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Informed Consent for Exome Sequencing Research in Families with Genetic Disease: The Emerging Issue of Incidental Findings

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Abstract

Genomic sequencing technology is increasingly used in genetic research. Studies of informed consent for exome and genome sequencing (ES/GS) research have largely involved hypothetical scenarios or healthy individuals enrolling in population-based studies. Studies have yet to explore the consent experiences of adults with inherited disease. We conducted a qualitative interview study of 15 adults recently enrolled in a large-scale ES/GS study (11 affected adults, four parents of affected children). Our study had two goals: (1) to explore three theoretical barriers to consent for ES/GS research (interpretive/technical complexity, possibility of incidental findings, and risks of loss of privacy); and (2) to explore how interviewees experienced the consent process. Interviewees could articulate study goals and processes, describe incidental findings, discuss risks of privacy loss, and reflect on their consent experience. Few expected the study would identify the genetic cause of their condition. All elected to receive incidental findings. Interviewees acknowledged paying little attention to potential implications of incidental findings in light of more pressing goals of supporting research regarding their own medical conditions. Interviewees suggested that experience living with a genetic condition prepared them to adjust to incidental findings. Interviewees also expressed little concern about loss of confidentiality of study data. Some experienced the consent process as very long. None desired reconsent prior to return of study results. Families with inherited disease likely would benefit from a consent process in which study risks and benefits were discussed in the context of prior experiences with genetic research and genetic disease.

Keywords

exome sequencing; genome sequencing; informed consent; incidental findings; genetic counseling; genetic testing

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INTRODUCTION

Exome and genome sequencing (ES/GS) technologies are increasingly utilized as tools in genetic research [Bick and Dimmock, 2011] and have the potential to determine the genetic cause for both single gene and complex disorders [Lupski et al., 2010; Tabor et al., 2011]. This technology brings with it potential benefits but also potential risks. Informed consent is the primary means by which these risks and benefits are communicated to research participants [Wolf et al., 2008]. The goal is that participants are aware of potential risks and benefits of a study and that they voluntarily agree to participate [National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1979].

Concerns regarding the adequacy of the consent process for ES/GS have emerged [McGuire and Beskow, 2010]. These include three primary areas thought to differentiate ES/GS from more conventional genetic research: (1) the complexity of the technical and interpretive aspects of ES/GS; (2) the likelihood of discovering incidental findings with clinical utility; and (3) the risk of loss of privacy and confidentiality related to data sharing of rare alleles [Tabor et al., 2011]. In recognition of these challenges, several groups have begun to explore how to best accomplish informed consent for ES/GS [McGuire and Beskow, 2010; Facio et al., 2012; Ayuso et al., 2013; Jamal et al., 2013; Rigter et al., 2014]. There have been calls for empiric data on how individuals pursuing ES/GS understand and experience the consent process [McGuire and Beskow, 2010; Tabor et al., 2011; Green et al., 2013; van El et al., 2013; Rigter et al., 2014]. The few studies addressing these issues have focused on healthy individuals enrolling in population-based studies [Facio et al., 2011; Kaphingst et al., 2012], participants asked to consider hypothetical genetic research studies or tests [Levenseller et al., 2013; Platt et al., 2013], and patients consenting to clinical ES/GS [Rigter et al., 2014].

We set out to address this gap through a semi-structured qualitative interview study of adult members of families affected by Mendelian disease who enrolled in an ES/GS research study. First, we aimed to explore participants' experiences with the three outlined theoretical challenges to informed consent: (1) technical and interpretive complexity; (2) the possibility of incidental findings; and (3) the risk of loss of privacy and confidentiality, as well as the effectiveness of our consent process. Second, we aimed to explore how interviewees experienced the consent process.

MATERIALS AND METHODS

Our institution is currently enrolling adults and children with suspected Mendelian conditions into a large-scale ES/GS study whose goal is to use ES/GS technology to discover the genetic basis of these disorders. The study will be referred to as the "Mendel Project" which is part of the National Human Genome Research Institute (NHGRI) Centers for Mendelian Genomics program. Solving diagnostic dilemmas is explicitly not a Mendel Project study goal.

