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Parental Perception of Self-Empowerment in Pediatric Pharmacogenetic Testing: The Reactions of Parents to the Communication of Actual and Hypothetical *CYP2D6* Test Results

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Abstract

Concerns about the ethical and social implications of genetics persist as more applications of genetic and genomic technology have become available. Pediatric testing for genetic influences on response to opioids like codeine is one area of application. We interviewed parents of children enrolled in a mixed-methods study following the communication of actual or hypothetical results for *CYP2D6*, which impacts opioid response. Forty-one parents of children naïve to opioids and 42 parents of children previously exposed to opioids participated in qualitative interviews. Findings did not differ by the child's opioid exposure or by actual versus hypothetical results. Parents' responses centered the experience of the parent(s) and the potential impact of that information on the parent, rather than the result's impact on the child. Parents also emphasized that the results did not impact their perceptions of the child, reaffirming that the child was still "normal" regardless of test result. When asked about the impact of receiving secondary results, parents' responses emphasized how the results would impact their ability to advocate for the child or impact their state of mind. While the answers reflect parents' role as surrogate decision maker for their child, they also reinforced concerns that healthcare decisions might be influenced by secondary parental concerns as much as the best interests of the child. Emphasis on the child's "normality" challenges concerns about the impact of genetic essentialism, but further research is required to see whether the type of testing done or the way results were communicated shaped this response.

Keywords

Genetics; Return of results; genetic essentialism; pharmacogenetic testing; incidental findings

The ethical, medical and social implications of genetics have been a concern for medical professionals, patients, and the broader public since the identification of genes at the dawn

of the twentieth century (Condit, 1999). These concerns persist as more applications of genetic technology become available. Communication scholars have examined these concerns in numerous contexts (e.g., Condit, Templeton, Bates, Bevan, & Harris, 2003; Galvin & Grill, 2009; Lynch, Parrott, Hopkin, & Myers, 2011; Silva, 2005). Most studies focus on diagnostic or predictive genetic tests that indicate whether a person has a condition or is likely to develop a condition, but pharmacogenetic testing, which identifies genetic influences on one's response to a drug, is a common form of testing that has received less attention as a health communication phenomenon (exceptions include, Bevan et al., 2003; Condit, et al., 2003; Lynch & Dubriwny, 2006). Furthermore, many studies have only offered *hypothetical* genetic results, and with the advent of research on the return of *actual* results, differences between actual and hypothetical results, if any, require further exploration.

Previous scholarship on genetics has identified the potential to foster “genetic essentialism,” or the belief that genetics influences one's identity, as a danger of genetic testing (Bates, Templeton, Achter, Harris, & Condit, 2003; Dar-Nimrod & Heine, 2011; Parrott, Kahl, Ndiaye, & Traeder, 2012; Parrott & Smith, 2014). This essentialism has been linked to fatalistic attitudes about health outcomes, as well as discriminatory or eugenic attitudes (Bates, et al., 2003; Condit, Parrott, Harris, Lynch, & Dubriwny, 2004; Parrott, et al., 2012). These attitudes typically reflect social norms about desirable physical and mental attributes. While Parrott et al. (2012) included a pharmacogenetics-related item in their scale for measuring attitudes of genetic determinism, Haga, Mills and Bosworth (2014) argue that pharmacogenetics does not seem to foster the discriminatory and stigmatizing attitudes that are the product of genetic essentialism. Whether these attitudes will be produced by pharmacogenetic testing is not clear, but previous studies indicate that lay people might not interpret information about pharmacogenetics in the ways that they interpret information about genetics generally. Public understandings of genetics focus on heredity and not the structural or functional nature of DNA (Condit, 2010). Although genetic testing is meant to identify specific gene differences, the purposes for gathering the information (e.g., determining the best drug or drug dosage versus whether a person will develop a specific medical condition) might alter the degree to which individuals perceive a test as involving heredity and thus the degree to which the test is perceived as genetic. In other words, pharmacogenetic testing might not be perceived as involving heredity and therefore might not activate essentialist attitudes about genes.

