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Communicating Unexpected Genetic Information with Family Members: A Multimethod Study of Secondary Findings Recipients

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Abstract

Communicating Unexpected Genetic Information with Family Members:
A Multimethod Study of Secondary Findings Recipients

Background: Medically-actionable secondary genomic findings (SF) can be life-preserving or life-prolonging for recipients but this benefit can only extend to family members if this information is shared with relatives. How SF recipients communicate this important genetic information with relatives, barriers and facilitators to this process, and SF recipients' lived experiences in communicating about their results over time remain largely unknown. Family communication is required for relatives of SF recipients to access cascade testing and the potential benefits of enhanced screening and management. Applying behavioral and implementation science theories and providing rich and deep descriptions of SF recipients' lived experiences in sharing their results with relatives may lay the foundation for the development of future studies of interventions to optimize this process.

Objective: The purpose of this study was to describe SF recipients' lived experience of sharing their results with family members and characterize self-reported determinants of this process.

Methods: This multimethod study was conducted in two Phases. In Phase 1, existing data from interviews of SF recipients was analyzed to characterize self-reported determinants of family communication. The COM-B (Michie et al., 2014) was employed as the theoretical framework for the thematic analysis of existing data to describe SF recipients' capability, opportunity, and motivation to share their results with their relatives. A novel interview guide based on this analysis was also developed in Phase 1. In Phase 2 purposive sampling to

emphasize diversity of family communication experiences was employed to conduct novel phenomenological interviews (Moustakas, 2011) with SF recipients to develop a deeper understanding of their lived experiences of sharing their results with their relatives over time. These data were also thematically analyzed and coded to describe textural and structural elements of the described lived experiences. A second coder, bracketing, and member-checking were employed to enhance trustworthiness of the data.

Results: A codebook mapped to the COM-B constructs of Capability, Opportunity, and Motivation was developed to analyze existing interview transcripts from 40 participants in Phase 1 of the study. Over a quarter of participants (n=13) demonstrated poor or uncertain knowledge (Capability) of their SF. Interpersonal and social factors affecting family communication (Social Opportunity) were described by 32 participants and over half of participants (n=22) described emotional closeness as a facilitator of family communication. Physical proximity and frequency of contact (Physical Opportunity) were also cited as determinants of family communication. Participants commonly discussed a desire to help relatives as a Reflective Motivator of family communication, and many also described worry or concern about how relatives might react to their sharing their SF (Automatic Motivation). Purposive sampling was used to assemble a cohort of 11 Phase 2 participants, and analysis of the novel phenomenologic interviews that characterized this Phase extended and deepened some Phase 1 findings. Two major themes emerged from analysis of Phase 2 data: 1) the experience of family communication of SF is one that engenders personal reflection and emotional responses, and 2) family communication of SF is strongly influenced by existing family dynamics. For Phase 2 participants the essential experience of sharing their SF with relatives was analogous to giving each family member an

important and valuable gift; sharing SF information was a personal and loving act, and they were very invested in, and affected by, how relatives received it.

Discussion: This study's theory-informed approach demonstrated key ways family communication of SF parallels what is known about how families communicate about genetic information generally and suggests some possible differences that may form intervention development for this understudied population. SF recipients may lack both knowledge of the medical implications of their findings and a shared familial understanding of how family health history may be related to their finding. As well, while SF recipients may be motivated to share their findings with relatives to improve their care, they are tasked with sharing unexpected medical information within complex existing family systems. The interplay of these factors suggests that interventions designed to optimize family communication of SF may need to address both gaps in knowledge and understanding as well as communication strategies employed in family systems.

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List of Abbreviations and Key Terms

ACMG: American College of Medical Genetics and Genomics

Genotype: Specific DNA sequence variant

GSRP: "Genomic Services Research Program;" the existing NIH study from which participants in the proposed study will be recruited.

NCATS: National Center for Advancing Translational Science.

Penetrance: The extent to which a particular genotype results in a recognizable phenotype

Phenotype: A physical, biochemical, or otherwise observable feature commonly associated with a particular genetic variant.

Proband: A genetics term to identify the first person in a family who comes to clinical attention because of a particular phenotype or genotype. In this document, the term "proband" is generally interchangeable with the term "index" participant or recipient.

SF: Secondary Finding

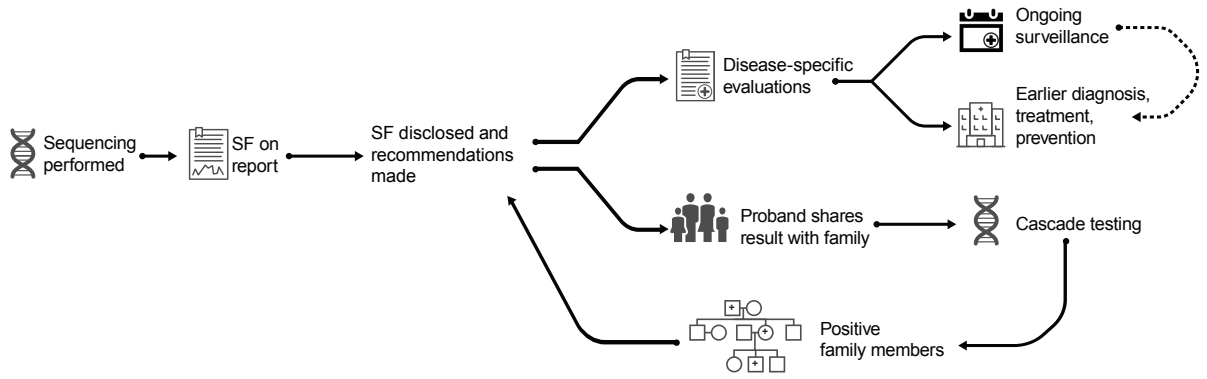
Chapter 1: Introduction

Overview

Effective communication of medically-actionable genomic secondary findings (SF) within families has significant potential to save and/or prolong lives (Kalia et al., 2017). SF are incidental genetic test results that reveal significantly increased risk for a treatable or preventable disease. In the United States, SF are returned to individuals via opportunistic screening recommended by the American College of Medical Genetics and Genomics (ACMG) (Katz et al., 2020; Miller et al., 2021). A typical example of a SF is a *BRCA1* mutation; this confers up to an 85% lifetime risk of developing breast cancer, and effective surveillance and treatment options are available to dramatically lower this risk (Petrucelli et al., 1993). Upon receipt individuals with SF generally receive two recommendations: 1) to seek additional evaluations to understand and reduce disease risk, and 2) to share their SF with relatives so that these family members can also seek genetic testing and receive personalized care. This general paradigm is shown below in Figure 1.

Figure 1

Idealized Secondary Findings Paradigm



The limited literature on family communication of SF demonstrates that strategic and effective family communication is the exception rather than the norm (Hart et al., 2019; Sapp et al., 2018; Wynn et al., 2018). While recipients of SF can benefit directly by engaging in specific life-prolonging or -saving health behaviors, their relatives can only benefit from the availability of SF if they are informed about these results. As such, understanding determinants and patterns of family communication in this population is an important research priority with direct implications for clinical practice as SF return becomes increasingly available. Opportunistic screening for medically actionable SF presumes that individuals who receive these findings will use them to obtain tailored, potentially life-saving interventions, and that strategic evaluation and testing of relatives will allow this benefit to extend to their family members.

Problem Statement

An extensive body of literature devoted to both family communication and downstream genetic testing of relatives describes determinants of both of these outcomes in families where genetic testing is conducted in an effort to understand the causes of a manifest disease in one or more family members (Elrick et al., 2017; Gaff et al., 2007; Menko et al., 2019; Wiseman et al.,

2010). In contrast, the literature describing outcomes generally, and family communication in particular, in SF recipients is sparse (Sapp et al., 2021). Unlike individuals who undergo genetic testing to evaluate a known indication, recipients of SF may lack a familial and social context within which to situate and discuss risk for genetic disease (Nycum et al., 2009). While the penetrance of disorders associated with SF in unselected families is expected to be reduced, accurate estimates may be years away (Katz et al., 2020). This fact imposes special considerations on both the clinicians counseling and the individuals receiving SF. While the information probands share when communicating genetic results derived from a phenotype-first diagnostic assay more closely resembles an explanation associated with a known risk, SF recipients may be asked to communicate information that can be characterized as a risk advisory absent any evidence of disease. Despite these potentially unique attributes, very little is known about the challenges family communication of an unexpected and unfamiliar, yet potentially high-impact, SF may pose for recipients.

Purpose and Research Questions

The purpose of this study was to explore and describe family communication experiences and processes and their determinants over time in individuals with a SF to understand possible unique attributes of this population and inform future research. The study's specific aims and accompanying research questions were:

> Aim 1: Describe the cognitive, logistic, and affective processes SF recipients engage in as they consider communicating with relatives about their results. RQ1: How do SF recipients describe the process of communicating their results with their family members?

Aim 2: Explore determinants of family communication among SF recipients. RQ2: How do SF recipients describe barriers to and/or facilitators of sharing their findings with relatives?

Aim 3: Understand the lived experience of SF recipients in communicating their findings with their families over time. RQ3: How does the lived experience of family communication in SF recipients evolve over time?

Statement of Potential Impact

Many elements of the opportunistic return of SF provide an important glimpse into the emerging era of precision medicine. Currently, genotype-first approaches to healthcare and public health, such as disclosure of potentially high-impact genomic variants, can only realize their maximum potential if recipients of this information effectively disseminate it to their healthcare providers and at-risk family members (Katz et al., 2020). This study expands upon the existing body of literature devoted to how families communicate genetic information in an important way by describing how communication by SF recipients may be similar to or different from how probands in selected families engage in this process and how family communication in SF recipients may evolve over time. This study provides foundational data upon which future investigations of strategies and interventions designed to facilitate family communication may be based.

Translational Nature of the Proposed Study

Various authors and entities broadly describe translational research as a sometimes linear process of moving basic science research discoveries into clinical practice to advance human health (e.g., (Drolet & Lorenzi, 2011)). The National Center for Advancing Translational Science (NCATS) conceptualizes translational research as involving interrelated and iterative

stages that build upon one another (NCATS, 2021).Some elements of this study build upon and are related to behavioral and observational studies that fall into the "Clinical Research" stage delineated by NCATS, in that this study aims to better understand and observe the effects of a policy/practice change in clinical medicine (Green et al., 2013). In other ways, this study sheds light on a complex process in an under-studied population and as such may be conceptualized as aligned with the NCATS "Basic Research" designation. The knowledge generated from this study seeks to inform and promote additional lines of inquiry with the ultimate goal of improving the health of both individuals and the public.

Conceptual Framework

This study sought to elucidate the lived experiences of recipients of secondary findings as they engage in one of two behaviors recommended at disclosure (communicating their results to their family members) with a downstream goal of facilitating the development and/or testing of interventions to optimize SF recipients' performance of this behavior. A multimethod qualitative approach was used to accomplish study goals. Qualitative descriptive techniques were employed to delineate the logistical, cognitive, and emotional processes SF recipients described when relating their experiences sharing their result with relatives and to describe participant-reported barriers and facilitators to family communication. A phenomenological approach elicited SF recipients' lived experiences of communicating about their results with family members over time.

The Behaviour Change Wheel (BCW) is a comprehensive framework synthesizing 19 different behavioral change theories, models, and frameworks to characterize how interventions should function to optimally address the physical, emotional, and cognitive antecedents of health behaviors (Michie et al., 2014; Michie et al., 2011). The COM-B (acronym expanded in bold)

model of behavioral change lies at the center or "hub" of the BCW; this model of behavior posits that individuals must have sufficient **C**apability, **O**pportunity, and **M**otivation to engage in the performance of a desired **B**ehavior (Atkins & Michie, 2015). The COM-B and the BCW within which it is situated were the major theoretical scaffolds informing much of study, particularly the study's first Phase.

Phenomenology, a philosophically-oriented research technique, allows the researcher to understand the lived experiences of a particular phenomenon or occurrence in order to arrive at a description that encapsulates the very "essence" of that experience (Creswell & Poth, 2018; Miller & Salkind, 2002; Moustakas, 2011; Usher & Jackson, 2014). Phenomenology's prioritization of the experience of the individual makes it a natural fit when investigating how patients/clients experience health-related phenomena (Usher & Jackson, 2014).

Methodology

This multimethod study, conducted in two Phases, employed existing and novel qualitative semi-structured interviews to describe and understand the lived experiences of SF recipients (Creswell & Poth, 2017; Moustakas, 2011; Usher & Jackson, 2014). The COM-B constructs mentioned above informed the primarily deductive and descriptive analysis of existing interview data (Mason, 2002; Michie et al., 2014; Michie et al., 2011). A novel phenomenological follow-up interview guide was designed following Phase 1 and used to conduct follow-up interviews with a sub-set of individuals purposively selected to maximize variation in family communication experiences and were analyzed accordingly (Moustakas, 2011).

This study was nested within an existing protocol investigating both the molecular/population genetics and social and behavioral aspects of opportunistic SF return, the

Genomic Services Research Program (GSRP; NIH protocol 16-HG-0017; NCT02595957). Briefly, the GSRP cohort comprises a diverse group of individuals who have received medically actionable secondary genomic findings as defined by the ACMG in the course of clinical care, consumer-initiated genetic testing, or as a result of research participation. Existing transcripts from semi-structured interviews conducted as part of GSRP were analyzed to address Aims 1 and 2. This analysis guided the development of a novel interview guide, which employed a subset of GSRP participants 6-12 months after their initial interview to address Aim 3. These novel phenomenological interviews primarily addressed family communication as it evolves over time.

Limitations

While GSRP is a broad research program seeking to enroll as diverse a group of SF recipients as possible, GSRP participants (and thus, this study's participants) may not be representative of SF recipients in general. This study utilized existing data from the early Phases of GSRP, and these participants are more likely to have received their SF in the context of participation in a research protocol rather than in clinical care.

Chapter Summary

This study utilized existing data to characterize attributes of family communication of SF and the determinants of this behavior in terms of the COM-B, a behavioral and implementation science framework that allows for an in-depth investigation of complex behaviors. A novel phenomenology of how families communicate about SF over time added to the richness of the data generated. Results of this study may inform development of interventions to optimize family communication in recipients of medically-actionable secondary genomic findings.

Chapter 2: Literature Review

Introduction: Topics, Purpose, and Methods

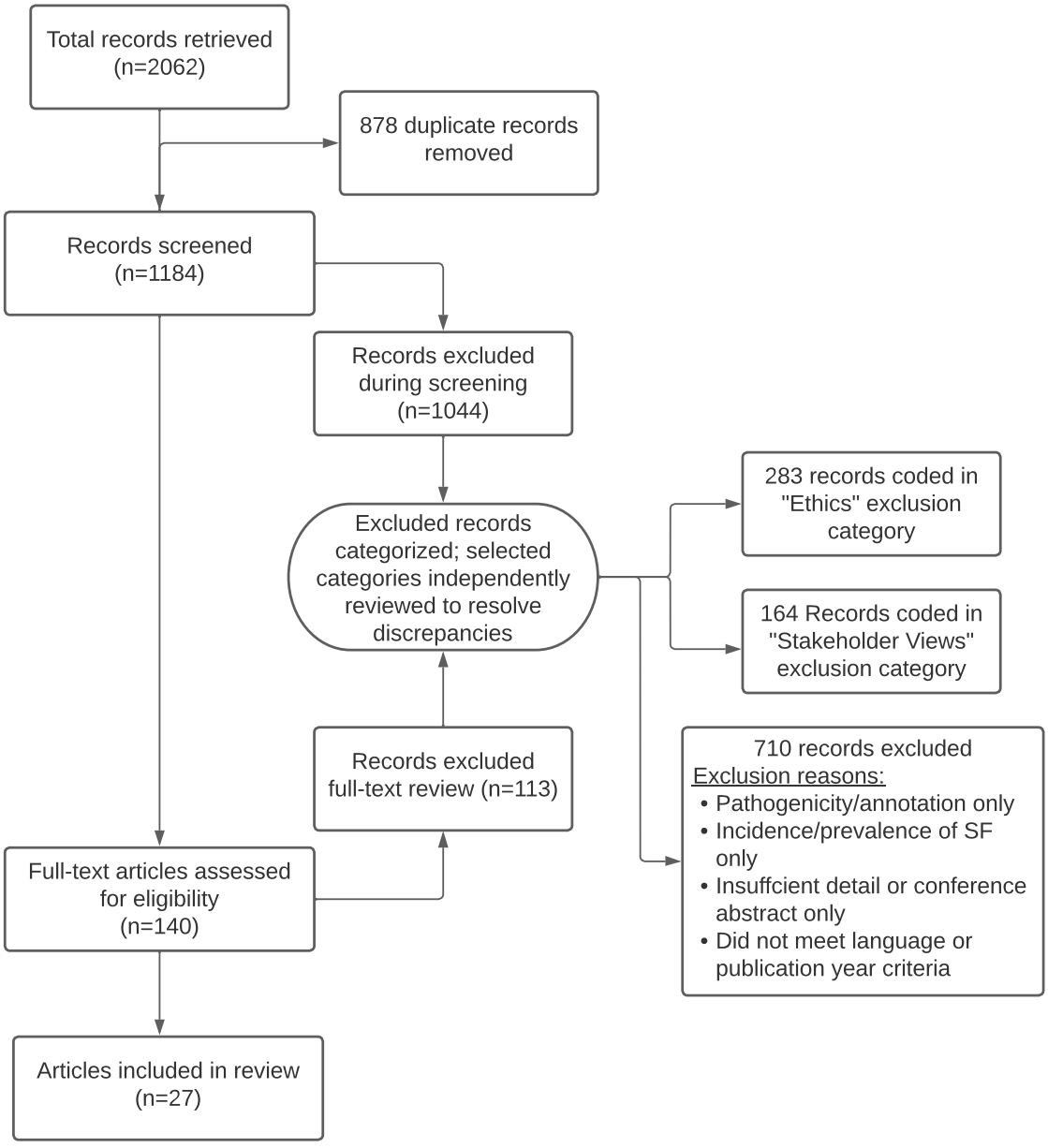
This literature review covers three major topics. The first section provides an overview of SF and what is known about specific outcomes related to family communication in individuals who receive these findings. The next section is devoted to summarizing recent existing literature devoted to communication of genetic information within families. Finally, the theoretical frameworks the current investigation relied on, the BCW/COM-B and phenomenology, are reviewed.

Medically-Actionable Secondary Findings

A search strategy employed in a recently published systematic review yielded most of the literature summarized in this section (Sapp et al., 2021). The goal of this search strategy was to answer a broader question, which encompassed the major area of interest for the study: *What is known about how SF from genomic sequencing are communicated to patients and how learning this information affects outcomes such as psychosocial impact, healthcare behaviors, and family communication?* Five major biomedical databases were searched: CINAHL, Embase, PubMed, Scopus, and Web of Science; the American Psychological Association's PsychInfo was also included but no publication year limit was set for this database. The search was restricted to include only records published in 2012 or later and in the English language. This strategy, shown below in Figure 2, yielded 27 articles for inclusion, some of which are summarized in this section. Additional literature, such as the initial and revised ACMG recommendations for SF return, which did not meet criteria for inclusion in the systematic review but is relevant to this study's goals is summarized as well.

