Title
Maternal Perspectives on the Return of Genetic Results: Context Matters

Journal
American journal of medical genetics. Part A, 161(1)

ISSN
1552-4833

Authors
Lakes, Kimberley D.
Vaughan, Elaine
Lemke, Amy
et al.

Publication Date
2012-12-13

Peer reviewed

Published in final edited form as:
Am J Med Genet A. 2013 January ; 161(1): 38–47. doi:10.1002/ajmg.a.35673.

Maternal Perspectives on the Return of Genetic Results: Context Matters

Kimberley D. Lakes[1], **Elaine Vaughan**[1], **Amy Lemke**[2], **Marissa Jones**[1], **Timothy Wigal**[1], **Dean Baker**[1], **James M. Swanson**[1], and **Wylie Burke**[3]

[1]Orange County Vanguard Center for the National Children's Study, Department of Pediatrics, University of California, Irvine; Irvine, California 92617; United States of America

[2]Institute for Health and Society, Center for Bioethics and Medical Humanities, Program in Genomics and Ethics, Medical College of Wisconsin; Milwaukee, WI 53226; United Stated of America

[3]Department of Bioethics and Humanities, University of Washington; Seattle, Washington 98195; United States of America

Abstract

The objectives of this study were to study maternal preferences for the return of their child's genetic results and to describe the experiences, perceptions, attitudes and values that are brought to bear when individuals from different racial and cultural backgrounds consider participating in genetic research. We recruited women with diverse sociodemographic profiles to participate in seven focus groups. Twenty-eight percent of participants self-identified as Hispanic; 49% as White, Non-Hispanic; and 21% as Asian or Asian American. Focus groups were conducted in English or Spanish and were audio-recorded and transcribed verbatim. Transcripts were analyzed using qualitative thematic methods. Results indicated that preferences and decisions regarding the return of results may depend on both research and individual contextual factors. Participants understood the return of results as a complex issue, where individual and cultural differences in preferences are certain to arise. Another key finding was that participants desired an interpersonal, dynamic, flexible process that accommodated individual preferences and contextual differences for returning results. Our findings indicate a need to have well-developed systems for allowing participants to make and change over time their choices regarding the return of their child's genetic results.

Keywords

genomic; genetic; research participation; return of results; context

INTRODUCTION

Rapid progress in the field of genomics has raised expectations that future research will radically change our understanding of health and disease, leading to major improvements in health and medicine by combining clinical experience, evidenced-based research and genomics-enabled approaches [e.g., Green et al., 2011; Borry, Evers-Kiebooms, Cornel, Clark, and Cietrickx, 2009]. An important step towards the promise of personalized

*Corresponding author: Kimberley D. Lakes, Ph.D., Assistant Professor, Department of Pediatrics, University of California, Irvine, 101 Academy Way, Suite 150, Irvine, California 92617, klakes@uci.edu.

The authors reported no conflicts of interest related to this study.

medicine is to develop a best practices approach to sharing genomic information [Caufield et al., 2008; Forsberg et al., 2009; Bookman et al., 2006; Fernandez et al., 2003; McGuire et al., 2008; National Institutes of Health, 1993].

Guidelines regarding the return of individual results in genetics research emphasize the clinical relevance and actionability of findings [Fernandez et al., 2003; National Institutes of Health, 1993; Wolf et al., 2008; Fabitz et al., 2010; Pociot et al., 2010; Hebebrand et al., 2010; Wilfond and Ross, 2009; Schulze, 2010]. However, some experts argue that personal preferences should determine which results are returned, rather than expert opinions of clinical relevance [Ravitsky and Wilfond, 2006; Kohane and Taylor, 2010], and evidence seems to suggest that parents and other potential participants in genomic studies overwhelmingly desire individual-level results [Kohane and Taylor, 2010; O'Daniel and Haga, 2011]. Currently, there are no consistent minimal suggestions for what information should be reported to participants in a genomic research study; how and when to disclose results [e.g., McGuire et al., 2008; Fabitz et al. 2010; Beskow and Burke, 2010; Bredenrood et al., 2011; National Academy of Sciences, 2006; Powell, Dunwoody, Griffin, and Neuwirth, 2007]; or what are necessary and sufficient decision-making criteria to be used by individual researchers, institutional review boards, or other regulatory bodies [Caufield et al., 2008; Kohane and Taylor, 2010].

Questions about how to return individual results are especially significant when vulnerable groups (e.g., children) participate in genomic research. In discussions about the return of results in pediatric genomic studies, often assumptions or claims are made about the potential psychological harm or psychosocial risks associated with receiving different types of individual findings within a research environment. Empirical research is needed to provide a broader basis for understanding possible benefits as well as harms of disclosure [e.g., LaKind et al., 2008].

THE PRESENT STUDY

In various parts of the world, large national efforts are underway to develop biobanks that include children's data [Hens et al., 2011]. In the US, the National Children's Study (NCS) is an example of such population-based, pediatric health research. This multi-site, observational, longitudinal study plans to examine the effects of environmental and genetic influences on the health and development of children across the United States, following them from before birth until age 21 years. Studies like the NCS have tremendous potential for research that will help society better understand, prevent, and treat childhood disorders, but appropriate guidelines and models for research practices, particularly related to informed consent and possible disclosure of different types of individual genetic results, are needed [Hens et al., 2011; Samuel et al., 2008]. Here we report on results from research conducted during the Vanguard (i.e., pilot) phase of the NCS at the University of California, Irvine (UC Irvine) Orange County Vanguard Center.