Research participants accrued to the Mendel Project at Johns Hopkins met with a board-certified clinical genetics provider who was trained to provide informed consent. Informed consent was typically obtained in a clinical appointment, though some participants were

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consented during a research visit or by telephone. On average, approximately 40 min was spent on the consent. Consent language used to describe incidental findings and other key consent elements are shown in Table I. The full consent form is available (Supplement A).

During the consent, potential participants were given a choice regarding which results they would like to receive, including: (1) no results; (2) only results related to the reason for enrollment; or (3) both. Enrolled participants, whether affected themselves or the parent of an affected child, were offered the choice of whether to receive incidental findings. We described the likelihood of a participant receiving an incidental finding using the phrase "a small chance" rather than estimating an individualized likelihood. Potential participants were also informed that they may never receive any results, either because their sample was not selected for sequencing or because no meaningful data were obtained. Risks related to loss of confidentiality through a lapse in security or by virtue of the collection of rare variants were also reviewed. Potential participants were informed that their biological sample and sequencing results would be stored at either Johns Hopkins or Baylor (our collaborating institution for the Mendel Project), and that results could be entered into the database of Genotypes and Phenotypes (dbGaP). Information regarding the existence and limitations of GINA, the Genetic Information Non-discrimination Act, was also reviewed.

Recruitment

Potential interviewees were identified from a pool of individuals who had completed the informed consent process within the preceding nine months, could speak English, and had not yet received any results. Adults who had either provided consent for their own participation or for their minor child were eligible. All individuals recruited to this study had been consented to the study by a study team genetic counselor so that the topics raised during the interview had been included in the original consent. Recruitment occurred via phone or email. This study was approved by the Johns Hopkins Institutional Review Board.

Interview Guide

We created the interview guide based on knowledge of the theoretical challenges to informed consent and our prior experience conducting informed consent for the study. Topics were organized into sections that included understanding of the purpose and goals, expectations and motivations for enrollment, perception of risks and benefits of participation, the process, risks, and benefits of receiving study results including incidental findings, opinions about confidentiality protections, general impression of the consent process, and whether reconsent at the time of return of results was of interest. We refined the probes being used after the first four interviews but made no changes to the core content of the interview guide. The final guide was then used for the remaining 11 interviews.

Data Collection

Study interviewers were unknown to the individuals being interviewed. Interviewers obtained verbal informed consent for this study and then conducted a semi-structured telephone interview using the guide. Interviews lasted 20–45 min and were recorded. Interviewees were offered a $25 gift card as compensation.

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Data Analysis

Recordings were transcribed and de-identified. Transcripts were then entered into Atlas.ti.7 software (ATLAS.ti GmbH, Germany) for qualitative analysis. Initial codes were developed based on the topics covered in the interview guide and we independently generated a list of secondary codes based on a reading of two transcripts. Four investigators applied the secondary codes to three additional transcripts, and the team compared the coded transcripts, discussed discrepancies, finalized secondary codes, and developed rules to make coding consistent. Each of the 15 transcripts was then coded within Atlas.ti.7 based on the finalized codebook by two independent coders. Codes were compared and discrepancies addressed until consensus was reached. Text coded with codes pertaining to the consent process and to the three theoretical challenges to informed consent (complexity of information, incidental findings, and risks to privacy) was organized and analyzed for common themes.

RESULTS

Study Population

Twenty participants were selected for this study. Contact was established with 17 (85%), each of whom agreed to participate. Two had scheduling issues that could not be overcome. Fifteen (75%) individuals from 15 unrelated families ultimately completed an interview. The elapsed time between the informed consent discussion and the interview was 2–13 months (median 7 months). Additional demographic information is presented in Table II. The key themes that emerged from analysis are reviewed below, accompanied by illustrative quotes.

Complexity of technical and interpretive information—We explored interviewees' technical understanding of ES/GS by asking them to describe in their own words what it meant to have their genome sequenced. Most were able to indicate their understanding that this type of testing interrogates a large portion of the DNA rather than one or a handful of genes.

