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Parent Perspectives on Pediatric Genetic Research and Implications for Genotype-driven Research Recruitment

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Abstract

As genetic research is increasingly conducted in children, it is important to understand how parents make decisions about enrolling their children and what they think about receiving their children's genetic research results. We conducted semi-structured phone interviews with 23 parents of children enrolled in genetic studies of autism or diabetes. Qualitative thematic analysis focused on two important components of genetic research and genotype-driven recruitment: participation in genetic research and return of results. Our findings suggest that parents' preferences and perspectives may be specific to their child's disease and the needs of the family as a whole. Assessing the expectations of target research populations will be beneficial for developing best practices for pediatric genetic research, return of results, and genotype-driven recruitment.

Keywords

informed consent; recruitment; risk; benefit; genotype-driven; autism; diabetes; ethics

Increasingly, parents of children with both Mendelian and complex diseases, as well as parents of healthy children, are being asked to enroll their offspring in genetic research studies. Several studies have explored why families enroll their children in pediatric genetic research (Bernhardt et al., 2003), how parents and children perceive the consent process for genetic research (Geller et al., 2003), disclosing the results of pediatric genomic research to

participants (Miller, Hayeems, & Bytautas, 2010), and the ethical implications of including children in large biobank studies (Gurwitz et al., 2009; Hens & Dierickx, 2010; Hens et al., 2009a, 2009b, 2011; Hens, Wright, & Dierickx, 2009; Kaufman et al., 2008).

Genetic researchers are also increasingly employing genotype-driven research recruitment, where researchers invite existing research subjects to participate in additional research because of genetic information that was generated in the original study (Beskow et al., 2010; McGuire & McGuire, 2008). This kind of recruitment can maximize the utility of data stored in databases while speeding progress toward the ultimate goal of benefitting human health. However, the approach raises ethical considerations about the use and disclosure of genetic information as part of the recruitment process, particularly when this kind of recontact was unexpected and not described as part of the original informed consent process (Beskow et al., 2011). Concerns exist around the tension between clearly explaining to participants the purposes of the additional research and avoiding the disclosure of genetic information that may be unwanted and/or uncertain (Beskow et al., 2010).

There are unique ethical challenges in pediatric genetic research studies that intersect with ethical issues involving genotype-driven research recruitment. In pediatric genetic research, parents are asked to give permission on behalf of their children for participation. In doing so, they are asked to weigh risks and benefits, to the children and the family as a whole, of initial research participation, of the return of genetic research results, and of any subsequent participation. Parents may view these decisions, in their role as decision-maker for their child, somewhat differently than adults view the decisions for themselves.

We conducted an interview study to evaluate parent perspectives on pediatric genetic research participation, and specifically on genotype-driven research recruitment. This project was part of a larger study that interviewed research participants about their perspectives on genotype-driven recruitment across a range of studies and disease populations (Beskow et al., 2011). This paper focuses on the subset of interviews conducted with parents whose children were participating in a pediatric genetic research study of either diabetes or autism. Understanding how parents make decisions about enrolling their children in genetic research and what they think about receiving their children's individual genetic research results is important for developing effective and appropriate approaches for primary research recruitment, return of results, and genotype-driven research recruitment in pediatric populations.

Methods

Parents were recruited from three studies in which genotype-driven research recruitment occurred: (1) the SEARCH for Diabetes in Youth Study (SEARCH), (2) the Autism Genetic Research Exchange (AGRE), and (3) the Study of Autism Genetic Exploration (SAGE) (Table 1).

We attempted to recruit all parents in the three studies who had been recontacted and recruited for additional research based on a finding in their children's DNA, as well as a subset of parents who participated in the original genetic study but were not recontacted for additional research. The original study investigators contacted parents to tell them about our study. Subsequently, our research team called the parents to provide additional information about our interview study and invited them to participate. Verbal consent was obtained at the beginning of each interview. The interviews were conducted using an interview guide that was developed as part of the larger genotype-driven research recruitment project (Beskow et al., 2011). The guide was organized around four topics: (1) recruitment and consent for the original study, (2) the recontact process, (3) return of genetic research results from the

original study, and (4) recruitment and consent for further research. Interviews lasted between 30 and 60 minutes. All interviews were audio-recorded and transcribed, and all identifiers were removed from the transcripts.

