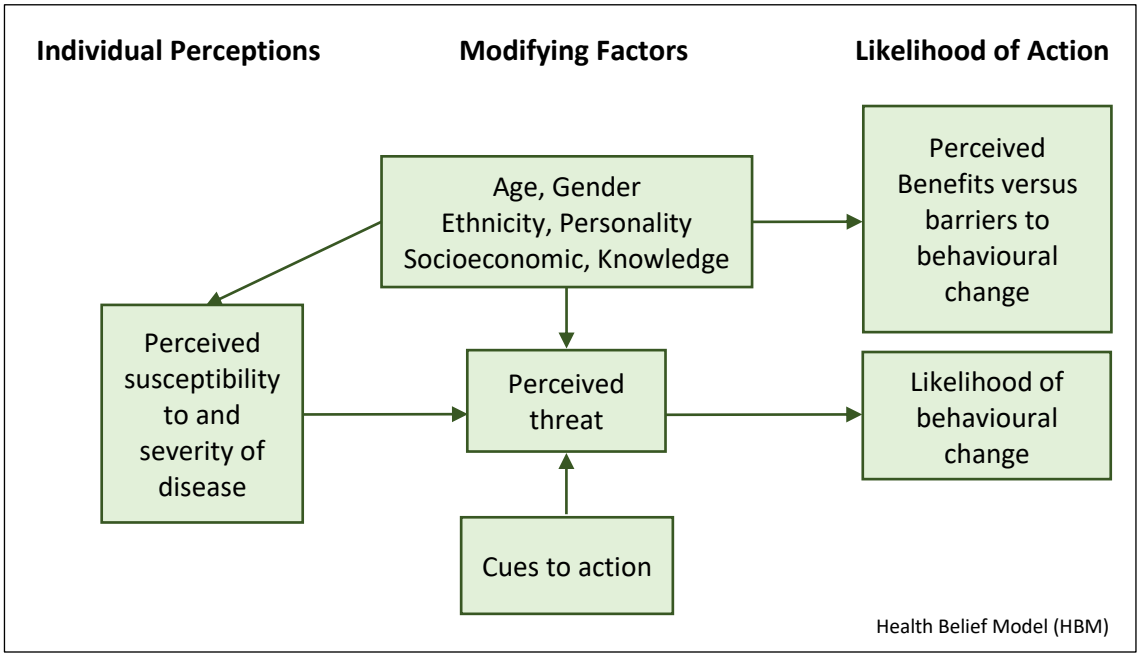
1. The desire to avoid illness or to get well.
2. The belief that specific health actions available to an individual would prevent undesirable consequences [295, 296].

HBM is divided into three components:

1. the individual's beliefs or perceptions about health
2. the modifying factors which includes demographic, socio-psychological and structural variables
3. the benefits of taking preventative measures

A review of HBM [165] found strong empirical support for the model's use in health education with perceived barriers being the most powerful predictor across all studies. Perceived susceptibility was a stronger predictor of preventative health behaviours than perceived benefits whereas the reverse was true for behaviours related to those who are ill [165]. Harrison and colleagues' 1992 meta-analysis found that in prospective studies benefits

Fig. 2.2 **Health Belief Model**

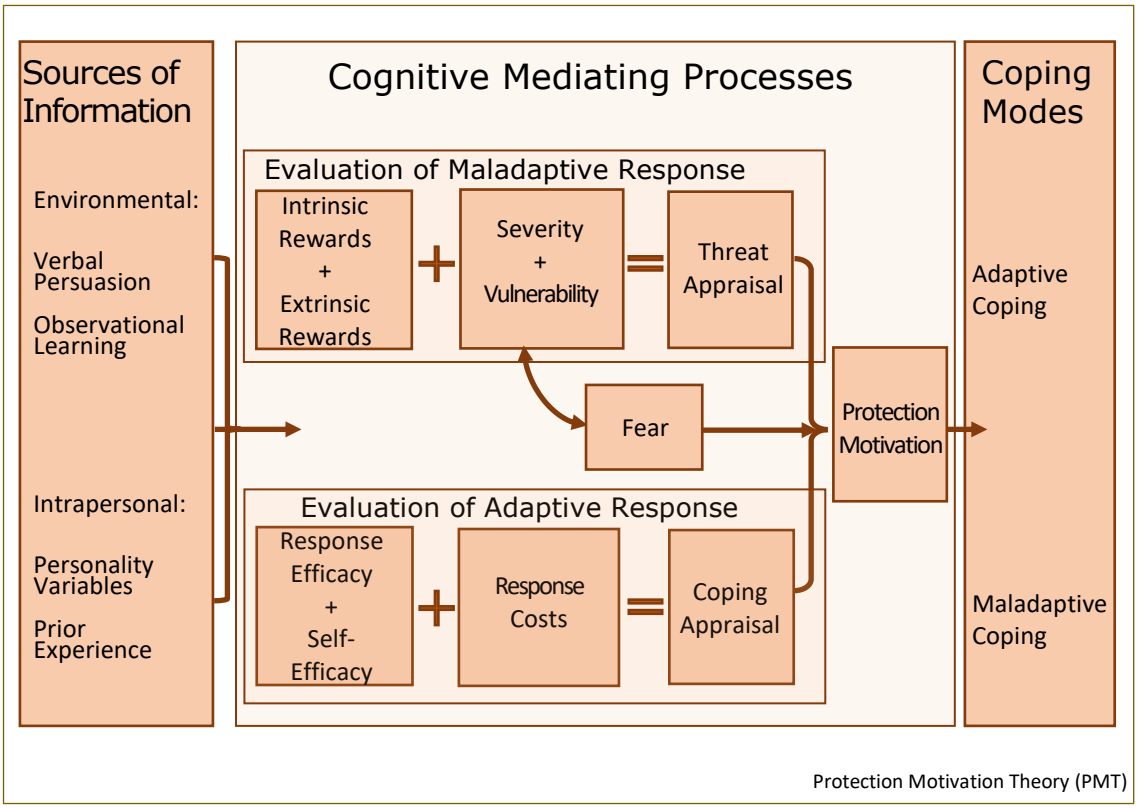


and barriers had significantly larger effect sizes than they did in retrospective studies, whereas severity had a significantly larger effect size in retrospective studies [139, 288].

2.4.4 Protection Motivation Theory

The Protection Motivation Theory (PMT), originally conceptualised in 1975 by Ronald W. Rogers to provide conceptual clarity to the understanding of fear appeals [261, 248], is an extension of Lazarus' 1968 primary and secondary appraisal process model [294]. Protection motivation refers to the motivation to protect oneself against a health threat and is usually defined operationally as the intention to adopt a recommended action [288]. PMT has been revised several times since 1975 [248], with Rogers and colleagues' 1983 version [262] presented in Figure 2.3. Both HBM and PMT are premised on expectancy-value theory and contain cost-benefit analyses and share an emphasis on the cognitive processes mediating attitudinal and behavioural change [248]. Specifically, PMT uses perceived vulnerability, perceived severity, response efficacy, and response costs in place of perceived susceptibility, perceived severity, perceived benefits, and perceived barriers in HBM [287].

Fig. 2.3 **Protection Motivation Theory**



The revised version of PMT (1983) classifies its cognitive mediating factors into two categories according to individuals' decision making stages [287].

1. threat appraisals, which include:
    - perceived vulnerability
    - perceived severity
    - intrinsic rewards
    - extrinsic rewards
2. coping appraisals, which include:
    - response efficacy
    - response costs
    - self-efficacy

The Self-Efficacy construct in PMT is taken from Bandura's 1977 Self-Efficacy Theory that is contained in his Social Cognitive Theory [262, 21]. Self-efficacy relates perceived self-efficacy with behavioural change [21]. Bandura's Social Cognitive Theory has been used extensively in its own right and is among the most used theories identified in health behaviour research [238]. Social Cognitive Theory specifies factors governing the acquisition of competencies that can profoundly affect physical and emotional well-being as well as the self-regulation of health habits; it addresses the sociostructural determinants of health as well as the personal determinants [22]. Social Cognitive Theory posits a multifaceted causal structure where self-efficacy beliefs operate with goals, outcome expectations, perceived environmental impediments and facilitators in the regulation of human motivation, action and well-being [22]. Perceived self-efficacy refers to beliefs in one's capabilities to organise and execute the courses of action required to produce given levels of attainments; it is a key causal factor because it operates on motivation and action both directly and through its impact on the other determinants [22].

People have little incentive to act unless they believe their actions can produce desired effects, so whatever else may serve as motivators, they must be founded on the belief that one has the power to produce desired changes by one's actions [22]. People fear and tend to avoid threatening situations they believe are beyond their coping skills, whereas they will undertake activities and act confidently when they judge themselves capable of handing what would otherwise be intimidating situations [21]. A sense of personal efficacy may entail regulating of one's own motivation, thought processes, affective states and behaviour patterns, or changing environmental conditions, depending on which aspects of life one seeks to manage [22]. Efficacy beliefs influence whether people think in a manner that is self-enhancing or self-debilitating, optimistic or pessimistic; what courses of action they choose to pursue, the goals they set for themselves, their commitment to them, their perseverance when faced with difficulties and setbacks, and the accomplishments they realise [20, 22]. Beliefs people hold about their capabilities affect whether they make good or poor use of the skills they possess; self-doubt can easily overrule the best of skills [22]. Health communications that heightened perceived self-efficacy rather than elevating fear were found to be more effective [20]. Two meta-analyses of PMT from 2000 [218, 93] found support for PMT's variables predictability of intentions and/or behaviours.

PMT argues that individuals' evaluations of the severity and the vulnerability of the potential threats, i.e. their threat appraisals, and the extent to which they can cope with said threats by undertaking certain health behaviour, i.e. their coping appraisals, determines their intentions to perform the health behaviour [287]. The threat must be perceived or identified before coping can be appraised [93]. PMT's purpose is usually to persuade people

to follow communicated recommendations; therefore intentions indicate the effectiveness of the attempted persuasion [93].

2.4.5 Technology Acceptance Model

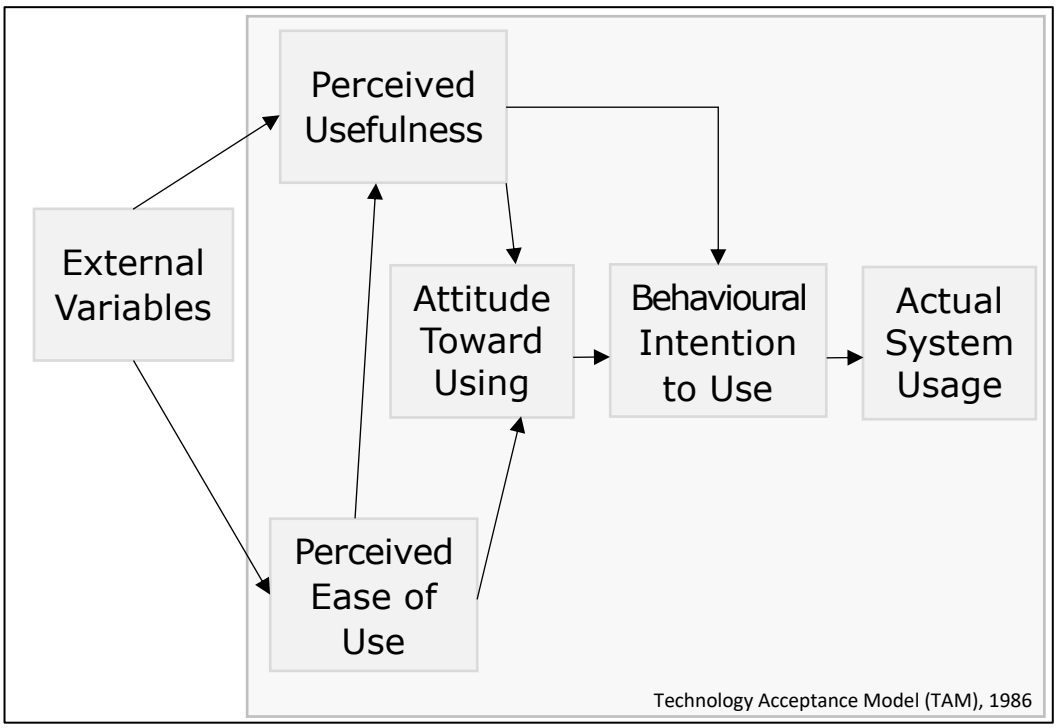
Technology Acceptance Model (TAM), illustrated in Figure 2.4a originates from the Theory of Reasoned Action (TRA), just as TPB does [125], however unlike TPB, TAM and its extensions have been developed to address technology acceptance, in particular, employee decision making about new information technology (IT) [317, 125].

TAM was first published in Fred Davis's PhD thesis [71] in 1986. TAM has proven to be highly predictive of computer system usage and has become the most widely employed model of IT adoption and use [317, 125]. Originally TAM, as illustrated in Figure 2.4a, included Attitude as one of its key constructs. However, by 1989, Davis and colleagues' empirical study of a group of university students' voluntary intention to use a particular word-processing package that had been made available to them found that Attitudes intervened between beliefs and behaviours far less than originally hypothesised [72]. The revised TAM, is illustrated in Figure 2.4b below the original 1986 version of TAM. The difference being the loss of the Attitudes construct from the revised 1989 version of TAM.

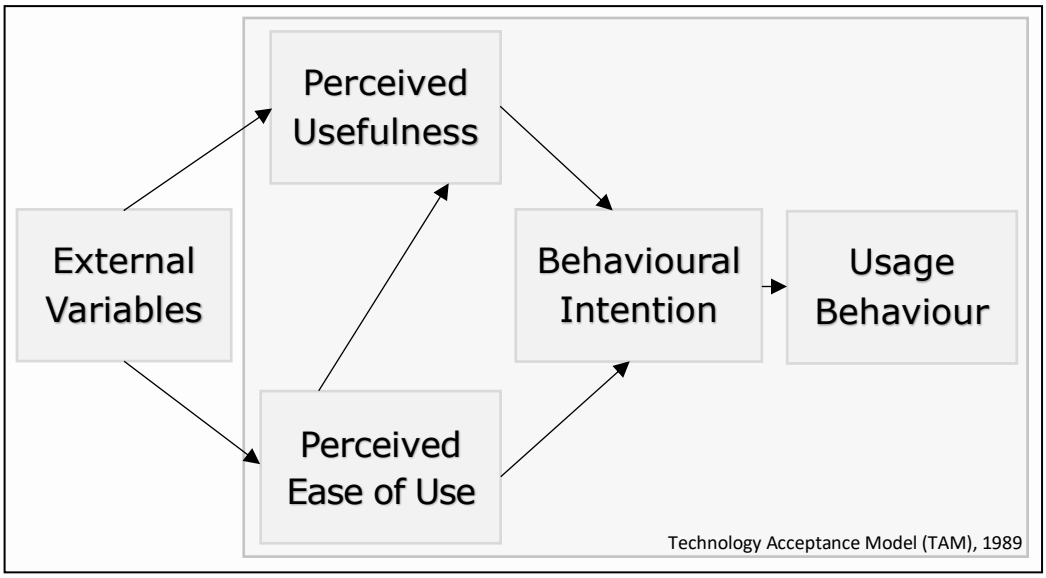
TAM is a parsimonious model that includes the constructs of perceived usefulness and perceived ease of use that determine behavioural intention, from which behaviour specifically related to use of new IT follows [317]. The four determinants of perceived usefulness and perceived ease of use recognised by TAM are individual differences, system characteristics, social influence and facilitating conditions [317]. In TAM, individual differences include personality and demographics; system characteristics are the salient features of a system that can help individuals develop their perceptions about the usefulness or ease of use of a system; social influence include social processes and mechanisms that guide individuals in formulating their perceptions of various aspects of an IT; facilitating conditions address organisational support to facilitate the use of an IT [317].

TAM2 extension [318], illustrated in Figure 2.5 was introduced to explain perceived usefulness and usage intentions in terms of social influence and cognitive instrumental processes. The determinants detailed for perceived usefulness in TAM2 are moderated by experience and voluntariness [318, 317]. Subjective norm and image are categorised as social influences whereas job relevance, output quality, result demonstrability and perceived ease of use are considered as system characteristics [317]. Perceived ease of use is also recognised as a direct determinant of behavioural intention in TAM2 [317]. Perceived ease of use in TAM3 is determined by individual differences and general beliefs about computers and computer use, which are grouped into three categories: control beliefs, intrinsic motivation, and emotion.

Fig. 2.4 **Technology Acceptance Model (TAM)**

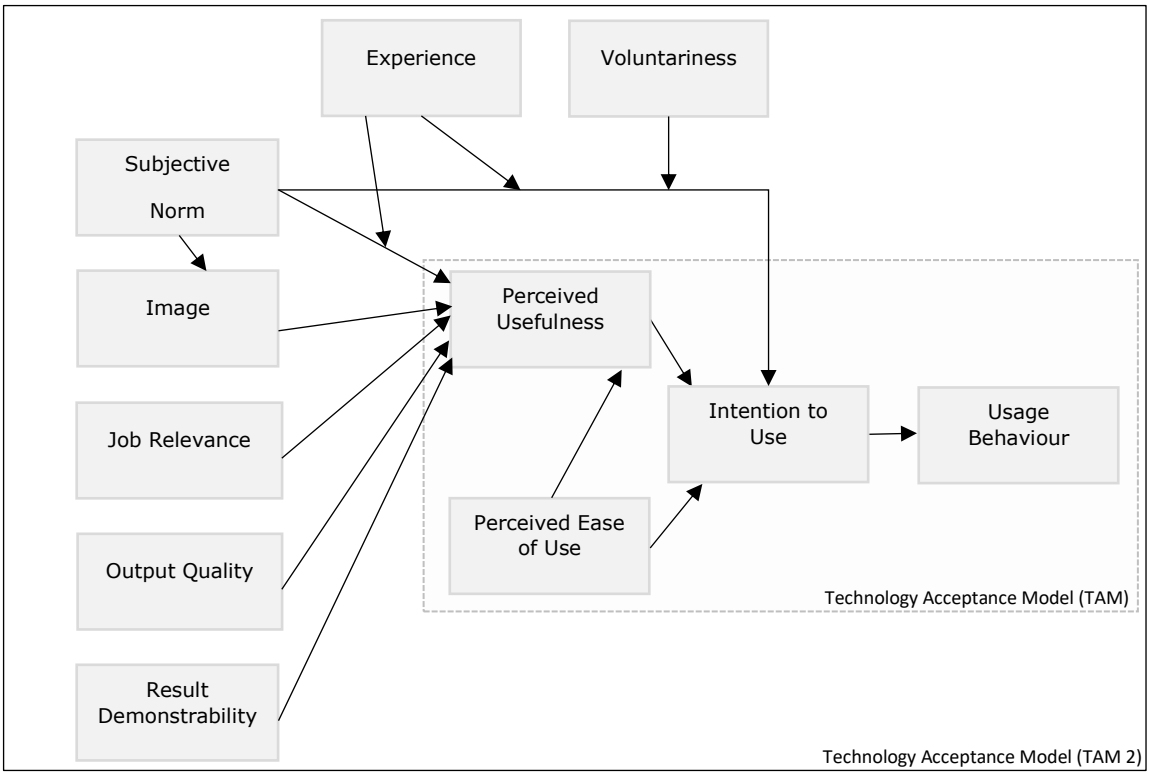


(a) TAM, original (Davis, 1986)



(b) TAM, revised (Davis et al., 1989)

Fig. 2.5 **Technology Acceptance Model 2 (TAM2) (Venkatesh and Davis, 2000)**



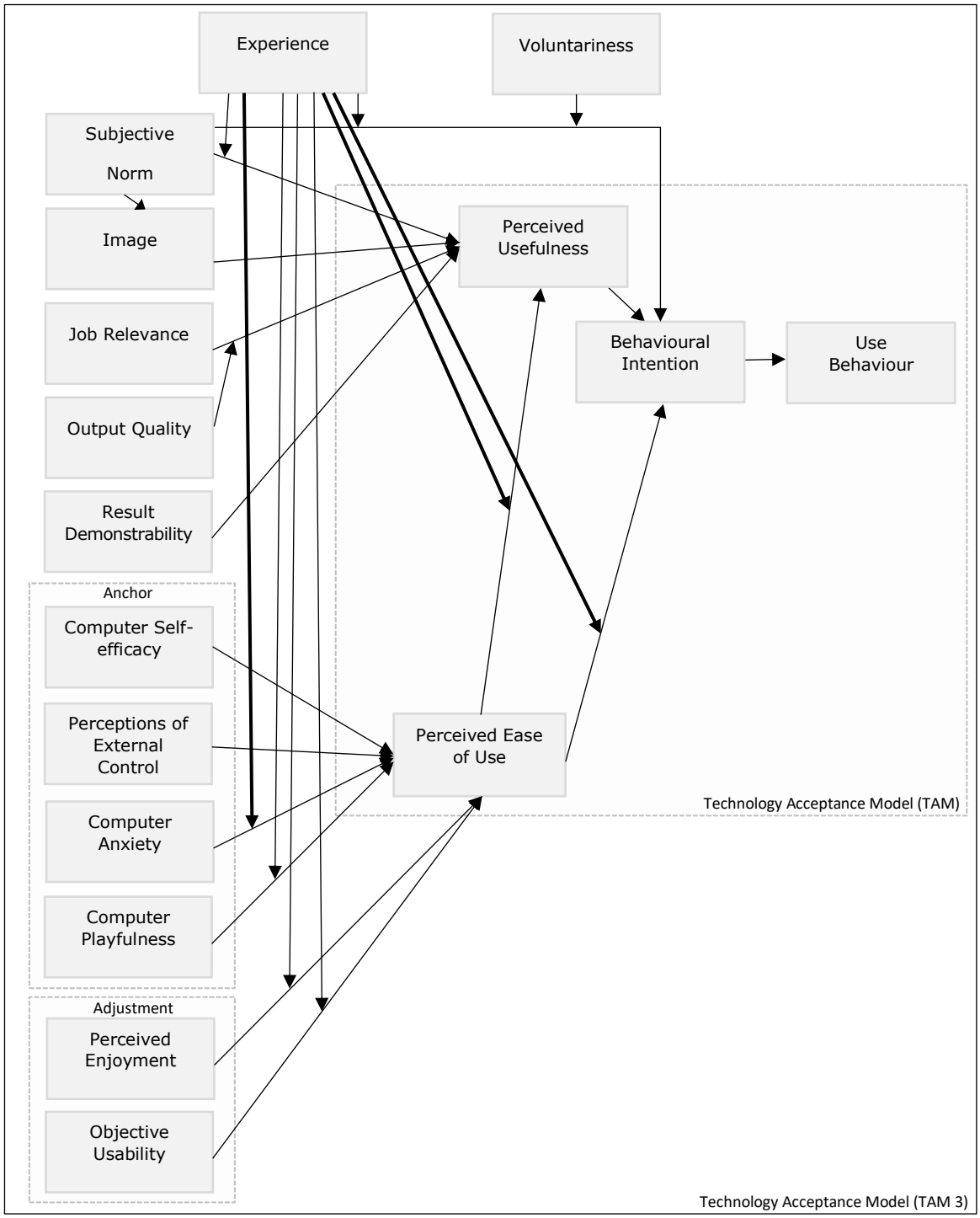
In TAM3, illustrated in Figure 2.6, perceived usefulness is viewed as a cognition (as opposed to emotion); it is conceptually similar to extrinsic motivation, and is an instrumental belief regarding the benefits of using a system [317]. Both TAM2 and TAM3 exclude attitudes but retain perceived ease of use and usefulness.

TAM3 was developed by combining TAM2 with a model of the determinants of perceived ease of use to create a more integrated model of technology acceptance [317]. In TAM3, the general pattern of relationships from the previous iteration holds but the model is more comprehensive.

Perceived usefulness in TAM3 is determined by subjective norm, image, job relevance, output quality and result demonstrability, as per TAM2 [317]. TAM3 model presents the following traits and emotions as specific determinants of perceived ease of use: computer self-efficacy, computer playfulness and computer anxiety as well as perceptions of external control, perceived enjoyment and objective usability [317].

TAM3 stipulates that the determinants of perceived usefulness will not influence perceived ease of use, likewise the determinants of perceived ease of use will not influence perceived usefulness [317].

Fig. 2.6 **Technology Acceptance Model 3 (TAM3) (Venkatesh and Bala, 2008)**



The assumptions and decisions made in designing TAM2 and 3 are due to the models' creators focus on use of technology in organisations [317]. Despite not being directly related to employment, WGS and similar multiple gene testing packages are offered via online IT accounts. Also, WGS may be offered to young professionals working in fields where such technologies are acceptable as a gift, benefit or prize.

2.4.6 Unified Theory of Acceptance and Use of Technology

The Unified Theory of Acceptance and Use of Technology (UTAUT) as illustrated in Figure 2.7a combines and adapts elements from major theories that explain individual acceptance to form a comprehensive model of acceptance [319] to predict behavioural intention to use a technology and technology use primarily in organisational contexts [320].

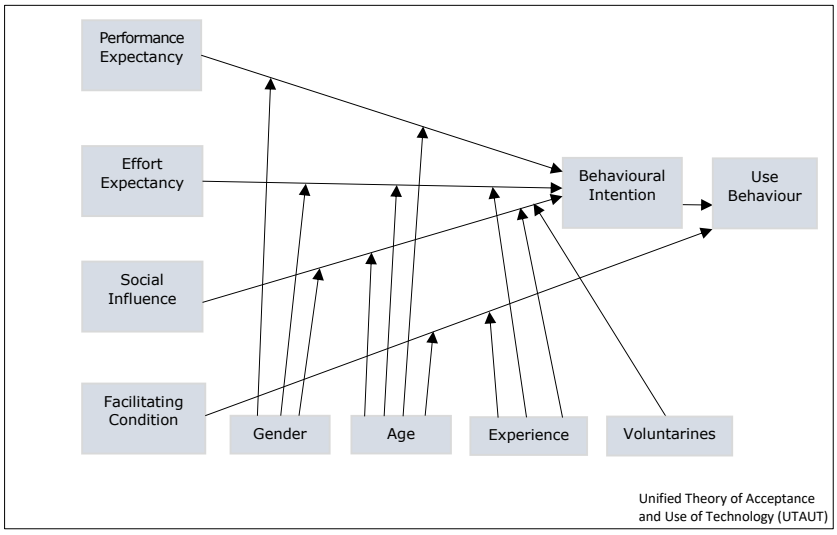
UTAUT is underpinned by TRA, TPB, TAM, the Motivational Model, a combined TPB/TAM, the Model of Personal Computer Utilization (MPCU), Innovation Diffusion Theory and Albert Bandura's Social Cognitive Theory [319, 231]. The key constructs of UTAUT are performance expectancy, effort expectancy, social influence, facilitating conditions, behavioural intentions and use behaviour [231].

TPB and TAM have already been described in this section as models for consideration in design of the survey and interview studies and as analytical models for use with the results, so they and their combined model will not be described here. TRA was previously discounted because TPB supersedes it so it too will not be described further here. Bandura's Social Cognitive Theory has previously been described as it is an underpinning theory of PMT, so there is no need to repeat its description here.

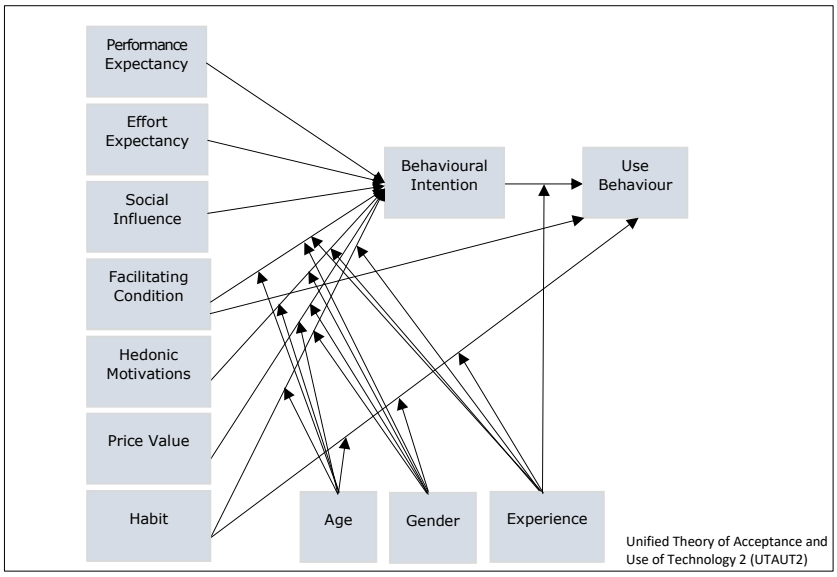
The Motivational Model represents a significant body of motivational theory work in psychology, incorporating both intrinsic and extrinsic motivation, to explain behaviour related to computer use in the workplace [73]. Extrinsic motivation describes the perception that the user's desire to perform an activity is because it is perceived to be instrumental in achieving valued outcomes that are distinct from the activity itself, such as pay, performance or promotion whereas intrinsic motivation refers to the perception that the user will want to perform an activity for no apparent reinforcement other than the process of performing the activity [319].

MPCU is derived largely from Triandis's 1977 theory of human behaviour for the evaluation of cross-cultural training effectiveness [306] which was adapted and refined by Thompson and colleagues in 1991 to predict PC utilisation [303, 319]. MPCU was incorporated into UTAUT because it was recognised as being particularly suited to predict individual acceptance and use of a range of IT and offers a competing perspective to TRA

Fig. 2.7 **The Unified Theory of Acceptance and Use of Technology (UTAUT) and UTAUT2**



(a) The Unified Theory of Acceptance and Use of Technology (UTAUT) Venkatesh, Morris, Davis and Davis (2003)



(b) The Unified Theory of Acceptance and Use of Technology 2 (UTAUT2) Venkatesh, Thong and Xu (2012)

and TPB [319]. MPCU's core constructs are Job-fit, Complexity, Long-term consequences, Affect Towards Use, Social Factors and Facilitating Conditions.

The Innovation Diffusion Theory is grounded in sociology and has been used to study a variety of innovations and disciplines since the 1960s [319, 183]. An innovation describes an idea, practice, or object that is perceived as new, whereas diffusion is the process by which an innovation is communicated over time among the members of a social system [260, 183], therefore potential users decide to adopt or reject an innovation based on beliefs and attitudes they have formed about the innovation based on five characteristics:

- relative advantage
- complexity
- compatibility
- trialability
- observability

These are used to explain end-user adoption of innovations and the decision-making process [183, 3].

UTAUT was developed from the point of view of implementation of new technologies within organisations, so for this reason its constructs are distinctly utilitarian in nature [263].

2.4.7 Unified Theory of Acceptance and Use of Technology 2

In 2012, UTAUT2 was proposed by Venkatesh and colleagues as making important theoretical and managerial contributions when applied to consumer IT use context [320]. UTAUT2, illustrated in Figure 2.7b, includes three new determinants added to those already employed by UTAUT [320]:

- hedonic motivation
- price value
- habit

The three new determinants are moderated by age, gender and experience. [320]. Because consumers' use of IT systems is assumed to be voluntary in nature, the construct "Voluntariness" was removed to design UTAUT2 [320]. As in UTAUT, Facilitating Conditions, moderated by age, gender and experience, have direct links to both Behavioural Intentions

and Use Behaviour [320]. Experience has an additional link to the point between Behavioural Intention and Use Behaviour, as shown in Figure 2.7b, Experience moderates the effect of Behavioural Intention on actual Use Behaviour. Given Experience with a behaviour, links made between cues and behaviour are strengthened, facilitating habitualisation, therefore the effect Behavioural Intention has on Use Behaviour decreases as Experience increases. "Hedonic Motivation" such as enjoyment are seen as important in consumer product and/or technology use, and is added as an determinant of intention to complement utility considerations in UTAUT [320]. "Price" is added to reflect consumers' responsibility for costs as this is viewed as a likely factor dominating adoption and it complements UTAUT's existing resource considerations [320]. "Habit" is added to UTAUT2 as a critical predictor that compliment's the theory's focus on intentionality as the overarching mechanism and key driver of behaviour [320].

2.5 Benefits and Constraints of the Theoretical Models

For individuals to place themselves in a hypothetical situation, or to view a situation from an other's perspective requires them to use their imagination to create a simulation. This feature is key to the capacity of participants to engage with the studies in this thesis, therefore ToM mechanisms are expected to occur and are accepted as part of the deliberations participants undertake when deciding how to answer questions.

The tables that follow present the benefits and constraints identified for each of the theoretical models considered in WGS research studies' design and as potential analytical tools for results of studies undertaken for this thesis. These benefits and constraints are offered in view of the subject area, YAs' attitudes to undertaking WGS and sharing their results.

The theoretical models included in deliberation for studies' design and analysis are HBM, PMT, TPB, TAM and UTAUT. These theories address human behaviour and behaviour change for either generic, health, or IT purposes with the premise that actions are based on intentions and behaviours [295]. Their benefits and constraints guide choices made for this thesis' study designs and analyses.

HBM requires measurement of the full range of factors that may influence a behaviour [116], however all of the factors for YAs undertaking WGS and sharing its results are not yet known. HBM is focused on perceived threat and health actions. Although WGS is usually health focused, it does not necessarily follow HBM's premise of a response to a particular threat [116] especially given healthy adults with no known history may pursue WGS. Before testing, the threat is of the unknown, after testing the perception threat will be informed

Model	Benefits	Constraints
Health Belief Model (HBM)	Perceived benefits, barriers, susceptibility, and severity all contribute equally to health behaviour. HBM emphasises rational, deliberate decision-making processes and behaviours. HBM is a systematic method to predict preventative health behaviour. 'Cues to action' represent normative beliefs. Self-efficacy tends to be the strongest predictor of behaviour where it is recognised as a distinct component of the model [220].	Perceived threat, susceptibility and severity concepts establish HBM's health-focus. HBM lacks 'intention to try' construct and has weak predictive power [296]. HBM accounts for health belief but not for other factors that influence health behaviours e.g. socioeconomic status, cultural factors, special influences, previous experience [304]. HBM is a list of variables rather than a theory based on adequately specified relationships between its core components [296].

by the results that are returned. WGS-based test kits are now increasingly commercially advertised products and services for personal and social use [182], therefore WGS needs to be seen beyond the health and healthcare lens.

Unlike HBM, PMT includes a coping appraisal where self-efficacy is a core component, as shown in Figure 2.3, however like HBM, PMT first requires a threat for the threat appraisal to be undertaken, prior to operationalising the coping appraisal mechanism. The distal nature of disease risks that may be revealed to healthy curious YAs undertaking WGS might limit their threat appraisal [91].

Receipt of WGS results and decisions to share will entail an emotional quotient and TPB lacks an account for emotional or knee-jerk reactions [14, 220]. This is not necessarily a constraint for researching healthy adults' attitudes to WGS as there is no urgency implicit in the situation denying individuals time to think through and consider their initial emotional responses when deciding whether to undertake WGS, what to do about receiving results and and how to act on them. TPB constructs require re-operationalisation when used in new settings [349]. TPB allows for exploration of antecedents to individuals' behaviours [27] and this appraisal of the antecedents of behaviour is agreeable to the exploration of YAs' attitudes to WGS.

Both TAM and UTAUT models use combinations of theories to address technology acceptance. Their focus on IT use is restrictive for exploring views of hypothetical users

Model	Benefits	Constraints
Protection Motivation Theory	PMT has been used to identify predictors of a range of health behaviours, including breast cancer genetic test [150], and undertaking WGS for screening purposes [91]. PMT includes self-efficacy and the intrinsic and extrinsic rewards of the maladaptive behaviour. As predictors of intentions and behaviours, self-efficacy has the strongest, most consistent and most robust effect [288]. Self-efficacy is a major factor in determining both motivation and health-protective behaviour [218]	PMT requires a threat in order to operationalise its threat appraisal first, then the coping appraisal. PMT is premised on negative appeals rather than on messages emphasising the benefits of the adaptive recommendation [248]. At times we engage in preventive health behaviours in anticipation of positive consequences, not because of fear [248]. Healthy users of WGS services may undertake WGS for positive planning. In some WGS results, when previously unknown threats become known, they may then be appraised via PMT. However, unidimensional measures of PMT appear not to be effective in capturing threat perceptions regarding multiple disease, as is the case in WGS [91].

in the studies' designs. The following discusses each of them in terms of their relevance to WGS.

When TAM is applied to a new technology, it is unclear which component or components of the particular technology are perceived to be useful and which ones are not, thus leading to a lack of practical lessons for design [27]. Understanding of usefulness requires detailed studies, however there are no theories of usefulness currently available to explain the relationships that can exist between users' perceptions and IT characteristics, as well as to identify the possible moderators of those relationships [27]. TAM does not provide a mechanism for the inclusion of salient beliefs such as trust, enjoyment or cognitive absorption, and its dominance as a model forces researchers to justify any additions [27] outside of those already contained within. This is contrary to the spirit of TRA from which both TAM and TPB were born [27]. In TRA, the original source of TAM, a variety of salient beliefs may be generated dependent on the specific context [27].

Although TAM is more parsimonious than TPB, and is arguably a better choice than TPB when performing an analysis of technology adoption [349], Straub and colleagues [284] recommend researchers consider whether it really is system usage they are trying to

Model	Benefits	Constraints
Theory of Planned Behaviour (TPB)	TPB emphasises rational, conscious, and deliberate behaviours [220]. TPB builds on TRA, taking social influence into account in terms of normative and control beliefs [297]. The left hand side of TPB model, (antecedents) can be opened up to identify salient beliefs relevant to the nature of the technological application, providing theoretical grounding to incorporate concepts into research models [27]. TPB is predictive in a variety of intentions and behaviours outside the health sphere. More than TAM, TPB provides specific information to guide development [196]. TPB was slightly better at predicting health screening intentions than HBM [220].	TPB does not break attitude down explicitly into affective, cognitive and conative (impulse, desire, volition) dimensions. TPB does not account for emotional or irrational behaviours e.g. heat of passion, spontaneous or knee-jerk responses [220, 14]. TPB overlooks affective beliefs and attitudes [96]. TPB does not include a focus on emotion and affect, which are increasingly being recognised as important predictors of health behaviours [220]. TPB does not take prior behaviour into account [282].

explain, as that is what TAM actually measures. TAM violates TRA's model, one of its foundational theories, when it makes a direct path from perceived usefulness to intention, bypassing attitudes [297]. For WGS exploration, attitudes are considered important, whereas measuring system usage, as is TAM's aim, is not the intended focus for research. Exploration of attitudes to WGS requires the ability to generate data to identify elements within constructs that determine behaviours associated with WGS, therefore a model focused on system usage is not directly relevant.

As models go, UTAUT is large, bringing together eight theoretical models to form one focused on technology acceptance and use, this primarily in workplace settings. As per TAM, UTAUT is not directly relevant to exploring WGS attitudes. UTAUT does contain theories that are relevant to WGS, others that are less so, if at all and some concepts from the different theories are very similar or overlap. TPB, Motivational Model, Innovation Diffusion Theory and Social Cognitive Theory within UTAUT have relevant constructs for WGS exploration, however overall emphasis on the use of IT systems in the workplace can only be legitimately extended so far. It is reasonably expected for WGS use to be based upon attitudinal beliefs beyond computer use as that element is possibly the least difficult one to overcome for those considering using WGS services, receiving results and sharing them. MPCU suits prediction of individual acceptance and use of a range of IT [319] and although it takes social norms into

Model	Benefits	Constraints
Technology Acceptance Model (TAM)	TAM (including TAM2 and TAM3) is a simplified adaptation of TRA to fit IT contexts [27]. TAM is tailored to model users' acceptance and use of information systems or technologies [178]. TAM has been extensively used in studies related to use of IT and is easy to apply across different research settings [268].	Based on TRA but focused on explaining IT system 'usage' [27, 284]. TAM only supplies very general information on users' opinion about a system [196]. TAM loses information richness from studies [268]. TAM measures users' perceptions of and intentions to use technology within and across organisations [13]. "Acceptance" not clearly delineated [284]. TAM predicts or explains system use as an amount or frequency [27]. TAM favours Perceived Usefulness and Perceived Ease of Use as having direct positive influencing effects on Behavioural Intentions rather than Attitudes [251]. Perceived usefulness and its antecedent, perceived ease of use are 'black boxes' with little investigation into what makes a system useful [27]. Little attention paid to antecedents of belief constructs, e.g. design, implementation, evaluation. Little attention paid to behavioural or performance consequences of adoption and acceptance. No mechanism for inclusion of other salient beliefs e.g. trust, enjoyment, cognitive absorption [27].

Model	Benefits	Constraints
Unified Theory of Acceptance and Use of Technology (UTAUT)	Facilitating conditions and social influences added to perceived use and perceived ease of use constructs from TAM, makes UTAUT similar to TPB [27]. Offers a view of how the determinants of intention and behaviour evolve over time [268].	Restrictive model focused on technology adoption and usage, rather than other measures or underlying factors [27, 284]. Refers to use of technology systems [268], mainly, but not always in organisations. Attitudes not explicitly recognised as directly determining intention, instead they are moderated by situational variables of gender, age, volutariness and experience [268]. UTAUT has over fifty constructs that would require examination and modification to suit context [4, 137].

Model	Benefits	Constraints
Unified Theory of Acceptance and Use of Technology 2 (UTAUT2)	Three new constructs are added to UTAUT, and one is removed to make UTAUT2, a model applicable to consumer context through utility appraisal, resource consideration and intentionality[320].	Although it is applicable to the context of consumers, UTAUT2, like UTAUT focuses on adoption and use rather than opening up antecedents of these factors to exploration. Habit and experience are unlikely to be useful constructs for undertaking WGS. UTAUT2 is expected to be inclusive. If additional constructs or elements are needed, UTAUT2 must be extended to include them.

consideration, it does this from the workplace perspective and is very much about personal computer usage [303].

UTAUT and UTAUT2 contain several models of value to WGS exploration but their aim is to understand use of IT systems, so as an analytical tool for the exploration of WGS, UTAUT models need to undergo several modifications. To explore WGS, UTAUT needs to be extended beyond its main concern of measuring technology acceptance and use. Attitudes and other relevant individual characteristics would need to be included for UTAUT to be applicable to different contexts [81]. Although UTAUT2 is designed for consumers, it remains a tool designed for considering systems' usage, rather than exploring factors, such as attitudes, that may be more useful to design and implementation than focus on usage measures. Elements that are similar to each other within the theories that support UTAUT and UTAUT2 have been distilled, brought together or otherwise managed to deal with frequent duplications and extensions of similar ideas, however it is likely to be elements from the theories within UTAUT models that are relevant to WGS exploration. Opening UTAUT and UTAUT2 constructs to explore considerations for undertaking new and as yet unestablished activities, such as WGS would result in an analytical tool lacking in the established validity offered by appropriate use of UTAUT models.

Exploration of WGS attitudes aims to learn what those who are not yet likely to be using WGS services think, which requires enquiry beyond use of an IT system. Even at the point of purchasing a DTC WGS service, specific online interfaces or other such aspects of WGS services are unlikely to be the key influencing factors impacting attitudes about undertaking WGS and receiving results and sharing them. If we focus on how easy it is to use WGS, as a technology it can now be as as simple as spitting into a lidded pot, posting it in a small package and interacting with an online account to access the results. It can be given as a gift or be part of a social event, shared with family or friends [182]; therefore the social aspects

related to attitudes associated with undertaking WGS, receiving results and sharing them are likely to include considerations about family, friends, health and well-being, research and personal information amongst others.

Rather than utilise UTAUT or TAM, it is preferred to use a comprehensive yet more generic model of behaviour to support the development of the thesis' studies. TPB is supported by Benbasat and Barki who recommended its theoretical grounding that allows incorporation of concepts relevant to the nature of the IT application being studied [27]. TPB utilisation allows the research design to be structured around the subject or setting to identify what antecedents to behaviour are at play. For these reasons, TPB is the analytical tool of choice for the studies that explore YAs' attitudes to WGS. To acknowledge and illustrate various theoretical models' use, the following section presents published research related to genetics or genomics that utilised some of these models.

2.6 Theoretically-based Studies Relevant to YAs and WGS

Attitudes of patients and research participants in the clinical genetic field have been researched in terms of sharing genetic results with relatives, friends and health professionals. Despite this, only a few clinical studies have considered TPB or other theoretical models as part of their research into attitudes about family communications and information sharing with health care professionals. Theoretically-driven efforts to examine testing interest across test types remain sorely needed [290].

The following studies, related to genetic or genomic testing, indicate use of theoretical models that have been introduced in this chapter. HBM, PMT and TPB appear in the literature for studies to genetics or genomics and are summarised below.

In 2010, Cyr and colleagues investigated associations between intentions to engage in genetic testing for colorectal cancer and HBM [63] using a postal survey with a sample living in rural Montana, USA. Cyr and colleagues found perceived benefits to be the best indicator of intention to undergo testing, followed by some elements from the perceived barriers and cues to action constructs, however susceptibility was not found to be a significant motivator, contrary to earlier findings in a 2002 telephone survey by Bunn and colleagues where, in order of magnitude, perceived barriers, susceptibility and benefits were found to significantly influence intention to test for colorectal cancer among adults living in three New England states in the USA [44].

Fisher and colleagues' 2012 single-blind randomised trial of Australians [91] included survey items in their study, drawn from the following theories to build their battery of

measurements to address effect of information bias on beliefs about and intention to undergo WGS:

- Protection Motivation Theory
- Consideration of Future Consequences,
- Uncertainty Avoidance
- Anticipated Regret

Fisher and colleagues found PMT provided a useful theoretical background for understanding factors underlying WGS screening intention [91], with coping appraisal variables emerging as strong predictors. However, much like HBM, PMT requires a high threat appraisal and a high coping appraisal [91]. The high threat appraisal requirement was not met by young adult participants (average age 19.4 years) when considering whether they would undertake WGS screening in the future [91]. It may be PMT's unidimensional measures are unable to effectively capture threat perceptions as a means of predicting intention to undergo WGS in future healthcare [91].

Milne and colleagues found coping appraisal was of greater utility than threat appraisal in predicting health-related behaviour [218]. Although two meta-analyses of PMT in 2000 [93, 218] found support to claim self-efficacy as the strongest, most consistent, and most robust effect on intentions and behaviour, Floyd and colleagues' meta-analysis found that their college-aged group showed a lower relationship between self-efficacy and protection motivation than other adults did, suggesting that this may indicate that as we mature we experience more successes in coping, generally, therefore our beliefs regarding effectiveness of coping strategies become more salient [93].

Although there may be threatening information revealed in results when apparently healthy YAs undertake WGS, it is not a straightforward process to define and appraise these threats from as yet unknown results from WGS in the conventional sense. Threat beliefs, i.e. perceived severity and perceived susceptibility, pertain to specific disease outcomes [289]. Because they cannot be directly mapped when used for tests that provide results about multiple disease outcomes, conventional threat beliefs do not make sense [289, 91]. This point is noted by Sweeny and Legg in 2011 [289] in relation to DTC genetic tests with results about a wide range of genetic health factors where they reject inclusion of perceived severity or perceived susceptibility in their study. The same point about tests with multiple results and traditional threat appraisals is made again in 2012 by Fisher and colleagues in relation to WGS screening [91], to explain the lower predictive ability that PMT's unidimensional measures held in their WGS screening study.

Apart from the coping appraisal variables from PMT, Fisher and colleagues found Uncertainty Avoidance was a strong predictor of intention to undertake WGS screening [91]. PMT will be relevant to some undertaking WGS, who have a family health history that concerns them in the same way that HBM does, because of its reflection of health-focused threat and benefits appraisals.

Quantitative studies to predict sharing of breast cancer genetic test results with relatives that address TPB constructs have been published [25, 221]. In Barsevick's 2008 study, attitudes, SNs and PBCs were all found to predict female participants' intention to share their breast cancer genetic test results [25], whereas, in 2013, Montgomery and colleagues found perceived control and specific social influence, i.e the sense of control participants had in relaying the results information and their perception of the relative's opinion of genetic testing, were associated with sharing breast cancer genetic test results [221]. Variance in the relative importance of attitudes, perceived behavioural control and subjective norms for different behaviours and among different populations does not negate the value of TPB, but rather suggests a need to be flexible in the weight assigned to each of its components for a given context [221].

TPB is evidenced as having the ability to predict health related behaviours and has the potential to incorporate and categorise a wide range of factors underlying genetic behaviours, including communication [296], however few empirical studies have utilised a behavioural model when addressing healthy adults' perceptions, intentions and choices when undertaking WGS, receiving results or sharing results' information. Relevant adult studies that have used TPB include a quantitative study by Wolff and colleagues addressing intention to obtain genetic testing with a sample from the Norwegian population [342] and a mixed-methods study of mainly healthy individuals' intentions to receive WGS results by Facio and colleagues' as part of ClinSeq, a larger clinical genomics study in the USA [87].
Sweeny and colleagues' 2014 systematic review of empirical work on predictors of genetic testing decisions, concluded that qualitative studies that addressed genetic testing interest, intentions or uptake using self-reporting methods and those that were focused on types of tests had far more consistent findings than quantitative research attempts to use objective predictor variables and studies that were disease-focused [290]. Wiens and colleagues' systematic review, published in 2013, that addressed genetic risk communication with family, identified factors relevant to communication of genetic risk information in families; these included perceived pressure to disclose information, shaped by genetic professionals, family members and society [335].

Wolff and colleagues extended TPB to include 'anticipated affective outcome' and used a separate measure of individuals' attitudes towards uncertainty avoidance [342]. When

participants were asked about their interest in taking the initiative to have a genetic test, Wolff and colleagues found that their interest was predicted by uncertainty avoidance, potentially negative consequences of testing and SNs [342]. Participants in Facio and colleague's study held positive attitudes toward receipt of WGS results information, including uninterpretable results, and they perceived the views of their SNs to be positive [87].

In the clinical genetic field, patients' and research participants' attitudes to sharing genetic results with relatives, friends and other health professionals have been researched. Some studies have addressed family communications and information sharing with health care professionals. Studies addressing the views of young, non-clinical, adult participants, towards genetic or genomic testing and results information, that also refer to a theoretical framework such as TPB or similar, remain rare with notable exceptions [190, 91].

Using TPB in its design and analysis, a survey of young university-based undergraduates' interest in a DTC genetic-testing kit [190] found that TPB, and in particular attitudes and SNs, accounted for a significant amount of variance in participants' intentions to use a personal genomic services. Family, friends and significant others provided a constellation of interpersonal influences on intention and engagement with genomic services, suggesting the need for future research into attitudes, subjective norms and their impacts on decisions [190]. In their 2013 systematic review, Wiens and colleagues [335] evaluated nine theoretical models for their appropriateness as guiding theories for framework development pertaining to communicating genetic risk information in families, they are as follows:

- Circumplex model of marital and family systems
- Double ABCX model of adjustment and adaptation
- The Beaver's systems model
- The McMaster model of family functioning
- Family communication patterns model
- Health Belief Model
- Protection Motivation Theory
- Social Cognitive Theory
- Theory of Planned Behaviour

Wiens and colleagues' five criteria for evaluating the theoretical models were:

1. relevance to family communication of genetic risk information (relevance)

2. ability to incorporate a wide range of factors which underlie communication of genetic risk information (range of factors)

3. ability to delineate or categorise target behaviours amenable to intervention (amenable behaviours)

4. ability to predict whether communication will occur in varying circumstances (predictive ability)

5. evidence of validity (validity)

Following their evaluation, Wiens and colleagues utilised TPB to identify factors relevant to genetic-risk information communication in families. They found perceived pressure to disclose information was shaped by genetic professionals, family members and society [335].

This small body of theoretically-aligned research has mainly focused on attitudes of patients and research participants about sharing genetic results with relatives, friends and other health professionals in clinical genetic settings rather than genomics and the personal genomic service arena. What they provide are illustrations of the theoretical models being incorporated into WGS-relevant research.

2.7 Gaps in Knowledge

YAs are coming of age in a more genomically informed era and may be adopting a more optimistic view of genomic medicine in general [236]. The literature reviewed highlights new areas for exploration. With a few exceptions, YAs' intention to undertake WGS, receive results and share genomic results with others has barely been explored [326, 316, 190]. As a group YAs are increasingly likely to encounter, use and be affected by new genomic services, making their views towards WGS worthy of exploration [140].

Apart from studies such as Hassan and colleagues in 2020 [140], Carver and colleagues' in 2017 [52], Giraldi and colleagues in 2016 [115], Mackert and colleagues in 2012 [190] and Rew and colleagues in 2010 [254], few research papers about knowledge and attitudes to genomics or genetics target YAs or report findings from adult sub-groups, meaning YAs' views cannot be ascertained from them. Many questions remain about the knowledge and attitudes of YAs to the complex matter of undertaking WGS and sharing such results, both within and beyond medically-mediated and research environments. The relationship between YAs' knowledge of genetics and attitudes towards its applications remains to be clarified with studies returning conflicting results [52]. Evidence for the relationship gender has with

knowledge and attitudes towards WGS also remains conflicted [162, 151]. YAs' views about how to receive results is an area that remains disputed. How genetic professionals and other domain experts respond to YAs' concerns demands research.

There is a lack of research addressing how services and systems could be developed to support those who undertake WGS, receive and share results with others. An exploration of theoretical frameworks, that could reflect YAs' views of WGS, shows technology acceptance models have developed from other more general theories and models. Technologies are either viewed through the lens of theoretical models or the models are adapted to fit new technologies. For the purpose of the YA studies that follow, TPB has been chosen as a generic model that requires an application or behaviour to recontextualise the contents of its constructs; its flexibility allows for the social and technical aspects of undertaking WGS, receiving results from WGS and sharing them with others. Genomics is in its commercial infancy and may be considered for reasons other than threat of ill health.

Although family health history has an influence, essentially, apparently healthy people undertake WGS out of curiosity to discover what information about themselves can be known from sequencing their DNA [356, 357]. As WGS becomes increasingly available people will undertake it in a desire to gather information for consideration in planning their future. Genomic sequencing DNA test kits were advertised and sold online, for example, in August 2020 Nebula Genomics was selling one for $299 [224]. UK customers may buy genetic products and services for themselves from well-known online retailers; these products and services are also marketed as gifts [1]. Independence from the influence of traditional relationships with healthcare providers means there is an additional need to better understand the interplay between YAs knowledge and attitudes so they may access appropriate information and guidance about undertaking WGS.

The YAs' studies that follow aimed to explore YAs' knowledge and attitudes to undertaking WGS, receiving results and sharing them with others. A large scale survey explored relationships between knowledge and attitudes. An in-depth interview study addressed YAs' considerations for undertaking WGS in more detail. The theoretical frameworks introduced in this chapter and the YAs' studies' findings informed the design of a proposed framework. The proposed WGS framework was evaluated with domain experts, who enhanced it. The WGS framework is contributed as part of an effort to assist YAs by offering guidance to them and those who may support them with such an undertaking.