> The geneticist that we're working with, she always uses this gesture where her hands are like spreading it out, almost like a big string….and so I see that picture in my mind over and over again, so I think about it – like laying out all of his genetic material in one big line. (Parent of affected child)

> As I understand it, there is a group of genes that have been identified as being linked and predictors for the condition. But the understanding is that there are others out there that have not been identified. And this study is working towards that goal of mapping out all of the genetic factors that can help identify people who have the disease. (Affected adult)

Interpretive complexity was also explored. Most interviewees expressed an understanding of the difficulty of interpreting some ES/GS results and many described their anticipation of uncertainty regarding the correlation of study findings to disease causality.

> But often, genetic testing will flag potential issues, but then the question of whether those issues are actually related is questionable. And there's uncertainty with that. (Affected adult)

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> I don't think they'll find "the" cause of the condition. I think they might find some contributing risk factors. But I think it's complicated. I think it's genetic, and I think there's probably something really that's environmental, or like virus, or something else that triggers it, as well as the genetic component. That' s probably going to be much harder to nail down than just by looking at the genome. (Affected adult)

Consistent with the interviewees' strong understanding of the technical and interpretive complexity of ES/GS analysis, few expected the study to identify the cause of their condition, although many were hopeful. No interviewee thought it was a certainty. None were motivated to join the study solely by expectations of personal benefit. Several individuals thought it was likely the basis of their condition would be identified. These individuals had valid reasons for optimism – typically because there were multiple affected individuals in the family.

> I believe they have a pretty good chance percentage wise, 80% hopefully, maybe better. They have my father and me and I think that's pretty good. I think they had my nephew in that study as well. They have multiple people in one family, I think there's a pretty good chance they'll find something. (Affected adult)

Several interviewees addressed the potential psychoemotional impact of the interpretive complexity inherent in ES/GS.

> And so it could potentially lead you down the rabbit hole, sort of chasing this thing that's not actually related….if we thought it was related, and then came positive, but it wasn't really the underlying cause, it could cause some sort of emotional distress. (Parent of affected child)

Incidental findings—Interviewees were asked to recall discussion from the consent regarding the possible identification of incidental findings. All were able to accurately describe the concept of incidental findings and many provided examples.

> From what I understood they could call me up and let me know I have cancer or some other kind of disease. (Affected adult)

> Not only will I may or may not be able to help them, they may not find that mutation in my genome but they will find other things that are known to cause serious illnesses of other gene mutations, whether it be a cancer or Alzheimer's or whatever the condition may be. (Affected adult)

> It might be revealed that my husband and I, or even [child's name], they might have some other underlying genetic issue going on that we didn't know about…we [find] out that when I turn sixty-five I might get Parkinson's Disease. (Parent of affected child)

All interviewees had elected to receive results related to their medical condition and incidental findings. When asked, almost all recalled having a choice about which results they wanted to receive, and could recall the selection that they had made. Interviewees were also asked about their perception of the likelihood of incidental findings, and many described this as a likely outcome.

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> I think what they said is that everybody…when they look at that [the genome], they're going to find some abnormality with your genes. I think everybody has certain issues. (Affected adult)

> There are abnormalities in any individual's genetic makeup. And those will be common–there'll be a lot of those, because everybody has a lot of them. (Affected adult)

When interviewees were asked to discuss the likelihood that they would themselves be the recipient of an incidental finding, almost all felt that this was unlikely. Many cited personal health beliefs as the basis for their belief.

> Low percentage hopefully. I really hadn't thought about it. I don't believe…I never thought that way that I'm sick, that there's something wrong with me. (Affected adult)

> I wouldn't think so mainly—our family comes from fairly healthy stock. (Parent of affected child)

Inattention to personal implications of incidental findings—Some interviewees, predominantly affected adults, acknowledged they had not thoroughly considered the likelihood or impact of incidental findings. Responses suggested that while they understood the concept of incidental findings, interviewees had paid little attention to the implications of these potential results in light of their more pressing goals of supporting research regarding their medical condition.