Qualitative thematic analysis was performed using NVivo 8 qualitative data analysis software (NVivo, 2008). We used an iterative approach to the qualitative content analysis of the transcripts (Hsieh & Shannon, 2005). The first set of codes was developed and applied through a collaborative cross-site coding process as part of the larger study (Beskow et al., 2011). The data were then reanalyzed by the Seattle research team to identify all comments that parents made about the impact of genetic research on their children. We also examined parents' responses to specific questions about their reasons for research participation, their perceptions about risks and benefits of receiving individual genetic research results, and their understanding of the goals of the research. Five team members (TB, JC, HKT, SMF, BW) reviewed and discussed the transcript segments on these topics and developed a list of content codes to be applied across all transcripts. Two team members (TB and JC) conducted a second pass analysis, applying the newly generated pediatric-specific content codes. Frequency tables were developed to examine which concepts were cited most frequently across transcripts and differences between disease groups. The group then fine-tuned these codes and three coders (TB, JC, and HKT) reviewed the transcripts for a third time, applying the more specific content codes where appropriate. The team reviewed all coded segments and any discrepancies were resolved by consensus. The study protocol was reviewed and determined to be exempt by the Seattle Children's Institutional Review Board (IRB).

Results

Twenty-three parents of children enrolled in SEARCH, SAGE, and AGRE were interviewed as part of this study. Of these, six parents experienced genotype-driven research recruitment and 17 did not (Table 2). Most of the participants were mothers, Caucasian, and had at least a Bachelor's degree (Table 2). While the two autism studies differ in their study design, we did not observe any significant differences in our result categories between parents from SAGE and parents from AGRE. The most apparent differences in any of the result areas were between the disease groups, i.e., between the Diabetes-SEARCH parents and the combined Autism-SAGE and Autism-AGRE parents. Therefore, our results are structured to compare the two disease groups rather than the three studies.

We present our results in two main categories: (1) participation in genetic research and (2) return of results.

Participation in Genetic Research

Parents' perspectives on their children's participation in genetic research centered on five themes: (1) avoiding harms, (2) time and convenience, (3) helping: an opportunity for altruism and positive action, (4) "rewards" of research participation, and (5) relevance of the study to the family and perceived importance to society.

Avoiding Harms—Many of the parents described wanting to protect their children from unnecessary harms or distress as a key factor in their decision about whether to participate in genetic research. They also described how they weighed these risks against the potential benefits of research participation. One parent said, "If there's anything that's not abrasive to my child and if I can help science, I'm all for it because nobody wants to have no answers" (Autism-AGRE-S09). Another parent described weighing potential psychological impacts of the research procedures for a child with autism: "I also look at what they're looking for, or how my child is going to be affected by this. If it's something they'll be so stressed out or

losing it, for days after, days before, anxieties, then it's something that it's not going to be a candidate for them" (Autism-AGRE-S07).

Parents, especially those of children with autism, expressed concern about the additional stress of blood draws as part of research participation. One parent discussed her experience in which researchers insisted that her son needed to voluntarily extend his arm for a blood draw, and how challenging this was for her child with autism.

I was a little startled at first when we had gone through everything and we thought everybody understood the extent of our son's handicap with this autism. That he wouldn't be an easy kid; he wouldn't be an easy participant with the blood draw. And so I was a little scared at first when...we were told, "Oh yeah, we can't hold him down. He has to willingly, gladly, extend his arm for this."... I mean even my...so-called "typical" child would have had to be coerced or something. So to expect an autistic child who is so severely handicapped to gladly, willingly extend his arm, that was a little shocking at first. (Autism-SAGE-S23)

Despite these concerns, no parents, when asked specifically, said that the blood draw alone would deter them from enrolling their child in genetic research that is relevant to their disease. Instead, some parents explained that they would have to weigh their view of the potential importance of the science in the study against possible distress.