METHODS

Study Sample and Recruitment

The Institutional Review Board of the University of California, Irvine approved this study. Women (ages 18–49 years) were invited to participate in focus groups conducted in seven socioeconomically diverse cities in Orange County, California. We intentionally recruited women who were not eligible for the National Children's Study due to their geographic location (to avoid placing an additional burden on communities that would be approached and asked to participate in the NCS), but who would be representative of the communities selected for participation in the NCS in Orange County [for a description of the household

probability sampling methods used to identify NCS segments, see Montaquila et al., 2010 and Baker et al., 2011]. The Orange County Vanguard Center community outreach team worked with community partners to distribute study flyers targeting mothers or expectant mothers in the selected communities. Interested women who called the study center were read a description of the study from the IRB-approved study information sheet, provided verbal consent to participate, and were enrolled via telephone. The self-identified racial and ethnic groups with which women identified (see Table I) approximated the racial/ethnic and socioeconomic diversity of the Orange County population.

Data Collection

Trained moderators facilitated seven groups using a focus group guide, which included nine core questions (see Supplement Ain Supporting Information online), some of which related to participation in genetic research and preferences regarding return of results. Results from other focus guide content areas (e.g., issues related to informed consent and perceived risks and benefits) have been reported previously [Lakes et al., 2012] and are not included here.

Each group consisted of around 10 participants, and the total number of participants was rounded down to 50 in accordance with the NIH rounding rule for the NCS, which requires that publications round the number of participants to the nearest 50. Two groups were conducted in Spanish by Latina facilitators. At the beginning of each focus group, the facilitator described the study, reviewed the IRB-approved study information sheet, and asked for verbal consent to proceed with the study. Participants were also asked to complete a demographic questionnaire and received $35 in cash at the completion of the group discussion. All focus groups were 90 minutes in length.

Analyses

Focus groups were recorded and transcribed for analysis. Spanish focus groups were translated into English prior to analysis. Qualitative thematic methods [King, 1998; Crabtree and Miller, 1999] were used to analyze the transcript data. Groups were analyzed throughout the study, and investigators stopped recruitment for new focus groups when theoretical saturation was achieved. Three investigators read transcripts together and developed initial coding schemes that represented themes that emerged in the discourse about return of individual results in a genomics or genetic research investigation. Subsequently, these investigators independently coded the transcripts and then met to review and discuss codes. Agreement on codes was tallied and used to compute inter-rater reliability: across the seven groups, the three researchers achieved between 95 and 99% agreement in their codes and identification of themes. Themes related to the return of results are reported in this manuscript. Descriptive data from the brief demographic questionnaire were analyzed using SPSS.

RESULTS

A common question across all focus groups was whether or not findings from genetic studies would be returned to individual participants. There was disagreement among participants about which results they would want to receive, particularly when it came to genetic testing. Some participants wanted all results, while others stated that they did not want any of the results. As participants discussed issues related to the possible provision of individual genetic or genomic results, they often referenced and inquired about procedures that would be associated with the results reporting protocol (for example, some wanted to know if a psychologist would be providing the results, particularly if they were perceived by the participant as negative), and referred to personal life circumstances, past experiences and other broader criteria to anticipate their decisions about and potential impact of the

information. The discussion revealed the following themes (see Table II for a summary of themes).

Theme 1: Preferences and decisions regarding return of results may depend on research context, particularly the nature of the results available and the implications for prevention or treatment

Preferences for the return of results were not equivalent for different research contexts. Some participants qualified their possible choice about the return of individual results and indicated that decisions would depend on specific circumstances, such as the nature of the disease studied or implications for quality of life. They struggled to answer the question about which findings they would want to receive, stating that in some cases they would want to know, and in others they would not. Often discussions about whether receiving individual-level genetic or genomics results would be desirable referred to hypothetical characteristics of the study that would factor into decisions to receive a child's genetic information. For example, in one focus group that included only Latina mothers, when considering the possibility of receiving individual genetic results about a child during pregnancy, before making a decision to receive individual results, participants wanted to know what type of follow-up provisions might be included in the study's procedures to educate participants about the meaning of the reported findings. For results with perceived medical or clinical significance, participants wanted to know if the research procedures regarding the return of individual findings would include a *"type of program… where the parents would get ready for when the baby arrives and know how to treat him and where to consult."* There was general agreement on these points. In another group, when considering whether individuals would or would not participate in the research or elect to receive individual results, some participants inquired about whether the research design presented an explanation at the time of informed consent about what they could expect to learn if they chose to receive individual results. Participants believed that features of the research protocol could potentially influence the emotional impact of any findings that were disclosed.

The nature of the result itself and its implications for prevention or intervention were seen as important considerations in deciding whether or not to receive the result—Participants mentioned several factors that could influence their decision about whether or not they would want to be informed of particular genetic results. For example, if a child had a particular genetic marker for a disease that was preventable, many participants wanted to know so that they could take additional steps to prevent the disease (e.g., "*I want to know cause* [short for "because"] *if there is a prevention for certain things I would take every step to prevent it. I think it's really important. When I was pregnant, I had full genetic testing done because we wanted to know what our situation was.")*

Participants also stated that researchers should communicate results when there was a particular level of risk, but noted that it was difficult to determine where to draw this line, especially if there was no known prevention [Supplement B (OSB), Q1 in Supporting Information online]. However, other participants still did not want to know the results because they stated that they believed they should take preventive measures regardless of genetic risk [OSB, Q's 2, 3].

Mothers differentiated between receiving results for themselves and results for their babies—Participants often responded to questions (addressing both participation in genomic research and preferences for return of individual results) by asking for clarification regarding whether or not the researcher wanted a response based on the

mother's preferences for herself or her baby, noting that in many cases, their answers for the two would be different. In every case when a participant described differences between preferences for herself and her baby, she indicated that she would be more likely to request more results for herself.