> Well, you brought up a couple good points that I really hadn't concentrated on too much… probably everybody's got five to seven things wrong with them, and how much of that do you want to know? And I never really thought about that as much because I was more focused on getting the gene information for my disease. (Affected adult)

> I'll be honest with you, I never really thought about that (incidental findings) and that was not the driving reason why I did this. (Affected adult)

> I guess I just never sat down to think about that… I just focused on the issue of just wanting to provide information about (my condition) …I didn't really sift through what that side effect would be for me. (Affected adult)

> I think a lot of us with the disease want to help you [researchers], want people to know more…, but we don't think. Just by the nature of this type of gene survey, you may find out a lot of things that you may or may not want to know. (Affected adult)

Perceived Benefits of Incidental Findings

When asked about the possible personal and family impact of receiving an incidental finding, most interviewees only described the potential benefits without mention of potential risks.

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> Well, I know it will be beneficial, so like if it was something hereditary, also because my two younger sisters don't have insurance, so if something came up where it is a family history, they could at least be aware also and make sure they watch out for it…it would be more beneficial to know the more risks that are possible versus Googling everything yourself and giving yourself every disorder out there. (Affected adult)

> And then as far as discovering other things, I mean, if there's something else going on, I'd like to know now so that if there's treatment or things that I'm doing that I need to stop doing, I'd definitely like to know that. (Affected adult)

Despite being further prompted with the possibility of receiving information for which there was no treatment or action to be taken, all participants stated they would still like to know. Some explained that their experiences living with their genetic condition adequately prepared them to adjust to additional genetic risks:

> I don't think anything would be shocking at this point (Parent of affected child)

> A couple years ago I might have answered that different…I think we just learned to live our lives the way we do and don't really let things affect us too much. (Parent of affected child).

Potential Loss of Privacy and Confidentiality

When asked about potential risks of ES/GS, several interviewees spontaneously mentioned concerns related to privacy and confidentiality of their genetic information.

> And you don't want them living their whole life in fear of that [insurance discrimination]. And you also don't want any outsiders to get that information and be able to hold it against you or your family in insurance costs or denying insurance, because they're afraid that there will be a catastrophic event or a more expensive need for services. (Parent of affected child)

> And I know that's even, you know– if President Obama did not get re-elected, you know looking at the healthcare reform, but I guess everyone is pretty much agreed on pre-existing conditions. So I guess that's always a concern, that somehow we're gonna get denied somewhere along the way. (Affected adult)

However, most interviewees did not explicitly state any risks associated with their participation in the project and, when prompted, denied feeling any personal risk related to loss of privacy or confidentiality of study data.

> Like these crazy movies they're based off of that information gets to the wrong people and somehow they do crazy stuff, but I don't see that happening. (Affected adult)

> Interviewer: Okay. You mentioned some concerns about recognizing that there are risks with privacy and people getting ahold of it [genetic information]. Although you recognize them, that didn't make you think twice about joining?

> Interviewee: No. It's not gonna do anything to me. (Affected adult)

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Participant reflections of the consent process—Toward the conclusion of the interview, interviewees were asked if there was anything in the consent process that they felt needed to be emphasized further, now that they had the chance to reflect on the process. None articulated a request for more information or a different emphasis of the information that was presented. The majority spontaneously indicated satisfaction with the consent process.

> I think she did a good job explaining any risks or anything like that and kind of a brief overview. (Affected adult)
>
> She was very, you know, neutral and clear about everything…she didn't sway one way or the other. (Affected adult)

Without prompting, several interviewees commented about the amount of effort and time that went into the consent process, indicating that the consent process was time-consuming for them and provided considerable detail.

> The consent process was very detail-oriented. I mean it was like a ten-page document…it was very, very detailed. Minutia. (Affected adult)
>
> Interviewer: What was most memorable about the information that they gave you about this study?
>
> Interviewee: We went over consents for a long, long time. So that's the thing that sticks out in my mind the most. (Parent of an affected child)
>
> I'm just surprised that so much effort has to go into the consent process….it just sounds like the whole process is much more burdensome than it should be. (Affected adult)
>
> Interviewee: We spent a lot of time (laughs)…. It was already a long day and then we finished with the consent which probably made it seem longer than it really was. She went over every page and then had to do it with me, and then we did it for (child), and then she had to do it for my husband, too. She didn't just do it all in one blanket thing. She did it with each individual person and so it was… (Parent of an affected child)
>
> Interviewer: Wow… that would be a long day.
>
> Interviewee: A long day <Laughter>.