Prior studies of communication about genetics have focused typically on adults who are responding to real or hypothetical results about themselves. However, genetic testing may occur in a pediatric context. In pediatric settings, parents are surrogate decision makers for their children until they become adults. Children are not legally allowed to consent to research, although they may be informed about research and concur (or “assent”) to a procedure for which their parent(s) or guardian(s) have offered legal consent (Avard, Senecal, Madadi, & Sinnett, 2011). This creates a “tripartite” relationship between the pediatric researcher or healthcare provider, the parent, and the child. Unlike most adult medical encounters, a pediatric medical encounter might require the researcher or healthcare provider to play a more active role in medical decision-making as a guardian for the child if a parent's surrogate decision-making does not consider the best interest of the child

(Wilfond & Carpenter, 2008). One area where the child's best interests might run counter to parental decision-making is the child's right to an "open future," where a child at some point in the future might not want to know genetic information that has an impact on their health (Wilfond & Carpenter, 2008; Avard et al., 2011). In the context of genetic and pharmacogenetic testing, parents could choose to be informed about their child's results when the child may not want to know them, especially about conditions that appear in adulthood. Parents choosing to receive information about their child's genome and the risks of adult-onset, untreatable conditions could detrimentally impact the child's future ability to make choices about their health information. Bioethicists have raised concerns that parents might choose to learn a child's risk of adult-onset and untreatable conditions in order to help other family members, thus harming the privacy rights and future autonomy of the child in order to benefit others (Avard et al., 2011). Studies suggest that a majority of parents wish to receive genetic results for their children that reveal information about untreatable, fatal, or adult-onset conditions (Fernandez et al., 2014; Tercyak et al., 2011). Additionally, genetic and pharmacogenetic studies might produce incidental findings, or information that was not being sought as part of the study yet has potential health or reproductive significance. While the American Academy of Pediatrics and the American College of Medical Genetics have produced recommendations for a variety of genetic tests, debate continues about which incidental findings to report back to children and parents. Nonetheless, a consensus exists that if a pharmacogenetic test could produce information with implications beyond drug response, these diagnostic or prognostic implications should be discussed before testing (Ross, Saal, David, & Anderson, 2013).

We treat the return of pediatric pharmacogenetic results to parents as a communicative act. Parents will have a range of motivations for agreeing to this communication, and they will respond in different ways to the results provided and the possibility of receiving further incidental findings. The genetic result communicated to parents was an actual or hypothetical result of a test for variants of *CYP2D6*. The *CYP2D6* gene produces an enzyme that contributes to the metabolism of more than 25% of drugs that are prescribed in a clinical setting, such as opioids like codeine (Leppert, 2011). Codeine is administered to children for post-surgical and injury-related pain management, as well as for cough suppression (Kaiser et al., 2014; Williams, Patel, & Howard, 2002). There are more than 80 variants of *CYP2D6* that contribute to a variety of metabolic phenotypes related to codeine metabolism (Leppert, 2011). Pharmacogenetic testing is available for *CYP2D6*, and the results from pharmacogenetic tests can assist in improving drug response and treatment efficacy by informing drug selection/dosing processes (Crews et al., 2014; Relling & Klein, 2011). In what follows, we report on a qualitative study of parents that aimed to (1) assess parental reasons for participating in research involving the return of their child's *CYP2D6* research results, and reactions to the receipt of results (hypothetical or actual), and (2) explore their responses to hypothetical incidental genomic research results.