Perceived benefits of results reporting and reactions to procedures for storing samples for later analysis could impact decisions about the return of results—Generally, participants viewed the potential return of results as a significant benefit of participation. In the NCS, not all information collected will be analyzed immediately; many samples will be stored in a repository for future analysis. Therefore, the moderator asked participants to discuss their thoughts about this as it would limit immediate return of results. Several participants stated that they understood that this might be part of the study and would not affect their decision to participate, as they understood the potential future benefit [OSC, Table III].

Participants in other groups that included women who had less formal education and were from households with lower income levels expressed a strong expectation to receive all results and were less open to the idea of storing samples for future use. This perspective was especially prevalent in groups that included Latina participants, where return of individual results was seen as a significant incentive to participate in a genetic study. Discussions revealed that some individuals believed that as a participant in a genetic study, they retained some form of ownership over or psychological investment in biological samples provided. For example, several mothers expressed expectations for future personal access to genetic samples or information if a health situation arose with the child where knowledge of certain genetic findings would be useful [OSB, Q4]. Some participants wanted to know about all possible studies that would be done in the future with their baby's sample and the security measures that would be employed to avoid mishandling or misuse.

Theme 2: Preferences and decisions regarding return of results may depend on individual contextual factors, including knowledge, experience, personality, emotion, and resources

Preferences for the return of results were not equivalent for different individuals. Some participants qualified their possible choice about the return of individual results and indicated that decisions would depend on individual circumstances, such as predispositions toward anxiety or the availability of social resources. Participants also described how timing could impact their decisions, describing how certain times could increase emotional risk (e.g., during pregnancy) as well as how life experiences could change their preferences.

There is significant variability among mothers in the perceived risks and benefits of the return of results, and differences are related in part to individuals' subjective reactions to and knowledge about family disease or medical history and prior experiences—Preferences for return of individual-level results in genomic research were rarely discussed in isolation of family history of disease and health, prior emotional reactions to particular disease experiences within the family, or prior beliefs about personal or family vulnerabilities to particular diseases and interfamilial relationships. Many participants referenced these factors when asked to consider how they would decide, if offered the choice, whether to receive various types of genetic or genomic information during the course of a study. For some participants, when there were known genetic risks for disorders in their families, obtaining genetic testing results was seen as a potential benefit of the study [OSB, Q5]. However, there was not agreement on how family history would influence decisions to receive and the impact of individual results, and one participant described how even within her family, individuals varied greatly in their preferences for what genetic testing results they would want [OSB, Q6].

Current life circumstances, including access to economic, healthcare and other resources, and beliefs about personal control over life events and outcomes, may attenuate or amplify potential harms of information disclosure and influence decisions to receive results—In focus groups that included participants from high-income households and with high levels of formal education, discussions about the anticipated impact of receiving individual genetic results for a child, and the perceived importance of having this option offered during a study, referred to alternative means of obtaining this information outside the context of a specific research study. Even though many of these mothers felt that receiving individual results during the course of research could act as an incentive for participation, many believed that there were alternative means available to them to receive this information, if desired, and this decreased the perceived importance of a study offering these findings. One participant in a high-income group explained and others agreed: "…*Well, anybody can get genetic testing right now. But people are choosing, I guess, to get it or not get it. So, just because the National Children's Study is doing the genetic testing, it shouldn't be like oh I will have to know. Well you can go out and get it on your own. If you really want this result…"* These themes were never mentioned in groups with women from low- income households, and in fact, participants from these groups felt it would be difficult to go many years in a longitudinal study without receiving any individual results.

The theme of perceived choice or alternatives for obtaining genetic information about a child was also raised when women in groups with greater economic resources discussed the emotional impact of the unavailability of individual genetic findings for many years into a longitudinal study. Again, they did not find this as distressing as they might have otherwise because they believed that other options exist for getting this information in a timely manner, if desired.

Participants perceived emotional risks of receiving results, anticipated negative emotions, and expected effects on quality-of-life and the parent-child relationship—Across all focus groups, participants mentioned multiple risks associated with the possibility of receiving individual results during the course of a genetic or genomic study. The anticipation of negative emotions from receiving certain findings, as well as the situation of being offered the choice, played a major role in reasoning strategies. Often participants referred to the anticipation of excessive worry and anxiety as a deterrent to agreeing to receive individual results, and expected that results could adversely affect quality-of-life for the parent, as well as how the parent interacted with the child. References to negative emotional responses pervaded discussions of concerns about the return of results question.

Anticipated worry and fear related to possible genetic findings that would be revealed in the course of a research study was discussed as a major consideration for the decision of whether or not to receive individual-level results. Anticipated emotions seemed to be weighted more in return of results decisions than probabilities of a disease outcome or the strength of an association between a genetic pattern and a disease outcome. Mothers described how worry over the possibility of a disease – that may or may not ever manifest itself in the child – could change their relationship and experience with their child negatively [OSB, Q7]. In another group, a participant described a personal experience in which she had decided not to have genetic testing because of the potential adverse emotional results (i.e., stress, anxiety) [OSB, Q8].

Theme 3: Participants desired an interpersonal, dynamic, flexible process that accommodated individual preferences and contextual differences for returning results

Participants described expectations and preferences for a return of results protocol that would include methods that would allow for individual preferences to be changed and would involve an interpersonal process with direct communication between researchers and participants.

Decisions about return of results are not perceived as immutable—Participants anticipated circumstances that could change previous decisions they would have made about receiving individual genetic results generated during a research study. Mothers acknowledged that changes in life circumstances could influence preferences. Many expressed the difficulty of deciding beforehand about whether individual results would be desired at some future time.