Interviewees were also asked whether they desired, or felt it necessary, to engage in a reconsent process when results become available. There was no indication from any subject that this was necessary or desirable. Further prompting from the interviewers about whether topics were raised during the interview that would cause individuals to change their mind about their choices again did not identify any interest in reconsent.

DISCUSSION

This qualitative study represents an early exploration of the consent experiences of members of families with Mendelian conditions enrolling in ES/GS research. Our study has three main findings. First, the consent process was effective as a means of alerting study

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participants to the potential risks of ES/GS research. Interviewees could accurately describe the goals and processes of ES/GS and incidental findings, to recall choices made related to return of results, and to identify risks related to privacy and confidentiality. Second, interviewees acknowledged paying little attention to potential implications of incidental findings and risks to confidentiality in light of their more pressing goals of understanding and supporting research into their own medical conditions, an area of potential concern in the consent process for this population. Finally, while it was largely effective, some interviewees experienced the consent process as very long and none desired reconsent prior to return of study results.

The use of ES/GS technology has led to concern in the genomics and bioethics communities about the ability of the consent process to adequately convey the information needed for individuals to make informed decisions about participating in this research [McGuire and Beskow, 2010]. Three areas of potential concern have been raised that differentiate ES/GS from conventional genetic research, including the technical and interpretive complexity of ES/GS, the likelihood of incidental findings, and the risk of loss of privacy and confidentiality related to data sharing [Tabor et al., 2011].

Appreciation of these potential challenges led to calls for empiric data on how individuals pursuing ES/GS understand and experience the consent process [McGuire and Beskow, 2010; Tabor et al., 2011; van El et al., 2013; Rigter et al., 2014]. Seminal work was done by Tabor et al. [2012] who studied perceptions of risks, benefits, and harms among members of two families with Miller syndrome being consented for GS research. Several studies followed which investigated consent experiences of individuals in population-based studies [Facio et al., 2011; Kaphingst et al., 2012; Facio et al., 2013] or undertaking clinical ES/GS [Rigter et al., 2014]. There has also been considerable study of a variety of stakeholders asked to consider hypothetical genetic research studies or tests [Levenseller et al., 2013; Platt et al., 2013]. More recently, Jamal et al. [2013] and Sapp et al. [2014] have reported interview-based qualitative studies of parents of children affected with severe potentially genetic health conditions enrolled in research-based ES/GS protocols. These studies focused on the rationale for choices about return of results [Sapp et al., 2014] and attitudes toward confidentiality [Jamal et al., 2013].

Several themes have emerged from these studies. With regard to the theoretical challenges to informed consent, a few studies suggested the consent process can improve knowledge of the technical and interpretive complexity of ES/GS [Kaphingst et al., 2012]. Individuals in some studies, however, struggle to comprehend the nature of testing [Tabor et al., 2012; Rigter et al., 2014]. These studies also demonstrated that most participants were interested in receiving primary study results and incidental findings [Facio et al., 2013; Sapp et al., 2014]. With regard to potential loss of privacy and confidentiality, individuals in families with potentially genetic disease express few privacy concerns [Jamal et al., 2013; Levenseller et al., 2013; Sapp et al., 2014], particularly when weighed against perceived benefits of participation, in contrast to individuals participating in a hypothetical genomic study [Platt et al., 2013]. Only two studies, one of which involved assessment of informed consent for clinical GS [Rigter et al., 2014], collected feedback about the consent process. These studies suggest that while participants appreciated the care taken with consent for ES/GS, they

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found the process long and, in the case of a study requiring 2–3 hr consent process, burdensome [Tabor et al., 2012].

Our study confirms and extends these findings. Our results are strengthened by two novel features. First, this is among the first studies to consider the consent experiences of adults with decision-making capacity who are affected by genetic disease. As suggested by our finding that adult interviewees paid little attention to personal implications of incidental findings — which is sharply different than parental attitudes reported in the literature [Levenseller et al., 2013; Sapp et al., 2014] — the weighing of risks and benefits to participation may be different in the affected adult population. Second, our study included feedback on how interviewees experienced the consent process of an active research study, data that are largely absent from the literature.