[The blood draw is] a traumatic thing for him. I would do it anyway. I would anyway, in a heart-beat. Simply because I feel like people have to be able to find out the information, somehow. And, overall, it's a little thing to do for something that could have a great import. And, you know, we have to have several people hold him down, but I would still do it, simply because I feel like information needs to be had. (Autism-AGRE-S01)

A parent of a child with diabetes voiced similar concerns about the physical and emotional burden of blood draws in the context of research participation. She said, "I would be less likely to send her in for [that]. She had a hard year last year with her diabetes. So we have just spent a lot of time at doctors and pokes. So I'm seeing it now more than any year. She's had [diabetes] for six years, but any extra pokes aren't okay" (Diabetes-SEARCH-S20).

Parents of children with autism were concerned about the ability of research staff to manage their children's special needs. This concern was raised with regard to the burden of the blood draw, as well as other research-related burdens for children with autism. One parent described how researchers' failures to understand challenges unique to children and families with autism mirrored those of the general population: "It's just real hard, you know, if we have to wait. They don't take into account that you have autistic kids at all, nobody does. Nobody really understands it, still" (Autism-AGRE-S12). Another parent said that she would be more likely to have her child participate in a research study if the staff had experience working with children with autism: "If I was taking her to a clinic that just deals with kids with autism or is used to dealing with them, then that would be a higher priority than just taking them to the random person" (Autism-AGRE-S02).

Time and Convenience—Parents also cited time and convenience as important factors when considering whether to enroll their children in genetic research. Parents of children with autism were explicit about balancing the burden of research visits with caring for their children. One parent commented that research participation is "typical[ly] time consuming, and convenience is all. Time is an issue for me in terms of managing the time I have, with the kids' condition and so on" (Autism-AGRE-S13). Another autism parent described balancing wanting to help through research participation with the other demands on her time from caring for her affected child/children:

...honestly, you're just kind of like in survival mode sometimes, so just, it's not that I don't want to help because I do, it's just honestly, like I know that sounds crazy, but just finding 20 minutes to sit down and write a questionnaire...just kids with autism keep you pretty crazy so it's not like you get a lot of free moments. (Autism-AGRE-S02)

Parents from both the autism and diabetes studies commented on the potential inconvenience of travel time to the research location. Parents also suggested that consideration of time burdens may be different for older children than for younger children, and that parents take their children's wishes about this burden into consideration as children's autonomy develops. One parent discussed the impact of these inconveniences on her teenage daughter: "I'm kind of in the middle on that one too just because it takes like, Tuesday when we come out she'll miss a whole day of school. And so it's a big deal for a high schooler" (Diabetes-SEARCH-S20).

Helping: An Opportunity for Altruism and Positive Action—Many parents across both diseases recognized that research participation might not result in direct benefit for their child. However, they described research participation as an opportunity for altruism and as a way to take positive action to help their child, even indirectly or in the distant future. Several parents described their desire to help their child who was living with the disease: "I just wanted to make sure that if there was anything else that can be done to help her [my daughter], you know, that I was there to provide it in whatever minimum way" (Diabetes-SEARCH-S03).

Parents also described participation in genetic research as providing potential benefits to their unaffected children. For example, one parent said that she was motivated to enroll her diabetic child in research because "I was hoping that they could find out the causes and hopefully how to delay it with my other children and have it not come about with my other children. So we were trying to help any way we could...I guess my huge goal...is that my other two don't get [diabetes]" (Diabetes-SEARCH-S20).

More broadly, parents described being motivated to participate in genetic research as a way of contributing to science and making progress towards finding causes or preventive measures, developing treatments, and/or helping other families with the same diseases. Other parents spoke about the desire to "help out in the community at large whenever we can" (Diabetes-SEARCH-S16).

"Rewards" of Research Participation—One of the benefits of research participation discussed by parents of children with autism and diabetes was the potential for research to lead to better interventions or services for their children. Three parents of children with autism described this in the specific context of obtaining school-based services. One autism parent described these kinds of nongenetic results as the "rewards" of research, in the form of reports that could be used to obtain educational services for their child from their public school.

I think [the research is] really good and the rewards are wonderful. It seemed like every time the study came up, especially when my kids were in public school district, that the timing was just perfect, and of course we would get a free report and more evidence showing the school district, you know, that my son and daughter needed the services. (Autism-AGRE-S15)

While these reports were not genetic results, these parents perceived the return of research information as a direct benefit to their child, even outside the medical/clinical context.