Figure 2

Search Strategy and Study Selection Process



Modern genomic interrogation techniques allow the exact nucleotide sequence of the DNA of a specific gene in a particular individual to be known and compared to a known "reference sequence." In this way, minute (as small as a "one-letter") differences in any given individual come to light. While almost all DNA sequence variations (i.e., genetic differences) in any person from the reference sequence are benign and do not cause disease, a tiny fraction are associated with genetic disorders with sometimes devastating consequences.

Until recently, most genetic tests sought to determine the sequence of a single gene or a handful of related genes. Increasingly, genetic tests are not limited to a specific set of genes – sequencing all or most of an individual's DNA is increasingly commonplace and is rapidly becoming a first-line diagnostic test. "Genome sequencing" refers to processes by which the sequence of all the 3 billion nucleotides that comprise a complete human genome can be known. Genome sequencing is rarely employed outside the research setting at present primarily because of its expense and the fact that most of the information it yields is difficult or impossible to interpret with current knowledge – only 1.5% of the nucleotides in the genome actually encode proteins (Green, 2023). "Exome sequencing" is the practice of reading through the protein-coding regions of all ~20,000 of an individual's genes to understand that person's unique genetic sequence. Currently, the main clinical application of this technology is diagnostic; it is employed when individuals present with a medical problem that is thought to be due to a DNA sequence variation in a gene (Biesecker & Green, 2014; Ginsburg & Willard, 2013; Koboldt et al., 2013; Mardis, 2008). Of course, a major feature of exome and/or genome sequencing is that these techniques yield information about the DNA sequence of **all** of a person's genes, not just a specific gene of interest. In this proposal, the term "sequencing" applies to exome sequencing, genome sequencing, or both.

By 2012, exome sequencing was becoming increasingly clinically available and multiple studies had shown its effectiveness as a diagnostic tool (for a contemporaneous review, see (Ng & Kirkness, 2010)). In response to the increasing clinical utilization of genomic interrogation techniques, the American College of Medical Genetics and Genomics (ACMG) released its first set of guidelines to define parameters under which a specific set of genomic variants should be sought and returned to individuals undergoing clinical sequencing (even if those variants were unrelated to the clinical indication for ordering the sequencing test) in 2013 (Green et al., 2013). The ACMG guidelines were designed to interpret medical actionability in a very strict sense. Only variants predicted or known to be deleterious or pathogenic in specific, well-characterized genes, where the relationship between mutations in that gene and the development of a disease was very strong and highly likely, were recommended for return. These variants are "medically actionable" because their presence dramatically increases a person's risk of developing a treatable, preventable, or ameliorable disease (e.g., breast or colon cancer). The ACMG described these findings as "secondary" because they are found incidentally when sequencing tests are ordered for another reason, for example, to learn the genetic cause of a child's unexplained illness.

The most immediate and direct impact of these guidelines may have been felt by clinical laboratories, who were now obligated to develop robust procedures to annotate the sequence data of samples they received, clinicians, who had to counsel patients about the possibility of receiving unrelated yet highly clinically-relevant results when recommending and ordering sequencing tests, and patients, who were the ultimate recipients of these secondary findings. These impacts, and the effects of these guidelines on research studies employing sequencing, continue to be reviewed and evaluated (Ormond et al., 2019). The ACMG has thus far released

two revisions to their initial set of guidelines; currently, 78 genes associated with 36 genetic disorders meet the identified criteria (Miller et al., 2022). Recent estimates suggest that SF are present in 2-3% of individuals undergoing sequencing (Johnston et al., 2012). The list of SF recommended for screening and return by the ACMG (Miller et al., 2022) at the time the interviews were concluded is provided in Appendix 1.

The desired and stated goal of efforts to return medically-actionable secondary findings (SF), as defined by the ACMG to individuals who are found to have them, is to allow those individuals to receive tailored and specific healthcare interventions, which have the potential to prolong or preserve life (Green et al., 2013; Kalia et al., 2017; Miller et al., 2022; Miller et al., 2021). Another benefit (the focus of this study) is the notification of family members who may share this genetic risk factor, so that they, too, may undergo testing and receive needed healthcare if found to be positive (Bowdin et al., 2016). Figure 1, above, provides a graphical description of this paradigm.

Communication with relatives about SF in this context has important public health implications, as the true benefit of SF can only be realized if at-risk family members are notified and then undergo "cascade testing" – targeted genetic testing to determine if they share their at-risk relative's SF. Among the 27 articles included in the systematic review, nine papers assessed family communication (Amendola et al., 2015; Basel & McCarrier, 2017; Hart et al., 2019; Haukkala et al., 2013; Ormondroyd et al., 2020; Rego et al., 2018; Sapp et al., 2018). These studies collectively described a total of 52 SF recipients communicating their results to at least one family member. None of these studies included detailed information about family structure; communication to 11 siblings, 16 parents, 11 children, and seven more distant relatives was reported in these articles. Twelve articles reported that cascade testing of at least one relative

had taken place for 27 index SF recipients (Amendola et al., 2015; Baldridge et al., 2017; Catenacci et al., 2015; Hart et al., 2019; Leppig et al., 2017; Mackley et al., 2018; Nestor et al., 2020; Ormondroyd et al., 2020; Papaz et al., 2019; Rego et al., 2018; You et al., 2019).

Participants reported in one article describe family communication about their SF as a complex process due to family and individual dynamics (Ormondroyd et al., 2020). One study, focused on understanding how recipients of SF communicate these results to their family members, invited three participants from a large biobanking study to receive SF as part of their investigation; two of these three individuals chose to share their finding with family members, and some of these family members underwent genetic testing and received recommended healthcare as a result (Leppig et al., 2017). A Finnish study of biobank participants who received specific SF associated with a risk of cardiac disease reported high rates of family communication and follow-up but also provided participants with specific and directed referrals and care (Haukkala et al., 2013). Sapp and colleagues and Hart and colleagues described both rates of family communication (~70% in both studies) and the range of relatives SF participants communicated with (Hart et al., 2019; Sapp et al., 2018).

Rates of cascade testing, while rarely reported, are low; only 45 family members of the 709 SF recipients included in the review were reported to have undergone cascade testing (Sapp et al., 2021). In describing three families who received SF, Leppig and colleagues reported that in one family, no family communication or cascade testing took place, and in the other two, incomplete family communication and cascade testing occurred (Leppig et al., 2017). Only one family out of 14 reported cascade testing (Baldridge et al., 2017). One additional report described an SF recipient's sister who underwent cascade testing (Rego et al., 2018).

Two very recent studies investigating family communication focused on cascade testing of relatives of participants in a large biobank study who received medically-actionable findings consistent with SF as defined above. Both studies employed the same chatbot technology to facilitate family communication and uptake of cascade testing; one focused on all biobank participants (Schmidlen et al., 2022) and the other focused on participants who had received results related to familial hypercholesterolemia only (Walters et al., 2023). Younger SF recipients were more likely to engage chatbots to share findings with relatives (Walters et al., 2023) and higher rates of cascade testing were observed in relatives who were engaged by the chatbot compared to relatives of SF recipients who declined to use the chatbot (Schmidlen et al., 2022).

Family Communication of Genetic Information

The literature search for this section was conducted in PubMed using the following search terms: family communication AND genetics, family communication AND genetic counseling, cascade testing, cascade screening. In addition, abstracts resulting from a committee member's previous searches were reviewed, and the citations from particularly salient articles were scanned. While more recent literature (2010 to date) exists, several review papers dating back to 2007 were included because of their relevance.

Family communication of genetic risk has been a feature of the practice of genetic counseling and medical genetics since the inception of these fields. Gaff and colleagues, in their 2007 review of the literature relating to communication of genetic results and risk in families, identified 29 studies, most of which pertained to familial forms of breast/ovarian and colon cancers (the genes involved in these disorders are included in the ACMG list; (Gaff et al., 2007)). Three major themes emerged from this body of literature: 1) individuals who learn of a

genetic risk or predisposition engage in a deliberative process as they decide whether and how to inform relatives, often considering when the "right time" might be to share information and imagining/anticipating the reactions of individual family members, 2) communication strategies employed vary greatly although the use of intermediaries is common and there is an expectation that a relative who is a parent is responsible for sharing the information with their offspring (i.e., a woman who learns of a gene change related to breast cancer may share the information with her aunt, rather than telling her aunt's children – her cousins – directly), and 3) uptake of cascade genetic testing by relatives, when assessed, does not approach 100%; the highest uptake rate in the included studies was 64% (Gaff et al., 2007).

Several additional systematic reviews of family communication and the factors influencing family communication have followed in the years since the Gaff et al. (2007) review. One review paper published in 2009 included only papers addressing communication in families affected by hereditary cancer syndromes and highlighted the tension experienced by probands when faced with the task of sharing their genetic test results with relatives; while these individuals are motivated by a desire to protect their family members from a serious disease (cancer), they are acutely aware that this will likely be upsetting information for family members to hear (Chivers Seymour et al., 2010). The following year, another review of largely the same body of literature (33 papers were included) emphasized that a number of factors, including perceived relevance, feelings of "closeness," relatives' anticipated reactions, and existing family communication patterns influence family communication of genetic findings/risk (Wiseman et al., 2010). In their 2019 systematic review of families with hereditary breast/ovarian and colon cancer, Menko and colleagues included 30 papers with cascade testing uptakes rates ranging from 15-57% of relatives in breast/ovarian cancer families and 41-94% in families with colon

cancer families; higher rates of cascade testing for both disorders were associated with programs where disclosure of the genetic risk to relatives was not initiated by the proband but rather facilitated by a cancer registry or other program with the proband's permission (Menko et al., 2019). Compared to patient-mediated contact, direct contact of relatives by the medical team resulted in higher rates of cascade testing and genetic counseling of relatives in a recent meta-analysis of 87 studies comparing contact methods (Frey, Ahsan, Bergeron, et al., 2022).

Theoretical Foundations

The literature summarized in this section comprises several seminal works reviewing and/or describing the COM-B and phenomenology. The theoretical underpinnings guiding the methodological approaches employed in this study are discussed below.

Phase 1 of the proposed study is heavily scaffolded on the Behaviour Change Wheel (BCW) framework. This comprehensive framework synthesizes 19 different behavioral change theories, models, and frameworks to characterize how interventions should function to optimally address the physical, emotional, and cognitive antecedents of health behaviors (Michie et al., 2014; Michie et al., 2011). The COM-B (acronym expanded in bold) model of behavioral change lies at the center or "hub" of the BCW; this model of behavior posits that individuals must have sufficient **C**apability, **O**pportunity, and **M**otivation to engage in the performance of a desired **B**ehavior (Atkins & Michie, 2015). The COM-B serves to facilitate the making of a "behavioral diagnosis" in that it allows for a thorough assessment of the major logistical, psycho-emotional, cognitive, social, and other attributes that contribute to behavior change. This behavioral assessment employing the COM-B constructs facilitates systematic consideration of interventions matched with COM-B constructs and tailored to the specific context in which behavior change should occur(Atkins & Michie, 2015). The Theoretical Domains Framework

(TDF) integrates numerous behavior change theories and greatly facilitates selection of intervention functions aligned with COM-B components. Taken together, the COM-B components and the intervention domains of the TDF comprise the "inner wheel" of the BCW (Atkins et al., 2017; Atkins & Michie, 2015; Michie et al., 2014).

Phase 2 of the study comprised novel phenomenological interviews with a subset of the GSRP participants who participated in the interviews analyzed in Phase 1. Phenomenology can be described as both a philosophical orientation as well as qualitative research technique (Moustakas, 2011). While variants exist, studies employing phenomenology all seek to systematically explore and understand the experience of being an individual human engaging in a particular lived experience in the world (Miller & Salkind, 2002; Moustakas, 2011; Usher & Jackson, 2014). Several studies in the genetic counseling literature seek to understand the "lived experiences" of various patient populations (Garza et al., 2020; Hamilton et al., 2016). A phenomenological approach was determined to be the best fit for this study as study aimed to understand how SF are communicated to relatives by exploring family communication processes, patterns, and determinants in individuals who have first-hand lived experience (Finlay, 2011; Miller & Salkind, 2002; Moustakas, 2011). Specific considerations relating to data collection and analysis using this approach and areas where procedures departed from pure phenomenologic inquiry are discussed in detail in Chapter 3.

Study Inferences

SF recipients are an understudied population and yet, the number of individuals receiving SF can only be expected to increase as genetic sequencing becomes increasingly affordable, ubiquitously applied in diagnostic settings, and more available in direct-to-consumer and non-diagnostic applications (Ormond et al., 2019). The existing literature describing family

communication in SF recipients can only be described as sparse and does little to contribute to an understanding of this complex process, let alone provide insight into what types of interventions may be designed and tested to enhance family communication (Sapp et al., 2021). Indeed, dedicated studies focused on understanding numerous outcomes after receipt of a SF has been highlighted as a research priority by several authors (Katz et al., 2020; Sapp et al., 2021; Williams et al., 2018). The degree to which processes, patterns, and determinants of family communication of SF resemble those observed in families communicating other types of genetic information remains largely unknown, although there is some evidence suggesting that SF recipients find family communication to be challenging for reasons similar to those described in the non-SF population (Ormondroyd et al., 2020).

This study sought to advance understanding of an important aspect of opportunistic screening for medically-actionable SF by exploring the lived experiences of recipients of SF over time. How family communication evolves over time after SF receipt has not been evaluated in the existing literature. The study explicated family communication determinants, patterns, and processes through the lens of the COM-B framework, thus providing the fuller picture afforded by the "behavioral diagnosis" allowed by this framework (Michie et al., 2011), filling an important gap in the genomics literature.

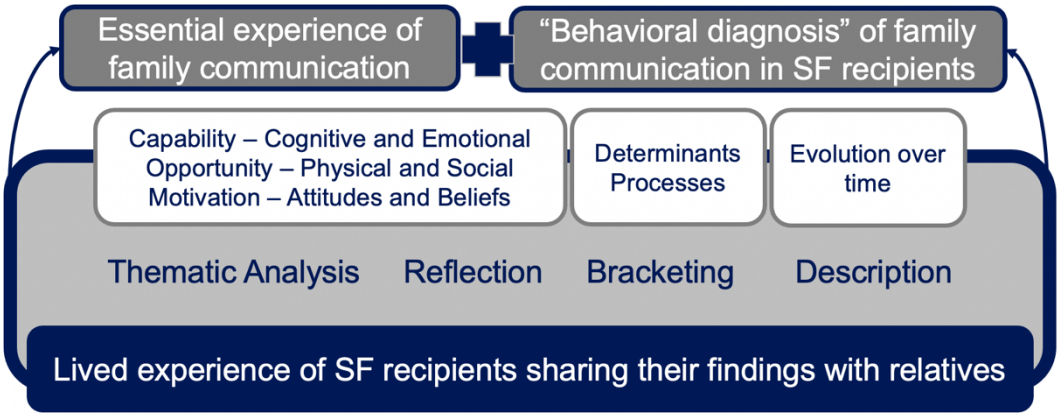
Conceptual Framework

This study merged the emphasis on the unique lived experiences of the individual characteristic of phenomenological inquiry with the practical framework of the COM-B. This approach allowed for a rich description and exploration of the experiences of individuals faced with communicating unexpected genetic information with their family members, contributing to a detailed and thorough "behavioral diagnosis" to guide the beginnings of intervention

development. The interplay between these two approaches is shown in Figure 3 below, where the lived experience of SF recipients formed the foundation of the line of inquiry and phenomenological techniques such as bracketing were employed while considering the COM-B framework and evaluating determinants, processes, and the effect of time. The ultimate outcome was a rich description of the essential experience of SF recipients.

Figure 3

Conceptual Framework



Chapter Summary

Family communication of genomic and genetic information is complex. Individual family attributes, such as the degree of emotional closeness shared by family members and family structure, are salient factors that influence how families communicate about genetic information. Much of the literature on family communication centers on families who have received diagnostic genetic information; genetic results that confirm an already known or suspected genetic predisposition to disease. How individuals who receive non-diagnostic, secondary genomic findings communicate these results with their families is largely unexplored. This study

relied on two theoretical approaches to investigate this problem. The COM-B is a behavioral science framework that allows researchers to investigate complex behaviors such as family communication. Phenomenology is an intensive qualitative technique which centers first-hand accounts of individuals undergoing a specific experience to capture the essence of their lived experiences.

Chapter 3: Methods

Overview

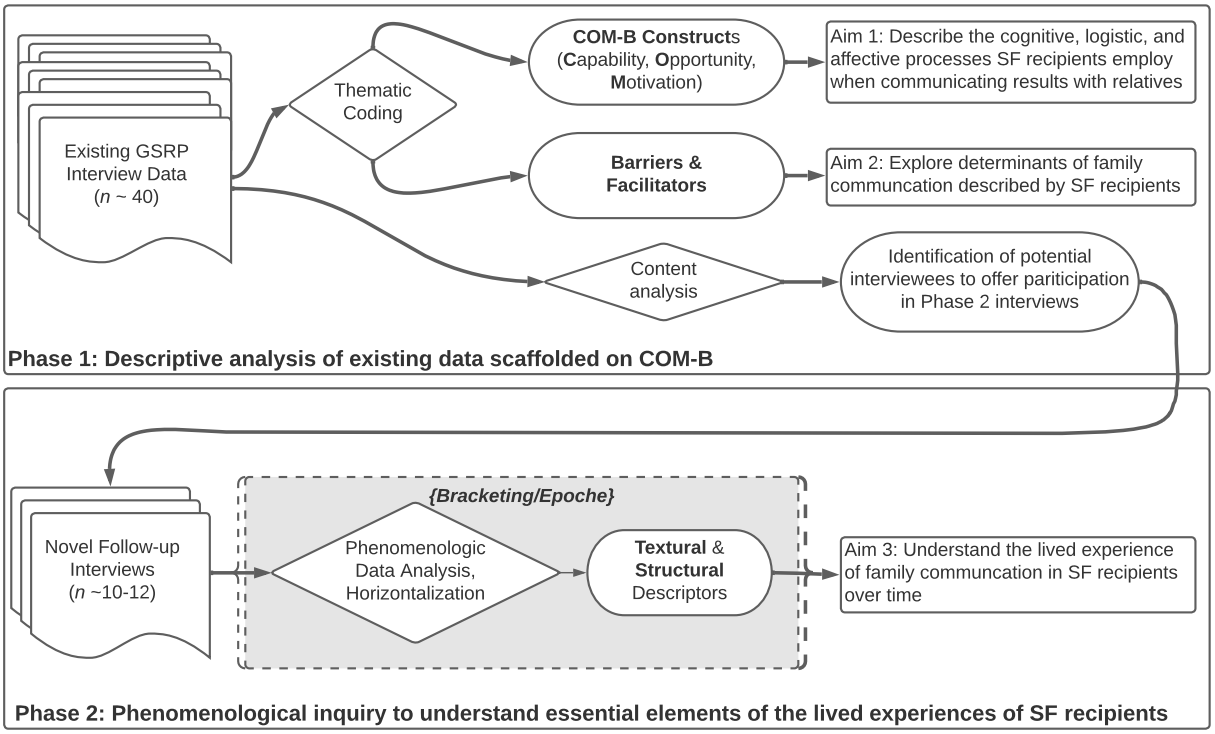
Broadly, the purpose of this study was to explore and describe family communication of SF by engaging directly with index recipients of these findings to understand processes and determinants of family communication and to develop a preliminary understanding of the lived experience of sharing unexpected genetic information with relatives. The study sought to describe aspects of family communication of SF to fill important gaps in existing knowledge. An additional study goal was to begin to inform future intervention development and therefore aligns with a pragmatic ontology (Corcoran, 2017) with a constructivist/interpretivist lean where "…people, and their interpretations, perceptions, meanings and understandings [are] the primary data sources" (Mason, 2002, p. 56). The study's theory-informed approach to utilize existing data and then collect additional data to generate a presupposition-free and thick description of the lived experiences of SF recipients is consistent with this ontology, incorporating constructivism to shed light on real-world problems. As outlined below, the study was conducted in two distinct Phases to address the research questions and specific aims outlined in Chapter 1.