2.8 Summary

Carrying out a detailed survey of the literature has helped shape the studies' designs. The objectives for studies contained in this thesis are to better understand YAs' attitudes towards undertaking, receiving and sharing information resulting from WGS, so a framework may be produced as guidance to support professionals and YAs when considering WGS. From the literature reviewed, there appears to be a gap in current academic research where YAs' views about genomics are elicited. In order for them to be best served, there is a need to understand views of YAs. WGS has become accessible to them where once it was only available to patients with complex and serious medical conditions and research participants in clinical studies. Questions about YAs' considerations for readiness include their genetic knowledge, attitudes and understanding of what to expect from WGS results, and the sharing implications that ensue.

Research to support YAs needs to be informed by the perspectives of YAs. Exploring their knowledge and attitudes will help identify elements important to YAs' considerations. Tools designed with YAs' views in mind would assist professionals to be prepared to offer services that are suited to support YAs' decision making requirements. Previous research, including a 2012 TPB-based study [190] for online Do-It-Yourself Genetic Assessment services provided a useful starting point to design a large scale survey for YAs about WGS for this thesis. Following the survey, in-depth interviews with a small group of the YA participants posed further questions about their considerations for undertaking WGS, receiving and sharing results.

YAs may benefit from a tool to indicate or emphasise considerations for decision making that they may not have already thought of. YAs may also need to make sense of WGS services and usage for themselves, without conventional pre-testing counselling. For a proposed framework to be designed, theoretical models introduced in this chapter were appraised in light of the findings of the YAs studies. What professionals thought about findings from the YA studies was important. Their views guide where emphasis may be placed or additional information deemed necessary for YAs' informed decision making. Findings from the YA studies were evaluated with knowledgeable domain experts to enhance its structure and contents. Empirical additions to the academic literature that offer a framework for undertaking WGS, from consent and sample provision to receiving results and sharing them, would help guide YAs and those who support them.

Chapter 3

Survey of YAs' Knowledge and Attitudes about Undertaking WGS and Sharing Results

3.1 Introduction

This study was a large scale survey to capture attitudes of YAs (18-25 year-olds) about undertaking WGS and their preferences for sharing results.

Aim: Following a literature review, quantitative methods were used to identify relationships between individual characteristics and preferences related to YAs' knowledge of and views about undertaking WGS and sharing results information with relatives.

Specifically, to answer the research question: Are there relationships between individual characteristics (such as gender, genetics course undertaken, completed educational level, field of study) and YAs' attitudes to undertaking WGS, receiving results and sharing them with relatives? Hypotheses were tested to identify relationships between participants' characteristics and their attitudes to undertaking WGS, sharing results with parents and siblings, and their desire to know their relatives' WGS results.

3.1.1 Theory of Planned Behaviour and Survey Study

TPB constructs were used to frame survey questions so that subjective norms, behavioural controls and attitudinal components of behavioural intentions could be examined. Data pertaining to External Factors in TPB were collected. In particular, hypotheses tested concern whether gender and indicators of knowledge affected participants' subjective normative beliefs and attitudes to WGS [10, 57, 9].

3.2 Methods

This is a large survey study collecting quantitative data about YAs' knowledge and attitudes to WGS. This section will describe participant recruitment, materials used to conduct the survey and method adopted for statistical data analysis.

3.2.1 Participants

This study initially recruited from the University population. This population contained YAs who were highly educated in terms of genetics through to those with no formal genetics education. This study aimed to gather and understand attitudes about WGS from a wide range of university-based YAs, therefore previous awareness of WGS was not an inclusion criterion. Instead, participants were sought, regardless of their level of subject-specific knowledge. It was recognised that the study's sample population would contain a higher proportion of individuals who were knowledgeable about genomics than found in the general public. The university-based population provided an opportunity to analyse relationships between formal education and YAs' attitudes to WGS.

The study's broadened scope to study university-based YAs with a variable awareness and knowledge of WGS reflected a recognition of increasing exposure and access this group will have to genomics services, either through referrals made by their HCPs or via DTC genomic services. Specialists, who attended public dialogue workshops, recognised how little knowledge of the science of genomics the public actually needed in order to make a valuable contribution, and that views belonging to members of the public did not diverge significantly from those held by genomics patients and their families [312]. On participant information sheets, YAs were directed to Genetic Alliance UK's and Genomics England's webpages to access introductory information about WGS.

The Urban Rural Sustainability's (URSUS) 2019 report *Evaluation of a public dialogue on Genomic Medicine: Time for a new social contract?* [312, 113], recognised commercial businesses as part of the genomic medicine ecosystem and the need to carefully frame these relationships for the public. The report concluded that an understanding of what the wider public (i.e. 'potential patients') thinks about genome data could help NHS England design its communications programmes to address targets set by the Secretary of State, in October 2018, to sequence 5 million genomes within 5 years. [312, 112].

The YAs study was approved by the School of Computer Science's Research and Ethics Committee at the University of Nottingham. A snowball method was used to recruit participants who were students or non-academic university staff, mainly by in-person canvassing activities of the lead investigator, as well as emails to contacts, University webpage adverts

and posters in University buildings. Four-hundred and fifty surveys were distributed between June and October, 2016. A voucher draw with prizes worth £40, £25 and £15 was offered to incentivise participation in the survey and in a follow-up interview study. All participants completed a consent form.

A further application to the School of Computer Science's Research and Ethics Committee at the University of Nottingham the study was approved, extending the study to all 18-25 year-olds, allowing those without affiliation to the university could enrol. Incentives, i.e. vouchers, were not available for this tranche of participants.

3.2.2 Materials

The survey was available to participants on paper or in an electronic format. The survey is provided in Appendix B.1. Study packs contained participant information sheets with weblinks to Genomics England's 'Understanding Genomics' webpage [110] and an introductory educational webpage from Genetic Alliance UK [100], consent forms, the survey itself, and envelopes for returning completed documents to the researcher. The survey began with multiple choice questions about participants' awareness of WGS, followed by a quiz adapted from one online [2] testing their principles knowledge of human genetics, i.e. basic theoretical information about functioning principles [283]. The main part of the survey combined questions adapted from a study of young people's attitudes to a DIY genetic test kit [190] together with some original questions, shaped by TPB [94], to explore WGS awareness and test hypotheses about attitudes towards sharing WGS results with relatives.

Although semantically differential scales, such as Likert, are often used for ease, there is no specified scale designed as a dedicated measure of factors associated with TPB [8]. Survey responses to attitudinal questions were collected using a method whereby users draw ellipses to indicate their response together with their perceived confidence in their answer [328]. This approach has not been used before in this context. This data capture method allowed participants to express their level of certainty when answering hypothetical questions as this is an area where uncertainty is likely to exist. These interval-valued questions were numbered with a prefix IQ to distinguish them from other questions.

In this present study, the central point of the ellipse, i.e. the mean of the endpoints, was taken as the response; the uncertainty was not used. Participants reported their gender, highest attained educational level, previous genetics education and field of study. Respondents were provided with a blank space on the questionnaire so they could self-identify their gender. Participants reported whether they had previously undertaken a genetics course at school or at university. If both, the higher level was used for analysis. Independent variables of gender, belonging to Science, Technology, Engineering, Maths or Medicine (STEMM) fields of

study, genetics quiz scores, completed educational level, and genetics course were compared to the following dependent variables:

- genetics quiz scores
- intent to consult a healthcare professional (HCP) prior to undertaking WGS
- interest in purchasing WGS services online
- concerns related to insurance policies,
- wanting a report to explain WGS results
- the desire to share WGS results with parents
- the desire to share WGS results with siblings,
- desire to know relative's WGS results

The survey was piloted and initially validated by three international PhD students at the University of Nottingham, who completed it, commented on any difficulties or concerns regarding the questions and made recommendations that were incorporated into the final version. All survey participants were invited to comment on the survey, either inline or in the comments section at the end. Following completion of the main survey, participants were asked questions on a separate survey sheet to ascertain their views about the use of ellipses. Responses to these questions were used to assess the face validity of the use of ellipses. All participants' responses were manually inputted into spreadsheets. During this process a sense-checking exercise was undertaken to assess internal consistency of individuals' responses, i.e. agreement between and among responses to survey items that reflected similar constructs, evidencing internal consistency reliability as well as criterion validity.

3.2.3 Data Analysis

Descriptive analysis of participant characteristics are presented in the Results section. Violin plots illustrate the shape of data distribution by adding a density trace to the box plot design [152]. The density trace highlights peaks, valleys and bumps in the distribution [152]. Violin plots in the Figures illustrate data distribution of responses to attitudinal questions, with markers for the minimum, median and maximum values. To inform inferential analysis of attitudinal questions' responses, a statistical power analysis was performed for sample size estimation. To detect a small to moderate effect (Cohen's d = 0.4) with an estimated means

SD of 2.5 on a scale from 0 to 10 and an alpha of 0.5, a sample size of 100 participants will produce power = 0.52.

Two-tailed Spearman's rank order correlation coefficient tests (r_s) were used to measure the strength and direction of association between two ranked variables. Two-tailed Wilcoxon-Mann-Whitney tests (U) were used for independent variables with two levels and Kruskal-Wallis rank sum tests (X^2) were used for independent variables containing three groups to test the null hypotheses that samples were from identical populations. Conover post hoc pairwise multiple comparison tests (t) with Bonferroni adjustments followed Kruskal-Wallis tests with p-values < 0.05 to identify which groups differed significantly. Following initial analysis described above, post-hoc, one-tailed Wilcoxon-Mann-Whitney tests (U) were used for selective two-level variables to identify whether observed differences between them were significant. Details of all the statistical test results are presented in Appendix B.2, together with their p-values, z-scores and effect-sizes (r). All statistical tests were performed using R version 3.3.2 statistical software [301].

3.3 Results

This section presents results analysed from the survey data. This includes description of participant characteristics, variables related to education and genetic knowledge and genetic quiz scores as well as statistical results related to attitudes for undertaking and sharing WGS.

3.3.1 Participant characteristics

One hundred and twelve YA participants between the ages of 18 and 25 completed the survey. Their mean age was 21.9 (SD = 2.28). Ninety two (82.1%) were full-time students and twenty (17.9%) were non-academic employees. One hundred were recruited from the University of Nottingham, nine from a Nottinghamshire school and three were conference attendees. For fifty eight participants (51.8%), this was the first time they had heard of WGS. The median quiz score of 80% was achieved or surpassed by 71 participants (63.4%). Of the 59 STEMM participants, 40 (68%) scored above the median on the quiz, as did 28 (53%) of the 53 non-STEMM participants.

Seventy nine participants (70.5%) wanted to learn more about WGS and the human genome. The highest completed education level attained was self-reported, translated to correspond with the eight levels of the UK Visas and Immigration Qualification Level list [311], then grouped into three completed educational levels. The first level included those whose highest educational level attained was secondary school education or equivalent

vocational qualifications; the second level included those whose highest attainment was a degree level qualification or equivalent, and the third level included those with a further degree, equivalent or higher. The STEMM group did not differ by gender, as confirmed by a chi-squared test ($X^2(1, N = 112) = 2.1458, p = 0.143$). The gender breakdown for participants' STEMM status, previous genetics courses undertaken and completed educational levels are detailed in Table 1.

Survey completion evaluation: use of ellipses

In the open-ended comments, most comments were participants expressing their interest in the topic. None of the participants commented on having any difficulties in completing questions using ellipses. It was observed that participants often responded with variable ellipse sizes placed at different points along the 0-10 range in response to the range of questions in the survey. This evidences their attention and ability to express their level of certainty for each question put to them, supporting face validity of the use of this method. Thirty six participants answered the separate questions concerning the use of ellipses. When asked how using ellipses affected their ability to express their opinion, of the 25 participants' who responded to this specific question, 20 described the method's effect positively, whilst five commented that it was not helpful.

Table 3.1 **Independent variable levels and participant numbers**

Variables	Description, numbers and percentages (%)		
Gender:		Female: 67 (59.8%)	Male: 45 (40.2%)
Educational levels Completed: Gender-split:	Secondary school or equiv.: 46 (41.1%) Females 28 : Males 18	1° degree: 42 (37.5%) Females 23 : Males 19	2° degree: 24 (21.4%) Females 16 : Males 8
STEMM: Gender-split:		STEMM: 59 (53%) Females 31: Males 28	Non-STEMM: 53 (47%) Females 36 : Males 17
Biology Course: Gender-split:	None: 17 (13.9%) Females 10 : Males 7	School: 73 (65.2%) Females 40 : Males 33	University: 22 (19.6%) Females 17 : Males 5
Genetics Course: Gender-split:	None: 86 (76.8%) Females 46 : Males 40	School: 10 (8.9%) Females 8 : Males 2	University: 16 (14.3%) Females 13 : Males 3

Quiz scores, education, and Science, Technology, Engineering, Maths and Medicine

The relationship between genetic quiz scores and attainment of a biology course was examined. The median quiz score for the 17 participants who had not undertaken a biology course was 70%. The 73 participants, who had undertaken biology at school, but not at university, achieved a median quiz score of 80% and the 22 participants who had undertaken university-level biology achieved a median of 90%. Those who had studied biology at university had

significantly higher scores than both those who had studied it at school, and those who never had. How genetic quiz scores related to participants' completion of a formal genetics course was analysed. Both the 86 participants who had never undertaken a genetics course and the 10 participants who had completed a genetics course at secondary school achieved a median score of 80%. The 16 participants who had undertaken genetics at university had a median score of 90%. Those who had studied genetics at university had significantly higher quiz scores than those who had never undertaken a genetics course. Genetic quiz scores were analysed in relation to participants' STEMM status. Both groups' median was 80%, despite this the Wilcoxon-Mann-Whitney test found significant distribution differences with overall higher scores for STEMM participants.

3.3.2 Statistical Test Results

Tables containing the statistical results are presented in Appendix B.2 and at the end of this section, Table 3.2 summarises the statistically significant relationships found between variables.

3.3.3 Attitudinal Results

The following refer to questions that required interval-valued responses (IQ1, IQ2, IQ3, etc) starting on the survey's forth page.

IQ 19. I would consult a doctor, nurse, or counsellor before undertaking WGS.

There was a high median recorded for participants' desire to consult with a health professional before undertaking genomic sequencing. When the relationship between participants' desire to consult a HCP prior to undertaking WGS (IQ19) and their completion of a genetics course was examined, those who had undertaken a genetics course at school were found to have a significantly lower intention to seek consultation than those who had studied it at university, as illustrated in Figure 3.1

IQ 20. I like the idea of purchasing WGS services over the Internet.

Exploration of the relationship between liking the idea of buying WGS services online (IQ20) and participants' STEMM background found those with a STEMM background were significantly more inclined to like the idea of buying WGS online than those wthout a STEMM background. This finding is illustrated in Figure 3.2

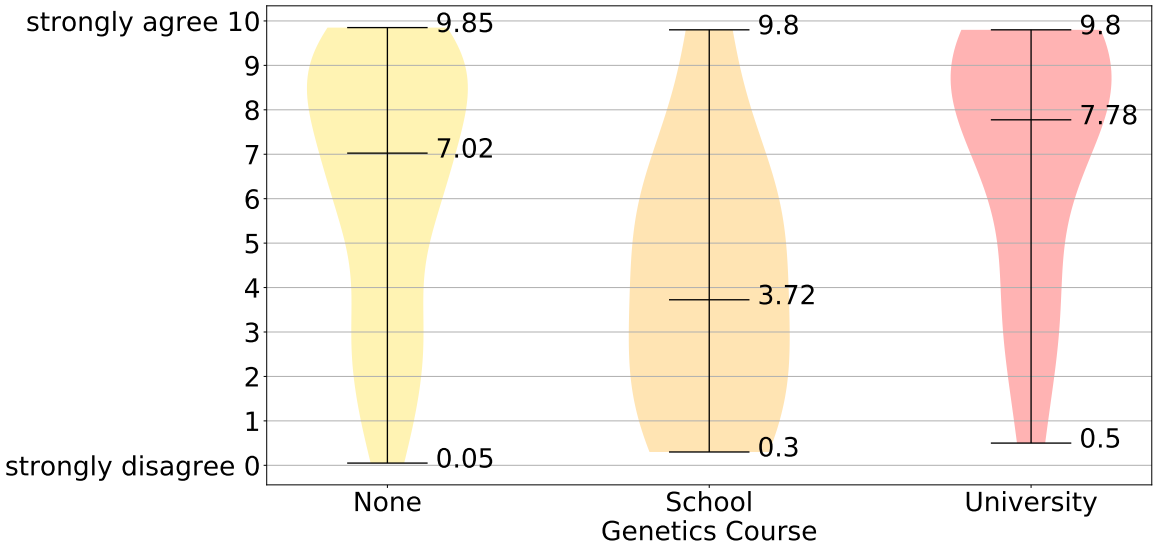


Fig. 3.1 **I would consult a doctor, nurse, or counsellor before undertaking WGS (IQ19).**

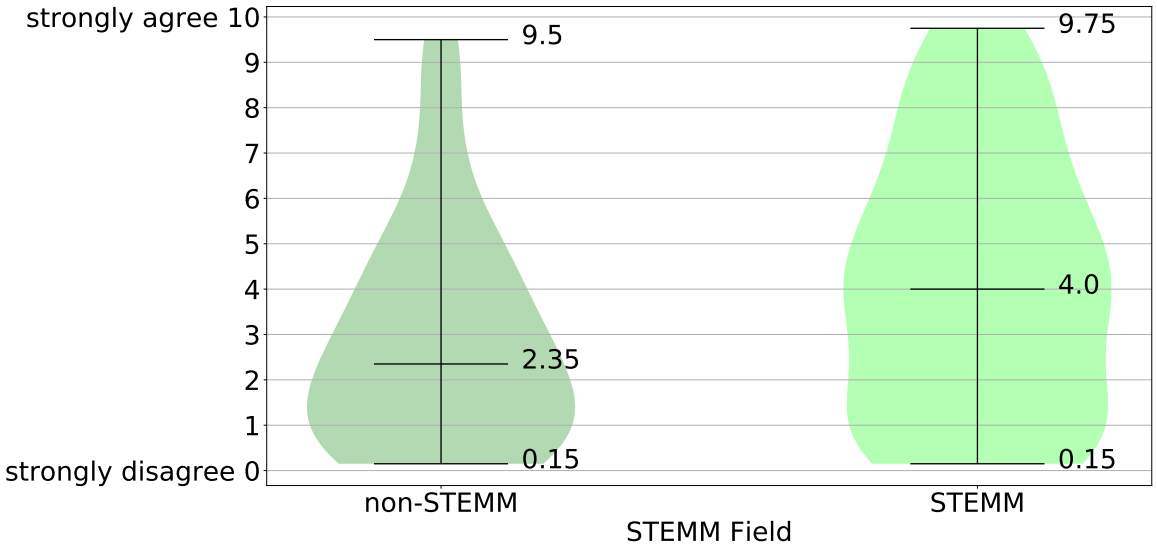
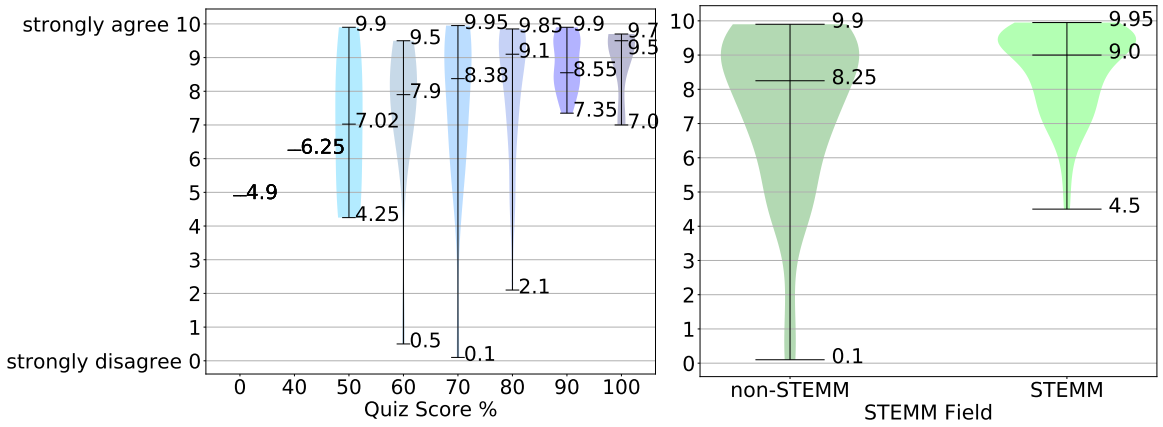


Fig. 3.2 **I like the idea of purchasing WGS services over the Internet (IQ20).**

IQ 17. I would want to receive a report that explains the results from my WGS.

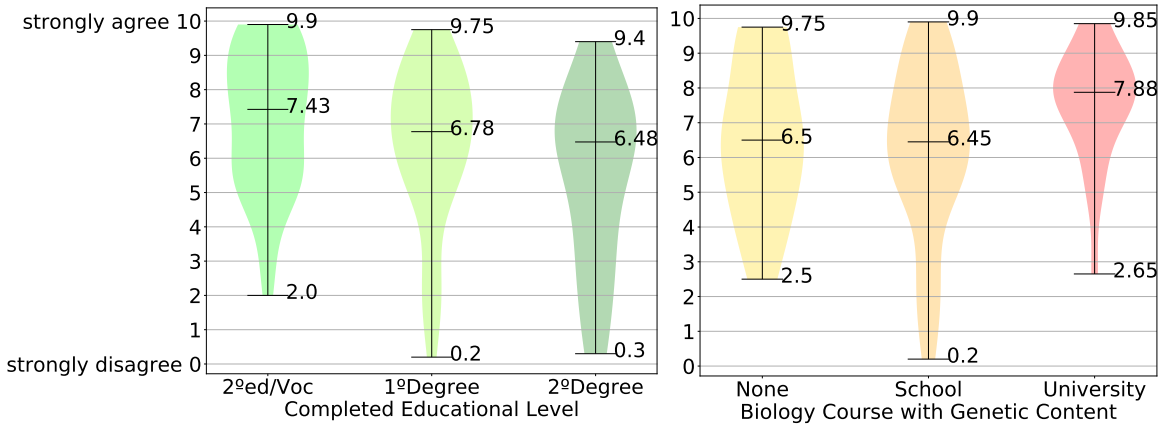
The relationship between the desire for a report to explain results (IQ17) and participants' quiz scores was found to have a significant positive correlation when explored using Spearman's Rho test. As quiz scores increased, the desire for a report also increased, see Figure 3.3a. When one's desire for a report to explain WGS results was compared to STEMM status, a significant difference between the groups was found with a greater desire expressed by STEMM participants, see Figure 3.3b.



(a) Want a report by quiz score

(b) Want a report by STEMM

Fig. 3.3 **I would want to receive a report that explains the results from my WGS (IQ17).**



(a) Insurance concerns by generic educational attainment

(b) Insurance concerns by biology course

Fig. 3.4 **I am concerned about possible insurance consequences of WGS results (IQ11)**

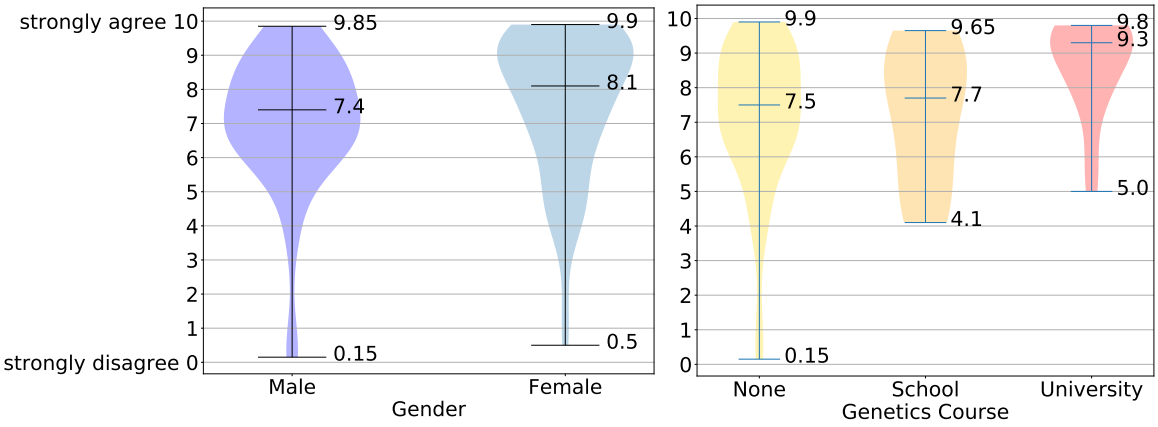
Participants with STEMM background had a greater desire to receive a WGS results report than those who did not come from these fields.

IQ 11. I am concerned about possible consequences the WGS results may have on insurance policies for health, travel or life.

YAs were asked about whether they had concerns for the possible consequences WGS results might have on insurance policies (IQ11). As YAs' generic educational levels increased, their insurance concerns decreased. Conversely, attainment of university-level genetics-specific education through a biology course was related to higher levels of concern. These findings are illustrated in Figure 3.4.

IQ 7. and IQ 5. I would inform my parents about the results of my WGS analysis and I would inform my siblings about the results of my WGS analysis

The survey examined the relationship between participants' gender and their intention to share their WGS results with parents (IQ7). The difference between the genders was significant, as illustrated in Figure 3.5a.



(a) Sharing by gender

(b) Sharing by genetics course

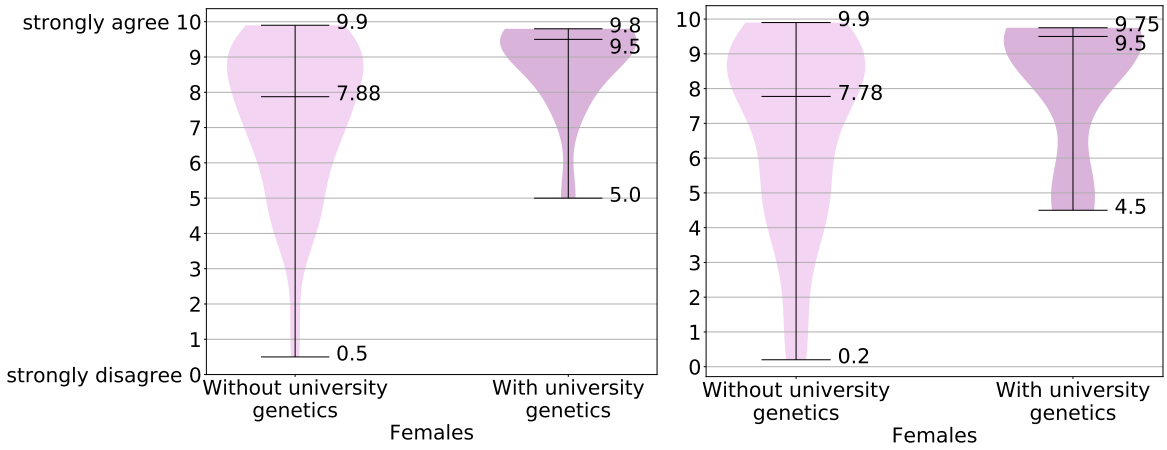
Fig. 3.5 **I would inform my parents about the results of my WGS analysis (IQ7).**

In relation to intention to share one's WGS results with parents and participants' genetics course attainment, those who had studied genetics at university had a significantly greater intention to share with parents than those who had not studied genetics at all, see Figure 3.5b.

The relationship between participants' intention to share with parents and their completed educational level was found not to be statistically significant. The relationship between intention to share results with parents and STEMM status was also found not to be statistically significant. Because intention to share with parents of participants who had previously studied genetics at university was higher than that of the female participants and due to the high ratio of females in the university-level genetics groups, females with and females without university-level genetics education were compared post-hoc for their attitudes to sharing with parents. Power for this analysis was low. Females who had studied genetics at university had a significantly greater intention to share with parents than the other females, Figure 3.6a.

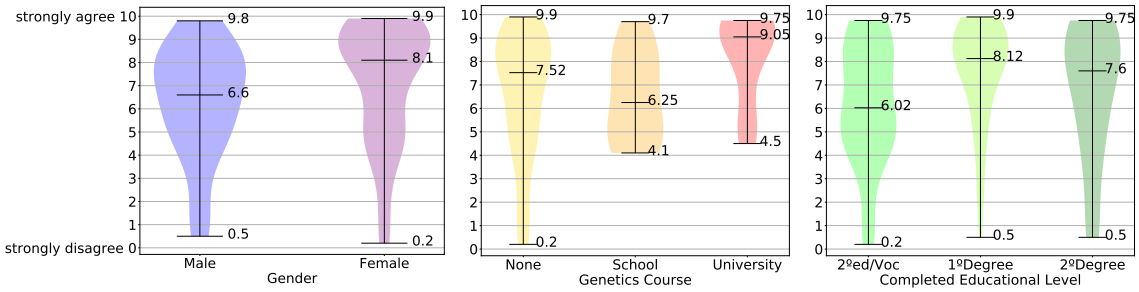
When the relationship between intention to share results with siblings (IQ5) and gender was examined, females were found to have significantly greater intention to share, see Figure 3.7a.

When intention to share one's WGS results with siblings was analysed in relation to participants' prior completion of a genetics course, those who had studied genetics at university had a significantly greater intention to share their results with their siblings



(a) I would inform my parents (IQ7) (b) I would inform my siblings (IQ5)

Fig. 3.6 **Females intention to share with relatives and university genetic education**



(a) Sharing by gender (b) Sharing by gen. course (c) Sharing by education

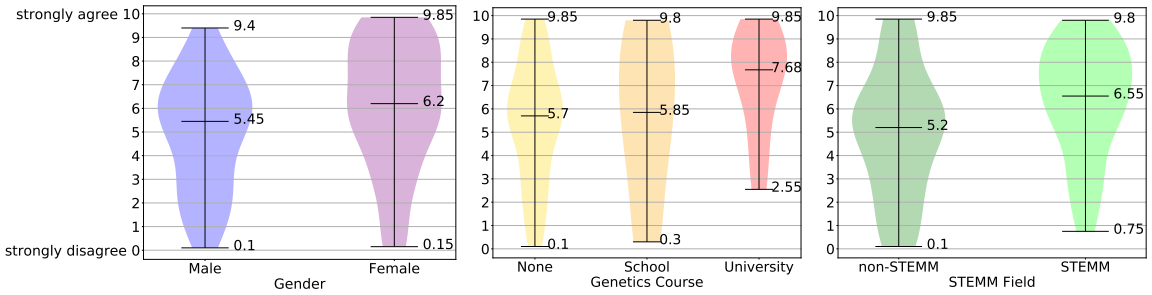
Fig. 3.7 **I would inform my siblings about the results of my WGS analysis (IQ5).**

compared to those who had never studied genetics, as per Figure 3.7b. Examination of how the desire to share WGS results with siblings related to educational levels found that those with a secondary-school / vocational-college education had a significantly lower intention to share with siblings compared to those with a 1st degree, see Figure 3.7c. Participants' intention to share with siblings and their STEMM status was not found to be statistically significant. Because intentions to share with siblings held by university-level genetics course participants were higher than those of female-gender group, females with and females without university-level genetics education were compared for their attitudes to sharing with siblings.

Females who had studied genetics at university were found to have a significantly greater intention to share with their siblings than the other females, Figure 3.6b.

IQ 22. I would want to know the WGS results of my relatives.

Examination of the relationship between the desire to know the WGS results of one's relatives (IQ22) and gender found that females had a significantly greater desire to know, see Figure 3.8a. The desire to know the results of relatives and participants' prior genetics education were compared. Those who had studied genetics at university had a significantly greater desire to know the results of relatives than those who had never studied genetics, see Figure 3.8b.



(a) Results by gender (b) Results by gen. course (c) Results by STEMM

Fig. 3.8 **I would want to know the WGS results of my relatives (IQ22).**

The relationship between desire to know relatives' results and completed educational level was found not to be statistically significant. The desire of those in STEMM areas to know the WGS results of relatives was significantly greater than non-STEMM, see Figure 3.8c. Because desire for relatives' results held by University-level genetics course participants was higher than that felt by females, a comparison was made between females with and without university-level genetics education.The difference observed in their attitudes was not statistically significant.

Table 3.2 summarises the independent variables that were found to have significant relationships with the attitudinal survey questions, statistical results are detailed in Appendix B.

3.4 Discussion

New insights into the knowledge and attitudes of university-based YAs about undertaking and sharing genomic results information are discussed here. Other studies have explored participants' desire to share genetic results with relatives, but most were in the context of clinical genetics, such as breast cancer [83, 221] or in paediatric settings [206, 272, 247]. Very few genomic studies have addressed YAs' views and even fewer considered their sharing preferences for genetic or genomic sequencing results in relation to their educational

Interview Questions	Independent variables						
	Genetics Course	STEMM	Quiz Score	Completed Education level	Biology Course w/genetics	Gender	Females ± Genetics Course
Q 19. I would consult a doctor, nurse, or counsellor before undertaking WGS.	X						
Q 20. I like the idea of purchasing WGS services over the Internet.		X					
Q 17. I would want to receive a report that explains the results from my WGS.			X				
IQ 11. I am concerned about possible consequences the WGS results may have on insurance policies for health, travel or life.				X	X		
Q 7. I would inform my parents about the results of my WGS analysis.	X					X	X
IQ 5. I would inform my siblings about the results of my WGS analysis	X			X		X	X
IQ 22. I would want to know the WGS results of my relatives.	X	X				X	

X = significant relationship found

Table 3.2 **Summary of Significant Relationships**

attainment or knowledge of WGS [190, 269]. Empirical studies addressing desires for genetic information resulting from a relative's testing are rare [83, 148]. TPB concepts and quantitative methods were used to explore participants' attitudes towards undertaking WGS, their desire to share their genomic results and to receive results of their relatives' WGS. Survey responses primarily addressed relationships between certain External Factors and aspects of participants' attitudes, subjective norms and perceived behavioural controls.

3.4.1 Participant characteristics: WGS awareness, education and quiz scores

The level of WGS awareness among participants supported the trend identified in another study that the public's knowledge of genetics had been improving over the preceding 14 years [130]. Despite opening the study to a wider group, the sample mainly attracted participants from the university setting. Having a sample of respondents with differing awareness of WGS indicated data captured a mixed group in terms of subject familiarity, a result of the effort to recruit a broad range of YAs' from the University population.

Participants were all given links to materials about WGS when they joined the study. They may have chosen not to read it. Attitudes were not compared to participants' previous awareness of WGS. Instead, the sample's demographic supported the proposal of statistical hypotheses about relationships between subject-specific genetics knowledge and attitudes about WGS.

Interest in genetic testing and previous genetics education was high among YA participants compared to previous findings [130]. The level of interest was due, at least in part, to the high proportion of university students studied here.

A smaller percentage of these YAs had undertaken any biology course compared to advertising undergraduates in a USA-based study, yet a large percentage of the YAs studied were from a STEMM background and had taken a genetics course at university compared to the USA-based advertising students [190]. These differences likely reflect the broader range of subjects undertaken at secondary school and in early university education in the USA, where 90% of university graduates may receive some genetics instruction through general education courses [41]. An earlier study of the public by Haga and colleagues [130] found those with a higher education level had more genetic knowledge. By contrast, our study found no relationship between educational level and genetic quiz scores. Instead, quiz scores, assessing theoretical knowledge of genetics were higher for those with university-level genetic education and those with a STEMM background. This finding indicated that previous formal genetic education was a good measure of genetic knowledge whereas having

a higher education was not. It also supported validation of the genetic quiz used as a proxy for genetic knowledge rather than simply being a general indicator of educational level.

3.4.2 I would consult a doctor, nurse, or counsellor before undertaking WGS (IQ19).

Most YAs indicated that they would want to consult with a HCP before undertaking genomic sequencing. Participants in earlier studies have expressed this desire [254, 192, 355] but empirically the proportion of them that actually do is lower than opinions described pre-testing and hypothetically [269, 356].

Finding those who had undertaken a genetics course at school were less willing to consult with health professionals than those who had either not studied genetics at all and those who had done so at university may be an indication that attainment of some genetic knowledge at school gave participants a greater sense of their knowledge and abilities than those with more actual genetic knowledge. In 2011, Leighton and colleagues warned that individuals' overestimation of their abilities to interpret findings correctly made it especially important to find optimal methods to present information and provide assistance in interpreting results [184] because of lack of understanding the meaning and significance of results may lead to false reassurance, an inappropriate change in future medical management or unnecessary anxiety.

3.4.3 I like the idea of purchasing WGS services over the Internet (IQ20).

Others have found levels of interest in purchasing WGS online varied by gender, country of study, with privacy concerns cited [62, 315]. Despite overall low levels of interest from all participants, STEMM participants were significantly more interested in buying online WGS services than others.

3.4.4 I would want to receive a report that explains the results from my WGS (IQ 17).

Participants with a STEMM background preferred the idea of receiving a WGS report to explain results as did those with higher genetic quiz scores. This finding refines previous findings that indicated those with higher education would retain personal responsibility for their health [157]. The findings reflect previously reported positive attitudes and perceived behavioural controls of the more knowledgeable to manage a results report independently as well as their perception that receiving such a report helps them to retain behavioural

control[157], specifically aligning desire for a WGS results report to knowledge of or familiarity with the field.

3.4.5 I am concerned about possible consequences the WGS results may have on insurance policies for health, travel or life (IQ11).

Impact of insurance policies appeared to have a relationship to education levels and to having undertaken a biology course with a genetic component. Educational levels were found to have an inverse relationship with insurance policy concerns. This large, diverse YAs sample showed higher levels of genetic knowledge were positively associated with having higher levels of insurance concerns whereas higher generic educational levels were associated with lower insurance concerns. This higher level of concern was contrary to findings of others looking at insurance concerns and generic educational attainment [356]; it offers new insight into differences in attitudes between educated participants and genetically knowledgeable ones in relation to insurance and WGS.

3.4.6 I would want to know the WGS results of my relatives (Q21).

The generic measure of Completed Educational Levels was found not to be associated with a desire for relatives' results; however, having undertaken a genetics course at university, being female or studying in a STEMM field was, see Figure 3.8.
These findings are contrary to Heaton and Chico's 2016 UK-based study [148] where lesser-educated participants had a greater desire to know their relatives results.

3.4.7 I would inform my parents about the results of my WGS analysis (IQ7) and I would inform my siblings about the results of my WGS analysis (IQ5).

Our study found that most YAs had a strong desire to share their WGS results with their parents and siblings, supporting previous findings [148] in which most respondents, from a wider age range, reported willingness to consent to sharing pertinent genetic information with their relatives. Participants' responses to attitudinal questions about sharing with relatives indicated many had made a positive evaluation of the potential outcome of these sharing activities when forming their attitudes. However, differences were found. Unlike another study that did not find any gender differences among YAs [190], we found that gender,

genetic education, and familiarity with a STEMM field were all significant variables for the sharing preferences of YAs. Having a university-level genetics education or being female was related to higher desire to share one's results with parents and siblings and to want to know relatives' results. It was found that females were significantly more willing to share their WGS results with parents and siblings. Additionally, female participants who had undertaken a university-level genetic course had significantly higher intentions to share their results with parents and siblings than females who had not studied genetics to this level, see Figure 3.6. The relationship between the female gender-group and a desire to share with siblings illustrated female participants' greater willingness to share their WGS results with siblings when compared to their male counterparts. The relationship between participants educated to a bachelor's degree level and desire to share WGS results with siblings was equivalent in strength to that of the female gender group, see Figures 3.7a and 3.7c. In many cases, women were found to be more likely to communicate genetic test results than men [65]. Women conceived themselves as having a moral obligation to inform family members they believed needed to know of potential risk of breast and ovarian cancer in Hallowell and colleagues' 2003 study [133]. In 2017, Bowen and colleagues' study [40] found being female was associated with higher communication frequency about family melanoma risk compared to being male. Three quarters reported their family's 'health informant' was female; 'health informant' was defined as the a person who kept track of family information about health.[40]

In 2005, Gaff and colleagues [98] reported that male participants in their study found advice given to them about which family members to inform helpful. Intervention by clinical staff appeared crucial in making some men aware of their responsibility to inform other family members; this contrasted with female participants who felt such discussions unnecessary because they were already aware of their responsibility to inform other family members [98]. Societal expectations about who should be caring suggest that gender may play a role in the meanings and duties constructed around sharing genetic risk information, and as testing becomes more commonplace, women may become disproportionately burdened with this kind of information [65].

In 2017, Lumish and colleagues [189] found younger age, lower education and lower genetic knowledge among the significant factors associated with genetic testing-specific distress.

In 2008, Barsevick and colleagues found a potential barrier to sharing genetic test results with parents was the sophisticated nature of the information and the highly technical terms involved, particularly for older parents, who may have had little access to scientific information [25]. Bowen and colleagues [40] found a lower frequency of communication

about melanoma risk with family for those with lower level of education when compared to frequency for those with high educational level.

This YAs study found attitudes towards sharing WGS results with relatives are likely to be more positive for YAs who had higher levels of genetic and genomic knowledge, female precipitants, and more so for females with higher levels of genetics knowledge obtained through subject-specific formal education. These groups want to share more, making them obvious conduits for communicating genomic information within families.

Appropriate education needs to be provided when implementing genomic testing to address the challenges identified [348]. To this end, information and advice designed for managing WGS results would benefit from including knowledge and attitudinal assessments that address sharing considerations.

Genomic service providers could support assessment of YAs' prior genetic education and sharing attitudes as part of personalised educational provision so the outcomes of WGS may be appreciated by the individual and others. These results raise further questions about what YAs think of sharing their results with health professionals, researchers, employers and others. Also, what genetic knowledge would be best to acquire for the purpose of undertaking elective screening using technologies such as WGS? The question of how best to support individuals to appropriately share results from genomic sequencing is also highlighted. Larger scale research is needed to further examine sharing attitudes indicated here. Additional research will be required to inform design and provision of educational materials that account for individuals' pre-existing genetic knowledge and attitudes towards sharing.

TPB was utilised in survey question design so that attitudes, subjective norms and perceived behavioural control elements of behavioural intention could be examined. Several new findings about YAs's attitudes and behavioural intentions towards undertaking WGS and sharing results were discovered. Intentions were related to gender, genetic courses undertaken, generic educational attainment level, genetic knowledge and STEMM status. These variables are likely to affect how WGS results are shared in families, affecting, for instance, relevant health promoting information may be withheld initially, not shared or miscommunicated.

3.4.8 Limitations

Limitations to this study include its narrow demographic make-up, made up mainly of university population, sample size and lack of ethnicity data. Only the largest differences were detectable with this sample size. The sample was drawn from populations based in educational establishments. They were expected to have higher educational attainment and

likely greater subject-specific knowledge compared to the general public. Further research is required to generalise these results to a wider population of YAs.

3.5 Summary

By utilising TPB constructs of attitudes, behavioural and subjective norms to frame the YAs survey questions, several novel insights regarding WGS were found that related to TPB constructs and External Factors. Gender, educational levels, genetic knowledge and STEMM background were External Factors that featured highly as independent variables that may affect YAs' behavioural intentions for undertaking WGS and sharing results.

In terms of intention to consult with a health professional prior to undergoing WGS, participants who had undertaken a genetics course at school reported lower intention to consult than either those who had not studied genetics at all or those who had studied genetics at university-level. With regards to willingness to receive WGS reports, those having a STEMM background or more knowledge of genetics were more willing to receive results reports. In contrast to previous findings, no direct link was found for interest in a report to manage genetic results and individuals' generic educational attainment level. Due to this apparent lack of interest among those with less genetic knowledge to having a results report, offering engaging educational material prior to provision of results is critical. In addition, if results are presented to YAs in an accessible format, tailored to their developing knowledge and designed with information sharing in mind, they may be better understood, acted upon and more effectively shared.

In terms of desire to share information with parents and siblings, females are more likely to want to share than males. This is mirrored in the fact that females are more likely to want to know results of relatives. These sharing tendencies are also exhibited by participants who had undertaken a genetics course at university. Additionally, female participants who had studied university-level genetics had higher intentions to share their results with parents and siblings than the females who had not. Those from a STEMM background were more likely to want to share results with their parents than non-STEMM participants. As generic educational level increased, concerns about the effect WGS results might have on insurance policies decreased, contrary to increased concerns among those who had specifically studied genetics. Subjective norms and attitudes were most relevant to WGS sharing preferences. Perceived behavioural controls were specifically indicated by concerns participants had regarding possible effects WGS results might have on future insurance policies. Responses to buying WGS using online services and insurance concerns are likely to reflect a perceived threat to YAs when considering sharing WGS results data with such parties. Public enthusiasm for

WGS is tempered by discrimination concerns, with great fears around information overload and breaches of privacy associated with it [62]. Overall, views contrast more by gender and genetic knowledge than by general educational levels. This is of particular interest to information provision and support before and after WGS to improve outcomes for individuals and their relatives. In order to address their preparedness to manage WGS results, it would be prudent to take account of gender differences and to assess YAs' prior genetic education and actual genetic knowledge.

There is a need to improve public and professional knowledge of genomics and personalised medicine [38] as it affects attitudes. An assessment of attitudes, social norms and perceived behavioural control as part of the process of undertaking genomic testing could better prepare individuals and report designs so that advice regarding sharing genomic information can be better presented and received. This is particularly important in relation to the increased availability of WGS services and the advancement of related WGS technologies.

Chapter 4

Interviews with YAs about Undertaking WGS and Sharing Results

4.1 Introduction

There are a small but growing number of studies that have explored the views about preferences held regarding genomic information in comparison to those that have explored such views for genetic testing. Understanding the factors most commonly associated with decisions to accept or decline WGS are required as it is virtually impossible to make a general statement about what the public thinks [19] and genomic information preferences, specific to YAs, remain unclear.

Sweeny and colleagues' 2014 systematic review of empirical work on predictors of genetic testing decisions concluded that qualitative studies using people's self-generated explanations for choosing whether or not to test were far more consistent than findings from quantitative attempts to use objective predictor variables [290], however, theoretically-driven efforts to examine testing interest across test types were sorely needed. This interview study was designed to explore details of YAs' preferences and intentions for undertaking WGS, receiving results, acting on them, and in particular, sharing genomic results with families, HCPs and others. In the interview design, constructs from the theory of planned behaviour (TPB) [159, 10, 9] were considered for undertaking WGS and acting on results. Interview questions generated responses about attitudes, perceived behavioural controls (PBC) and subject norms (SN). As such, it was expected that TPB would be relevant to the results. The fit between the results of the YAs studies and theoretical models, including TPB, will be presented in Chapter 5.

4.2 Methods

4.2.1 Aim and Objectives

This study aimed to explore what influenced YAs' considerations and behavioural intentions for undertaking WGS, receiving results information and sharing them with others.

To achieve this aim, the literature reviewed for Chapter 2 informed the design of semi-structured interviews that gathered numerical data regarding preferences for WGS and qualitative data related to undertaking WGS. Outputs included a novel representation of WGS as a process map, themes derived from qualitative analysis and descriptive findings from the informal hypotheses tested.

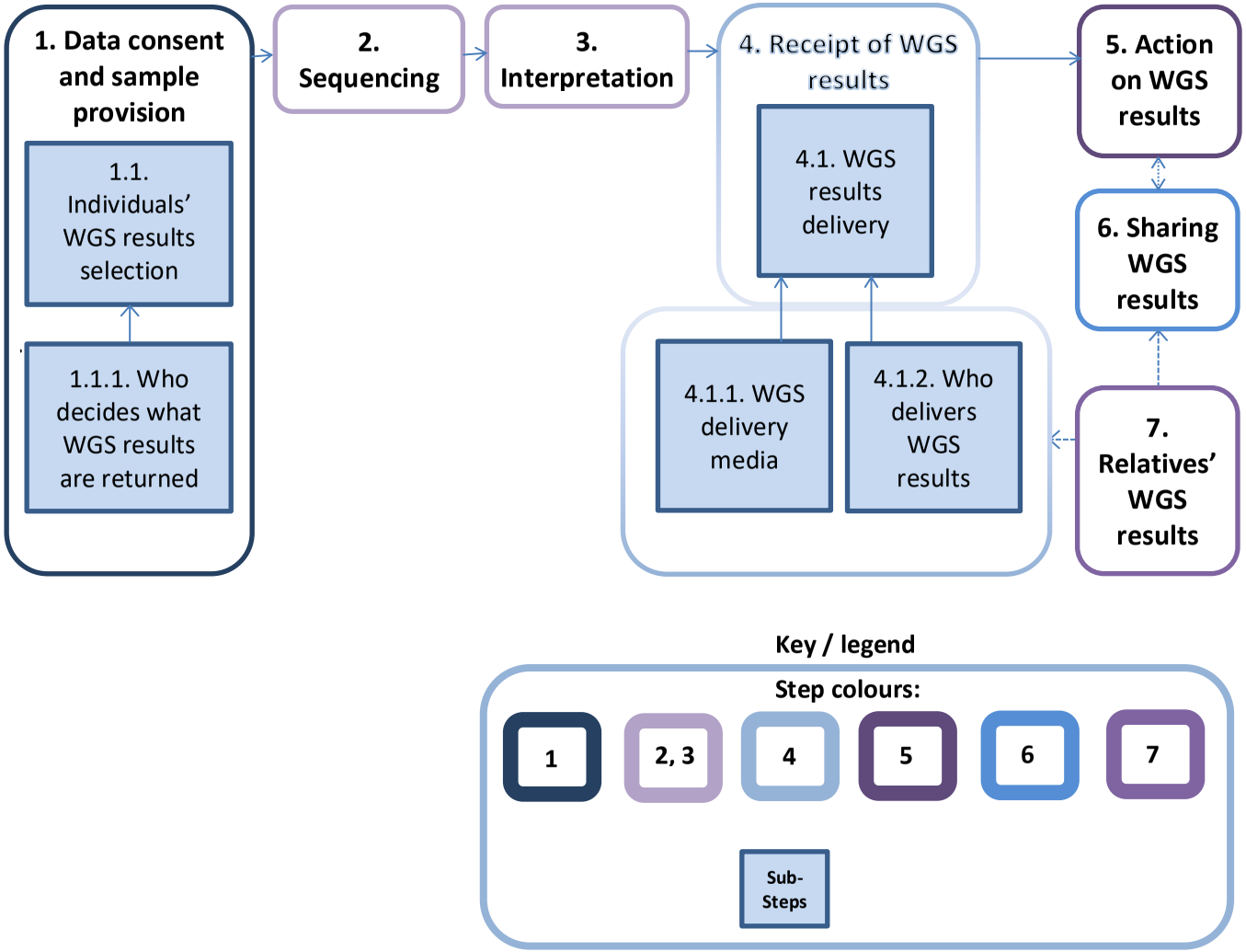
4.2.2 Designing the Proposed WGS Pathway

The first step in creating the interview schedule was to design the pathway around which interview questions could be organised. An automated genomic pipeline to produce routine diagnosis from WGS was described in the UK's Chief Medical Officer's (CMO) 2016 Annual Report [70]. The CMO's pipeline reflects the UK's determination to harness genomic medicine at scale. By considering how each step would translate to individual users of WGS services, the CMO's pipeline has been redesigned to conceive a Proposed WGS Pathway, as illustrated in Figure 4.1. This adaptation reflects events individuals may encounter rather than organisational activities.

To correspond with the CMO's step for gaining consent and a sample from the patient to perform sequencing, the Proposed WGS Pathway's first step is 'data consent and sample provision' which primarily includes selecting WGS results, including views about who should decide what results are returned (i.e. made available to the user) when undertaking WGS. The CMO's steps of 'sequencing' and 'interpretation' are included in the Proposed WGS Pathway as steps 2 and 3. Those two steps reflect a period of waiting from when individuals provide their DNA sample or data till receipt of their results at step 4. Step 4 is where 'WGS results media' and 'who delivers WGS results' are included as part of WGS results delivery. Because access to HCPs can vary dependent on what WGS service is used, the 'clinical' step from the CMO's pipeline is replaced with 'action on WGS results'. In this way, 'receipt of results' allows for HCP's clinical input and 'action on WGS results' represents further activities with results including sharing, with HCPs, researchers, family and others. An optional step related to both 'sharing WGS results' and 'receipt of results' is 'relatives' WGS results'. This option accounts for individuals' receipt of potentially important shared familial genomic information from relatives' WGS results. This form of sharing may

lead one to take further WGS-related actions. The Proposed WGS Pathway design provided a sequential basis to organise interview questions.

Fig. 4.1 **Proposed WGS Pathway**



4.2.3 Hypotheses

The following informal hypotheses were guided by literature reviewed.

1. Participants' selections will vary and may even contradict each other dependent on how WGS result options are categorised and presented to them.

2. Participants will want genomic results information because of an interest in pre-existing family health conditions for their health planning intentions.

3. Participants will want to collect their personal information because of an interest in self-discovery and for life planning intentions beyond health purposes.

4. Sharing preferences will be related to participants' perceptions of seriousness of their results information, interests of family members and HCPs, and their desire to contribute to genomic and health research.

5. Considerations influential to participants' preferences will emerge at later points in the Proposed WGS Pathway.

Hypothesis 1 supposed that participants would make selections that may vary and be contradictory when different presentations of categories for possible results were used. This was tested in the first two exercises, where participants selected types of results they would want to know about in two different formats, first by clinical-utility categories, then by diagnostic names for health conditions.

Materials have been presented to research participants under many different conditions with varying results [30, 351, 18, 352, 353].

Genomics and health are commonly considered together and therefore current research into human genetics and genomics are often contextualised in terms of health-related concerns [15, 214, 210, 134]. Current genomic trends and markets place value on the promise of health benefits derived from genomics [17, 128].

This interview engaged with the context of health psychology. It asked individuals to consider their health-related choices as well as exploring other contexts such as ancestry and other topical items. Relatives were recognised as obvious co-participants in genetic studies as well as being sources of knowledge about genetic conditions in a family.

Literature addresses relatives as joint participants in studies and in terms of the communication of genetics within families. In previous studies with children, 95% of participants [172] indicated that they would want to know if there was a disease running in their family. Adoptees are a group who may benefit from learning about hereditary conditions and ancestry

otherwise inaccessible to them [23]. This study concerned people entering adulthood, who could more easily act independently on their own views to find out.

Hypothesis 2 and Hypothesis 3 addressed what reasons participants give for wanting to know results. This is addressed when offering selection of results in the two formats as well as in other elements of the interview.

Hypothesis 2 supposes that interest in results will be related to family health conditions and health-related planning. Participants' interest in results will be to inform their plan for a healthy future. This hypothesis is guided by findings from an earlier study where the information wanted by adolescents who have cancers and their parents was about immediate and future health needs [89]. Early adopters of genomic services cited two main reasons to undergo genomic sequencing; they were to gain health-related information and to learn about individual genetic risk factors [200]. Serious conditions, especially those where there is potential for prevention, are expected to generate more interest for receiving results [148]. Some of the interest in receiving results, such as those identified in earlier studies, are expected to stem from pre-existing conditions in the family. In a study of adults about to undertake WGS [87], 98% (299/306) were motivated to receive results because of a personal or family history, with many noting cancer, heart disease or other condition. One third of participants expressed a general desire to know health information, many believing all knowledge is positive [87].