Parents of children with both diabetes and autism also discussed their hopes for improving treatment through genetic research. Some parents drew a direct connection between participation in research and improved treatment, although they did not explain the timing of these potential benefits relative to their participation.

Because they [the researchers] would see the traits in other people and they would see the traits in my own genes or my son's genes and people with diabetes and the people without diabetes, to see how they can get the cure or the...better use of the insulin, instead of having all the low sugars and the high sugars and the deterioration of your kidneys and liver and pancreas. So it would help out. (Diabetes-SEARCH-S14)

Relevance to the Family and Perceived Importance—Parents were asked about their willingness to have their children participate in research about diseases other than the one affecting their child. Many parents expressed a preference to have their children participate only in research that is relevant to their family and their family's health. This included the primary diseases in our sample (autism or diabetes), as well as other conditions that exist in their family. Several parents indicated that they would be less interested in participating in studies on other diseases. No parents expressed any hesitancy about participating in additional genetic research related to their child's disease.

Parents also talked about the perceived "importance" or "value" of a study to society as influencing their decision to participate in future research. Some distinguished important questions about health and disease from "trivial" questions.

Whether or not I feel that there's value in the study. That it's an important study, I guess not just personal value, but do I see a long-term value to society in finding out the information that that study is looking at. Not that I've ever been contacted about a study that I thought was frivolous, but if the study was trying to figure out why girls like the color pink or something, I wouldn't be as interested. (Autism-SAGE-S24)

Return of Results

Parents described several different themes surrounding return of genetic research results, both in general and in the context of genotype-driven research recruitment, including: (1) psychological impact of results, (2) clinical, reproductive, and personal utility of results, and (3) results as an incentive for further research participation.

Psychological Impact of Results—In their responses to hypothetical scenarios about return of results, as well as prompts about concerns, none of the parents from either disease group mentioned any possible negative psychological impact *on their child*. This may be due to the wording of the hypothetical questions in the interview, or the absence of a specific question in the interview guide about this issue. However, a majority of parents described concerns about the psychological impact that receipt of results could have on parents in general, particularly results that had uncertain meaning or for which no treatment was available.

Some parents of children with autism also described psychological implications for *themselves* of receiving their children's individual genetic research results, including blame, guilt, and fault. None of the diabetes parents mentioned these types of psychological implications. One autism parent described a possible negative psychological impact of learning causal genetic information, saying, "It would vary by person, everybody is different but, you know, especially if it's genetically, one person might want to blame another [for the

child's disease], a spouse, they might not have enough information and run with what little they have and thinking that, thinking the wrong thing..." (Autism-AGRE-S04). Another autism parent anticipated possible relief, stating, "I mean, can you imagine what a relief it would be to say, "No, your son does not have any marker that would indicate heart disease." Well, then I would say, "Oh! He got that from me, because my family doesn't have it, and boy, what a relief!" (Autism-AGRE-S01).

Another parent explicitly cited the value of genetic results to relieve guilt about possible nongenetic exposures that might have caused their child's autism.

I still think it's beneficial to know that a gene had caused it. There's a lot of theories out there about what causes autism, I think it's a relief just to know sometimes it's a gene and that you didn't cause it by getting immunizations or having your child immunized, you know, too close together or feeding them the wrong food or, you know, knowing that it's a gene is kind of a relief, in a way. (Autism-AGRE-S18)

The most common concerns of parents from both disease groups about receiving results were worry, stress, fear, and depression. One parent said:

I think researchers need to treat us like individuals because everybody takes things differently. Some people cannot handle knowing what [sic] to happen to them because the genes they carry, and that it could be, you know, they can get into some anxiety by thinking this will happen down the road to them, and that's not helping. (Diabetes-SEARCH-S17)

Because of the potential for negative psychological impacts, parents in both disease groups expressed a desire to be able to decide whether or not they want individual genetic research results returned to them.