Our results indicate that, by and large, the consent process implemented for the Mendel Project worked as a means of alerting study participants to the three areas of concern expressed by theorists. We found interviewees could accurately describe the basic differences between ES/GS and more traditional single gene tests, articulate the possibility of learning about incidental findings, and identify risks related to loss of confidentiality. Although direct comparisons are not possible, interviewees' abilities to articulate their understanding of ES/GS in this study appears somewhat better than that described by Tabor et al. [2012] and had similar to the level of understanding described by Facio et al. [2011] in a general-population ES/GS research study.

When interviewees were asked to apply their conceptual understanding of aspects of ES/GS to their own lives, we identified one area of potential concern. A substantial proportion of adult participants explained that their goal of improving understanding of their own condition led them to pay relatively little attention to implications of incidental findings and other study risks. While prioritizing results that might have eventual implications for themselves, family members, and others is reasonable, it could lead to incompletely considered potential risks. Notably, this finding differs substantially from studies of parents of children enrolled in ES/GS research [Sapp et al., 2014] or considering hypothetical ES/GS research [Levenseller et al., 2013], who viewed incidental findings as a parental responsibility.

While many interviewees articulated their belief that all people have variations in their genes that could be detected by ES/GS, almost none believed an incidental finding would be discovered in them. It is possible that this finding is further evidence that our consent process worked well, resulting in research participants who understood that that all people carry some disease causing genes and that that the chance of finding ones unrelated to their reason for enrolling in the Mendel Project was small. However, interviewees articulated their reliance upon personal health beliefs as their rationale for their low estimate of personal risk of incidental findings, rather than recall of study goals and processes. Some attributed their confidence in handling any result that might come to their experience living with a chronic medical condition, a finding that has also been seen in a recently published study of parents of affected children enrolling in an ES/GS research study [Sapp et al., 2014]. It, therefore, may be more likely that this finding represents optimistic bias, a well-

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established phenomenon in certain subgroups of the population [Cooper et al., 1988; Rutter et al., 1998; Delfabbro and Winefield, 2000; Rogers and Webley, 2001; Weinstein et al., 2005]. Our cohort, consisting of early-adopters of ES/GS technology who desire all results from testing, may represent a subgroup that demonstrates a bias toward optimism when considering the risk of receiving incidental findings. This is further supported by our data that interviewees provided responses heavily weighted toward the positive potential implications of receiving incidental findings.

Combining our findings with the literature, we suggest that patients and family members of individuals with inherited disease have a higher tolerance of risks associated with participation in ES/GS research in comparison to the general population. This tolerance appears to be associated with (1) increased potential benefit for themselves, family members, or their disease community; (2) confidence in their ability to adjust to incidental findings; and (3) lower perception of personal risk of study findings given their existing medical situation. Families with inherited disease may benefit from a consent process in which study risks and benefits were discussed in the context of prior experiences with genetic research and genetic disease.

Data from this study also suggest how best to balance providing a comprehensive ES/GS informed consent with time constraints of both participants and the researcher. It has been suggested that the technical specifics of ES/GS may not need to be explicitly described during informed consent, as such details may not be relevant to the goals of the research or to the benefits and risks [Tabor et al., 2011; Levenseller et al., 2013]. Our findings support the measures to streamline consent for ES/GS research, as some interviewees indicated that the consent process was very long. Our discovery that interviewees had no interest in reconsent and no suggestions for additional elements to add to the consent process is consistent with this theme.

While our consent process was effective, all underwent consent with a board certified genetic counselor. These results may not be applicable to informed consent with professionals not formally trained in genetics. As ES/GS research expands, ensuring informed consent will require further exploration of not only the minimal information to be conveyed, but also the preparation of clinical investigators and staff who enroll participants.

Our study was small and may not be generalizable. All interviewees chose to receive incidental findings, which is not true of all who enroll in ES/GS research. Additionally, the time from the initial consent for the Mendel Project and the interview for this study varied among interviewees, which may have influenced responses. Given the size of our sample, we were not able to reach conclusions about differences between parents of affected children and affected adults.