Due to the nature of genomic information, and how it has been portrayed in the media, it is possible that participants will recognise a value to themselves beyond managing a health condition. This is tested with hypothesis 3 that considers reasons beyond health for wanting WGS results.

Questions about sharing results address Hypothesis 4's expectation that participants will want to share with their relatives, health professionals and researchers involved in WGS. Relatives and HCPs are recognised parties who genetic service users need to consider in terms of who to share results with [190].

A third of participants undertaking WGS as part of a large clinical study wanted their results specifically so they could inform their relatives [87].

Just under 11% of 122 participants who were DTC genetic testing customers chose to share their results with their doctor, genetic counsellor or other similarly trained medical professional and fewer than 25% of participants were able to answer the questions about interpreting results put to them correctly [202]. The sharing preferences of our participants is expected to be moderated by their belief that their medical professional can help.

Study participants who have experienced cancer want to support research by donating their data [89]

Those with experience of cancer desired results reports to address long-term outcomes and to offer suggestions, indicating that they had thought about this [89], however it cannot be expected that all aspects of results and sharing will be considered by those who are otherwise well, such as the YA participants. Hypothesis 5 concerns this aspect and will attempt to identify what YAs omit to address when considering undertaking WGS.

4.2.4 Materials

Following a literature review of attitudes and preferences for genomic and genetic testing and results, the structured interview schedule was developed. See interview schedule in Appendix C. It contained structured elements that produced quantitative data and interview questions that required a more qualitative approach.

The interviews explored YA participants' views of undertaking a WGS, with a focus on preferences for receiving, managing and sharing resulting genomic information. A priori hypotheses related to literature in the field were incorporated into the interview schedule design. Resulting variables and themes were explored to identify what influences participants. Influences were categorised and indicated at points along the Proposed WGS Pathway where they were relevant to behavioural intentions.

Interviews were undertaken with YAs who had previously completed the WGS survey and had agreed to being re-contacted for an interview study. TPB has the potential to incorporate and categorise a wide range of factors underlying genetic behaviours, including communication, and there is evidence for TPB's ability to predict health related behaviours [296].

Interview Schedule

An interview schedule was designed to address considerations as related to attitudes, perceived behavioural controls and subjective norms along the Proposed WGS pathway's steps, as illustrated in Figure 4.1 and test the specific hypotheses described above. The YAs were given a copy of the interview schedule, see Appendix C.1 at the start of their interview. The schedule was broken down into the following sections:

- Introductory quotation
- Select WGS results by clinical categories: What disease types would you want to know about?
  - Why this choice?

  - What affects your desire to know more or less, sooner or later?
  - Who should decide what should be reported in WGS results?

- Select WGS results by disease or condition name: Would you want results about these conditions?
  - Why this choice?
  - What affects your desire to know more or less, sooner or later?
  - Who should decide what should be reported in WGS results?

- Who would you want to receive your WGS results from?
- How would you want to receive your WGS results?
- What resources and tools would be important to help you (a list of suggestions presented to participants)?
- Action on WGS results: What would you want to use your WGS results for?
- Who would you want to share your WGS analysis results with?
- What would you describe as your support needs?
- (When) would you want to know about WGS results undertaken by another family member?
- What would you consider an ideal process for undertaking WGS?
- What would you see as your personal challenges if you had WGS done?

Some elements were designed to collect quantitative data, whereas others also gathered thematic data, relaying participants' specific preferences and tested the five hypotheses. Exploration of attitudes, perceived behavioural controls and subjective norms were integrated into the interviewer's questions and prompts.

To set the scene for the interview, a quote from a 2014 paper by Kathryn Philips and colleagues was printed on the front page it reads:

"If an entire genome is sequenced, almost everyone tested will have multiple findings—each with its own measure of validity, utility, and possible interventions and outcomes. These results are likely to include incidental findings that are not related to the reason for testing [. . .] For example, a person being sequenced to determine susceptibility for breast cancer may be discovered to have Huntington's disease, which has no cure. There has been much

controversy about how to address incidental findings and what findings should be reported, including debates about whether experts should determine which incidental findings will be reported to all patients or whether patients should decide what specific results they want to know." [244].

The YAs were asked to imagine they had had their WGS undertaken. Equipped with a copy of the structured interview schedule proforma and a pen, they were asked to complete tick-box selections and discuss their responses as they proceeded through the interview schedule-proforma. The questions were designed to encourage elaboration on preferences and reasons for them.

The YAs indicated the types of WGS results they were interested in by selecting those they would or would not want and those they were unsure about from listed items. First, they were presented with a list of clinically orientated categories for types of results that could be derived from genomic sequencing [30, 18]. They were then shown a list of named diseases and conditions for potential WGS results adapted from a focus group study [352]. Ancestry was added to the bottom of this list and was explained as additional information that may be gained from WGS, should they be interested. As with the previous list, they indicated items they would want to receive results about, those they would not, and ones where they were unsure. The YAs were asked who should decide what WGS results are returned to them. This was the key question posed by the quote they had read at the start of the interview schedule [244]. They then indicated on tick-box tables who they would want to receive their results from and how they would like to receive them. They indicated who they would want to share their results with. Further questions related directly to their interest in knowing WGS results belonging to their relatives, resources and support they would like to have when undertaking WGS, what actions they would consider taking with their results. Near the end of the interview, they were asked what they thought their ideal process for undertaking WGS and their greatest challenges might be if they undertook it. Throughout the interview, the YA participants were prompted to give reasons for their selections and elaborate on their responses.

4.2.5 Participants

The eleven participating YAs were students or non-academic staff from the University of Nottingham. They were all between 18 and 25 years of age when recruited, between July and October 2016. They were a subset of the 112 18-25 year-old participants who had previously completed the Whole Genome Sequencing (WGS) survey reported in Chapter 3. None had previously undertaken WGS themselves. Ethical approval was provided by the School of

Computer Science at the University of Nottingham. Consent forms were completed by all interviewees.

4.2.6 Data analysis

The interview (audio) files were transcribed by PB. This first pass was an opportunity to be reacquainted with the participants' responses in their own voices.

Descriptive analysis

The tick-box selections made in the interview offer quantitative data about participants' choices.

Theme-based content analysis

Researchers cannot free themselves of their theoretical and epistemological commitments, and data are not coded in an epistemological vacuum [42]. In the 1950's, Bernard Berelson developed content analysis as a quantitative approach to increase consistent coding for a range of textual media content across a group of coders [29, 330, 249]. Berelson influenced Robert Philip Weber to account for context in content analysis as well as Matthew B. Miles and A. Michael Huberman's methods for qualitative data analysis [249, 216, 330]. These works further influenced approaches described as theme based content analysis (TBCA), qualitative content analysis, among others [223, 249].

Themes may be derived through manifest content, i.e. respondents' actual words form concepts, or through latent content, whereby concepts are derived from interpretation and judgement of participants' responses [249]. Contextual meaning is facilitated through theme development from the textual data [249].

Weber states that having "identified the substantive questions to be investigated, relevant theories, previous research, and the texts to be classified" researchers may proceed to code data [330]. Themes were generated using a theoretical approach to coding data [42] in so far as the reviewed literature influenced research questions and interview schedule design, including key constructs from TPB. Interview questions address attitudes, SNs and PBCs, however TPB was not the focus of data analysis. Instead thematic analysis aimed to capture participants' views about undertaking WGS [42]. A detailed thematic analysis of the data focused on TPB would be expected to generate elements supported by TPB constructs [42]. This will be explored in Chapter 5.

Because genomic literature influenced research questions, participants' responses in this study, and groupings and classifications applied to their responses were meaningful to said research questions and background literature.

Essentially, a matrix is the intersection of two lists, presented as rows and columns in a tabular format; it collects and arranges data for easy viewing in one place, permitting detailed analysis [215]. Classification matrices were used to present raw data themes: ideas in the raw text (transcripts of participants responses) that stood out as noteworthy. Synonymous ideas or concepts from raw data themes were clustered into intermediate order themes (with associated frequencies), and appropriately abstracted terms were applied. Higher order themes encompassed the intermediate themes [215]. Terms used for lower order themes could remain if abstraction was not deemed necessary. This is an iterative process that incorporates checking and questioning of themes as they are generated [249, 223]. Matrices were revised as required during this process of selecting and condensing [215]. Researcher judgement and flexibility is needed as themes are not necessarily measured in frequency, but rather on whether they capture something important about the data in relation to the research question, and represent some meaning or level of patterned response within the data set [42].

Neale and Nichols described TBCA methods [223] in a step-by-step process, incorporating elements of both quantitative and qualitative analysis. TBCA offers a structured and consistent way to analyse and present detailed information about YAs' considerations (Sharples, S. 2021, pers. comm., January 6th).

The TBCA procedure used has five fundamental elements:

1. Data collection: Verbal responses from interviews were audio recorded and transcribed along with participants' selections from tick-box table options.

2. Data collation: once collected, the data from individual's responses were grouped according to the questions addressed. Responses to the tick-box tables were also collated. The data is tagged with participant numbers so the origin is traceable. This takes form as a document with headings and sub-headings for topics addressed in interviews with responses organised under them. This data collation document was easy to view and analyse.

3. Theme definition and classification: The author, Pepita Barnard (PB) had an initial discussion about the research aim, interview questions and hypotheses with a second researcher Lorena Macnaughtan (LM). These two researchers classified the data into raw data themes independently. Data chunks (words, phrases, sentences), for the responses to questions, were manually identified and coded. The process of coding the

participants' comments to thematically analyse the data was undertaken manually by PB, whereas LM used qualitative analysis software NVivo to do this. The two sets of raw data themes were compared and discussed by the two raters. Adjustments were made in response to discrepancies and raw data themes were agreed by consensus between the two in line with the study's aim, hypotheses and literature reviewed. The number of data chunks from participants' responses falling into each raw data theme was indicated in the relevant matrix. From this point, the sub-headed collation document was used to populate matrices, one for each topic addressed, using rows in the far left column to present raw data chunks from individuals' responses, and subsequent columns to summarise the data chunks into raw data themes. These matrices were retained throughout the iterative process of theme definition and allocation.

4. Higher order theme selection: Following this, more general themes (intermediate order and higher order themes) were defined independently by PB and LM. A set of codes requiring a higher level of inference than a raw data theme can be described as a higher order theme and a number of levels of themes may be assigned with increasing levels of grouping and inference. During this step, the two researchers' themes were compared for agreement and final themes were designated with the number of data chunks falling into each higher order theme indicated.

5. Presentation of classification matrix: Matrices of the raw data, raw data themes, intermediate order themes, higher order themes and frequencies (number of data chunks per theme) provided a clear representation of the data so that commonality and popularity of themes relevant to genomic results information receipt and sharing could be accounted for.

Cohen's kappa was calculated during the higher order theme selection step of theme-based content analysis. Cohen's kappa is a statistical coefficient that represents the degree of accuracy and reliability in a statistical classification. Kappa tests the null hypothesis that the extent of agreement is the same as random (kappa = 0). Cohen's kappa takes account of the hypothetical probability of chance agreement, providing a measure of the level of agreement, over and above chance, made between two raters categorising nominal data, in this case themes, into mutually exclusive categories [176, 179].

4.3 Results

Eleven YAs undertook structured interviews. Four of the seven who identified as male had a Science, Technology, Engineering, Maths or Medicine (STEMM) background as did one of the four who identified as female.

4.3.1 Interview Questions and Hypotheses

Table 4.1 indicates which hypotheses the interview questions addressed, and corresponding results' sections.

4.3.2 Theme-based content analysis

Transcribed data were processed and analysed according to the methods described above. In the final comparison, there were two themes identified by PB that LM did not agree with (1. perceived utility and 2. autonomy v dependency) which were retained. There was disagreement about the theme 'actionability', PB against and LM in favour. It was subsequently eliminated as it appeared to be contained within perceived utility. The data were recoded accordingly. Additionally, there were three themes that both PB and LM agreed to eliminate as items could be better categorised under other themes already identified and agreed by both (1. care plans, 2. right to know and 3. access health and social care). The final list, agreed by PB and LM contained 236 themes, grouped into fewer themes.

Each theme (raw, intermediate or higher-level theme) counts as one case for Cohen kappa calculation. R statistical package was used to calculate Cohen's kappa and test the null hypothesis that the extent of agreement is same as random (kappa=0). Interrater reliability was measured with 98.7603% level agreement found. Cohen's kappa Index Value was calculated with a result of k = 0.6604, p-value = 0.0228, z = 1.9999, 95% CI = 0.2786 to 1.0423. According to guidelines, this is a substantial level of agreement above that expected from chance alone [179].

Results from tick-box selections, the classification matrices containing a detailed breakdown of the themes that were identified from the data, and the raw data from which they were sourced, are presented in Appendix D. Detailed thematic analysis, including cross-checking classification matrices with the developing hierarchical list of themes was undertaken using hard copies of the two documents by PM. LM printed outputs from NVivo software for interrater comparisons to be made. The matrices are organised to match the order in which questions were asked of YAs, which was generally aligned to the Proposed WGS Pathway, Figure 4.1. This allows easy location of the raw data and the topics being addressed by

Interview Question(s)	Hypothesis(es)	Results Section(s)
Select WGS results: •by clinical categories •by diseases and clinical condition.	H1	Select WGS results by clinical categories. Select WGS results by diseases and clinical condition.
With reference to above selections: Why this choice? What affects your desire to know more or less, sooner or later? What would you want to use your WGS results for?	H2, H3	Select WGS results by clinical categories. Select WGS results by diseases and clinical condition. Action on WGS results
Who would you want to share your WGS analysis results with?	H4	Who would you want to share your WGS analysis results with?
Who would you want to receive your WGS results from? How would you want to receive your WGS results? Who would you want to share your WGS analysis results with? What resources and tools would be important to help you? What would you describe as your support needs?	H5	Who would you want to receive your WGS results from? How would you want to receive your WGS results? Who would you want to share your WGS analysis results with? What resources, tools and support needs would be important to help you?

Table 4.1 **Interview Questions, Hypotheses and Results Sections**

theme. See Appendix D.4 for a table that contains the hierarchical list of themes from the theme-based content analysis and the classification matrices from which the hierarchy of themes emerged in Appendix D.5.

4.3.3 Select WGS results by clinical categories

When clinical-utility categories for genomic results were offered, all eleven interviewees wanted some form of WGS results returned to them. See Appendix D.1 for table of selections regarding clinically-categorised results wanted.

All eleven wanted to receive results related to treatable conditions that were found to be present or were preventable in the future. All eleven also wanted pharmacogenetics results. Most who did not indicate they wanted certain results actually indicated they were unsure; number of refusals are indicated here. Ten wanted results related to the reason they would have undergone WGS for. Ten participants wanted results pertaining to their carrier status with one refusing such information. Nine wanted results about traits that meant they had a high predisposition for certain complex diseases. Nine wanted results about variants of uncertain significance with one declining such results. Eight wanted to receive results pertaining to untreatable diseases that were present. The same eight wanted results about diseases expected in the future that were unpreventable and untreatable with one refusing results of this nature.

The overriding higher order themes for responses about the offer of WGS results by clinically recognised categories were: perceived utility followed by autonomy and dependency. The intermediate order themes were: health planning, WGS results related to uncertain future conditions, self-discovery, concerns about lack of actions for WGS results, consumerism issues, and WGS results affecting the next generation. The thematic classification matrix for this interview question can be found in Appendix D.5, the classification matrices for TBCA.

4.3.4 Select WGS results by diseases and clinical conditions

When offered a list of 27 diseases and conditions to consider for receipt of results with the additional option of also getting results about ancestry, most ticked the box for all results, whereas three YAs indicated diseases or clinical conditions they were not sure of or uncertain about receiving results for, see Appendix D.2. The thematic classification matrices for responses to these interview questions can be found at the beginning of Appendix D.5, the classification matrices for TBCA.

Two of the three participants, who had been selective when offered the list of clinical categories, chose to receive all results from the list of diseases and conditions including items that would be included in clinical categories they had previously indicated objection to or had been unsure about.

The overriding higher order themes were: perceived utility as well as autonomy and dependency. The intermediate themes were: health planning, life planning, treatability, open

future for self, open future for family planning purposes, self-discovery, ancestry, medical terminology.

Only a few participants were particular about which diseases they wanted results for and gave reasons for their choices. One participant (P5M) prioritised conditions known to the family on one hand i.e. Alzheimer's disease, cancer, ADHD and diabetes but felt uncertain about receiving results for conditions he was not familiar with e.g. Factor V Friedreich ataxia, fibromyalgia, macular degeneration and sickle cell on the other. A second (P97F) did not want results for addiction because it would be dependent on your personal circumstances, nor for Huntingdon's disease as there is no treatment. She was torn about receiving information about Alzheimer's conditions despite there being no cure as her family may benefit from knowing so they could be prepared, she also expressed uncertainty for allergies as one could outgrow those, ADHD because it was behavioural and learning difficulties as she believed one might live better not knowing about having such a difficulty. The third selective participant (P74F) described not wanting results that would scare her, especially conditions that related to family planning, those far into their future or where treatment would not be available or appropriate, she declined wanting results about Alzheimer's disease, ADHD and Down's syndrome. All bar one participant wanted results related to ancestry genealogy, one said it was a waste of money but chose to tick 'yes' because if available he considered all results to be his. Many of the rejected WGS results were for diseases or conditions directly related to neurological function, i.e. Huntingdon's disease, Alzheimer's disease, ADHD, learning difficulties and Down's syndrome.

4.3.5 Who should decide what should be reported in WGS results?

The YAs were asked who they thought should decide what results are returned to them. The two higher order themes were: autonomy vs. dependency and ownership. The intermediate order themes were: expert decision maker, patient choice and consumerism. YAs preferred an expert to decide about whether or not to report results because of potentially negative impact, uncertain results and for state-subsidised or free WGS. However, the preference for consumers or patients to decide which results were returned was voiced more often. The thematic classification matrix for this interview question can be found in Appendix D.5, the classification matrices for TBCA.

4.3.6 Who would you want to receive your WGS results from?

When indicating on a pick list, from whom they would be happy to receive their results, ten were happy if a doctor returned their WGS results and nine were happy for a genetic

counsellor to do so. Only two were happy for a relative to give them their results. When asked to elaborate on their choices for who they would or wouldn't want to receive their results from. The higher order themes were: complexity of information, intimacy, perceived ownership and impact on self. The intermediate themes were: professionals to help with complex information, professionals to maintain confidentiality and privacy to manage impact of results, close network (relative, partner or professional), negative impact on family dynamics and constraints getting genomic information needs met. Four elaborated on reasons for who they would not want their results from. They described lack of relatives' knowledge, wanting to know about themselves before relatives did and general negativity if results were from relatives. Two were uncertain about the role or abilities of genetic counsellors to meet their information needs and one expressed concern that 'doctors like to jump into treatment' (P74F). The responses to this interview question can be seen in Appendix D.3, with reasons given in Appendix D.5, the classification matrices for TBCA.

4.3.7 How would you want to receive your WGS results?

Participants were asked to indicate from a selection what media they would prefer to receive their results in. All eleven selected an in-person meeting. Two wanted a letter to follow an in-person meeting and one preferred a letter first, then an in-person meeting. Four indicated they would be happy to receive results by email or via a secure website. Only three wanted results by letter with another three being unsure about this medium. Phone calls and video calls were least popular though they were mentioned by one as an alternative to waiting for an in-person appointment. All selected 'in-person' making that the most popular medium to receive WGS results in. In descending order, a results report of WGS findings was desired by: email, secure website, then letter, phone and video-call. Most were happy to receive their WGS results report before, during, after, or sometimes instead of meeting professionals for results. This was conditional on whether results contained bad news or were psychologically distressing for any other reason. Participants recognised that results report format would influence their understanding. All desired a step by step guide to a results report. Most wanted bar charts or graphs to compare their risk to others. The majority wanted their results report to use simple language though two expressed some reservations that this would oversimplify the information. Computer graphics were least desired; participants expressed a belief they would be difficult to interpret. The thematic classification matrix for this interview question can be found under the heading Media preferences for results in Appendix D.5, the classification matrices for TBCA.

4.3.8 What resources, tools and support would be important to help you?

Participants were asked whether the following tools and resources would be important to them when undertaking WGS. Some participants expressed views about all resources listed where others commented on a subset. The list included: more knowledge about genomics, simple language in reports, a step-by-step guide as part of the results report, bar charts and graphs, computer graphics, genetic counselling and an explanation from a qualified health care professional (HCP), see the heading: Tools and Resources to Support WGS Process, in Appendix D.5.

The YAs recognised they would have support needs for the WGS process. The intermediate themes for support needs were: education to understand results, explanation of results after WGS, professional support to deal with results as well as professional information and support needs prior to undertaking WGS. All participants desired an explanation of their results from a qualified HCP. Of the seven who expressed an opinion about genetic counselling, all said they would want it; two specifically wanted genetic counselling after WGS, not before. All expressed a desire to have a step-by-step guide within the report, however one described reservations that it could make the report too long. Eight described wanting more knowledge about genomics, though only one described wanting such knowledge before undertaking WGS. All indicated they would want some genetic knowledge. Of the eight who commented on "simple language in the results report", six said this would be a good idea. Two commented that they would not want simple language, with one elaborating that the report should not be "dumbed down". Seven out of eleven expressed an interest in bar charts and graphs as they could be used to compare their results to wider population. Of the four that did not want bar charts, one said that such comparisons would not be reassuring and another three said charts and graphs would be difficult to read, messy or overwhelming. Three out of the eight participants who expressed an interest in computer graphics to present results also described a need for them to be additive, simple and few. The other five, who did not want computer graphics, described concerns they would be unhelpful and difficult to interpret.

4.3.9 Action on WGS results

The higher order themes regarding actions considered for WGS results were perceived utility, belonging, autonomy vs dependency and information ownership. The intermediate themes were life planning, relatives' shared interest, sharing widely, family tree and withholding results from doctor. From a list of potential actions, the YAs indicated, in descending

order, what they would do with their WGS results: contribute to their health record (11), support self-care e.g. lifestyle, activities, medication, treatment (9), re-sequence or additional future analysis (9), ancestry family tree (5), support family planning decisions(2), share and compare results with family members (2) and considerations around withholding information from relatives or doctors(1). The thematic classification matrix for this interview question can be found under the heading Actions on WGS in Appendix D.5.

4.3.10 Who would you want to share your WGS analysis results with?

All interviewees expressed a desire to share WGS results with someone. In descending order, the parties indicated for sharing WGS results with were genetic counsellor, clinical geneticist and other HCPs, followed by researchers. Family members were next. Mother was selected by most. A few considered sharing with support groups or online forums. None wanted to share with employers and only one thought they would want to share with insurance companies. One participant added 'partner' to the list. HCPs were favoured by more YAs to share their results with than other parties. Least popular were insurer and employer. Figure 4.2 presents YAs' preferences for who they would want to share their WGS results with. The thematic classification matrix for this interview question can be found under the heading Reasons for choices re. sharing WGS results in Appendix D.5. Noteworthy details are presented below including raw and intermediate themes.

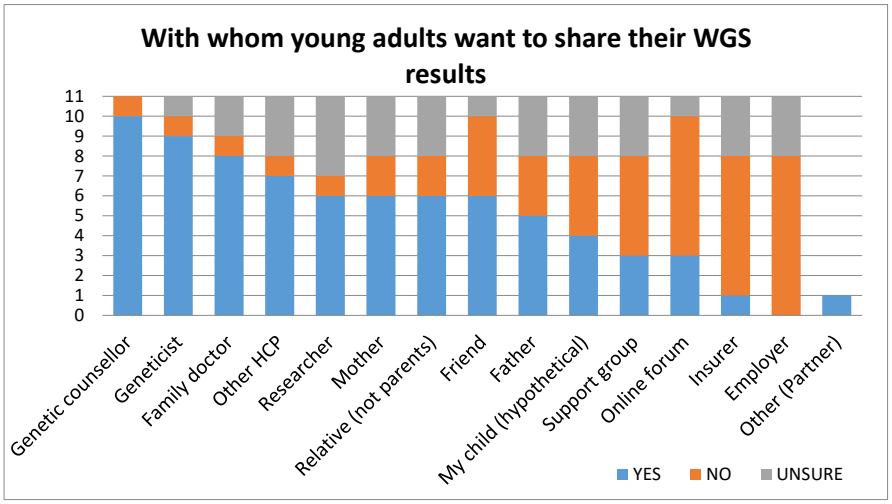


Fig. 4.2 **YAs' preference for who to share their WGS results with**

The following themes were identified from reasons given for wanting to share WGS results information. The three higher order themes were: autonomy vs dependency, perceived

utility and trust. The intermediate theme of belonging included: close network of relatives and partners, a wider community of interest including friends, health professionals, and researchers, for whom the act of sharing would be for shared interests. Health planning, as an intermediate theme, included: accessing professional health, social care and support services, health declarations to access care and support, employer's occupational health requirements and insurance policies. Three participants considered situations where they might withhold results information from health care professionals or from their health records.

Six selected 'yes' to sharing WGS results with researchers on the tick-box table. One non-STEM participant selecting 'no' to sharing with researchers; of the four who selected 'unsure', three were STEMM participants. The two raw data themes about sharing their WGS results with researchers were trust and the type of research. Eight actually described a willingness to share with researchers though the same four who had ticked 'unsure' said their willingness to share their WGS results with researchers depended on the type of research involved. Further exploration identified that four out of the five STEM and two out of the six non-STEM participants clearly stated they would have conditions about researchers or would want to approve specific research studies that their data might be sought for.

Six participants expressed a willingness to share with family members. Though reservations existed pertaining to uncomfortable or negative interactions, sharing with family was considered in terms of accessing their support, protecting and preparing them for impact of serious results, informing them of shared risks and comparing results with them. Despite knowing it would cause an argument, one participant described how she would still tell her father about undertaking WGS and resulting information. Relevance of results information was a raw data theme for sharing with employers and for insurance the raw data themes were costs and trust.

4.3.11 (When) would you want to know about WGS results, if undertaken by another family member?

When asked about their desire to know their relatives' WGS results, the higher order themes were relative's consent for sharing, impact on family included psychological impact of bad news and practical support their relative may need, impact on oneself included shared risk and intimacy related to shared interest and discovery. The thematic classification matrix for this interview question can be found under the heading Desire for relatives' WGS results in Appendix D.5.

4.3.12 Ideal Process

Nine participants described what they thought would be an ideal WGS process. The thematic classification matrix for this interview question can be found under the heading Ideal process in Appendix D.5. The themes were normalisation of genomics, professional interventions post-WGS, then pre-WGS, perceived utility, accessing family support, consent and security of sensitive personal data. Significant points raised from their descriptions are presented here. One participant (P98M) described wanting his family to join him to undertake WGS together and have process described beforehand to them all, staying together as much as possible throughout the process as well as the desire for the process to be more normal, so it would be treated like a blood test and that more people would undertake WGS so results are compared to averages that are less skewed by people who are likely to get certain diseases dominating the sample.

One (P20F) said she would want to take parents with her, have access to a counsellor and a report to keep for future reference. One (P74F) said she felt the process so deserved privacy that she would only want her mother to go with her and not share with others until she is ready. One participant (P97F) described a desire for a specialist to provide information beforehand and contacts to use if wanted upon receipt of WGS results. Two participants (P99M, P5M) specifically described wanting to meet with HCPs before and after WGS, with one (P5M) indicating a desire for several such meetings beforehand and a protracted period of time to weigh up his decision whether to consent to undertake or not whereas the other (P99M) indicating a few sessions after to talk about results. One (P14M) described wanting results returned with a text if all was normal like some blood test results are, so his mind could be put at rest quickly, or an appointment arranged with the doctor if needed. One (P30M) wanted a results table that informed him of his risk for diseases and actions he could take. One (P2M) described the desire for children to be educated at school about the process so everyone would receive a basic level of awareness as a way to normalise genomics in society.

4.3.13 Greatest challenge

When asked what their greatest challenge would be if undertaking WGS, the following raw data themes were indicated from eight participants' descriptions. The potential impact their results may have on them, the impact of sharing with family, concerns regarding their sensitive personal data security, shortage of medical professionals to help with WGS results, difficulty taking health promoting actions, where to go for WGS, concerns about societal burden and burden on public services and insurance to finance WGS services. The thematic

classification matrix for this interview question can be found under the heading Greatest Personal Challenge in Appendix D.5.

4.3.14 Summary of Findings

The following section contains two tables to summarise the key findings from the interviews. Table 4.2 refers findings to headings from the interview schedule headings corresponding with sub-headings in this results section. Table 4.3 summarises the study's findings that correspond with the informal hypotheses posed. For each hypothesis, the results sections corresponding to the interview schedule items examined are listed.

4.4 Discussion

Interview sections have been combined to support coherent discussion of related topics. Ideal processes and greatest challenges are discussed first. These refer to the entire Proposed WGS Pathway. Participants' WGS results selections and considered actions for results follow Hypothesis 1 is addressed by analysis of the selections. Reasons for selections and desired actions with results address the points pertinent to Hypotheses 2 and 3. Who should decide what should be reported in WGS results was the question posed by the opening quote for the interview and is discussed next. The next group of questions addressed are Who to receive results from, how to receive them and what resources, tools and support needs would be important for WGS results. Hypothesis 5 is addressed with this group of questions. Hypothesis 4 and 5 are discussed as part of Sharing WGS results. The final interview question discussed relates to the desire to know relatives' WGS results.

A rich categorised dataset of participants' considerations was created from theme-based content analysis of the transcriptions, including frequency tables and thematic matrices. The five hypotheses were proposed to gain insight about what influenced intentions. Their discussion is framed within the wider findings and in the context of the Proposed WGS Pathway.

4.4.1 Ideal processes and greatest challenges

Ideal processes and greatest challenges were considerations identified by participants, following prompts at the end of the interviews, as relevant to the whole process. The two topics are related, the presence of one may reflect the absence of its counterpart, i.e. where an ideal process is not available, a challenge is likely to be raised, and vice-versa, a lack of challenges likely reflects ideal processes in place. There were several requirements perceived

Interview Schedule Items		Findings
4.3.3	Select WGS results by clinical categories	Most interest in treatable and preventable conditions, pharmacogenetics and carrier status.
4.3.4	Select WGS results by diseases and clinical conditions	Most wanted results about all diseases and conditions presented, and ancestry. Results for neurological conditions were least desired.
4.3.5	Who should decide what should be reported in WGS results?	Experts for potentially negative impact of results, uncertain results, for free or state-subsidised WGS. Overall prefered for consumers or patients to decide.
4.3.6	Who would you want to receive your WGS results from?	Most wanted a HCP to deliver their results. 2 wanted family. Consulting a HCP if results may contain bad news.
4.3.7	How would you want to receive your WGS results?	Face to face, secure websites and e-mails, rather than letters.
4.3.8	What resources, tools and support would be important to help you?	All 11 wanted a step-by-step guide to report. 8 wanted more knowledge about genomics, only one described wanting this before undertaking WGS. 7 wanted bar charts / graphs, compare risk to others.
4.3.9	Action on WGS results	All 11 would contribute results to health record. 9 wanted to act to support self-care e.g. lifestyle, activities, medication, treatment as well as re-sequence or get additional future analysis.
4.3.10	Who would you want to share your WGS analysis results with?	10 selected HCPs, some specified which. 6 selected researchers; some wanted to know more about research before approving the use of their data. 6 selected a family member. 3 considered withholding from HCPs or health record. Concerns about employers and insurance.
4.3.11	(When) would you want to know about WGS, if undertaken by another family member?	Important for relatives to have consented to sharing their WGS information with them. They envisioned impact on the family, including psychological impact and practical support for relative if bad news. Impact on self from shared risk and intimacy related to shared interest and discovery.
4.3.12	Ideal process	Sense of utility, access to a HCP, to consent to data use, assurances to satisfy privacy and security concerns. Some wanted family support: Mum or whole family. Some wanted WGS normalised, made commonplace, representative comparative data, children educated.
4.3.13	Greatest challenge	Selecting WGS provider, understanding insurance and commercial implications, sensitive personal data. Health system capacity, i.e. access to qualified HCPs, undertaking healthy actions, impact on self and family.

Table 4.2 **Findings by Interview Schedule Items**

	Informal Hypotheses with Results Sections	Findings
4.3.3 4.3.4	H1. Participants' selections will vary and may even contradict each other dependent on how WGS result options are categorised and presented to them.	Discrepancies in selections made. Participants expressed specific concerns when presented with the list of diseases and conditions, especially ones related to neurological problems.
4.3.3 4.3.4 4.3.9	H2. Participants will want genomic results information because of an interest in pre-existing family health conditions for their health planning intentions.	Health records, self, care, medication / treatment, WGS results related to uncertain future conditions, WGS results affecting the next generation, treatability, open future for self, family planning purposes, concerns about lack of actions for WGS results and medical terminology, further / re-analysis.
4.3.3 4.3.4 4.3.9	H3. Participants will want to collect their personal information because of an interest in self-discovery and for life planning intentions beyond health reasons.	Lifestyle activities, consumerism issues, ancestry and further / re-analysis.
4.3.10	H4. Sharing preferences will be related to participants' perceptions of seriousness of their results information, interests of family members and HCPS, and their desire to contribute to genomic and health research.	10 wanted to share with HCPs; 6 with a relative. 3 said they may actively withhold information from HCPs or health record. Desire to share with researchers was trust-dependent. Concerns about employers and insurance policies.
4.3.6 4.3.7 4.3.8 4.3.10	H5. Considerations influential to participants' preferences will emerge at later points in the Proposed WGS Pathway.	Despite importance of family health history in selecting results to receive, family dynamics and relationship issues were not described then. Communication skills and trust concerns were considered even later in interviews. Participants mainly did not want greater genetic knowledge prior to WGS, but rather after.

Table 4.3 **Findings by Informal Hypotheses**

by participants as facilitating an ideal process and a number of challenges identified. Ideally, participants desired normalisation of the WGS process. Several participants wanted access to qualified professionals, this included desire for support to manage their information needs and concerns, the impact of result and their privacy and data security concerns throughout the process. Greatest challenges identified related to selecting a WGS provider, undertaking health-promoting actions, understanding insurance and commercial implications and concerns about the capacity of the health system and access to health professionals.

A genomic carrier screening study, [276] characterised those who desire all possible resulting information because of the sense of control this knowledge adds to their family planning decisions as 'certain individuals'. This contrasted with 'hesitant individuals' who actively choose to not know something because they believe it as easier than coping with the stress of knowing, especially when that information is perceived as uncertain, undesirable, or scary. Concerns about receiving results may be attributable to such personality characterisations.

Those participants who desired an extended WGS consent process, over a protracted period, with several meetings with health professionals for information, were comparable to 'hesitant individuals' [276]. Participants who desired support from professionals and family throughout the decision making process thus an evaluation of desire to share is included from the start of the WGS process.

From a study of University students, it has been pointed out [316] that some of those who believed they would not be worried about results could become worried when they actually receive them.

In a study of genomic test consumers [68] it was found that those who had fewer concerns about the process and fewer insurance concerns before undertaking DTC genomic testing were more likely to share their results with their doctor or other health care provider yet their actual resulting genomic risk estimates and family medical history did not influence their sharing behaviour with their health professionals. The YA participants did not consider insurance and employment concerns until these were mentioned to them later in interviews when asked about who they would want to share their results with. It is possible that these participants, and other YAs living in the UK considering undertaking analysis of WGS independently, would not be fully considerate of these parties until they had undertaken WGS if they were not mentioned to them. Managing concerns about undertaking, receiving and sharing WGS results is clearly important so individuals may engage with genomic services in a manner conducive to their health and well-being. The YA participants' concerns regarding capacity of the health system, including access to appropriate professionals to support people are on a long list of ethical, legal and societal issues [229] that have arisen because DTC testing originates outside of established traditional clinical genetics practices. Also of concern were misleading advertising, scientific validity and utility of tests, secondary use and privacy of consumers' data, non-consensual uses of testing and regulatory problems [229]. The ethical issues raised by YA participants in this thesis' study and from previous research may yet grow as the scope of available genomic services expands in absence of support services for WGS service users and regulatory frameworks to provide for and protect them and their relatives.

Efforts that could be implemented to maintain autonomy and increase utility obtained from DTC tests include: clear communication prior to testing to prevent false misconceptions on the potentials and risks so expectations are better managed, tailoring disclosure of results, matching customers' needs with technical support from test providers, scaling down ambiguity, demonstrating competing risks rather than absolute risks, offering reward systems to incentivise behavioural change as well as education in schools and for the public [54]. These same points are applicable to other WGS services, including third-party interpretation

tools. The challenge for individuals in selecting a WGS provider will be in making an overall assessment of how well their requirements will be met along their journey on the Proposed WGS Pathway, see Fig 4.1.

4.4.2 Select WGS results and action on WGS results

This section combines how selections were made when participants were offered possible WGS results in two different ways with the actions they intended to take with their results. Hypothesis 1, addressed what selections were made under different conditions. Their reasons for selections and intended actions addressed Hypotheses 2 and 3.

Participants' selection of the type of results they would prefer to have and subsequent intentions to act did differentiate by the way selections were offered, see tables in Appendices D.1 and D.2. Evidence found to support Hypothesis 1, that participants' selections would vary and may even contradict each other dependent on how WGS result options were categorised and presented to them, included discrepancies in preferences for WGS results dependent on whether selecting from a list of clinical utility terms or a list of diseases and conditions. The discrepancies observed may indicate that participants were more specific about their concerns when given a list of diseases and conditions as opposed to a list of clinical-utility categories, or it may simply indicate they were not fully cognisant of discrepancies in their selections for results for either one or both presentation of options. Contradicting statements and selections have been reported in previous studies [285]. The way ancestry was presented also appeared to affect whether it was selected or not. When offered on a list of conditions, about which results could potentially be returned if one was to undertake WGS, ten selected ancestry information. Later in the interview, when considering ancestry from a short list of discrete actions that could be taken following WGS, five indicated a desire to get their ancestry information. If the 'hesitant' or 'certain' personality characterisation is applied to receiving all genomic results including carrier information, then eight out of eleven YA participants were 'certain individuals' who wanted information about untreatable diseases, present or future as well as carrier information. The high proportion of 'certain individuals' found here is consistent with previous findings [271] that despite concerns about potential psychological impact, 74% of personal genome sequencing research participants from the HealthSeq project who gave reasons for wanting to know about unpreventable conditions.

People's desire for more information than is usually offered in most settings, including VUS, is evident from the YAs. A previous study where participants from the general population undertook genome sequencing also found that 94% of those who undertook genome sequencing wanted all of their WGS results[271]. This desire for VUS results indicated participants perceived utility or placed value in receiving results that health professionals were

likely to categorise as lacking clinical utility. Elaboration and harmonisation of the different guidelines and protocols developed to date on managing VUS and incidental findings related to untreatable conditions, late-onset conditions or those with familial implications has been advocated for [39].

Evidence to support Hypothesis 2, that participants would want genomic results information because of an interest in pre-existing family health conditions for their health planning intentions emerged from the YAs' reasons for WGS results they would want to receive when they were offered a selection of named diseases and conditions for WGS results. Participants' expressed interest in conditions known to exist in their family was the single most prominent raw data theme and was specifically relevant to considerations about health planning. There were several underpinning reasons given by the YAs for their health choices.

More than half of self-selected participants with an interest in personalised medicine [121] were motivated to participate by their hope to find out their risk for a particular condition. Healthy participants [271, 121, 315, 316, 286] were motivated by curiosity to undertake personal WGS, a desire to obtain health-related information, to know their disease risk and to improve their health. These earlier studies' findings were congruent with results presented here.

Reasons given by the YAs for their sensitivity or selectiveness regarding receiving certain results ranged from receipt of bad news about themselves, conditions with no cure, those characterised as needing behavioural management rather than medical treatment or results that would influence family planning. These findings reflect those of an earlier study of DTC consumer responses to genomic testing, where differences were related to individual disease perceptions [35], those participants were more sensitive to receiving results for conditions that are characterised as more serious and entailing lower levels of perceived control.

The decision to learn everything is not necessarily an informed one as the ability to opt out of additional results relies on recognising that the option exists and having confidence that declining is a reasonable course of action [258], as such, deciding to learn about one potential finding but not another requires greater understanding of the scope and magnitude of potential returnable results.

In descending order, the reasons given by university student participants [316] for refraining from DTC genomic testing were receiving worrying results, lack of validity, utility, privacy concerns, cost and scepticism about genetic testing. The university student participants' concern about receiving worrying results was not related to whether their fields of study were science and technology or humanities orientated [316]. Medical student participants' [114] main reason for undertaking DTC genetic testing was to be made aware of genetic predisposition to disease affecting them and risk of passing onto children a predisposition to

disease, those not willing to participate in DTC testing cited lack of confidence in results first as well as worrying results as reasons. The YAs in this interview study expressed reservations about genomic results of an uncertain nature, reserving an open future and other concerns similar to those found in other studies [316, 114], despite this, the YAs were willing to receive most if not all results that could be made available to them through WGS.

The provision of information to individuals that address the utility of specific results about diseases, conditions or otherwise would offer context to both the matter being considered for investigation and terms related to utility, clinical or otherwise. This would facilitate education so informed choices about the types of results wanted could be made.

Evidence to support Hypothesis 3, that participants would want to collect their personal information because of an interest in self-discovery and for life planning intentions beyond health purposes was provided by finding most participants selected ancestry information when it was offered on a long list alongside diseases and conditions. Later in the interview, ancestry was offered again, on a short list as potential actions with WGS results. At that stage, five indicated they wanted ancestry information and raw genomic data delivered. They wanted the raw data so they may learn more from resulting information in the future by re-analysing or re-sequencing their genome.

Because several hundreds of thousands of DTC customers had purchased ancestry services, and over a third of general population participants who undertook WGS mentioned interest in ancestry as a motivator to undertake WGS [271], offering ancestry information can act as a mechanism to encourage people to seek useful health-related genomic information and broaden public interest beyond early adopters [271]. Genealogy was found to act as a motivator for DTC genome-wide testing [286].

The YA participants' desire for raw genomic data in this thesis' study is reflected elsewhere [271] where 89% of their participants wanted their raw data returned to them. Because only one participant addressed it, and none of the eleven described profiting themselves from their data, it seems most of the YA participants were unlikely to be aware of the huge commercial interest in commoditising their data by genomic service providers [177, 128].

4.4.3 Who should decide what should be reported in WGS results?

After making their WGS results selections, participants responded to the question introduced at the start of the interview: 'Who should decide what WGS results are returned?'. Although most participants wanted to act autonomously and choose for themselves what results are returned to them from WGS, they valued experts to decide on their behalf about returning uncertain or distressing results. Participants mentioned their need for genetic education most, to enable them to understand their results. However, like their desire to engage with health

professionals, more indicated they would need genetic knowledge when results were returned rather than beforehand. However, as indicated by McGrath and colleagues in 2016, DTC customers were more likely to be able to understand their test results if they had read the supplemental material that came with the testing kit or were in the middle or higher income band i.e., US$50,000 or more [202], in other words, the more informed.

The recognition of need for content-specific knowledge by this thesis' YA interviewees was also found by others results [355] where participants with greater pharmacogenetics knowledge were more receptive to accurate test results. Findings from these interviews reconfirmed Chapter 3's survey findings [24] and those of Ostergren and colleagues who studied DTC customers [237], where numeracy, genetic knowledge and education-level knowledge predicted comprehension of genomic results information.

4.4.4 Who, how, resources, tools and support needs for WGS results?

Responses to these four questions are discussed here as they relate to preparing for, receiving and perceived support needs for WGS results:

- Who would you want to receive them from?
- How would you want to receive your WGS results?
- What resources and tools would be important to help you?
- What would you describe as your support needs?

Hypothesis 5 stated that considerations influential to participants' preferences would emerge at later points in the Proposed WGS Pathway. Support for this hypothesis included participants' description of support needs they thought they might have if they were to undertake WGS. They more frequently expressed a desire to have genetic education and input from HCPs after completing WGS, rather than before.

Individuals' comprehension of their results is likely to be influenced by the parties and media used to deliver them [202]. The YA participants indicated ways in which they would accept their results; in-person being most favoured and other media also acceptable. They were far more favourable to receive their results from a doctor or genetic counsellor than from a family member, primarily influenced by their desire to receive a knowledgeable explanation of their complex information, professional input to manage the impact of receiving results. Patient participants [132] expected health professionals to interpret their results in context of their personal and family medical history and that results would be presented in an understandable manner that was not overwhelming.

The provider undertaking WGS will indicate what and how results are returned. This places a great deal of responsibility in their hands to deliver results that are understandable and support appropriate sharing for individuals. Opinion [131] suggests that laboratories could offer user guides to explain each section of a results report and signpost to further information as well as providing two versions of the genomic test report to meet the informational requirements of a range of recipients with variable health literacy and educational levels. Personal genomic services with recognised accreditation and inclusion of professional interventions may appeal to those who desire choice, support and reassurance. Consideration of media and parties returning WGS results was important to YAs and may in turn affect intentions to act on results, including sharing them with others.

4.4.5 Sharing WGS results

Participants' reasons for sharing often related to their needs for support and resources. As these are interrelated, sharing, with whom, and what for are addressed together. Hypotheses 4 is discussed in this section. Hypothesis 5 is further discussed in relation to sharing. Hypothesis 4 pertained to reasons for wanting to share WGS results and hypothesis 5 tested whether there were considerations that only emerged as part of later steps in the Proposed WGS Pathway that were actually relevant to the earlier steps.

YA participants identified a number of different parties with whom they would share their WGS results and reasons to share. Both the parties considered for sharing results with and the reasons given for sharing with them are directly influential to individuals' sharing intentions.

Evidence to support Hypothesis 4, that sharing preferences would be related to participants' perceptions of seriousness of their results information, interests of family members and HCPs, and their desire to contribute to genomic and health research, included finding that accessing health, social care and support services, supporting research and interests of relatives were dominant Intermediate order themes for participants desire to share their WGS results. Unexpectedly, more YA participants selected researchers to share their results with than family members, as seen in Figure 4.2.

Most of the YA participants were willing to share their results with health professionals, mainly for explanation of results and treatment, if needed and to add information to their health records. They expressed a desire for input from health professionals after receiving WGS results more often than wanting input before WGS, though that was also desired by a few. In one study [329], DTC consumers found their genetic test results easy to understand with help of a genetic counsellor; less than half indicated they would have been able to work through the results on their own. DTC genomic testing consumers' high intention

to share results with primary care health care professionals was moderated by what they considered to be serious and clinically actionable results [314]. Higher genetic risk predicted a greater likelihood of sharing information with one's doctor [35] and those who had results indicating high pharmacogenomic risks were significantly more likely to share these with their physicians than those with results indicating low pharmacogenomic risks [34]. Only 10.7 percent of DTC consumer participants [202] actually shared their results with a health care professional.

For DTC services, where specialist health professionals are not necessarily offered, individuals might approach their usual health provider for advice and expert knowledge [197, 33]. This may prove to be a challenge to health professionals' abilities and resources [265, 120, 127], potentially leaving individuals with unmet information or psychosocial needs [201, 314, 197].

72% of university student participants [316] were willing to contribute their genetic data to research with science, engineering and medical student participants significantly more motivated to use DTC genomic testing to be able to contribute to research than humanities students who were more motivated by learning genetic information about themselves. 67% of medical student participants [114] were willing to undertake DTC testing and have their data made available for research.

91% of research participants who undertook genome sequencing [271] were willing for their data to be used by the study's researchers for related research, and 60% for unrelated research, 60% for use by other institutions for studies related to the one they were participating in and 37% were willing to share their WGS data with the USA's National Institute of Health's managed database for international accessibility to researchers. The YA participants were primarily interested in WGS to learn about themselves and though most were willing to share with researchers, more than half wanted to be able to approve specific research studies that their data might be sought for. Dynamic consent for reuse of personal genomic data and information would be a necessary feature applied to genomic information management services for genomic service users to have the level of control desired to approve their data contribution to individual research projects. Participation in research is highlighted as an aspect of personal utility that genomics can have for users [316]. Contributing to research was found to act as a motivator for DTC genome-wide testing [286]. Contributing to research is valued by almost all participants in this YAs' study, and as individuals become more autonomous in accessing and sharing their genomic information it would benefit from further exploration.

The YAs' reasons for sharing WGS results with family members was primarily for their shared interest, to access their support, prepare them for serious results and inform them of

shared risks. Challenges associated with sharing genetic test results within families include incomplete understanding of test results or poor communication skills by the person sharing the information and emotional distance among family members [66]. A family genetic risk communication framework using TPB has been designed [335].

Genetic information impacts inter-familial relations, where an initial inclination to share genetic risk information with relatives can become problematic in reality [39]. Several barriers for those who have undertaken genetic testing to share familial genetic risk have been described, including a limited understanding of which family members to inform about what, reduced motivation due to the desire to protect relatives or self, e.g. from negative emotions, and self-efficacy, i.e., feeling unable to inform relatives as not being able to reach them or not confident about informing them correctly [74]. This led to a proposed psychosocial intervention delivered to improve knowledge regarding which at-risk relatives to inform and what information to disclose, motivation to disclose, and self-efficacy [74]. However, others have found that the communication skills intervention they provided did not affect their participants' sharing behaviour, nor their distress when sharing with family, indicating that such interventions need to be designed to address other pertinent sharing-related factors [221].

The YA participants were least willing to share their results with employers and insurers; for health declaration purposes, they described relevance of results as a condition for disclosure to employers, and privacy, distrust and premium costs as reasons not to share with insurers. The YA participants did describe willingness to share with employers and insurers if it would benefit them to do so. Following specific education about the Genetic Information Non-discrimination Act (GINA), 25 % of prospective participants in the MedSeq Project declined to participate in sequencing for fear of insurance discrimination cited as their primary reason [123, 271]. 6 out of 10 participants who provided additional details about their privacy concerns specifically cited insurance related concerns [271].

Further evidence to support Hypothesis 5, a likelihood to not have fully considered aspects of WGS prior to undertaking WGS, was indicated by participants' limited, prompted and late consideration of data security, privacy, trust and their own communication skills.

4.4.6 Desire to know relatives' WGS results

The YA participants were interested in knowing the results of their relatives, primarily to be able to support them, to be made aware of shared risks for reasons of shared interests and interest in self-discovery. Most insisted that their relatives would have to be willing to share their WGS information. The most important factor affecting an at-risk relative's desire to know genetic information was the preventability of the disease to which the information

relates and disease seriousness; even when a test indicated in a small increased risk of developing a disease, at-risk relatives may still want to be informed if there are actions possible to modify this risk of onset [148]. It is speculated [148] that this may be due to decisions being based upon attitudes towards possession of any available information about oneself per se, the familial nature of the information, or perhaps simply a difficulty in understanding quantitative genetic risk.

4.4.7 Limitations

This study enlisted eleven self-selected YA participants from a university environment. They offer a particular hypothetical perspective of potential future genomic service users that is not representative of the general public. Participants in the present study were positive about acting on their WGS results if they would benefit from doing so. As these are hypothetical responses of a few individuals, their enthusiasm cannot be generalised by virtue of their self-selection to participate in the study and expression of interest in WGS. They are likely to be more interested in undertaking WGS and more proactive with their WGS results than other prospective participants who did not accept any of the time-slots offered to them for an interview. A grounded theory approach, utilising open interviews may have produced alternative themes to those elicited from utilising a TBCA approach to analyse semi-structured interviews.

4.5 Summary

Using an interview design, this study has contributed empirical data as themes about YAs' considerations and tested hypotheses related to choices they made along the Proposed WGS Pathway. The result of tested hypotheses are summarised: When choosing what WGS results they wanted, YAs were found to vary and even contradict themselves, depending on how options for WGS results were presented to them. They wanted genomic information primarily because of an interest in health and health planning. They also wanted the information for reasons of self-discovery and life-planning beyond health purposes. Seriousness of results was an important reason for YAs to share their results. When given options for who to share with, HCPs and researchers were selected more by YAs than family members. There was evidence that YAs did not think about important considerations until later in the interview and the proposed WGS Pathway process. This studies findings provide valuable insights into YAs' thoughts regarding WGS that would benefit professions related to genomic medicine, health psychology and those who use their services.

This study used content-based thematic analysis methods in its aim to explore YAs' considerations, preferences and behavioural intentions for undertaking WGS, receiving results information and sharing them with others. As a group, YAs are likely to be exposed to and use emerging genomic services, therefore their perspectives about the process are important to understand. University-based YAs were interviewed to explore their views. Themes and frequencies from interviews were discussed in the context of undertaking WGS and sharing results. Responses to questions addressed informal hypotheses related to preferences.

There was a desire for more results information than would normally be supplied. Additionally, there were discrepancies in selection for potential WGS results dependent on whether they were offered as clinical categories or diseases and conditions. Service users may benefit from having a comprehensive range of results to choose from, presented as specific diseases and conditions alongside terms to indicate utility, clinical or otherwise for results. This would allow for discrepancies in choices made across categories to be highlighted to individuals and offer an opportunity for clarification and education.

The YA participants' interest in ancestry results indicated many had a desire for genomic information to facilitate self-discovery beyond health. Proactive health care reasons did predominate for undertaking WGS, and family health history was considered important to participants when selecting conditions to receive results about. Yet more participants favoured sharing with HCPs and researchers than with family members or other parties. HCP input to deliver results in-person was most desired; they were wanted for their expert knowledge, support and access to services, clearly indicating that there is an expectation that receiving results may be difficult to cope with alone. Reference to domain experts offers opportunities for HCPs to meet individuals' needs and support appropriate sharing with family.

Participation in research was valued but participants wanted to control when, how and by whom their genomic information is later used, however the control at this level is not traditionally an option when accessing WGS services. This tension will become increasingly apparent as genomic services and data sharing capabilities develop in this arena to support users to have greater control over their genomic data and information sharing.

Personal genetic information, by nature is derived from data one shares with relatives yet more attention needs to be given to help individuals communicate genetic risk information with them. YAs did not discuss family dynamics and relationship issues until after they had selected what test results they would want to receive. This was despite taking family health history into consideration for desiring certain results. They considered their own communication skills and trust concerns even later in the interview process. Additionally,

their desire for knowledge prior to WGS did not feature as highly as their desire to have this after WGS.

Informed by current literature, a novel characterisation for a Proposed WGS Pathway was produced, taking individual service users' perspective rather than an organisational automated pipeline as depicted in 2016's CMO's report [70].

Results from this study and significant findings from Chapter 3 will populate a proposed research framework in the next chapter. Theoretical models introduced in Chapter 2 will be appraised against the findings with YAs for the best-fit model to categorise the research findings.

Chapter 5

Theoretical Appraisal: Framework for Undertaking WGS and Sharing Results

5.1 Introduction

The survey and interview studies were designed to explore YAs' considerations for undertaking WGS, receiving and sharing WGS results information with others.