Making decisions beforehand is difficult—Participants recommended that researchers allow individuals to make decisions about what results they would like to receive, but they noted that it would be very hard to make this decision with limited information about the range of results that would be possible [OSB, Q9].

Experience may lead to different choices over time—Another emergent theme was that individuals may make different choices over time as the result of personal experiences. One mother described how her decision not to have testing early in her child's life would have been different if she'd known what she knows now [OSB, Q10].

The timing of the return of results could influence the possible emotional risks and benefits of genetic information—For some individuals, the timing of and life circumstances surrounding information disclosure could amplify or reduce the emotional consequences of receiving genetic or genomic information. Participants expected and worried that if adverse genetic analysis results were obtained during pregnancy, this would be emotionally traumatic, particularly within the context of decisions of whether or not to continue the pregnancy. In one of the Latina groups, participants described a culture in which parents would proceed with the pregnancy regardless of the results, noting that this would be difficult [OSB, Q11]:

The methods used to return results could reduce or increase harms—Across groups, there was an expectation that if researchers were to share a result that was perceived as negative, researchers should also make referrals to help address those results. This was described as a potential benefit of participation in genetic research, particularly when something was discovered that could be prevented. In Latina groups, participants described an expectation for intervention, rather than simply a referral [OSB, Q12]. Receiving a perceived negative result without intervention or referral for intervention was viewed as harmful.

Interactions between themes: Decisions about the return of results and the impact of disclosure of individual findings can be affected by the interaction between characteristics of the person and the research context

Certain features of the research protocol related to the return of results may be more important for decision-making and the potential impact of individual findings for some participants than others, and groups that differed in their sociodemographic profile placed an emphasis on different details of a study's procedures. For example, some Latina participants noted that having a family history of disorders that are thought to be genetically-based might increase interest in receiving individual findings during the course of a research study. For

those participants who expected to have choices outside of the research setting in obtaining genetic information about a child, they placed less emphasis on the importance of decisions about return of results in a research setting. Strong perceptions of control over life events and outcomes also led some participants to remark that decision-making about receiving individual results would depend on how much personal control they had over preventing or minimizing the impact of a disorder on a child's life, whereas in other groups, participants associated control over a possible disorder with not just personal actions, but also with other agents such as a health or medical care program that would follow-up with the parent after individual findings were disclosed.

DISCUSSION

Advances in genomic research have sparked discussion about the standards and principles that should be used to make decisions about the return of results to research participants, including parents of children who provide biological samples for analysis [Green, 2011]. Previous studies often have conceptualized and measured preferences and response to genomic information without reference to broader contexts that likely influence choice behavior and psychosocial responses. As a result, current literature may underestimate the complexity of these decisions. Our findings suggest that preferences for return of individual results are not determined in isolation, but instead incorporate the nature and scope of the research context and individual factors such as pre-existing beliefs about family disease history, perceptions of family or personal vulnerability to particular diseases, beliefs about "ownership" of biological samples provided in a research study, and life circumstances. In addition, the impact of receiving genetic information could be affected by the timing of return of results and provision of follow-up education or guidance in interpreting the meaning of results.

Our results have some similarities with but also important differences from recent recommendations by national advisory boards, proposing clinical utility and analytical validity as the key determinants of whether specific individual results should be reported back to participants [Wolf et al., 2008; Fabitz et al., 2010]. In addition to clinical utility, participant preferences for return of results seem to be highly influenced by the anticipation of negative emotions associated with receiving certain results, more so than by considerations about probabilities and strength of associations between genetic patterns and disease states. Preferences were not viewed as immutable and participants anticipated circumstances that would change previous choices and decisions about receiving genetic results for a child participating in a research investigation. Results are consistent with recent observations that life circumstances can change preferences for genetic or genomic information [Foster et al., 2009] and support suggestions for a tiered re-consent or flexible consent process for the return of individual results [McGuire and Lupski, 2010].

Context, Timing, and Potential Harms

Participants discussed repeatedly the potential emotional impact of receiving results that suggest a risk for a particular disorder or adverse health condition. They were concerned that knowledge about a risk could cause unnecessary worry, with potential adverse lifelong consequences for their relationship and experience with their child.

Participants also described how timing could amplify the emotional risks; as noted previously, in one Latina focus group, there was strong consensus that receiving genetic results during pregnancy could be traumatic for mothers in a culture where terminating a pregnancy may not be considered an option. Similar to decision-making in other domains [Johnson and Weber, 2009; Slovic et al., 2004], the decision-making process for return of individual results is thus highly influenced by the anticipation or experience of negative

emotions. Our findings are also consistent with bioethicists' concerns about possible emotional harms of returning individual results under certain conditions [Cameron et al., 2009] and the need to develop protocols that anticipate and recognize the central role of emotions in parents' decisions and reactions regarding the return of a child's genetic information.

Harms may be greater for individuals who are predisposed to anxiety or worry, individuals who lack certain resources (money, insurance coverage, access to counseling or other services) or individuals who have particular pre-existing beliefs about family health or medical history and vulnerabilities. Harm may be greater for individuals who interpret findings as more significant or influential to their personal health or the health of their child, while having fewer options to pursue alternative means of obtaining clarity about the findings, or beneficial genetic and medical information [Beskow and Burke, 2010]. Alternatively, decreased potential for harm regarding the return of results may be present for those who have greater social support [Kisinger et al., 2009], when results are more communicable [Kohane and Taylor, 2010], and when participant' expectations for the information and the research process are not violated [Lakes et al., 2012].