Materials and Methods

Participants

Participants were parents of children who were enrolled from two pediatric hospitals, under a protocol approved by IRBs at both institutions. Parents enrolled from Cincinnati Children's Hospital Medical Center (CCHMC) were part of a larger mixed methods study consisting of parents whose children were previously enrolled in one of three protocols in which stored DNA was accessible for further research. After the stored DNA samples of the participants' child were genotyped for *CYP2D6*, the *CYP2D6* research results were disclosed by phone at a pre-arranged time. Following the return of their child's result parents were asked to complete a telephone survey. At the close of the survey, a subset of parents was asked to participate in a qualitative telephone interview to gain an in-depth understanding of their reactions to their child's *CYP2D6* results, as well as hypothetical responses to incidental results. Parents had the option of completing the interview immediately after the survey was completed, or they could schedule the telephone interview during the two weeks after the return of results. Half of these parents had children who were naïve to opioid (controls), and half had children who were previously exposed to opioids (cases). Parents were provided a \$10 incentive after completing the interview.

Participants enrolled from Boston Children's Hospital (BCH) consisted of parents of children who were previously enrolled in another study at BCH in which DNA samples were studied. However, because *CYP2D6* testing was not approved for use at BCH, this study was conducted using return of hypothetical *CYP2D6* results. Parents were told that they would receive a hypothetical *CYP2D6* result for their child and would then be asked to complete a telephone survey and to base their answers on the hypothetical result. A subset of parents were also asked to participate in a qualitative telephone interview to gain further knowledge about their reactions to the results, had the results been actual *CYP2D6* results. Here we report the findings from the qualitative portion of our dual-institution mixed methods study.

CYP2D6 Pharmacogenetic Test/Results Disclosure

Samples from CCHMC participants' children were assayed in the CLIA-approved and CAP-accredited CCHMC clinical molecular genetics laboratory. The laboratory returned genotypes in standard “* allele” nomenclature to a research team member (CP) who interpreted the genotypes and assigned predicted metabolizer phenotypes (i.e., how the person would metabolize codeine) using recommendations from national guidelines (Crews et al., 2014).¹ The same team member returned the research results to participants. Result-specific scripts were used to assure consistency in messaging. Scripts were formatted to indicate metabolizer status by using descriptive language indicating whether the child would experience an analgesic effect from a normal dose of codeine (a common opioid in pediatric settings) and whether the child was at normal or increased risk for side effects from a normal dose of codeine. Using an online randomization program, BCH participants were randomly assigned to one of three results phenotypes. This phenotype result was then returned to

¹Descriptions of metabolizer statuses and distribution of actual and hypothetical metabolizer statuses in the sample are available upon request from the corresponding author. Descriptions of hypothetical metabolizer statuses used in the study are also available upon request from the corresponding author.

participants in the same manner as at CCHMC using the same result-specific scripts for consistency, and was used as a basis for survey and interview responses.

Data Collection

The qualitative interview guide questions aimed to develop an understanding of the reasons, expectations, and perceptions that shaped parents' participation and attitudes towards their child's research results. Questions were open-ended, and they addressed reasons for participating, reactions to results, perceived benefits of hypothetically receiving incidental findings, and perceived harms of hypothetically receiving incidental findings. Three CCHMC interviewers and two BCH interviewers were trained to conduct interviews using the qualitative interview guide and encouraged to use impromptu probes to elicit participant elaboration on the issues discussed. Interviewers underwent training including practice interview sessions over a two week period prior to interviewing participants. Interviews were audio recorded, and the recordings were transcribed verbatim by an outside transcriptionist at CCHMC and a research team member at BCH.

Data Analysis

Codes were initially identified by the research team at CCHMC, both inductively based on a reading of 20% of the transcripts and deductively based on issues raised in the literature or by members of the research team. Codes were added as new issues were identified in subsequent interview transcripts. Coding was conducted at CCHMC using ATLAS.ti (Version 7.5, ATLAS.ti Scientific Software Development GmbH) by two coders who were trained to apply codes according to the code guidebook.

Inter-rater reliability was established after both coders coded the first 13 transcripts, and the first 20% of transcripts were used to calculate Cohen's kappa in which a 0.60 cut-off for agreement was used. Cohen's kappa was determined to be 0.670 for Reasons for Participating, 0.660 for Reactions to Results, 0.773 for Perceived Benefits of Hypothetical Incidental Findings, and 0.741 for Perceived Harms of Hypothetical Incidental Findings, which all indicated substantial inter-rater reliability. After inter-rater reliability was established, coding was reviewed by the second coder (JL) every 5 transcripts to monitor consistency in code application.