The following theoretical models HBM, PMT, TPB, TAM and UTAUT were introduced in Chapter 2. They are designed to capture determinants of intention and behaviour. They each have their own perspective, so despite overlaps, they each contain a unique group of constructs to help explain the phenomenon they are applied to. HBM, PMT and TPB are well known models used to understand health behaviours. TPB, in particular, is a generic model that has been applied to a variety of contexts. TAM and UTAUT offer technology adoption perspectives that may be applicable to the findings. This appraisal will examine the theoretical models in relation to the YAs studies' findings. This offers an opportunity to identify how best the findings fit with each of them, and in turn where there are deficits in how well the models represent the concepts from the studies' findings. Constructs from the theory of planned behaviour (TPB) [159, 10, 9], were considered in the designs for the YAs' studies, as such it was expected that the results would fit well with this theory.

5.1.1 Aim and Objectives

Aim: This theoretical study is an exploratory investigation to examine the associations between theoretical models introduced in Chapter 2 and the findings from the YAs' studies in Chapters 3 and 4 to inform the development of a framework of considerations for YAs' on the WGS Pathway.

5.2 Methodology

The empirical studies with YAs produced a combination of quantitative and qualitative data, including a WGS Pathway that offers a structure for undertaking WGS, receiving results, and acting on them, including sharing them with others.

Results from the following were applied to the theoretical models.

- From Chapter 3's quantitative survey study:
  - statistically significant variables
- From Chapter 4's qualitative interview study:
  - WGS Pathway
  - emergent themes
  - frequency tables

The theoretical models that were introduced in Chapter 2 are considered, in turn, to ascertain their potential to support a framework for the results of the previous studies with YAs:

- TPB
- TAM, TAM2 and TAM3
- UTAUT and UTAUT2
- HBM
- PMT

TPB, illustrated in Figure 2.1 was considered best suited for designing the YA studies because it was designed so that its constructs are open for antecedents to intentions and actual behaviours to be categorised under generic constructs of Attitude, Perceived Behavioural control and Subjective Norm (SN) and recognises demographics, experience and similar variables as external factors. It is generic in that it does not claim to represent a specific domain, such as health or information technology systems. TPB is the first model the studies' findings are applied to. TPB is followed by TAM and UTAUT models, that engage with information technologies as their foundations are theoretically aligned to TPB. The health-focused HBM follows the technology-focused models. Last to be appraised is PMT that considers fear appeal communications for changes to attitudes and behaviour.

To support the development of a framework of considerations, this appraisal identifies constructs from the theoretical models introduced in Chapter 2 that studies' findings map to. To be assured that findings from YA studies were accurately reflected in the models' appraisals, quantitative findings from Chapter 3 and the classification matrices from Chapter 4 were considered in relation to the theoretical models' constructs. The outcome will be a proposed research framework reflecting findings from the YA studies through the lens of the preferred theoretical models' constructs.

5.3 Results: Theoretical Models' Appraisal

This section presents appraisals of the key theoretical models, introduced in Chapter 2, against the YAs' studies findings from Chapters 3 and 4. The survey's findings are summarised in Table 3.2 on page 70. The interview study's findings are smmarised in Table 4.2 on page 100 and Table 4.3 on page 101. The themes identified from the interview transcripts begin on page 254 in Appendix D.

The studies considered TPB of value to their design because it offered a generic model where the antecedents to attitudes, perceived behavioural control and subjective norms could be explored, therefore TPB will be the first model for the findings to be appraised against. After TPB, the technology acceptance models are appraised incrementally. First TAM, followed by TAM2, TAM3, then UTAUT, and finally UTAUT2. Appraisal of the health-focused HBM follows the technology acceptance models. PMT is last to be appraised, with threat appraisal as a key concept.

Elements of the theoretical models that were introduced in Chapter 2's literature review are considered in relation to the findings from the two studies undertaken with YAs, in Chapters 3 and 4, to identify models that could act as analytical tools to frame the findings.

5.3.1 Theory of Planned Behaviour

TPB constructs of Attitude, PBC, SN and External Factors are used to organise the characteristics of significant variables from the survey study and the themes from the interview study. Artefacts and parties identified are influential at each step of the WGS Pathway, and are relevant to the themes that emerged.

The creator of TPB [159] argued for criteria to be carefully considered for addition to TPB constructs in preference of using separate measures to predict behaviour and recommends use of terms that allow for measurement of alternative behaviours [9]. TPB terms are generated from relevant characteristics of the influences and themes identified in the interviews. The

resulting themes and frequencies from the YA studies are matched to TPB model by a process where the raw, intermediate and higher order themes are examined. The themes identified from the interview data are categorised under the indicative, relevant TPB terms. The frequencies are also considered for indications of relatedness to the model's constructs.

Participants' considerations related to these artefacts and parties are examined at the various thematic levels, including reappraisal of the source raw data to classify whether participants are describing attitudes, perceptions of behavioural control, subjective norms or factors considered to be external to TPB constructs yet influential to them.

TPB and survey findings

This section describes how statistically significant results from the survey study are categorised under TPB constructs. TPB's External Factors include the demographic independent variables of gender, education, genetic knowledge, and STEMM status. Attitudes describe the evaluation that is made when participants respond to the attitudinal questions concerned with preferences for WGS. A distinction between autonomy and dependency-related attitudes and utility-related attitudes will not be made from the survey findings as the both types of attitudes may be reflected in responses. Although gathering attitudinal responses, PBCs are relevant to the responses to attitudinal questions in the survey. The survey questions ascertain views about aspects of undertaking WGS. Differences found varying relationships between the measures of knowledge, i.e. External Factors of educational levels, genetic knowledge, and STEMM status, and the participants' attitudes to aspects of WGS undertaking, indicating PBC's relevance to the attitudinal responses. The construct SN becomes relevant where other people are involved, as is the case for Attitudes towards consulting a HCP beforehand, sharing with relatives, the desire for relatives' WGS results and insurance concerns. Thus, all TPB constructs are operationalised when the survey's results are considered. The remainder of this appraisal of TPB will focus on the interview data, starting with the ideal processes and greatest challenges. Participants answered these global question at the end of their interviews. Ideal processes and greatest challenges are described first as they offer broad views that are relevant to all steps of the WGS Pathway.

Ideal processes and challenges and TPB

Using TPB constructs to categorise themes identified as important by participants in an ideal process and indicating them at each step of the WGS Pathway allows for their explicit consideration. Attitudinal factors of 'usefulness of communicating(ion)' for information and 'desire to share' were classed under the higher order theme 'perceptions of utility'; 'desire

for support' was categorised under the higher order theme 'perceptions of autonomy and dependency'. These attitudinal factors were relevant to each step of the WGS Pathway, as described by participants. It can be argued that TPB items categorised under 'utility' attitudes are also relevant to 'autonomy and dependency' attitudes and vice versa however the distinction emerged from individuals' responses to interview questions, the raw data, and are reflected in TBCA themes. Attitudes towards insurance and commercial entities, in relation to WGS, should be considered as part of useful communications involved in consent and provision of ones DNA sample. These considerations are also addressed as privacy and data security factors within PBC. One's 'ability to access' and the 'ability to choose', i.e. perceived ability to choose from options for support and information, were categorised under the PBC construct as were concerns for control over 'privacy' and 'data security' factors throughout the process. The desire for 'normalisation of WGS' process was perceived as a facilitating factor, categorised under PBC and indicated at all steps in the pathway. One's perceived 'ability to undertake health-promoting actions' is another PBC factor that can be relevant to decisions at various points in the pathway.

Who should decide which WGS results are returned?

Our participants described individual characteristics such as education and knowledge of genetics as being pertinent to their decision about what to receive because they impact understanding of results, and in turn decisions to share. These characteristics are recognised as factors external to TPB constructs that affect behavioural intentions by influencing attitudes, PBC and SN.

Participants expressed a preference to participate in deciding what WGS results are made available to them, along with a desire for expert guidance, thus reflecting a combination of TPB factors. From TBCA, attitudinal factor 'desire to plan' and 'desire to protect' could be identified. These two factors were categorised under a broader factor, 'perceptions of utility' which reflected the most frequently indicated of the higher order themes that emerged from TBCA. The 'desire for choice', 'desire for support' were identified from these findings and categorised under 'perceptions of autonomy and dependency', the second most strongly indicated of the higher order themes.

PBC factors found in the results were 'ability to choose', 'ability to understand', 'coping skills', 'perceived ownership', 'ability to access', 'data security', 'privacy', 'normalisation of WGS' and 'ability to undertake health-promoting actions' for this step of the process. Participants described expectations as members of 'society' and they value the views of 'domain experts' so these parties are included as factors in the SN construct for decisions about what results are returned.

The considerations listed below are for 'who should decide which results are returned' are relevant to sub-step 1.1.1. of Figure 4.1.

- **Attitudes related to perceptions of utility / usefulness**
  - desire to plan
  - desire to protect
- **Attitudes related to perceptions of autonomy and dependency**
  - desire for choice
  - desire for support
- **PBC**
  - ability to choose
  - ability to understand
  - coping skills
  - ownership
  - ability to access
  - data security
  - privacy
  - normalisation of WGS
  - ability to undertake health-promoting actions
- **SN**
  - domain experts
  - society

Individuals' WGS results selection and intended actions

TPB factors related to what resulting WGS information, if any, individuals may want to receive, Step 1 in Figure 4.1, included attitudinal factors 'desire to plan', 'desire to protect', 'perceptions of relevance', 'usefulness of communication', 'desire to share', 'perception of seriousness', 'perceptions of treatability', 'perceptions of certainty', 'perceptions of temporality' for distant future outcomes of specific result types and 'perceptions of value-for-money'. These were all categorised under 'perceptions of utility'. Attitudinal factors

of 'desire for choice', 'desire for support' and 'interest in self-discovery' were added and categorised under 'perceptions of autonomy and dependency'. The 'ability to choose', 'ability to understand', 'coping skills' and 'perceived ownership' were included as PBC factors. SNs identified were domain experts and society for Step 1 of the WGS Pathway.

For actions on WGS results (Step 5 in Figure 4.1) participants described the following attitudinal factors that influenced their intentions to act on WGS results. 'Desire to plan', 'desire to protect', 'perceptions of relevance', 'usefulness of communication' and 'desire to share' were categorised under 'perceptions of utility'. Under 'perceptions of autonomy and dependency', attitudinal factors, were 'desire for choice', 'desire for support' , 'interest in self-discovery', 'desire to offer support', 'perceived shared interest' and 'perceptions of rights and responsibilities' were added. From the findings, PBC factors identified were 'ability to choose', 'ability to understand', 'coping skills' 'perceived ownership', 'family dynamics and relationships' and 'communication skills'. The interests of 'relatives', 'professionals' and 'society' will influence one's intentions and these parties are SN factors.

WGS results delivery: media and parties

TPB factors identified for participants' considerations about the media in which YAs would want their results are indicated in sub-step 4.1.1. of Figure 4.1. They are similar to the consideration factors for who YAs would want to receive results from indicated in sub-step 4.1.2. of Figure 4.1. The factors for sub-step 4.1.1, addressing considerations for the media which YAs would want their results in are as follows:

- **Attitudes related to perceptions of utility**
  - desire to share
  - complexity
  - desire for privacy
  - desire to plan
  - desire to protect
  - relevance
  - usefulness of communicating(ion)
- **Attitudes related to perceptions of autonomy and dependency**
  - desire for choice
  - desire for support

- **PBC**
  - ability to choose
  - ability to understand
  - ownership
  - coping skills
  - ability to access
  - data security
  - privacy
  - normalisation of WGS
  - ability to undertake health-promoting actions
- **SN**
  - domain experts (HCP)
  - society

Step 4.1.2, for who delivers WGS results, contains the factors indicated above in sub-step 4.1.1 apart from the' desire to plan', which is not present, and two additions, as listed below.

- **PBC**
  - family dynamics and relationships
- **SN**
  - relatives

These sub-steps are almost identical except for the attitudinal factor 'desire to plan', which was indicated when participants considered 'how' to receive results but not 'who' to receive them from, the PBC factor 'family dynamics and relationships' and the SN 'relatives' which were only indicated when considering the sub-step of 'who' to receive WGS results from but not 'how' results should be delivered in terms of media or report format. Most expressed a preference for HCPs, in recognition of experts and qualifications, as 'who' they would want to deliver their results. They generally did not consider relatives when asked about 'how' they would want the results to be delivered. Relatives were only considered as a potential source of WGS results when questions caused them to consider their relatives delivering results to them or being involved in the receipt of results. Participants, on the whole did not want relatives to deliver results.

Sharing WGS results: with whom and reasons

Participants' considerations for sharing their WGS results are categorised under TPB constructs. For attitudinal factors categorised under 'perceptions of utility', we found 'desire to plan', 'desire to protect', 'perceptions of relevance', 'usefulness of the communicating(ion)', 'desire to share' 'perceptions of complexity' and 'perceptions of seriousness'. Attitudinal factors for sharing considerations categorised under 'perceptions of autonomy and dependency' were 'desire for choice' 'desire for support', 'interest in self-discovery', 'desire to offer support', 'perceived shared interests' and 'perceptions of rights and responsibilities'. PBC factors indicated were 'ability to choose', 'ability to understand', 'coping skills', 'perceived ownership', ' ability to access', 'data security', 'privacy', 'family dynamics and relationships' 'communication skills' and' trust'; all specifically indicated by participants at this step when sharing WGS results was contemplated. The desire to share was influenced by the following SNs, domain experts – HCPs, society, relatives, researchers and commercial entities which could include the WGS service provider, employers or insurers.

Desire to know relatives WGS results

Participants considerations for their desire to know WGS results of their relatives contained fewer items when compared to their considerations for sharing their own WGS results.

- **Attitudes related to perceptions of utility**
  - desire to plan
  - desire to protect
  - relevance
  - usefulness of communicating (ion)
  - desire to share
- **Attitudes related to perceptions of autonomy and dependency**
  - interest in self-discovery
  - desire to offer support
  - shared interests
  - rights and responsibilities
- **PBC**

  - ownership
  - ability to access
  - data security
  - privacy
  - normalisation of WGS
  - ability to undertake health-promoting actions
  - family dynamics and relationships

- **SN**
  - society
  - relatives

Summary of TPB's fit

TPB provides a good fit for the YAs studies' findings because it is a generic model that operationalises its constructs in relation to the specific context it is applied to. This makes it easy to apply TPB to undertaking WGS, or other subjects. For reference, the YAs' studies' findings are summarised in Tables 3.2 on page 70, 4.2 on page 100 and 4.3 on page 101. The themes identified from the interview transcripts begin on page 254 in Appendix D. These informed the analysis of TPB model and were used to analyse the models that follow. Each of the following theoretical models contain constructs that differ from TPB's. TAM models are next to be appraised to identify whether their constructs illustrate the findings more precisely.

5.3.2 Technology Acceptance Models

Due to the technological acceptance aspect of undertaking WGS, this appraisal of TAM, TAM2 and TAM3's constructs aims to identify whether they offer superior categories for the YA studies' results that relate to computer or technology acceptance and the workplace. A combination of technological use aspects and work or study organisational matters are required for the findings to be truly represented by TAM models' constructs. Employers are not assumed to be involved in the WGS Pathway, so the findings do not automatically map to TAM's technology workplace context.

Much as TPB does, TAM recognises demographic variables as 'External Factors'. Attitudes related to utility from TPB's appraisal that relate to technology acceptance or use at work may map to TAM's 'Attitude Toward Using' construct as published in Fred Davis, Jr.'s

1986 thesis [71], as illustrated in Figure 2.4a. However, this construct, 'Attitude Towards Usage', was dropped from TAM when it was revised, in 1989, to what became its more recognised form [72], illustrated in Figure 2.4b. This loss means that research findings relevant to technology acceptance use and work, categorised as utility-related attitudes in TPB, would have to be classified under 'perceived usefulness' (PU) in TAM instead [72]. As there is no equivalent in TAM, Findings characterised as PBCs in TPB that relate to technology acceptance or use at work may map to 'perceived ease of use' (PEOU) in TAM. Attitudes relevant to technology acceptance or use and the workplace, that have been sub-classified in TPB appraisal as autonomy and dependence-related may relate to either 'perceived ease of use' or 'perceived usefulness' aspects. The appraisal will distinguish where findings fit with TAM, TAM2 and TAM3.

In TAM2 [318], illustrated in Figure 2.5 utility-related attitudes relevant to computer use may be classed under one of the seven constructs that determine PU or 'Intention to Use'. The same applies to TAM3 [317], illustrated in Figure 2.6, where 'Intention to Use' is called 'Behavioural Intention'. Social influence and cognitive instrumental processes are noted by TAM3's creators as theoretical processes that explain the relationships between PU and its determinants [317]. These seven constructs align with utility-related results from the YAs' studies that are both technology and work-related.

No SN construct exists in the original nor in the revised TAM [71, 72], as it does in TPB. TAM provides no obvious alternative classifier for influential others who were classed as SNs in TPB's appraisal. SN appears as a construct in TAM2 and TAM3, determinant of PU. Where SNs from TPB's appraisal refer to technology acceptance or use and the workplace, they map to SNs in TAM2 and TAM3. The construct of 'Image' from TAM2 and TAM3 is closely related to SN as it refers to an individual's desire to maintain a favourable standing among others [194] in the work setting. The 'Job Relevance' construct may be relevant to the findings where themes refer to sharing WGS results with employers. TAM2 and TAM3's PU determinants of 'Output Quality' and 'Result Demonstrability' are likely to be relevant to some of the utility-related Attitudes from TPB appraisal. 'Voluntariness' is a construct in TAM2 and TAM3 that determines PU and directly determines 'Intention Towards Use' in TAM2 or 'Behavioural Intention' in TAM3. 'Voluntariness' is assumed in the YA WGS studies. Any exceptions will be indicated if they exist. The YAs who were studied had no 'Experience' with WGS or similar technologies, whether work-related or otherwise, therefore 'Experience', like 'Volunariness' is assumed not to be relevant and exceptions will be indicated if they exist in the findings.

TAM3's creators [317], point out a lack of empirical and theoretical basis to expect social influence and cognitive instrumental processes to play any role in forming judgments

about PEOU. Instead, they consider PEOU in terms of individuals' self-efficacy beliefs and procedural knowledge, which requires hands-on experience and execution of skills, suggesting that individuals form their perceived ease of use about a specific system by anchoring their perceptions to the different general computer beliefs and later adjusting their perceptions of ease of use based on hands-on experience with the specific system. TAM3's developers argue that processes related to social influence, i.e. compliance identification and internalisation, in the context of IT adoption and use represent how important referents present the instrumental benefits of using a system but they argue that it is unlikely an individual will form stable perceptions of ease of use based on the views of others over their own general computer beliefs and hands-on experience with the system [317]. TAM3's Anchors and Adjustment-related constructs are unlikely to be relevant to the research findings. Exceptions will be indicated if they are found to exist.

Survey findings and TAM

From the survey findings, the following are relevant to the technology related aspects of TAM but not to its work focus. To a statistically significant level, participants from STEMM fields were found to relate to greater:

- interest in purchasing WGS online,
- desire for a WGS results report and
- interest in knowing relatives' WGS results.

STEMM participants' interest in these outcomes may be relevant to acceptance and use behaviour with technology. In particular, their interest in the idea of purchasing WGS online and their desire for a results report are both, by nature likely to involve technology acceptance and use. Despite the professional demographic and relation to computer or technology use, the survey findings do not refer to workplaces.

Ideal processes and greatest challenges

In the interview study, the setting through which WGS could be undertaken was left open, so traditional and online DTC services could be considered. Participants' desire for consent, their concerns about insurance and for the security of their sensitive personal data are relevant to TAM's focus on technology acceptance and use. YAs' lack of desire to share with employers, as per Figure 4.2 means the workplace is considered problematic for sharing WGS results.

Individuals' WGS results selection and intended actions

Although differences in participants decisions about what results they selected may be relevant to how technologies are used to present options to users, they remain directly irrelevant to places of work or study.

WGS results delivery: media and parties

In the interviews, participants were asked about their preferences for how results could be returned. YAs' generally accepted using technology to receive results, however there was no discussion about this being related to work.

Sharing WGS results: with whom and reasons

The construct 'Job Relevance' in TAM2 and TAM3 highlights the point that YAs interviewed were least willing to share WGS results with their employer. They considered only sharing with employers what they were obliged to as part of occupational health declarations or similar. Their preference is not to share for fear that WGS will negatively impact them in their workplace.

Desire to know relatives' WGS results

The desire to know relatives' results is not relevant to organisational workplaces, nor directly relevant to technology use, although technology may be used to receive results from relatives.

Summary of TAM's fit

The main problem TAM models pose for the findings from the YA studies, summarised in Tables 3.2, 4.2 and 4.3, are their focus on organisational computer use. To credibly align more TAM constructs to WGS, TAM models would need to be removed from their organisational context.

Where results were relevant to technology acceptance or use were indicated. Relevance to organisations, or lack of, have been indicated.

Some of the studies' results could be framed using TAM, however, TAM's determinants do not highlight the specific issues raised by participants, In fact, TAM's categories aggregate many of the studies' findings so valuable meaning is lost.

The lack of a clear attitudinal element in the 1989 revised TAM and the additional specialised constructs in TAM2 and TAM3 are not helpful to classifying the themes and dependent variables from the YAs' studies.

TAMs' attention to computer-related traits does not relate much to considerations raised by the YAs as these are unlikely to cause them particular difficulty.

Because the revised TAM, TAM2 and TAM3 exclude attitudes and subjective norms, many of the results from the YA studies would be diluted, abstracted or potentially lost to fit into TAM2 and TAM3's categories. TAM's organisational-workplace context also does not support the studies' findings. TAM2 and TAM3 contain 'Voluntariness' and 'Experience' as moderators of 'Perceived Usefulness' of IT systems. The studies with YAs assume they would undertake WGS voluntarily, rendering 'Voluntariness' redundant unless one views it in terms of individuals' full cognisance of the detailed terms under which they have undertaken WGS. Even so, this question of volition is not work-related.

None of the participants studied had previously undertaken genetic testing, at work or elsewhere. Where individuals undertaking WGS have previously undertaken genetic testing, 'Experience' is likely to moderate behavioural intentions about undertaking WGS.

UTAUT is the next model to be appraised against the YA findings.

5.3.3 Unified Theory of Acceptance and Use of Technology model

The synthesis of many TAM-related studies has resulted in UTAUT [319], a model structurally closer to TAM's early form, mainly reliant on a simplified TRA structure for IT contexts [27, 72, 319]. TAM [72]. The addition of 'Social Influences' and 'Facilitating Conditions' constructs cause UTAUT to resemble TPB, itself an extension of TRA [27]. These two new UTAUT constructs overlap considerably with TPB's SN and PBC, respectively [27]. Although UTAUT brings together a number of useful theories, its focus, like TAM, on acceptance and use of IT systems in organisations, limits UTAUT's applicability to the studies' findings. This appraisal will highlight occasions where its constructs are useful to describe specific findings.

Survey findings and UTAUT

The technology-related findings described in TAM appraisal related to STEMM participants' interests to buy WGS online, receive a WGS results report and know their relatives' WGS results. 'Experience' is not a relevant construct because the YAs studied were not WGS users. The STEMM variable does not appear to have an appropriate construct in UTAUT. UTAUT's designers highlight age and gender because studies' results revealed patterns and interplay between them [319]. They acknowledge researchers will identify underlying influential mechanisms other than age and gender, such as computer literacy, social or cultural background and others [319]. This allows for STEMM field of study or work to be considered

as an influential variable. However, as was the case for TAM, the survey's technology-related findings do not fit with UTAUT's purpose as an organisational workplace-situated model.

Ideal processes and greatest challenges

UTAUT's organisational workplace focus makes it problematic when attempting to align the YAs' interview findings, given participants expressed their desire to keep WGS results from their employers, as per Figure 4.2.

Individuals' WGS results selection and intended actions

Differences in YAs selections for WGS results depended on how choices were presented. This may be relevant to technology acceptance and use, but not to their place of work.

WGS results delivery: media and parties

YAs considered using technology to receive WGS results, however this was not related to places of work nor study.

Sharing WGS results: with whom and reasons

YAs' desire to keep WGS results out of the reach of employers highlights UTAUT's contextual mismatch with the studies' findings.

Desire to know relatives' WGS results

Although technologies may be used to communicate relatives' results, the desire to know them is not directly related to technology use, nor to organisations, and therefore not a good fit with UTAUT.

Summary of UTAUT's fit

Like TAM models, UTAUT provides a tool for workplace managers to assess and intervene for successful acceptance and use of new systems [319]. This is not congruent with the YAs studies' findings, as summarised in Tables 3.2, 4.2 and 4.3. UTAUT does not consider consumer or health-related aspects, nor does it have a discreet construct for attitudes.

5.3.4 Unified Theory of Acceptance and Use of Technology 2

UTAUT2's focus on consumers' use of IT systems offers the potential of a closer coupling for the YAs' studies to be appraised against than UTAUT and TAM models do.

TPB and TAM are two theories contained in UTAUT and UTAUT2 appraised above. Other theories incorporated into UTAUT models include the Motivational Model, Model of Personal Computer Utilization (MPCU) and Innovation Diffusion Theory. The Motivational Model's internal and external motivators are relevant to findings as are most of MPCU's constructs. WGS raises issues around the innovation-based characteristics that the Innovation Diffusion Theory focuses on, i.e. relative advantage, complexity, compatibility, trialability and observability. The studies presented a hypothetical situation to YAs without WGS experience, however, Innovation Diffusion Theory constructs would be better applied to WGS users.

Construct changes made to UTAUT to form UTAUT2 include the removal of 'Voluntariness' and the addition of 'Hedonic Motivations', 'Price Value' and 'Habit'. UTAUT2's new 'Habit' is not expected to moderate behavioural intentions in YAs who have no experience of undertaking WGS or a similar procedure. 'Experience' in UTAUT2 is unlikely to be helpful for the same reason.

Survey findings and UTAUT2

Interest from STEMM participants towards purchasing WGS online, receiving a WGS results reports and knowing their relatives' WGS results are relevant to the consumer context of IT. However, employment or educational demographics are not represented among UTAUT2's individual difference variables. UTAUT2's designers recognise the need for future work to examine other key constructs salient to different contexts [320]. 'Experience' in UTAUT2 refers to someone's experience with the technology being evaluated and moderates the effect of Behavioural Intention on Use Behaviour. 'Experience' in UTAUT2 does not refer to individuals' relevant knowledge, occupation nor educational status. For interest in purchasing WGS online and desire for a WGS report, 'Performance Expectancy' and 'Effort Expectancy' are likely to be engaged. Additionally, 'Facilitating Conditions' may be relevant to WGS online and results reports. 'Hedonic Motivations' may be involved, however motivations were not explored in the survey study. With regards to the desire for relatives' results, there is no clear construct that determines it. It may be that 'Social Influence','Performance Expectancy', 'Effort Expectancy', 'Facilitating Conditions' and 'Hedonic Motivations' are all determinant.

Ideal processes and greatest challenges

The desire for WGS to be normalised is a 'Facilitating Conditions' to increasing acceptance and use of WGS services. 'Performance Expectancy' and 'Effort Expectancy' both play a part in concerns about lack of professionals to help with WGS results. One's decision to undertake WGS may be affected if the one fears their need for professional input with results will go unmet. UTAUT2's 'Facilitating Conditions' is the most appropriate construct for participants' desire for consent, concerns about insurance and security of their personal data. However, these themes may be better placed in constructs designed especially to recognise consumers' specific consent and data protection concerns. 'Price Value' is best suited to capture concerns raised by participants about use of public taxes to finance WGS and requests for non-useful data. Public funding of WGS must be justifiable to address these concerns.

Individuals' WGS results selection and intended actions

The way selections are presented to participants affects how options and reasons are considered. Some choices are dependent on whether clinical utility categories or conditions' names are offered which is relevant to WGS consumers. Consumers are enabled to provide consent when 'Facilitating Conditions' support them to make well-informed selections. 'Social Influence' impacts selections as participants' interest in conditions known in the family demonstrates. Interest held by several participants in ancestry information may be categorised under 'Hedonic Motivations'

WGS results delivery: media and parties

Desire to have a step-by-step report and professionals to deliver results could be mediated remotely. These preferences may be 'Facilitating Conditions' to support WGS service users.

Sharing WGS results: with whom and reasons

Participants' considerations for who to share their WGS results with and why may be classed under UTAUT2's 'Social Influence' construct. Sharing results may be undertaken to receive further advice, information or support and therefore seen as a 'Facilitating Condition' if the 'Performance Expectancy' is sufficiently high and the 'Effort Expectancy' is sufficiently low.

Desire to know relatives WGS results

'Social Influence' is a relevant construct for desire to know a relative's WGS results given that the themes include:

- relative's consent for sharing
- impact on family including:
  - psychological impact of bad news
  - practical support their relative may need
- impact on oneself including:
  - shared risk
  - intimacy related to shared interest and discovery

The importance of relatives' consent to share their results fits with wider consent, data protection and privacy challenges the YAs described, highlighting the point that, other than 'Facilitating Conditions', UTAUT2 has no other constructs to satisfactorily categorise consent, data protection and privacy challenges.

Summary of UTAUT2's fit

UTAUT2 [320] extends the original UTAUT to the consumer's context by adding new relevant constructs.

'Hedonic Motivations' are relevant to those who may undertake WGS for fun, however the studies' findings, summarised in Tables 3.2, 4.2 and 4.3, indicate that YAs may have other reasons, such as using WGS results information for ancestry purposes, life and family planning. UTAUT2's 'Habits' were not reflected in the studies' findings. The addition of 'Price' reflects consumers' responsibility for costs as a likely factor dominating adoption and complements UTAUT's existing time and effort resource considerations [320]. Concerns related to consent, data protection and privacy appear to only fit into UTAUT2's 'Facilitating Conditions'. UTAUT and UTAUT2 would benefit from a construct better tailored to address these types of concerns. As this thesis is written, more genetic and genomic services for WGS are becoming available. Yet, for the majority of YAs considering undertaking WGS, including those studied here, 'Experience' with WGS was non-existent, making this construct irrelevant, along with 'Habit', unless experiences or habits are discovered that determine WGS acceptance and use.

5.3.5 Health Belief Model

HBM addresses personal demographic variables (gender, age, socioeconomic status, education and knowledge), individuals' personal perceptions of susceptibility, seriousness, cues to

action, and benefits and barriers regarding action towards a disease. Generally speaking, as HBM is focused on health matters, themes from the YAs studies related to perceived utility are much better represented than autonomy and dependency ones.

Survey findings and HBM

In HBM, demographic variables are classified under Modifying Factors. The survey study's significant results found relationships between demographic independent variables, i.e. gender, education, genetic knowledge and STEMM status, with dependent variables about attitudes to undertaking WGS, receiving results and sharing them with people who are influential. On the whole, the significant dependent variables, i.e. the attitudes identified from the survey, do not have a clear category within HBM's constructs; also lacking a clear place are influential people to share results with. Consulting with a HCP prior to undertaking WGS may create a Cue to Action, i.e. lead to someone undertaking data consent and sample provision, Step 1 of the WGS Pathway. Interest in purchasing WGS online does not have a place in HBM for healthy YAs who do not perceive vulnerability from a threat. However the perceived susceptibility to a threat from disease construct and severity of said disease would be important determinants for those undertaking WGS due to a specific threat. The desire for a WGS results' report may be dependent on one's perceived threat or may be viewed as a benefit of undertaking WGS. The quality of the results' report that is offered may be a Cue to action. Sharing one's WGS results with relatives and receiving relatives' results may depend on perceived susceptibility and severity under Individual Perceptions, or under Modifying Factors, the demographics and Cues to action that raise awareness of sharing. Concerns about insurance policies may be a barrier to undertaking WGS or sharing results. The remainder of this HBM appraisal will focus on the interviews' findings.

Ideal processes and greatest challenges

The theme, normalisation of WGS, indicates participants' apparent desire to move past disease threat when considering WGS is very relevant to this appraisal. Healthy YAs undertaking WGS are not necessarily responding to a specific disease, instead they perceive utility in planning for a healthier future, therefore perceived susceptibility and severity may only take effect if results returned to them indicate the threat of a disease or diseases. Knowledge, experience and personality traits, such as 'hesitant' and 'certain', as expressed by participants are categorised under HBM's Modifying Factors. The desire for professional intervention before or after WGS, or accessing family support may be classed in HBM's Cues to Action under Modifying Factors or in Perceived benefits versus barriers under Likelihood

of Action, however neither of those HBM constructs sufficiently describe the themes found. Concerns about a shortage of professionals to help with WGS results, taxation to finance WGS services and insurance policies are all potential barriers to WGS as are the potential impact results may have on oneself, the impact of sharing results with family and the difficulty taking health promoting actions are also potential barriers. Preferences around the consent process, concerns regarding data security and privacy, and deciding where best to go for WGS are themes best placed under Perceived benefits and barriers. Barriers to undertaking WGS may be overridden by Cues to action or other constructs in HBM that increase threat perception.

Individuals' WGS results selection and intended actions

Individuals' deliberations about who should decide which results are returned to them balanced autonomy against dependency and ownership. This may reflect some of the demographics, such as personality and knowledge.

The way options are offered for WGS results could affect Perceived susceptibility and severity. These HBM constructs are more relevant to individuals who have made an assessment that certain diseases are of personal concern, as indicated by the dominant raw theme 'health conditions known in the family'. For many healthy YAs considering undertaking WGS; the threats are as-yet-unknown potential illnesses. Treatability or actionability of diseases results pertain to is important to YAs considering WGS. All participants indicated that they would want to receive results about pharmacogenetics and for conditions that could be acted on; treatability may be categorised in HBM's Perceived benefits versus barriers under Likelihood for Action.

Interest in health and life planning, self-discovery, ancestry and consumerism may be broadly classed under Cues to action or even Perceived benefits and barriers but they seem too generic for HBM's disease focus. Concerns about having an open future, lack of actions for results, uncertain future conditions, and results affecting the next generation have some relation to perceptions about susceptibility and severity as well as to Perceived benefits and barriers, however the place for these themes in HBM is not clear.

WGS results delivery: media and parties

The emergent themes related to who to receive results from refer to a desire for professionals' help when receiving results. Face-to-face is most preferred media, along with a step-by-step report; these are followed by email and secure website. Themes related to WGS results' delivery are not represented in HBM's constructs.

Sharing WGS results: with whom and reasons

When the perceived threat is the information from WGS results, HBM does not easily align to wider activities, even those that are potentially health-related, such as sharing results from WGS. HBM does not provide clear categories for sharing health information with influential people such as health professionals, researchers, family members and others with a shared interest. Sharing with family members, health planning, access to professional health, social care and support services, after receiving results, health declarations for insurance or employer occupational health requirements could be classed as Cues to action, however some of these themes may also be classed as Perceived Benefits vs Barriers to sharing WGS results. It is hard to see where HBM would categorise the themes of trust and belonging in the context of sharing WGS results.

Desire to know relatives WGS results

The relative's consent for sharing, practical support needs of their relative, could be classed as Cues to action The psychosocial impact on family and self, including psychological impact of bad news and shared risk, may be classed as Perceived threats. Like trust and belonging from the previous section, it is hard to place intimacy related to shared interest and discovery under HBM constucts.

Summary of HBM's fit

HBM holds a number of relevant constructs for the findings of the YAs' studies about considering undertaking WGS, as summarised in Tables 3.2, 4.2 and 4.3. However HBM would need to be accompanied by another theory as it lacks self-efficacy, an important construct for individuals considering undertaking WGS. In addition, it does not address the non-health aspects of the studies' results.

5.3.6 Protection Motivation Theory

PMT focuses on communications in terms of fears. PMT's perceived vulnerability, perceived severity, response efficacy, and response costs are equivalent to HBM's perceived susceptibility, perceived severity, perceived benefits, and perceived barriers [287]. PMT, as illustrated in Figure 2.3 includes Self-Efficacy as a construct in the Coping Appraisal, under Evaluation of Adaptive Response, and Intrinsic and Extrinsic Rewards constructs, in the Threat Appraisal, under Evaluation of Maladaptive Response.

The constructs in the Threat Appraisal require a known fear in order to be operationalised. As mentioned previously, for many healthy YAs undertaking WGS there may not necessarily be a specific fear, in terms of a known disease or genetic trait. This renders PMT's premise of a fear and its threat appraisal proposition inapplicable to them. Self-efficacy, i.e. the strength of people's convictions in their own effectiveness is likely to affect whether they will even try to cope with given situations [21]. This construct offers a place for categorisation of themes related to personal effectiveness. To appraise PMT, one must view it as potentially relevant to a proportion of otherwise healthy YAs, e.g. those concerned about their family's health history.

Survey findings and PMT

PMT focuses on fear appeals. To appraise PMT, one must view it as potentially relevant to a proportion of otherwise healthy YAs, e.g. those concerned about their family's health history. For them the survey's significant dependent variables address attitudes related to undertaking WGS and sharing results with others which are mainly classified within the Coping Appraisal that sits under the Evaluation of Adaptive Response in PMT. The cost-benefit analysis, upon which evaluations for attitude formation and perception of behavioural controls are based [335, 16], are not specified in PMT, however they would occur in either the Threat Appraisal or the Coping Appraisal constructs of PMT, which, in turn, are influenced by Sources of Information. Those who are perceived as influential individuals and groups are not specified in PMT, however the others' influence may a Source of Information. This does not address the entirety of the role of important others, as they may not be the sources of information, but rather have a vested interest in the decision of the person considering WGS.

Insurance concerns seem best positioned in the Threat Appraisal from the Evaluation of Maladaptive Response as they may deter individuals from seeking WGS, but where exactly to place such concerns within the threat appraisal is not clear. This categorisation assumes undertaking WGS is the "adaptive" thing to do.

The desire to consult with a HCP prior to undertaking WGS and interest in receiving a WGS results report could both be classed as Sources of Information that feed into Response Efficacy and Response Costs in the the Coping Appraisal at different points on the WGS Pathway i.e. Step 1: Data consent and sample provision and Step 4: Receipt of WGS results, respectively.

The act of seeking consultation, buying WGS online, receiving results and sharing them with others is the outcome from Protection Motivation, i.e. the Coping Mode on the right-hand side of the PMT model, as illustrated in Figure 2.3, Chapter 2.

Ideal processes and greatest challenges

Participants' desire for normalisation of genomics, so that undertaking WGS was commonplace, points to PMT's immediate limitation due to its foundation as a fear appeal model, much like HBM is but more generalised to wider fears. A number of themes from ideal processes and challenges of WGS do not have a single clear place in PMT. The theme, perceived utility, aligns well with PMT's goal of assessing whether a behaviour is likely to be useful in an effort to protect oneself. Concerns about insurance policies and where to access WGS services highlight appear to represent fears that PMT could process. Concerns about public taxation to finance WGS services may reflect a Response Cost, in that lack of government funds would mean paying personally to undertake WGS or not being able to because of the cost. Participants' concerns about 'consent and security of sensitive personal data' may be either Extrinsic Rewards within the Threat Appraisal for undertaking WGS or Response Costs in the Coping Appraisal. For instance, seeking access to professionals, either pre-WGS or post-WGS, could be classed under Sources of Information, a Response Efficacy or Coping Modes. Concerns about a shortage of qualified professionals to help with WGS results could indicate a Response Cost of WGS, i.e. cost of not being able to easily get support for results, or a deficit in one's Self-Efficacy to manage the results independently. The theme, accessing family support, is also open to interpretation and may align to a number of PMT's constructs. Family support may be a Source of Information before or after WGS, access to family support may affect the Response Efficacy in the Coping Appraisal or maybe it is the Coping Mode that comes if the fear being deliberated is whether or not to seek out family after WGS. Avoiding the potential impact results may have on oneself and on one's family may be classed under Intrinsic Rewards. Not undertaking WGS, not receiving results, not acting on them or not sharing them may be intrinsically rewarding as tactics to avoid stress. The impact of results on self and on family could also be classed under Response Cost, something one has to accept as a potential cost of undertaking, receiving or sharing WGS results. Difficulty undertaking health promoting actions could contribute to one of the Threat Appraisal's constructs or be classed as a deficit in one's Self-Efficacy or a Response Cost one may not want to pay.

Individuals' WGS results selection and intended actions

Autonomy against dependency and ownership are key themes in deliberations about who should decide which results are returned, this may reflect views about Self-Efficacy. The most popular selection for WGS results was for treatable conditions and pharmacogenetics, this reflects a recognition of the utility of knowing about threats where Response Efficacy

is perceived as adequate. Themes such as treatability, health planning, life planning, self-discovery, ancestry, results affecting the next generation, results related to uncertain future conditions, not understanding medical terminology, concerns about unactionable results and conditions known in the family all affect views about results' utility and contribute to perceptions of Response Efficacy and Self-Efficacy.

The Intrinsic Rewards for not undertaking WGS and Response Costs of undertaking WGS may be reflected in concerns about having an open future for oneself and for family planning purposes. Consumerism is a theme that may be influenced by Sources of Information, advertising in particular.

WGS results delivery: media and parties

The results report is classed as a Source of Information in PMT. Preferences for results delivery, such as in-person meetings with professionals to receive help with results and the desire for a step-by-step report may be relevant to several PMT constructs, i.e. Sources of Information, Self-Efficacy, Response Efficacy and Coping Modes.

Sharing WGS results: with whom and reasons

Sharing results with influential people, such as health professionals, researchers, social care, support services, family members and others who have a shared interest, to gain protection from one's WGS results, is a Coping Mode influenced by the Threat Appraisal and the Coping Appraisal for sharing with each person or group. From the Threat Appraisal, Intrinsic and Extrinsic Rewards and the Severity and Vulnerability factors implicit in sharing the WGS results are involved. The theme health planing can be classed under Coping Appraisal, where the Response Efficacy, Self-Efficacy and Response Costs of sharing with individual parties all play a part in sharing considerations.

Sharing with insurance companies or employers are primarily seen as something to fear and therefore, resulting in a Coping Mode that reflects this.

Desire to know relatives' WGS results

In PMT, relatives' WGS results may be classed under Sources of Information. The theme pertaining to the relative's consent could be a condition of accepting Sources of Information for relatives' results.

The desire to know a relative's results so one may be able to offer practical support is a Coping mode that depends on a Threat Appraisal about the potential impact of WGS results on oneself and family, shared risk and intimacy related to shared interest and discovery,

including psychological impact of bad news. All elements of the Coping Appraisal for knowing this information, i.e. Response Efficacy, Self-Efficacy and Response Costs are represented in participants' considerations about wanting to know relatives' results.

Summary of PMT's fit

PMT, like HBM suggests healthy behaviours are more likely to be pursued if the individual perceives a personal, specific risk [32]. Given that current consumer genomic reports emphasise relative risks, one suggestion is to adapt 'perceived vulnerability' to the context of genomic risk information to shed light on how individuals integrate novel, personalised genomic information into their individual constructions of health and disease risk [32]. The findings from the YAs studies, summarised in Tables 3.2, 4.2 and 4.3, did not focus on relative risk. However, examining threat appraisals for as-yet-unknown threats that may be uncovered by undertaking WGS, including perceived vulnerability for multiple risks for healthy adults, would be useful to further understand decision making for WGS. PMT does not have explicit categories for some of the themes but it offers a way to consider communications related to WGS.

The following section summarises the models appraised in this section. Their characteristics are summarised in terms of fit between their constructs and the studies' findings.

5.3.7 Theoretical models and the proposed WGS framework

The theoretical models appraised for the studies' findings are TPB, TAM, UTAUT, HBM and PMT. When designing the YAs' studies TPB was chosen because it is an open generic model operationalised by the behaviour being examined [171]. As expected, the findings, summarised in Tables 3.2 on page 70, Table 4.2 on page 100 and Table 4.3 on page 101, mapped to TPB's constructs.

Like TPB, TAM and UTAUT models use TRA as an underlying theory. TAM, TAM2, TAM3, UTAUT and UTAT2's constructs are relevant to the technological aspects related to undertaking WGS, receiving results and sharing them. They were appraised against the YAs studies' findings for their relevance to identified technological aspects of WGS.

Although TAM was originally tested in a study of voluntary acceptance of technology by university students on a course [72], such organisational-based applications still remain far removed from the context for undertaking WGS. TAM models are only relevant when WGS is related to work or study organisations. Few of the YAs' studies' findings are strictly about technology, so to match the remaining results to TAM, TAM2 or TAM3 requires abstracting or excluding many findings altogether.

Health beliefs specific to WGS are not easily incorporated into TAM models and the model would need adaptation or additions to support health-related and other non-work findings from the YA studies.

UTAUT is another organisational tool, designed for managers [319] and because of these characteristics, UTAUT causes the YAs' findings to be abstracted beyond usefulness, with much left unaddressed due to the studies' findings' wider context.

UTAUT and UTAUT2 are both lacking constructs that specifically addresses consent, data protection and security-related challenges. Studies are already extending UTAUT2 with additional variables to deal with shortcomings. In 2019 Shaw and Sergueeva modified UTAUT2 by including 'Perceived privacy concerns' and replaced 'Price Value' with 'Perceived Value'[279]. The findings from the YAs' studies would support Shaw and Sergueeva's inclusions. The issue of consent and contracts, also known as terms and conditions of service, could be addressed under these headings. For their study of determinants for smartwatch adoption and use among Malaysian adults, Beh and colleagues [26] added what they deem to be potentially overlooked moderating threat appraisal factors of 'perceived vulnerability' and 'perceived severity' to UTAUT2 in order to better answer their research question. HBM contains perceived susceptibility and severity, notably missing from UTAUT2 [26]. HBM's constructs address health-related concerns raised by the YAs studied, however it lacks 'self-efficacy' or a similar construct. If used as an analytical tool for the findings, HBM would require support from other theories to compensate for its narrow focus.

Fear may be a factor for some considering undertaking WGS, receiving results and sharing them. PMT is useful when considering communications with individuals to manage their fears so they may be better prepared, than they would otherwise be, to make informed decisions about undertaking WGS, receiving results and sharing them. Each model contributed its own perspective to classification of the studies' results, yet the open, generic nature of TPB remains a dominant reason to adopt it as the model for the results to be categorised against. It does not assume context and therefore does not preclude results from inclusion nor is there a requirement to adapt the model to fit the findings. Formulation of a WGS framework will be discussed in the following section.

5.4 Discussion

The theoretical model appraisal offered an examination of the appropriateness of the constructs to represent the findings from the YAs' studies. The models each focus on a particular context. TPB addresses antecedents to planned behaviours and is generic with respect to the types of planned behaviours it can be applied to. TAM models and UTAUT are focused

on technology acceptance and use in organisational settings. UTAUT2 is a re-working of UTAUT for the consumer end of technology acceptance and use. HBM is a health belief focused model. PMT is a fears appeal model, designed to address communications and their impacts. Although each model offers useful constructs, most are either missing elements needed to represent the studies' findings or contain constructs that are not helpful for this purpose.

5.4.1 Proposed research WGS framework

Following the comparisons made between the studies' findings and the theoretically-based models, the constructs from TPB remain most relevant to findings. They allow for further detailed elaboration, addition and sub-categorisation to support the themes identified in the studies.

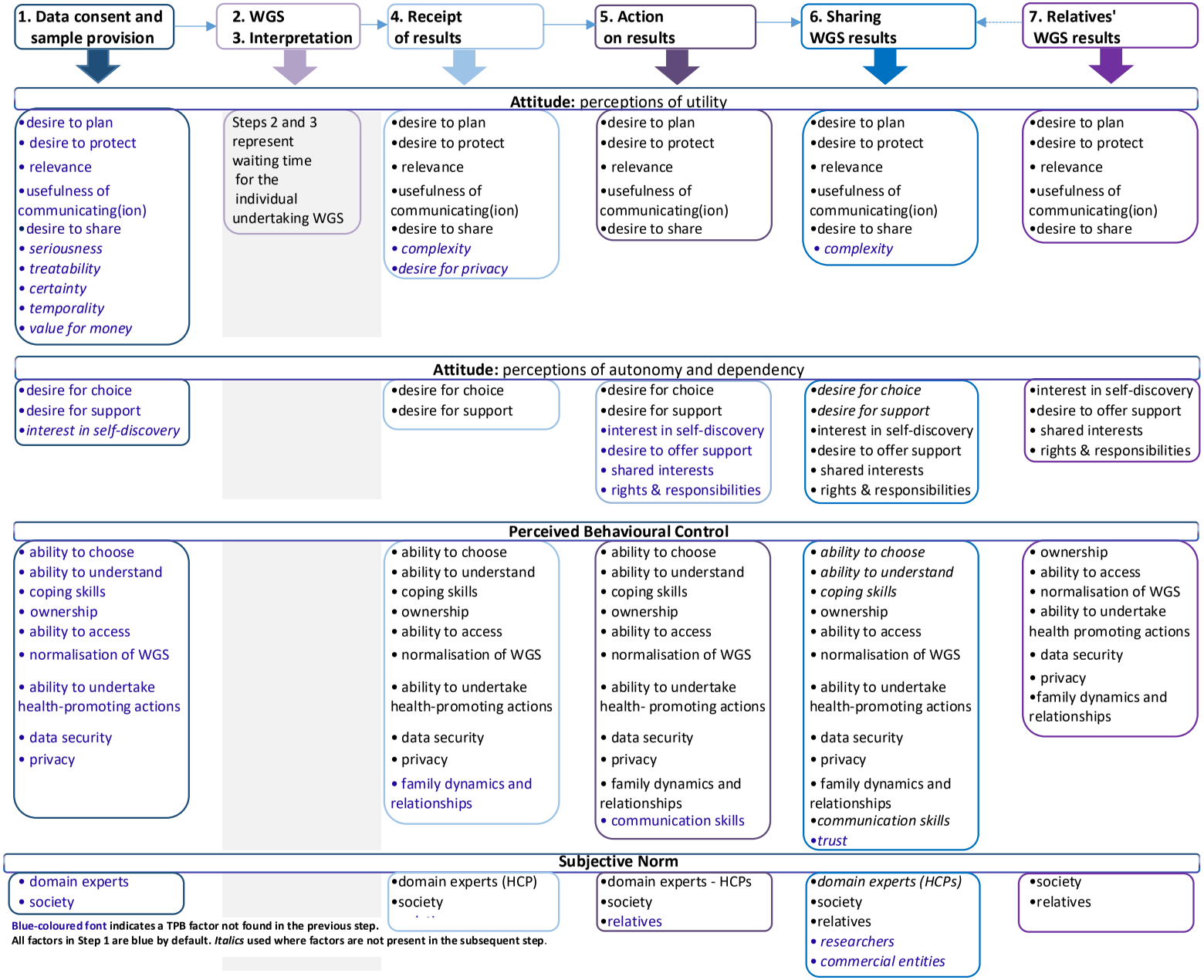
Benbasat and Barki advocated that the antecedents to individuals' behaviours can be explored using TPB constructs [27]. Due to this best-fit between its constructs and the studies findings, TPB is chosen for continued use as an analytical tool to scaffold the proposed WGS framework.

By utilising TPB-compatible constructs and factors, findings from the survey and interview studies may be captured at an appropriate level of granularity to categorise influential factors in the proposed research framework. Although health beliefs are not specified in TPB, the model is well recognised and valued in health settings as the level of detail TPB allows makes it possible to highlight health considerations where they are indicated in the findings. TPB is open to having non-health related considerations incorporated because of its expectation to have its constructs re-operationalised for each context it is applied to [349]. Like genetic tests, purchasing WGS is likely to require a substantial amount of thought and deliberation making TPB applicable [167].

The results of the quantitative survey with the YAs identified variables known as External Factors that are recognised as influential upon behavioural intentions. Influential factors identified from the themes in the classification matrices from the interview study with the YAs may be proposed in a framework utilising TPB-compatible terms and the WGS Pathway from Chapter 4 that contextualises the interview process, see Figure 4.1. These characteristic features are incorporated into the proposed WGS framework, illustrated in Figure 5.1. TPB is used as the theoretical model to frame the research findings along the WGS Pathway, as illustrated in Figure 4.1. Seven steps are proposed that an individual would take from undertaking WGS through to sharing genomic information and the optional step of receiving relatives' WGS results. Themes emergent following TBCA of YA interviewee transcripts, and frequencies gathered from their tick-box selections, are re-categorised as proposed TPB

factors that may influence YAs' behavioural intentions for undertaking WGS and sharing results. At each step, the proposed WGS framework presents newly indicated and previously recognised TPB factors considered at steps on the WGS Pathway.

Fig. 5.1 **Proposed WGS framework of considerations**



TPB factors are categorised and defined under their corresponding TPB constructs. These are listed in Appendix E.

All seven steps of the proposed WGS framework are illustrated in Figure 5.1. Step 1 is 'Data consent and sample provision'; this includes factors related to 'Who should decide which results are returned'.

For the purposes of the interview study's aim, steps 2 and 3 represent waiting time for the individual and are not explored further.

Step 4 in Figures 4.1 and 5.1 incorporates factors indicated at sub-steps 4.1.1 'WGS results delivery media' and 4.1.2 'Who delivers WGS results', respectively. These sub-steps represent preferences about either the parties or artefacts involved at that point in the process. The only differences to note between these two sub-steps were that participants gave consideration to their desire to plan when addressing their views about sub-step 4.1.1 'WGS results delivery media', however at sub-step 4.1.2 'Who delivers WGS results' they did not discuss matters related to planning. Family dynamics and relationship issues were considered by participants at this point, mainly in response to the researcher's question asking if they would want to receive their WGS results from a relative, where nine out of the eleven said they would not want this. For the optional step where YAs considered receiving relatives' results, the attitudinal factors categorised under 'perceptions of utility' were: 'desire to plan', 'desire to protect' 'perception of relevance', 'usefulness of communication' and 'desire to share'.

For receiving relatives' results the attitudinal factors categorised under autonomy and dependency' were: 'interest in self-discovery', 'desire to offer support', 'perceived shared interests' and 'perceptions of rights and responsibilities' reflected comments about relative's consent to share. In PBC terms, participants mostly deferring to relatives' right to consent as being necessary before receiving results about them, this was categorised as 'perceived ownership'. Use of insistence to convince a relative to share their results was categorised as PBC factor, 'family dynamics and relationships'. The relatives are the main party involved in this sharing activity and as such they and societal pressures are indicated in SN.

Evidence to support Hypothesis 5, from the previous chapter's interview study, is indicated in the proposed WGS framework. It can be seen in the proposed WGS framework that factors identified by participants emerge and abate along the pathway, therefore it appears that individuals do not consider some important and relevant issues until later in the WGS process which they may benefit from being made aware of earlier. A number of attitudinal factors related to characteristics of test results were indicated at Step 1 but not indicated at Step 4. They were perceptions of 'seriousness', 'treatability', 'certainty', 'temporality', and 'value for money'. Factors indicated at Step 4, when results are received, but not reflected

in factors at Step 1, when selecting results to have returned, included attitudes related to perceptions of 'complexity' of the information and 'desire for privacy', PBC of 'family dynamics and relationships' as well as SN of 'relatives'.