Inquiry Description

Both study Phases employed thematic analysis of transcripts of interviews conducted with recipients of SF enrolled in GSRP. The distinct data collection and analysis plans and corresponding philosophical/methodological approaches to be employed are mapped to the specific aims of the study and summarized below in Figure 4.

Figure 4

Study Methods Mapped to Aims



In Phase 1, a sub-set of existing transcripts (n = 40) from GSRP were thematically coded and analyzed to describe determinants of family communication, along with the logistical, cognitive, affective, and other processes, SF recipients report when describing their experiences in sharing their SF with relatives (Creswell & Poth, 2018; Mason, 2002). GSRP has undergone several protocol revisions; interview data from the first and second versions of the interview used in GSRP were used in Phase 1. These existing, structured interviews, loosely informed by the Health Belief Model, included other topics in addition to family communication (including understanding of medical implications of the SF, adherence to recommendations, interactions with healthcare providers, and risk perception), and were designed to gather broad and

exploratory descriptions of a variety of outcomes of SF receipt (see Appendix 2 for the interview guide). While participants were invited and encouraged to share their "lived experiences" after receiving a SF, distilling the essence of the common meaning of receiving a SF, as is intended in phenomenological studies, was neither the stated nor philosophical goal informing these interviews (Creswell & Poth, 2018). Content analysis of the transcripts helped in determining a sampling strategy to maximize the potential for diversity in participant experiences for Phase 2, discussed in detail below. As reflected in Aims 1 and 2, the goal of Phase 1 was to describe how the process of family communication maps to COM-B constructs and to characterize barriers and facilitators of family communication experienced by SF recipients.

The intentional, novel phenomenology of the lived experience of communicating a SF with relatives over time characterizes Phase 2. Purposive sampling of existing GSRP participants was conducted to maximize potential for diversity in experience and facilitate a heterogeneous cohort of SF recipients with a target *n* of 10-15 interviews (Finlay, 2011; Munhall, 2007). Achieving an understanding of a phenomenon free from preconceived notions is a major, goal of phenomenology (Creswell & Poth, 2018; Miller & Salkind, 2002; Moustakas, 2011; Usher & Jackson, 2014). As such, extensive bracketing (also called epoche) of the researcher's own experiences (e.g., coding and analyzing the Phase 1 data, professional experiences working with SF recipients) was necessary to maximize the "fresh-perspective" potential of the Phase 2 interviews (Creswell & Poth, 2018; Moustakas, 2011). A novel interview guide (Appendix 3) was developed for the Phase 2 interviews structured around the two central questions commonly employed in the phenomenological tradition typically identified with Moustakas: "What has the experience of sharing your SF with family been like for you?" and "What temporal, situational, cultural, familial, and other contextual factors have affected how you've communicated your

finding with your family?" (Creswell & Poth, 2018; Moustakas, 2011). Textural (the "what" of lived experience) and structural (the "how" of participants' lived experience) themes were inductively coded and evaluated (Creswell & Poth, 2018; Moustakas, 2011). As reflected in Aim 3, the goal of Phase 2 was to provide an understanding of the essential components of the lived experiences of SF recipients as they communicate with their families about their results (Miller & Salkind, 2002; Moustakas, 2011; Usher & Jackson, 2014).

This study relied on existing and new data from participants enrolled in the National Human Genome Research Institute's Genomic Services Research Program (NHGRI, 2020). Launched in 2019 this protocol is designed as a hybrid implementation-effectiveness study investigating social and behavioral, genomic, and epidemiologic aspects of returning medically-actionable secondary genomic findings as defined by the ACMG (Bauer et al., 2015; Miller et al., 2022). Participants in this protocol are recruited from clinical laboratories, research studies, direct-to-consumer genetic testing products, and large-scale sequencing efforts such as the Geisinger Health MyCode initiative after they have received SF as a result of clinical care, consumer-initiated testing, or research participation. GSRP participants may be offered clinical evaluation and cascade testing and complete a number of social and behavioral interventions.

In Phase 1, existing data from 40 randomly selected GSRP participants was analyzed to contribute directly to Aims 1 and 2 and to allow for the development of a novel interview guide to generate the data necessary to address Aim 3. Discussion of family communication in existing GSRP interview transcripts was thematically coded and analyzed using the COM-B constructs and to describe participant-reported determinants of family communication (Creswell & Poth, 2017). These existing interviews were not designed with these constructs in mind, rather, participants were asked to describe their experiences sharing their SF with relatives in a general

way, including some exploration of barriers and facilitators. These qualitative data were used to select a heterogeneous sample of GSRP participants to invite to participate in follow-up interviews to address Aim 3.

Analysis

Qualitative data analysis software (MAXQDA) was used for coding and analysis of transcribed interviews in both study Phases. A primarily deductive approach was employed in the analysis of interview transcripts in Phase 1 (Braun & Clarke, 2006; Creswell & Plano Clark, 2011; Mason, 2002). The COM-B constructs informed the development of the codebook in order to describe cognitive, logistical, affective, and relational processes SF recipients employ in sharing their results with family members. Codes describing participant-reported barriers and facilitators of family communication inductively emerged from the data. GSRP interviews were conducted in a structured manner where family communication is addressed in a clearly distinct part of the interview. As such, while the entirety of each transcript was reviewed, most codes were applied only to the "family communication" portion of each transcript. Coding of new transcripts was halted when meaning/thematic saturation was achieved (Braun & Clarke, 2021). After limited training in the COM-B constructs and how they could be applied to the data, an independent second coder not involved in the study (AH) independently coded 20% of the transcripts (Kurasaki, 2000; O'Connor & Joffe, 2020).

Analysis of Phase 2 transcript data employed a number of phenomenological techniques, beginning with developing descriptions of the textural and structural lived experiences of family communication in SF recipients (Creswell & Poth, 2018; Usher & Jackson, 2014). Participant transcripts were reviewed to identify statements and descriptions of family communication uttered by participants, the research/interviewer, or both parties that highlighted important

elements of the participants' lived experiences. Moustakas describes these "significant statements" (Moustakas, 2011) as those that correspond to textural (the "what" of lived experience) and structural (the "how" of participants' lived experience) themes. These significant statements were reviewed and coded inductively to identify thematic "meaning units" to reduce and combine themes.

Analysis of themes within and across participants focused on developing an understanding of what participants experienced in communicating about their SFs with relatives as well as underlying dynamics or contextual elements that affected how they experienced communication over time (Miller & Salkind, 2002; Moustakas, 2011). A version of the Stevick-Colaizzi-Keen method modified from Moustakas's description (Moustakas, 2011) was employed to accomplish this. Textural-structural descriptions of participants' experiences in sharing their SF with their families were compiled and synthesized to develop a composite description representing how participants' unique perspectives contributed to a more holistic understanding of the "essence" of the lived experience of family communication (Eddles-Hirsch, 2015; Miller & Salkind, 2002; Moustakas, 2011). Bracketing, in the form of a written series of personal statements relating the researcher's own experiences as a genetic counselor and in coding the Phase 1 data, was employed as part of this process (Creswell & Poth, 2018; Moustakas, 2011). Member-checking was employed to maximize trustworthiness; general impressions were reviewed in a brief follow-up phone call with two Phase 2 participants, and a brief summary was sent to all Phase 2 participants inviting them to contact the researcher with comments and thoughts.

Trustworthiness

Specific elements of this study's design, conduct, and analysis were employed to optimize the trustworthiness of the study's analysis and conclusions (Creswell & Poth, 2017; Usher & Jackson, 2014). To address credibility, theory-informed approaches were employed in both study phases: the COM-B in Phase 1 and Moustakas's conceptualization of phenomenology, including his modification of the Stevick-Colaizzi-Keen analysis method (Atkins et al., 2017; Moustakas, 2011). Self-reflection in the form of bracketing and epoche was employed to explore the author's own experiences (Usher & Jackson, 2014). In addition, member-checking was employed as described above.

Although not designed to generate broadly generalizable knowledge, several elements of the study's design were employed to enhance the potential applicability of the findings. To enhance transferability, both study Phases employed thick-description: Phase 1 transcripts were analyzed until noticeable recurrence of major themes took place, and Phase 2 interviews were designed and executed in a manner that allowed for full and meaningful descriptions' of participants lived experiences to come through (Creswell & Poth, 2017).

The theory-informed deductive coding scheme and use of a second coder in the analysis of the Phase 1 data together with the author's bracketing of her own experiences working with SF recipients as a clinician and an individual operating within an existing and unique family system during data collection and analysis in Phase 2 enhanced the dependability and credibility of its conclusions (Mason, 2002; Moustakas, 2011).

Eligibility

Phase 1 was conducted using 40 existing GSRP transcripts available upon initiation of the study. Fifteen existing participants were invited to participate in the Phase 2 interviews

(GSRP participants consent to participate in follow-up studies and interviews; participant uptake of these follow-up procedures approaches 100%). Four of these individuals did not respond to invitations and one declined, citing a busy work schedule, and the remaining 11 participated in the Phase 2 interviews. As the aim of the phenomenological inquiry of Phase 2 was to capture the essence of the lived experiences of SF recipients communicating with family over time, participants who first received their findings greater than a year ago were prioritized for potential recruitment for Phase 2. Other participant attributes, such as the nature of the SF, family structure, age, gender, racial/ethnic identity, and the depth at which family communication was discussed in the initial interview were considered to maximize the potential for diversity in Phase 2.

Human Participants and Ethics Considerations

The GSRP protocol is approved by the NIH Intramural Research Program IRB (NCT02595957). This NIH protocol was amended and approved to include the study procedures listed here and inclusion of George Washington University as an added site. A reliance agreement with the George Washington University School of Medicine and Health Sciences IRB was negotiated and approved in April 2022. The GSRP protocol consent form is attached in Appendix 4 and the interview guide and verbal consent procedure that was employed for Phase 2 of the study is attached in Appendix 3.

The research activities described here and in the GSRP protocol from which participants were recruited represented minimal risk to participants; participants in the GSRP may have also directly benefitted from participation in this protocol through clinical encounters, expert consultation, and clinical genetics services. The semi-structured interviews conducted for this study did occasionally touch on sensitive subjects such as family estrangement and the heritable

risk for serious diseases. The interviewer was a genetic counselor with over 17 years of clinical experience working with families and in conducting qualitative interviews. None of the interviewees who participated in this study exhibited unusual levels of distress.

Chapter Summary

This study employed deductive and inductive approaches in two Phases to understand how SF recipients communicate with their families about their results. In Phase 1, existing (n = 40) interview data was analyzed using the COM-B framework to understand SF recipients' capability, opportunity, and motivation to share their findings with relatives, characterize participant-identified determinants, and inform the development of a novel interview guide. Eleven individuals participated in novel phenomenological interviews designed to investigate the lived experience of family communication over time in Phase 2. Data from both study Phases were analyzed thematically. Design and analysis choices were made in both study Phases to maximize trustworthiness.

Chapter 4: Results

Overview

Phase 1 comprised descriptive analysis of existing transcripts scaffolded on COM-B constructs. Purposive sampling of Phase 1 participants was employed and the novel phenomenological interviews which comprised Phase 2 were transcribed and analyzed. Participant data from each study Phase are presented and followed by Phase 1 and Phase 2 analysis and results.

Participants

Existing interview data from 40 participants was analyzed in Phase 1. Two-thirds of participants (n=25) had SF associated with cancer predisposition syndromes and were female (n=26); this reflects the GSRP population (unpublished data). Participants received their SF between 2015 and 2021 from clinical care, research/biobank participation, or through direct-to-consumer genetic testing. Mean time from initial SF receipt to initial interview participation was one year and ranged from two months to almost five years. Participant characteristics are shown below in Table 4.1.

Table 4. 1 *Participant Characteristics*

Nature of Secondary Finding (*genes*)	*n* (%)
Cancer predisposition syndrome	**25(63%)**
Hereditary Breast and Ovarian Cancer (*BRCA1, BRCA2)*	17 (43%)
Other (*BMPR1A, RET)*	4 (10%)
Lynch syndrome (*PMS2*, *MSH6*)	3 (8%)
Cardiac disorder	**9 (23%)**
Dilated or hypertrophic cardiomyopathy (*MYBPC3, MYH7)*	6 (15%)
Long QT/Brugada Syndrome (*KCNH2, SCN5A*)	2 (5%)
Arrhythmogenic right ventricular cardiomyopathy (*DSC2)*	1 (3%)
Other	
Familial hypercholesterolemia (*APOB, LDLR)*	5 (8%)
Vascular Ehlers Danlos Syndrome (*COL3A1)*	1 (3%)
Self-reported race	
White	33 (83%)
Black or African-American	4 (10%)
More than one race	3 (7%)
Self-reported ethnicity	
Hispanic	2 (5%)
Non-Hispanic	32 (80%
Other or not reported	6 (15%)

Eleven participants whose initial interview data were analyzed in the first Phase of the study were re-contacted and invited to participate in the novel interview comprising Phase 2. These individuals were purposively selected to maximize the potential variation in lived experience in sharing their results with their family members. Attributes such as race/ethnicity, gender, nature of the SF, and time since SF disclosure and initial interview were considered. However, the depth and content of the discussion regarding family communication in the initial interview was prioritized. Table 4.2 refers to each of the Phase 2 participants by pseudonyms and describes some of these characteristics.

Table 4. 2 *Phase Two Interviewee Characteristics*

Pseudonym	**Age at Second Interview**	**SF Gene**	**Time since SF receipt**	**Time since first interview**
Kesha	28	*BRCA2*	2.2 years	2.1 years
Donovan	46	*BRCA2*	2.3 years	2.2 years
Theresa	52	*BRCA1*	3.4 years	3 years
Patricia	84	*SCN5A*	2.9 years	3.6 years
Samantha	47	*KCNH2*	4 years	3.3 years
Evan	52	*MYBPC3*	3.1 years	4 years
Farah	61	*BRCA2*	2.7 years	1.8 years
Melanie	48	*BRCA2*	7.8 years	2.9 years
Jethro	48	*RET*	2.3 years	1.4 years
Camilla	56	*LDLR*	3.8 years	2.9 years
Max	72	*COL3A1*	2.4 years	1.5 years

All verbatim quotes from participants presented here appear in italicized font and are attributed with pseudonyms and the relevant SF gene along with age at time of interview. Words used repeatedly by the speaker ("filler" words such as "uh," and "you know") were removed from verbatim quotes along with speech errors when their removal did not affect the meaning of the text. Transcriptions of non-verbal expressions (e.g., <laugh>) were generally retained, and slang (e.g., "wanna," "cuz") words used by participants were generally not replaced. Verbatim quotes were restricted to the participants' words unless the interviewer's spoken words were required to understand or clarify what participants said; the term "GC" is used to indicate the interviewer's speech. Ellipsis points ("…") are used to indicate breaks in transcribed utterances and/or to remove statements from the interviewer. Non-italicized words in brackets (e.g., [words]) represent necessary clarification by the author and/or replacement of un-transcribed audio with the author's estimation of the participant's words based on listening to audio files.

Phase 1 Findings

The codebook employed for analysis of the Phase 1 transcripts was developed by prospectively applying COM-B constructs to the behavior of family communication and then iteratively refined as the first several transcripts were coded. Participants' discussion of their own knowledge of their SF and skills to share this knowledge were coded under the "Capability" domain. Participants' statements concerning their self-reported social/normative and physical opportunities to share their SF with relatives were coded under the "Opportunity" domain, and their discussion of attitudes, emotions, and beliefs influencing family communication were coded under the "Motivation" domain. Thirty total codes encompassing the COM-B constructs, three distinct codes describing participant-reported facilitators of family communication, and four distinct codes describing participant-reported barriers to family communication were employed across the 40 Phase 1 transcripts (see Appendix 5). Ten transcripts were independently coded by a second coder and the study author (JCS) and the second coder achieved 92% agreement on these transcripts.

Capability

The "Capability" domain of the COM-B describes the psychological knowledge and skills an individual employs when considering or engaging in a behavior (Michie et al., 2014). Participants described variable understanding or knowledge of their SF with some participants succinctly summarizing key points about their SF, including the name of the involved gene and the health implications associated with variants in that gene:

> *They told me that I had [a] gene mutation on something called the RET….Yeah, basically they told me that I had this genetic mutation that put me at increased risk medullary thyroid cancer.* (Wilson, *RET*, age 70)

Others described their findings primarily in terms of health implications or recommendations they remembered such as this participant, who, when asked to describe her finding replied *"Just to see a cardiologist…That's all I really understood this to mean."* (Samantha, *KCNH2*, age 44).