Our findings highlight the consent experiences of both parents of affected children and adults themselves affected with genetic disease enrolling in ES/GS research. The consent process implemented by board certified genetic counselors and geneticists was largely effective at conveying study goals and processes, the concept of incidental findings, and potential risks related to confidentiality. Affected adults paid little attention to personal risks

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of incidental findings and confidentiality in light of their more pressing goals of understanding and supporting research into their medical conditions. As individuals and families with genetic disease will be likely to participate in ES/GS research, it will be important to further investigate how to make the consent process for this population most effective. In particular, further exploration of the experiences of adults affected with inherited disease would be valuable as our study hints that their experiences and priorities in enrolling in ES/GS research may differ from both parents of affected children and adults in the general population. We also encourage further exploration and dialogue regarding balancing meaningful informed consent with time constraints.

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TABLE I

Consent Element Definitions Used in the Mendel Project

Mendel project consent elements	Language used in Mendel project consent form
Purpose of the Mendel Project (consent form page 1)	*This research is being done to identify the genetic cause for inherited syndromes and health conditions (called "Mendelian disorders").*
Description of ES/GS (page 2)	*We will try to find the genetic cause for your rare syndrome or disorder by studying all or nearly all your genes through a new method called genome-wide sequencing. In genome-wide sequencing we will look for disease causing mutations in your entire genome.*
Incidental findings (page 3)	*A previously validated genetic cause for other serious medical conditions which you will likely develop as a result of a mutation we discover.*
Choices for return of results (page 4)	• Please contact me if you discover the genetic cause for my disorder or medical condition • *Please contact me if you discover that I have a genetic mutation likely to cause in me a serious medical condition other than the condition that led me to take part in this study.*
Clinical confirmation of research results (page 4)	*Either of these results would need to be confirmed in a clinical laboratory and study team members would help you with clinical testing, if you want, though your insurance would need to pay for this testing.*
Timing of return of results (page 4)	*It may take many months, or even years, before we complete our research. So it may be several months or years before we may contact you about any important results. ε It is possible we may never contact you.*
Risks associated with incidental findings (page 5)	*If we learn that you have a genetic mutation likely to cause in you a serious medical condition other than the condition that led you to take part in this study, the information you learn may be distressing to you. This information may also cause distress for members of your family who may carry the same genetic mutations.*
Sample storage (page 3)	*Your cell sample, DNA, and/or cell line may be stored indefinitely in a biologic repository at Johns Hopkins or Baylor College of Medicine, our collaborating site for this project*
Data storage (page 9)	*As part of this study genetic information from your biologic samples and health information will be sent to a public, controlled database maintained by the National Institutes of Health (dbGaP). Standard identifying information ε will not be sent to any database. The submitted data will be coded and will not contain information that identifies you directly. Genome-wide sequencing data will be shared with other qualified researchers at other institutionsε*
Risks of data storage (page 9)	*Although it would be unlikely, the following could occur with your coded data: Your identity could become known to people outside the study either through a lapse in security or by virtue of collection of genetic variants in your genome that are specific to you. Information could be revealed that could lead to denial of employment or insurance for you or a relative. Information about you could be released to law enforcement agencies. The possible loss of privacy could cause stress, anxiety, or embarrassment.*

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TABLE II

Demographics of Study Participants

Variable (n =15)	N (%)
[0,1-2]Gender	
Male	8 (53)
Female	7 (47)
Type of Participant	
Affected adult	11 (73)
Parent of affected child[a]	4 (27)
AGE (Years)	
18–29	1 (7)
30–39	6 (40)
40–49	2 (13)
50–59	3 (20)
60–69	3 (20)
Diagnosis/Clinical Findings	
Arrhythmogenic right ventricular cardiomyopathy	7 (46)
Schwannomatosis	4 (27)
Multiple congenital anomalies with autism	2 (13)
Connective tissue disorder with developmental delays	1 (7)
Lipoatrophy/hemifacial microsomia	1 (7)
Time Between Mendel Project Consent and Interview (Months)	
1–2	4 (27)
3–6	3 (20)
7+	8 (53)

[a]One subject was both the parent of an affected child and was mildly phenotypically affected themselves; we chose to include this individual as a parent of an affected child for our analysis.