At Step 5, when actions are considered, consideration of 'complexity' and 'desire for privacy' were no longer apparent, instead new attitudes emerged related to 'desire to offer support', 'perceptions of shared interests' and 'perceptions of rights and responsibilities'. Additionally, 'communication skills' appears as a new PBC. At Step 6, when considering sharing results 'complexity' and 'seriousness' reappear, 'trust' emerges as a new PBC factor, and 'researchers' and 'commercial entities' appear as new SNs.

At the optional Step 7, receiving relatives' WGS results, a number of factors that were considered at Step 6 for sharing one's own WGS results were no longer apparent. These included attitudinal factors related to perceptions of 'complexity' and 'seriousness', 'desire for choice' and 'desire for support', PBC factors related to 'ability to choose', 'ability to understand', 'coping skills', 'communication skills' and 'trust'.

Concerns about receiving results, whether one's own or that of relatives may be attributable to 'hesitant' and 'certain' personality characterisations and as such are classed as factors external to TPB constructs that are influential upon them.

Research is needed to explore the WGS Pathway for further contributory parties, artefacts, activities or considerations that have not been identified in these studies. Studies that addressed similar subjects using TPB are described in the next section.

Theory of Planned Behaviour factors compared to other relevant studies

Identification of TPB factors from findings of earlier studies support the proposed WGS framework. Like others [241], these studies have found that a plurality of dimensions need to be considered and integrated into studies about receiving genetic information.

Earlier studies that addressed undertaking genetic testing and used TPB to underpin their design included Wolff and colleagues [342] who surveyed random Norwegians and Mackert and colleagues [190] who surveyed University students in the USA. Whereas both Wiens and colleagues [335] and Montgomery and colleagues [221] considered sharing genetic results with family. Their respective findings included aspects of TPB or information to inform TPB constructs and factors that influence individuals undertaking genomic or genetic testing and sharing genetic results. The proposed TPB factors or influencers derived from themes and variables resulting from Theme Based Content Analysis of interview data from the YAs were

compared to results related to TPB factors from each of these particular studies. From this comparison, TPB factors not previously identified in the earlier studies [342, 190, 335, 221] and the factors that were identified may be indicated.

TPB constructs of attitudes and SNs were significant predictors of intention to use genetic services, but no specific TPB factors were categorised under those major constructs in Mackert and colleagues' study [190], therefore it was excluded from further consideration for TPB factors. Some of the differences identified between proposed factors and those described in the remaining three studies compared may reflect this research's purpose to address individuals' considerations for undertaking WGS as well as receiving and sharing results, utilising a qualitative methodology to elicit participants' hypothesised views.

Factors classified under TPB constructs and external factors by Wiens and colleagues [335] could all be aligned to the findings from the YAs' studies.

Montgomery and colleagues' discussion on TPB constructs indicated that although attitudes are predictive of intentions to share, only PBC and SN were predictive of actual sharing, proffering a few TPB factors.

	Mapping Factors from Wolff et al. 2011 to TPB terms	
	Beliefs and factors about intention to obtain genetic testing (Wolff et al. 2011)	**TPB factor items from current study, congruent to factors from Wolff et al. (2011)**
Attitude	Disease characteristic: penetrance	Perceptions of relevance
	Disease characteristic: fatality	Perceptions of seriousness
	Uncertainty avoidance	Perceptions of certainty
	Negative consequences	Desire to protect
		Desire to plan
	Positive consequences	Desire to share
		Interest in self-discovery
	Future effects	Desire to plan
	Information	
PBC	Future effects	Ability to choose
	Negative consequences	Coping skills
	Information	Ownership
SN	Information	Relatives
	HCP suggestion	Domain experts - HCP
	Positive consequences	Researchers

Table 5.1 **TPB factors translated from Wolff et al. 2011**

Despite using TPB in their study's design, Wolff and colleagues [342] did not present attitudinal and PBC findings as discrete TPB factors. Further extrapolation was undertaken to map their findings to TPB factors, as presented in Table 5.1.

Fig. 5.2 **TPB factors from others' studies and new TPB factors identified in YA studies**

	TPB factors from previous genetic testing studies and TPB factors newly identified with young adults in this study				
	TPB factors from Wolff et al. (2011) re obtaining genetic test, and Weins et al. (2013) and Montgomery et al. (2013) re. sharing genetic test results.			**Summary of TPB factors from Wolff et al. (2011), Weins et al. (2013) and Montgomery et al. (2013)**	**TPB factors found in this study but not indicated in Wolff et al., Weins et al. and Montgomery et al.**
	Wolff et al.(2011)	Weins et al. (2013)	Montgomery et al. (2013)		
Attitude	• desire to protect • perceptions of relevance • desire to share • perceptions of certainty • perceptions of seriousness • desire to plan • interest in self-discovery	• desire to protect • perceptions of relevance • perceptions of rights and responsibilities • usefulness of communicating(ion)	• desire to share • perceptions of certainty	• desire to protect • perceptions of relevance • desire to share • perceptions of certainty • perceptions of seriousness • desire to plan • perceptions of rights and responsibilities • usefulness of communicating(ion) • interest in self-discovery	• perceptions of treatability • perceptions of temporality • perceptions of value for money • perceptions of complexity • desire for privacy • desire for choice • desire for support • desire to offer support • perceptions of shared interests
PBC	• ability to choose • ownership • coping skills	• communication skills • ability to understand • coping skills • family dynamics & relationships	• communication skills • ability to understand	• coping skills • communication skills • ability to understand • family dynamics & relationships • ability to choose • ownership	• ability to access • data security • privacy • normalisation of WGS • ability to undertake health-promoting behaviours • trust
SN	• relatives • domain experts - HCP • researchers	• relatives • domain experts - HCPs • society	• relatives	• relatives • domain experts - HCP • researchers • society	• commercial entities

Figure 5.2 shows TPB factors indicated from the three previous genetics studies with a column that brings those factors together, then in the final column are new TPB factors identified in this thesis' YAs' studies that were not identified in the earlier studies. All terms for the proposed WGS framework of considerations are in the last two columns of Figure 5.2.

The proposed WGS framework is designed to support researchers concerned with events that YAs may experience with WGS. By framing antecedents to behavioural intentions as TPB factors along a WGS Pathway, this proposed WGS framework offers a novel theoretical perspective for the YAs' studies that recognises a sequence of behavioural events. It is because of the wider perspective taken by this thesis that TPB factors identified in previous research do not sufficiently reflect the data captured in the YAs' studies.

5.5 Limitations

This theoretical appraisal was limited to certain models and their constructs. Alternative models exist, however those selected for appraisal were deemed most relevant to the research context. None of the models appraised address either user-interface or user-experience, yet these are relevant to how WGS services and products are presented online to users. In particular, participants views about selecting results to receive and the WGS results report would benefit from a category that recognises the technical importance of how information is presented to those using WGS services.

TPB, though chosen as the best-fit for the studies' findings, is not without its drawbacks. Although it recognises External Factors, i.e. individual characteristics, such as demographics, these are not distinguished for special recognition. UTAUT and UTAUT2 distinguish gender, age and experience, but not knowledge. When tested in the survey study, gender, knowledge and education were statistically significantly related to YAs' attitudes to WGS. Without any experience of undertaking WGS, those with relevant genetic knowledge or from a STEMM field had differing views from other participants. Knee-jerk reactions are not the focus of TPB because it refers to planned behaviours. This may be a drawback because of how WGS may be accessed. If a WGS service or product is bought as a gift, this may compromise considerations or limit planning due to the social pressures that may be involved in receiving such a gift.

Although further attuning and validation is required, care was taken to word endpoints in such a manner to allow implications of statements to be considered in either a positive or a negative light, as per TPB construct formulation [7]. The proposed research framework requires evaluation with persons experienced in sharing and managing sensitive information with individuals and families so proposed TPB factors may be evaluated and further items

identified by them. The proposed framework and factors may be further developed, refined and validated through testing with a prospective group of individuals undertaking WGS or similar technology or those who already have.

5.6 Summary

Following examination of TPB, TAM, TAM2, TAM3, UTAUT, UTAUT2, HBM and PMT, TPB constructs of Attitudes, PBC and SN were used, along with the WGS Pathway to structure the framework within which the findings related to behavioural intention may be categorised. The other models had some useful elements, however they were too focused on either acceptance and use in terms of organisational and consumer technology, or health and fears. The WGS Pathway and constructs from the Theory of Planned Behaviour (TPB) [159, 5, 9] were utilised to frame factors from YAs'considerations for WGS. TPB allowed a more open exploration of the findings than other models appraised and the WGS Pathway provided a chronological structure for the steps in the process. The proposed WGS framework contained the seven-step proposed WGS Pathway. TPB categorises the demographic results from the quantitative survey study as External Factors and the themes from the interviews were classified under the Attitudes, PBC and SN constructs.

TPB factors derived from emergent themes following TBCA are presented within the proposed research framework where they were indicated by participants. This dynamic perspective shows the different combinations of factors engaged in as each step was considered. Individuals appeared not to consider some important and relevant issues until later in the WGS process, which they may have benefited from being aware of earlier. In the next Chapter, evaluation and further development with informed participants, such as health domain experts experienced in sharing complex health information with WGS service users, help evaluate the framework. The aim is for the framework to recognise individuals' considerations as a process of steps over time so acceptable interventions may be designed and best placed.

Following appraisal of theoretical models, this chapter proposed a seven-step WGS framework that presented the flow of YAs' considerations as TPB factors in the context of the WGS Pathway steps. This is a novel way to breakdown WGS to account for late or transient considerations. The next chapter will present an evaluation study of the framework and its factors with domain experts working in fields related to WGS.

Chapter 6

Evaluation of proposed research framework with domain experts

6.1 Introduction

The WGS Pathway, as illustrated in Figure 4.1, was developed to frame interview questions with the YAs. From the quantitative and qualitative results of the YAs' studies, the WGS Framework was devised. It is underpinned by TPB, illustrated in Figure 2.1 and the WGS Pathway. The proposed WGS Framework, as shown in Figure 5.1, represents the YAs' considerations for genetic behavioural intentions on their WGS Pathway. It has the potential to inform design of tools to help YAs assess their readiness and prepare them for undertaking, receiving and acting on, including sharing genomic results. The proposed WGS Framework would benefit from an evaluation study with informed experts. The domain experts evaluated the WGS Pathway and the TPB factors for consideration in the proposed WGS Framework so it could be further developed.

Extreme differences in attitudes have been found to exist between members of the public and genetic health professionals, whereas non-genetic professionals' attitudes broadly align with those of the public [212]. The factors indicated from the YAs studies were compared to views of experts with experience of sharing genetic information in clinical, research, educational, consumer or other genetic health technology contexts. The domain experts were engaging with their professional knowledge and experience of working in this field with YAs. The experts were asked, in simple terms, to engage their imagination and utilise their Theory of Mind (ToM) mechanisms to produce a simulation as they perceived a YA would if considering WGS. They were expected to engage theoretical and process driven efforts to respond to the questions related to YAs' considerations.

6.2 Research Aim and Objectives

Aim: This study used surveys and interviews with domain experts to evaluate the Proposed WGS Pathway and the proposed WGS framework's factors that were generated from applying the results of the YAs' studies to TPB.

The objectives were to design a survey and interview that could be administered in-person or remotely, for domain experts to:

- Evaluate the steps in the Proposed WGS Pathway and indicate whether they need to be edited or added to.
- Rank the proposed WGS framework's factors by how likely and important each is for YAs to consider
- Identify WGS Pathway steps and WGS framework factors that were not found in the YAs' studies' results.
- Express views about the steps, factors and the wider context of the study.

6.3 Method

By revisiting the Proposed WGS Pathway, illustrated in Figure 4.1, and the individual TPB factors from the last two columns on the right-hand side of Figure 5.2, health-related professionals' prioritisations were elicited to evaluate the proposed WGS Framework, illustrated in Figure 5.1.

Evaluation was in the form of a survey and an interview designed so domain experts could choose to undertake a survey, have an interview or both. Both could be completed remotely or in-person. Introductory slides with important information about the study were included for the domain experts to familiarise themselves with.

6.3.1 Domain Experts

Because the factors considered by the YAs studied varied at the individual level, experienced practitioners (health researchers and practitioners) were recruited to undertake an evaluation. A domain expert study was chosen to elicit views from experts who had accumulated tacit knowledge about groups and individuals they had worked with. Domain experts are formally educated professionals with trained understanding of issues associated with undertaking WGS and sharing results [11]. They are familiar with knowledge in their expertise domains

and have a clear understanding of the attributes, relationships, and possible operations of the data they are being asked to evaluate [343].

Due to pressure on their time, a representative role for domain experts was opted for, rather than a researcher or liaison role [11] which would have required more time and effort. High demands on specialised experts' time was a recognised factor likely to limit their motivation to be more actively involved in the study [343]. A representative role recognised the study's demand on experts to offer their professional perspective about the WGS Pathway's steps and the TPB factors as well as channel YAs' likely views about the factors.

Experts who were familiar with the return of genetic or genomic health information, including to tested individuals' relatives or others, were recruited. They could describe their work as being relevant to one or more of the following:

- YAs
- young people
- adults
- adolescents
- families

Experts could describe themselves as:

- Health professionals involved in working with one of the groups mentioned above or similar including returning clinical results.
- Health researchers involved in research with one of the groups mentioned above or similar including returning clinical results.
- Health technology researchers or practitioners designing for one of the groups mentioned above or similar.
- Academics or educators addressing knowledge in the field
- Any of the professional roles above, i.e. health professionals, health researchers, health technology researchers, health technology practitioners, academics or educators, who are involved in returning health information (test results) that include sharing information with relatives of an individual and others.

For both the question about groups of people relevant to one's work and self-description of profession, there was an 'Other' option, in case the design failed to precisely describe options for either that are relevant to the eligibility criteria.

No financial incentives were offered for participating in the study. Experts were able to consent to be publicly identifiable for their contribution to the study. Because experts were likely to belong to hard-to-reach, specialist groups, meeting was optional to the protocol. The purpose for meeting with professionals, in-person or otherwise, was not always to undertake the study itself, but rather to facilitate a personal introduction to the study, so individuals might feel more comfortable about volunteering their consent to such a domain expert study.

6.3.2 Recruitment

Experts were recruited by a convenience method known as snowball sampling. In this instance, the term snowball sampling is used to refer to a non-probability approach to sampling design for hard-to-reach populations [149]. This was the case for genetic professionals, who remain a small population relative to the general population, geographically dispersed, highly sought after and recognised as being scarce and hard to come by [265, 43, 245, 201, 166]. These busy professionals and their networks are difficult for outsiders to engage with. Each professional engaged with was asked to recommend additional domain experts. The researcher did not directly canvas for any professionals who worked for the NHS, neither through NHS email nor on NHS property.

Experts were recruited from an international pool with the offer of in-person interviews in the UK and San Francisco Bay Area in California.

In-person meetings, interview dates and surveys were offered in the UK, as this was the study's home base, and in California's San Francisco Bay Area due to the large number of genetics professionals working there combined with capacity to offer in-person interviews there. Online surveys or remote interviews were offered to all domain experts.

Recruitment efforts consisted of many methods of convenience including:

- in-person canvassing with known individuals in relevant fields,
- LinkedIn searches, using a Premium account, to find professional domain experts,
- Twitter searches for domain experts,
- emails sent to all domain experts for whom addresses could be sourced,
- tweets posted on Twitter for those who had Twitter handles
- adverts posted on LinkedIn

- meetings offered to domain experts

One hundred and thirty-three domain experts were contacted directly using e-mail addresses. Four were sent messages on LinkedIn only. Recruitment tweets mentioning experts' Twitter handles were posted to Twitter. Due to their professional and geographical proximity to sought-after domain experts, thirty-two individuals, who were not themselves eligible to participate, were emailed to ask them to share study information with eligible experts they were in contact with. Domain experts were asked to consent to take part in a study evaluating an early-stage framework designed for YAs undertaking, receiving, acting on and sharing genomic results.

All domain experts completed a consent form prior to data collection. For those willing to be interviewed in-person, a range of dates were offered and they were asked to pick a location and time to be interviewed.

By using online methods to recruit and complete the study, it was possible for experts to undertake the study outside of the UK, independently, or with the researcher. The study recruited internationally and was directed to individuals working in the field of genetics to gather from a diverse group of domain experts. Advertisements for surveys and interviews specifically targeted experts in the San Francisco Bay Area, California, USA and England, UK.

6.3.3 Materials and Procedure

The study was made available as an online survey, using an organisational account for the University of Nottingham's approved website. It was accessible on paper, as a Word document and in pdf format. The researcher was available to undertake the surveys with the domain experts, where the opportunity for an interview allowed a discussion when domain experts could elaborate on their views.

Before completing the questionnaire, the experts were provided with a mandatory "Proposed WGS Framework Introduction" PowerPoint presentation containing a copy of the WGS Pathway 4.1, the proposed WGS Framework 5.1 containing TPB-related factors indicated at each step of the WGS Pathway, the statistically significant External Factors and definitions for all factors presented. They were given an additional PowerPoint presentation about the YAs' research studies that informed the proposed TPB factors. They could access this PowerPoint presentation if they wanted to know more about the YAs' studies. The questionnaire was completed after experts indicated they had viewed the PowerPoint presentation titled, "Proposed WGS Framework Introduction", in Appendix F.2.

If they wanted to talk or correspond to discuss the study yet complete it independently, this was facilitated. If a consent form was completed during a meeting, an audio recording was made of the dialogue or filed notes were taken of proceedings that followed consent.

Experts' submitted their responses to the survey in a manner convenient to them, with the choice to enter responses themselves or verbally respond to the researcher asking the questions. With consent, audio recordings of interactions were made using a digital voice recorder. Alternatively, field notes recorded responses when interacting with experts and were used in analysis.

Surveys and interviews were offered to the professionals using a mode of their choice, including any combination of the following: in-person (where possible), phone or internet call, by email or other text based format (e.g. using a word or pdf document), or on paper. For those who completed the survey remotely, it was provided online using Bristol Online Survey B.O.S, and as a document (Word or pdf), for the domain experts to enter their responses onto and return to researcher along with any other files they created and sent. All were advised that they could ask questions or be supported to complete the study at any point. They were shown the steps in the WGS Pathway, the proposed WGS Framework the four statistically significant External Factors from the YAs' survey study and the categorised TPB factors designed following the YAs' interview study findings. Quotes and paraphrases from experts who were audio-recorded were used to identify additional factors and provide context for their responses.

- Domain experts were asked to select their areas of interest, professional practice and the groups of people they worked with from a list. They could select all that applied to them and specify 'Other' options.
- Experts were asked to comment on the WGS Pathway
- Experts were asked to describe any changes they would suggest for the pathway.
- From the list of TPB factors, the experts were asked to indicate those they thought were likely to have been considered by a YA *before* embarking on undertaking WGS.
- From an identical list of factors, experts were asked to indicate those they thought were important for a YA to consider *before* embarking on undertaking WGS.
- Experts were asked to state any changes they wanted to see in the factors or additions they wanted to contribute.

- Experts were asked to add any further comments, if they had any. Additional comments were captured using a dedicated space on the survey as well as audio recordings and field notes where applicable.

The domain experts' survey can be found in Appendix F.1.

Audio recordings and researcher's notes were analysed to identify any additional factors raised by the experts and to gain a richer picture of YAs engaging in WGS from the experts' verbally associated responses and conversations that emerged from participation in an interview. These discussions were further opportunities to identify additions or corrections the experts wanted to make to the steps in the framework and to the list of factors presented to them in the survey.

The evaluation was structured in this way to make it possible for the WGS Pathway and the factors to be appraised separately from each other and to contextualise responses. The WGS Pathway is a key structural component of the proposed WGS Framework's design as it provides the points when individual factors were considered. The factors were evaluated so domain experts could indicate their views of how likely it was for the factors to be considered by YAs, how important each factor identified by the YAs was, whether any should be changed and if any previously unidentified factors should be added. The components evaluated in the proposed WGS Framework tested the validity of the steps providing structure to the process and the interpretation of YAs' considerations as TPB factors from the perspective of domain experts, a source of personal knowledge about the target group [11].

6.4 Data Analysis

From the survey data collected, the experts' profession, areas of interest and the groups they work with were identified. These variables were chosen to allow for elements of their expertise to be validated without having to identify them. Experts' identities were protected, except when they indicated explicitly in their consent form that they wanted to be publicly identifiable for their contribution to the study.

For the question regarding the design of the WGS Pathway, experts' suggestions were considered for inclusion. For the two questions asking experts to select factors from a list, selections were collated so that frequencies could be presented. Additional factors were either entered into the survey or identified from transcripts of the interviews. New factors, identified by domain experts, were added to the list of factors and presented in the Results section.

In accordance with Saldana's Coding Manual for Qualitative Researchers, intriguing quotes were identified from transcriptions and field notes [267]. These data were recognised

for their potential as key pieces of the evidence to support propositions, assertions, or theory, as well as serving as illustrative examples [267]. Quotes or passages deemed worthy of attention were highlighted as "codable moments" [267]. Quotes offered insight into the context of experts' views. "Codable moments" in the form of direct quotes were reported where they presented a clear expression of individuals' views. Direct quotes and paraphrased summaries are presented in the subsection, Experts' Contextualisation of YAs on a WGS Pathway, following the Survey Responses and Additional Factors subsections.

6.5 Results

6.5.1 Experts' Demographics

Seventeen experts completed the survey. Seven experts were met during the study period. Four experts consented and completed the study's survey with the researcher present. Of those four, three provided interviews, for which transcripts were created. One expert had sufficient time to complete the survey in-person but left without wishing to make further comment. Meetings served to introduce the study to three other experts who later consented and completed the survey without further involvement from the researcher.

P1 worked in the UK, whereas P2 and P3 worked in the USA. A dataset of three interviewed experts is of limited value for comparisons, geographical or otherwise. What the interview material offered was the contextualisation of the perspectives of three domain experts for whom WGS and working with people is familiar ground.

6.5.2 Survey Responses

The professionals' appropriate expertise were verifiable, however their identities remain confidential, except to acknowledge two experts who consented to be publicly identifiable as the creators of work they produced as part of the study. They were Janey Youngblom and Aneil Mallavarapu, who each completed a survey, following introductory meetings. Experts' response to the profession-related demographic questions are summarised in the Figures 6.1, 6.2 and 6.3.

There were five experts who identified with one area of professional interest each. The remaining twelve experts selected more than one area of professional interest. Five selected two areas of interest; three identified with three areas and another three identified with four areas. One expert selected five areas of interest. Figure 6.1 shows that thirteen experts described their areas of interest as being in the field of clinical genetics or genomics. The

seven who identified with medical genomics also identified with clinical genetics or genomics interest group. Nine had an interest in sharing medical information with individuals. Of those nine, seven also had an interest in sharing medical information with relatives of such individuals.

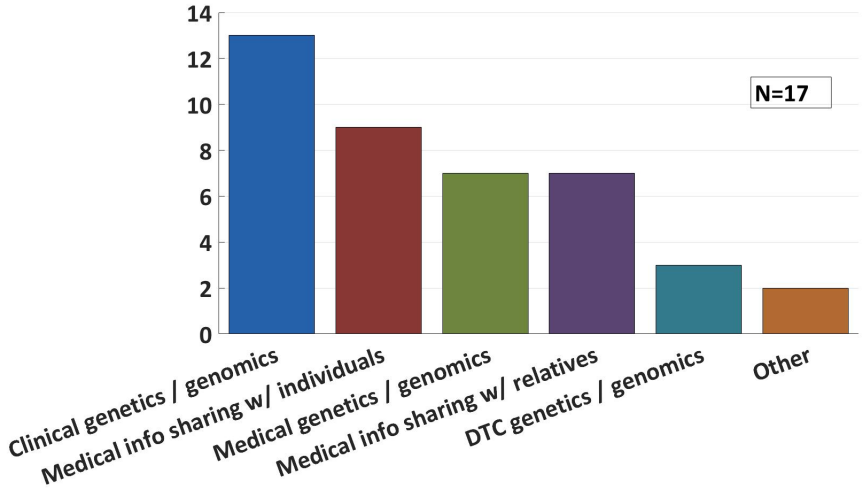


Fig. 6.1 **Professionals' Areas of Interest**

Figure 6.2 presents a summary of the professional groups the domain experts identified with. Eleven experts identified as belonging to a single discrete professional group on the selection list in the survey. Three experts indicated that they belonged to two professional groups and another three experts identified with three of the professional groups listed. The four most common professional groups that domain experts indicated they belonged to, with four experts in each of them, were:

- genetic or genomic counsellors
- clinical geneticists or genomicists
- medical specialists who are not geneticists or genomicists
- academics or educators

The remaining five professional groups each had two experts identifying with them:

- medical geneticist or genomicists
- health services researchers
- health technology researchers

- health technology developers
- DTC providers

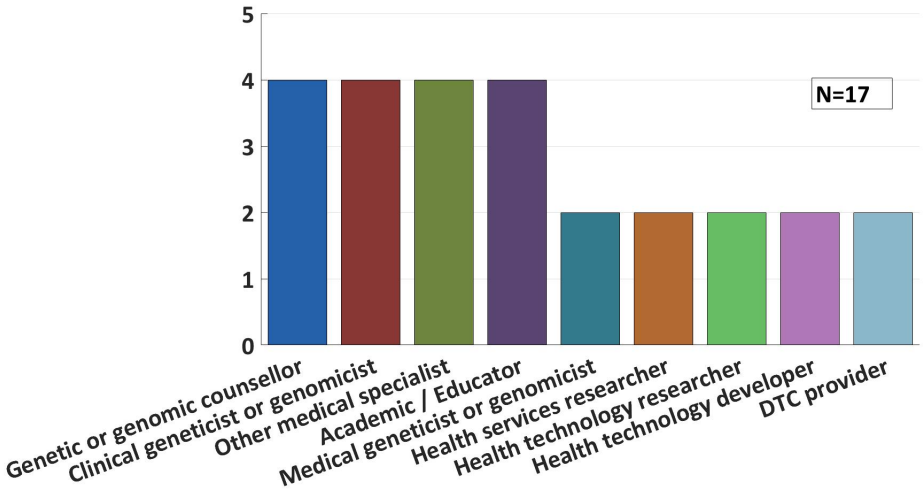


Fig. 6.2 **Experts Professions**

The groups experts worked with are summarised in Figure 6.3. The two most selected groups, 'YAs' and / or 'adults' captured all of the experts, most of whom selected both and other groups.

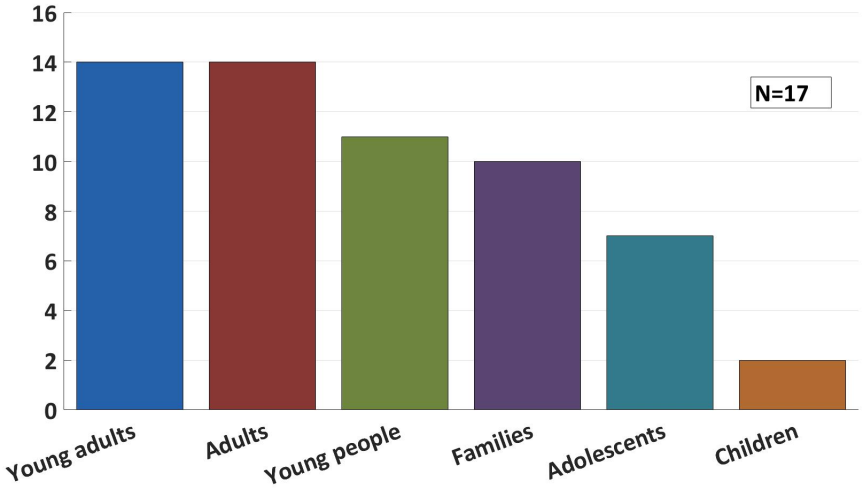


Fig. 6.3 **Groups the Professionals work with**

6.5.3 Likely to be considered *before* embarking on undertaking WGS

The factors that the experts thought were likely to have been considered by YAs *before* embarking on undertaking WGS are summarised in Figure 6.4.
Listed below are the factors that ranked highest among those selected by experts as likely to be considered by YAs, and the number of experts who selected them:

- Value-for-money (12)
- Interest in self discovery (10)
- Desire to plan (9)
- Data security (9)
- Treatability (7)
- Relevance (7)
- Privacy (7)
- Ability to understand (7)
- Desire for privacy (6)
- Seriousness (5)
- Ability to Choose (5)

Factors selected most often as likely to be considered by YAs, were those categorised as Attitudes related to utility; they included value-for-money, desire to plan, treatability, relevance, desire for privacy and relevance. Among the top scoring factors, interest in self-discovery was the only attitudinal factor related to autonomy and dependency selected by the experts as likely to be considered by YAs. Factors related to Perceived Behavioural Control account for the remaining top ranking factors likely to be considered: data security, privacy, ability to understand and ability to choose. The items that TPB categorises as External Factors, i.e. gender, STEMM status, genetic and generic education were selected by a small minority of experts as being likely.

There were six factors that none of the experts selected as likely to be considered by YAs:

- desire to offer support
- rights

- responsibilities
- shared interests
- communication skills
- normalisation of WGS

Attitudes related to autonomy and dependency were among those factors not selected; they were desire to offer support, rights, responsibilities and shared interests. The remaining two factors, communication skills and normalisation of WGS, were both categorised under the construct Perceived Behavioural Control. See Figure 6.4 for the ranking of all factors used to examine likelihood.

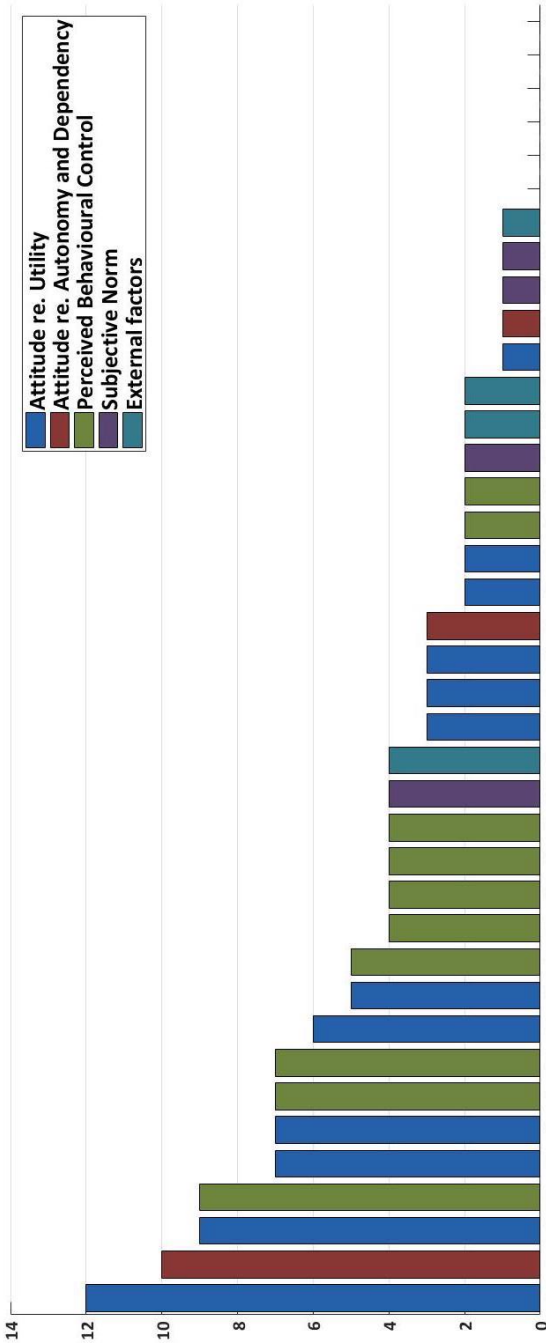


Fig. 6.4 **Factors experts thought were likely to have been considered**

6.5.4 Important to consider *before* embarking on undertaking WGS

The factors the experts thought were important for YAs to consider *before* embarking on obtaining WGS are summarised in Figure 6.5. Listed below are the factors that ranked highest among those selected for importance by experts, and the number of experts who selected them:

- Relevance (14)
- Data security (14)
- Ability to understand (13)
- Privacy (13)
- Seriousness (12)
- Treatability (12)
- Desire for privacy (11)
- Desire to plan (10)
- Family dynamics & relationships (10)
- Ability to choose (9)
- Coping skills (9)
- Ability to undertake healthy actions (9)

From the factors selected most often as being important, relevance, seriousness, treatability, desire for privacy and desire to plan are categorised as Attitudes related to utility. Other important factors listed above are related to Perceived Behavioural Control. None of the Attitudes related to autonomy and dependency made it into the top ranking important factors listed above.

Most factors that the TPB categorises as External were selected by a small minority of experts as being important for YAs to consider, with gender not being selected by any expert. See Figure 6.5 for the ranking of all factors used to examine importance.

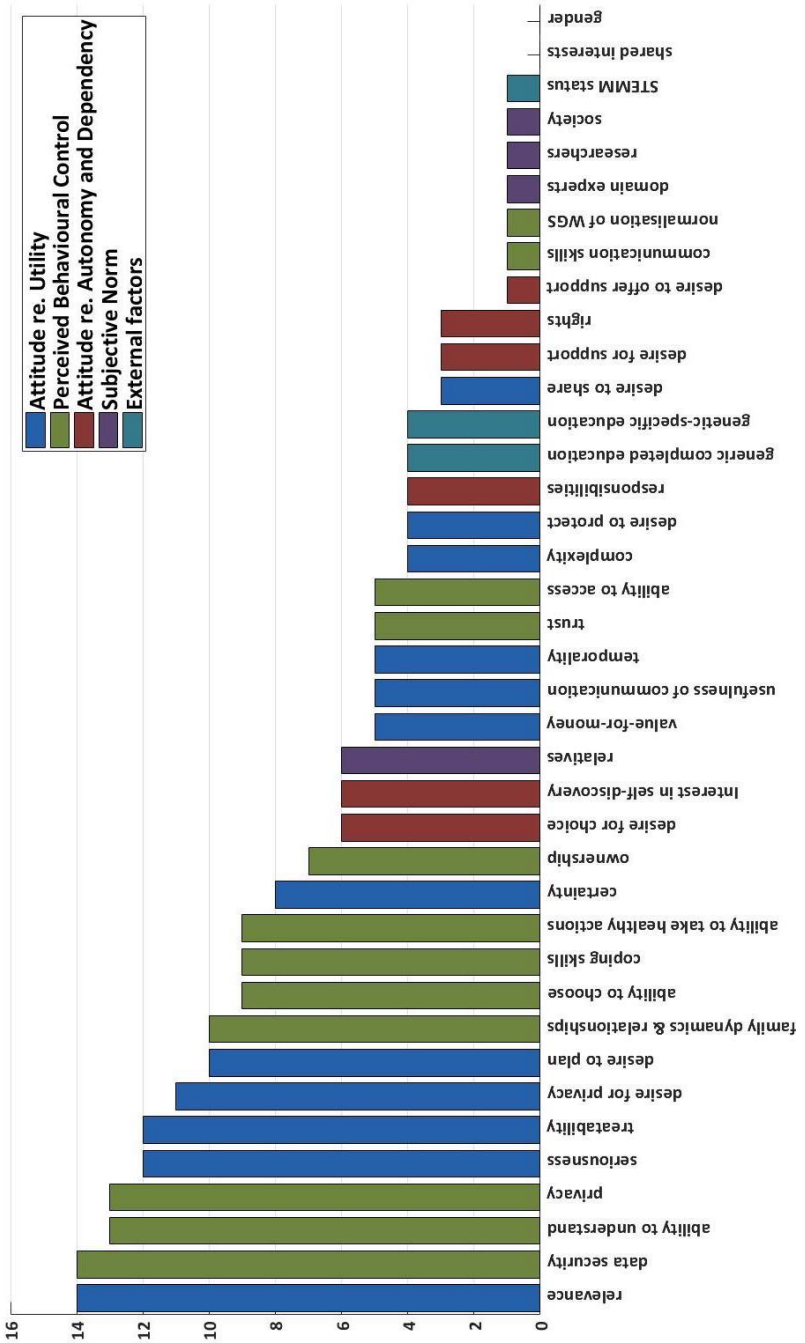


Fig. 6.5 **Factors experts thought were important for consideration**

6.5.5 Additional Factors

All surveys had a space for the domain experts to identify further items they would want to have included in the list of factors. In order to capture additional factors if they were to arise during the meeting, additional audio recordings were made with four experts who completed the survey in-person. Initial audio recording attempts failed due to a technical problem with the recorder, therefore field notes were taken on the occasion where additional comments were made. Field notes were shared with the affected expert to make further edits and comments. The expert undertook these and returned the edited transcript with corrections and additional comments. The recording device issue resolved for further interviews.

From the surveys and audio recordings, domain experts identified the following additional important items for inclusion.

- Culture
- Religious beliefs
- Prior exposure to others with genetic disorders
- Exposure to advertising
- Settings within which WGS takes place
- Individuals' views of their current health state
- Perceived reliability of resulting data and its interpretation
- Insurance implications
- Friends
- Co-workers

6.5.6 Contextualisations of YAs on a WGS Pathway

Almost all experts indicated in their survey responses that the steps on the WGS Pathway, as illustrated in Figure 4.1, did not need any changes. The three experts who engaged in an interview discussed adding a pre-WGS step for individuals considering undertaking WGS, with only one clearly indicating what needed to be changed on the survey. The following presents sections of text which are either direct quotes or paraphrases from the rich data collected with P1, P2 and P3 that contextualise their views and captures additional information about YAs' consideration factors, the WGS Pathway and the proposed WGS

Framework's design. The three experts spoke succinctly and meaningfully, so much of the content of their transcripts were reported. Direct quotes were maintained where they provided the clearest expression. The Discussion section will address the quantitative findings from survey responses and contextual issues raised from the three audio recordings.

Autonomy and Dependency

P3 described YAs as acting more autonomously, doing things on their own, going online to find information when older physicians do not have the information, wanting control over themselves and their health, leading healthier lifestyles, wanting information at their fingertips to help them manage their lifestyle, and don't want others to tell them what to do.

P3 stated, "It is the case that people choose to share their results with HCPs over family members. Sharing with professionals applies to 'you' and you want to have that discussion about you. It's an 'I' Generation, where families are not so close and people are moving away. We talk about nuclear families, we don't talk about extended families anymore." P3 stated, "Younger is healthier so its about planning."

P1 stated, "In my experience, they are very 'me' focused at that age". P1 also pointed out that "they grow, so a 25 year old will be quite different to an 18 year old. That is a really big change in that space of time."

P1 stated, "The young women that we see, they are pretty switched on, you know, but they are not used to necessarily thinking of their own autonomy. They are still very guided by family, and won't always make decisions that are the right ones for them because of all the other things that come in, it's interesting."

P1 continued, "Even coming down to things like prenatal testing, we did a study years ago that showed that if you were married you were more likely to undertake an amniocentesis in response to a raised screening risk than if you weren't married, yeah. And that's about a woman's ability to exert her own individual autonomy, that if you are married, your ability to exert your own autonomy is slightly diminished by that perceived need for your husband, with whom you have a legal relationship, to be able to exert his autonomy. And men are much more black and white than women. And men, 'there's a problem, there's a solution'. And for women it doesn't work like that, you know, 'there might be a problem, but in creating a solution we might create a whole heap of other problems that I don't really want to think about at this stage, so actually I'd rather not solve the problem because I might not like the solution and the solution might create a whole heap of other problems [...] and there may not be a problem in the first place', yeah, whereas the men are very black and white, 'you are telling me there is a risk, you are telling there is a test, the test will tell me absolutely about the risk so we must take the test. Okay, if the test creates a heap of different consequences,

we will get there.' And it was very interesting, if you were in a relationship but you weren't married, it didn't seem to matter as much. Actually, *being married*, yeah, [...] yeah. And this, understanding your own autonomy, understanding what you hope for, why you are doing it in the first place, what you hope to gain from it before you..."

P1 questioned whether they understand that they can choose not to go down this road or that there are other choices that might be less than WGS but still provide information.

Pre-WGS appraisal

P1 stated that most individuals who choose to undertake testing of this nature are likely to expect the results to indicate everything is fine so the test is viewed as evidence to confirm their positive expectation.

P1 stated, "I'd add pre-test exploration of hopes. What do these young people hope to get from it? Certainly they may be hoping to get information about seriousness, treatability, certainty, all of that. But it may also be that there is nothing to worry about and it'll be alright, and reassurance, they are hoping for reassurance. We know with testing in pregnancy, most women go into it believing it'll be okay, yeah".

P1 saw a pre-WGS appraisal as very important opportunity for the individual to understand what they are hoping and expecting from undertaking testing and how that relates to what the test results may return because there may be a mismatch, as often found in their experience of individuals undergoing multiple-test screening.

P1 expressed concern that individuals undertaking such testing are "opening up a box", a reference to Pandora [1], or going up an escalator to an unknown destination without giving due consideration to deciding not to undergo WGS.

P1 stated that if you don't do 'pre-exploration', they get on escalator and they feel they cannot get off or they feel the escalator is going that way and they thought the escalator was going to take them another way.

P1 stated that "an exploration of those things were really, really important because that was going to guide what testing you do and how you deliver the results.[...] considerations for the reasons for undertaking, the hope of what the test will give you..."

P1 stated, "So they are not actually going into it looking for something bad, they are actually going into it for something good."

[1] In Greek mythology, Pandora is the first mortal woman sent by Zeus on a revenge mission to earth, with a box whose evil contents would infect the world and harm mankind when she opened it. Or, in another version of events, the box contained all the world's blessings that should not be allowed to escape. When Pandora opened the box, only hope remained to assuage the lot of humankind.
Pandora's Box describes a process that generates many complicated problems as the result of unwise interference in something. http://www.oxfordreference.com/view/10.1093/oi/authority.20110803100303595

P1 stated that they don't want something bad but they have a 'head in the sand' approach and therefore do not realise what they are potentially opening themselves up to.
P1 also stated that it's not just this type of testing where this approach is taken, mammography, cervical screening, all the screening tests, everybody does them because they believe it will provide them with reassurance and nobody goes into it thinking what will happen if it doesn't, or very few do.

P1 also described "women who do opt out of pregnancy screening programmes because they know it won't change anything they do, they are making a very positive decision, 'I'm not going to get on that escalator because if I got to the top and it told me there was a problem, I'm still going to do this anyway'. You would not go for a mammography if there was no way in the world that you would let anybody treat you for breast cancer."
So P1 felt that an ultrasound or having multiple blood tests can be viewed almost the same as WGS. You are not just looking for a single thing, you are looking for multiple problems that could come from having what the person expects to be a reassuring blood test.

P1 advocated for a young person embarking on WGS to "have an understanding why, why am I doing it? What am I hoping to get out of it and what might happen once we take a lid off the box?".
P2 stated that most people want reassurance when they go for testing, they are not after bad news. So, then that can be a real wake-up call, when it happens.
Until recently, P2 had worked for a company that received tests ordered by physicians, via insurance, some private. Some customers ordered online with a remote assessment by a physician, the physician then placed the order. P2 noted that some employers were subsidising the cost of having genetic testing or paying for it, as a perk to their employees. Companies were competing to have a feature to attract skilled employees (engineers etc.), genetic testing is one of those cool things at the moment. The employer does not see results. The employees benefit if they know things they can act on and the employer benefits from the actions the employee may adopt. P2 reflected that those who get genetic testing for free (where their employer pays) were much less thoughtful compared to those who were concerned about a health issue.

P2 stated, "Customers are saying either, 'this is cool, high-tech, I saw an ad on TV', or they have a family history. The healthy young person doesn't seem to put their curiosity in check. Then they want the raw data, they use software analysis tools from third party interpreters (TPI), cheap US$10. They play around, not very accurate, then the person may or may not need to see a genetic counsellor at the company. Sometimes the person doesn't get same result when they run the raw data through the TPI system as a previous sequence result had shown. False negatives are common. Some people who take a direct to consumer test

(eg. 23&Me, Ancestry, etc) download a copy of their raw sequencing data and then analyse it using third party software tools from the internet (eg. Promeathase is one service available for $10). That third party software tries to identify mutations (eg. Outside the areas covered in the original test report). Mutations found by this type of third party software analysis are often false positives (eg. 40% of the time in Invitae's data). There's a variety of reasons for this, some of which are due to technical issues (eg. Coverage of that region of the DNA) or interpretation issues (what information are they using to call something a mutation vs a benign variant)."

P3 thought that people are more inclined to do genomic testing because a lot of the information that would have previously been passed through the family no longer was, so the only way to really know what you are at risk of is probably doing genomic screening.

P2 said "some people struggle with timing and choice. With WGS you don't know what you'll find. Can't counsel for all of it, can do general categories."

P3 felt that where YAs will struggle will be "...as this new information is coming, there is a lot we do not understand about genomic data that is coming out.". P3 continued, "We do not know what the clinical significance of all of this information is."

P3 indicated that their company was only returning certain information because of the limitations of what is currently known. P3 stated that YA will forget their results, and described a vault to contain an individual's genetic information that they could access at later dates.

P2 stated that at their previous employer, customers who were under-21 years old were phoned *before* testing to warn them of long term impact [...], things that may affect their partner, reproductive issues, things that may not need to be actioned till later.

P2 stated that the over-21s were not called until *after* testing to have such a discussion. P2 pointed out that under-21s may not have considered the many insurance implications including life insurance, limitations of the Genetic Information Nondiscrimination Act [GINA, is a federal law in the USA], variable legal and employment implications.

P2 stated that pre-test assessments may be less needed for those who have read up, able to get into genetics and those who need to be tested urgently due to upcoming decisions for their cancer treatment.

P1 viewed a pre-WGS appraisal learning package as something that could be offered online for individuals to complete independently.

P1 stated, "you could do an electronic learning package that took you through the things you need to think about. If you are signing up for financial advice, they will send out a fact sheet on how you understand what sort of risk you're willing or able to take when investing money. It's the same thing. You are trying to explore people's hopes and expectations from where they invest their money. So if you have loads of money but you hope to make really

big bucks, and if you lose it, that bit of it, you are not going to be crying into your soup, you might be a high risk taker. If that money is very precious to you and no matter what happened, you could not afford to lose that money, you'll be a low risk taker; and the way financial advice is given, aims to explore where you are in that process. It ought to be possible to put a package together to take you through a form of exploration that understands what you need to get out of it at the end and what your fears are".

P1 indicated that professionals working with individuals who undertake such testing were best placed to inform contents of a learning package to appraise an individual's hopes and expectations in relation to the testing decision as they have "seen the unforeseen consequences, the things that people getting on the escalator at the bottom can't see because that's what you need to bring to them, 'So if I get on this escalator what's waiting for me at the top and what's at the top that I never saw coming, and how would I cope with that? And is it worth me getting on the escalator, are the benefits going to outweigh the potential risks?' ".

Sharing WGS Results

As for communicating results with family, P3 indicated that this is great for genomics but it doesn't really happen in real life as there are so many family dynamics, people don't talk to each other and they don't want to share the information. P3 stated that it is important to emphasise to these people the importance of sharing the information, it's really critical because there could be other people who could benefit from that information. P2 stated that for people who already have kids, often passing this [bad news] on is a consideration but the younger ones are not yet thinking about children.

For parents having genetic screening of their unborn baby, P1 described how they inform parents in their leaflet that occasionally things will be found that do not affect the baby as a baby but might affect the baby as an adult and might have implications for other family members, "so when we take the lid off the box we have to be prepared for everything, we don't very often find things but the BRCA gene [for breast cancer] is one that can be picked up because it is a big gene change and identifiable, and we can pick it up and of course that has implications for that child and the family".

P2 stated, "I do think that it is important to go to somebody like a healthcare provider to work with you on results.".

In terms of sharing data for the benefit of others, P3 did not know how many people really have an altruistic mode anymore.

When asked how people responded to this exchange, of sharing data to support research and help others, P3 said it would come from anonymous sharing but she indicated that although people say they will share, they feel differently when they find they have something they

struggle to deal with.
People using the services of the company P2 worked for had a choice to have their sample saved or discarded. However P2 indicated that in a public healthcare lab, the choice is not necessarily explicit.

P2 described concerns of customers, post-election of President Trump, "they say things like, 'I don't necessarily trust the current administration to protect the data' and 'What will they take next.', they don't trust them not to just cancel the GINA protections". P2 added, "In general guidelines for who can access clinical genetic testing are stricter in Canada than in the US".
Regarding following-up with individuals about variants of unknown significance, P1 described informing individuals about databases such as the Human Gene Mutation Database that collects genetic results information related to variants of unknown significance from around the world.

Using their knowledge and experience, the three interviewees described contexts for the concepts presented to them. They highlighted considerations related to autonomy, dependency, preparedness for WGS and sharing results. They suggested the importance for YAs to be well-informed in preparation for considering undertaking WGS. The experts approved of the seven steps proposed in the WGS Pathway, shown in Figure 4.1. Those interviewed specifically raised the need for a pre-WGS step, creating an enhanced eight-step process. This additional step offers individuals an opportunity to consider whether potential results relate to their hopes, expectations and concerns of undertaking WGS. The ranked consideration factors, illustrated in Figure 6.7, are relevant to step 1 in both the originally proposed WGS Pathway and the Enhanced WGS Pathway shown in Figure 6.6.

6.6 Discussion

The findings from this framework evaluation are discussed in relation to the YAs studies and published literature. Demographic data collected validated credibility of the professional domain experts, knowledgeable in fields related to genetics and genomics, and experienced in working with relevant groups. The domain experts approved and enhanced the WGS Pathway and the framework. They prioritised the factors YAs identified by likelihood and importance and contributed additional factors for YAs' to take into consideration.

6.6.1 WGS Pathway and Factors for Considerations

To reflect experts' opinion, a pre-WGS step was incorporated into the amended WGS Pathway presented in Figure 6.6. This draft form requires further empirical exploration for its validation.

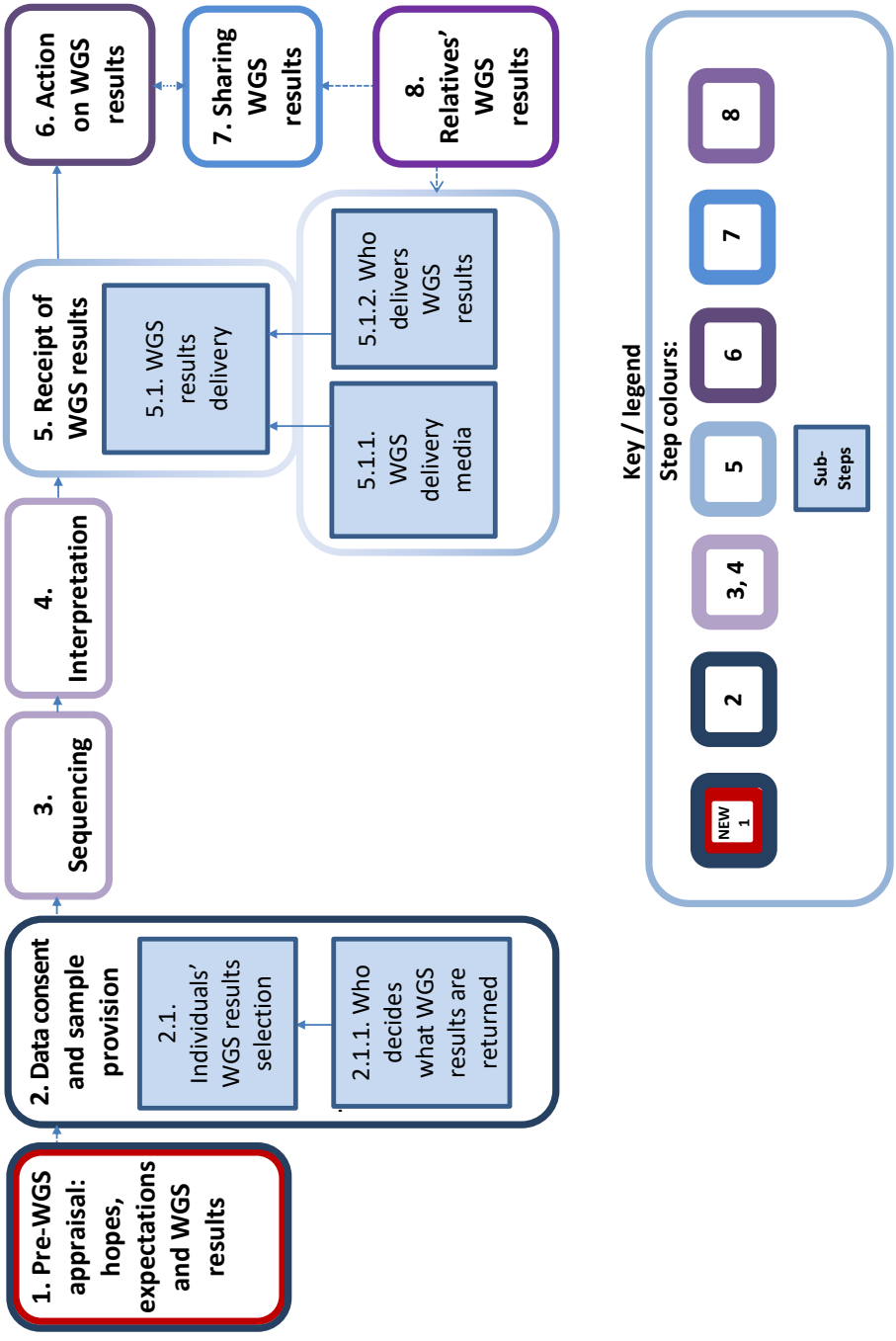
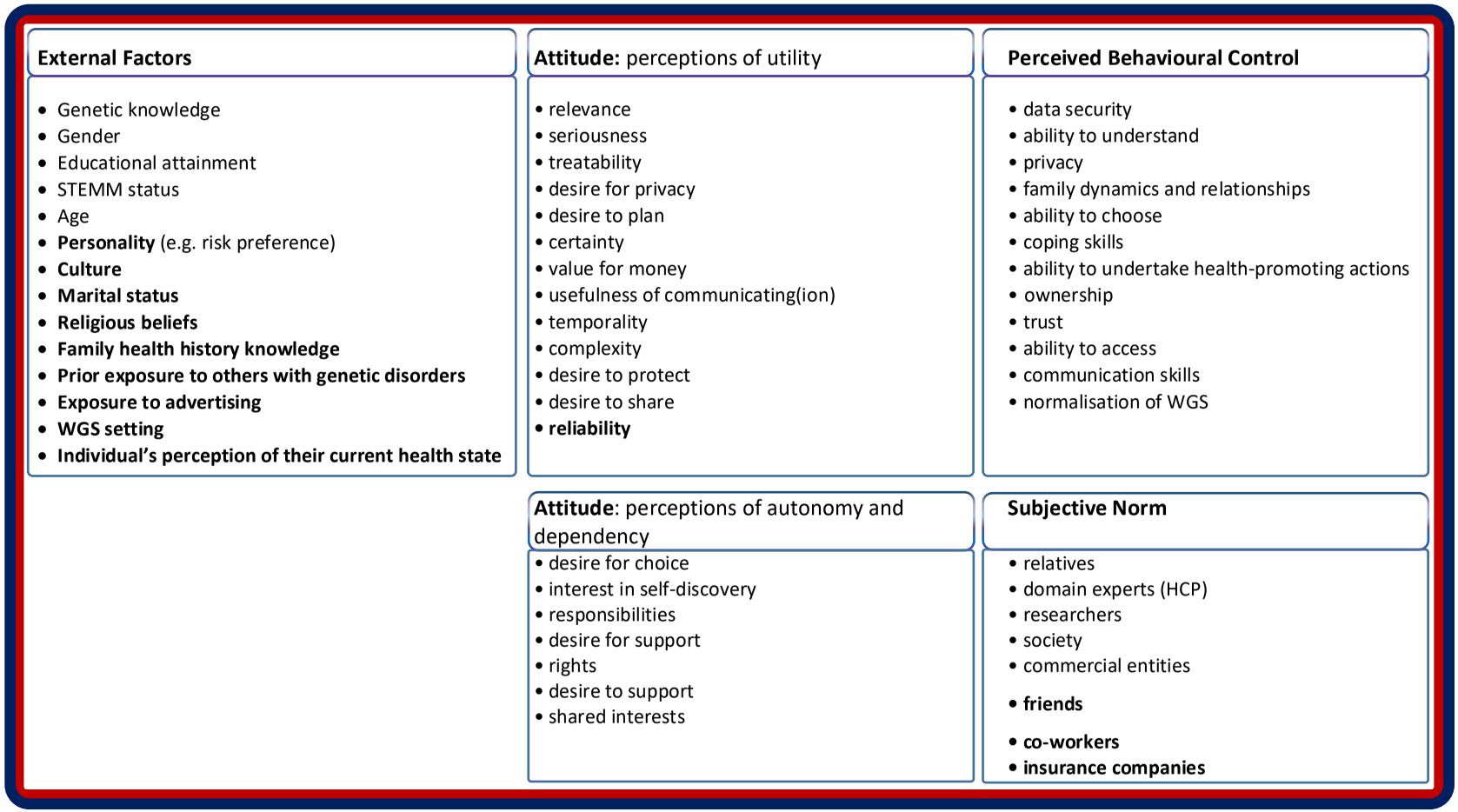


Fig. 6.6 **Enhanced WGS Pathway**



Factors are listed by construct, then in order of importance as prioritised by the domain expert study participants. Additional factors, newly identified by the domain experts are bullet-pointed **in bold**.