Coding was then reviewed by the research team to identify any themes that cut across the coding categories. Themes were confirmed using researcher triangulation where members of the research team individually identified potential themes, and the final themes were determined by consensus (Denzin, 1970). The CCHMC coding guide was then used in the coding of interviews completed at BCH. All interviews were coded by two BCH study staff members. Codes were then compared and disagreements were resolved by consensus for each transcript.

Results

Sample Characteristics

A total of 83 participants were enrolled in the study (Table 1). Interviews at CCHMC ran from five to 27 minutes, with an average duration of 11:06, and interviews at BCH ran from four and a half minutes to twenty-five minutes, with an average duration of 9:35. The forty-one parents in the control group had children who were naïve to opioids (i.e., they had never been given an opioid-based medication): Thirty-one parents at CCHMC received an actual *CYP2D6* result for their child, and ten parents at BCH received a hypothetical *CYP2D6* result for their child. The forty-two parents in the case group had children who were previously exposed to opioids (i.e., they *had* been given an opioid-based medication): Thirty parents at CCHMC received an actual *CYP2D6* result for their child, and twelve parents at BCH received a hypothetical *CYP2D6* result for their child. No major differences were seen between case and control groups regarding participant characteristics or coding and themes across transcripts. The majority of participants were mothers (n=78), of whom four identified as “adoptive mother.” Most identified solely as white (n=77), had four or more years of college (n=59), and had incomes of more than \$74,999 (n=49). Additionally, all participants had health insurance, and nearly half of the parents involved in this study identified with working in healthcare, healthcare-related industry, or in biomedical research in the past (n=38).

Reasons for Participating: Health Empowerment, Altruism, and Trust

Participants identified a range of reasons for participating in our study and receiving actual or hypothetical research results, but the most prevalent responses thematically emphasized *health empowerment* either through increased health knowledge or through making better health decisions. This theme captures two codes: learning about health and helping their child. “Learning about health” was the most common reason coded for participation (n=48), although at BCH this reason was hypothetical in nature. One parent stated, “I just think it’s a better awareness of his health. He has to acknowledge that anything he takes, even if he thinks he’s got a headache that everything interferes with your body. It’s all chemicals, and changes happen” (74). ‘Helping their child’ was identified as a reason for participation by more than one-third of participants (n=35), the majority of whom came from CCHMC due to the hypothetical nature of result return at BCH. Parents indicated that the information they received will help them make medical/health decisions for their child. For example, one parent stated, “There’s always new treatments and everything coming out through the course of his life that something we had done, say, to see his genetic makeup. That could possibly make a difference in his future treatment” (84). This is consistent with previous studies that have found that parents consent to genomic research for reasons related to helping their child or learning about their child’s health (e.g., Burstein, Robinson, Hilsenbeck, McGuire, & Lau, 2014).

While the most prevalent reasons for participation centered on empowering parents to improve their child’s health, three other reasons were raised. The first two of these reasons are primarily *altruistic*. Twenty-eight parents discussed contributing to research as a reason for why they participated in this study. One parent stated that, “Anything that would research

into why people react the way they do is valuable” (24). Sixteen parents identified helping others as a reason for participating. Parents who articulated this reason often stated simply, “I wanted to help” (10). Parents receiving hypothetical pharmacogenetic results instead of actual pharmacogenetic results were more likely to offer altruistic reasons. A final reason for participation was trust in the institution. Eleven parents discussed that they participated specifically because of CCHMC or BCH, whether it was because of clinical care or the institution’s research profile.