Thirteen participants described poor understanding of their SF, and four reported that they could not remember many details about their results and/or results disclosure conversations. One participant explicitly labeled his understanding as "basic:"

> *I just know that it's not super common, but my chances are higher of getting it. Just, I mean, just from what I read, it's just kind of basic things, just checking for early signs or anything like that. And just avoiding too much sun exposure and stuff along those lines. This is just pretty basic knowledge, I think.* (Fletcher, *BRCA2*, age 29)

Like the participant quoted above, another participant discussed his fairly superficial knowledge of his SF, associated health implications, and its heritability:

> *I guess I'm just supposed to watch what I eat maybe and exercise just…*[GC prompts for additional thoughts about what participant remembers about result] *So, um, I didn't, get any, um, I didn't go see a cardiologist or anything. No, I, if I remember right, they didn't really go too much into detail what kind of heart disease it might be. Um, yeah, I just, I just thought they said increased risk for heart disease. I think they just left it at that….I think they, I, I don't, I don't really remember them, uh, bringing, bringing up anything about how it could have been inherited.* (Jorge, *MHY7*, age 22)

One participant who received a SF associated with breast cancer risk admitted being confused about his results prior to some clarification from the interviewer and then expressed gratitude for the clarification:

> *Now the part I wasn't real clear what cancer it could [be] because there's different types of cancer. I just know that I have to at least try to have a healthy lifestyle. What I mean by healthy lifestyle, stay on top of all my checkups because I already go every five years for colon cancer because my dad had colon cancer.* [Interviewer clarifies that the SF this individual received is related to increased breast cancer risk]*... I don't remember her talking about it. I knew cancer in the beginning of the call, I don't remember which type. I knew I had the cell that might be in my genetic makeup, but I can't remember which particular cancer it could be. And again, now that I know it could be breast, I'll just go get myself checked. It's probably good you did the follow-up call because I totally forgot that.* (Walter, *BRCA2*, age 48)

Participants who expressed poor understanding of their SF often asked questions about their results and what recommendations they should follow. These participants used words like "cryptic" and "mixed messages" to describe their understanding of information they had received about their SF and offered their unanswered questions in describing their understanding:

> *My question is, since I have these findings, it doesn't mean that I will follow in my father's footsteps? Or does it mean you have a higher percentage to follow into your father's footsteps with the heart condition and the high cholesterol in my life?* (Camilla, *LDLR*, age 53)

While few participants (n=15) discussed their perceived skills to share their SF with relatives, when they did, most described their skills as poor (n = 5) or uncertain (n = 6). Two participants described not knowing what to say or how to say it:

> *"I'm like, you know, I'm just gonna throw this out. I don't know what it means. I don't know what, I don't know if you want to mention it to your physician."* (Lydia, *MYBPC3*, age 51)

> *"…there was so much, I didn't understand, is this a death sentence? Is this, what do I do with this information? …Um, but I don't know how to tell him*."(Kristina, *BRCA2*, age 58)

Only four participants described their process of sharing their SF with relatives as "easy" or "not difficult;" two of these individuals cited their own experiences in managing their SF *("I talk to them about, you know, my experience and what it might mean, and the pros and cons of testing"* (Brian, *BRCA2*, age 58) and two others attributed their lack of difficulty to their family's communication style generally *"Yeah, it was fine. I mean, we're pretty cut and dry people, so it wasn't really a hard thing"* (Ariel, *BRCA1*, age 29).

In several cases, participants' understanding of their SF aligned with their assessments of their skills to share their results with relatives. All four participants who described their ability to share their results with their relatives as "easy" also had an excellent understanding of their

SF. One participant described being in close communication with her family but also others with hereditary cancer syndromes in a support group, saying

> *I certainly know a lot of information now just from my own experience. Um, and I'm always happy to talk to people and sort of give them my, um, experience, like, you know, tell them my story, um, and what I did and why I chose to do it, but I never say, well, that's what you should do too. And I mean, I happen to have these conversations all the time now with strangers because people, I was so open with it, I guess…*(Danica, *BRCA1*, age 40*)*

Conversely, five participants with a poor or uncertain understanding of their SF also described their ability to share information about their SF with relatives as poor or uncertain, as expressed by this participant:

> *And especially pretty early, I didn't know a lot myself. So I was like, I can't really tell you a whole lot, but here's what I know so far kind of.* (Donovan, *BRCA2*, age 44)

Reflecting on her own knowledge, another participant expressed a desire to know more about her finding to clarify her communication with her relatives.

> *I think with a little more information, I would definitely have a conversation with them… Yeah, knowing more about it, and I don't know, I'd like to know more about it so I can say, "Okay, because you're genetically related to me, this could come up in your genetic history as well?"* (Camilla, *LDLR*, age 53*)*

Only one participant demonstrated excellent understanding of her SF along with a strong sense of uncertainty of how exactly to impart that information to relatives. Although this participant, "Melanie," would eventually share her results broadly with family members, she described a delay in family communication:

> *It took me quite a bit of time to figure out how to do it. From the very beginning when I received the information, I felt like I would like to share it with my family but didn't know how.* (Melanie, *BRCA1*, age 46)

Opportunity

Normative and social influences and the resources and environmental context that contribute to an individual's behavioral choices comprise the "Opportunity" domain of the

COM-B (Michie et al., 2014). Interpersonal, cultural, and social factors affecting family communication were cited by 32 participants and most of these (25) mentioned more than one social factor. Emotional closeness with relatives was the most frequently citied contributor to participants' opportunities to share their SF with family members. More participants (n = 22) described feeling emotionally close with relatives as a facilitator of family communication than those who felt that their opportunity to share their findings was limited by emotional distance (n = 16). Many participants described open family communication as a function of positive emotional attachments with relatives and almost always described these relationships as "close," or "emotionally close." This sentiment is typified by this participant's description of her positive relationship with her parents and straightforward and intentional discussion with them about her SF:

> *My parents and I are very close, so with them, I could have an open conversation about it. I was very forthcoming with I'm going to get the confirmation testing and my next moves and trying to make sure that they feel like it wasn't their fault that I have this or I'm not aiming it at one particular parent. That's why I wanted to have the conversation with them both together because we won't know until they both get genetic testing, possibly down the road.* (Angela, *BRCA2*, age 32)

Participants who described emotional distance with relatives did so using a much broader set of descriptors and circumstances, although the phrase "not close" was often part of this discussion. Like several others, this participant expressed a desire to share her SF with a specific family member while providing an explanation of the complex interpersonal barriers that made it difficult for her to do so.

> *I have a brother. We're not close anymore. He's kind of not close to anybody in the family. I did Facebook... He has heart issues, but we always thought his was due to his lifestyle, because he's overweight, and drinks, and did drugs. But then when I got this news, I was like, "Well maybe it's his lifestyle and this gene." He's my only full brother.* (Lisbeth, *DSC2*, age 51)

Ten participants described some family relationships by using the terms "estranged" or by saying that they "don't talk/speak" to certain relatives, as expressed by this participant:

> *"I am estranged from a lot of my family, unfortunately. So, in regard to the ones that I haven't spoken to on told of my risk, it's due to that, um, we just no longer have a relationship* (Johanna, *BRCA2*, age 34).

Physical affordance or ability and how it influenced family communication was mentioned by 28 participants. Seven participants mentioned text-based tools or approaches that they employed when communicating with family members. Three participants reported using an existing family group text or chat to share their results and four utilized family notification letters provided to them by a genetic counselor or other clinician:

> *Oh yeah so I got this letter. And then from the genetic counselor after the fact that just said that just, you know, show your family, if you want to. Then I said, okay, and then I showed my parents.* (Carrie, *BRCA2*, age 45)

The presence or proximity of relatives was the most frequently cited physical affordance affecting family communication. Eleven participants described their "regular contact" with relatives as a factor in their communication with them. This participant's description of her communication with her children is characteristic of this sentiment:

> *You know what? My daughter works for me. So I see her every single day. So really nothing happens without her knowing. And my son, I probably see two or three times a week. We live in the same community.* (Lydia, *MYBPC3*, age 51)

Eight participants described both close and distant relationships in their families, and several (5) participants described how physical distance combined with emotional distance affected their family communication. Two examples are listed below, where the first participant described this as a longstanding pattern, while the second describes a slow degradation of family relationships over time exacerbated by the unique circumstances of the COVID-19 pandemic:

> *It's not intentional. It's just that, that, aunt and her family are, I just have never been close to my other brothers and sisters are a bit older than I am. So, um, they kind of, uh, grew up more around all their cousins and aunts and uncles. Whereas I, I kind of wasn't for some reason, by the time I came along, they, you know, my parents were, were not into as many family gatherings and things like that. So, I didn't really have a lot of those relationships that, you know, my brother and my sister may have had.* (Melanie, *BRCA1*, age 46)

> *Right. We, we, uh, we don't keep in touch. Like we used to, uh, yeah, I'm 68 and I'm the youngest of the family….my parents both, uh, passed away pretty early in my life. Uh, just sort of don't we never stayed close knit. Okay. Because everybody, uh, sort of went their own way. My, my one brother lives in Florida, the other one lives in the town is not too far away. And, uh, we just don't, uh, don't keep in touch. Like we used to. Especially with, uh, with what's going on now with the pandemic.* (Grant, *BRCA2*, age 68)

Motivation

In the COM-B, "Motivation" and how it affects behavior is subdivided into psychological evaluations, attitudes, and belief toward the behavior ("Reflective Motivation"), and automatic or impulsive desires or emotions associated with or driving the behavior ("Automatic Motivation") (Michie et al., 2011).

The most commonly used code in this study was applied to statements where participants expressed the belief that sharing their information with relatives was important for their relatives' healthcare; this attitude was shared by 31 participants and coded 52 times. These individuals wanted their relatives to know about their SF both to inform care relatives were already receiving and so that their relatives could potentially benefit from recommended screening and surveillance procedures to reduce risk. This participant connected her SF related to heart rhythm differences with her father's cardiac history:

> *One of the main reasons being my father also had a PVCs and I just wanted him to be aware that that might be something that he needs to be tested for and see if he needs followup because he's getting up there*. (Samantha, *KCNH2*, age 44)

This father described his rationale in sharing his cancer-related SF with his daughters in terms that clearly outline his hopes that they could benefit from enhanced screening:

> *Um, it had a lot to do with #1) When did the doctors say we should tell them as a medical matter and the answer there was as your oldest daughter approaches 30, it would be bad parenting, you would be remiss not to tell her, because even though she probably wouldn't get breast cancer until her forties, you know, if you didn't tell her and then something was growing inside and then she didn't get her first mammogram until, you know, 35, you'd never forgive yourself. So first it was governed by the medical knowledge* (Brian, *BRCA2*, age 58)

The above quote also exemplifies a communication pattern where participants expressed their belief that notifying family members was both medically important and motivated by concern or love for their relatives. Feelings of concern and love were described by 19 participants as they discussed their rationale for sharing their SF, and 12 of these individuals invoked these dual motivations. This participant's simple but poignant description provides another example of this duality:

> *My granddaughter who's 13 knows. She's the reason I did all these surgeries. She's the reason…oh, god I hate when I cry.* (Kristina, *BRCA2*, age 58)

Close to half (n = 18) of participants described concern, hesitancy, or worry about the consequences of sharing information about their SF with their relatives as they discussed family communication. In some cases, participants explicitly stated fear about how their relatives would react and how those reactions could affect relationships:

> *Interviewee: I mean, I just struggled with, at times just feeling like... When I told family, I wondered if I was over reacting or, if they thought I was overreacting. That has been hard for me, and the risks that make it so, that I can't get information that I would like to know. I would say the family part has been harder.*
>
> *GC: What about that? Just worrying that you were worrying people unnecessarily?*
>
> *Interviewee: Yes. And did they think it was over reacting, or wanting attention?* (Stella, *BRCA2*, age 42)

Other participants expressed concern about worrying or upsetting their relatives, particularly in the case of aging relatives or relatives who were already struggling with health concerns (e.g., *"Then with my dad, I think because he has been so sick, I just didn't want to worry him.* (Lisbeth, *DSC2*, age 51)).

In some cases, participants cited specific emotional attributes of relatives that explained their concern or hesitancy in sharing their SF:

> *My niece, she gets nervous pretty easily. So that's why we haven't shared that with her yet because I wanted to see, well, if my sister doesn't have it, then that's it. You know, that all, we don't have to worry her. I mean, she didn't know about me. I don't, I don't mind that part, but I don't want her to worry.* (Donovan, *BRCA2*, age 44)

> *Yes. Yes. I was probably a little bit more careful in how I phrased it with my daughter, because she is I think, is a more fragile person. But she didn't miss the point and I wasn't beating around the bush. I simply chose my words.* (Patricia, *SCN5A*, age 82)

Twenty participants described beliefs about heredity as motivating and influencing family communication. Some inherently prioritized sharing their SF with relatives with closer degrees of biological relationships, as described by this participant, who when asked by the interviewer why she shared her SF with only her siblings and parents replied "*I guess it's a combo of just they are the closest to me and then the gene line down the gene pool."* (Carrie, *BRCA2*, age 45). Several participants prioritized one side of the family when making decisions about disclosing to relatives. In some cases, participants hypothesized that one side of the family was more likely to be the origin of their SF because of family history of disease associated with the SF, as expressed by this participant, who had only informed his maternal relatives at the time of the interview:

> *Yeah. So I guess I started off with my parents and sister because they would be the ones, you know, I don't know, a hundred percent that it's from my dad's side, but I feel like it there's just because of my grandmother, since she had both ovarian and breast cancer fairly early, um, that's probably where it comes from. So that's all, we haven't focused as much on my mom's side of the family yet. And on her side of the family, like they there's like personally no cancer. Um, I think my mom had a cousin that had liver cancer, but*

> *she had been an alcoholic for 40 something years. So it was more environmental than probably genetic.* (Donovan, *BRCA2*, age 44)

Another participant with a SF in *BRCA2* common in individuals of Ashkenazi Jewish descent described extensive efforts to notify even distant paternal relatives who she was not in close contact with because of this shared ancestry:

> *I think I just said, "I have, this and there's a chance you guys might have it. And I suspect it was dad's side, because Ashkenazi Jewish." So just letting them know about it, and that they could have it…Yeah, I felt it was my responsibility to let her know, and my dad's half sister. Because their dad is my dad's dad, I don't know for sure, but he was Jewish, so I'm assuming the mutation was passed on from him. So I let them know. And I'm not particularly close to either of them, especially not to my dad's half sister, but I think I contacted them through Facebook, and let them know.* (Stella, *BRCA2*, age 42)

Only two participants who described family communication decisions as influenced by heredity based these beliefs on knowledge derived from cascade testing by relatives. In one case, a participant whose parents were divorced and did not have a close relationship with her father shared her results with paternal relatives after learning that her mother had tested negative for her SF. She describes feeling motivated to reconnect with these relatives to inform them of her SF and her feelings of gratitude about the outcome:

> *It basically left me knowing it came from my dad's side of the family. I shared that information with him and his extended family so that they could do any screening that they wanted to. And in fact I had not talked to my dad's extended family in 20 years and I was kind of thankful because it pushed over the edge to reconnect with them. So I talked to my, yeah, my grandma and my aunts for the first time and then ended up seeing them the next year when we were out to visit in Colorado. So in a ways too, for me, it ended up being positive about it. I had some family benefits from it too.* (Jennifer, *MSH6*, age 39)

For the individual quoted below and five other participants, the motivation to share their SF with relatives was influenced by their own desire to better understand their SF, particularly in the context of their own understanding of their family history:

> *I'm thinking about this in a more serious way, right? So I'm going to be talking to my sister now in the meantime, she knows and then she talked about my cousins and*

> *everybody else and we talked about my parents, what they died from.* (Colin, *MYBPC3*, age 64).

Another participant described reaching out to several relatives over four months after first learning her SF related to high cholesterol and only after reviewing her family history with GSRP staff while scheduling the interview:

> *And that pushed me because with the last interview or last time when I talked to the last woman* [GSRP study staff]…*Yeah. And she's talking to me about all of the extent in my family, I'm like, I don't know a lot of what I should know. And that's when I started having the targeted conversations and talking to people about, Hey, I got this genetic results. Can you tell me about our family history? And I talked to probably 10 or 12 different people and Hey, what have you experienced? And what do you know about the extent of our family? And I got so much information.* (Joy, *APOB*, age 42)

Seven participants described not sharing their SF with relatives because they did not believe doing so would have an impact on their relatives' health. Two participants described not sharing their SF with their brothers because "*He wouldn't care*" (Kesha, *BRCA2*, age 26) or because *"…it will not affect his life. If I tell him this or not, it won't change anything*" (Angela, *BRCA2*, age 32). Others chose not to share their information with relatives because, in the words of one participant, "*There doesn't seem to be any medical reason for them to know.* (Paul, *SCN5A*, age 51) or because they did not perceive sharing their result as medically urgent: "*I don't think there's ever going to be urgency to tell everyone in the family.* (Jorge, *MYH7*, age 22)

"Automatic motivations" such as emotional drives or impulses other than feelings of obligation or responsibility were rarely invoked by participants as they discussed how they shared their SF with family members. Ten participants described these feelings as motivating their family communication decisions and patterns. Phrases such as "I needed to," "I had to," and "I was obligated to" were commonly employed, and one participant described this in moral and empathetic terms:

> *Well, I mean, you find something like this, it was a such surprise to me, and I would want someone ... I would have wanted someone in the family, if they knew about this, to let me know, and even if you didn't like the person, I mean, I just [inaudible 00:38:23] by not sharing this kind of news with people who are potentially affected. I think it would be too immoral to not let people know. You know?* (Wilson, *RET*, age 70)

For four participants, feelings of responsibility were jointly expressed along with beliefs about the autonomy of their relatives, as described by this participant:

> *I, I, felt like I needed to tell them because if I got it, there is a possibility, it's not a for sure thing that they have it and then if they have it, their kids would have it. And so that made me say, I got to at least tell them. What to do about it? That's their choice.* (Lena, *RET*, age 64)

Participant-Described Facilitators of Family Communication

Three themes emerged as facilitators of family communication. Contextually, these themes were coded separately from COM-B constructs when participants emphasized them as distinctly contributing to their thoughts, feelings, and decisions regarding sharing their SF with relatives. One participant explicitly stated that sharing her SF with her relatives was a very easy and straightforward process because *"…we talk about anything and everything. It's like one of those open families. We talk about <u>everything</u>."* (Sophia, *LDLR*, age 56). Other participants explicitly cited their strong belief that their relatives would benefit from their sharing their SF as facilitating their communication processes. For this participant, this belief facilitated her continuing communication with relatives to encourage them to act on the information by pursuing cascade testing:

> *I guess that's where my, my, my biggest impetus was. And then from that point, if they tested positive, I never wanted to, you know, push on them. What I felt like, you know, what I did, I guess it's a personal decision for everybody. But at that point I had, I felt more comfortable knowing that they had gone to see a doctor or genetic counselor, because that's how they got the test. Right. So they were under the care of someone that was going to be giving them the recommendations.* (Danica, *BRCA1*, age 40)

Finally, several other participants cited a shared understanding among relatives of their family history of health concerns potentially related to their SF as a facilitator of initial or ongoing conversations:

> *And my mom was always, she's kind of old school, so she was skeptical about this. And when I told her she was kind of just like yeah, I could have told you that and brushed it off. But the more we talked about it, the more she was like, oh, it was interesting and it's good to know that it's hereditary. Because she was kind of the same with me, she knew that it was in our family, but wasn't exactly sure if it was just bad luck or it was genes.* (Fletcher, *BRCA2*, age 29)

There is overlap between these themes and COM-B constructs; open communication within a family provides a normative opportunity for communication and beliefs about heredity and that sharing family health information will benefit loved ones serve as motivators of communication.