Implications for Methods of Returning Results

Study results have implications for the methods that are used to return results. One potential method for returning genetic results involves using web-based systems where participants can log in and view private results with educational information that can be used to interpret and respond to results [Kohane and Taylor, 2010]. This approach usually assumes that participants will understand the information provided and seek additional services or referrals when necessary (i.e., by contacting a genetic counselor or discussing results with their physicians). The participants in our study described an expectation for a much more personal process; participants in all focus groups described an expectation for referral at a minimum, with participants in Latina groups describing expectations that went beyond referral to intervention to include a preference for personal guidance for follow-up. Expectations for intervention ranged from providing educational information about preventive steps mothers could take to reduce the risk of a disorder to actually providing a program to educate parents on how to "treat" their child. Although a web-based tool can encourage individuals to seek genetic counseling if needed, lack of resources (e.g., money, time) or cultural factors (e.g., language, familiarity with the field of genetic counseling) may have a negative impact on an individual's ability to obtain quality counseling or discuss results with a knowledgeable physician. Individuals of lower socioeconomic status may also have difficulty accessing the web portals that provide information about results. Our results suggest that such efforts, while holding promise for large-scale studies, should consider carefully contextual factors that will impact how individuals respond to and use the information they receive and should develop complementary strategies to address these contextual factors.

Participants in our study acknowledged that individuals will differ in their preferences for the return of results and wanted to be able to specify which results they would receive if they were participating in the NCS. However, they also identified challenges. They noted that it would be difficult to make choices ahead of time. Participants would need to have a substantial amount of information at the time of consent to make choices, including what studies would be conducted, the potential results that could emerge, and the meaning of those results. This information will not be available for studies like the NCS, where future research using the samples has yet to be determined. Participants also noted that their choices might change over time as a result of life experiences, pointing to a need for a flexible, dynamic system for allowing participants to make choices about the return of their child's results, based on ongoing communication with researchers.

Implications for Recruiting Socially and Culturally Diverse Populations

Perceived personal control over life events and circumstances differs across ethnic, social and socioeconomic backgrounds within the United States [Bandura, 2002; Betancourt and Lopez, 1993; Landrine and Klonoff, 1992; Vaughan and Dunton, 2007; Fang et al., 2006; Senior et al., 2002], and beliefs about and the importance of personal control over life events have been associated with health decision-making, distress and ways of coping with medical risks [Landrine and Klonoff, 1992; Vaughan and Dunton, 2007; Fang et al., 2006; Senior et al., 2002], as well as with the psychological impact of receiving information about a genetically-based disease in a child [Lipinski et al., 2006]. In the present study, a recurrent theme was the notion of personal control over outcomes and general expectations of choice regarding access to genetic results. If participant populations in genomic research are truly representative of and reflect the cultural and socioeconomic diversity in society, protocols for the return of results may need to consider how variability in pre-existing control beliefs and access to resources might lead to unequal psychosocial impacts of information, and therefore a greater need for support or counseling for some participants. In a contextual perspective on return of results, Beskow and Burke [2010] suggest that researchers' obligations should take into account whether participants have other avenues for obtaining genetic information.

As genomic research initiatives commit effort and resources to increase the representativeness of participant populations, it is likely that differences in certain cultural perspectives will present researchers and institutional review boards with the question of how to or plan for reporting ambiguous or negative individual genetic information to diverse individuals. For example, our analysis revealed that Latina mothers, like others, wanted more information about whether personal actions could help prevent a particular disease before deciding to receive individual genetic findings for a child. However, they also expected that the actions of others (e.g., those affiliated with programs or resources outside of the study) would assist in coping with the implications and understanding of findings. This expectation of tangible support from others may not reflect a misunderstanding of the research endeavor, but rather a cultural orientation that frames the goal of achieving control over life circumstances beyond personal actions to include the actions of others working on one's behalf [Bandura, 2002]. This cultural orientation seems to vary in prevalence among different cultural and ethnic groups in the United States, and for individuals with different life experiences [Bandura, 2002; Landrine and Klonoff, 1992].

Broader Implications of Study Results

Although our study focused on the return of genetic results within a research study, our findings offer important insights for clinical practice. The clinical use of whole genome and whole exome sequencing is increasing feasible, due to falling costs of sequencing and expanding knowledge about the implications of human genetic variation for health [Gonzaga-Jauregui et al.,, 2012]. Such testing will typically be done to answer a specific clinical question; however, the technology will produce a broad array of incidental genetic findings. As a result, clinicians will increasingly face challenges regarding the return of test results that are similar to those faced by researchers. Clinicians will need to determine how to inform patients of potential incidental findings, elicit preferences for the return of finding, and provide appropriate counseling support and guidance after results are provided. Data from the research setting provide a starting point for addressing these questions. In particular, our data suggest that patients' desire for information may include results with personal rather than clinical utility, and may be influenced by the anticipation of emotional reactions to information. Cultural differences and social context may also represent important factors influencing both preferences of information and the support needed by patients after information is provided.

Limitations and Directions for Future Research

One limitation of our study was that it focused on participant preferences for a broad range of the types of results that might emerge from the NCS; Beskow and Burke [2010] described how aspects of research such as the scope of the study, depth of relationship between participants and researchers, and nature of the study population may matter to decisions about offering individual results in a particular study, indicating that there may be great variability across studies on this issue due to the importance of contextual factors. A contextual perspective also suggests that the potential risks, benefits, and impacts of genetic information can vary depending on participants' cultural values, goals, prior beliefs, experiences, family medical history, baseline psychological health, social support and life circumstances [Kohane and Taylor, 2010; Beskow and Burke, 2010; Gritz et al., 2005]. However, most studies have measured preferences for and the potential psychosocial impact of genetic findings in isolation of psychological and social processes that likely contribute to individuals' reactions to certain genetic information in a research setting [O'Daniel and Haga, 2011; Beskow and Burke, 2010]. Future research should examine participant preferences for results and the impact of receiving results with close attention to research and individual contextual factors. As clinical uses of genome-scale testing increase, comparable research is also needed in clinical settings, examining preferences for and impact of returning incidental findings from genomic studies.