It could be an option available for people to decide whether or not they want that information, it depends, because some people prefer more information and other people get scared of more information, so by leaving it up the person to decide whether or not they want that, I think that would be the best way to do it. (Diabetes-SEARCH-S16)

While most of the potential psychological impacts described were negative, a small number of autism parents also discussed the potential of receiving results and feeling relieved or empowered. One parent made an analogy to a friend with cancer learning more about his disease, saying, "I think it's always helpful [to learn more], even if it's bad news. Sometimes it still is, it's a sense of empowerment" (Autism-AGRE-S11).

Clinical, Reproductive, and Personal Utility of Results—While both groups of parents discussed the possibility of individual genetic research results having utility for their children, their families, or future generations, they discussed the concept in slightly different ways. Parents of children with diabetes were more likely to perceive individual genetic research results as having clinical utility related specifically to diabetes. They described the potential for family members to change behavior and possibly prevent the disease as a benefit of receiving individual research results. One parent of a child with diabetes said, "They might know that because they've got one strike against them, maybe that will encourage them to live more healthfully in other areas to make themselves stronger to compensate for the weakness" (Diabetes-SEARCH-S16).

A parent of a child with diabetes who received individual genetic research results from the first study described how the results might affect her daughter's diabetes treatment: "I was excited [when I received the results]. I wrote down the questions, like 'Do we need to

continue with the insulin? How often do you want us to test her blood sugar?’ Just a couple of those questions, written and ready to show to the doctor” (Diabetes-SEARCH-S08).

Parents of children with autism spoke more vaguely about the clinical utility of results specifically for autism. One parent said that by sharing results with their child’s doctor, “there might be something you could do about the information” (Autism-AGRE-S04). Another parent said that if the gene for autism was found, “there might be better therapies” (Autism-AGRE-S06).

Both groups of parents described potential utility of individual genetic research results in terms of knowledge that could be used for proactive health behaviors and treatments, now or in the future.

As I said before, knowledge is power. The more you know about your health, the better you can map out your plan. If you find out that you have a genetic predisposition to cancer or heart disease, you can eat better! Which, you know, you know how to do those things anyway. But, actually knowing that you have the predisposition could be the goose someone needs to get going! (Autism-AGRE-S01)

Several parents of children with autism talked about the utility of research results for reproductive planning. Autism parents discussed the impact and utility for a variety of people beyond just their affected child, including themselves, their unaffected children, their other relatives, and society in general. None of the diabetes parents discussed the use of results for reproductive planning. One autism parent described her perceived value of this information: “It’s information that it’s good to know, that it could be passed on. If my oldest son, who’s only mildly autistic, should decide to have children, I mean, at least he can know that he doesn’t have it to pass on” (Autism-AGRE-S01). Several autism parents stated that their desire for information related to reproductive planning increased as their unaffected children became adolescents and young adults. One parent said, “I’m starting to think about my oldest [who] is 18, you know, he gets married and wants to have children. Are they finding that there is a genetic link? It becomes a little more important than when they were five” (Autism-SAGE-S21). Another autism parent noted: “When my kids, my typical kids, have kids, it would be nice...to know before they decide to have kids, what their likelihood would be of having a child with autism. That would be helpful information” (Autism-AGRE-S02).

Reproductive planning was most often discussed as a benefit of receiving research results. However, some autism parents expressed concern about the use of genetic information for this purpose, and perceived it as a potential harm to their children, other children with autism, and society. One autism parent described how she might have felt if genetic information had been given to her in the past, when she was deciding whether or not to have more children, and related her experiences to the potential use of the information for her unaffected children’s reproductive decisions.

If they would have told me I had 80% chance of having another child with autism, I might not have had any more kids... I guess the problem I could foresee is maybe if my kids got the percentage they would decide not to have kids, which, that would make me sad, too. So, maybe having people have too much information and maybe having abortions or choosing not to have kids because they are too scared of the percentages, that’s the only thing really negative I can think of. (Autism-AGRE-S02)

Results as An Incentive for Further Research Participation—Several parents of children with autism stated that receiving genetic results from a research study would be a strong incentive to participate in future related research activities. None of the parents of children with diabetes expressed this perspective. One autism parent said, “I think that it would be helpful [to get results from the first study] because that could be the motivating factor that would make someone accept to be in the study or not” (Autism-AGRE-S01).