Participant-Described Barriers to Family Communication

One overarching theme distinct from the COM-B discussion above emerged from participants' descriptions of barriers encountered when sharing their SF with relatives: family dynamics. This participant's introductory statement when beginning to review her communication pattern with the interviewer summarizes this theme well:

> *The dynamics between my parents and then my siblings is just not easy. In fact, I took a survey before I met with you and there was a set of questions and answers about your family relationships. It talked about parents, siblings, spouse and children. Well my dynamics with my spouse and my children are very different than siblings and parents. I feel like I have a much healthier relationship with my husband and my children, not as close and good with the others.* (Melanie, *BRCA1*, age 46)

Like this participant, several others situated themselves as "different" or "outsiders" in relation to their families. One participant had clear insight into how this status affected her communication with relatives, proposing two other alternatives, and concluding with a reflection of how she felt like a "bad guy" when sharing her SF with relatives:

> *"I have a reputation in the family as being the artistic sort of a little nutty one. And so I wasn't the right messenger for this information. Um, ideally there would be a system where my doctor would talk to their doctor who would talk to them, um, so that it would come with more authority. Um, second best would be a website designed for people like me designed by a group like the NIH or some other authoritative group that would just have all the different genetic disorders and what the implications are to send that you can say, I got this diagnosis and here's a website to share with you about it, you know? And I could send that by email. And then I think that would be less fraught, because it would appear as if the NIH was the bad guy in this scenario rather than me.* (Farah, *BRCA2*, age 59)

Phase Two Findings

Phase 2 findings are described here in textual ("what" participants experienced when sharing their SF with family members) and structural ("how" participants experienced this phenomenon) terms. Two major themes emerged from synthesizing the meaning units identified in each transcript and the textural and structural elements of these themes are displayed in Table 4.3 below.

Table 4. 3 *Themes with Textural and Structural Elements*

Theme	Textural Elements	Structural Elements
Personal impact and reflection	Methods of communication, personal investment of time or energy, medical procedures and their outcomes, new disclosures	Emotional responses to family, challenges and struggles, evaluations of family's actions
Effect of family culture	Descriptions of family culture, continuation of exiting communication patterns	Durability or influence of connections or estrangements

Theme 1: Personal Impact and Reflection

Family communication was described by Phase 2 participants as an experience they were open to sharing more about; none of these participants struggled to find words to describe their experiences and how communication had evolved (or not) over time. Participants told their stories of how they communicated with their relatives in the same familiar way they might have

described a movie they had seen many times before. Even if they did not love the plot or the outcome, all the characters were well-known and the story was deeply resonant and familiar. Participants described their experiences in sharing their SF in terms of this experience's impact on their feelings and the outcomes of their investment of time and energy.

Textural elements participants described included their reflections on the methods they used to communicate with their family members and the perceived effort involved or effectiveness of these communication techniques. One participant, Max, described his efforts to share his results with relatives over time using several different methods. His sense that technologies such as email and text messaging were variably helpful was palpable, and his final conclusion was that he felt that conversations with relatives were the most fulfilling and successful when they occurred in a conversational way.

> *Sometimes it wasn't easy to communicate and get immediate answers. So it is just a matter of trying different communication avenues and keep on, uh, reminding my folks to, you know, reply and, and read, read the information that I gave them. I ended up, mailing copies of the information I received, because not all of us are that up to date with modern technologies of using the phone and sending things through the email and stuff like that. So I ended up mailing things out to a few of my family members and then, you know, we talked face to face about results and issues that they may have had and texted back and forth, just used all that modern stuff to, to communicate. It seemed like, you know, when I was face-to-face or on the telephones speaking with people, and we've both had the information in front of us...that worked good.* (Max, *COL3A1*, age 72)

Like Max, Theresa also initially shared her *BRCA2* SF with relatives via email but then followed up with one aunt who had been diagnosed with breast cancer 20 years ago by telephone. Theresa described this telephone conversation as helpful and important on several levels: she learned more about her aunt's experience and prompted her aunt to take action that she hoped would be beneficial to her aunt's daughter (her cousin).

> *What I did was I drafted an email to the concerned parties and just explained what had happened with me and my findings… then I called my aunt directly and had a really good*

> *conversation with her and just got her whole, cuz I, I mean I had known what had happened to her and everything, but I never really had a personal long visit with her to get all the details and just what a horrible thing she went through and survived. And I think it helped me doing the more personal approach versus the impersonal email. I think it helped me just talking to her and just saying, you know, from my perspective, I would wanna know if I had it or not because I have two daughters and so I would be worried about them. And so then yeah, then she kind of decided that yes, it would be smart for her to go get tested.* (Theresa, *BRCA2*, age 52)

Samantha reflected on the impact of her SF for herself and relatives in the context of her family's additional medical concerns, straightforwardly describing the importance she assigned to family communication in relation to other tasks.

> *Everything in my family right now has been medical for the last 15 years. I mean, I shared it, the information, but I guess we're just kind of desensitized to things…it's just kind of something that goes to the back burner, I guess. Until it's affecting me, I, you know, it may become more relevant if something happens.* (Samantha, *KCNH2*, age 47)

Several participants described ongoing communication in their families about their SF. For Max, in-person gatherings were an opportunity to revisit previous discussions:

> *Well, you know, every time I physically see them, you know, I'll bring it up and, and mention it to 'em. I said, you know, finding out where, where they stand on this.* (Max, *COL3A1*, age 72)

Evan similarly described straightforward and periodic check-ins with family members prompted by his own reassuring cardiac surveillance evaluations:

> *Our communication is usually after a doc, after the yearly checkup we discuss it. But you know, like I said, so far it's been, everything's checked good. And we just move on till the next year, I guess is the best way to put it. Knock on wood. Hopefully it goes smooth for a long time.* (Evan, *MYBPC3*, age 52)

Five participants reported new disclosures since their last interview. Melanie and Theresa shared their breast-cancer-related SF with newly-adult daughters and both reported framing these disclosures as ones that prioritized their daughters' health but also their autonomy to make decisions about pursuing cascade testing and beginning additional surveillance. In describing her conversation with her daughter, Melanie said:

> *So it's been more just the last time I talked with her about, it's probably within the last month, I did say "Now that you're 20, you're getting a little closer to the age that if you did have the same gene that they would start doing some screening and testing, and then if you did have it that you could just be a little bit more proactive." And she just did the look like, "Okay, I didn't ask Mom," type thing, so I just left it at that.* (Melanie, *BRCA1*, age 48)

Theresa similarly described her and her husband's choice to share Theresa's SF with their daughters and her comfort with allowing her children to make decisions about how and when to move forward:

> *I was, we just felt like they were old enough that they could have the information, and then they could choose to do what they wanted with it. And they have both chosen to wait. Um, my youngest is getting married this summer and she's thinking she will wait until she's had children and then go get tested. And my eldest, um, I think she just said she just kind of wants to wait till she's 30 maybe before she goes and tested. Um, yeah, she's just not really sure.* (Theresa, *BRCA2*, age 52)

Farah and Donovan both described how children of their siblings had become aware of their SFs. Farah shared her results with a nephew and described her experience positively and as an opportunity to share accurate family history information:

> *So the whole thing was good because it turns out that he didn't know that my dad died of pancreatitis. He thought my dad had died of cancer. My father died in 1980 way before he was born. And so I guess somehow the family lore got changed. But anyway, so it was good to be able to share with him the family history of pancreatitis. And so that opened up a nice conversation.* (Farah, *BRCA2*, age 61)

Donovan did not communicate with his niece directly but was certain that his parents relayed the information to her:

> *Donovan: I know my niece is aware; she just turned 18 so she may choose to get tested in a few more years. I don't know, but I haven't actually spoke to her about it in particular.*
>
> *GC: Got it. How do you know that she knows? Just through the grapevine, through your sister?*
>
> *Donovan: I think my parents told her.* [Because] *she lives with my parents. So I'm pretty sure, yeah, I know for sure that they, that they told her* (Donovan, *BRCA2*, age 46)

Kesha concluded that she was much more likely to have inherited her *BRCA2* variant from her father, whom she had never met, after she reviewed her mother's negative cancer family history. Kesha made a concerted effort to track down members of her paternal family, even though they did not live in the United States, by connecting with distant relatives via Facebook Messenger. She was able to connect with a paternal half-sister using this medium to share her SF with her.

> *So I tried to find some of my relatives, and I did find a half-sister, and I think it ended there. I don't think she ever got testing, but I felt like at least I* [did] *share, I let them know. Then after that, well, I couldn't find anyone else, so it kind of ended there from that side.* (Kesha, *BRCA2*, age 28)

All participants described structural elements which shaped how they experienced communicating their SF with relatives. Both Jethro and Donovan cited their own feelings of frustration when describing their ongoing experiences in communicating with their families Donovan, for example, described persistent attempts to persuade his sister and father to pursue cascade testing for his *BRCA2* variant. Donovan, a father of two girls, experiences communication with his sister as concerning and frustrating as he worries about the health implications of his sister's unwillingness to consider cascade testing both for her and for her daughter:

> *I mean, probably the only frustration on my end was like, my sister, she just doesn't wanna be tested. She doesn't wanna know. And that's her decision and that's, you know, she can certainly do that. But in the beginning I was a little more pressured, like, don't you wanna know, like, don't you [want to know] and why wouldn't you get tested? And then you've got a daughter, and so it would be nice if you could find out that you don't have it, so then you don't have, and she doesn't have. to worry about it either.* (Donovan, *BRCA2*, age 46)

Although the niece described is the same niece Donovan reported as having learned about Donovan's results through his own parents, rather than her mother, Donovan's sister, Donovan remains frustrated at the indirect nature of this disclosure. Later, Donovan described making an

active decision to try to relieve his sense of obligation and responsibility over his sister's choices regarding cascade testing:

> *I mean, we, we still talk about it, but I don't push. I just, that was something I kind of finally decided was even for my own self, like I don't wanna feel obligated that I have to try to convince her to do it…after we talked about it several times and she was like, you know, I just don't wanna know.* (Donovan, *BRCA2*, age 46)

Donovan described a months-long process working with his father and his father's physicians to obtain cascade testing for his father and appropriate followup care for his father with his own oncologist. His relief in the end result of these efforts is evident in his summary statement describing his father's current care:

> *Once he got the result back and it was positive, his doctor was just kinda like, well, I mean this doesn't really change anything. And I'm like, oh yes it does. Like, no, you need to, you know, get some additional screenings done that maybe you're not already getting. I have had to kind of help push and prod and say: Hey, I see this oncologist [and it] might be good for you to see this oncologist. He's doing 'em* [tests recommended by the oncologist]. *So that was good. So that's good. But it was a little bit of a hurdle of getting through his, his initial doctor who just didn't think any of this was important* (Donovan, *BRCA2*, age 46)

Jethro similarly describes his relatives' inaction after repeated attempts to spur them to take action, stating: *"I was irritated. Yeah. Irritation and frustration."* (Jethro, *RET,* age 48). Jethro, who underwent a prophylactic thyroidectomy, which revealed a 2mm malignancy, remains mystified that relatives would not want to seek clarity on their thyroid cancer risk status:

> *Oh, every time I talk to 'em, I keep asking 'em, did you get it done yet? Did you get it done yet? Wow. Are you gonna get it done? Are you getting tested? 'Cause I care about them and I at least want 'em go, go get tested. If it's negative, great. Wonderful. Don't ever worry about it again. I won't bring it up again, but otherwise, yeah, every time we talk, even a text message, you know, Hey, like, we didn't talk for, you know, a few weeks or a month. Hey, how's it going? Hey, did you go get tested yet? I keep throwing it in there.* (Jethro, *RET*, age 48)

Emotional responses to communicating with family members were described by all participants. Unlike the frustration described by Jethro and Donovan, Patricia, Melanie, Farah,

and Kesha experienced family communication as disappointing, surprising, and/or painful. The following description from Farah exemplifies some of these feelings well:

> *Well, it's been shocking. I learned a lot about my family. I'm surprised that they don't take my word for it, but this is not a death sentence…My father's side have been like, they just want to bury their head in the sand. They don't want to know about it because they're afraid that it would increase their anxiety if they got a positive result. Also, the fact that my mother won't move on it and she's an only child, means that each side of the family can blame the other side and fantasize that it's the other side of the family that the BRCA2 came from. And so it's been quite disappointing…I'm disappointed with everybody, but I'm disappointed, especially with my sister, because she's an MD, but she doesn't want to know either.* (Farah, *BRCA2*, age 61)

In reflecting on their experiences, both Melanie and Kesha described how their own coping with learning about their SF and how it influenced family communication:

> *Well, in the beginning it was very shocking for me. I just remember, I didn't know what a genetic mutation was….I guess it was very shocking to me as accepting that I had one, that it was affecting me. And, so it took me while, I wasn't in a good, place. I wanted to accept it before I could share it.* (Kesha, *BRCA2*, age 28)

Melanie described an ongoing and highly complex process involving her own coping and both concern **for** her relatives and **about** how they would react to and perceive the information she shared:

> *I think for me it has been a process, so being able to just first take in what was being explained to me but then also to think about that it affected more than just me or could affect an impact more than just me, and then try to, within the range of my own relationships at that time, figure out what's my responsibility now that I have this information, with the information, and how can I respect my own feelings while also trying to reach out to people who I felt like could get benefit from the information.* (Melanie, *BRCA1*, age 48)

Melanie later elaborated on this after discussing how, despite feeling prepared to share her personal knowledge and familiarity with genetics, discussing her SF with relatives remains an emotionally fraught process:

> *So I think in that way I was prepared intellectually, academically, but I think that part was easy. I think the most difficult aspect has been the emotional, the psychological in*

> *some ways, the relationships pieces to it, and the processing of my own... In some ways, because I leaned so much into the academic intellectual piece to it, I feel like I'm still grappling with how do I feel about it.* (Melanie, *BRCA1*, age 48)

Melanie further described a poignant sense of emotional hurt and deflation in the aftermath of her sharing her SF with her mother and sisters. She met with a genetic counselor to discuss her results and this individual provided her with a family notification letter. Melanie's deep and persistent sadness about the way her mother and sisters reacted to her use of this letter to facilitate disclosure of her SF is palpable:

> *And apparently, there's a lot of angst that's harbored in that, and it's hard because I thought I was doing a good thing to share the information, and I did it the best way I could. And I felt like I was using a genetic counselor in a way by doing it that way because the information directed them to contact the genetic counselor, and it would be at no cost to them. So I thought that they would get professional help, and I'm not a professional…. I think it's just uncomfortable so much because it's "Why were you so impersonal about this?" Or "How do you think it feels to get told this way, and blah, blah, blah?" I'm saying it in a nice way compared to how I was feeling when it was being said to me and some of how it was said to me. But I think that's part of it, and to me it just felt dehumanizing to think that that's how they feel about my attempt. And I think that's the piece to it that's really hard is just that I was trying to do something helpful, but it seems like it was taken as something that hurt them.* (Melanie, *BRCA1*, age 48)

Like Melanie, Patricia's disclosure of her SF with her daughter was motivated by her desires and hopes to benefit her daughter. Patricia's resignation and disappointment are clear as she relayed her thoughts and feelings about what these discussions with her daughter were like:

> *Patricia: "I don't, I don't care what, what happens, I don't wanna know." This was what I was getting from her. And my saying, "It has nothing to do with me. It has to do with your health and your future." And her saying," I don't care." I mean, she's, she's depressed, she's always been depressed. And so, you know, after a while I, I gave up. I couldn't convince her, and I knew, you know, I'm a therapist, I knew that you, you don't convince people, they have to come to it themselves. And, there was no way after a while that I could see that I could help her come to it herself.*
>
> *GC: Sounds really painful on a number of levels.*
>
> *Patricia: It is.* (Patricia, *SCN5A*, age 84)

Theme 2: Effect of Family Culture

Participants framed past, current, and planned communication about their SF with relatives in terms of their unique family cultures and compositions. Structurally, "what" participants described was a continuation and extension of existing communication patterns in the family. While variability emerged as participants discussed physical factors, such as distance between relatives and family structure or emotional factors such as estrangement, a key similarity across participants was how these attributes influenced family communication. Just as participants had no trouble relating and reflecting on the personal impact sharing their SF with their families had on them, they were similarly able to discuss, apply, and interpret how their individual families (and their unique positions within the family) influenced family communication. Participants experienced communication about their SF as taking place in the setting of a familiar and largely static family system.

Several textural elements described participants' family cultures and systems. Many participants referenced how frequently they spoke with or saw their relatives. Some, like Evan, described regular contact and close proximity with relatives:

> *I mean we, like I said, I got two sisters and you know...we live within 15 minutes of each other…we don't have any trouble communicating.* (Evan, *MYBPC3*, age 52)

Others provided detailed descriptions of family communication patterns and how they had developed over time. Here, Jethro describes how his siblings grew apart after the death of their mother and how their relationships with one another changed as they matured. Despite this gradual emotional and physical distancing, Jethro described maintaining ties and connections with his siblings that facilitated his communication about his SF:

> *…We all once my mom did pass away, then everybody just kind of, you know, I don't know, fizzled, I don't wanna say fizzled out, but everybody has their own families, you*

> *know. I mean, I still talk to almost all of them and, and see them a couple times a year. So that's not the problem…only one is really geographically far away. She lives out in Michigan…We're not all that close and, you know, spending all the holidays together and everything like that, 'cause we all have our own families. But it's still, but we still, like I said, stay in contact, so that's not an issue.* (Jethro, *RET*, age 48)

Theresa described a long-standing family grapevine involving women in the generation above hers. She readily admitted that while this facilitated information-sharing in the family, some viewed this as invasion of privacy:

> *We have what we call the, my cousin and I have coined it the aunt hotline <laugh>. As soon as there's any sort of family news, all the aunts on both sides, both my mom's side and my dad's side, they all call each other and it's discussed and hashed out and, um, you know, gossiped about and all of that kind of stuff…With the person's best interest…originally at heart, but then it can kind of get carried away into, you know, and more into gossip. But I think some members of my family, like my brother who's a bit more private, um, and he's very religious and he, I think he takes offense to the thought that, you know, something that affects him has been analyzed and discussed by all of these people in his family, mostly females.* (Theresa, *BRCA2*, age 52)

Long-standing family communication patterns and ways of relating with one another were referenced by several participants as contributing to what their communication with relatives about their SF was like. Theresa, quoted above, revisited some of what she previously described about her brother, elaborating on her explanation of why she believed he was unlikely to ever act upon the SF information she shared with him:

> *I believe my brother is of the mindset that don't speak it out loud, then you won't get it, um, kind of deal. So they don't like talking about disease or illness or that kind of thing. And so I think that's where they're at is they're just going to ignore it.* (Theresa, *BRCA2*, age 52)

After disclosing her SF to family members, Farah relayed how unconcerned they seemed to be, repeatedly using the term "meh," but also how unsurprised she was by this reaction:

> *GC: You've said that a lot. It sounds like everyone has this, just this meh reaction.*
>
> *Farah: It's a very meh reaction that I find very odd, but this isn't the first time I found the reaction, meh and odd.* (Farah, *BRCA2*, age 61)

Kesha expressed similar feelings when talking about her communication with her siblings, stating: *"I mean, my siblings never really, they didn't really care, I think"* (Kesha, *BRCA2*, age 28).