CONCLUSION

Our findings indicate that as researchers consider methods for returning results to participants in a genomic research study, it will be important to develop strategies that involve an interpersonal, dynamic, flexible process designed to accommodate individual preferences and contextual differences. Participants in our study understood the complexity of returning genetic results, particularly when the implications for treatment or prevention are limited. They also understood how individual and contextual differences would affect individual preferences and the potential impact of a finding that conveyed some level of risk for a particular health problem. Of particular importance were the participants' descriptions of how receiving results could have both an adverse and a positive impact on parenting behaviors and relationship with the child, and how psychosocial outcomes depend on contextual factors. This presents a challenge for researchers, as it suggests that potential risks from the disclosure of a result a participant may perceive as adverse depend in part on individual contextual factors. It also provides insights into the challenges to be addressed as genome-scale testing enters clinical practice. Standardized methods of returning results, such as current web-based programs, hold great potential as flexible and dynamic systems for allowing individuals to make choices. However, in order to address and minimize potential risks associated with individual contextual factors, direct communication between researchers and individual participants is necessary. Future research should examine methods involving both web-based and relational approaches to sharing results from genetic research, and should explore the potential for similar tools to be adapted to clinical practice.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was conducted through the Orange County Vanguard Center, which has two PIs (Drs. James Swanson and Dean Baker). Staff members, student interns, and community partners contributed to the study by helping with recruitment and data collection. These contributions are gratefully acknowledged.

Funding for this study was provided through the Orange County Vanguard Center National Children's Study contract awarded by NICHD to the University of California, Irvine. The National Children's Study is a partnership involving four federal agencies: 1) The Eunice Kennedy Shriver National Institute of Child Health and Human Development; 2) the National Institute of Environmental Health Sciences; 3) the U.S. Environmental Protection Agency; and, 4) the Centers for Disease Control and Prevention.

The research described also was supported by the National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant UL1 TR000153. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

References

Baker D, Ignosci J, Waffarn F, Wadhwa P, Yang H, Swanson J. The National Children's Study: Effectiveness of Household-based Recruitment. Epidemiology. 2011; 22:S285.

Bandura A. Social cognitive theory in cultural context. Appl Psychol: Int Rev. 2002; 51:269–290.

Beskow LM, Burke W. Offering individual genetic research results: Context matters. Sci Transl Med. 2010; 2:2–5.

Betancourt H, Lopez SR. The study of culture, ethnicity, and race in American psychology. Am Psychol. 1993; 48:629–637.

Bookman BB, Langehorne AA, Eckfeldt JH, Glass KC, Jarvik GP, Klag M, Koski G, Motulsky A, Wilfond B, Manolio T, Fabsitz RR, Luepker RV. NHLBI Working Group. Reporting genetic results in research studies: Summary and recommendations of an NHLBI working group. Am J Med Genet A. 2006; 140:1033–1040. [PubMed: 16575896]

Borry P, Evers-Kiebooms G, Cornel MC, Clarke A, Cietrickx K. Genetic testing in asymptomatic minors. Background considerations towards ESHG Recommendations. Eur J Hum Genet. 2009; 17:711–719. [PubMed: 19277061]

Bredenoord AL, Charlotte Onland-Moret C, Johannes JM, Van Delden JJM. Feedback of individual genetic results to research participants: In favor of qualified disclosure policy. Hum Mutat. 2011; 32:861–867. [PubMed: 21538687]

Burke W, Diekema DS. Ethical issues arising from the participation of children in genetic research. J Pediatr. 2006; 149:S34–S38. [PubMed: 16829241]

Cameron LD, Sherman KA, Marteau TM, Brown PM. Impact of genetic risk information and type of disease on perceived risk, anticipated affect, and expected consequences of genetic tests. Health Psychol. 2009; 28:307–316. [PubMed: 19450036]

Caufield T, McGuire AL, Cho M, Buchanan JA, Burgess MM, Danilczyk U, Diaz CM, Fryer-Edwards K, Green SK, Hodosh MA, Juengst ET, Kaye J, Kedes L, Knoppers BM, Lemmens T, Meslin EM, Murphy J, Nussbaum RL, Otlowski M, Pullman D, Ray PN, Sugarman J, Timmons M. Research ethics recommendations for whole-genome research: Consensus statement. PLOS Biology. 2008; 6:430–435.

Crabtree, BF.; Miller, WL. Using codes and code manuals: A template organizing style of interpretation. In: Crabtree, BF.; Miller, WL., editors. Doing Qualitative Research. 2. Thousand Oaks, CA: Sage; 1999. p. 163-178.