Another autism parent described how experiencing intellectual satisfaction from return of results would motivate future research participation, saying, “I could see a satisfaction of some curiosity at this point. And maybe the other benefit would be to inspire a person to keep on to maybe participate in other studies” (Autism-AGRE-S09). This concept was echoed and reinforced by another parent who felt that without the return of the results, parents might be reluctant to participate in additional research: “I think they should [give results back from the first study]. I think that makes a person more wanting to do the research if it’s something they found. Otherwise it puts them in the dark, why am I doing this again?” (Autism-AGRE-S07).

Some parents realized that there might not be clear clinical utility of some results, or that they might not understand them or know what to do about them. However, they still expressed a strong desire to receive such results because they would provide hope, and motivation to participate in further research as part of that hope. One autism parent explained, “You know, whether I understood it [the result] or whether I would think it was worth it, I don’t know, that’s another story, but if I choose, if it sounds helpful and hopeful and they explained it appropriately, it seems to me that it’d make me more motivated to do the [additional] study” (Autism-AGRE-S12).

An autism parent who had experienced genotype-driven research recruitment described this motivation to participate in a genetic research study as a way of helping researchers learn more about what the change in their DNA means.

It was interesting too ... when they contacted us and said that two of the family members carry this, and then after the test finding out that [my child] carries it, I would, actually it would be good to go on another study and figure out, “OK, well what does this mean then?” So yes, I would say it’s good for them to tell us. (Autism-AGRE-S15)

In this case, the return of “uncertain” research results was perceived as a benefit that would allow the family to participate in follow-up research that would potentially improve researchers’, as well as the family’s, understanding of the meaning of the result itself.

Discussion

This qualitative study of parents of children participating in genetic research focused on challenges related to two important components of genetic research: research participation and return of genetic research results. While some other studies have addressed these issues in the pediatric setting, none have focused on them in the emerging context of genotype-driven research recruitment. Pediatric genotype-driven recruitment is likely to become more common as genetic research in children increases, and as exome and whole genome sequencing result in the identification of large numbers of genetic results of possible clinical significance that will require further study.

Genotype-driven recruitment in a pediatric context presents ethical issues that are distinct from those encountered in an adult context. Parents will be required to make decisions for their children about the potential harms and benefits of participating in ongoing genetic

research. They will also need to consider the risks and benefits of a range of genetic information that might be returned as part of recruitment of their children, or families, to participate in further research, including uncertain information and information about future disease risks to their children and potential grandchildren. We examined parents' motivations for enrolling their children in genetic research and their perceptions of what individual genetic research results might mean to get a sense of how these issues might best be addressed in the context of genotype-driven research recruitment.

Perhaps not surprisingly, both autism and diabetes parents identified the need for blood draws as a potential deterrent to participation in pediatric genetic research because they did not want to see their children unhappy or physically uncomfortable, even for a short time. Parents may be more likely to have their children participate in genetic research using stored samples, such as blood spots collected at birth (Tarini et al., 2010), leftover samples taken in clinical care (Brothers, 2011) or DNA from other sample sources (e.g., buccal swabs).

Parents expressed a variety of motivations for having their children participate in genetic research. The theme of "helping" as a motivation to participate in research has been explored in various populations (Kohane & Altman, 2005; Reddy, 2007; Treloar et al., 2007), and was a common motivation among the parents interviewed for this study. "Helping" was mentioned in the context of several different possible beneficiaries. Parents wanted to help their affected child, and particularly in the case of autism, felt that research was one way to feel like they were "doing something" in the context of uncertainty about the disease and treatment. They also wanted to help their unaffected children, future children and grandchildren, and society more broadly. This suggests that parents make decisions about participation in genetic research based on possible benefit to a range of family members and stakeholders beyond just their affected child.

Much of the debate about return of genetic research results has focused on the actionability of results (Fabsitz et al., 2010; Wolf, 2008). In the context of pediatric genetic research, this has led to the suggestion that genetic research and return of results should not include results related to adult-onset conditions or results related to reproductive planning (Burke & Diekema, 2006; ASHG & ACMG, 1995; Committee on Bioethics, 2001). Our results suggest that despite the potential for negative psychological impacts of receiving results, parents are interested in receiving these kinds of genetic results about their children. They are interested for a variety of reasons beyond near-term clinical utility for an affected child. These reasons include explanation of disease etiology, psychological benefit, and reproductive decision-making in the future for their unaffected children and extended family. These findings are consistent with previously reported interviews of parents of children in autism research, who cited a desire to explain the cause and answer the question "why?" (Miller et al., 2010).