Camilla described a specific and long-standing difficulty communicating with one of her sisters who she described as having lifelong learning challenges:

> *So if I was to talk to my younger sister, she wouldn't understand it….And it, it's just wasting your breath…It's actually hard. And like, it's, what's the word I want to use? It's painful. You know, it's painful. So she doesn't really listen to what I, I mean, she may listen, but she doesn't understand.* (Camilla, *LDLR*, age 56)

Kesha's ability to communicate about her SF with some relatives was affected by language issues. Kesha is bilingual but many of her relatives speak only or primarily Spanish. Explaining her results and what they meant in Spanish to her mother (first quote below) and other relatives was challenging for her.

> *I just didn't know how to kind of, like, not only am I saying, you know, all this scientific terms and all this medical terms to her, but also in Spanish, and then in addition to that, it's like, in a way that she could understand. Yeah. But just itself, just communicating what it means was difficult.*
>
> *Well, yeah, like I said, Spanish, my first thing was Spanish…I don't really have the, the language, like the medical terminology in Spanish. I had to learn. It was a challenge.* (Kesha, *BRCA2*, age 28)

For most participants, these textural descriptions and elements of family culture were intimately linked with the structural elements of their lived experience – how family culture and existing family relationships affected their experience of family communication. Melanie's complex disclosure story is one illustration of this. Melanie learned of her SF in the context of diagnostic genetic testing for two of her children with congenital anomalies who died shortly after birth. She described sharing her findings with her mother and sisters as a terribly painful experience and as *"…a pretty ugly confrontation to be honest"* (Melanie, *BRCA1*, age 48). As

noted earlier on page 53, she described how her mother and sisters berated her for beginning the conversation by sharing a family notification letter she received, and how hurtful this was for her particularly because *"…we were getting genetic testing because I'd had two children who died, and …we were experiencing a lot of traumatic events…and it really did take a lot for me to get out of all of that and set all of that aside in order to share with them that we have this gene that you might want to know about."* (Melanie, *BRCA1*, age 48). As she further described:

> *And so when it got received in such a negative way, it also at the same time discounted that we have all of this other stuff that's very heavy and difficult and that we could use a lot of love and support for. It just amplified that they have ignored all of that, and that it's all about them, and I'm supposed to be taking care of them while I'm also taking care of all of these other things that are really complicated and hard to take care of.*
>
> *And so I think that component makes it that much more hurtful is that it wasn't... There was no acknowledgement of, "Wow, you're going through a lot, and you were trying to get these answers that you didn't even get, and instead you got this other answer, and that must be also hard to hear. And even though it's hard for me to hear that you're sharing this, I can see that you love me enough that you thought that it could be helpful for me, and so I appreciate that you did that."* (Melanie, *BRCA1*, age 48)

Melanie described this dynamic as static and longstanding and contributing to feelings of alienation and difference. She pointed out several ways in which she feels fundamentally different from her closest relatives, stating,

> *So I think that the culture is more just that we clash, I think, in my family…. And so that does really play a part in our experience of being able to share it openly.* (Melanie, *BRCA1*, age 48)

The profound loneliness of Melanie's experience is evident in a concluding statement describing how she and her mother and sisters communicate about screening studies related to her SF: *"But I keep trying. I don't know if I'm ever going to really connect, but…"* (Melanie, *BRCA1*, age 48).

Farah's experience of sharing her SF with her relatives was also shaped by her family's specific culture and her sense of being an outsider in her own family. In her words, *"I've always been sort of odd compared to the rest of the family."* She described herself as *"...involved politically. I have opinions about things in the world. I'm engaged with my health"* and, in contrast, described her family as *"...just fish in a school, just going along with whatever waves come along*" (Farah, *BRCA2*, age 61). She relayed significant distress when considering how to communicate with nieces and nephews because her brother and sister did not seem interested in learning more about her SF or pursuing cascade testing (Farah's feelings of disappointment are evident in her quote on page 52 above). For Farah, there is a direct connection between her current communication challenges and the trauma she experienced in childhood. For Farah sharing her SF with her family is experienced as a familiar and tiring recapitulation of patterns and processes established years ago:

> *Oh, my brother, too. Now we've got the same problem with him about the generations, because he's got three kids. And so when do I tell them if he's not going to tell them? And they're all really young now, but I guess I'll wait till they're 21 and hopefully I'm still alive...*
>
> *This was always my role. This was always my role in the family. Now I'm getting mad. My mother has borderline personality disorder, and my father had narcissistic personality disorder, and I'm the oldest kid. And the rest of the family doesn't seem to have a personality disorder, but they are passive, as you mentioned. Anyway, in my immediate family, which we live far away from the rest of the extended family, it was always my role to keep the family together. And that was both oppressive and isolating because I was just a kid. But also, it always made me different. I was the kid who didn't have a childhood. I was a parentified child, so I was always different.*
>
> *And it makes me mad that this is coming up again, that I have this role that now it's like, "Do I tell their kids, because they won't do it in order to protect their health?" Again, it's not my role, but who else is going to do it? So I've been at this place many times before and I've really worked in my life to withdraw from that role and to let people make their own mistakes.* (Farah, *BRCA2*, age 61)

Like Melanie and Farah, participants commonly described themselves as contrasting with relatives or their family system as a whole. Donovan described this in terms of personality differences when discussing how he and his siblings and parents approach discussions about cascade testing and screening evaluations:

> *But for me, I'm, I'm more of the very analytical type person and so I want to know; to me information is power. Cuz now it's like, now I can make sure I get my, annual physicals and all the different tests and I can check it off each year and be like, yep, I've done everything. But you know, everyone's different.* (Donovan, *BRCA2*, age 46)

Kesha described a similar sense of feeling more proactive and in control of her health compared to her family members. She described challenges in talking about her SF and the screening studies she had with her mother and other relatives because of their skepticism that her cancer risk was increased. In her words, many family members questioned her choices, saying *"I think they don't understand why I am focusing on something that I don't have*" (Kesha, *BRCA2*, age 28). The family's religious background, especially her mother's Catholic faith, added additional challenges and provided another point of comparison between Kesha and her family.

> *I mean, like, my family is Catholic, um, and they, I mean, it's hard to communicate when it comes to science… They, they wanna put everything on faith…I'm not saying they don't believe in cancer or anything like that. It's just they want to believe that there's a higher power, that there's, um, that, you know, God will prevent everything.*
>
> *And, um, and for me, I don't think [that], so I feel like I need to make that happen for myself. I put it in the way that I put it to my mother is, "okay, maybe God gave me the, the knowledge to know I have [the] BRCA genetic mutation, so then I could take, do all the things that I need to do to, to be healthy." You know, I have the tools.* (Kesha, *BRCA2*, age 28)

Other longstanding family dynamics shaped how participants experienced communication about their SF. Patricia's difficult and strained relationship with her daughter predated any communication about her SF by decades and remained unchanged afterwards:

> *Well, it's not, I mean, this particular subject was not the problem, per se. Although that was the thing talked about, it was just, you know, the coin of the realm. And it was, it was the thing that got played out. But we had a difficult relationship. And so she was unhappy with me on and off.* (Patricia, *SCN5A*, age 84)

Camilla's estrangement from her older brothers, due to her history of childhood sexual abuse they perpetrated, continued as a protective action as she did not contact them to share her SF. In her words, *"I choose not to engage with them."* (Camilla, *LDLR*, age 56).

For Samantha, her family's complex medical history and ongoing medical concerns contributed to her sense that communicating about her SF was more like an item on her long to-do list rather than something exceptional or urgent:

> *Um, well, like I said, to be honest, <laugh>, everything in my family right now has been medical for the last 15 years. So I mean, I shared it, the information, but I guess we're just kind of desensitized to things…we've been dealing with, um, his illness since 2005. Right. So, you know, we were talking 11 years in and, on top of, that, my granddaughter who now lives with me, she has a disability and we have in-home nursing for her as well as my son. So it is just, everything has been medical for so long that, um, yeah, it's just another thing to add to the list, I guess.* (Samantha, *KCNH2*, age 47)

Textural-Structural Composite Description

The 11 participants interviewed for Phase 2 of this study described the experience of sharing their SF with their relatives as a series of conversations with people they knew well and cared about. These conversations were important, and participants engaged in them with the hope that their loved ones would value the information and act on it for their benefit. The information they had to share was not only important, it was important to them to share it; doing so fulfilled both obligations and desires to help and to make a meaningful difference in their families.

This group of participants shared their SF results with their relatives according to their best judgment and in the manner that felt best to them and that they anticipated would suit their

relatives well. Communication about the SF was not a one-time occurrence; in contrast, participants described ongoing conversations taking place over a period of months and years. Even if the content of the conversations was clinical and factual, these were emotionally-laden conversations that participants mulled over, revisited, and processed over time, sharing their feelings openly with the interviewer.

The inherent familiarity of relatives and relationships established over decades was the foundation upon which family communication about participants' SF was built as well as the scaffold upon which it evolved. Participants' underlying assumptions and preconceived notions about how relatives would respond upon disclosure deeply affected how they themselves experienced these conversations. How participants situated themselves within their unique family systems was the most durable, notable, and important factor in how they experienced sharing their SF results.

The experience of communicating important, yet unexpected, genetic information in the form of a SF, whether it was difficult or easy, continuous or episodic, revelatory or expected, was, above all, deeply meaningful for participants. Sharing their SF was an act of love, of hope, of concern, and of caring; these participants were gifting their families something incredibly personalized and valuable. Like anyone giving a loved one a present, participants were acutely aware of and highly sensitive to how their offerings would be received. Even as relatives responded in predictable, hurtful, grateful, or dismissive ways, this did not diminish the value of this interaction for participants. Sharing SF with family members was how participants gave of themselves and a reflection of their regard for their families.

Participant-Reported Recommendations

Two participants (Melanie and Farah) volunteered detailed opinions and thoughts about interventions that they wished had been available to them. While the rationale underlying their recommendations may align with the themes described across Phase 2 participants, they alone provided suggestions. Rather than completely filtering these experiences out, their inclusion here is more in alignment with a narrative or case-study approach rather than with phenomenological methods (Creswell & Poth, 2018; Moustakas, 2011).

Melanie's suggestion was for counseling and support specifically directed toward family communication that included strategizing about the use of communication tools, anticipatory guidance regarding relatives' responses, and follow-up supportive care:

> *But I think when I was at* [redacted name of clinic] *and asking if I could get the letter that I could send with the little page that had the medical information about the gene, and maybe if we could have sat down there and talked about, "Well, if you sent this, what potentially could be the consequence for how it's received?" Kind of like what you do as a genetic counselor when you're saying, "Okay, here's the gene that you have, and here's potentially the consequences because this gene is a part of who you are." I think doing that same thing, but in the social way… I don't even know what all the options would be, but maybe somebody professionally could have some of those ideas, maybe scripted or maybe practice role-playing how you could share this with them. I think also maybe just having somebody you could go back to and vent to and be like, "I just got yelled at because I sent this letter and I'm feeling really, really vulnerable right now about that. What do I do about this?"* (Melanie, *BRCA1*, age 48)

Farah's thoughts on a potentially helpful intervention were both extremely specific to her unique family culture and situation. While she expressed a strong desire to remove herself from communication with family members as much as possible, she also felt very strongly that any communication that she did not directly participate in be highly tailored to align with her perceptions of how her relatives would react. She began by suggesting the development a website designed for relatives of SF recipients:

> *Simple things that could have helped is just some website that was straight and to the point, so it didn't take too long to read, that was developed by a psychologist about denial. Why do people deny health outcomes, especially with BRCA? What are the advantages of not denying?... That would've been really helpful if there was something I could point to, because it would've been less fraught.* (Farah, *BRCA2*, age 61)

After discussing the informational content of such a website, Farah added *"But addressing the psychological denial is important, I think."* The interviewer's use of the word "proactive" in clarifying the main messages on an educational website prompted the following exchange, highlighting Farah's sense that tailoring messages to suit her specific family was both important and difficult:

> *Farah: Yeah, but proactive is a bad word.*
>
> *GC: In your family?*
>
> *Farah: I know. You have to get into their brains. It's really hard to do.* (Farah, *BRCA2*, age 61)

Chapter Summary

Interview data from 40 Phase 1 participants was analyzed by coding each participant's discussions of family communication in terms of their capability, opportunity, and motivation (the COM-B constructs) to engage in this behavior. Participant's knowledge of their SF varied, and over a quarter of participants described poor understanding of their SF, with some of these reporting poor skills to share their results. Participants described the opportunities they had to share their SF with relatives primarily by citing physical proximity to relatives and emotional closeness. Over three-quarters of participants (n = 31) described high levels of motivation to share their SF with relatives, expressing the belief that doing so was important for their families. Participant-reported facilitators included existing open communication patterns, strong desires to help their relatives, and a shared understanding of the medical significance of the SF. Complicated or difficult family dynamics were the main barrier to family communication cited

by participants. Eleven individuals participated in the Phase 2 interviews and two major themes emerged from the textural and structural descriptions of family communication in these individuals: 1) the personal impact of family communication, and 2) the effect of family culture on family communication. The lived experience of these participants as they shared their SF with their families was complex and involved even as it largely mirrored existing family relationships. This experience was universally described as generating meaningful emotional responses in participants.

Chapter 5: Discussion

Achieving the true clinical potential of opportunistic screening for medically-actionable secondary genomic variants (i.e., SF) requires both direct actions by SF recipients to modify their own healthcare and effective communication of these findings with family members so that they may also reap the benefits of more personalized medical care (Green et al., 2013; Katz et al., 2020). This study explored family communication of SF in individuals who had received such findings through a variety of genomic interrogation mechanisms. A phased approach was employed to investigate the phenomenon of family communication of SF through the lenses of both behavioral science (Atkins et al., 2017) and the deep narrative approach of phenomenology (Moustakas, 2011; Usher & Jackson, 2014). Taken together, this study's findings shed light on this important dimension of precision medicine and expand our understanding of how communication about SF overlaps with and differs from what is known about how families communicate about other kinds of genetic data.

Knowledge or understanding of a genetic finding affects how an individual communicates about that finding with relatives (Makhnoon et al., 2021; Mellon et al., 2006; White et al., 2004; Wiseman et al., 2010). Participants in Phase 1 of the study described significant variation in both their knowledge and understanding of the relevant medical details associated with their SF as well as the degree to which they felt equipped to be able to share this knowledge with relatives. While some participants accurately and completely described their SF in terms of both medical actionability and heritability, over a quarter (n =13) of participants demonstrated difficulty in explaining, naming, describing, or remembering their SF and/or associated risks, and these participants often posed questions to the interviewer highlighting

specific knowledge gaps while discussing their findings. A notable interaction between poor understanding and feeling ill-equipped to share SF information with relatives was observed. Close to half of the individuals who reported poor skills to communicate with relatives also described poor understanding of their SF (n = 5) while, conversely, all four participants who reported feeling confident in their skills to share demonstrated excellent understanding of their SF.

Emotional closeness and family cohesiveness, shown to be facilitators of family communication of genetic findings generally (Wiseman et al., 2010) and in specific studies of families sharing genetic results related to cancer (Kenen et al., 2004; Peters et al., 2011; Wiseman et al., 2010) and heart disease (Shah et al., 2019) was also described as an important determinant of SF communication by participants in both of this study's Phases. Described in Phase 1 in terms of social opportunity, SF recipients explained how interpersonal relationships within their families both facilitated and inhibited communication about their SF. Physical opportunities described by SF recipients in Phase 1, including geographic distance and communication frequency, have also been reported as determinants of family communication about melanoma risk (Loescher et al., 2009), heart disease (Shah et al., 2019), and cancer (Finn et al., 2022).

Previous work has demonstrated that individuals faced with sharing genetic information with relatives are simultaneously motivated by a desire to help their relatives and concerned about the potential emotional and familial ramifications of disclosure (Chivers Seymour et al., 2010; Gaff et al., 2007; Wiseman et al., 2010). This study's findings support both of these conclusions and align them with the COM-B constructs of reflective and automatic motivation (Atkins et al., 2017). Participants frequently cited their belief that communicating their SF with

relatives was important and valuable for relatives' healthcare. Even as concern for relatives was cited as a powerful motivating factor described by 31 participants, a substantial number (n = 18) were worried about the consequences of sharing their results, describing hesitancy stemming from worry or fear of how relatives would react to and feel after learning this information.

Phase 2 participants' vivid descriptions of family communication as an act of giving that is centered in concern and hope, while shaped by complex family relationships, aligns with studies of genetic communication informed by a family systems approach (Harris et al., 2010; Shah & Daack-Hirsch, 2018; Shah et al., 2019; Zhao et al., 2022). In one longitudinal follow up study focused on communication blocking behavior in families communicating about genetic cancer risk, situational and interpersonal factors influenced the durability of blocking behavior (Peters et al., 2011). Longstanding communication patterns specific to families shaped how Phase 2 participants experienced family communication as well. One of the essential structural elements of the lived experience of Phase 2 participants, the emotional responses communication engendered, is cited in a study of family dyads communicating about genetic cancer risks (Campbell-Salome & Rauscher, 2020). This study described discrepant dyads characterized by emotions of tension and frustration resulting from different coping mechanisms and approaches to risk management (Campbell-Salome & Rauscher, 2020).

Clinical and Translational Implications

While there is overlap between the results reported here and the sizable existing literature describing family communication of genetic information, the SF recipients in this study differ from other recipients of genetic information reported in the literature because of the unexpected, unanticipated nature of their results. This study's findings related to capability and motivation to

communicate their SF suggest how this difference may be clinically important and suggest possible areas for intervention development.

Genetic knowledge as an individual-level factor is known to affect family communication (Makhnoon et al., 2021). A substantial number of SF recipients reported poor or uncertain knowledge and/or recall of their SF result. While common understanding and experience of a particular health condition shared by family members influences how these families communicate after receipt of a diagnostic result (Campbell-Salome & Rauscher, 2020; Harris et al., 2010), this shared understanding may be muted or absent in SF recipients. While beliefs about heredity and heritability influenced the communication motivations of 20 Phase 1 participants, only two cited concrete knowledge informed by cascade testing. The lived experience of Phase 2 participants was characterized by emotions such as frustration and disappointment about their relatives' appraisals of the importance of their SF. These findings reinforce the idea that SF recipients may be tasked with *establishing,* rather than entering into, a shared understanding of the significance of their findings as they communicate with relatives. Interventions designed specifically for SF recipients to promote family communication may be most successful if they address knowledge gaps, connect family medical history data to the SF, and assess family systems. Melanie's suggestion for anticipatory counseling explicitly outlines some aspects of this approach.