Duan J, Sanders AR, Gejman PV. Genome-wide approaches to schizophrenia. Brain Research Bulletin. 2010; 83:93–102. [PubMed: 20433910]

Fabitz RR, McGuire A, Sharp R, Puggal M, Beskow LM, Biesecker LG, Bookman E, Burke W, Gonzalez Burchard E, Church G, Clayton EW, Eckfeldt JH, Fernandez CV, Fisher R, Fullerton SM, Gabriel S, Gachupin F, James C, Jarvik GP, Kittles R, Leib JR, O'Donnel C, O'Rourke PP, Rodriguez LL, Schully SD, Shuldiner AR, Sze RK, Thakuria JV, Wolf SM, Burke GL. Ethical and practical guidelines for reporting genetic research results to study participants. Circ Cardiovasc Genet. 2010; 3:574–580. [PubMed: 21156933]

Fang CY, Daly MB, Miller SM, Zerr T, Malick J, Engstrom P. Coping with ovarian cancer risk: The moderating effects of perceived control on coping and adjustment. Br J Health Psychol. 2006; 11:561–580. [PubMed: 17032484]

Fernandez CV, Kodish E, Weijer C. Informing study participants of research results: An ethical imperative. IRB. 2003; 25:12–19. [PubMed: 14569989]

Forsberg JS, Hansson MG, Eriksson S. Changing perspectives in biobank research: From individual rights to concerns about public health regarding the return of results. Eur J Hum Genet. 2009; 17:1544–1549. [PubMed: 19471310]

Foster MW, Mulvihill JJ, Sharp RR. Evaluating the utility of personal genomic information. Genet Med. 2009; 11:570–574. [PubMed: 19478683]

Gonzaga-Jauregui C, Lupski JR, Gibbs RA. Human genome sequencing in health and disease. Annu Rev Med. 2012; 63:35–61. [PubMed: 22248320]

Green ED, Guyer MS. National Human Genome Research Institute. Charting a course for genomic medicine from base pairs to bedside. Nature. 2011; 470:204–217. [PubMed: 21307933]

Gritz ER, Peterson SK, Vernon SW, Mirani SK, Baile WF, Watts BG, Amos CI, Frazier ML, Lynch P. Psychological impact of genetic testing for hereditary nonpolyposis colorectal cancer. J Clin Oncol. 2005; 23:1902–1910. [PubMed: 15774782]

Heaney C, Tindall G, Lucas J, Haga SB. Researcher practices on returning genetic research results. Genet Test Mol Biomarkers. 2010; 14:821–827. [PubMed: 20939736]

Hebebrand J, Scherag R, Schimmelmann BG, Hinney A. Child and adolescent psychiatric genetics. Eur Child and Adolesc Psychiatry. 2010; 19:259–279.

Hens K, Nys H, Cassiman K, Dietrickx K. The return of individual research findings in pediatric genetic research. J Med Ethics. 2011; 37:179–183. [PubMed: 21059631]

Johnson E, Weber EU. Mindful judgment and decision-making. Annu Rev Psychol. 2009; 60:53–85. [PubMed: 18798706]

King, N. Template analysis. In: Symon, G.; Cassel, C., editors. Qualitative methods and analysis in organizational research: A practical Guide. Thousand Oaks, CA: Sage; 1998. p. 118-134.

Kinsinger SW, McGregor BA, Bowen DJ. Perceived breast cancer risk, social support, and distress among a community-based sample of women. J Psychosoc Oncol. 2009; 27:230–247. [PubMed: 19337931]

Kohane IS, Taylor PL. Multidimensional results reporting to participants in genomic studies: Getting it right. Sci Transl Med. 2010; 2:19–23.

Lakes KD, Vaughan E, Jones M, Burke W, Baker D, Swanson J. Diverse perceptions of the informed consent process: Results from formative research for the National Children's Study. Am J Community Psychol. 2012; 49:215–232. [PubMed: 21671109]

LaKind JS, Aylward LL, Brunk C, Dizio S, et al. Guidelines for the communication of Biomonitoring equivalents: Report from the Biomonitoring Equivalents Experts Workshop. Regul Toxicol and Pharmacol. 2008; 51:S16–S26.

Landrine H, Klonoff EA. Culture and health-related schemas: A review and proposal for interdisciplinary integration. Health Psychol. 1992; 11:267–276. [PubMed: 1396496]

Lemke AA, Halverson C, Ross LF. Biobank participation and returning research results: Perspectives from a deliberative engagement in South Side Chicago. Am J Med Genet Part A. 2011; 158(5): 1029–1037.

Lipinski SE, Lipinski MJ, Biesecker LG, Biesecker BB. Uncertainty and perceived personal control among parents of children with rare chromosome conditions: the role of genetic counseling. Am J of Med Gen C Semin Med Genet. 2006; 142:232–240.

McGuire AL, Caufield T, Cho MK. Research ethics and the challenge of whole genome sequencing. Nat Rev Genet. 2008; 9:152–156. [PubMed: 18087293]

McGuire AL, Lupski JR. Personal genome research: What should the participant be told? Trends Genet. 2010; 26:199–201. [PubMed: 20381895]

Montaquila JM, Brick JM, Curtin LR. Statistical and practical issues in the design of a national probability sample of births for the Vanguard Study of the National Children's Study. Statist Med. 2010; 29:1368–1376.

National Academy of Sciences. Human biomonitoring for environmental chemicals. Vol. Chapter 6. Washington, DC: National Academy Press; 2006.

National Institutes of Health [Internet]. Protecting human research subjects: 199 Institutional Review Board guidebook: Human genetic research. Office for Protection from Research Risks; 1993. Available from: http://www.genome.gov/10001752

O'Daniel J, Haga SB. Public perspectives on returning genetics and genomics research results. Public Health Genomics. 2011; 14:346–355. [PubMed: 21555865]

Pociot F, Akolkar B, Concannon P, Erlich HA, Morahan G, et al. Genetics of type 1 diabetes: What's next? Diabetes. 2010; 59:1561–1571. [PubMed: 20587799]

Powell M, Dunwoody S, Griffin RJ, Neuwirth K. Exploring lay uncertainty about an environmental risk. Public Underst of Sci. 2007; 16:323–343.