While parents of children with autism and parents of children with diabetes emphasized similar ideas about what influences their research participation, these two groups of parents differed in their interpretation and expectations around the return of individual genetic research results. Both groups emphasized the potential psychological impacts of receiving research results and their perception of clinical, reproductive, and personal utility of results. However, only parents of children with autism talked about results as an incentive for further participation in research about their child's condition, a concept that is most clearly linked to genotype-driven recruitment. Additionally, only autism parents discussed a desire for individual genetic research results for reproductive decision-making for themselves and their family members. These differences suggest that parents of children with different diseases may have different perceptions of the risks and benefits of research participation, return of results, and genotype-driven recruitment.

Some of our findings are similar to those from interviews with adult research participants in the larger genotype-driven research recruitment project (Beskow et al., 2011). Specifically, some adults expressed concerns about potential psychological impacts of results (Cadigan et al., 2011), and some were interested in results for future reproductive decision-making (Namey & Beskow, 2011). This suggests that some of the issues related to return of results in this context may not be unique to parents making decisions about their children's participation, but may also apply to adult research participants in some study contexts.

Best Practices

Pediatric genetic research, like most biomedical research and genetic research in general, is not a one-size-fits-all enterprise. Parents of children with different diseases may differ in their perceptions of the risks and benefits of both participation and individual genetic results, and may differ from parents of healthy children. Researchers may have more involved relationships with participants, such as clinical relationships and long-term research relationships, or less involved relationships, such as for cross-sectional studies. In some situations, a researcher using a genotype-driven approach may be a new investigator with no prior relationship to the participant. These different relationships may translate to a range of obligations to return and communicate findings. Furthermore, the nature of the results driving genotype-driven recruitment, and the nature of the follow-up research studies for which participants will be recruited, are also likely broad and varied in their potential impact (Beskow et al., 2004; Ravitsky & Wilfond, 2006). For these reasons, it is difficult to develop guidelines for genotype-driven recruitment of children that will apply in all situations. However, the findings from this study suggest at least five important factors that should be taken into consideration by researchers and IRBs (Table 3).

First, when discussing the study with parents of potential participants, researchers may need to address possible benefits and risks to a range of different stakeholders beyond the enrolled child (e.g., parents, siblings, future children and generations). This would need to take place at the time of recruitment and consent, both for the original study and any unanticipated follow-up research activities involving genotype-driven recruitment.

Second, researchers should consider the time involved and inconvenience of research participation for parents and families, particularly those with sick children. This requires considering how family structure and disease context might affect parental perceptions of the amount of time available to devote to research and how to balance the child's daily needs with the demands of a research study. In particular, parents may be reluctant to have their child participate in blood draws beyond the scope of clinical care. Concerns about blood draw burdens may be greater for parents making decisions for their children than for adults making decisions for themselves.

Third, our interviews with autism parents suggest that researchers should consider providing training or using staff experienced with children with autism in order to address parent concerns about stress and anxiety for their children and families. Fourth, if individual genetic research results are offered to parents, there should be a clear explanation of the meaning and certainty of the results. Parents expressed the potential for psychological impacts, and a particular interest in receiving genetic results related to their condition that will affect future reproductive decision making. These findings suggest that researchers should consider offering genetic counseling during return of results and the process of genotype-driven recruitment to avoid misinterpretation and possible subsequent harms, at least for some results and in some populations.

Fifth, our findings suggest that offering individual research results as a part of genotype-driven recruitment, even uncertain results, may motivate parents to have their children

participate in future research. This presents a challenge: researchers may feel obligated to return results as part of genotype-driven recruitment, either in the spirit of fully informing families of why they are being contacted, or out of a sense of reciprocity to families in exchange for their time and contribution to the research study. However, researchers will need to avoid miscommunication about uncertain results, or unintentionally pressuring parents to participate by offering results.