Fig. 6.7 **YAs' Consideration Factors for Step 1 of Enhanced WGS Pathway**

The pre-WGS appraisal, which is Step 1 in the Enhanced WGS Pathway as seen in Figure 6.6, aims to allow individuals the opportunity to prepare for the decision as to whether or not they want to undertake WGS. The table of factors has been reorganised to prioritise factors as indicated from the experts and previous studies from this thesis. The list of factors in Figure 6.7 should be considered as part of an individual's decision making process for undertaking WGS and sharing results. Factors listed for consideration during the pre-WGS appraisal may be relevant at any other subsequent steps in the WGS Pathway. The proposed steps for pre-WGS appraisal, as indicated by domain experts, are as follows:

- Assess hopes, expectations and concerns about WGS results and their impact.
- Relate these to both likely and unforeseen WGS results.
- Appraise impact of results if not as expected or reassuring.
- Decide if and when to receive results.
- Consider how and with whom information will be shared.

6.6.2 Factors for YAs' consideration

In Figure 6.7, factors previously identified with the YAs are prioritised by the experts, along with additional factors the experts indicated as missing.

Most experts believed YAs considering undertaking WGS were likely to prioritise getting value for money, their interest in self-discovery and their desire to plan when considering WGS. The top three factors selected as likely by the domain experts were similar to the motivational factors indicated by genetic professionals in a previous study where they undertook WGS of their own genomes [356]. Those genetic professionals [356] were primarily motivated by their professional enhancement, curiosity about the technology and personal health benefits.

The factors selected by most experts as being likely considered by YAs prior to undertaking WGS coincided with items considered by the YAs interviewed at the point when they were asked about consenting to data and provision of their sample.

None of the experts thought YAs were likely to consider communication skills, with only one expert selecting this as an important factor for YAs' consideration. The YAs' interview data indicated that they had not made any reference to their communication skills during the initial step of considering undertaking WGS. Communication skills were considered later in the interview, when 'Action on Results' was addressed with the YAs. Others have

recognised communication of genetic risk with relatives as sub-optimal, especially with ambiguous or indeterminate results [197] or for extended family members (second-degree or more distant) [98, 313], emotionally distant relatives [156], or where relationship dynamics lacked flexibility to cope with changes [138]. Non-disclosure might be active due to the desire to protect; it may be passive, caused by social, geographical or genetic distance, or non-disclosure may be unconscious, where the individual is completely unaware of the (distant) relatives' risks [98].

Five of the six factors that all of the experts decided YAs were not likely to have considered prior to undertaking WGS were factors that the YAs had failed to mention in interview when discussing the first step in the proposed WGS Pathway. The five factors identified by the experts were desire to offer support, rights, responsibilities, shared interests and communication skills. Normalisation of WGS was not selected as a likely factor, however it had in fact been considered by YAs. Normalisation of WGS was identified by the YAs as relevant to the whole WGS process, later in their interviews, following additional prompts asking about ideal processes and challenges to undertaking WGS. This correlation of five out of six factors represents a high level agreement between what the experts believed would be neglected by YAs and what the YAs neglected to mention in their interviews.

There was a higher level of agreement among the experts for the factors deemed important for YAs' consideration than for there was for those they believed YAs were likely to actually consider prior to undertaking WGS. This difference is illustrated by comparing Figures 6.4 and 6.5.

Although most felt YAs were likely to prioritise getting value for money, their interest in self-discovery and their desire to plan when considering WGS, the experts most frequently deemed relevance of undertaking WGS, data security issues, and the ability to understand undertaking WGS and its results as important considerations. Double the number of experts thought it was important for YAs to consider relevance compared to the number who thought YAs were likely to take relevance into consideration.

Patients who wanted to receive their genomic information often wanted to know results even in the absence of clinical utility [28]. Standards of clinical utility, such as those used for public health evaluations are not identical to those used for individual valuations of utility [45]. In fact, personal approaches towards the significance and usefulness of genetic information challenge the notion of clinical utility [45].

Genetic health care professionals [305] favoured WGS analysis limited to medically relevant results as opposed to the general public who emphasised that medical relevance was subjective and disclosure of findings should not be based on clinical relevance alone. Lay participants insisted individuals interpret relevance and seriousness differently, therefore

patients should not be offered results filtered by professionals into pre-categorised packages [305]. They wanted to exercise their autonomy and right to choose what findings they receive, stating they accepted the consequences of any potential anxiety and uncertainty [305]; these assertions challenge the professional preference and raise the question, relevant according to whom? Consumers of genomic services may pursue acquisition of their genetic data and attribute personal utility to genetic information even after being informed of current clinical limitations [45]. Some have argued that the patient's evaluation of personal utility of genetic information should inform disclosure of findings when clinical utility is unclear [305, 353].

In clinical genetic settings informed consent has to be given, including pre-test information and genetic counselling, especially where high risks or serious diseases are involved [58]. This process addresses knowledge gaps and expectations of testing, however there remains concern that, for DTC services at least, consent may be reduced to a box-ticking exercise because of limitations faced by users interacting with a company's process over the internet [58].

Value-for-money was selected by the most as a likely factor YAs would consider, however less than a third viewed value-for-money as important for YAs' consideration. For consumers looking to use their own resources to access such services, they have a legitimate interest in value for money, or cost effectiveness of genetic tests that have been proven to have demonstrable health impact [124]. People can gain personal and social value from genetic testing in the form of entertainment, learning, or as a way to relate to others [309]. What YAs consider as good value for money is likely to differ from views of clinical experts [309].

Almost double the number of experts identified the ability to understand as important compared to the number who thought it was likely that YAs would consider it. Interviewed experts elaborated about the importance of understanding the potential outcomes in advance of undertaking WGS. The ability to understand is recognised as one of many new challenges genomics presents. HCPs will be called on to interpret results patients bring to them from DTC tests, requiring them to be able to assess, interpret, and make clinical decisions using complex data generated by genomic tests [132]. It is worth acknowledging that, in the case of DTCs, these traditionally clinical challenges are transferred to individuals, since, as consumers, they may or may not seek professional assistance to make sense of received results.

Privacy, to be more specific, one's perceived ability to control privacy, is related to data security. Privacy was ranked seventh by the experts as a likely to be considered by YAs but it was considered forth most important factor for YAs to consider. Bietz and colleagues point out in 2019 that this is problematic, particularly because YAs have fewer or limited privacy

concerns, or they may not perceive as many consequences from information disclosure than older adults [31].

Data security and related issues exist concerning the context of DTC genomic testing in Europe and USA, where medico-legal boundaries are fragmented privacy and information offered to consumers about possible re-identification is lacking [228, 226, 168, 278]. Despite attempts by the Food and Drug Administration in the USA to regulate safety and effectiveness of tests offered by DTC companies, they are not obliged to protect the data they collect from their customers except in certain circumstances. In the USA, GINA prohibits discrimination in employment and health insurance, it does not address life, disability, or long-term care among other insurance and discrimination contexts [123]. As the Presidential Commission for the Study of Bioethical Issues guideline states: "Clinicians owe stringent fiduciary duties to patients, which entail an obligation to act in furtherance of the patient's best interests. Non-clinician DTC providers have less stringent duties, including duties that might be limited or circumscribed by contract. Consumers should be made aware of these distinctions prior to consenting to undergo DTC testing." (p. 103–104, 2013) [226]. 23andMe's website explicitly stated that its database-sifting scientific work "does not constitute research on human subjects," meaning it is not subject to the rules and regulations that are supposed to protect experimental subjects' privacy and welfare [278].

In a study comparing views of clinical geneticists and general practitioners towards DTC genetic testing, clinical geneticists were significantly more concerned about risks such as reliability of test results, provision of information or counselling, understanding of results and advertisement than general practitioners were about these aspects [232]. Others have identified geneticists' concerns [232] that chimed with finding ability to understand was the third most selected important factor. Individuals among the experts added 'reliability' and 'advertisement', noting that these factors had not been identified by the YA participants. Reliability, specifically 'perceived reliability', was identified as a missing factor by one expert. 'Reliability' has been identified by others as an important concern [119, 114] but it had not been explicitly identified in the proposed framework informed by the YAs. It is possible that reliability issues may have been coded as certainty, but it required recognition as a distinct factor. For some YAs, reliability risks may have been accepted, assumed or not considered, given the hypothetical situation they were engaged in. It is as important for HCPs to address technical and clinical limitations of genomic technologies as well as the potential benefits [132]. For the purposes of the proposed framework's development, reliability is classified as an attitudinal factor related to utility.

Few experts selected any of the External Factors, on the list presented to them, as being either likely or important for consideration. Gender was only selected by one expert as a

factor that YAs were likely to consider. However, gender was found to be a significant genetic information sharing factor for the YAs studied, those findings did not answer questions about the YAs' awareness of gender as a relevant consideration. Gender differences related to sharing needs have been observed by others [98], with males expressing a need for guidance or support to communicate their genetic test results for colorectal cancer with their relatives.

Genetic education was a low-ranking External Factor selected by only two experts as likely to be considered by YAs. In the quantitative survey study with YAs, genetic education was found to significantly affect their sharing decisions. However, their awareness of their genetic knowledge and its impact was not examined with the YAs. More YAs interviewed indicated a preference to receive genetic education *after* undertaking WGS, i.e. upon receipt of their results, rather than *before* embarking on obtaining WGS.

Despite the low ranking of External Factors presented to experts, most of the facotrs they identified as missing from the framework could be categorised as External Factors. They included culture, religious beliefs, exposure to advertising, settings for undertaking WGS and individuals' views of their current health state. Prior exposure to others with genetic disorders was classed as an External Factor but could also indicate a person with a genetic disorder, such as a relative or friend, acting as a Subjective Norm for the individual making decisions for WGS. Personality was added to the list of External Factors for consideration. It was referred to by P1 when comparing the decisions for WGS to financial risk-taking. Some YAs interviewed appeared more 'certain' about undertaking WGS, whereas others took a more 'hesitant' stance. Risk preference, as a factor, has recently been found to share the psychometric structure of major psychological traits [97].

Friends and co-workers were specifically indicated as important additional Subjective Norms. Insurance concerns are also categorised as Subjective Norm; they are a sub-set of commercial entities, along with genomic service providers. Individuals may have relationships, enshrined with expectations, with their insurance companies or genomic service providers. Such External Factors are recognisable variables from literature however they need to be brought together in a manner that allows their influences to be considered.

6.6.3 Experts' Contextualisations

Experts interviewed raised a number of concerns when describing YAs and WGS. They recognised that young healthy adults act in their own self-interest, first and foremost. However, they also indicated that healthy YAs were more likely to open a Pandora's Box of information without being particularly concerned or perturbed by the possible outcomes. They recommended a pre-WGS appraisal step to precede data consent and sample provision These concerns make the production of accessible and engaging educational information

that balances benefits and risks of undertaking WGS with YAs' hopes, expectations and concerns all the more important. The increasing variety of ways that a person may gain value and experience utility from WGS is expected to foster a more nuanced understanding of the types of test results, which will in turn highlight new ethical and regulatory challenges that influence regulatory framework development [309].

6.6.4 Limitations

Limitations included limited research project resources, contributing in part to other limitations of reduced sample size, international coverage.

There were 17 domain experts. Small sample size is related to difficulties accessing individuals from relevant professions. Recordings of conversations were only created with three domain experts, limiting the data available to identify new factors and contextualise responses to the survey questions. Experts were mainly based in the UK or the USA, though a couple were based in Brazil, and one had Australia and USA connections. The number of experts and the limited international coverage represented by their geographical locations limits the findings' generalisability to a wider population of genetic professionals.

Experts were asked to utilise their imagination to simulate views they believed YAs were likely to hold. Domain experts' ToM is limited by their knowledge and experience as well as their abilities to include and exclude mental states they attribute to YAs appropriately, and their ability to avoid allowing their own state to creep into the simulation as this would contaminate it [118]. Due to the limitations, the list of important factors for consideration for a pre-WGS appraisal step in the Enhanced WGS Pathway, as presented in Figure 6.7, is proffered in draft form. Further research is required to identify additional factors and prioritise them, as well as to validate factors in WGS user-studies.

6.7 Summary

Following the YAs' studies and formulation of the proposed WGS framework, this study aimed to evaluate the proposed framework and factors, identified from the YAs' studies, with domain experts. TPB was used as a model to underpin this study's design because its constructs have been shown to predict decision making very well in a variety of health care settings. TPB was appraised in the previous chapter against the YAs' findings. The TPB factors used here were informed by the results of the YAs' studies.

Although interest in self-discovery, an Attitude related to autonomy and dependency, was second highest on the list of factors likely to be considered, it was the only autonomy

and dependency related attitudinal factor among those selected as important by five or more experts. The factors most selected by experts as likely to be considered by YAs were utility-related Attitudes ones followed by Perceived Behavioural Controls.

There was far more agreement among expert respondents for what were the most important consideration factors for undertaking WGS. At the same time, the items that were not selected by the domain experts as being likely considerations by YAs were in fact the very ones YAs did not recognise when deliberating their first step in undertaking WGS. This would indicate experts were attuned to what YAs did not consider.

Several External Factors related to previous experience and personal characteristics were added to the list of considerations by the domain experts. The addition of so many External Factors indicates this category might be particularly relevant to individuals' deliberations. Further research could help identify what and how External Factors affect YAs' decision making process for undertaking WGS and sharing their results.

YAs are not expected to understand TPB or work out what the variables mean or what categories they fall under. Rather, having a clear understanding of what influences young people's decisions can inform and support the design of systems and services to meet their needs.

Developments in the field of WGS and related techniques are likely to extend the way people interact with their genome. This includes: what for, how this may happen, also, who their data may be shared with, for what purposes it is shared, and how it may be used and reused. For these reasons, the factors found here, and others as yet unidentified, require careful consideration. Given current and near-future commercial offerings, technical capabilities and regulatory frameworks, this consideration is already lacking in many settings.

Chapter 7

Conclusions

7.1 Introduction

Technologies such as WGS are becoming cheaper and increasingly accessible to YAs. Their attitudes and preferences are important indicators of how they are likely to interact with WGS services. Research needs to reflect one's reaction to genomic results for what it is, a dynamic process modulated by experience [234]. To that end, YAs' considerations for undertaking WGS, receiving results and sharing them were examined using a WGS Pathway to provide a chronological structure. Domain experts' perspective provided insight into gaps between what YAs were likely to consider and what would also be important for them to take into account.

7.2 Contributions

The overarching aim was to explore variables associated with YAs' behavioural intentions towards undertaking, receiving and sharing information resulting from WGS. This was achieved by undertaking YAs studies informed by the literature related to their knowledge and attitudes about genomics, including theoretical models relevant to health-related behaviour and technology acceptance. Following quantitative and qualitative data collection studies with YAs, an appraisal of theoretical models for technology acceptance used the studies' results to identify the best-fit model. The Proposed WGS Pathway and factors for consideration were evaluated with genetic professionals who informed an Enhanced WGS Pathway, prioritised considerations and contributed new factors to the WGS framework's design. In achieving the aim and objectives, the following contributions were identified from the research activities undertaken:

1. The literature review gives an overview of WGS landscape related to YAs' knowledge and attitudes, and theoretical models that may frame such studies.

2. The survey discovered several novel insights about relationships, knowledge and attitudes of YAs to undertaking WGS, receiving results and sharing WGS information.

3. The interviews identified themes from YAs' considerations, preferences and intentions for undertaking WGS, receiving results and sharing them with others.

4. The models' appraisal proposes a novel, theoretically underpinned WGS framework to perceive YAs' considerations for undertaking WGS along a pathway.

5. The survey of domain experts prioritised YAs' considerations for WGS and added a pre-WGS appraisal step to enhance the WGS Pathway and WGS framework.

7.2.1 Literature Review

Chapter 2's objective was to undertake a literature review related to YAs' engagement with genetics and genomics focused on knowledge and attitudes, and relevant theoretical models, to identify gaps in published knowledge, informing the thesis' studies. This was achieved by reviewing articles relevant to adults, with a focus on younger adults. Further, literature identified relevant theoretical models to describe behavioural antecedents and these were introduced. To the fields of behavioural psychology and genomics, the review contributes a collection of published literature illustrating the complex landscape YAs undertaking WGS are presented with and theoretical models much needed for unifying and grounding studies in this field [99].

7.2.2 Survey of YAs' Knowledge and Attitudes to WGS

Chapter 3's objective was to better understand YAs' preferences for undertaking WGS and sharing information. This was achieved using quantitative methods to identify relationships between individual characteristics and preferences related to YAs' knowledge of and views about undertaking WGS and sharing results information with relatives.

Hypotheses tested found statistically significant differences in YAs' attitudes about sharing WGS information related to genetic knowledge, educational attainment, STEMM background and gender. Knowledge and familiarity with the subject, rather than generic educational attainment, appeared to impact attitudes for several aspects of undertaking WGS and sharing results. Being female was a consistently significant factor for more positive attitudes to sharing with relatives. In addition, females with a university-level genetic

education engendered a significantly greater desire to share with their relatives than that expressed by other females.

Many attitudinal studies in the genetics field have been all-female or had a high percentage of female participants [192], with many addressing breast and ovarian cancer [83, 347, 333, 348]. Studies that have addressed gender differences have conflicting results or not found a difference [190, 129]. This study recruited YA males and females allowing for gender comparisons in this age group. The findings not only highlighted significant differences in views between males and females regarding sharing information with their family members, but also significant differences between females with and those without genetics education.

The findings highlighted differences in attitudes between educated participants and those who had subject-specific knowledge, contrary to other attitudinal studies that did not compare those in STEMM or WGS-relevant subjects and those in unrelated subjects [322, 99, 148]. These findings indicate that obtaining a genetic education to a high level, prior to undertaking WGS or receiving results, may affect outcomes. Those with higher genetic knowledge may be more able to recognise the benefits and risks of receiving results information and sharing them with significant others.

One's familiarity with genetics matters, but in different ways. Those in fields related to STEMM were more confident about purchasing WGS and managing the results material on their own than others. However, they might not be cognisant of support needs and sharing issues that might arise for them. Additionally, 'a little knowledge' of genetics from school-level biology class, engendered lower insurance-related concerns in YAs when compared to those who had taken this subject at university. This implied that those with lower domain-specific knowledge were not likely to question how their data might be used. As more people, who have less subject familiarity, come to use WGS and similar services, they may choose to do so without consulting a HCP and not to educate themselves about the technology. Many studies assume genetic or genomic counsellors will manage the educational needs and psychological expectations [291, 350], yet this may not always be the case with DTC services [190, 235, 341, 193]. The experience of negative impacts due to unpreparedness for unexpected and unreassuring results are likely to occur and persist unless tailored interventions to better prepare for and manage undertaking WGS are used [235, 323].

To the field of genomic medicine, Chapter 3 contributes several novel insights into YAs' attitudes regarding undertaking WGS, receiving results and sharing WGS information. Gender, educational levels, genetic knowledge and STEMM background were highly featured variables that may affect YAs' behavioural intentions towards undertaking WGS and sharing results.

7.2.3 WGS Interviews with YAs

Chapter 4's objective was to explore what influenced YAs' considerations and behavioural intentions for undertaking WGS, receiving results information and sharing them with others. Qualitative methods, specifically theme-based content analysis were used to explore aspects of YAs' considerations, preferences and behavioural intentions for undertaking WGS, receiving results information and sharing them with others to identify themes from the data. Chapter 4's interview study contributed insights for genomic medicine, health psychology, related professions and their service users. Empirical data presented as themes about YAs' considerations and tested hypotheses related to their choices along the Proposed WGS Pathway offer rich data about their thoughts regarding WGS.

Others have addressed public motivations and preferences [274]. This study contributes knowledge about YAs' perspectives related to undertaking WGS, receiving results and sharing them with others. The YAs described proactive health planning as their dominant reason for undertaking WGS. This is consistent with studies of adults [274, 271]. Individuals' selections for desired WGS test results were affected by how options were categorised and presented. More information about categories, conditions, and greater granularity in the selection process may assist in informing individuals [285]. Any apparently conflicting or contradictory selections could be highlighted. This would add an opportunity for individuals to be able to check their selections against their actual preferences and intentions, and make changes to selections as desired, adding a layer of validation to indicate that selections are based on a decision making process where conflicts in preferences are used as an opportunity for genuine consideration.

Although family health history was important in selection of results to have returned, slightly more YA participants favoured sharing their WGS results with HCPs and researchers over family members. The insights offered illuminate YAs' WGS sharing priorities and preferences as previous studies [68, 314, 202] have done for the public. Self-discovery, which adds to one's self-identity was a reason to want personal genomic information. YAs' desire for ancestry results for family-tree purposes illustrates their interest in genomic self-discovery beyond health utility. This finding shows YAs have similar non-health interests as ostensibly healthy adults from a broad age range [273, 271].

The YA participants wanted strict control over re-use of their genomic information for research, more than that traditionally offered. This tension will only increase as genomic services and data sharing capabilities develop to increase users' control over their genomic data. Most seemed unaware of the commoditisation of their data by genomic service providers, only one mentioned it, none described profiting themselves. Others have found adolescents and young adults may not have as many privacy concerns as older adults [31].

The YA participants were concerned about their personal genomic information, however they did not recognise its market value as a commodity. An individual's genomic information, be it health-related, ancestry or other, offers new elements for individuals to balance, along with other aspects of self-knowledge when integrating sources of information about themselves into their overall perception of personal identity. Factors identified by YA participants emerge and abate along the WGS Pathway indicating that important considerations are not being fully addressed early enough in the process such as trust, communication skills, family dynamics, rights and responsibilities, desire for privacy, and shared interests with others.

7.2.4 Theoretical framework appraisal for undertaking WGS and sharing results

In light of the significant findings from Chapter 3's survey and themes from Chapter 4's interview study, Chapter 5's objective was to appraise the theoretical models introduced in Chapter 2, and propose a structured WGS framework for YAs' considerations along the Proposed WGS Pathway. In genomics, attitudinal research is wanting for theoretically underpinned design [348]. The appraisal exercise applied empirical data to theoretical models, revealing their characteristics' strengths and weaknesses.

After an examination of the theoretical models, the constructs from TPB of Attitudes, PBC and SN were used with the Proposed WGS Pathway to structure the proposed WGS framework because of its applicability to the range of YAs' considerations involved.

The other models each had useful elements, however they focused either on acceptance and use, in terms of organisational and consumer technology or on health and fears, limiting their applicability. TPB's generic characteristics allowed more findings to be easily included.

Appraisal of theoretical models against empirical data from the YAs' studies supported using TPB for the proposed WGS framework because it offered a broader and more inclusive lens for the studies' results than the other models. A few other genetics studies have utilised TPB [190, 335, 342, 221]. The proposed WGS framework, underpinned by TPB, contributes a novel way to perceive considerations for undertaking WGS as a process over time, using the Proposed WGS Pathway, as per Figure 5.1. This representation contributes to psychological and behavioural science, providing a theoretically underpinned perspective of the WGS process.

7.2.5 Survey with domain experts: an evaluation of proposed research framework

The objective of Chapter 6's study was to evaluate, with domain experts, the Proposed WGS Pathway, the WGS framework's structure and the likely and important factors from those identified from the YAs' studies. Views about motivators and important considerations have been sought of domain experts [120, 154, 169], however these studies did not apply theoretical models, nor were they specific to YAs.

Professional domain experts identified utility-related attitudes and PBCs as more important than factors categorised under TPB constructs of SNs or External Factors. The Proposed WGS Pathway was enhanced with a pre-WGS appraisal step and additional factors, as suggested by the domain experts. The WGS framework, containing the Enhanced WGS Pathway, contributes to the fields of genomic medicine, human factors, and psychological and behavioural science. It may be used to appraise, support and design for YAs undertaking WGS, receiving results and sharing them.

In the past, genetic professionals have been much more willing to return incidental findings from WGS than their professional recommendations advised [353]. They have also been found to be more conservative than non-genetic professionals, researchers and the public [212]. Gaps were found in expectations between what factors most domain experts thought were likely to be considered and the ones they viewed as most important. Designing to bridge these gaps by bringing what may be important yet unconsidered factors to the fore, YAs may address what experts would recommend they prioritise, improving their ability to make more effective decisions about using genomic information to achieve their goals. Before one decides to undertake WGS, there is a logical opportunity to appraise ones hopes, expectations and concerns in relation to undertaking WGS, receiving and sharing results.

Building on the 100,000 Genomes Project in the UK, the NHS Genomics Service included pre-WGS genetic counselling, and established patients' choice in the formalisation of processes for clinical implementation of WGS for clinical diagnostic use and data sharing for 21 rare diseases and 4 cancer indications [86]. These processes were established to comply with current understandings of governance across the clinical and research interface [86]. Early adulthood population-based carrier status screening using WGS has already been shown to be highly cost-effective for diagnosis, risk stratification, and clinical management of several conditions [354], including cancers [46], coronary artery disease [161], and Alzheimer's Disease, highlighting value in prevention interventions in early and mid-life [147].

Publicly-funded use of WGS in the NHS for YAs will become increasingly compelling, driven by the motivation to encourage individuals with elevated risk to pursue lifestyle or medical interventions to prevent the onset of sub-clinical disease [161]. Proportionality and

autonomy must be guaranteed, and in collectively funded health-care systems the potential benefits must be balanced against expenditures [75]. The public will need to know a little bit about what genomics is, and be motivated to take part, in order for a new genomics social contract, reliant on solidarity, altruism, and reciprocity, to succeed in the NHS [113, 312]. The distinguishing characteristic of screening is not so much its context (i.e. whether public health or health care), but the lack of an indication for having this specific test or investigation in those to whom screening is offered [75]. Until NHS Genomics Service provides whole-population WGS screening to whoever wants it, individuals will be motivated to pursue commercial genomics for themselves.

This personal motivation was voiced by Lord Bethell when he bore witness at the Science and Technology Committee's (House of Commons, UK) inquiry into commercial genomics convened in June 2020 [277]. Several years prior, Lord Bethell, a self-described early adopter, used a USA-based DTC company to test for a genetic mutation for Parkinson's disease. A positive result would have indicated a 30%-70% chance of developing Parkinson's disease, like his father, compared to 1% chance in the general population [277]. Lord Bethell was keen to find out how genomic services could contribute to research, encourage people to engage in their health, as it had for him, and how the actual individual insight might change the way people lead their lives [277]. Lord Bethell referred to his common sense and ability to mediate complicated information; he had not sought counselling before undertaking the commercially purchased genetic test, stating that, had he received a positive result he would have then sought counselling [277]. Like Lord Bethell, the STEMM YAs studied in Chapter 3, had greater self-confidence to purchase WGS and receive results independently. Additionally Lord Bethell reflected views of most of the YAs, interviewed in Chapter 4, who also expressed an interest in counselling after WGS results, if needed, but not before.

However, concern remains that if selecting genomic testing on the open DTC market as part of a tick-box purchasing procedure continues, with inherent presumption of knowledge, then YAs' true appraisal of options, including not undertaking WGS, is less likely [122]. The findings of this thesis recognise that young adults do not take in a full range of considerations for WGS and would benefit from some guidance when considering WGS.

Demographics, socioeconomic status, culture, and prior experiences can all influence an individual's health behaviours; this holds true for those pursuing WGS [158]. Expectations and trust among different groups of YAs, including those who seek WGS commercially, those for whom WGS is clinically recommended and offered by their HCP (e.g. through the NHS Genomic Service), and those who decline sequencing, require exploration; unrealistic expectations could lead to worse outcomes [158]. Future research that captures the wider

population's experience of WGS will produce a more generalisable understanding of the clinical, psychosocial, and economic outcomes of pursuing or declining sequencing [158].

Quality of analysis, life-changing implications results may have, and whether counselling was indicated, were among concerns of various submissions to the 2020 Science and Technology Committee's inquiry into commercial genomics [277]. Providing evidence, Dr Tara Clancy, a Council Member of the Nuffield Council on Bioethics, advocated that adequate information provision, consent, and interpretation of results as critical in protecting consumers [277]. When presenting evidence to the inquiry, Graeme Tunbridge, Director of Devices at the Medicines and Healthcare products Regulatory Agency (MHRA), described commercial genomic tests as an in vitro diagnostic device (IVD), currently classified under the lowest risk category, and thereby lacking pre-market scrutiny through regulatory processes [277]. Mr Tunbridge recognised concerns raised about validity of results generated by commercial genomic companies as legitimate; in addition, he stated that there was relatively little in the way of regulation where the test is provided outside the EU [277].

To keep their reputations and revenues, DTC genomic companies need customers' continued experiences to remain positive. Findings from this thesis were shared with those approached for the domain expert study from Chapter 6. One genomics company noted the finding that YAs' had limited interest in results for diseases and conditions affecting mental capacity. They subsequently confirmed this finding was influential in their decision not to pursue such products at that time. It is likely other commercial companies would also choose to pursue genomic results that are most likely to be positively accepted, and marketable, rather than focus on areas that are more challenging.

If trust in privacy protection and access to expertise were enhanced through regulation, DTC WGS markets could increase significantly [62]. As they continue to offer more information to customers, some DTC genomic companies, who do not already offer counselling before WGS, may choose to add such support services for those who need it. It would be beneficial to individuals if systems were correctly designed to proactively support customers' information needs for decision making rather than only offering counselling for those who need it when results are returned. Offering potential customers an appraisal opportunity is good for service users [348], but it has the potential to reduce uptake of the companies' products.

This points to a need for regulatory oversight to enforce the provision of appraisal mechanisms or address the need for more education so users of WGS services can engage with the process in a manner that would indicate true informed consent [12]. A tool or service is required to offer support for a genuine appraisal of WGS; this needs to be attractive enough to get the attention of those YAs who may not know much about genetics, yet are in

the market for WGS. Without the enforcement of a structured appraisal before undertaking WGS, it is unlikely that DTC genomic companies would offer it as their interest is to seek to accentuate the benefits of testing and make the customer experience as painless as possible, so provision of consumers' data is not impeded.

The Enhanced WGS Pathway and the proposed likely and important factors form a theoretically underpinned framework of considerations that requires further evaluation and validation so a tool may be developed to raise awareness of issues and inform intervention designs to support YAs considering WGS in different settings. Findings from this thesis contribute to an evidence base that can further inform current debates and development of standards and good practice guidelines for YAs and WGS (in relation to commercial genomic companies and publicly-funded healthcare services. The findings presented here pave the way for further work in this area, particularly timely given the UK Parliament's current inquiry.

Results from this thesis contribute knowledge to a number of fields including genomic medicine, psychological and behavioural science, and human factors. The WGS framework, with the Enhanced WGS Pathway, contribute to genomic medicine, human factors and psychological and behavioural science. Results about YAs knowledge, sharing preferences and considerations for WGS offer valuable insights to inform genomic medicine service provision and future direction of studies. The Enhanced WGS Pathway and the WGS framework of factors ranked by experts lays out YAs' considerations about undertaking WGS, receiving results and sharing them that may inform design for YAs' or appraisal of their needs, contributing to human factors, genomic medicine, and psychological and behavioural science.

7.3 Dissemination and Impact

Individual pieces of work from this thesis have been disseminated. Details of venue and format are as follows:

One peer reviewed journal article publication, April 2019:

- Barnard, P, Sharples, S, Thomson, B and Garibaldi, J, "YAs' attitudes to sharing whole-genome sequencing information: a university-based survey", BMC Medical Genomics, 2019, 12:55 Venue: BMC Medical Genomics, Springer.

One conference workshop, September 2016:

- A research workshop with individuals interested in genomics to explore participants' considerations for undertaking WGS at a conference focused on medicine, patients

and technology. Venue: Medicine X 2016 conference. Stanford University, Palo Alto, California, USA.

Four conference presentations:

- May 2016: Oral presentation of research plan to Postgraduate Children and Childhood Network Annual Conference, University of Nottingham. Venue: Council Room, Trent Building, University of Nottingham, UK.
- September 2017: Oral presentation of previous year's workshop and findings from interviews with YAs at a conference focused on medicine, patients and technology. Venue: Medicine X 2017 conference. Stanford University, Palo Alto, California, USA.
- May 2018: Oral presentation to conference with a focus on medical education and technology. Venue: Medicine X | Ed 2018 conference. Stanford University, Palo Alto, California, USA.
- September 2019: Oral presentation of findings from the domain expert study at conference focused on medicine, patients and technology. Venue: Medicine X 2019 conference. Stanford University, Palo Alto, California, USA.

Three invited presentations:

- June 2018: Conference presentation of findings from workshop and interview with YAs at a conference focused on emerging commercial healthcare technologies. Venue: iCEE.health conference, Grand Cinema & More, Bucharest, Romania.
- September 2018: Class presentation to cohort of genetic counselling students on a course offered by University of California San Francisco and Kaiser Permanente in Oakland, California. Venue: The Oakland Kaiser Hospital, Oakland, California, USA.
- October 2018: Oral presentation of survey and interview findings with YAs to Horizon industry partners, academics and researchers. Venue: Jubilee Conference Centre, University of Nottingham, UK.

Two poster presentations:

- October 2016: Poster presentation of study plan to Horizon industry partners, academics and researchers. Venue: Jubilee Conference Centre, University of Nottingham, UK.

- May 2019: Poster presentation of findings from the domain expert study at conference focused on use of big data in health. Venue: Big Data in Precision Health, Stanford University, Palo Alto, California, USA.

The impact of the studies goes beyond genomic medicine, psychological and behavioural science and human factors.

The results may have an impact on:

- epidemiology: insights from understanding what influences YAs' sharing preferences may inform epidemiological studies and public health screening programmes.
- computer science: identification of important user requirements in terms of consideration factors and the structure provided by the Enhanced WGS Pathway and WGS framework are useful to software designers.
- business studies: information about YAs' considerations, preferences and needs related to WGS inform where efforts may be targeted to maximise benefits. This is relevant to health and leisure, specifically DTC sectors.

There are plans to disseminate findings to audiences in the UK and abroad who have an interest in WGS in relation to YAs.

7.4 Limitations

Limitations to the studies included sample size, lack of ethnicity data, socioeconomic demographic make-up of participants in terms of and elements of the methodology. These were mainly due to limited resources, including time and finances, to undertake alternative studies. Numbers and reach of the studies were primarily limited to the geographical mobility of the researcher and opportunities to access participants.

For the YAs' survey, the sample size was relatively small so only the largest differences were detectable. That sample contained a large proportion of students, drawn mainly from the population of University of Nottingham's UK campus-based individuals. This population's educational attainment and genetic knowledge was likely to be higher than that of the general public. The use of ellipses in collecting data in the YAs' survey was novel in this context. This should also be considered when interpreting results.

Sample size for the interview study with YAs was the main limitation. Thematic analysis was carried out on the qualitative data, however the quantitative data gathered from the tick-box elements of the interview schedule could only be presented as simple descriptions.

Sample size for the domain expert study was the main limitation of that study. Expert genetic professions were a difficult group to recruit participants from. Because of the limited number of participants it was not possible to carry out statistical analysis on their data. Basic descriptions and presentation of expert participants' responses could be presented.

7.5 Future Work

Further research related to or repeating the thesis studies with a wider demographic of YAs and domain experts, would help identify how generalisable the results found here are likely to be. Ethnicity data should be captured in future studies so the relationship they have with attitudes may be tested.

The list of prioritised consideration factors and the Enhanced WGS Pathway that were drawn up following findings from the domain expert study require further research and development. This includes research with YAs, who have undertaken WGS, to identify factors they prioritise from their experience as important to consider before undertaking WGS. Understanding differences in the considerations of those YAs offered WGS by their HCP as opposed to those who seek commercial genomics services will make a valuable addition to knowledge. Elicitation of additional factors YAs may have experienced that have not already been indicated from research to date would be beneficial to developing an appraisal tool to address concerns from pre-WGS onwards. Dissemination of this thesis' findings will contribute to current debates by providing evidence to support those developing good practice guidelines for WGS and YAs both in the UK and abroad. Sharing findings about YAs considerations, particularly the gaps identified by the domain experts have the potential to inform commercial companies' choices and regulatory development for commercial and publicly-funded genomic offerings.

External factors feature highly among those added by genetic expert participants to the list of important factors for YAs to consider. External factors cover a great deal of ground and deserve more attention with further research so services may be designed to meet indicated requirements.

The version of Enhanced WGS Pathway and the prioritised list of factors that would follow any additional validation research with an experienced group of YAs would require re-evaluation. This re-evaluation could be done by involving genetic professionals in another domain expert study. The experts may wish to further amend the WGS Pathway and the prioritised list of factors. This re-evaluation would be well served by inclusion of a larger numbers of domain expert participants from various countries than were available for this thesis.

New questions arise from the findings of the expert study and the literature. Those questions include:

- How does undertaking WGS oneself affect genetic professionals' expectations of otherwise healthy YAs to consider undertaking WGS?
- What motivates genetic professionals themselves to undertake WGS or not?
- How does this compare to what motivates YAs to do the same?

Re-use of samples held by WGS service providers may be allowed for a variety of other purposes with very few regulatory protections in place in the case of offerings from DTC companies. This aspect was not the focus of this research, but given that there was a desire to share results with researchers so others may benefit, it is relevant to future research. YAs' desire to decide who uses their data will only be realised if terms and conditions of sample provision indicate it. It may be that individuals are making ungrounded assumptions about what WGS service providers will do with their data. This deserves greater attention in future research, given how increasingly accessible and cheap WGS is becoming.

Analysis of the interval data gathered from YA participants who used ellipses when answering survey questions has yet to be undertaken. Use of ellipses in this context remains a technique requiring further research to assess its usefulness for gathering more nuanced information about uncertainty held within participants' responses. Interval data, captured on a scale, allows for more sensitive analysis of views.

Development of engaging educational tools that will prepare individuals for the potential outcomes of WGS by addressing their expectations and increase their facility to manage results will benefit from additional research and development activities as listed above.

7.6 Conclusions

This thesis presented studies that have contributed novel insights into YAs' preferences and considerations for undertaking WGS and sharing results. The WGS framework proposed illustrates the WGS Pathway. TPB supported the YA studies' design and was found to be most suited to categorising results from the findings in a meaningful manner, therefore YAs' considerations were framed as TPB factors in the proposed WGS framework. The Proposed WGS Pathway was enhanced by domain experts to include a pre-WGS step. They prioritised the factors and added new ones.

Gender, genetic knowledge and STEMM backgrounds were statistically significant variables related to YAs' behavioural intentions regarding sharing results. Proactive health planning was the dominant reason for wanting to undertake WGS. Despite this, individuals were interested in a selection of results that extended beyond clinical utility. YAs wanted more results information than is usually offered. Discrepancies in participants' selections for WGS results indicate that their need for clearly defined presentation of their selections and for any potential contradictions in their selections to be highlighted to them. Some important factors may not be considered by YAs including communication skills and trust. Sharing preferences indicated that more education would support informed decisions about who to share one's DNA and genomic information with and why. Domain experts addressed the Proposed WGS Pathway in an evaluation study of the proposed WGS framework. They prioritised TPB factors presented to them and added others they felt were missing to create an Enhanced WGS Pathway with a pre-WGS step.

Access to and engagement with educational materials appears to be key to informed decision making about WGS. Undertaking a structured, informed appraisal of WGS before deciding to undertake it would help fill gaps between what is likely to be considered and what would be important for consideration. This would be an opportunity to design to raise awareness and better inform individuals about undertaking WGS.

Questions about YAs' intentions and behaviours remain outstanding. This thesis contributes a theoretically and empirically underpinned WGS framework containing key factors and a WGS Pathway process that may be utilised for future research design, analysis, and for practical interventions.

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Appendix A

Searches: Dates, Terms and Sources

A.1 Searches by date order

3/11/2015: Google Scholar search terms: relationship kinship family member relatives parent child adolescent patient attitude perspective understanding engagement behaviour outcomes data sharing health medical genomic genetic return results, limited to 2010-2015 – 303 results, 18 results downloaded. Google scholar search terms: children families relatives perspective genomics results findings informed decision-making, limited to 2010-2015 – 12,000 results, 84 downloaded. 19/1/16: Springer Link Library of Journals search terms: "genomic results" and "genomics results patient" and "genomic results adolescent" Refined by English, Articles, 2011-2016 – 1,819 results, 45 results downloaded.

20/1/16 and 21/1/16: Springer Link Library of Journals search terms: "genetic genomic results adolescent" 2011-2016, English – 2,383 results found, 28 results downloaded.

9/2/16: NU Search Primo Central search terms: genomic results young adult human - 38 results, none relevant adolescent adult genetic genomic genome exome exomic report results - 5 results, none relevant genetic genomic genome exome exomic report results - 79 results, 0 relevant family adolescent perspective genetic genomic genome exome exomic report results - 2 results, none relevant family adolescent perspective genetic results -17 results, 0 relevant family adolescent perspective genetic genomic genome exome results - 58 results, 5 results downloaded.

10/2/16-11/2/16: NU Search Primo Central search terms: student attitude perspective genomic results; (in last 10 years) -182 results, 21 articles downloaded NUSearch led to ERIC website's educational literature resource. Search terms: genomic, adolescent, genetic - 12 results downloaded

11/2/16: Google Scholar search terms: genomic results young adult human - 0 relevant results on 1st page of returns family adolescent perspective attitudes genetic - 2 relevant

results on 1st page of returns, downloaded Article found led to an opportunistic search through the Journal of Research in Adolescence Wiley Online Library Search terms: genome AND attitude - 7093 results, 29 results downloaded

23/2/16: SCOPUS search terms: “public” refined to find “genome” refined again to find “attitude”, refined again for “young” - 477 results, 15 results downloaded

24/2/16: Google Scholar search terms: genomic report attitude OR perspective OR view OR opinion OR share OR sharing (in the last year) - 18,400 results, 9 results downloaded "public OR lay OR adult OR adolescent OR teenager OR student OR young OR people" AND "attitude OR opinion OR view OR perception OR acceptance OR communication" AND "Genomic OR genetic OR exomic OR exome" AND "result OR report" – 39,900 results, 14 results downloaded

Further materials were sourced from reference lists of relevant articles and search updates.

Appendix B

Supplementary information for YAs' WGS Survey

B.1 Copy of YAs' WGS survey

Whole Genome Sequencing Study: My Genomic Life Survey

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

Welcome to this survey designed to explore your views about receiving and sharing information from **Whole Genome Sequencing (WGS), the process of sequencing a person's entire DNA**. Analyses are performed on the sequence to provide results on various health conditions. You may fill in this survey electronically by using "text comment" or "draw free form" functions found in the "Comment" menu, (see the top right of this PDF's toolbar) and return completed survey with your consent form and prize draw coupon by e-mail to pepita.stringer@nottingham.ac.uk OR you may complete printed forms. Completed consent form, survey and prize draw coupon may be returned by post or scanned and emailed. Postal address: Pepita Stringer, Room B38, School of Computer Science, University of Nottingham, Jubilee Campus, Wollaton Road, Nottingham England NG8 1BB
If you have any questions, please get in touch with Pepita by email.

1. How did you first become aware of WGS? Tick all boxes that apply to you.

   a. Through this study ☐
   b. On the Internet ☐
   c. A video on the Internet ☐
   d. In a movie ☐
   e. On TV ☐
   f. A printed magazine or newspaper ☐
   g. A book ☐
   h. Academic journal article ☐
   i. A friend ☐
   j. A family member ☐
   k. A health professional ☐
   l. At school ☐
   m. At university ☐

   If you answered "Yes" to any of the above, please describe an example (or more).

   _____

   _____

   _____

2. Since hearing or reading about WGS, have you looked for more information about it?

   ☐ Yes ☐ No

3. If you answered "Yes" to Question 2: Where did you seek additional information?
(please tick as many options from the following that apply to you)

   a. Web links from study's information sheet ☐
   b. Academic journals ☐
   c. Books or other printed materials ☐
   d. Other internet sources ☐
   e. Friends ☐
   f. Family members ☐
   g. Work colleagues ☐
   h. Health professionals ☐
   i. Other, please specify _____

Please answer the following questions about the human genome. It is not expected that you have all the answers.

4. Genes come in pairs, with one copy inherited from each parent.

   ☐ I don't know ☐ false ☐ true

5. The chromosomes of men and women are similar except for one pair.

   ☐ I don't know ☐ false ☐ true

6. For some disorders to be inherited, a mutation must come from both parents.

   ☐ I don't know ☐ false ☐ true

7. Males and females have the same number of chromosomes.

   ☐ I don't know ☐ false ☐ true

8. A gene is a disease.

   ☐ I don't know ☐ false ☐ true

9. Parents with no sign of ill-health can have a child with an inherited disease.

   ☐ I don't know ☐ false ☐ true

10. The carrier of a disease gene may be completely healthy.

☐ I don't know ☐ false ☐ true

11. Some genetic conditions express themselves later in adult life

☐ I don't know ☐ false ☐ true

12. How many pairs of chromosomes do humans have?

☐ a. 23
☐ b. 24
☐ c. 27
☐ d. 28
☐ e. I don't know

13. In DNA, the Adenine nucleotide bonds with which nucleotide to form a base pair?

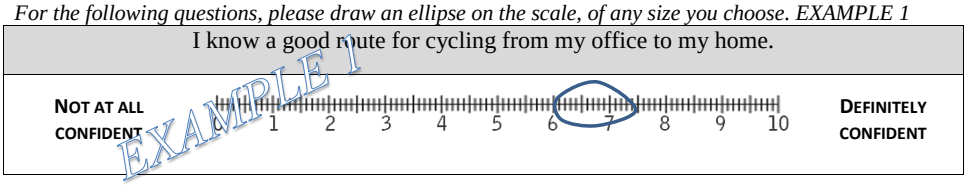
☐ a. Guanine
☐ b. Cytosine
☐ c. Thymine
☐ d. Uracil
☐ e. I don't know

14. Approximately how many protein-encoding genes do humans have?

☐ a. 20,000 to 25,000
☐ b. 35,000 to 40,000
☐ c. 70,000-75,000
☐ d. More than 100,000
☐ e. I don't know

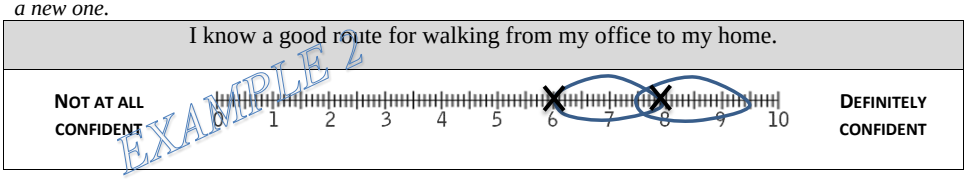
For the following questions, please draw an ellipse on the scale, of any size you choose. EXAMPLE 1

I know a good route for cycling from my office to my home.



EXAMPLE 2: To correct a mistake, make crosses at both sides of an incorrect ellipse (6 - 8), then draw a new one.

I know a good route for walking from my office to my home.



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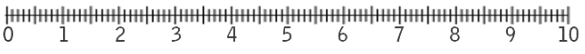
Draw your ellipses as you see fit for each of the statement below.

1. I am confident I can find information on whole genome sequencing (WGS).

STRONGLY DISAGREE  **STRONGLY AGREE**

2. I am confident I would understand the relevant information about results from a WGS analysis.

STRONGLY DISAGREE  **STRONGLY AGREE**

3. I think the development of WGS is a medical progress which may have positive impact

STRONGLY DISAGREE  **STRONGLY AGREE**

4. I approve of using WGS for better management of diseases.

STRONGLY DISAGREE  **STRONGLY AGREE**

5. I would inform my siblings about the results of my WGS analysis.

STRONGLY DISAGREE  **STRONGLY AGREE**

6. I would inform my children about the results of my WGS analysis.

STRONGLY DISAGREE  **STRONGLY AGREE**

7. I would inform my parents about the results of my WGS analysis.

STRONGLY DISAGREE  **STRONGLY AGREE**

8. I would want to know if I had a hereditary disease.

STRONGLY DISAGREE  **STRONGLY AGREE**

9. I think having the results of my WGS analysis would help me take more responsibility for my health.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

10. Knowing the results from WGS analysis could change a person's future.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

11. I am concerned about possible consequences the WGS results may have on insurance policies for health, travel or life.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

12. I only want to know about diseases that can be treated.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

13. I would prefer not to undertake WGS.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

14. I want my WGS to help me learn about my ancestry and my family tree.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

15. The idea of WGS frightens me.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

16. I would like to have my own WGS done.

STRONGLY DISAGREE 0 1 2 3 4 5 6 7 8 9 10 **STRONGLY AGREE**

17. I would want to receive a report that explains the results from my WGS.

STRONGLY DISAGREE	0 1 2 3 4 5 6 7 8 9 10	STRONGLY AGREE

18. I would want to receive the raw data from my WGS.

STRONGLY DISAGREE	0 1 2 3 4 5 6 7 8 9 10	STRONGLY AGREE

19. I would consult a doctor, nurse, or counsellor before undertaking a WGS.

EXTREMELY UNLIKELY	0 1 2 3 4 5 6 7 8 9 10	EXTREMELY LIKELY

20. I like the idea of purchasing WGS services over the Internet.

STRONGLY DISAGREE	0 1 2 3 4 5 6 7 8 9 10	STRONGLY AGREE

21. My relatives would want to know about my WGS results.

STRONGLY DISAGREE	0 1 2 3 4 5 6 7 8 9 10	STRONGLY AGREE

22. I would want to know the WGS results of my relatives.

STRONGLY DISAGREE	0 1 2 3 4 5 6 7 8 9 10	STRONGLY AGREE

23. I would consider knowing my WGS analysis as:

HARMFUL	0 1 2 3 4 5 6 7 8 9 10	BENEFICIAL

24. I would consider knowing my WGS analysis as:

WORTHLESS	0 1 2 3 4 5 6 7 8 9 10	VALUABLE

25. I consider myself…

VERY UNHEALTHY  VERY HEALTHY

Please fill in the blanks and make a tick in the circles ☑ that apply to you:

26. Please state your age: I am_____years old

27. Please state your gender: I am _____

28. Have you studied genetics as part of a biology course?

◯ no ◯ yes (at school) ◯ yes (at university)

29. Have you been on a course specifically about genetics?

◯ no ◯ yes (at school) ◯ yes (at university)

30. What is your highest completed level of education? _____

31. Are you employed?

◯ no ◯ yes, part-time ◯ yes, full-time

If you are employed, what is your current role(s)?_____

32. Are you a student?

◯ no ◯ yes, part-time ◯ yes, full-time

If you are a student, what is your field of study?_____

33. Do you teach or do research?

◯ no ◯ yes

If you teach or do research, what is your field?

_____

34. What country have you mainly resided in for the last 6 months?

_____

35. Would you want your genomic data to be available to wider health research studies?

◯ no ◯ yes, but only if I'm not re-identifiable ◯ yes, if I can be re-identified and contacted

◯ other response, please describe_____

36. Would you like to learn more about WGS or the human genome?

◯ no ◯ yes

Please make comments_____

_____

_____

_____

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This survey used the following method to gather your opinions, see the example below:

Please draw an ellipse on the scale to reflect your views.

I like using this method to answer questions about my opinion.		
STRONGLY DISAGREE		**STRONGLY AGREE**

36. Please describe how the method used in this survey affected your ability to express your opinions.

_____

_____

Many surveys use the following format for gathering opinions:

Please click the dot to select your response from those below:

I like using this method to answer questions about my opinion.

Strongly Disagree	Disagree	Slightly Disagree	Neither	Slightly Agree	Agree	Strongly Agree
○	○	○	○	○	○	○

37. Would you have been able to express yourself better using this method?

_____

_____

38. Please select words below that reflect your opinion of the method used in this survey (select all that apply).

◯ Realistic	◯ Confusing	◯ Intuitive
◯ Easy	◯ Time-efficient	◯ Correct
◯ Natural	◯ Vague	◯ Cryptic
◯ Clear	◯ Difficult	◯ Time-consuming

Please write three words below to describe your thoughts about using the method above to answer the questions in this survey.