Perceived Normality

When asked about their reactions to the research results, parents offered reactions that were coded into nine different categories. The first theme drawn from these reactions was an emphasis on the child’s perceived normality, characterized either as *my child is medically normal* or *my child is socio-culturally normal*. *My child is medically normal* reflects parents’ recall of the results returned (i.e., whether their child was able to break down codeine into morphine, and whether codeine was likely to work for them) and their statements that the test results do not indicate the child’s treatment for pain should be changed. One parent, when asked to describe their understanding of the results, said, “He would be OK to get a normal dose of pain medication; that he should react the way the medicine is meant to react” (34). Another parent said, “From what I understood of the way it was explained to me... he can take pain medication, and it’s not going to affect anything [negatively]” (28).

My child is socio-culturally normal characterized responses to questions about the meaning of the results for the child and influence of the results on parent-child interactions. The majority of remarks coded under ‘changes nothing’ (132/153) fits into the second theme of “the child is socio-culturally normal.” For example, one parent stated, “I’m not gonna look at him any different because he can’t take codeine” (52). Another parent said “I don’t think she would view herself as any different than any other kid just because her body doesn’t process a drug the same way. It’s not visible *per se*” (111). Another parent said “I feel fine. I’m glad to know ‘em, but they’re not gonna change the way I do anything” (38). Parents indicated the test results will not change how they view their child or how their child views himself or herself, indicating that “normalcy” did not reduce to genetic essentialism.

Parents’ Emotional Appraisal Filtered by Expectations

The second theme about parents’ reactions to results was *parents’ emotional appraisal filtered by expectations*: parents’ reactions were shaped by their expectations when they consented to participate in this study. There was substantial overlap among the codes constituting this theme, which were not mutually exclusive. Parents articulated multiple, sometimes conflicting, expectations. For example, because the return of pharmacogenetic results was outside of their experiences, many participants who received actual results for their child indicated that they had no prior expectations (n=40), but then identified a specific reaction or expectation they had. For example, one parent stated,

I don’t know that I had any true expectations. I wanted to learn as much as possible, and when they said that they were gonna do a gene study to find out how [my child] might react to some medicines, I was interested in finding out what the results of

that might be so we don't give him medicines that aren't effective, things that aren't gonna work. I didn't really have any expectations, because I didn't know what to think about it.

This parent indicated her lack of experience with pharmacogenetic testing meant she did not "know what to think" about it, but she also was curious to learn more about her child's reactions to medication so that she could use that information in the future.

For those receiving actual results, a few (n=6) described the result as expected/unsurprising. For these parents, their child's previous experience with pain medication predisposed the parents to expect a certain type of result, which they in fact received. For example, one parent said "I think it was pretty much what I expected to learn. I think I kind of understood what they were looking for when they were doing the research, and I had seen the way my son responded with the medication they had given him" (32). Out of the six parents who were not surprised by their child's *CYP2D6* results, four children received results indicating a normal dose of codeine should work to lower pain, and the other two children could partially metabolize codeine and a normal dose of codeine might lower pain.

Eight parents expressed surprise toward their child's research result in terms of the amount of information and the degree of detail in the results. One parent said, "I wasn't expecting anything, and the fact that they had specific details about my child and what her body can handle and what it couldn't was kind of a surprise" (121). Twenty-seven parents expressed that the information was interesting, and two parents expressed worry toward the research result in terms of what the information indicated about their child and health or pain management issues that might arise. One parent said "I guess a little bit worried... I don't know if it's good knowing ahead of time and worrying yourself and worrying them" (005). The amount and detail of the information provided led to surprise, interest and worry for parents.

Three parents expressed that they wanted to seek information in addition to the actual results they received, and seven parents who received hypothetical results imagined they would seek more information if the results they received had been actual results. Of the three who received actual results, two of the parents discussed wanting to seek additional information about their child's risk for disease, and the other parent discussed wanting further information to give to the child's physician. In terms of wanting information about the child's risk for disease, one parent said, "I was interested in finding out about different diseases, if he would be at risk for anything, either now as a childhood disease or further on down the road as an adult" (081). The parent who discussed wanting further information for the child's physician said they wanted to seek "more information that I could give a pediatrician or something down the line if he were to require pain medication" (010).