There are several important limitations of this study. We interviewed only 23 parents from three pediatric genetic research studies. Our participants varied across studies in ways that may influence perspectives on these issues, such as target research population, study design, relationship with the primary and secondary researchers, as well as the nature of the kind of genetic information that was the basis of the genotype-driven recruitment. Also, given the small sample sizes, it is possible that the participants we interviewed are not representative of the larger population of participants in those studies. Parents of children in other studies or with other diseases, or parents of healthy children, might have different perspectives on these issues. However, this study adds important new data by including participants who participated in studies where genotype-driven recruitment occurred.

Research Agenda

Further empirical research is needed about parent perspectives on recruitment and return of results in pediatric genetic research, and perspectives about pediatric genotype-driven recruitment specifically. It is important to characterize whether and how parents' perspectives differ across disease groups, or between parents of sick children and healthy children. This information will be necessary to develop ethical approaches to these challenges across a range of study contexts and populations involving children. It is also important to learn how adolescents feel about these issues, and whether their perspectives align with those of their parents. Finally, it would be helpful to follow parents who experience genotype-driven recruitment over time, in order to evaluate how they interpret results that characterize the long-term risks and benefits. Many of these issues would be best studied prospectively in pediatric genetic studies in which genotype-driven recruitment either is possible or is actually planned, across a range of disease and healthy populations.

Educational Implications

Researchers, IRBs, and institutions should consider pediatric genotype-driven recruitment as the intersection between two important ethical challenges: research recruitment and return of individual genetic research results. Our findings suggest that parents may consider different factors when deciding to have their children participate in research, which may be specific to their particular disease and the needs of the family as a whole. They are also very concerned about blood draws for their children, although this concern may not by itself prevent them from participating in research. Approaches to recruitment and informed consent will be most effective if they are developed to take these issues into consideration. Our results suggest that parents of children with different diseases have a range of perspectives about the benefits and meaning of results that might be returned. Assessing the hopes and expectations of the target research populations will be beneficial for developing best practices for return of results in general, and in genotype-driven recruitment specifically.

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TABLE 1

Characteristics of Studies.

Name of Study	Study Population	Goal of Study	Description of Genotype-driven Recontact	Number Interviewed
Study of Autism Genetics Exploration (SAGE)	Families with children ages 2–17, diagnosed with autism	Identify genes involved in autism	Parents of children with a potentially causative CNV were given their results. They were then asked to participate in the second phase of the SAGE study.	1 Recontacted 4 Not recontacted
Autism Genetic Resource Exchange (AGRE)	Families with 2 or more children diagnosed with autism	Create an open-access repository of clinical and genetic information	Parents of children with a CNV at 16p11.2 CNV recontacted by AGRE, and then recruited by other research groups to participate in deeper phenotyping/genotyping.	3 Recontacted 9 Not recontacted
SEARCH for Diabetes in Youth	Population-based study of people who were diagnosed with diabetes before age 20	Understand the natural history of diabetes	Parents of children who were either <1 year of age at diagnosis or with residual insulin secretion and negative diabetes autoantibodies, were tested for the known genetic causes of permanent neonatal diabetes or mature onset diabetes of the young (MODY). They were then invited for confirmatory testing and participation in further research.	2 Recontacted 4 Not recontacted

TABLE 2

Study Participant Characteristics.

	<i>n</i>	%
Age: Mean = 49; range = 42–56		
Education		
High school	3	13
Some college	6	26
Bachelor's degree	10	43
Graduate degree	3	13
Missing	1	4
Sex		
Female	20	87
Male	3	13
Race		
Caucasian	17	74
African-American	3	13
Other/Mixed Race	3	13
Recontacted about follow-up study	6	26

TABLE 3**Five Best Practices for Pediatric Genotype-Driven Recruitment.**

1	During research recruitment, address possible benefits and risks to a range of different stakeholders.
2	Consider the time involvement and inconvenience of research participation for families.
3	For autism-related studies, consider providing training or using staff experienced with children with autism.
4	When offering results, provide a clear explanation of the meaning and certainty of results.
5	Avoid miscommunication about uncertain results, or unintentionally pressuring parents to participate in future studies by offering results.