- _____
- _____
- _____

Completed consent form and survey to be returned by email to pepita.stringer@nottingham.ac.uk, by post to Pepita Stringer, School of Computer Science, University of Nottingham, Wollaton Road, Nottingham England NG8 1BB, in person or as directed. **Thank you for your participation, it is very much appreciated!**

B.2 Statistical Results from YAs' WGS survey

n = 112 **Statistical Test Results**

Statistical Test ⇒	Mann Whitney (U)	Mann Whitney (U)	Spearman's Rho (r_s)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)
Single test alpha	$\alpha = 0.05$	$\alpha = 0.05$	$\alpha = 0.05$	$\alpha = 0.05$	$\alpha = 0.05$	$\alpha = 0.05$
Multi-test alpha	$\alpha = 0.001$	$\alpha = 0.001$	$\alpha = 0.001$	$\alpha = 0.001$	$\alpha = 0.001$	$\alpha = 0.001$
Variables	**Gender (f, m)**	**STEM (n, y)**	**Quiz Score**	**Completed Ed-Level (grouped)**	**Biology course (none, school, university)**	**Genetics course (none, school, university)**
Quiz Score	U = 1486 p = 0.8975 z = 0.128 r = 0.012095	**U = 1079.5** **p =.00359** ****** **z = 2.821** **r = 0.266559**		$X^2(2) = 0.4513$ p = 0.798 ns	**$X^2(2) = 22.796$** **p = 1.122e-05** ******** **----------** **Conover post-hoc test result for University x School** **t(110) = 4.441** **p < 0.0001** **r = 0.38991** **----------** **Conover post-hoc test result for University x none** **t(110) = 4.49** **p < 0.0001** **r = 0.42610**	**$X^2(2) = 18.809$** **p = 8.235e-05** ******** **----------** **Conover post-hoc test result for University x none** **t(110) = 4.596 p < 0.0001** **r = 0.40136**
consulting with HCP prior to WGS (Q19)	U = 1629.5 p = 0.471 z = -0.724 r = -0.06841	U = 1451 p = 0.513 z = 0.656 r = 0.061986	r_s =-0.0007 S = 234310 p = 0.993 ns	$X^2(2) = 2.267$ p = 0.3218 ns	$X^2(2)$ = 0.33506 p = 0.8458 ns	**$X^2(2) = 6.4329$** **p = 0.0401** ***** **----------** **Conover post-hoc test result for School x University** **t(110) = 2.531,** **p < 0.05** **r = 0.23458**

n = 112		**Statistical Test Results**				
Statistical Test ⇒	Mann Whitney (U)	Mann Whitney (U)	Spearman's Rho (r_s)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)
Single test alpha **Multi-test alpha**	$\alpha = 0.05$ $\alpha = 0.001$	$\alpha = 0.05$ $\alpha = 0.001$	$\alpha = 0.05$ $\alpha = 0.001$	$\alpha = 0.05$ $\alpha = 0.001$	$\alpha = 0.05$ $\alpha = 0.001$	$\alpha = 0.05$ $\alpha = 0.001$
Variables	**Gender (f, m)**	**STEM (n, y)**	**Quiz Score**	**Completed Ed-Level (grouped)**	**Biology course (none, school, university)**	**Genetics course (none, school, university)**
wanting a report to explain WGS results (Q17)	U = 1754.5 p = 0.143 z = -1.466 r = -0.13852	**U = 1218** **p = 0.0441** ***** **z = 2.013** **r = 0.190211**	**r_s = 0.279** **S = 168590** **p = 0.002794** ****** **z = 2.939** **r = 0.19637**	$X^2(2) = 1.1982$ p = 0.5493 ns	$X^2(2) = 5.3363$ p = 0.06938 ns	$X^2(2) = 2.288$ p = 0.3185 ns
concerns related to insurance policies (Q11)	U = 1590 p = 0.626 z = -0.49 r = -0.0463	U = 1247.5 p = 0.0659 z = 1.842 r = 0.174053	r_s = -0.014 S = 237640 p = 0.875 ns	**$X^2(2) = 6.3042$** **p = 0.04276** ***** **----------** **Conover post-hoc test result for Secondary School x 2nd degree** **t(110) = 2.549,** **p < 0.05** **r = 0.23616**	**$X^2(2) = 6.4392$** **p = 0.03997** ***** **----------** **Conover post-hoc test result for University x School** **t(110) = 2.572,** **p < 0.05** **r = 0.23817**	$X^2(2) = 3.2182$ p = 0.2001 ns

n = 112		**Statistical Test Results**				
Statistical Test ⇒	Mann Whitney (U)	Mann Whitney (U)	Spearman's Rho (r_s)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)
Single test alpha	α = 0.05	α = 0.05	α = 0.05	α = 0.05	α = 0.05	α = 0.05
Multi-test alpha	α = 0.001	α = 0.001	α = 0.001	α = 0.001	α = 0.001	α = 0.001
Variables	**Gender (f, m)**	**STEM (n, y)**	**Quiz Score**	**Completed Ed-Level (grouped)**	Biology w/ genetics	**Genetics course (none, school, university)**
sharing WGS results with parents (Q7)	**U = 1856** **p = .0388** ***** **z = -2.068** **r = -0.19541**	U = 1288 p = 0.108 z = 1.605 r = 0.151658	r_s = 0.184 S = 190930 p = 0.051 ns	$X^2(2)$ = 3.5372 p = 0.1706 ns	$X^2(2)$ = 5.0899 p = 0.07848 ns	**$X^2(2)$ = 8.273** **p = 0.01598** ***** ---------- **Conover post-hoc test result for University x none** **t(110) = 2.906** **p < 0.05** **r = 0.26701**
sharing WGS results with siblings (Q5)	**U = 1849.5** **p = 0.04258** ***** **z = -2.03** **r = -0.19182**	U = 1287 p = 0.107 z = 1.611 r = 0.152225	r_s = 0.118 S = 206360 p = 0.212 ns	**$X^2(2)$ = 6.1039** **p = 0.04727** ***** ---------- **Conover post-hoc test result for Secondary School x 1st degree** **t(110) = 2.518, p < 0.05** **r = 0.23344**	$X^2(2)$ = 5.4783 p = 0.06463 ns	**$X^2(2)$ = 6.8617** **p = 0.03236** ***** ---------- **Conover post-hoc test result for University x none** **t(110) = 2.529,** **p < 0.05** **r = 0.23441**

n = 112		**Statistical Test Results**				
Statistical Test ⇒	Mann Whitney (U)	Mann Whitney (U)	Spearman's Rho (r_s)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)	Kruskal-Wallis (X^2)
Single test alpha	α = 0.05	α = 0.05	α = 0.05	α = 0.05	α = 0.05	α = 0.05
Multi-test alpha	α = 0.001	α = 0.001	α = 0.001	α = 0.001	α = 0.001	α = 0.001
Variables	**Gender (f, m)**	**STEM (n, y)**	**Quiz Score**	**Completed Ed-Level (grouped)**	**Biology w/ genetics**	**Genetics course (none, school, university)**
wanting to know WGS results of a relative (Q22)	**U = 1912** **p = 0.0164** ***** **z = -2.404** **r = -0.22716**	**U = 1104.5** **p = 0.00753** ****** **z = 2.675** **r = 0.252764**	rs = 0.184 S = 190950 p = 0.051 ns	$X^2(2)$ = 1.723 p = 0.4225 ns	$X^2(2)$ = 3.493 p = 0.1744 ns	**$X^2(2) = 6.2077$** **p = 0.04488** ***** ---------- **Conover post-hoc test result for University x none** **t(110) = 2.533,** **p < 0.05** **r = 0.23476**

n = 67	**Statistical Test Results**
Statistical Test ⇒	Mann Whitney (U) – post-hoc test
Single test alpha **Mult-test alpha**	α = 0.05 α = 0.0166
Variables	**Females without and females with university-level genetics course**
sharing WGS results with parents (Q7)	**U = 179.5** **p = .00336** ****** **z = -2.71121** **r = 0.331227**
sharing WGS results with siblings (Q5)	**U = 204.5** **p = .01044** ***** **z = -2.31484** **r = 0.282803**
wanting to know WGS results of a relative (Q22)	U = 254 p = .06301 ns z = -1.53001 r = 0.186920
	Interpretation of effect size (r): **r = 0.1 = small effect** **r = 0.3 = medium effect** **r = 0.5 = large effect**

Appendix C

Copy of Interview Schedule Template used with young adults

C.1 Interview Template: Young Adults Study

Whole Genome Sequencing Study Interview

REPORTING RESULTS TO PATIENTS

If an entire genome is sequenced, almost everyone tested will have multiple findings—each with its own measure of validity, utility, and possible interventions and outcomes. These results are likely to include incidental findings that are not related to the reason for testing […] For example, a person being sequenced to determine susceptibility for breast cancer may be discovered to have Huntington's disease, which has no cure. There has been much controversy about how to address incidental findings and what findings should be reported, including debates about whether experts should determine which incidental findings will be reported to all patients or whether patients should decide what specific results they want to know. (Phillips et al. 2014)

Imagine you have had your WGS undertaken…

- **What disease types would you want to know about?**

Pick from list of possible results categorised by condition

Categories for the possible genetic information obtained from Whole Genome Sequencing (WGS) would you want results from these categories?				
CATEGORIES	**YES**	**NO**	**UNSURE**	**THOUGHTS?**
• **Useful genetic findings about the condition that led you to undertake WGS analysis**				
• **Any clinically relevant genetic findings, which may have immediate benefits for you related to diseases or clinical conditions that are present.**				
• **Diseases that are present for which possible treatment is available**				
• **Diseases that are present with no treatment available**				
• **Genetic mutations related to high risks for diseases in the future.**				
• **Information about risks of preventable or treatable future diseases**				
• **Information about risks of non-preventable, non-treatable future diseases**				
• **Information about carrier status of mutations for an X-linked or an autosomal recessive disorder impacting reproductive life decisions.**				
• **Information of variable risk for future diseases: Genetic traits that may be translated into high predisposition for certain complex diseases**				
• **Pharmacogenetic variants – helps identify what medicines will / won't work for you.**				
• **Information of unknown significance.**				

Adapted from Ayuso et al. (2013)

- Why this choice?
- What affects your desire to know more or less, sooner or later?
- Should experts decide what should be reported or should patients decide?

WOULD YOU WANT RESULTS ABOUT THESE CONDITIONS IF YOU HAD YOUR WHOLE GENOME SEQUENCED? Make a mark in the box you agree with and share your thoughts. (1 of 2)				
Condition	**YES**	**NO**	**UNSURE**	**SHARE YOUR THOUGHTS**
All Results on this list				
No Results on this list				
Alzheimer disease				
Heart disease				
Lupus				
Addiction				
Sarcosis				
Bowel Cancer				
Breast and Ovarian Cancer				
Other Cancer types				
Diabetes				
Allergy				
Gastrointestinal conditions				
Learning disabilities				
Ancestry				
High blood pressure				

- Why this choice?
- What affects your desire to know more or less, sooner or later?
- Should experts decide what should be reported or should patients decide?

WOULD YOU WANT RESULTS ABOUT THESE CONDITIONS IF YOU HAD YOUR WHOLE GENOME SEQUENCED? Make a mark in the box you agree with and share your thoughts. (2 of 2)				
Condition	**YES**	**NO**	**UNSURE**	**SHARE YOUR THOUGHTS**
All Results on this list				
No results on this list				
Cystic Fibrosis				
ADHD				
Stroke				
Collagen disease				
Factor V Friedreich ataxia				
Down syndrome				
Fibromyalgia				
Haemoglobin E/Thalassemia				
Huntingdon disease				
Macular degeneration				
Parkinson disease				
Sickle cell				
Thyroid problems				
Familial hypercholesterolaemia				
Other: Please Specify				

- Why this choice?
- What affects your desire to know more or less, sooner or later?
- Should experts decide what should be reported or should patients decide?

Who would you want to receive your WGS results from?				
PERSON	**YES**	**NO**	**UNSURE**	**YOUR THOUGHTS**
From a genetic counsellor				
From a doctor				
From a family member				
Other, please specify:				

How would you want to receive your WGS results?				
MEDIA	**YES**	**NO**	**UNSURE**	**YOUR THOUGHTS**
Letter				
Secure website				
E-mail				
Phone call				
Video-call				
In-person				
Other, please specify				

- What, from the following, would be important to help you?
    - More knowledge about genetics and genomics?
    - Simple language in a report?
    - Step by step guide to results?
    - Bar graphs or other similar charts?
    - Computer graphics?
    - Genetic counselling?
    - Explanation from a qualified health care professional?
    - Other?

ACTION ON WGS RESULTS

- What would you want to use your WGS results for?
    - Support or improve self-care, e.g. lifestyle activities, medication, treatment
    - Add information to my health record
    - Add information to your family tree / ancestry records
    - Re- analyse in the future to learn more
    - None of the above
    - Other, specify
    - What would you see as your personal challenges if you had WGS done?

Who would you want to share your WGS analysis results with?				
PEOPLE	**YES**	**NO**	**UNSURE**	**YOUR THOUGHTS**
No-one, keep to myself				
Mother				
Father				
My child				
Other family member				
Family physician				
Clinical Geneticist				
Genetic counsellor				
Other health professional				
Researcher				
Friend				
Employer				
Insurer				
Support group				
Online forum				
Other, specify				

- What would you describe as your support needs?
- (When) would you want to know about WGS results undertaken by another family member?
- Ideal process?
- What would help?
- Challenges?

Appendix D

Young Adult Interviewees' Responses

D.1 WGS results selections by clinical categories

Categories for the possible genetic information obtained from Whole Genome Sequencing (WGS) would you want results from these categories?					
CATEGORIES	YES	NO	UNSURE	THOUGHTS	TALLY YES – NO - UNSURE
• Useful genetic findings about the condition that led you to undertake WGS analysis	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P98M, P99M		P97F		10-0-1
• Any clinically relevant genetic findings, which may have immediate benefits for you related to diseases or clinical conditions that are present.					
• Diseases that are present for which possible treatment is available	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P97F, P98M, P99M				11-0-0
• Diseases that are present with no treatment available	P5M, P8M, P14M, P20F, P30M, P73F, P98M, P99M		P2M, P74F, P97F		8-0-3
• Genetic mutations related to high risks for diseases in the future.					
• Information about risks of preventable or treatable future diseases	P2M, P5M, P8M, P14M, P20F, P30M, , P97F,P73F, P74F, P98M, P99M				11-0-0
• Information about risks of non-preventable, non-treatable future diseases	P5M, P8M, P14M, P20F, P30M, P73F, P98M, P99M	P74F	P2M, P97F		8-1-2
• Information about carrier status of mutations for an X-linked or an autosomal recessive disorder impacting reproductive life decisions.	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P98M, P99M	P97F			10-1-0
• Information of variable risk for future diseases: Genetic traits that may be translated into high predisposition for certain complex diseases	P2M, P8M, P20F, P30M, P73F, P74F, P97F, P98M, P99M		P5M, P14M		9-0-2
• Pharmacogenetic variants – helps identify what medicines will / won't work for you.	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P97F, P98M, P99M				11-0-0
• Information of unknown significance.	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P98M	P99M	P97F	P73F: not sure it'll be useful	9-1-1

D.2 WGS results selections by disease

SELECTION OF WGS RESULTS BY DISEASE CONDITIONS

WOULD YOU WANT RESULTS ABOUT THESE CONDITIONS IF YOU HAD YOUR WHOLE GENOME SEQUENCED?				
Condition	**YES**	**NO**	**UNSURE**	**TALLY**
All Results on this list	P2M, P8M, P14M, P20F, P30M, P73F, P98M, P99M	P5M, P74F, P97F		8-3-0
No results on this list				
Alzheimer disease	P5M	P74F, P97F		1-2-0
Heart disease	P5M, P74F, P97F			3-0-0
Lupus	P74F, P97F			2-0-0
Addiction	P74F	P97F	P5M	1-1-1
Sarcosis	P5M, P74F, P97F			3-0-0
Bowel Cancer	P5M, P74F, P97F			3-0-0
Breast and Ovarian Cancer	P5M, P74F, P97F			3-0-0
Other Cancer types	P5M, P74F, P97F			3-0-0
Diabetes	P5M, P74F, P97F			3-0-0
Allergy	P5M, P74F		P97F	2-0-1
Gastrointestinal conditions	P5M, P74F, P97F			3-0-0
Learning disabilities	P74F		P5M, P97F	1-0-2
Ancestry	P5M, P74F		P97F	2-0-1
High blood pressure	P5M, P74F, P97F			3-0-0
Cystic Fibrosis	P5M, P74F, P97F			3-0-0
ADHD		P74F	P5M, P97F	0-1-2
Stroke	P5M, P74F, P97F			3-0-0
Collagen disease	P5M, P74F, P97F			3-0-0
Factor V Friedreich ataxia	P74F, P97F		P5M	2-0-1
Down syndrome	P5M, P97F	P74F		2-1-0
Fibromyalgia	P74F, P97F		P5M	2-0-1
Haemoglobin E/Thalassemia	P5M, P74F, P97F			3-0-0
Huntingdon disease	P5M, P74F	P97F,		2-1-0
Macular degeneration	P74F, P97F		P5M	2-0-1
Parkinson disease	P5M, P74F, P97F			3-0-0
Sickle cell	P97F,		P5M	1-0-1
Thyroid problems	P5M, P74F, P97F			3-0-0
Familial hypercholesterolaemia	P5M, P74F, P97F			3-0-0
Other: Please Specify				

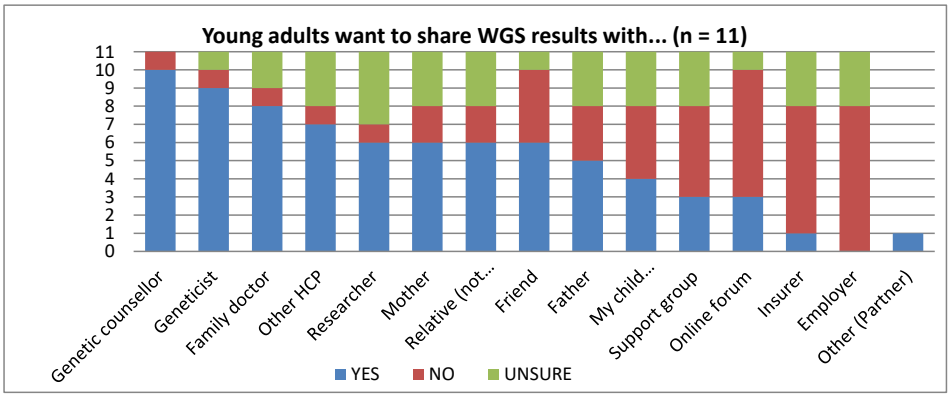
D.3 Receiving WGS Results and Sharing

Tickbox tables from Interviews

Who would you want to receive your WGS results from?					
PERSON	**YES**	**NO**	**UNSURE**	**THOUGHTS**	**TALLY**
From a genetic counsellor	P5M, P8M, P14M, P20F, P30M, P73F, P74F, P98M, P99M,		P2M, P97F,		9-0-2
From a doctor	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P97F, P98M, P99M,		P74F,		10-0-1
From a family member	P5M, P98M	P2M, P8M, P14M, P20F, P30M, P73F, P74F, P97F, P99M			2-9-0
Other, please specify: P98M: girlfriend – YES **P98M**: friend – NO					

How would you want to receive your WGS results?					
MEDIA	**YES**	**NO**	**UNSURE**	**THOUGHTS**	**TALLY (RANK)**
Letter	P8M, P97F, P98M	P5M, P14M, P30M, P73F, P74F	P2M, P20F, P99M		3-5-3 (4)
Secure website	P8M, P30M, P73F, P98M	P2M, P5M, P20F, P74F, P97F, P99M	P14M	P14M, not website for positive results	4-6-1 (3)
E-mail	P8M, P30M, P73F, P98M	P5M, P20F, P74F, P97F, P99M	P2M, P14M	P14M, not e-mail for positive results	4-5-2 (2)
Phone call	P14M, P97F, P99M	P5M, P8M, P20F, P30M, P73F, P74F, P98M	P2M		3-7-1 (5)
Video-call	P8M, P14M, P99M	P5M, P20F, P30M, P73F, P74F, P97F, P98M	P2M		3-7-1 (5)
In-person	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P97F, P98M, P99M				11-0-0 (1)

The following Figure illustrates who eleven young adult participants would want to share their WGS results with.



Who would you want to share your WGS analysis results with?					
PEOPLE	**YES**	**NO**	**UNSURE**	**THOUGHTS**	**TALLY and RANK**
No-one, keep to myself		P2M, P5M, P8M, P14M, P20F, P30M, P73F, P74F, P97F, P98M, P99M			
Mother	P5M, P8M, P20F, P73F, P98M, P99M	P14M, P74F,	P2M, P30M, P97F		6-2-3 (6)
Father	P5M, P20F, P73F, P98M, P99M	P8M, P14M, P74F	P2M, P30M, P97F		5-3-3 (7)
My child	P5M, P8M, P98M, P99M	P2M, P14M, P74F, P97F	P20F, P30M, P73F		4-4-3 (10)
Other family member	P2M, P5M, P8M, P74F, P98M, P99M	P14M, P73F, P97F	P20F, P30M	P74F: siblings in family only	6-3-2 (9)
Family physician	P2M, P5M, P8M, P14M, P20F, P30M, P98M, P99M	P74F	P73F, P97F	P2M: did not have a GP	8-1-2 (3)
Clinical Geneticist	P2M, P5M, P8M, P14M, P20F, P30M, P97F, P98M, P99M	P74F	P73F		9-1-1 (2)
Genetic counsellor	P2M, P5M, P8M, P14M, P20F, P30M, P73F, P97F, P98M, P99M	P74F			10-1-0 (1)
Other health professional	P2M, P8M, P14M, P20F, P30M, P98M, P99M	P74F	P5M, P73F, P97F		7-1-3 (4)
Researcher	P2M, P5M, P8M, P14M, P97F, P98M	P74F	P20F, P30M, P73F, P99M		6-1-4 (5)
Friend	P2M, P5M, P20F, P73F, P74F, P99M	P8M, P14M, P97F, P98M	P30M,		6-4-1 (8)
Employer		P5M, P8M, P14M, P73F, P74F, P97F, P98M, P99M	P2M, P20F, P30M,		0-8-3 (14)
Insurer	P2M,	P5M, P8M, P14M, P73F, P74F, P97F, P98M	P20F, P30M, P99M,	P99M YES if I benefit	1-7-3 (13)
Support group	P2M, P97F, P98M,	P14M, P20F, P73F, P74F, P99M	P5M, P8M, P30M,		3-5-3 (11)
Online forum	P2M, P98M, P99M,	P5M, P8M, P14M, P20F, P73F, P74F, P97F	P30M,		3-7-1 (12)
Other, specify	P8M: partner				

D.4 Hierarchical List of Themes

Aggregated THEMES from INTERVIEWS (236)

RAW THEMES (172)		INTERMEDIATE THEMES (46)	HIGHER THEMES (18)
Want step-by-step guide within results report (11)	Common process(2)	Health planning (9),(10)(41) = 60	PERCEIVED UTILITY (11), (1), (9), (16), (8), (1), (12), (32) (41), (2)= 133
Results media: In-person (11)	Can live well not knowing (2)	Professionals for explanation of results (6) (3) (15) (10)(11) (1)= 45	Autonomy vs. Dependency (4) (6), (11), (14),(38), (2) = 75
Want explanation from qualified HCP (11)	Concern re. untreatable conditions (1),(1) = 2	life planning (6),(1),(2), (32), = 41	Professional interventions - post-WGS (15),(2), (1), (16), (4)(20) = 58
Add results to health record (11)	Want to know about treatable diseases (1)	Belonging = 38	Results document (45), (10) = 55
Support or improve self-care, e.g. lifestyle activities, medication, treatment (9)	Value For Money (1)	Close network - Relative or partner(25)(3) = 28	Impact on self (2), (3), (12), = 17
Receive relative's results: If / when relative is willing (9)	Cannot change one's carrier status (1)	Access health, social care and support services (23)	Belonging (13)
Future re-analysis / re-sequencing re. self (8)	Panic re. possible future conditions (1)	Health declaration (18)	Impact - on family (4), (5), (4) = 13
Patient or Consumer choice (1), (2), (5) = 8	Guessing game re. possible future conditions (1)	Relatives' shared interest (12) (7), (2) =21	Patient education for genomics (13)
Want more knowledge about genomics (8)	Scared by results re VUS (1)	Impact on family/relatives (4),(5), (4) = 13	Complexity (6), (4) = 10
Not insurer – dis-benefit (8)	Reaction to bad news re. untreatable conditions (1)	Professional support to deal with results (7) (1)(9) = 17	Consent (9), (1) = 10
Want bar charts and graphs (7)	Makes no difference re. VUS (1)	Access professional health care (16)	Professional interventions pre-WGS (3), (5) = 8
Use bar charts to compare results (7)	Conditions not known to the family (1)	Impact of bad news on self (7),(4), (3) = 14	Intimacy (3),(2), (1), (1) = 7
Want genetic counselling (7)	Fear passing condition down to next generation (1)	Community of shared interest (1), (13)	Ownership (2),(3), (1) = 6
Conditions known in the family (7)	May "evolve" (outgrow) the problem (1)	Patient education to understand WGS results (13)	Normalisation of genomics (5)
Want all results (6)	Problem may be psychological (1)	Explanation of results after WGS (3), (9) =12	Trust (4)
Psychological support for results (6)	Do not know what the condition name means (1)	Self-discovery (4), (6), (1), (1) = 12	Sensitive personal data security (4)
Simple language in the results report (6)	Participant does not understand terminology - treatable vs curable (1)	Personal health insurance plan (12)	Societal cost (3)

Share results with: Researchers – to support research (6)	Waste of money – re. Ancestry (1)	Support research (11)	Access family support (2)
Lifestyle Planning - responding to results = (5)	Prefer family to inform, not genomics – re. Ancestry (1)	Not treatable (3), (8) = 11	
Impact on family (4)	Results from: Doctor for explanation (1)	Consent (9), (1) = 10	
Receive relative's results: Results relative may need help with (5)	Results from: Genetic counsellor – explanation for patient choice (1)	Access support (7)	
Computer graphics difficult to read (5)	Results from: All options- I'm not shy re. results (1)	Decision - Expert decision maker (6)	
Add results to family tree / ancestry records (5)	Results from: Not family – lack of knowledge (1)	Fear of results re. uncertain future conditions (6)	
Knowledge to prepare for results (4)	Results from: Not doctor – they jump to treatment, not meet information needs (1)	Occupational health (6)	
Results media: e-mail or secure website (4)	Results media: Letter then in-person (1)	Pre-WGS professional information and support needs (5)	
No treatment available (3), (1) = 4	Results media: Phone or video call to reduce wait (1)	Decision - Patient choice (5)	
Share results with: HCPs – to receive advice (4)	Want more knowledge about genomics ***before*** WGS (1)	Access family support (3),(2) = 5	
Share results with: Clinical geneticist – for advice (4)	Bar charts to compare results NOT reassuring (1)	Trust (1),(1), (2) = 4	
Share results with: Employer (unsure) depends on relevance (4)	Support with understanding analysis (1)	Open future for self (4)	
Not for family tree (4)	Education about why undertaking WGS (1)	Consumerism (2), (2) = 4	
Results: from Doctor or genetic counsellor – good explanation (4)	Education about results (1)	Impact on self - discomfort (4)	
Want to know about self (4)	Education with cohort of similar (1)	Friend - shared interest (3)	
Impact of bad news on self (4)	Doctor-patient relationship (1)	Data security concerns (3)	
Information about actions to take – after WGS (4)	Information from specialist before (1)	Societal cost (3)	
Share results with: Researchers (unsure) – depends on research (4)	Entire process supported by family (2)	Concerns re actionability of results (3)	
Share results with: Genetic counsellor – for advice (3)	Protracted informed consent process to undertake WGS (1)	Lack of understanding of diseases or medical terms (2)	
Share results with: Support group – for serious illness (3)	Explanation about what WGS results could mean – before WGS (1)	Not interested in WGS for Ancestry (2)	
Receive relative's results: Relatives' results that may affect me (3)	Process and results Information before WGS (1)	Professionals (for results) – to manage Impact re. privacy, confidentiality (2), (3) = 5	
Family planning (1), (2) = 3	Information about life changes-after WGS (1)	Genetic counsellor – constraints / challenges to meet information	

		needs (2)	
Want to know what may be coming (2), (1) = 3	Contact to talk after results (1)	Autonomy vs dependency (2)	
Simple explanation of results - after WGS (3)	Personal disease risk table (1)	Professionals' area of interest (2)	
Unnecessary worry re. possible future conditions (3)	Want to know what's coming (1)	Inform relatives of shared risks - (2)	
Results from: Not family – impact on dynamics(3)	Share results with: Parents –conduit to family communication (1)	Normalisation of genomics (5)	
Results media: letter (3)	Share results with: Parents – they'd be interested (1)	Impact on self– negative interactions (2)	
Results media: unsure about letter (3)	Share results with: Relatives – they'd be interested (1)	Withhold from doctor (1)	
Bar charts and graphs difficult to read (3)	Share results with: Children – for their interest (1)	Close relative for privacy (1)	
Want simple computer graphics (3)	Share results with: Relatives – to encourage them to undertake WGS (1)		
Sensitive personal data security concerns (3)	Share results with: Relatives - to prepare for a condition I may get (1)		
Share results with: Partner – for their interest (2)	Share results with: Children – inform of shared predisposition (1)		
Share results with: Parents – (unsure) serious results only (2)	Share results with: Relatives – forewarn of their potential risks (1)		
Share results with: Not support group – discomfort (2)	Share results with: Not children – protect from panic (1)		
Share results with: Not online forum – discomfort (2)	Share results with: Children (unsure) cannot hypothesise (1)		
Share results with: HCP (unsure) – if action needed (2)	Share results with: Not parents – annoying (1)		
Share results with: GP – for advice (2)	Share results with: Not father- don't get along (1)		
Share results with: Support group (unsure) – depends on ailment (2)	Share results with: Not parents – not to worry them (1)		
Share results with: Online forum – support (2)	Share results with: Not friends – annoying (1)		
Share results with: Insurer – if I benefit (2)	Share results with: Best friend – for their interest (1)		
Receive relative's results: Reciprocal exchange of results (2)	Share results with: Not friends – too personal, unless reciprocal (1)		
Support lifestyle and choices regarding procreation / next generation (2)	Share results with: Friends – if sharing is reciprocal (1)		
Compare to family members' WGS results (2)	Share results with: HCP – for their interest (1)		
Time to manage impact on self(2)	Share results with: Not HCP – if not relevant (1)		
Impact on self of risk uncertainty (2)	Share results with: Online forum – anonymous addition to database [research] (1)		