Press N, Yasui Y, Reynolds S, Durphy SJ, Burke W. Women's interest in genetic testing for breast cancer susceptibility may be based on unrealistic expectations. Am J Med Genet. 2001; 99:99–110. [PubMed: 11241466]

Ravitsky V, Wilfond BS. Disclosing individual genetic results to research participants. Am J Bioeth. 2006; 6:8–17. [PubMed: 17085395]

Samuel J, Ries N, Malkin D, Knoppers B. Biobanks and longitudinal studies: Where are the children? GenEdit. 2008; 6:1–8.

Senior V, Weinman J, Marteau TM. The influence of perceived control over causes and responses to health threats: A vignette study. Br J Health Psychol. 2002; 7:203–211. [PubMed: 14596709]

Schulze TG. Genetic research into bipolar disorder: The need for a research framework that integrates sophisticated molecular biology and clinically informed phenotype characterization. Psychiatr Clin of North Am. 2010; 33:67–82. [PubMed: 20159340]

Slovic P, Finucane ML, Peters E, MacGregor DG. Risk as analysis and risk as feelings: Some thoughts about affect, reason, risk and rationality. Risk Anal. 2004; 24:311–322. [PubMed: 15078302]

Tabor, H.; Yu, J.; Civan, A.; Crouch, J.; Kuwana, E.; McMillin, M.; Stock, J.; Dent, K.; Anderson, N.; Lakes, KD.; Specker, B.; Burke, W.; Murray, J.; Swanson, JM.; Bamshad, M. "My46," an innovative web-based tool for management of results return from exome and whole genome sequencing studies. Presented at the National Children's Study Research Day at the National Institutes of Health; Bethesda, Maryland. 2011.

Vaughan E, Dunton G. Difficult socio-economic circumstances and the utilization of risk information. Health Risk Soc. 2007; 9:323–341.

Weber EU, Hsee CK. Culture and individual judgment and decision-making. Appl Psychol: Int Rev. 2000; 49:32–61.

Wilfond B, Ross LF. From genetics to genomics: Ethics, policy, and parental decision making. J Pediatr Psychol. 2009; 34:639–647. [PubMed: 18647793]

Wolf SM, Lawrenz FP, Nelson CA, Kahn JP, Cho ML, Clayton EW, Fletcher JG, Georgieff MK, Hammerschmidt D, Hudson K, Illes J, Kapur V, Keane MA, Koenig BA, Leroy BS, McFarland EG, Paradise J, Parker LS, Terry SF, Van Ness B, Wilfond BS. Managing incidental findings in human subject's research: Analysis and recommendations. J Law Med Ethics. 2008; 36:219–248. [PubMed: 18547191]

Table I

Demographic Characteristics of Participants (n=50*)	%
Do you consider yourself to be Hispanic or Latino?**	
Yes	28
No	72
Which group best represents your Hispanic origin or ancestry?**	
Mexican	73
Central/South American	7
Other	20
Participant race**	
White	49
White/African American	2
White/Native American or Alaskan	2
Asian	21
Iranian	4
Pacific Islander	6
No Response/Other	17
Age	
18–24	11
25–34	23
35–44	38
45 and older	21
No response	8
Marital status	
Single	8
Married	77
Divorced	8
Separated	6
No Response	2
Primary language spoken	
English	62
Spanish	23
English/Spanish	2
Chinese	2
Korean	2
Korean/English	2
Japanese	2
Farsi	4
No Response	2
Religion	
None	13

Demographic Characteristics of Participants (n=50*)	%
Buddhist	4
Catholic	44
Christian	31
Jewish	2
Protestant Denomination	4
Other	2
Education level	
High School Incomplete	4
High School Diploma/GED	8
Some College/Vocational School	23
Bachelor Degree	42
Advanced Degree	19
No Response	6
Current employment status	
Full - Time	21
Part - Time	23
Work From Home (Child Care, etc.)	11
Not working, but I'm looking	11
Not working by choice (Housewife, Retired)	34

Notes:

* In accordance with the NCS guidelines for disclosure, the N has been rounded to the nearest 50. The percentages may not sum exactly to 100 due to rounding.

** These categories are based on categories used for the United States census.

Table II

Themes

Theme 1: Preferences and decisions regarding return of results may depend on research context.
The nature of the result itself and its implications for prevention or intervention were seen as important considerations in deciding whether or not to receive the result.
Mothers differentiated between receiving results for themselves and results for their babies.
Perceived benefits of results reporting and reactions to procedures for storing samples for later analysis could impact decisions about the return of results.
Theme 2: Preferences and decisions regarding return of results may depend on individual contextual factors.
There is significant variability among mothers in the perceived risks and benefits of return of results, and differences are related in part to individuals' subjective reactions to and knowledge about family disease or medical history and prior experiences.
Current life circumstances, including access to economic, healthcare and other resources, and beliefs about personal control over life events and outcomes, may attenuate or amplify potential harms of information disclosure and influence decisions to receive results.
Perceived emotional risks of receiving results, anticipation of negative emotions and expected effects on quality-of-life and parent-child relationship.
Theme 3: Participants desired an interpersonal, dynamic, flexible process that accommodated individual preferences and contextual differences for returning results.
Decisions about return of results are not perceived as immutable.
Making decisions beforehand is difficult.
Experience may lead to different choices over time.
The timing of the return of results could influence the possible emotional risks and benefits of genetic information.
The methods used to return results could reduce or increase harms.
Decisions about the return of results and the impact of disclosure of individual findings can be affected by the interaction between characteristics of the person and the research context.