Impact of Hypothetical Incidental Findings Centered on Parents

Parents' responses to questions about the benefits and harms to their child of possibly receiving incidental research findings focused on how the parents would react to that knowledge. In terms of benefits, parental responses emphasized a theme of *enabling*

proactive responses to potential health threats (n=74, including all 22 BCH participants). For example, one parent stated,

Knowing what could be coming, whether it's treatable or untreatable at that particular moment in time, is going to be a benefit to the parents and to the child's pediatrician, potentially, so that you can be on the lookout for symptoms and catch those much earlier than maybe you would otherwise. (124)

Four codes were covered by this theme. A benefit for the parents that was identified by 28 parents from CCHMC and 17 parents from BCH was making better decisions. One parent noted, "In some instances, it would give you choices about what to do and even if there isn't anything you could do, you would at least be sort of forewarned" (17). An additional thirteen parents discussed the ability to advocate for the child in future medical encounters. In each case, the receipt of information or the ability to use it as the basis for advocacy or decision making was viewed as a benefit because it enabled proactive responses by the parents to potential health threats.

Parent's consideration of potential harms framed those potential harms as *harm to the parent's mental or emotional well-being*. Over three-fourths of parents identified stress or anxiety as a potential harm (n=64). One parent described the harm related to incidental findings, stating, "The worry, the fear, if you let it take over your life, if you're one of those types of individuals who will sit there and dwell on the negative, as opposed to figuring out how to handle it" (19). Another parent worried that they could be "shunned by their family for sharing a genetic result [that affected the family] that they didn't want to know." Sixteen parents expressed that receiving results related to an untreatable disease could be a harm. For example, one parent stated, "If it were something that's untreatable and incurable and maybe is happening later on in life, I don't think that I would like to know that. I think it would be too much information, and I would worry about it all the time" (52). Nine parents stated that unanticipated environmental or genetic factors could alter the value of incidental findings. As one parent stated, "You might think that you could get a disease and you could think that you're gonna get it through your whole life and never get it" (100). For this parent, an incidental finding of a predictive, rather than pharmacogenetic, value could result in a lifetime of stress and worry, especially if other environmental or genetic factors altered the outcome. The one exception to this theme was concern about insurance: 11 parents were concerned that a hypothetical positive incidental finding could impact the family or child's ability to get some type of insurance in the future.

Discussion

Across all the questions reported here and across the conditions of receiving actual and hypothetical results, parents offered opinions and raised concerns about the return of pharmacogenetic tests and the possibility of receiving incidental findings in the future that centered the experience of the parent(s) and the potential impact of that information on the parent. They agreed to participate because the health information might empower the parent to advocate for or help their child. Many of the parents' claims about their child's perceived normality reinforced the information provided during the return of *CYP2D6* test results, but some parents also extended claims about normalcy beyond "normal doses of codeine" to

make claims about their child's socio-cultural normalcy. When asked about potential harms and benefits to their child caused by incidental findings, parents reframed the issue as either an impact on their ability to respond proactively to health threats or an impact on their state of mind. On the one hand, the focus on parental experiences is not surprising since parents have an obligation to make healthcare decisions for their child, which can produce a psychological burden. Parents would naturally have their obligations as surrogate decision makers in mind when considering the return of results about their child. Parent's emphasis on being proactive in choosing to receive these results and thinking proactively about hypothetical future results suggests they are considering the utility of this information. On the other hand, this focus on the parents' experiences reaffirms concern about the "tripartite relationship between researcher, child, and parent(s)" (Avard, et al., 2011, p. 593). The tripartite relationship raises concerns that parents might impair their child's future autonomy and decision-making by receiving genetic information about their child that would be relevant only later in life (e.g., *APOE4* variant status, which can increase risk for Alzheimer's disease), or access genetic information about their child in order to benefit the *parent's* own health and reproductive decision-making rather than directly benefiting the child (Avard, et al., 2011; Wilfond & Ross, 2009). While our study cannot offer any solution to the tensions raised in pediatric clinical and research situations, it reinforces that the tripartite relationship must be accounted for when clinicians and researchers return pharmacogenetic results and should be kept in mind for pediatric health communication generally.