Impact on self of certainty (2)	Share results with: HCP (unsure) – share but NOT for health record (1)		
Adult autonomy (2)	Share results with: Employer – if immediately relevant (1)		
Education about WGS (2)	Share results with: Not employer – not relevant (1)		
Explanatory supplementary information to address lack of knowledge (2)	Share results with: Insurer – useful for policies (1)		
Brochure / leaflet to provide explanation (2)	Share results with: Insurer (unsure) (1)		
Discussion with Doctor to ascertain readiness (2)	Receive relative's results: Insist on knowing relative's results (1)		
Meeting HCP before WGS (2)	Receive relative's results: Conversation piece – good news(1)		
Medication efficacy (2)	Future re-analysis / re-sequencing re. children (1)		
Fears knowing conditions far into the future (2)	No reanalysis (1)		
Treatment not needed - not appropriate (2)	Forewarn family with WGS results (1)		
Allowing for future to remain unknown (2)	Publish WGS results (1)		
Expert decision maker if WGS state-subsidise or free (2)	Keep some information from the doctor (1)		
Expert decision maker – to manage uncertainty (2)	Impact of unexpected results on self (1)		
Expert decision maker- to manage reaction to results (2)	Impact of results while on own (1)		
Results from: Professionals - to inform me before others (2)	Professional support for Impact of results (1)		
Results from: Close family – someone linked by result (2)	Impact - Difficulty taking health action (1)		
Results from: Unsure genetic counsellor – concerns re. ability to give a full explanation (2)	Impact - Personal financial burden – insurance (1)		
Results media: In-person then letter (2)	Choosing Provider (1)		
NOT simplify language in the results report (2)	Burden on public services (1)		
Genetic counselling after WGS only (2)	Results comparisons to represent population (1)		
Societal burden (2)	Share results with: HCP – Trust (1)		
Share results with: Not Insurer – do not trust (2)	Share results with: Researcher – Trust (1)		
Meet HCP after WGS for explanation (3)	Disease, risk and actions table in results report (1)		
Common knowledge(2)	Private process, mum only (1)		
Planning - responding to results (2)	Life planning: quality of life (1)		

```
Both raters (P.S. and L.M.): agreed to include 233 themes,
P.S.-only: categorised 2 themes (which was included in final list of theme
s),
L.M.-only: categorised 1 themes (which was excluded from final list of the
mes),
Both raters (P.S. and L.M.): agreed to exclude 3 themes
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D.5 Classification matrices for TBCA

Classification Matrices from Theme-based Content Analysis (TBCA)

The frequency counts (in brackets within the Theme tables) refer to the number of data chunks that fit within each theme, unless otherwise stated. This may include more than one chunk per individual participant.
Participants' have a unique alpha-numerical code that ends with the letter M or F, indicating the gender they identified themselves with.
Participant STEM background:
STEM participants: P14M, P30M, P73F, P98M, P99M
Non-STEM participants: P2M, P5M, P8M, P20F, P74F, P97F

Clinical categories:

When clinical categories for genomic results were offered, all 11 wanted to receive results related to treatable conditions that were found to be present or were preventable in the future. All 11 also wanted pharmacogenetics results. 10 wanted results related to the reason they would have undergone WGS for as well as their carrier status. Nine wanted results about traits that meant they had a high predisposition for certain complex diseases as well as variants of uncertain (or unknown) significance (VUS). Eight wanted to receive results pertaining to untreatable diseases that were present as well as those expected in the future that were unpreventable and untreatable.

Themes: Reasons for wanting results by clinical categories (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P20F: I like to plan P99M: I think you would want to know that right? [laughs] so you can act accordingly.	Planning - responding to results (2)	Health planning (9)	Perceived Utility (11)
P98M: um, I'd like to have **kids** one day, so **carrier status** would be useful	Family planning (1)		
P14M: [re. pharmacogenetics] Medicines which will or won't work I think that's probably more useful. P98M: Medicines and stuff that would or wouldn't work for me, would be useful because I could save time and effort and taking unnecessary medication.	Medication efficacy (2)		
P97F: I want to know if I have diseases that can be treatable.	Want to know about treatable diseases (1)		
P14M: I think I'm nosey so I'd like to know what I'm going to have, I guess.	Want to know what's coming (1)		
P98M: to be honest I would probably want to know as much information as possible so I certainly want to know about things that may come up in the future. P98M: knowing what I'd be more likely to get would also be interesting.	Want to know what may be coming (2)		
P30M: I mean at the end of the day it's your information you get to choose who gets to read it.	Consumer choice (1)	Consumerism (2)	
P30M: if I put no for some of them, is the sequencing cheaper? **R:** No. **P30M:** so technically I'd just that yes to everything because I'd want to get the most that my money's worth.	Value For Money (1)		
P5M: [re. information of unknown significance], it might be just interesting to know. I'm kind of interested in knowing about myself. P8M: well I'd want them all, just because I'd like to know, yes I want to know everything. If I was just told you've got this mutation but we don't know what it means, that's fine. P20F: I'm a glutton for punishment, I want to know everything. Knowledge is power.	Want to know about self (4)	Self-discovery (4)	Autonomy v Dependency (4)

P30M: If you're going to go for it, you want the whole experience.			

Themes: Reasons for NOT wanting results by clinical categories (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P97F: it's the same reason but this one is more important because it's concerning your children, for example, and if I know that I can have a disease that my children will have but I can do nothing about that, I prefer not to know that. Yeah, I think I prefer not to know, than knowing that I will give something to my child	Cannot change one's carrier status (1)	Results not actionable for next generation (1)	Perceived utility. (1)

Themes: Reasons for being UNSURE about wanting results by clinical categories (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P5M: [a] disease which you could develop but you don't know and I'd rather not know about that and then worry, kind of unnecessarily. P97F: and for 'unsure', I think it's delicate, like to know we have a disease and we're not sure that it can be treated, and if I know that maybe it'll like put me in the wrong situation or an unsure situation. P97F: and if I didn't know this information maybe I would be living better.	Unnecessary worry re. possible future conditions (3)	Fear of results re. uncertain future conditions (6)	~~P~~erceived utility. (9)
P14M: [re. variable risk for complex diseases], once it starts getting to a "may", thinking I'll just get a lot of panic if somebody said you may get cancer.	Panic re. possible future conditions (1)		
P5M: yeah, it is kind of a guessing game about what might develop then it's probably best.	Guessing game re. possible future conditions (1)		
P14M: unknown significance, I think that would just scare me too much [ticked 'yes' despite fear.	Scared by results re VUS (1)		
P2M: the ones I had me a little bit concerned were those that weren't treatable	Concern re. untreatable conditions (1)	Concerns re actionability of results (3)	
P14M: [re. untreatable, unpreventable] once I knew I'd probably be upset about knowing but beforehand I would want to know.	Reaction to bad news re. untreatable conditions (1)		
P98M: Um, unknown significance, I'd probably put yes as well, um, but it's, I guess it depends on what the information would be, if it's something that I as a non-medical person would have absolutely no clue and makes absolutely no difference to my life that all, probably not.	Makes no difference re. VUS (1)		

Diseases/clinical conditions:
When offered a list of 28 diseases and clinical conditions, 8 out of 11 wanted results for all of those presented to them. The 3 remaining participants (P5M, P74F, P97F) were more selective about which conditions they would want results for.
Two participants (P74F, P97F) did not want results about Alzheimer's disease.
One (P97F) also did not want results for addiction and Huntingdon's disease.
One (P74F) did not want results for ADHD and Down's syndrome
Two participants (P5M, P97F) were unsure about receiving results for learning difficulties and ADHD.

One (P5M) was also unsure about receiving results about addiction, Factor V Friedrieich ataxia, fibromyalgia, macular degeneration and sickle cell.

Themes: Reasons for wanting results by disease / clinical condition (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P5M: OK, there's some I'd like to prioritise because knowing my family history already, [Alzheimer's disease, other cancers, diabetes]. P5M: Yeah, so the particular ones which I've highlighted are ones that members of my family have had those either recently diagnosed or a long time ago and there is a possibility I'd have it so it's kind of close family with these conditions. P14M: quite a few people in my family with cancer uh and high blood pressure and things so I know I have a few people, and diabetes, so I guess quite a few of them are relevant. That would motivate me to want to know more, I mean some of them are cancers caused by smoking and things, and the diabetes been caused by sugar intake and stuff so I guess maybe its susceptibility or not, I don't know. P14M: the cancer ones, quite a few people in my family with cancer uh and high blood pressure and things so I know I have a few people, and diabetes. P20F: my grandma's got Alzheimer's, my dad's got diabetes, so they are ones that run in the family especially you would want to know about P20F: my cousin's got Down's syndrome so maybe there's just personal interest P98M: I was specifically looking out for ones the I already I already know exist in my family, so I'm already aware of, I have a predisposition, the only one that for as would be diabetes and some allergies. So those would be a definite yes, I'd want some information about those.	Conditions known in the family (7)	health planning (10)	Perceived utility (16)
P98M: if in having the genome sequence result back, I learnt more about things like other diseases that I might be susceptible because of my joined heritage of two families, but neither of the two families were susceptible by themselves, then yes I would want to know so I'll probably put 'yes' for all the results on both of the lists.	Conditions not known to the family (1)		
P14M: [re. Down's syndrome] my child has a high chance it might make me reconsider. P20F: It's about how I spend the rest of my life, **children, things like that**.	Family planning (2)		
P20F: It's about **how I spend the rest of my life**, children, things like that. P14M: I think they're all quite serious from what I can tell […] What motivates me is things like Huntington's and things like Parkinson's which will affect me more later in later life so I'd want to know because I'd probably make some life decisions now if I knew. P14M: right now I don't really travel much but I want to later on and things like this, or if I wanted a family and stuff it'd probably make me reconsider maybe delaying those decisions. So the family one, yes, of passing it on and	Lifestyle planning – responding to results (6)	Life planning (6)	

also things like if I wanted to travel I may consider doing it more now. Basically moving a lot of my decisions forward or some more forward and some more back. Like travelling I'd do now, family …might wait. P98M: I think it's useful to have more information about what could affect me. P99M: I think I'd prefer all of them [wants ALL results on 1st list of conditions] , as in if you knew you are going to have Alzheimer's, then I'd rather know so I can live my life, maybe like, save less and kind of act. Yeah I kind of spend all my money like now, rather than later [laughs] rather than save it for later [laughs]. P99M: [re. chooses ALL results on 2nd list of conditions] I guess it's the same reasoning again really.			
P30M: I mean like you just get told everything first, […] and whether you use the information or not, it's up to you later on, but you don't want to be like, oh I why did I miss, rejected it, later on it could become apparently useful or something. P8M: there might be a few [conditions] **that I don't know [what they are].** I think **'yes' to all of them, I'd want to know** [the results**]. I'm not a doctor so I'm not going to know about all these.** P14M: I kind of feel I want to know all of them, let's go with all. P2M: I think the more information you have, the better always in all scenarios, P2M: know results ([R: so there are some there that a treatment wouldn't necessarily be available but you would still want to know.] P2M: um hmm [yes] P8M: I like to know everything, it's not just with medical conditions, I like to look into things and find out about them and to know as much as I can.	Want all results (6)	Self-discovery (6)	Autonomy v dependency (6)

Themes: Reasons for NOT wanting results by disease / clinical condition (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P97F: addiction, no again I think it's very personal like addiction, I don't know, you cannot know what will happen in your life and sometimes maybe you will be addicted to something and then no. I prefer not to know. P97F: because I don't want it to affect my life, like maybe I can get addicted to something. R: yeah yeah yeah, if it adds anxiety. P97F: yes	Allowing for future to remain unknown (2)	Open future for self (4)	Perceived utility (8)
P74F: just because it happens much in the later age and it would just be nice to not know if I'm going to have Alzheimer's, or am predisposed to Alzheimer's, so then I don't scare myself […] like about something that is way in the future is scary	Fears knowing conditions far into the future (2)		
P74F: I think because for ADHD and Downs Syndrome, say if I'm a carrier and I'm passing it down to my children, I don't want to know so that I don't scare myself into say, not having children.	Fear passing condition down to next generation (1)	Open future re. procreation (1)	
P97F: I had tried to explain badly what Huntington's disease is, um but you've picked 'no' for that one, and again is that treatability aspect of it? P97F: Yes	No treatment available (3)	Not treatable (3)	

P74F: you'll never, some things like this, especially when it's with the brain, and your memory, it can just be old age and something you can never recover with medication P74F: I don't find ADHD, I just find ADHD is just like the behavioural thing, it's not like a condition that needs to be treated, same for Down syndrome, so maybe if I knew then it would just be like management classes, it's nothing of like, Oh find me a cure for Down's syndrome, because it's not something that you can cure.			

Themes: Reasons for being UNSURE about wanting results by disease / clinical condition (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P97F: when you have Alzheimer's there is no treatment, but I think if someone could tell me if I had it, now I'm not sure	No treatment available (1)	Not treatable (8)	Perceived utility (12)
P97F: Alzheimer's is the really difficult disease because it's concerning your family.	Concern re. untreatable condition (1)		
P97F: ADHD I am not sure, it's my personal opinion, but some people you needed treatment when you have ADHD and some others think no. R: and you are obviously with the 'no' camp. P97F: Yes. P97F: So it's not really important for me, but it depends on the level of the allergy you have.	Treatment not needed - not appropriate (2)		
P97F: So, allergies, um, I'm not sure and I think that you can evolve, for example I was allergic to something when I was younger and I'm not, I think it depends if you are	May "evolve" (outgrow) the problem (1)		
P97F: I think sometimes it's like, I don't know how to say it, psychological. You are allergic to something and then you don't know why you are not any more.	Problem may be psychological (1)		
P74F: and it would just be nice to not know if I'm going to have Alzheimer's, or am predisposed to Alzheimer's, so then I don't scare myself. P97F: Um learning disabilities, I don't know because it can really again affect your whole life I think and maybe you can live with it, with this and going good with this without knowing it, so I prefer not to know.	Can live well not knowing (2)		
P5M: I don't know what that is. I know, put unsure, for things I'm not sure about. P5M: This [ADHD] is 'unsure', I know what it [ADHD] is, the other 'unsure' ones is because I don't know what the condition is.	Do not know what the condition name means (1)	Lack of understanding of diseases or medical terms (2)	
P30M: [re. collagen disease] and it is not treatable? R: um, some will be treatable because it has rheumatoid arthritis, lupus, some of them are treatable, yes. They are not curable, but they are treatable. P30M: OK, Oh they are not curable? R: not curable, but treatable.	Participant does not understand terminology - treatable vs curable (1)		
P30M: Oh boy, sounds like a massive waste of money.	Waste of money – re. Ancestry (1)		

P97F: ancestry, I think I prefer to have real experience, like people of my family telling me the story of my family and not have science giving me information on that.	Prefer family to inform, not genomics – re. Ancestry (1)	Not interested in WGS for Ancestry (2)	

Themes: Who should decide what results are returned (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P30M: if I'm already paying like a ridiculous amount of money I want to know everything. P30M: I mean at the end of the day it's your information you get to choose who gets to read it.	Consumer choice (2)	Consumerism (2)	Ownership (2)
P8M: I think it should be the patient's decision, so some people might not want to know about any of them, that's fair enough, because some people might have the view that its psychological as well, and you might be more predisposed to if you're aware, but yeah I think it should be the patient's decision. P14M: [re. should individual or expert decide?] I'd like to consider myself quite a sound and reasonable person, umm, so I'd say they should just tell me everything, P30M: it depends sort of on like the motives for the test, so if people really want to go for the test because they want to try and see what they are like susceptible to like everything, like if they are already making an informed decision then they should be allowed to know about like, get all the results. P30M: treat it like a blood test […] tick what we want tested, like we have sort of full control about it, yeah. P74F: it would have to be patient's decision to ask for what I want and what you can hold it to yourself, and things I don't want to know.	Patient/ Customer choice (5)	Patient choice (5)	Autonomy vs. Dependency (11)
P30M: [re. if you were not paying anything] yeah, so like if you had nothing to lose or like it was relatively cheap then I think the argument become stronger for the experts to make a call. P30M: if it was cheaper, I think experts should make the decision, because like how doctors treat their patients.	Expert decision maker if WGS is state-subsidised or free (2)	Expert decision maker (6)	
P5M: I think a degree each way, if its things that will affect you in the future or say you are a carrier for a certain thing, I think you should know, um, but with unknown significance stuff, then it would really be up to an expert to decide that, so a bit, a bit of leeway, knowing about yourself but then also knowing that whoever is conducting this and has the information knows a lot more about what this means than you do. P14M: [re. reasons for expert to make decision] how high the chance was and also sort of how serious the disease was or… if they said to me, for example, like you have a high risk of diabetes or something for example, there are things you could be doing now, I guess that'd be something that'd be better, or even if they said like there's a 50/50 risk of diabetes, you should consider. Wheras if they said there's a high risk, or there's a *some* risk of getting Huntington's but it's moderate, then maybe I wouldn't	Expert decision maker – to manage uncertainty (2)	Expert decision maker (6) Perceived utility (1)	

want to know that as much. I don't know how you even do that in a world of spreadsheets, decide which one.			
P14M: but then I also know quite a few people who are hypochodriacs in my family, so my mother for example, and if you said you had a risk of this it would immediately make her panic more. And she'd think she'd be dying for the whole week. So I don't know, sometimes I feel like there should be professional judgement involved still just because I think for some people perhaps knowing it…[might be a bit] dangerous. P30M: if you tell some guy you going to get cancer, it's like oh he's going to live his entire life in fear of getting cancer, so that's like not exactly good. So there's ah, I feel like for the more serious diseases, maybe a doctor should make the call and like based on the chances of them actually contracting the disease or whether it's like 100%. So like if it's very known where possible then they might not have to inform you.	Expert decision maker - to manage reaction to results (2)		
P30M: It's not just information, it's also the quality of life.	Life planning: quality of life (1)	Life planning (1)	Perceived utility (1)

When filling in tables to indicate their preferences, 10 participants were happy if their WGS results were returned to them by a doctor and 9 were happy for a genetic counsellor to do so. Only 2 would be happy for a relative to be the one to give them their results. The following tables present their quotes classified into themes.

Themes: Reason for who young adults would want WGS results from (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P97F:[re. why 'yes' for doctor] because I think that if it's the doctor who gives me the information, maybe he could have a different approach[from a genetic counsellor], and explain me maybe better the disease.	Doctor – expect a better explanation (1)	Professionals – explanation of complex information (6)	Complexity (6)
P30M: [re. P30M questions the skills of a genetic counsellor] they are not necessarily a *genetics* specialist, their specialty is a counselor. That's right isn't it? R: their specialty is as a *genetic* counselor, so. P30M: so they do know the science stuff about the genetics. [P30M selects "YES" for genetic counsellor and doctor] P5M: I think I'd be happy from any of them. **P5M:** so I think from a doctor or genetic counsellor it'd be kind of a broad gamut. P98M: I don't think that I'm, shy or withheld about the information that I would receive from this, so I'd certainly say yes for the top two, and probably also 'yes' for from my family member. P98M: I'd rather have it as [from] a professional.	Doctor or genetic counsellor – good explanation (4)		
P74F: genetic counselor I would think that they are advising you or they are talking about the disease, so then you have a better understanding and then you make your own choice of treatment.	Genetic counsellor – explanation for patient choice (1)		
P8M: I'd go with the genetic counselor or the doctor. Family member 'no', because I'd like it to be me that knows first. P14M: I don't know what a genetic counsellor is. I can guess by the name but I didn't know that was a job.[…] I'd go for the first two [chooses doctor and genetic counsellor] but	Professionals - to inform me before others (2)	Professionals (for results) – to manage impact re. privacy,	Impact on self-confidentiality (2)

certainly not from a family member. Just because, I think I'd be upset my family knew before I did about me.		confidentiality (2)	
P5M: if there's something in particular that a family member might share already. **R:** So where the family member has information that's going to impact on you, you want to hear it [results] from them [family member]. **P5M:** yeah P98M: I'd rather have it as [from] a professional,[or] someone that is close to me and as a result, is linked by the results, um but someone who just knows me as a whole, I'd probably say 'no'. I'll be cheeky and add another group if you don't mind four. Girlfriend, and say 'yes' because if I have had disposition, sorry a predisposition towards the disease and I have children, my children may have a predisposition to what's that disease and so its information that my girlfriend may wish to know.	Close family – someone linked by result (2)	Close network (3) Relative or partner	Intimacy (3)
P98M: I don't think that I'm shy or withheld about the information that I would receive from this, so I'd certainly say yes for the top two, and probably also 'yes' for from my family member.	All options- I'm not shy re. results (1)	Close network (1) Relative or professional	

Themes: Reason for who would NOT want or UNSURE for WGS results (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P2M: definitely not a family member because they have the talent to unnerve me, but yeah, a doctor P14M: I'd go for the first two [chooses doctor and genetic counsellor] but certainly not from a family member. Just because, I think I'd be upset my family knew before I did about me. P74F: And I just don't want my family because I'm just, you know [gesture?]	Not family – impact on dynamics(3)	Professionals to manage privacy, confidentiality (3) (not family)	Perceived ownership (3)
P30M: I don't want a family member, they know nothing.	Not family – lack of knowledge (1)	Family - genomic knowledge (1)	Complexity (4)
P74F: doctors like to jump into treatment so, when they go oh you have this um disease and then they jump straight into treatment and cure.	Not doctor – they jump to treatment, not meet information needs (1)	Doctor – constraints /challenges to meet Information needs (1)	
P2M: what is the genetic counselor? **R:** a genetic counselor is, usually at the moment, tends to be a nurse, who works in genetics, who has had specific training to prepare people for genetic testing. **P2M:** OK, so I'll mark that as 'unsure'. But it would definitely be a 'yes' assuming that the genetic counselor would be trained to deal with tough information. P97F: [re. why 'unsure' for the genetic counselor] I'm not sure if it's a genetic counselor, he could like give me the same advice[as a doctor] and, I'm afraid he would just give me the results and um not have an analysis behind the results.	Unsure of genetic counsellor – concerns re. lack of ability to give a full explanation of information (2)	Genetic counsellor – constraints / challenges to meet information needs (2)	

Media preferences for results:

Participants were asked what media they would prefer to receive their results in. All 11 participants selected an in-person meeting. 2 wanted a letter to follow an in-person meeting and 1 preferred a letter first, then in-person. 4

participants indicated they would be happy to receive results by email or via a secure website. Only 3 participants wanted results by letter with another 3 being unsure about this medium. Phone calls and video calls were least popular though they were mentioned by 1 participant as an alternative to waiting for an in-person appointment.

Media preference for results (11 participants)	**Intermediate level themes**	**Higher level themes**
In-person (11)	Professional interventions after WGS (11), (2), (1), (1) = 15	Professional interventions after WGS (11), (2), (1), (1) = 15
In-person followed by letter (2)		
Letter followed by in-person (1)		
e-mail or secure website (4)	Results document type / format =10	Results document =10
letter (3)		
unsure about letter (3)		
Phone or video call to reduce wait (1)		

Tools and Resources to support WGS process:
Participants were asked whether the following tools and resources would be important to them when undertaking WGS. They could tick from a list of items on the page and they were given opportunity to elaborate. The list included: more knowledge about genomics, simple language in reports, a step-by-step guide as part of the results report, bar charts and graphs, computer graphics, genetic counselling and an explanation from a qualified health care professional (HCP). Not all 11 participants expressed an opinion about these resources.
8 wanted to more knowledge about genomics, though only 1 described wanting such knowledge before undertaking WGS. None said they would not want such knowledge.
Of the 8 who commented on "simple language in the results report", 6 said this would be a good idea. 2 commented that they would not want simple language, with 1 elaborating that the report shouldn't be "dumbed down".
All 11 participants expressed a desire to have a step-by-step guide within the report, however 1 described reservations that it could make the report too long.
7 out of 11 expressed an interest in bar charts and graphs as they could be used to compare their results to wider population. Of the 4 that did not want bar charts, 1 said that such comparisons would not be reassuring and another 3 said charts and graphs would be difficult to read, messy or overwhelming.
3 out of 8 participants expressed an interest in the use of computer graphics to present results. However they described a need for them to be few in number, simple and additive. The 5 that did not want computer graphics described concerns that they would be unhelpful and difficult to interpret, with 1 participant expressing a dislike for what he thought would be "90's-style animated bar graphs".
All 11 expressed a desire to receive an explanation of their results from a qualified HCP.
Of the 7 who expressed an opinion about genetic counselling, all said they would want it; yet 2 of them described wanting genetic counselling after
WGS, not before.
The data matrix below distils the data presented above about tools and resources into themes.

Tools and resources preferred for WGS (11 participants) – Raw themes	**Intermediate themes**	**Higher order themes**
Results: simple language in the results report (6)	Results document type/ format (45)	Results document (45)
Results: NOT simplify language in the results report (2)		
Want step-by-step guide within results report (11)		
Want bar charts and graphs (7)		
Use bar charts to compare results (7)		
Bar charts and graphs difficult to read (3)		
bar charts to compare results NOT reassuring (1)		
Want simple computer graphics (3)		

Computer graphics difficult to read (5)		
Want explanation from qualified HCP (11)	Health professionals for explanation of complex data (11)	Health professionals after WGS (20)
Want genetic counselling (7)	Health professionals to deal with results (9)	
Genetic counselling ***after*** WGS ***only*** (2)		
Want more knowledge about genomics (8)	Patient education to understand WGS results (9)	Patient education for genomic knowledge (9)
Want more knowledge about genomics ***before*** WGS (1)		

Action on WGS results:

All participants were asked to respond to prompts of possible actions they might take with their WGS results. The following table summarises the results into themes.

Themes: Actions on WGS (number of data chunks)			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P2M✓: OK, that would be the point of doing the whole genome sequencing thing I think, to improve on what you can improve and what you can't improve, just find some way of dealing with it. Um, yes I think I would be in for all of these. P5M✓: would be quite handy [to use results to support or improve self-care]. P8M✓: if you are more careful with what you eat or something, yes that would be useful to know. P30M ✓: P73F✓: P74F ✓: I think it's really more on the lifestyle, so then I'd know, say if I am predisposed to cancer than it is mostly lifestyle changes or management, it's more of taking care of myself then if it's going to be diseases, P97F✓: P98M ✓: I certainly think I would like to use it to improve myself care. If it says I'm susceptible to disease but as I do these steps I will be less susceptible than I would certainly like to do those steps just to sort of improve might quality of life and length of life. P99M ✓: I guess also, analysing my future, if I am going to become ill while I might as well prepare for that. Yeah so I can enjoy life.	Support or improve self-care, e.g. lifestyle activities, medication, treatment (9)	Life planning (32)	Perceived utility (32)
P8M✓: Yes I think it should go on the health record as well. P14M✓: yes, my doctor. P73F✓: P2M✓: like a central database. Imagine I was out jogging, I had an accident, I was taken to hospital, would that doctor have access to this kind of information? I think that will be like one of the top priorities. If you do it and keep it at home and then you are unconscious what good can that do? P20F✓: I suppose maybe my health record. Again it will be linked with planning and passing it on to other people P74F✓: maybe things like, things that would threaten my life say, if I was going to have cancer, then yes, it has to go on my record, so anything I do then it safeguards me, in a way P99M ✓: I guess that would be helpful ~~from~~ [for] professionals, rather than like myself. P5M: I don't know about adding to health record because of what insurance things like that. Might be an issue, but it could be quite	Add results to health record (11)		

[…] useful, so if you found something that you were allergic for example would be useful to have that. Depending on the results, it would be useful to have certain aspects. If it was something you felt might affect health insurance, travel insurance, life insurance… then you don't want something like that in your record. [It'd be] something to be aware of and maybe talk to a health professional about but um but not for [health record]. (N.B. the above P5M quote is also referenced in section about sharing WGS results with insurance) P30M✓: so I guess this is the important one. Add information to my health record, that's us would have given isn't it? P30M: someone like me that's been living around, like all over the place, then one doctor wouldn't necessarily have a dependable record of my life. Well if I keep it, if I get it and probably have a copy of it for myself, but that's about it.[R: would you want the doctor to also have a record of it, any doctor you happen to be seeing at the time.] P30M: it depends if they ask for it, or I could tell them about it if I, I mean I could tell them just things I find relevant to something am talking about when I go see them. P98M✓: I'd add information to my health record as a result of the sequencing if it would be of a benefit to medical profession for it to be there, sorry medical person, for it to be there. So if I go in for some screening or something and it says oh predisposition to these diseases or history this stuff and that's useful to the person, that would be great but, if I go in for a bog standard meeting and they have to sift through four pages of stuff, I wouldn't want it to water down any of the important information that's already there.			
P30M ✓: P73F✓: P99M ✓: P2M✓: the resequencing, yeah definitely. If it can be improved I mean, that's the whole point. P5M✓: that would be pretty good because then you might, umm you actually get it 10 years down the line or something and then you'd see actually see, this is more of a developing thing. P8M✓: I suppose it's keeping it for comparison yeah, I can use it further. P74F ✓: maybe sort of when I have a child, say if I were carrier for something and then I have a healthy child, I would just want to retake it, just to make sure that, hey is this sort of, was it the same result as before, that I have a predisposition to a disease but if I take these steps can I won't, then I would want to re-analyse and see how I'm doing down that route, and if that's helping me. P97F✓: I think so, uh, but depending on the disease they predict me.	Future re-analysis / re-sequencing re. self (8)		
P20F✓: Again it will be linked with planning and passing it on to other people P74F✓: but if it's going to be something that I am a carrier for, and I might have a fa[mily], I would want to increase my knowledge on the things, on these diseases or conditions, then I am able to just take care of the future better.	Support lifestyle and choices regarding procreation / next generation (2)		
P98M✓: I'd definitely like to re-analysing the future, especially if it says.	Future re-analysis / re-sequencing		

	re. children (1)		
P14M×:[re. reanalysis] probably not.	No reanalysis (1)		
P2M✓: I guess that could be interesting, but I mean to some extent, how useful can it be in the sense of helping your whole family. Because I'm thinking of my family but my neighbours, they live spread out all around the world. I don't see how they would benefit from it, but beats me, maybe helpful? P8M✓: It is important for the family tree because if you've got something that passed down, don't know the word for it but you pass on to someone else, um it would be important to know. P74F ✓ : I'd want to know yeah, my family tree like, who was carrier of what and then how did this come about. P98M ✓: certainly add information to my family tree on the basis that if I were to sit and look back at my family tree, having that information earlier in the family tree would be useful and would be interesting to see and so I believe that in later generations, if they were to look back they may wish to see that and if it's of benefit to them then yes I would want to do that. P99M ✓: I think that, there is probably the most for ancestry. So it's kind of interesting to see, like say, where my further family would come from in history and stuff like that. So that would be out of interest really. That's probably the main thing that I would. **R:** so that is number one for you, it's adding to your family tree. **P99M:** Yes I would like that.	Add results to family tree / ancestry records (5)	Relatives' shared interest (12)	Autonomy vs dependency (14)
P5M✓: I'd want to tell kind of family umm and have some way to, or I'd just tell people, make it known, people who are related to me. Yes, so they can see and also the might be able to say maybe this set comes from Dad's side and then other members of that family side, watch out for this.	Forewarn family with WGS results (1)		
P8M✓: I suppose if my family had it done, compare it with theirs to see if there's any differences in what they are? P98M: I possibly want family members and / or like a partner to have the same thing happen as well, and to compare between us. But I think that's more for sort of providing a localised version of those averages. Um just the sort of see well, OK my dad's very likely to have this disease, but I'm not, and to see that comparison. [R: so you're interested in the intergenerational change.] P98M: yeah.	Compare to family members' WGS results (2)		
P5M×: never really done any of that stuff, never been that interested. No. P14M×: no P20F×: never been particularly interested in a family tree P97F×:	Not for family tree (4)		
P14M✓: I would be interested in publishing it as a thing, I kind of feel like if we are collecting all this data, it should be used in research as well.	Publish WGS results (1)	Community of shared interest (1)	
P97F×: [re. sharing with doctor] I'm not sure because sometimes they just predict things that maybe will not happen so, I'm not sure that my doctor [would] have to know everything. I think I would just keep it for me.	Keep some information from the doctor (1)	Withhold from doctor (1)	
On its own, a tick (✓) indicates participant's response to the prompt was a positive tick without any further verbal or written comment.			

The following classification matrix presents themes for the reasons young adults would or would not want to share their WGS results.

Themes: Reasons for choices re. sharing WGS results (number of data chunks)					
Raw data	**Raw data themes**	**Intermediate order themes**	**Intermediate order themes**	**Intermediate order themes**	**High order themes**
P73F: it'll spread around like wildfire	Parents – conduit to family comms (1)	Relatives' shared interest (7)	Close network (relative or partner) (25)	Belonging (38)	Autonomy v dependency, (38)
P98M: I'd certainly share it with my mum and dad. I'd like to think that they would be interested as well.	Parents – they'd be interested (1)				----------
P98M: I would probably share it with other family members but only to a certain extent, only if they are somewhat closely related to me by blood. Sort of from both my sets of grandparents, down from them, probably within that sort of cone, I'd share with.	Relatives – they'd be interested (1)				Perceived Utility (41)
P20F: dependent on whether, when the child's a bit older, they want to know. […]the sort of attitude they have got towards it. P8M: I don't have any kids. If I did, I probably would.	Children – for their interest (1)				
P8M: I would share with my partner definitely. P20F: re. other family members] I think it would just be dependent on the family member, so like a partner, yes, uncle, um [maybe not].	Partner – for their interest (2)				
P2M: if I did this, if I do this, because now I'm thinking about, I'd definitely advise my younger brother to do it as well, and my cousins, everyone who should.	Relatives – to encourage them to undertake WGS (1)				
P97F: [re. Alzheimers] and so if I know that I will have this one, and maybe I will forget like the people who love me or something, I would like to tell them that maybe I'm going to have this, to just prepare them for that.	Relatives - to prepare for a condition I may get (1)	Access family support (3)			
P2M: [re. sharing with parents] if it was something really serious with which I wouldn't be able to deal was on my own, but even then they can be a little bit nagging. P97F: mother, it depends 'unsure', it depends on the gravity, sorry, the importance, sorry I'm in 'French'. Mother, father. R: so if it was more grave, would you want to? P97F: if it	Parents – (unsure) serious results only (2)				

is really, yes if it's really grave I would tell my mother, my parents, my mother and my father.					
P98M: and certainly share with a child if I would have one because well my predisposition towards things would be linked to theirs.	Children – inform of shared predisposition (1)	Inform relatives of shared risks - (2)			
P8M: Other family members, that would depend on how close family they are, so possibly my aunt's and my grandparents and things, and if it said that I have something that's that passed on from the family. Let others know, so I suppose that's the sort of 'yes'.	Relatives – forewarn of their potential risks (1)				
P14M: I don't have any children. [R: if you have children?], probably not, it would just panic them.	Not children – protect from panic (1)	Impact on relatives (4)			
P73F: all of these 'unsures' are, well I don't have children so I don't know how I'd feel.	Children (unsure) – cannot hypothesise (1)				
P14M: Parents are annoying.	Not parents – annoying (1)				
P8M: I'd share it with my mum. P8M: My dad, no I don't get on with my dad so.	Not father- don't get along (1)				
P14M: my normal thing is not to talk about my health to anyone, I probably wouldn't share with my mother, it would probably worry her more.	Not parents – not to worry them (1)				
P14M: Friends, oh they'd be annoying.	Not friends – annoying (1)				
P20F: [re. support group] I don't really see me doing that. P99M: I just feel probably uncomfortable in a support group.	Not support group – discomfort (2)	Impact on self - discomfort (4)			
P8M: an online forum, probably not. P20F: [re. online forums (same response as Support Group)] I don't really see me doing that.	Not online forum – discomfort (2)				
P74F: best friend	Best friend – for their interest (1)	Impact on self– negative interactions (2)			
P98M: Probably wouldn't share it with a friend, um, it's incredibly personal and there is not necessarily a relation between the two; **if the friend is also sharing theirs.**	Not friends – too personal, unless reciprocal (1)				
P98M: if the friend is also sharing theirs.	Friends – if sharing is reciprocal (1)	Friend – shared			

P98M: Um other health professional, I'd say yes but on the basis that it would be to do with what they do in their jobs or what they research.	HCP – for their interest (1)	interest (3)			
P98M: Um, so if it's not a case of, and providing information to someone where it's completely unrelated to what they'd care about. Um, 'cause at that point they are just sort of a stranger. be that, whether they are involved with genome sequencing or whether they are involved with preventative measures for a disease that involved in the sequencing or curing the disease or things like that.	Not HCP – if not relevant (1)	Professionals' area of interest (2)	Community of shared interest (13)		
P2M: Researchers, I'm all for supporting research or I wouldn't be here otherwise. Friends, I would be telling them to do it as well. P14M: Yes and [I **trust]** researchers, um but I think I'm quite private usually on those things. P14M: yes, the researcher obviously I've already said this. P97F: Researcher, 'yes', the same, if it can help. P8M: researchers, yes but I'd need to know about them, the actual research, yes. P98M: A researcher, with the same sort of point of view, 'yes' if it's of benefit to their research. P97F: [97F data chunk taken from response to "support needs" question] Um, I think I will share it with research or anything.	Researchers – to support research (6) ---------- Researcher: Trust (1)				
P20F: [re. sharing with researchers] depends who's researching P30M: I see no clear reason why you would want to tell them, so that really depends on the results. P73F: [re. 'unsure' of sharing with researcher] Depends on what they're doing research on, so, and how they're doing it. P99M: I'd be more sure if, if they used my genome sequencing to help combat that disease maybe.	Researchers (unsure) – depends on research (4)	Support research (11) ---------- Trust (1) ----------			
P98M: Online forum, um, ah yes but with another qualifier of anonymity. Um, I'm all for being able to see averages from these results and those averages have to be collected from somewhere and so if I can help in collecting those averages by	Online forum – anonymous addition to database [research] (1)				

submitting my results as an anonymous participant, then yes I would to aid that. Um if it prompted me to specified personal details such that I could provide the details to an online forum, then no I probably wouldn't.					
P8M: and other health professionals who might need to know. P14M: I **trust** Healthcare professionals most, clearly. P20F: [re. share with professionals], looking to for information and advice P30M: the reason why you would want to share, I would think, I mean these are professionals so if you're going to them in your sharing it with them it's mostly because you are seeking advice or help and the more information you give them the more they will be able to help you.	HCPs – to receive advice (4) ---------- HCP -Trust (1)				
P30M: And the other people like, I see no clear reason why you would want to tell them, so that really depends on the results. P73F: [re. sharing results with professionals] and the rest of it and just unsure about because it would depend on circumstances, so if it's something that I need to take action on.	HCP (unsure) – if action needed (2)	Access professional health care (16) ---------- Trust (1)	Access health, social care and support services (23)	Health planning (41)	
P97F:[re. family doctor / physician] I want to share, but if I share it would be recorded somewhere? R:probably it would become part of a record. It depends on whether you give it to them to look at or whether you actually hand it over. If you handed over then it's going to be. P97F: well this one I am unsure [family physician]. R: OK, again it's back to your previous, saying that you weren't sure if you wanted it to be part of the health record.	HCP (unsure) – share but NOT for health record (1)				
P14M: Yeah I can go with genetic counselling. P97F: genetic counselor, yes because it's the people who would advise me, or something. P98M: The same with the genetic counselor.	Genetic counsellor – for advice (3)				
P2M: [clinical geneticist] sure why not, and genetic counselor yeah, other health professional, I mean the idea would have to have the	Clinical geneticist – for advice (4)				

database for any health professional who interacted with me could use. P97F: geneticist, 'yes' if he can help to improve something. P97F: geneticist, 'yes' if he can help to improve something. P98M: Clinical geneticist, I see no reason why I wouldn't share it; it's their job to be interested in things like that. I think it might help their work if they had more information from more people.					
P8M: [GP], yeah they can know. Anyone that's an expert in it. P14M: I would probably want it to be shared with my family physician [GP] one man in the thousands of GPs who work at Cripps. I don't know who my actual GP is, but the person whoever is there. So I'd probably like it to be shared with them, but I wouldn't really want to go with my results to them.	GP – for advice (2)				
P2M: Support group, ah I've been reading about this since I've come to the UK, because we don't really have that many back home. Uh I guess so, if I had some really serious ailment, I would want someone to talk about it with. P8M: A support group, I am not in any so I don't know. I suppose if I were in a support group for a condition I found I had through this, then yes, (but Ticked UNSURE). P98M: I probably wouldn't share all of it, if it were support group for persons with the disease or likely to get disease, being uncurable, I think like Huntingdon's or something and I were to start attending the support group as a result of my sequencing, um, then yes' I'd probably share with them by being there that I am susceptible or have Huntingdon's disease. I wouldn't share any more information about the rest of the results.	Support group – for serious illness (3)				
P8M: A support group, I am not in any so I don't know. I suppose if I were in a support group for a condition I found I had through this, then yes, but otherwise, no [participant ticks 'unsure']. P30M: Probably won't go to a support group, I don't know maybe. I	Support group (unsure) – depends on ailment (2)	Access support (7)			

mean like it depends on how sick you are, what disease you are likely to get [selected 'NO' on Table but expressed uncertainty so this COMMENT has been put under UNSURE].					
P2M: online forums, I'll mark it [yes], I consider it both the same [same as support group]. P99M: where[as] online I could just dip in and out kind of thing.	Online forum – support (2)				
P98M: unless it, by 'it' I mean the sequencing presented something that I should be aware of in the immediate future.	Employer – if immediately relevant (1)				
P2M: Employers, mm, what point could that be, not sure, I mean if you had some kind of accident at work but, but then again if you had it in your database, you wouldn't need to tell your employer. P2M: [re. sharing with employer], I will mark it as unsure because I think it would depend on the ailment. I don't know, something that would be really de-humanising, really demeaning I wouldn't like them to know. P20F: employer, it would be dependent on whether it would crop up during that role, or batch of employment, P30M: employer, hmm, I was going to tick 'no' but I was thinking if they think if I'm likely to be sick they might treat me better.	Employer (unsure) depends on relevance (4)	Occupational health (6)	Health declaration (18)		
P8M: Employers, no. P98M: Employer, um, I'm the younger and in my mind a lot of the unpreventable diseases and whatnot are way off in the future so applying for jobs right now I am trying not to think about them, um so I'd probably say 'no' unless it, by 'it' I mean the sequencing presented something that I should be aware of in the immediate future.	Not employer – not relevant (1)				
P2M: [re insurers], I suppose so, that would come in handy.	Insurer – useful for policies (1)				
R: If the terms were different and you actually were to somehow benefit by giving your whole genome sequence results to an insurance company, would that change your mind about? **P98M**: yes I think it	Insurer – if I benefit (2)	Personal health insurance plan (12) ----------			

would, um, it seems like a selfish viewpoint because I am aware that its, at current point of view would negatively affect the insurer, but I would change my mind if it was of benefit to me, […]Yes I would change my answer for that. P99M: [P99M selected NO on the Table but then said] Yes, if I benefit.		(dis)trust (2)			
P5M: If it was something you felt might affect health insurance, travel insurance, life insurance… then you don't want something like that in your record. P8M: Insurers, the answer to the question 'would I want to?', they probably try and put your premium up or something. [participant ticks 'no'] P14M: dis**trust** of insurance companies and employers. P14M: Certainly not an insurer, that's a very big no. D**istrust** of insurance companies… P97F: Insurer, it's complicated this one because it can be better for your insurance if you have nothing or it can be really bad for your insurance if there is a lot of bad results. I would say 'no' [insurer] P98M: [re. sharing with Life Insurance] I'd say no then because if I were to get a disease and I knew I was going to get that it would only limit the quality of Life Insurance I could get, there wouldn't be any benefit for me doing that, there would be of a benefit for the insurer but from my point of view I don't know how that would help me, so no I wouldn't want to. so based on the terms of the insurance company, it's going to benefit and you won't. P98M: but it's an incredibly personal thing and it's completely related to my life and how long I will live for, um and so I think in that respect being selfish is OK for that. P99M: (P99M selected NO BUT said…) I have ticked it in the negative way, insurance [laughs], if I benefit from it [laughs]	Not insurer – dis-benefit (8) ---------- Not insurer – not trust (2)				
P20F: insurer's prices might bump up?	Insurer (unsure) – (1)		Trust (4)		Trust (4)

Themes: Desire for relatives' WGS results			
Raw data	**Raw themes**	**Intermediate order themes**	**Higher order themes**
P5M: I think I'd like to know **when they are comfortable with saying**, […] P14M: **Only if they wanted to tell me, I wouldn't want to be told unless they wanted me to be told,** P14M: **it would be up to them how I would be told**. P14M: I still think it's, **it's a very personal thing** still to someone so **I expect them to have the consent**. P14M: [R: family member who had their whole genome sequenced and there was something and their **result that they thought might be of interest to you**, would want them to come directly to you and tell you.] yes, in those situations. P74F: I grew up in a family where they **only share if they want to**, P98M**: I think I would**, **if they would be willing to disclose** it to me. P98M: **I wouldn't want to know if they didn't want to tell me**. P98M: Um, especially if it would be **things that would affect me, in terms of their quality of life, then needing to go into care early** or anything like that P74F so if they're holding it back then fine, **if you wanna keep a secret it's fine**, P20F: Not more for myself, but more to know **what to expect with them**. P20F: Just [want to know at the point] when the results came back, if there was **anything to worry about for them**, not for me. P73F: if it was **bad news about my parents**, I think I would want to know at any point, just because, **to prepare myself** I guess. P5M: **stuff which I can help support with** P5M: if it's obscure information, you don't know what it means, it doesn't matter. If it's not important things that's fine but **if it's either they are going to need certain care or treatment later on in life** P5M: **stuff that might affect me** P5M: **they are a carrier of something and then I have a strong chance of that as well or something which means I could also have that.** P98M: if it's things them having or being likely to get means **that I'm going to get it or I'm likely to get it**, and things like that. Um, so yes I would want to know. P74F: **I'd only want to know if I feel ready to share my results**, 'cause it would be a conversation of **tell me your results and then I'll tell you mine**, so then **I have to be confident and ready with my own results to share, and then this conversation can happen**. P74F: **if they're gonna share it and then encourage me to do this whole genome, then I might**. P20F:[re. wanting to know results of a relative if that person is considered genetically close] I'd want to know, but no, **I probably would push it**, I'd, I'm not going to lie. P73F: Um, if it's **good news about my parents**, again any time I don't think it would matter, **it would just be something to talk about**, I guess.	Receive relative's results: If / when relative is willing (9) Receive relative's results: relative may need help with (5) Receive relative's results: results that may affect me (3) Receive relative's results: Reciprocal exchange of results (2) Receive relative's results: Insist on knowing relative's results(1) Receive relative's results: Conversation piece – good news(1)	Consent (9) Impact on family (5) Impact on self – bad news (relatives' results) (3) Relative's shared interest(2) ---------- Discovery (1), (1)	Consent (9) Impact on family (5) Impact on self (3) Intimacy (2), (1), (1)

Themes: Greatest Personal Challenge: data chunks from Challenge question in middle and the one at end of interview			
Raw data	**Raw Data themes**	**Intermediate order themes**	**Higher order themes**
P74F: I think it would be the sort of, the **data that I didn't know,** but then I wanted to know, so if, it wasn't, so say my parents are diabetic yeah. Oh I might be predisposed to diabetes, but then if it's something like cancer I've never seen in my family and then I sort of predisposed to it. P2M: [I] am currently **living on my own, without anyone e**lse, and I had a bad result or untreatable. I think that could be an issue, so perhaps include like a line at the end of the whole genome sequencing, to ask **whether you have some way of dealing with possible negative results**? …at some point in the process before being sequenced. P14M: I'd go into it promising myself I wouldn't be a hypochondriac, and then I know the hardest thing would be for me to not to **panic about results**, um, which is why I thought about having sort of umm a **Healthcare professional to try and rationalised the thoughts**, and how in relation to the general population you are. To try and rationalise what you've got. P99M: , if that was known to become, say like Huntingdon's disease, which is like 40-ish. It's kind of **coping with the fact that I know that I won't be around for that long mayb**e. So maybe it would be like some kind of like grace period where I could be kind of struggling to cope with... **R:** after you get the results, there's going to be a, at some point you feel there **might be a period where you have to get your head round.** P20F: I suppose it's alright me saying, now I want to know, but then I'd probably kick myself if something came back saying, oh, I was better off not knowing, but that's, I think for me that'd only be in the **initial shock stage, I think once I'd had time to sit down and process it and look it up and x,y,z, depending what it was, I'd be OK.** P30M: I mean if he's **gonna tell me like I'm going to die soon then it would be quite surprising** [laughs]	Impact of unexpected results on self (1) Impact of results while on own (1) Impact of bad news on self (4) Professional support for Impact of results (1) Time to manage impact of WGS results on self(2)	Professional support for Impact of results (1) Impact on self - bad news (7)	Professional intervention – after WGS (1) Impact - on self (14)
P2M: perhaps **deciding, with whom or where to do it** [where to go to get WGS undertaken].	Choosing Provider (1)	Choosing Provider (1)	
P98M: I also think that having knowledge about predisposition to diseases and where that puts you as a **standpoint between you and the life insurer**, I think that would cause a problem as well because obviously they would be less likely to insure you,[R: or deteriorate the policy], yeah.	Impact on self- Personal financial burden – insurance (1)	Impact on self- Personal financial burden – insurance (1)	
P14M: Cos I think it's um, it's easy to look at someone and say you've got to 25 per cent risk of something, of cancer but then that's [probably lower than the general population], but then if somebody said oh you've got one in four chance, it's **really scary until you realise what that actually means**. So I think my **biggest challenge would be not to be a hypochondriac**. I don't know if it's really hypochondriac or just... chondriac. P98M: the other personal challenge that I think I would see is, **if it says you are 50 per cent likely to have this disease that unavoidable and untreatable, how that would affect me mentally** and how I would be able to cope with **knowing that**	Impact on self of risk uncertainty (2) ---------- Impact on self of certainty (2)	Impact on self (4)	

later in life I'm going to get a disease that I cannot do anything about and I can't cure anything, and it's sort of **knowing that my life's expectancy is lower** as a result of that.			
P98M: if I'm likely to get disease but I won't if I take the steps, **the first challenge would be can I take those steps, can I adjust myself such that I can avoid that disease**.	Impact on self- Difficulty taking health action (1)	Impact on self- Difficult taking action (1)	
P99M: yeah, I say less, for like, for me, but if someone had, **say if I had a family in like five years and then I had that disease, then I would be kind of, that would be worse for me** then. P20F: my dad is very like anti-this, he is kind of like 'we shouldn't know', he doesn't want me to be an organ donor, he doesn't want me to, I want to donate my body to science, he doesn't want me to do that sort of thing, um, he thinks what will be we will be sort of thing, he wouldn't, and he'd be arguing, and **he would be upset** if you knew I was going to get these things, it would be moreover, it wouldn't bother me, I'm all, it's going to happen anyway, sort of thing, so I'd rather know and prepare, but he, I think it would be a family, **become a family argument**, a family constraint. I'd probably still tell him I anyway. P97F: If I know that I can have an important disease, **to know if I have to tell my family or not**, sharing the information. P97F: The **challenge is um, telling my family or not.**	Impact on family (4)	Impact on family (4)	Impact - on family (4)
P8M: I suppose the challenge for me this sort of having my DNA mapped on a computer somewhere. At some point **someone could replicate it or something**, and **how much information are you prepared to give, because there is all the stuff about data protection and companies using your information**. I don't think it'd be a major problem for me, but be something I think about it. Probably **I'd want to check that it's not going somewhere random or being sold to people, or experiments I don't agree with**, and things.	Sensitive personal data security concerns (3)	Data security concerns (3)	Sensitive personal data security (3)
P98M: well obviously there's the cost incurred to it, um, and having it sort of **become the norm** would be incredibly expensive for that to happen, um and I guess then people would be charged for not doing it, if ever, we have to pay **tax** and has some of that money go toward genome sequencing, there would be people that are against it that sort of say why am I paying for it if I'm not having my sequencing.	Societal burden (2)	Societal cost (3)	Societal cost (3)
P14M: medical practitioner time is probably the hardest, uh, I can imagine it being, if this is something that is done on a larger scale I can imagine there being a shortage of medical practitioners, it's already hard enough to see a GP, um, or a nurse, or any one. Anyone who's ever tried to get into a GP's practice will know, so if it's something that is more widespread I imagine there's going to be a lot of challenges in how you deal with this	Burden on public services (1)		

Themes: Support needs			
Raw data	**Raw data themes**	**Intermediate order themes**	**Higher order themes**
P20F: I think you would need education about firstly **what** genome sequencing is, **why** you've had it done, and then **what the results are**. P20F: And then maybe some, don't know what to call them, like **classes** where you mixing **with people with the same sort of risk or predisposition or condition** as you. P99M: maybe if they, like supplied, kind of a **supporting information**, like say a **brochure or a leaflet** with it, to help you learn more about it. So when they get to tell you might, say if they bring up say like, say if we've talked about different diseases and I've not known some of them, so it's like if they had that, like a **brochure** of all the different things and **explained what it is, and all the different aspects of genetics that I might not know beforehand**, then maybe that **supplementary information** would be helpful. P2M: I guess if or when I go into it **I will definitely want to know as much about it as I can, like everything that could come out of it,** in the sense of, you do it, you **know what you're doing**, then **you'll be able to deal with whatever comes out of it. What could go wrong**. P2M: whether you would be prepared to **deal with you having an incurable or untreatable disease**, that would be separate issue	Education about what WGS is (2) Education about why undertaking WGS (1) Education about results (1) Education with cohort of similar (1) Explanatory supplementary information to address lack of knowledge (2) Brochure / leaflet to provide explanation (2) Knowledge to prepare for results (4)	Patient education to understand WGS results (13)	Patient education (9)
P2M: whether you would be prepared to deal with you having an incurable or untreatable disease, that would be separate issue; that would require, I suspect, some kind of **doctor-patient relationship** on some level. So as to, the **doctor being able to ascertain whether you would be prepared**. R: so before the result, or before the test. **P2M**: yeah. R: **the discussion around, maybe some of the more, um, how would I put it, so some of the things that may come later in life, or maybe some of the more uncertain ones, or the untreatable ones** amongst those. **P2M**: especially those. P5M: **explaining what this [results] could mean**. P99M [ideal process described in terms of "no challenge"]: as long as they supplied me with the right information, so that I would know what was going to happen and know what my results are then I don't think there would be any challenges.	Doctor-patient relationship (1) Discussion with Doctor to ascertain readiness (2) Explanation about what WGS results could mean – before WGS (1) Process and results Information before WGS (1)	Pre-WGS professional information and support needs (5)	Professional interventions - pre-WGS (5) ---------- - post-WGS (16)

P8M: It would depend on the results that I got, but a clear **simple explanation of what the results mean** and **implications of those results** and **how my life might change** because of them, so is it that **I need to go to hospital or to do something**. P30M: they should start telling you how you should, for example **stuff it needs or like certain things to avoid** more. P30M: example if you have a list of diseases, you have a likelihood of contracting it. So like if you, if I imagine it like **some kind of table, so it would be like 'disease', and 'percentage'**, so for those that you might get, you want to know **how you can possibly reduce the risk of contracting them** and then for **those that you will inevitably get** […]for an adult most likely you still want to give the adult the authority if they want their entire results, so basically it's like you go take the test and they tell you like for the safe ones, **you might get this**, this, this, this, **you should do that**, that, that, that, and that's it really. **R**: OK so like an ABC, this is your disease, this is your chances, and here's what you should do about it? **P30M:** yeah. P97F: I want to, **me know the information** and decide what is good for me.	Simple explanation of results - after WGS (3) Information about life changes-after WGS (1) Information about actions to take – after WGS (3) Information about risk reduction – after WGS (1) Personal disease risk table (1)	Explanation of results after WGS (9)	
P2M: Depending on where I would be at my life when doing it, I suppose some kind of **psychological support** could be helpful, I mean, I don't know, I am not an unhappy person right now, but suppose going through a rougher stage in life, later. P97F: And the support,[…] like a gentician [geneticist] **analysis when I receive something** about it. P97F: And, **doctor, if I think I have to consult him, for example if I think that I'm concerned with something grave, I want to share with the doctor,** so the **doctor's support, they have people support** P14M: so I think that would be more useful, and I think **people are probably better at calming other people down** so I imagine a **health professional would be better at delivering bad news or good news,** especially bad news, in **calming people down as opposed to just a letter or e-mail.**	Psychological support for results (6) Support with understanding analysis (1)	Professional support to deal with results (7)	
P30M: […]for an adult most likely you still want to **give the adult the authority if they want their entire results**, P97F: I want to, me know the information and **decide what is good for me**.	Adult autonomy (2)	Autonomy vs dependency (2)	Autonomy v dependency (2)

Themes: Ideal process			
Raw data	**Raw data themes**	**Intermediate themes**	**Higher order themes**
P20F: and then [after 16] it's your own choice, I'd probably still **take my mum and dad** anyway. P98M: I would want to **do it with family** and having them do it at the same time that might be useful **…probably having the entire process […] described to me.** P97F: So**, first have information by a genetician [geneticist] or a person specialising** in it, and **then doing it**, P99M: if **you met a professional beforehand to talk you through this, so the process** that was going to happen. P5M: **meeting with some health care professional first, a few times**, […] P74F: I think it's more of, um, something **private**, so something that not everybody in the family knows, say its **just me and my mum** and then we do this in private, results are collected in private, nothing is shared until I'm ready, that sort of process.	Entire process supported by family (2) Information from specialists beforehand(1) Meeting HCP before WGS for information (2) Private process, mum only (1)	Access family support (2) ---------- -- Professional to explain results of WGS (3) ---------- -- Close relative for privacy (1)	Access family support (2) ---------- ----- Professional interventions before WGS - decision making (3) ---------- - Sensitive personal data security (1)
P5M: […] and if it was protracted **over a period of time,** then you could have **time to think about what you were going to do** and kind of weigh it up properly and then kind of go through.	Protracted informed consent process to undertake WGS (1)	Consent (1)	Consent (1)
P14M: in the simplest of terms where **you will get a text message or you will get GP's appointment if it's positive.** P20F: I would want **access to like the counselors** and stuff you were talking about. P97F: **receive the results**, **have analysis of the results** and **people I can contact if I want to.** P99M: then I guess going and actually having your genome sequenced, and then say **a few sessions after talking about your results and what that means**.	Contact to talk after results (1) ---------- Meeting HCP after for explanation of results (3)	Professional support to deal with the results (1) ---------- Professional to explain results of WGS (3)	Professional interventions Post-WGS (4)
P2M: if children were taught about this at school, not in the sense of 'oh go and do it', just, there's this thing out there called whole genome sequencing and you could do it, and just give them some kind of **basic level of awareness**, I think that could be cool. P14M: **the way that a lot of blood tests are done now**, in the simplest of terms where you will get a **text message or you will get GP's appointment if it's positive**, I feel like that is actually quite an ideal process because, you know they sit down, they tell you the results and what it means and the treatment for it, if there is any. Obviously **putting people's mind at rest as soon as possible is the best way**, and I think a positive result by text message means that they would have to have an appointment which means a lot more waiting still, um and a negative result by text obviously means they get peace of mind sooner, so I think any process	Common knowledge(2) Common process(2) Results comparisons to represent population (1) ----------	Normalisation of genomics (5) ----------	Normalisation of genomics (5) ----------

whereby you can maybe give people some comfort as soon as possible would be the best process. P98M: but be **common knowledge**, commonly known, so it wasn't a case of, I say to a friend of mine 'oh I'm going off for this next stage of sequencing' and they say 'what is that?' For it to just be sort of **normal,** like saying 'I'm going for a blood test', it's like a I'd like it to sort of **become common enough that it's not completely out of the norm for us to go and do this**, such that the results in **comparison with averages would be representative of a population**, rather than, only people who go and get sequencing are likely to get this disease, and so the results are **skewed** as a result of that. P20F: I'd want it done and then I'd want like **a letter and something I can keep for my own record** to pass onto whatever crops up in the future. P30M: I imagine it like some kind of table, so it would be like **'disease', and 'percentage', so for those that you might get, you want to know how you can possibly reduce the risk of contracting them and then for those that you will inevitably**	Results report for personal record (1) ---------- Disease, risk and actions table in results report (1)	Life planning (2)	Perceived utility (2)

Appendix E

Definitions and Categories for Factors

The TPB factors are defined below, under their corresponding TPB constructs. From the findings of the survey with the young adults, the external factors that were indicated as influential on behavioural intention were:

- Gender: male or female
- Genetic-specific education: none, school, university
- STEMM status: yes or no
- Generic Completed Education: (subject studied not specified), school, 1st degree, 2nd degree

The attitudinal factors that were identified and categorised under 'perceptions of utility' were:

- Desire to plan: urge based on personal evaluation of planning for self or others
- Desire to protect: urge based on personal evaluation of acting to protect oneself or others.
- Relevance: personal evaluation of how pertinent or connected one is, or others are, likely to be with the matter at hand.
- Usefulness of communicating(ion): personal evaluation of likelihood communication (incl. reports, conversations etc.) will be useful oneself or others
- Desire to share: urge based on personal evaluation of sharing with others.
- Seriousness: personal evaluation of how important, weighty, severe, grave or harmful the outcome(s) of the matter at hand is.

- Treatability: personal evaluation of how responsive the matter at hand is to treatment.
- Certainty: personal evaluation of how sure one is (how much one believes) that something is factual, true or will occur.
- Temporality: personal evaluation about timeframe of events in relation to oneself or others; e.g. present, near-future, far-future, next generation.
- Value for money (VFM): personal evaluation of utility gained or intended outcomes achieved for the monetary resources required to do so.
- Complexity: Personal evaluation of how complex or intricate the matter at hand is.
- Desire for privacy: urge based on personal evaluation of importance of privacy to oneself or others.

The attitudinal factors identified categorised under 'perceptions of autonomy and dependency' were:

- Desire for choice: urge based on personal evaluation of being able to choose from options
- Desire for support: urge based on personal evaluation of receiving support for oneself.
- Interest in self-discovery: urge based on personal evaluation of receiving new information that may be added to one's sense of self-identity.
- Desire to offer support: urge based on personal evaluation of providing support to others.
- Shared interests: personal evaluation of interests one may have in common with others. May refer to interest in same things for similar or for different reasons.
- Rights: personal evaluation of one's legal, social, or ethical principles of freedom or entitlement
- Responsibilities: personal evaluation of one's obligation to support the legal, social, or ethical principles of freedom or entitlement of others.

The factors identified and categorised as perceived behavioural controls were:

- Ability to choose: Personal evaluation of beliefs about the power of facilitators and inhibitors to being able to choose in context of the matter at hand.

- Ownership: Personal evaluation of beliefs about the power of facilitators and inhibitors to ownership in context of the matter at hand.
- Ability to access: Personal evaluation of beliefs about the power of facilitators and inhibitors to being able to access what is wanted.
- Data security: Personal evaluation of beliefs about the power of facilitators and inhibitors to data security in context of the matter at hand.
- Privacy: Personal evaluation of beliefs about the power of facilitators and inhibitors to privacy in context of the matter at hand.
- Normalisation of WGS: Personal evaluation of beliefs about the power of facilitators and inhibitors to normalising WGS in context of the matter at hand.
- Family dynamics and relationships: Personal evaluation of beliefs about the power of facilitators and inhibitors to relationships and family dynamics in this context.
- Trust: Personal evaluation of beliefs about the power of facilitators and inhibitors to one's ability to trust in the context of the matter at hand.
- Ability to understand: Personal evaluation of beliefs about the power of facilitators and inhibitors to one's ability to understand in the context of the matter at hand.
- Coping skills: Personal evaluation of beliefs about the power of facilitators and inhibitors to one's ability to cope in the context of the matter at hand.
- Ability to undertake health promoting actions: Personal evaluation of beliefs about the power of facilitators and inhibitors to one's ability to undertake health promoting actions for the matter at hand.
- Communication skills: Personal evaluation of beliefs about the power of facilitators and inhibitors to one's ability to effectively communicate information in the context of the matter at hand.

The factors identified and categorised as subjective norms were:

- Domain experts: Function or relationship between one's beliefs about the expectations of domain experts (e.g. genetics and genomics related scientific researchers and HCPs) and the motivation to comply with those expectations.

- Society: Function or relationship between one's beliefs about the expectations of society and the motivation to comply with those expectations. NOTE: as a member of society, an individual might subjectively consider their personal expectations as proxies for society's.
- Relatives: Function or relationship between one's beliefs about the expectations of their relatives and the motivation to comply with those expectations.
- Researchers: Function or relationship between one's beliefs about the expectations of researchers and the individual's motivation to comply with those expectations. NOTE: focus on this SN was particularly related to participants' discussions about the research study protocols and objectives of research.
- Commercial entities: Function or relationship between one's beliefs about the expectations of companies and other legal personalities and the motivation to comply with those expectations.

Appendix F

Survey with Genetic Experts

F.1 Survey Template: Genetic Expert Study

Participant Research Number**:** _____

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

Whole Genome Sequencing (WGS) Framework Evaluation Survey

In the context of **'elective screening',** surveys and interviews using hypothetical situations were undertaken to further understand factors which may influence young adults decision to engage with whole genome sequencing (WGS). Derived themes were then abstracted and the Theory of Planned Behaviour used to produce a proposed framework for factors impacting young adults' decisions on WGS.

The WGS framework represents young adults' considerations at different points on the WGS pathway**.** For the purpose of this study, it is acceptable to think the individual may choose to undertake WGS through existing, emerging and potential service delivery models, including Direct-To-Consumer (DTC) companies, specialist clinical genetics departments, with or without genetic clinician input or others.

Please tick box to indicate you have viewed the MANDATORY PowerPoint slideshow "Proposed WGS Framework Introduction" that presents the framework to be evaluated in this study ❒.
If you want more detailed information, please view Slideshow titled 'Studies that informed WGS framework (OPTIONAL EXTRA).
Please write / type your results on this questionnaire.
You may complete the survey independently. Please contact the researcher, Pepita Stringer, on pepita.stringer@nottingham.ac.uk for support, optional interview (phone call or messages) and to return completed questionnaires.
Thank you.

1. Please select as many of the following which best reflect your area of interest or work.

   ❒ Clinical genetics or genomics
   ❒ DTC genetics or genomics
   ❒ Medical information sharing – with the individual concerned
   ❒ Medical information sharing – with relatives of the individual concerned
   ❒ Other – please specify_____

2. Please select as many of the following which best reflect your professional practice.

   ❒ Genetic or genomic counselor (counsellor)
   ❒ Medical / clinical geneticist or genomicist
   ❒ Health services researcher
   ❒ Health technology researcher
   ❒ Health technology developer
   ❒ Primary care doctor
   ❒ Nurse practitioner
   ❒ Medical specialist - other than geneticist
   ❒ DTC provider
   ❒ Other – please specify_____

3. Please select as many of the following which best reflect the groups you work with.

❒ Young adults

❒ Young people

❒ Adolescents

❒ Adults

❒ Families

❒ Other – please specify_____

4. The Individual WGS pathway is presented in Slide 3 of slideshow, 'Proposed WGS Framework Introduction'.

a) Are the WGS pathway steps acceptable as presented or would you change them?

❒ **YES,** WGS pathway steps are acceptable as they are.

OR

❒ WGS pathway steps would benefit from being changed.

b) If you would change any of the steps in the pathway, please describe changes by editing the following:

1. Data consent and sample provision

2. WGS (sequencing)

3. Interpretation

4. Receipt of Results

5. Action on Results

6. Sharing WGS Results

7. Receiving relatives' WGS

In the next two questions, the following abbreviations are used to prefix the list of factors:

- *External Factors (Ext.)*
- *Attitudes related to Utility (AU)*
- *Attitudes related to Autonomy-Dependency (AAD)*
- *Perceived Behavioural Controls (PBC)*
- *Subjective Norms (SN).*

Definitions for these prefixes are available in the previously mentioned MANDATORY Slideshow titled 'Proposed WGS framework Introduction', see Slide 4's notes section.

5. Imagine a young adult who has not had any professional input, or access to the framework before embarking on obtaining WGS. Which factors do you feel they are LIKELY to have considered, prior to starting?

- ☐ Ext: Gender
- ☐ Ext: Genetic-specific education
- ☐ Ext: STEMM status
- ☐ Ext: Generic completed education
- ☐ AU: desire to plan
- ☐ AU: desire to protect
- ☐ AU: relevance
- ☐ AU: usefulness of communicating(ion)
- ☐ AU: desire to share
- ☐ AU: seriousness
- ☐ AU: treatability
- ☐ AU: certainty
- ☐ AU: temporality
- ☐ AU: value for money
- ☐ AU: complexity
- ☐ AU: desire for privacy
- ☐ AAD: desire for choice
- ☐ AAD: desire for support
- ☐ AAD: interest in self-discovery
- ☐ AAD: desire to offer support
- ☐ AAD: shared interests
- ☐ AAD: rights and responsibilities
- ☐ PBC: ability to choose
- ☐ PBC: ability to understand
- ☐ PBC: coping skills
- ☐ PBC: ownership
- ☐ PBC: ability to access
- ☐ PBC: data security
- ☐ PBC: privacy
- ☐ PBC: normalisation of WGS
- ☐ PBC: ability to undertake health-promoting actions
- ☐ PBC: family dynamics and relationships
- ☐ PBC: communication skills
- ☐ PBC: trust
- ☐ SN: domain experts (HCP)
- ☐ SN: society
- ☐ SN: relatives
- ☐ SN: researchers
- ☐ None

6. Which factors do you feel are IMPORTANT to be considered by a young adult prior to starting?

- ☐ Ext: Gender
- ☐ Ext: Genetic-specific education
- ☐ Ext: STEMM status
- ☐ Ext: Generic completed education
- ☐ AU: desire to plan
- ☐ AU: desire to protect
- ☐ AU: relevance
- ☐ AU: usefulness of communicating(ion)
- ☐ AU: desire to share
- ☐ AU: seriousness
- ☐ AU: treatability
- ☐ AU: certainty
- ☐ AU: temporality
- ☐ AU: value for money
- ☐ AU: complexity
- ☐ AU: desire for privacy
- ☐ AAD: desire for choice
- ☐ AAD: desire for support
- ☐ AAD: interest in self-discovery
- ☐ AAD: desire to offer support
- ☐ AAD: shared interests
- ☐ AAD: rights and responsibilities
- ☐ PBC: ability to choose
- ☐ PBC: ability to understand
- ☐ PBC: coping skills
- ☐ PBC: ownership
- ☐ PBC: ability to access
- ☐ PBC: data security
- ☐ PBC: privacy
- ☐ PBC: normalisation of WGS
- ☐ PBC: ability to undertake health-promoting actions
- ☐ PBC: family dynamics and relationships
- ☐ PBC: communication skills
- ☐ PBC: trust
- ☐ SN: domain experts (HCP)
- ☐ SN: society
- ☐ SN: relatives
- ☐ SN: researchers
- ☐ None

7. Please indicate any changes that, in your opinion, would make the framework more accurate or complete (e.g. re-naming, re-grouping, separations, re-categorisation of factors or any other suggestions). Please give an explanation for your suggested changes. If you would not make any further changes please state 'none'. Continue onto next page if more space is needed.

8. Please use this space to add any further comments or questions you may have. Use other side of paper if you need additional space.

Thank you very much for your time. Please return your completed survey to Pepita Stringer.

Pepita Stringer, School of Computer Science, The University of Nottingham, Jubilee Campus, Wollaton Road, Nottingham NG8 1BB

Tel: +44 (0)7791443894 pepita.stringer@nottingham.ac.uk

PLEASE USE THIS PAGE FOR ADDITIONAL COMMENTS, IF NEEDED:

F.2 Presentation: Proposed WGS Framework Introduction

Proposed whole-genome sequencing framework introduction:
Your views about young adults attitudes for receiving and sharing WGS information

Image credit: www.macroevolution.net

Author: Pepita Stringer, MSc
University of Nottingham, England

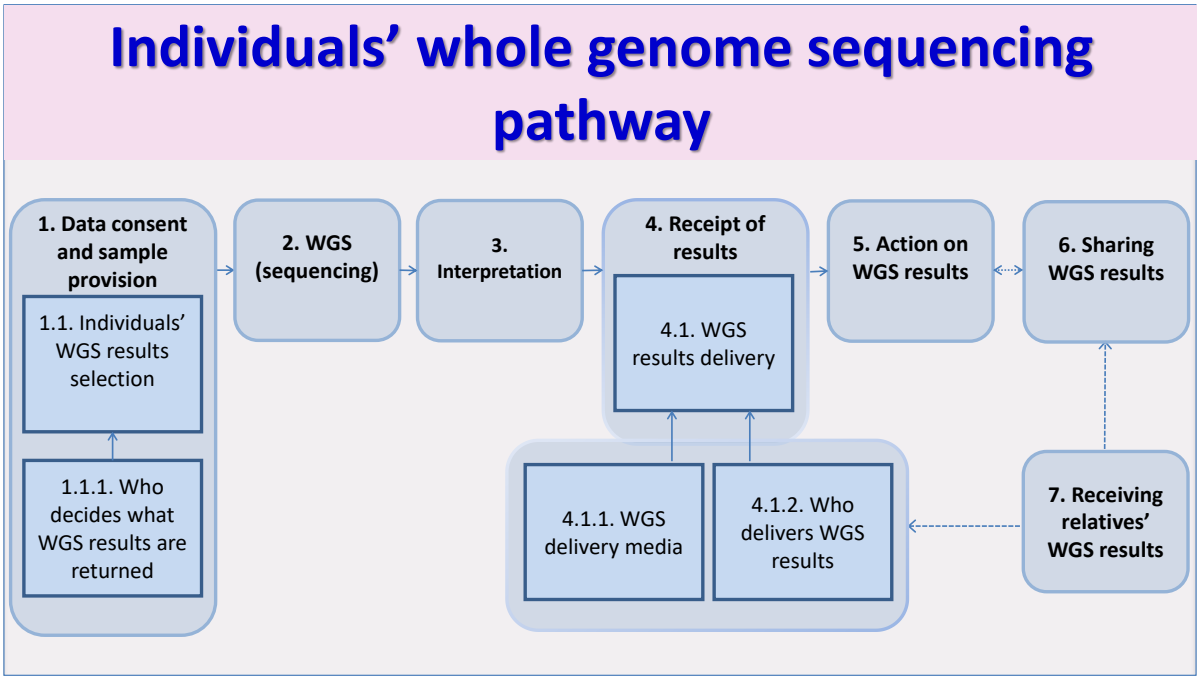
Please read Notes section

Please be aware that there is detailed information in the notes between presentation slides.

NOTES

- **The participants in the studies that have informed the proposed framework were young adults, aged 18-25.**
- **Those studies explored factors that may affect young adults' attitudes to whole genome sequencing (WGS) with young adults. They are a group likely to use emerging genomic services, so their perspectives are important to understand.**
- **In the context of 'elective screening', surveys and interviews using hypothetical situations were undertaken with young adults to create the proposed framework of factors, The WGS framework represents young adults' considerations at different points on the WGS pathway.**
- **For the purpose of this study, it is acceptable to think the individual may choose to undertake WGS through existing, emerging and potential service delivery models, including Direct-To-Consumer (DTC) companies, specialist clinical genetics departments, with or without genetic clinician input or others.**

Individuals' whole genome sequencing pathway



NOTES

The process map was derived from the Chief Information Officer's pipeline and maps to the structure of the interviews.

- **Participants were asked what WGS results they would want.**
- **They were offered categories with clinical-utility terms then a list of diseases / conditions to select from.**
- **Participants were asked who they thought should decide what results are returned to them.**
- **It is assumed that an individual would generally be waiting in Steps 2 and 3.**
- **Participants were asked about preferred receipt of results, actions they would consider undertaking with results and who they would want to share WGS results with.**
- **Additionally, participants gave their views about receiving results that belongs to relatives who have had their WGS undertaken. Dotted arrows at Step 7 indicate how this optional step in the pathway may relate to the other steps.**
- **Participants were also asked about their perceived resource needs, what they thought an ideal process would be like and what challenges they perceived if undertaking WGS.**

Whole genome sequencing framework: factors that influence behaviour

- **External factors (Ext.):**
  - Gender
  - Genetic-specific education
  - STEMM status
  - Generic Completed Education
- **Subjective Norms(SN):**
  - domain experts (HCP)
  - society
  - relatives
  - researchers
- **Attitudes, Utility-related (AU):**
  - desire to plan
  - desire to protect
  - relevance
  - usefulness of
  - communicating(ion)
  - desire to share
  - seriousness
  - treatability
  - certainty
  - temporality
  - value for money
  - complexity
  - desire for privacy
- **Attitudes, Autonomy-Dependency related (AAD):**
  - desire for choice
  - desire for support
  - interest in self-discovery
  - desire to offer support
  - shared interests
  - rights and responsibilities
- **Perceived Behavioural controls (PBC):**
  - ability to choose
  - ability to understand
  - coping skills
  - ownership
  - ability to access
  - data security
  - privacy
  - normalisation of WGS
  - ability to undertake health-promoting actions
  - family dynamics and relationships
  - communication skills
  - trust

NOTES

Previous slide presents a list of factors for consideration. Constructs from the Theory of Planned Behaviour (TPB) were used in study design and to classify the framework's factors.
The constructs used are: 'External factors' (Ext.), 'Attitude' (A), 'Perceived Behavioral Control' (PBC) and 'Subjective Norm' (SN).

External (Ext.): individual differences and environmental influences such as age, gender, experience (family or personal history), **knowledge , education, personality type, social class, and socioeconomic status.**
Which influence the other constructs.
Attitude (A): An overall positive or negative evaluation of one's (behavioural) beliefs about the outcomes of a particular behaviour, event, concept, object or person. Attitudes are subdivided based on themes our participants identified.

- **Attitude related to Utility (AU): evaluation of beliefs primarily related to usefulness or utility of the outcome.**
- **Attitude related to Autonomy-Dependency (AAD) : evaluation of beliefs primarily related to autonomy and dependency of the outcome.**
- **Perceived behavioural control (PBC) : One's perceived control over the performance of a particular behaviour. PBC is predicted by one's (control) beliefs about factors likely to facilitate or inhibit the behaviour and an evaluation of the power each factor has to affect one's behaviour.**
- **PBC unifies two types of control, perceived self-efficacy (ease or difficulty of performing a behavior) and perceived controllability (beliefs about the extent to which performing the behavior is up to the individual). It captures the belief that one is capable of engaging in a particular behaviour. For our purposes, on the WGS pathway.**

Subjective norm (SN): A function of one's (normative) beliefs about the expectations of important individuals or groups weighted by one's motivation to comply with them. Subjective Norms can also be described as perceived social pressure to perform the behaviour.
Further constructs in the Theory of Planned Behaviour (TPB) model are:
Intentions: are the most immediate and important predictor of whether people perform a behaviour.
Behaviour: is the performance or non-performance of an act. In our studies, the behaviours in question are those related to the steps along the Individuals' WGS Pathway.

Thank you for reading this introduction.
You may now complete the study's survey.

If you would like more information about the research studies that informed the framework, the framework structure and definitions for the factors listed in Slide 4 please see the following slideshow: 'Studies that informed WGS framework (OPTIONAL EXTRA)'.

Thank you.