Exclusive reliance on recipients of genetic information to communicate their findings to relatives has long been recognized as suboptimal; provider facilitated and non-patient-mediated communication mechanisms have been a persistent focus of research and result in higher cascade testing uptake (Frey, Ahsan, Badiner, et al., 2022; Frey, Ahsan, Bergeron, et al., 2022; Menko et al., 2019). Two recent studies to promote family communication via chatbot deployed this

intervention in a biobank population where recipients of genetic data were similar to SF recipients in that they learned their findings via biobank participation and the findings were thus unexpected/non-diagnostic (Schmidlen et al., 2022; Walters et al., 2023). These studies did not investigate factors influencing chatbot usage in SF recipients or their relatives beyond simple correlates such as age and use of electronic health records, and many participants (42%) declined to utilize the chatbot intervention (Schmidlen et al., 2022). While none of the current study's participants reported engagement with a chatbot, a handful reported communicating with family members via text message or by sharing a family notification letter. However, many participants in both Phases of the study described situations where chatbot usage may not be possible or attractive, such as the numerous cases of estrangement described by a quarter of Phase 1 participants. As well, several Phase 2 participants described very specific and unique communication patterns similarly resistant to this approach. Farah's desire for a highly specific and tailored communication aide provides an additional example where chatbot technology may be suboptimal. A major strength of a behavioral diagnosis based on the COM-B is the potential to recognize how a seemingly simple behavior may occur within a complex system. In turn, this facilitates systematic selection of intervention functions targeting specific behavioral contributors (Atkins et al., 2017). In Table 5.1 below, the COM-B components identified in this study are linked with salient domains of the TDF and potential intervention functions and options, with promising areas for intervention development shaded in grey.

Table 5. 1 *Relationships Between COM-B components, TDF Domains, and Interventions*

COM-B component	Linked TDF Domain	Relationship to study findings	Intervention function	Suggested interventions
Psychological capability	Knowledge	Understand SF and associated risks and surveillance	Education	Develop educational materials to increase SF recipient knowledge
	Cognitive skills	Know how to describe/explain SF to relatives	Training	Train SF recipients to improve skills to share SF with family
Social opportunity	Social influences	Anticipate and appreciate role of family system in SF communication	Modeling	Identify supportive individuals within the family system
Physical opportunity	Environmental context and resources	Be able to contact relatives	Environmental restructure	Direct communication with relatives
Automatic motivation	Reinforcement	-	Provide incentives	Provide rewards/punishments
	Emotion	Cope with feelings about SF related to self and family	Support	Provide ongoing support for SF recipients
Reflective motivation	Beliefs about capabilities	Feel prepared and able to share SF with relatives	Enabling	Supportive counseling to improve SF recipients' self-efficacy
	Beliefs about consequences	Value outcome of SF communication	Enabling Support	Counseling to support SF recipients' own surveillance behaviors
	Intentions	Motivation/desire to help relatives	Support	Support SF recipients' desire to help relatives

This study's findings suggest potential areas for intervention development across all three COM-B constructs. The highlighted interventions listed above address SF recipients' specific needs and are aligned with existing interventions to improve family communication about genetics. Addressing SF recipients' specific informational needs, assessing and improving SF recipients' communication skills within their specific family systems, and supportive counseling to enhance SF recipients' feelings of control and promote self-efficacy are promising areas for

future research supported by this study's findings. Similarly, the findings and existing research support the notion that certain intervention functions ought to receive lower priority. For example, it may be impossible to connect SF recipients with estranged or otherwise not-contactable relatives and for this reason, environmental restructuring to enhance physical opportunities for family contact is perhaps a low priority. Identifying what needs to change in order to promote a desired behavior is a core strength of the BCW, and taken together, this study's findings suggest a possible roadmap to selecting and implementing interventions to optimize family communication of SF. Many of the intervention functions that this study's findings highlighted as priorities for future investigation have relevance for the practice of clinical genomics and genetic counseling in particular. Genetic counselors are front-line providers of genetic test results and secondary findings, and they receive extensive training in patient education, communication, and psychosocial assessment and support (Austin et al., 2014; Biesecker et al., 2017). Educational interventions to enhance knowledge, decision and communication aids and supports, and psychosocial assessments are all interventions that are frequently developed, tested, and applied in genetic counseling practice (Burns et al., 2023; Underhill-Blazey et al., 2021). Furthermore, in addition to disclosing genetic test results including SF, genetic counselors are frequently involved in consenting both clinical patients as well as research participants to exome and genome sequencing where SF may be returned (Facio et al., 2012; Sapp et al., 2018; Schwartz et al., 2018). While this study only investigated outcomes downstream of SF receipt, some study findings may have practice implications for genetic counselors working with individuals and families considering sequencing tests where SF may result. Providing anticipatory guidance about family communication and assessing an

individual's or family's communication needs prior to testing may enhance outcomes should SF be found (Rost et al., 2020; Similuk et al., 2021).

Relatively few theory-informed approaches to intervention development to optimize family communication have been reported (Zhao et al., 2022). This study described family communication in SF recipients using the constructs of the COM-B and enriched understanding of this phenomenon by incorporating thick descriptions of SF recipients' lived experiences of family communication (Atkins et al., 2017; Moustakas, 2011). SF recipients are an understudied population, and there is a dearth of research describing outcomes associated with receipt of SF, including family communication (Sapp et al., 2021). Translating genetic data into advances in clinical care is an important priority for genomics moving forward and is the focus of several studies aimed at bringing genomics knowledge to practice (Cragun et al., 2021; Green et al., 2020; Jones et al., 2022; Manolio et al., 2013; Schwartz et al., 2018). The local knowledge generated in this study may be applied to develop and test communication interventions leading to more generalized knowledge, a key step in dissemination and implementation research (Bauer et al., 2015; Brown et al., 2017).

Limitations

This study investigated family communication of SF in a small sample of SF recipients already enrolled in and recruited from an existing research study. Participants received their SF from a variety of genetic testing modalities, and this study did not control for disclosure processes. The demographics of this sample population are less representative than might be expected in a general population study. Cultural, educational, and other factors may be particularly salient as individuals with diverse backgrounds engage with genomic data, and this is an urgent research priority. Phase 1 data were derived from transcripts from existing

interviews, and these interviews were not designed specifically to assess COM-B domains. As such, this analysis may lack depth of investigation into these constructs as they related specifically to family communication of SF. While strategies to ensure trustworthiness such as the use of a second coder were employed, the possibility of researcher bias cannot be excluded. This is especially relevant in phenomenological studies where an examination of the experience of interest free from bias is important, and extensive note-taking and self-reflection were employed to bracket out the researcher's experience as much as possible.

Chapter Summary

A major strength of this study was its theory-informed approach demonstrating how SF recipients overlap with and differ from recipients of other genetic data reported in the literature. Data analysis using the COM-B as a theoretical framework coupled with rich descriptions of SF recipients' lived experiences of family communication may contribute to the "behavioral diagnosis" necessary to guide the beginnings of intervention development. The local knowledge generated in this study fills important gaps and may promote additional lines of inquiry with the ultimate goal of translating knowledge to improve health.

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Appendices

Appendix 1: Current ACMG Gene List with Associated Disorders

Appendix 2: Interview Guide Used to Conduct Phase 1 Interviews

Appendix 3: Consent Procedures and Interview Guide Employed for Phase 2

Appendix 4: Consent Form for GSRP Study

Appendix 5: Code System for Phase 1 Interviews

Appendix 1: Current ACMG Gene List with Associated Disorders

Adapted from Miller et al., 2022

Condition	Gene	Age of onset
Hereditary Breast and Ovarian Cancer	*BRCA1*	Adult
	BRCA2	
	PALB2	
Li-Fraumeni	*TP53*	Child/Adult
Peutz-Jeghers	*STK11*	Child/Adult
Lynch Syndrome	*MLH1*	Adult
	MSH2	
	MSH6	
	PMS2	
Familial Adenomatous Polyposis	*APC*	Child
MYH-Associated Polyposis; FAP type 2	*MUTYH*	Adult
Juvenile Polyposis	*BMPR1A*	Child/Adult
	SMAD4	
von Hippel-Lindau	*VHL*	Child/Adult
Multiple Endocrine Neoplasia type 1	*MEN1*	Child/Adult
Multiple Endocrine Neoplasia type 2a,b	*RET*	Child/Adult
Familial Medullary Thyroid Cancer (in MEN2A)	*RET*	Child/Adult
PTEN Hamartoma Tumor Syndrome	*PTEN*	Child
Retinoblastoma	*RB1*	Child
Hereditary Paraganglioma-Pheochromocytoma Types 1-4	*SDHD*	Child/Adult
	SDHAF2	
	SDHC	
	SDHB	
	MAX	
	TMEM127	
Tuberous Sclerosis Complex	*TSC1*	Child
	TSC2	
WT1-related Wilms Tumor	*WT1*	Child
Neurofibromatosis type 2	*NF2*	Child/Adult
Retinoblastoma	*RB1*	Child
Vascular EDS	*COL3A1*	Child/Adult
Marfan syndrome	*FBN1*	Child
Loeys-Dietz	*TGFBR1*	Child

	TGFBR2	
	SMAD3	
Familial Thoracic Aortic Aneurysms and Dissections	*ACTA2*	Child/Adult
	MYH11	
Hypertrophic Cardiomyopathy	*MYBPC3*	Child/Adult
	MYH7	
	TNNT2	
	TNNI3	
	TPM1	
	MYL3	
	PRKAG2	
	MYL2	
	ACTC1	
Dilated Cardiomyopathy	*LMNA*	Child/Adult
	TNNT2	
	FLNC	
	MYH7	
	DSP	
	SCN5A	
	TTN	
Fabry disease	*GLA*	Child/Adult
Pompe disease	*GAA*	Child/Adult
Catecholaminergic polymorphic ventricular tachycardia	*RYR2*	Child/Adult
	CASQ2	
	TRDN	
Arrhythmogenic right ventricular cardiomyopathy	*PKP2*	Child/Adult
	DSP	
	DSC2	
	TMEM43	
	DSG2	
Long QT syndrome	*KCNQ1(1)*	Child/Adult
	KCNH2(2)	
	SCN5A(3)	
	TRDN	
Brugada Syndrome	*SCN5A*	Child/Adult
Familial hypercholesterolemia	*LDLR*	Child
	APOB	
	PCSK9	
Hereditary hemorrhagic telengiectasia	*ACVRL1*	Child/Adult
	ENG	
Malignant hyperthermia	*RYR1*	Child/Adult
	CACNA1S	
Wilson Disease	*ATP7B*	Child

Ornithine Carbamoyltransferase deficiency	*OTC*	M=Newborn F=Child
Hereditary Hemochromatosis	*HFE*	Child/Adult
Biotinidase deficiency	*BTD*	Child/Adult
MODY	*HNF1A*	Adult
RPE65-related retinopathy	*RPE65*	Child/Adult

Appendix 2: Interview Guide Used to Conduct Phase 1 Interviews

The text below is copied verbatim (including formatting) from Appendix C of NIH Protocol 16-HG-0017 and comprises the interview guide that was used to conduct the Phase 1 Interviews for the current study.

APPENDIX C: INTERVIEW GUIDE

Last Updated: 13DEC2021 (v.3)

This interview guide was informed by the Health Belief Model and the Theory of Planned Behavior. The questions are meant to indicate general topics to be covered during the interview and need not be read verbatim. Substantial modifications that may affect the risk/benefit ratio of the study will be submitted to the IRB for review prior to use. The Background Information, Health Behavior Recommendations Summary, Family History & Risk Perceptions sections are to be filled out by study staff based on available data from surveys & family history and are used to inform the interview questions, which begin in the section called "INTERVIEW GUIDE"

Background Information

- **ID Number:**
- **Participant Name:**
- **Referral Source:**
- **Disclosure Date:**
- **Gene:**
- **Interview Date & Time:**
- **Contact Number:**
- **Notes from Intake and Scheduling (e.g., testing indication, major health problems, what they call the disease(s) they are at risk for, communication style):**

Family History

A 3-generation family history is attached and includes notation about whether each family member has been told about the SF. The family history should be used to complete the Family Communication portion of the interview, during which the interviewer asks about facilitators of/barriers go telling each family member.

Health Behavior Recommendations & Adherence Survey Data Summary

We have abstracted survey data for reference in the 'Health Behavior Adherence' section of the interview (below), in which the interviewer asks about barriers & facilitators of taking recommended actions.

Health Behavior	Understanding of What is Recommended	Participant Adherence (# Times Since Result)	Participant Intended Adherence

Risk Perception

We have abstracted his/her survey data on several aspects of risk perception and list them here for reference in the 'Risk Perception' section of the interview (below).

Condition	Subjective Risk Perception *How likely do you think it is that you will develop each of the below conditions at some point in your future?* (Very Unlikely – 1 to Very Likely – 7)	Comparative Risk Perception *How do you think your chance to develop the below conditions compares with someone else your age and sex?* (My Risk is Much Lower – 1 to My Risk is Much Higher – 7)	Change in Risk Perception *Since receiving my result, I feel that my risk to develop DISEASE is ___ than I thought before.* (Much Lower Than I Thought Before, Somewhat Lower…, The Same As…, Somewhat Higher Than…, Much Higher Than…)

Page Break

INTERVIEW GUIDE

General Intro

You recently agreed to complete an interview with me about your experience getting a genetic testing result. During this interview I will ask you questions about getting the test result and what you did with it because we want to learn from our participants how to best handle these kinds of results. I know that you have already completed a family history, which I have in front of me and will reference during our conversation. You also took a survey recently and I have the relevant responses here. You may find that I ask about some of the same topics on the survey – the purpose of this is to give you a chance to build on the survey responses and so that we can learn new things beyond what the survey captured.

Is this still a good time for us to spend 20-30 minutes talking about your result?

- (If yes) Do I have permission to record our conversation?
    - (If yes) Ok, now I will turn on the recorder and I need to ask you again on tape if it is ok with you if I record this.
    - (If no) Ok, no problem, I will just need to pause during our conversation a few times to jot down some notes

- (If no) If this is not a good time, can we set up another time for me to call?
    - (If yes, arrange time, thank participant, and end call)
    - (If no) I hope you don't mind if I ask you one more question, it is always helpful for us to know what might be leading you to not be interested or able to speak with us about this – can you tell me a little about that?" (Then thank them and end call.)

Rapport Building

These are not being coded as of 11.25.21 and so they are optional questions and can be used by interviewer at her discretion.

- Can you tell me about how you learned this result?
- What were your reactions to the result?

Information Seeking

I would like to start off by asking you a little about how you know what you know about this gene finding.

- Where are you getting you information/can you describe the sources of information you have used to learn about your result?
    - Did you seek it out or was it provided to you (active vs passive)? How often have you done research on your own?
    - How useful are these resources? Do you use them?
    - If you get information from a person/provider, how often do you interact with them? Is there back-and-forth communication?
- What lingering or unanswered questions do you have about your result?
    - About the health behaviors that are recommended for you?
    - About sharing the result with your family?

Healthcare Behavior Adherence

Next, I want to talk about how the result has impacted your healthcare. I have a list of a health behaviors that are sometimes recommended to people with a result like yours & whether you have done each them according to the answers you gave on your survey. I would like to hear more about why you did/did not do each of these things. *List **<u>each</u>** health behavior recommendation from Health Behavior Recommendations Summary on page 1…*

- *If they did the behavior…*
    - What were the reasons you did X? (*The below prompts are factors that have arisen in earlier interviews and are not on the survey, so should be asked about)*
        - Insurance
        - Personality (*when this comes up, be sure to ask how the participant sees their personality playing a role in adherence – e.g., when they say, "I'm just laid back" – does that make them more or less adherent and why?)*

        - Provider reaction
    - Were there any reasons that you considered not doing X?
- *If they did not yet, but intend to…*
    - What were the reasons you did not?
    - How likely are you to do this in the next 3 months?
    - What things, if any, would increase the chances that you would do X in the future?
- *If they did not yet and do not intend to because…*
    - *They do not realize it's recommended → no further questions*
    - *They know it is recommended, but will not/cannot…*
        - What were the reasons you did not?
        - What things, if any, would increase the chances that you would do X in the future?

- Are there other things you have changed about your healthcare or lifestyle since receiving your result?
    - What were they and why?
        - Seen new providers?
        - Had tests/screenings/procedures?
        - Changed diet/exercise/medications?
- To what extent do you think you need long-term care related to this condition/risk?
    - Who is responsible for coordinating/organizing this care?
    - How will that person/entity make sure you get the healthcare you need on time?
    - What will your role be?
        - To what extent do you feel like you can carry out your role?
        - What would you like your role to be?

Risk Perception

- On your survey, we asked about your risk to develop health problems related to your result. Talk with me about how convinced/certain are you that there is a relationship between your result and risk for DISEASE.
    - We would like to know more about what goes into your thinking about your risks for DISEASE.

Patient Communication of Results

NOTE for MyCode Participants: These individuals were asked by MyCode if they told each of the following relatives about their results: mother, father, full siblings, children & grandchildren. Then they are asked whether each of those individuals had testing and the outcome (positive, negative, don't know) and about the reasons they thought it was important to tell, the problems they had in telling and the reasons not to share (all of these topics are asked about with

quantitative checkbox options that I cannot see). We will not have access to those data – however, this may make some of the below feel duplicative.

Next, I want to talk about sharing your result within your family. I have your family history here and want to go through each family member and hear more about why you have/have not told him/her.

- List ***each*** *family member from the pedigree*
    - *Told them already*
        - Why did you tell them?
        - Were there any reasons that you considered not telling them?
    - *Did not tell them, but intend to*
        - Why not?
        - What things would increase the chance that you would tell them?
    - *Did not, do not intend to*
        - *Does not realize it's recommended → No further prompts*
        - *Knows it is recommended, but will not*
            - Why not? What things, if any, would increase the chance that you would tell them?
- What did you tell them? How did you describe the result? Can you talk me through what you said/wrote? You are welcome to pretend that I'm a relative you've talked to if that helps?
    - How much detail did you give them and about what aspects of the results?
        - To what extent did you describe genetic counseling/testing for them as a recommendation vs option?
        - How much did you talk about health behaviors recommended for you? For them (if they are positive)?
        - Did you provide specifics in terms of conditions at risk for and how high the risk was or was the information more general?
    - Who helped you with that process?
- How would you describe your role in sharing this result with your family members?
    - Fully responsible (tell, educate, ensure they follow-up)/Middle man (tell and refer, but passive)/Shielding/Other?
    - Does that differ for different family members?
    - What would be the optimal way for your family members to be made aware of this result (if different from what you are doing)?
    - What are the limits of your role?