Parents' overall focus on treatment and helping their child might reflect how the results were returned to them. Genotype information was not used to explain the results; rather results were discussed in terms of actionability and what types of medication like codeine could or should not be prescribed to a child. This partly reflects how pharmacogenetic test results are provided at CCHMC, where test results emphasize whether changes in medication, dosing, etc., are required. Previous studies have shown that when parents receive positive genetic testing results related to disease predisposition or diagnostic genetic testing, they have more anxiety and show more concern for their child (Grosfeld, Beemer, Lips, Hendriks, & ten Kroode, 2000; Lalatta et al., 2010). However, there are significant differences between pharmacogenetic testing and predisposition and diagnostic testing. Predisposition and diagnostic testing has the potential to provide more life-altering information, regarding issues like life expectancy or what to expect from the natural history of a disease, and predisposition and diagnostic testing clearly invokes concepts about heredity and the familial implications of genetic conditions. Pharmacogenetic results may inform drug selection or dosing for participants and are only relevant if a patient needs specific medication. Lay people may not perceive these results as involving heredity or having familial implications. Although these types of clinical testing are different, they are similar in that they are both providing health information to parents regarding their child.

Although there is evidence in the literature about "genetic essentialism," or the belief that genetics influences one's identity (Dar-Nimrod & Heine, 2011; Parrott, et al., 2012; Parrott & Smith, 2014), the parents in our study results did not regard their children differently based on *CYP2D6* research results. The majority of parents emphasized that test results would not alter their behavior toward their child or their child's attitudes toward themselves.

Many parents conveyed that the results changed nothing or described their child as “fine” regardless of the specific *CYP2D6* pharmacogenetic result they received for their child. When asked about meaning of the results for the child or how the results would affect interactions with the child, some participants answered with responses related to the child being “medically normal.” One parent mentioned the genetics result being “normal.” Within *CYP2D6* pharmacogenetic testing, many parents interpreted (or understood) their child as socio-culturally normal if the test results indicated no change in how the child would receive medication or indicated no increased risk of side effects.

Parents’ emphasis on proactive empowerment and their assertion that their children were “fine” regardless of the specific result received offers interesting possibilities regarding the communication of genetic, genomic, and pharmacogenomic test results that should be addressed in future research. Specifically, was the reduced expression of genetic essentialism a result of *test type* or *how test results were communicated*? It is possible that pharmacogenomic testing does not raise issues of genetic essentialism in the same way that other types of clinical genetic tests do, in part because the test’s focus on changing the prescription of pharmaceuticals does not fit the lay conception of “genetics.” The differences in test type might have been on the minds of parents who said that possible incidental findings could be misconstrued as implying an unwarranted genetic determinism and ignoring environmental and lifestyle risk factors that influence health outcomes. Yet, it is also possible that expressing results in terms of *actions to be taken* mitigated any potential increase in parents’ genetic essentialism. The communicative acts of returning disease-focused genetic test results and returning pharmacogenetic tests results should be compared to identify how undue genetic essentialism as well as general anxiety about health outcomes might be reduced in these contexts.

Finally, one major exception to the focus on parental concerns, mindsets, and actions appeared when parents raised the topic of insurance. Eleven parents discussed that they had concerns about how insurance companies might view or use the information from an incidental finding to the detriment of themselves or their child. Parents discussed “insurance” generically, except for one parent who identified life insurance, so it is not clear what types of insurance coverage were meant. It is possible that parents feared an impact on their child’s ability to get health insurance, despite the 2008 Genetic Information Non-Discrimination Act (GINA). A recent study has shown that with regard to receiving incidental findings, parents consider their own and/or child’s ability to receive insurance in the future (Fernandez, et al., 2014). Although ability to receive insurance was an issue to consider, parents still showed great interest in receiving incidental findings (Burstein, et al., 2014; Fernandez, et al., 2014). Other studies have also found that even when incidental findings and/or secondary findings are a possibility within genetic testing for children, parents show great interest in receiving those results even when other concerns are presented (Levenseller et al., 2014; Sapp et al., 2014). Future research could examine the specific types of insurances that parents are concerned about, and if health insurance is identified as a concern, then future public outreach should reaffirm the protections provided by GINA.