Informed Choice

Looking back, what do you think about your choice to have this genetic testing and receive results like this one?

- How would you describe the amount of information you had about potential results that you could receive when you made the decision to have this testing?
    - What other things do you wish you had known then?

Other

- How has your primary condition/general health affected your view of your SF? (especially around increased or decreased adherence)
- If you had to give a brief summary, how has learning this result affected you? How would you describe the experience and its impacts overall?

Thank you very much for taking time to speak with me about this.

Interviewer Notes (e.g., counseling provided post-interview, etc.):

Appendix 3: Consent Procedures and Interview Guide Employed for Phase 2

The text below is copied verbatim (including formatting) from Appendix C of NIH Protocol 16-HG-0017 and comprises the interview guide that was used to conduct the Phase 1 Interviews for the current study.

Appendix K: Family Communication Follow-up Interview

Purpose:
Investigate family communication of secondary findings over time

Employed dates:
November, 2022 – [end date to be determined and will be submitted with a future amendment]

Invitation procedure:
Protocol staff will contact enrolled participants (typically by phone) to describe the interview study using the language below. Participants who agree to take part in the interview will complete the verbal consent process described below and record of verbal consent will be added to their record in our secure database/server (e.g.,TrakGene).

Invitation script:
Thank you for the opportunity to speak with you today. I am calling to tell you about a follow up interview we are conducting as part of our study of people who have received unexpected genetic results (secondary variants). The goal of this interview is to understand how families communicate about their genetic results over time. As you may remember, we asked you about family communication during the first interview you were kind enough to take part in in [DATE]. Many of the questions in this new interview will be similar and it should take about 30 minutes. You don't have to do this interview if you don't want to and your decision to do the interview will have no effect on your participation in the study. If you decide to do the interview, we would like to offer you a $10 gift card for your time. Does this sound like something you might be interested in?

If YES → thank participant and make a plan for record permission for interview and interview time/date following procedure outlined below
If NO → thank participant for their time

Documentation of permission to participate:
Thank you for your interest in this follow-up interview. You do not have to take part in this interview – it is completely voluntary. Your decision to take part in this interview will not affect your participation in any of the other parts of the study.

The purpose of this interview is to learn more about how families communicate about genetic test results over time. In the interview, we may reference some of your previous responses about how you have shared your results. We will also ask you to reflect on how you are currently communicating with your family.

The interview may take 20-40 minutes to complete and it will be recorded and transcribed. Only people directly involved in this study will have access to the recordings or transcriptions and we will remove all identifying information from recordings and transcriptions. You will receive a $10 gift card for your time and effort in participating in this interview.

Some people may find answering questions about their families uncomfortable. You do not have to answer any questions in the interview you don't want to.

Would you like to move forward with the interview?

☐ "Yes" _____

Investigator name, signature, and date

☐ "No" _____

Investigator name, signature, and date

Participant Name and GSRP ID: _____

Interview Guide:

Version #/date: v.1/November 2022

This interview guide is used to support a phenomenological inquiry into the lived experiences of secondary findings recipients as they communicate their genetic variant results and the impact of these results over time. The questions are meant to indicate general topics to be covered during the interview and need not be read verbatim; this is typical in phenomenological inquiry typically associated with the work of Moustakas (Moustakas, 2011). Substantial modifications that may affect the risk/benefit ratio of the study will be submitted to the IRB for review prior to use. The Background Information, Health Behavior Recommendations Summary, Family History & Risk Perceptions sections are to be filled out by study staff based on available data from surveys & family history and are used to inform the interview questions, which begin in the section called "INTERVIEW GUIDE"

Background Information

- **ID Number:**
- **Participant Name:**
- **Disclosure Date:**
- **Date of last interview**
- **Gene:**
- **Interview Date & Time:**
- **Contact Number:**

Family History

The previously-generated 3-generation family history is attached and includes notation about whether each family member has been told about the SF. This family history along with notes from the prior interview will be referenced frequently during this interview.

INTERVIEW GUIDE

General Intro

You recently agreed to complete an interview with me about your experience sharing your genetic results with your family over time. You were kind enough to share some of this with me during our last interview in DATE. I may reference what you shared with us then during our conversation today.

Is this still a good time for us to spend 20-30 minutes talking about your result?

- (If yes) Do I have permission to record our conversation?
    - (If yes) Ok, now I will turn on the recorder and I need to ask you again on tape if it is ok with you if I record this.
    - (If no) Ok, no problem, I will just need to pause during our conversation a few times to jot down some notes
- (If no) If this is not a good time, can we set up another time for me to call?
    - (If yes, arrange time, thank participant, and end call)
    - (If no) I hope you don't mind if I ask you one more question, it is always helpful for us to know what might be leading you to not be interested or able to speak with us about this – can you tell me a little about that?" (Then thank them and end call.)

Rapport Building
The interviewer will begin by summarizing the family communication information that the participant shared with the group; this will vary greatly from participant to participant. Some sample language to build rapport is listed below:
The last time we talked with you about how you shared your results with your family, you mentioned that you had shared your results with several people (interviewer may list individuals here). Is this consistent with what you remember?

Lived Experience
In this interview, our main goal is to understand the lived experience of what sharing your results with your family has been like for you.

- We expect that this "lived experience" is very different from person to person and I would love to hear your unique perspective. I'll stop here and see if you have thoughts or comments on this.
    - How would you describe the experience of sharing your result?
    - Can you share with me aspects of this experience that were particularly easy or difficult?
    - How did your experience sharing your result differ for different people in your family?
- How have your conversations with your family members about your results changed over time?
    - Who (if any) are family members you have shared your results with for the first time since our last interview (examples may be provided)?
        - Why did you tell/not tell him/her?
    - How has the language you have used to talk about or share your results with people in your family changed over time?
- What do you say to people in your family when you talk about your results? How did you/do you describe them? Can you talk me through what you said/wrote? You are welcome to pretend that I'm a relative you've talked to if that helps?

Contextual Factors (Temporal, Situational, Cultural) Affecting Communication
Next, I have some specific questions where I hope to develop a deeper understanding about how sharing your result with your family has been like for you as a specific and unique person.

- Are there things about you or your family that you think are very specific or individual that have played a role in how you communicated your result?
    - Language
    - Distance
    - Norms
    - Structure
- How comfortable do you feel talking about your specific result with your family members? Are there parts of this that are more comfortable for you and less comfortable?
- Can you imagine ways in which you and your family are different from other families when it comes to talking about genetics and health information in general?

- Can you talk to me about the timing of how you and your family members have talked about your result? What about that timing was important to you and your family?
- How would you describe your unique family culture? Has it stayed the same over time? How has talking about your result fit into or changed your family culture?

Conclusion

Thank you so much for sharing all of this information with me. Is there anything about what this experience has been like for you that I forgot to ask about or that you think is important to share?

Appendix 4: Consent Form for GSRP Study

The text below is copied verbatim (including formatting) from the currently approved version of consent form for the NIH Protocol 16-HG-0017; all participants in this study were consented using this form or a previously-approved version. All versions of the consent form included discussion of interview procedures and the possibility of recontact. Administrative headers and footers have been removed.

PRINCIPAL INVESTIGATOR: Leslie G. Biesecker, MD
STUDY TITLE: Genomic Services Research Program
STUDY SITE: National Institutes of Health Clinical Center (CC)
Cohort: Index
Consent Version: December 13, 2021

WHO DO YOU CONTACT ABOUT THIS STUDY?
Principal Investigator: Leslie Biesecker, 301-402-4041; lesb@mail.nih.gov
Associate Investigator: Julie Sapp, 301-435-2832; sappj@mail.nih.gov

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.
You are being asked to take part in a research study at the National Institutes of Health (NIH). Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers. Taking part in research at the NIH is your choice.
If the individual being enrolled is a minor then the term "you" refers to "you and/or your child" throughout the remainder of this document. If the individual being asked to participate in this research study is not able to give consent to be in this study, you are being asked to give permission for this person as their decision-maker. The term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research, throughout the remainder of this document.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY
You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

Most often, people have genetic testing for a specific reason – for example, to diagnose a health problem. Sometimes, important genetic test results are found that are not related to the reason why the testing was done. These results are called "secondary" or "incidental" results because of this. Secondary results are shared with people because they are often important for a person to know about. The goal of this study is to understand more about what learning secondary result could mean in a person's or family's health.

WHAT IS INVOLVED IN THE STUDY?

We will ask you some basic questions about the secondary result you learned. We will also ask you some questions about your health and your family's health. We may ask you to send us medical records like the secondary result report or results of any screening visits you have already had.

The main parts of the study are phone interviews and/or surveys. We want to understand what it was like for you to learn about this secondary result. We will record any interviews you take part in so that we can make a written transcript. We will destroy the original audio of your recording once your interview has been transcribed and verified by our team. We will not put any identifying information about you on any of the interview or survey results.

The interview will take about 20-30 minutes. The interviewer will ask you questions about this result, what you understood about it, your thoughts and feelings about it, and any health or behavior changes you have made since learning about it. The interviewer will also ask you about any communication you have had with your family about this result.

The survey will take about 20 minutes to complete and you can do it online. The survey will ask you questions about yourself and how you feel about genetic testing.

We may ask you to participate in a short follow-up interview and/or survey in the future.

Secondary genetic test results may put a person at an increased risk to have health problems. Medical tests can help screen for these problems. Each secondary result has a different set of recommended tests. Doctors or genetic counselors on our study may recommend that you have additional medical tests based on your genetic result and the records you share with us. We will talk with you about what the tests are and why we are asking you to have them. Our study team members may help you find a place near you to have the tests that they recommend. Some people may be invited to come to the NIH Clinical Center (NIH CC) to have tests. We will only do tests that are considered standard medical care. Not all the tests are right for each person and you may join our study even if you choose not to have some or all of the tests. You should understand what we are recommending and why. If we have not made it clear, please ask us to do so.

We may invite you to share information about this study with your family members, and we may be able to offer genetic testing to your family members as part of our study. If one of your family members joins the study and has genetic testing in our study, we may ask you for a saliva (spit) sample for research purposes and to help us interpret your relatives' results.

WHAT KIND OF RESULTS CAN I EXPECT TO GET FROM THIS STUDY?

You will not get any individual results from the interview or the survey in this study. We will share information with you about your specific result and may be able to help you find local resources. If you come to the NIHCC for an evaluation, we will share all results of all the testing you had, either in-person at the end of the visit or after the visit by phone or mail. A visit to the

NIH CC will include genetic counseling and doctor recommendations about health effects of this secondary result and how to manage them. If we get a saliva sample from you for research purposes, we will not share results from this research testing with you.

WHAT ARE THE RISKS OF PARTICIPATING IN THE STUDY?
Survey/Interview: You may find participating in the interview or survey to be upsetting.
Saliva Sample: There are no associated risks with collection of spit sample.
Psychological or Social Risks
It is possible that talking about genetics and health risks could cause emotional or psychological harm.
If other people in your family join the study, family information such as parentage and adoption may be discovered in the course of this research project. It is our policy not to disclose such information unless it has direct medical implications for your family, which is unlikely.
Some of the tests we could do at the NIH for your standard clinical care have risks. Those will be discussed with you depending on what the tests are. You can decide at that time whether you want to have the tests or not.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?
You may not benefit directly from being in this study.
The results of this study may benefit the public in the future by improving our knowledge of the relationship between genes and health. In addition, the results of our study may benefit other people with your genetic variant. Your responses to the interview and survey will help us to understand the impact of learning about secondary results.
Possible benefits to you could include:
Confirmation or knowledge of a genetic predisposition to develop health problems and information about things you can do to reduce the chance to have those health problems
Talking with our study staff and learning the information we will share with you about your result.
Learning information about your secondary result that could be useful for the health of your relatives.

WHAT ARE MY OTHER OPTIONS?
You do not have to join this study if you do not want to. Alternatives to being in this study include: (1) having a medical genetics evaluation, (2) having genetic counseling to assess your family history for health problems related to your secondary result.

WHAT IF I CHANGE MY MIND ABOUT BEING IN THIS STUDY?
You may quit this study at any time. If you quit the study, please tell us if you do not want to hear from us again. We need to know if you want us to destroy any samples you have sent to us. In rare instances, participants may be removed from this study at the discretion of the Principal Investigator.

PAYMENT
Will you receive compensation for participation in the study?

Participants will be offered up to $20 in gift cards for their time and effort. Participants will be offered $10 after the family history call and $10 after the interview. If you are the primary caregiver of a minor participant or an adult participant who is unable to consent, you will be offered compensation for completing the study activities on their behalf.
If you are unable to finish the study, you will receive compensation for the part that you do complete.

REIMBURSEMENT
Will you receive reimbursement or direct payment by NIH as part of your participation?
In this study, we are able to reimburse or directly cover some expenses related to participation. Travel to and from the NIH CC from within the U.S., lodging expenses, and some meal expenses will be paid for by the NIH directly in most cases. Some expenses (such as the cost of checked baggage) may fully or partially reimbursed.

COSTS
Will taking part in this research study cost you anything?
NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH CC.

CLINICAL TRIAL REGISTRATION and RESULTS REPORTING
A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY
Confidentiality and availability of the data we will generate
Everyone in this study will be assigned a code number which will be used on all study-related materials and files. Only people directly working in this study will have the "key" to the database that links names with codes.
We will keep any medical records or other information you send to us safe. We will keep physical materials (like CDs with imaging studies on them, for example) in a locked cabinet. We will keep electronic materials (like scanned copies of records you send to us or digital audio files of interviews) in a secure database. We will not share information about you with anyone without your permission. This includes your family members. We may publish what we learn in a medical journal or book but we will not identify you or anyone else in the study by name.
As with other information you send us, if you send us a saliva sample, it will be coded. Only medical and scientific staff directly involved in this study have access to the database that links participants' names and their samples or DNA.
Will your medical information be kept private?
We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government agencies, like the Food and Drug Administration (FDA), which are involved in keeping research safe for people.
- National Institutes of Health Intramural Institutional Review Board

- Other qualified investigators

The researchers conducting this study and the NIH follow applicable laws and policies to keep your identifying information private to the extent possible. However, there is always a chance that, despite our best efforts, your identity and/or information about your participation in this research may be inadvertently released or improperly accessed by unauthorized persons.
In most cases, the NIH will not release any identifiable information collected about you without your written permission. However, your information may be shared as described in the section of this document on sharing of specimens and data, and as further outlined in the following sections.
Further, the information collected for this study is protected by NIH under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality
To help us protect your privacy, the NIH Intramural Program has received a Certificate of Confidentiality (Certificate). With this certificate, researchers may not release or use data or information about you except in certain circumstances.
NIH researchers must not share information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if requested by a court.
The Certificate does not protect your information when it:

- is disclosed to people connected with the research, for example, information may be used for auditing or program evaluation internally by the NIH; or
- is required to be disclosed by Federal, State, or local laws, for example, when information must be disclosed to meet the legal requirements of the federal Food and Drug Administration (FDA);
- is for other research;
- is disclosed with your consent.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research.
The Certificate will not be used to prevent disclosure to state or local authorities of harm to self or others including, for example, child abuse and neglect, and by signing below you consent to those disclosures. Other permissions for release may be made by signing NIH forms, such as the Notice and Acknowledgement of Information Practices consent.
Privacy Act
The Federal Privacy Act generally protects the confidentiality of your NIH medical records we collect under the authority of the Public Health Service Act. In some cases, the Privacy Act protections differ from the Certificate of Confidentiality. For example, sometimes the Privacy Act allows release of information from your medical record without your permission, for example, if it is requested by Congress. Information may also be released for certain research purposes with due consideration and protection, to those engaged by the agency for research purposes, to certain federal and state agencies, for HIV partner notification, for infectious disease or abuse or neglect reporting, to tumor registries, for quality assessment and medical audits, or when the NIH is involved in a lawsuit. However, NIH will only release information from your medical record if it is permitted by both the Certificate of Confidentiality and the Privacy Act.

Policy Regarding Research-Related Injuries

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

Problems or Questions

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Leslie Biesecker, lesb@mail.nih.gov, 301-402-2041. Other researchers you may call are Julie Sapp, at 301-435-2832 and Katie Lewis at 301-594-3063. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

Consent Document

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Legally Authorized Representative (LAR) for an Adult Unable to Consent: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I am legally authorized to make research decisions on behalf of the adult participant unable to consent and have the authority to provide consent to this study. As applicable, the information in the above consent was described to the adult participant unable to consent who agrees to participate in the study.

Signature of LAR	Print Name of LAR	Date

Parent/Guardian of a Minor Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I give permission for my child to take part in this study.

Signature of Parent/Guardian	Print Name of Parent/Guardian	Date
Signature of Parent/Guardian	Print Name of Parent/Guardian	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date

Witness should sign below if either:
A short form consent process has been used to enroll a non-English speaking subject or
An oral presentation of the full consent has been used to enroll a blind or illiterate subject

Signature of Witness*	Print Name of Witness	Date

Appendix 5: Code System for Phase 1 Interviews

The code system below was employed in analysis of Phase 1 interviews; code sets were created to map to COM-B constructs. Additional codes to describe participant-reported barriers to and facilitators of family communication emerged from the data.

Capability
- C – Skills to Share – Uncertain
- C – Skills to Share – Poor
- C – Skills to Share – Good
- C – Self-Knowledge - Poor
- C – Self-Knowledge - Medium
- C – Self-Knowledge - Good

Opportunity – Physical (Affordance)
- OPP – Physical – Gathering or Reunion
- OPP – Physical – Difficult to Contact
- OPP – Physical – Family Letter or Document
- OPP – Physical – No Regular Contact
- OPP – Physical – Regular Contact

Opportunity – Social (Interpersonal Factors & Culture)
- OPP – Social – No Health Talk in Family
- OPP – Social – Hasn't Come Up
- OPP – Social – Emotionally Close
- OPP – Social – Family Dynamic/Culture
- OPP – Social – Not Emotionally Close
- OPP – Social – Health Talk Normal in Family
- OPP – Social – Disclosee Too Young

Motivation – Automatic (Emotional Reactions/Desires)
- MOT – Automatic - Responsibility
- MOT – Automatic - Emotion

Motivation – Reflective (Goals, Beliefs, Attitudes)
- MOT – Ref – Belief – Autonomy of Relatives
- MOT-Beliefs - Violation of privacy
- MOT-Ref-Belief - Family=Unhelpful
- MOT-Ref-Goal-Learn more about family health
- MOT-Ref-Beliefs about Consequences - No difference
- MOT-Ref-Beliefs-SF not relevant to health
- MOT-Ref-Belief about heredity/heritability
- MOT-Ref-Belief about Consequences - Upset Family
- MOT-Ref-Concern/Love
- MOT-Ref-Important for Care

Barrier - Family dynamic or complexity
Barrier-Family might worry
Barrier - No regular contact
Barrier - Low concern about SF
Facilitator - Family communication easy
Facilitator - Belief that it will help
Facilitator - Relative has possible manifestation