Two notable limitations to our study exist. First, there is the fact that our study examined the return of pharmacogenetic results within the context of pediatric *research*, rather than

pediatric clinical care or direct-to-consumer genetic testing. Pediatric research has requirements for consent, the balancing of risks and potential benefits, etc., that differ markedly from clinical care and commercial direct-to-consumer genetic testing. The difference in context might influence parents' responses.

A second limitation is the demographic homogeneity of the research participants. Parents were predominately well-educated white mothers from households with incomes well above the national average. Additionally, nearly half of the participants in this study previously worked in healthcare, a healthcare-related industry, or in biomedical research. Parents' work experience could influence their knowledge and attitudes about pharmacogenetic testing, as well as their willingness to participate in the study. Parents' race could mean that issues of trusting healthcare professionals and medical research are not as salient as they are for non-white parents in the United States. Parents were more educated and wealthier than the population in many studies regarding reactions to genetic testing. Those advantages of wealth and education might allow them to process information related to the pharmacogenetic results in ways that minimize attitudes or beliefs, like genetic essentialism, that could be detrimental to making health decisions on behalf of their child. Although access to resources could reduce anxiety for pharmacogenetic results, some parents still expressed concerns such as anxiety for some types of hypothetical incidental findings that were disease-focused.

Future studies should try to expand the racial, gender, educational, and socio-economic diversity of the research participants. Future studies could also examine claims about the child's medical or social normalcy to identify any interaction or overlaps between the claims and how they might impact the reception of future genetic and pharmacogenetic results. Finally, as noted earlier, parental concerns about insurance should be examined further, especially with a more diverse sample whose access to health insurance might be limited, to see how those concerns are discussed.

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Table 1**Demographic Information**

Demographic Characteristic	CCHMC Cases n=30	CCHMC Controls n=31	BCH Cases n=12	BCH Controls n=10	Total (n=83)
<i>Parental Identity</i>					
Biological Mother	26	31	9	8	74
Biological Father	2	0	2	0	4
Adoptive Mother	2	0	1	1	4
Adoptive Father	0	0	0	0	0
Legal Guardian	0	0	0	1	1
<i>Age</i>					
20–29	0	0	0	0	0
30–39	13	3	2	1	19
40–49	12	16	5	4	37
50 and up	5	12	5	4	26
<i>Race/Ethnicity</i>					
Black or African-American	1	0	0	0	2
White or Caucasian	25	31	11	10	77
More than one race	0	0	1	1	2
Other	4	0	0	0	4
<i>Education</i>					
High school graduates or have their GED	3	8	0	0	11
Some college or a 2-year degree	8	4	1	0	13
4-year college graduates	13	15	6	6	40
More than a 4-year college degree	6	4	5	4	19
<i>Income</i>					
Unknown	0	1	0	0	1
Refused to share	1	7	0	0	8
Less than \$25,000	2	1	0	4	7
\$25,000–49,999	3	3	1	0	7
\$50,000–74,999	3	7	1	3	14
\$75,000–99,999	9	4	3	3	19
More than \$100,000	12	8	7	3	30
<i>Employment</i>					
Employed	23	19	9	7	58
Unemployed	7	12	3	3	25
Worked in healthcare, healthcare related industry, or in biomedical research in the	14	16	4	4	38

Demographic Characteristic	CCHMC Cases n=30	CCHMC Controls n=31	BCH Cases n=12	BCH Controls n=10	Total (n=83)
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