Published in final edited form as:
J Empir Res Hum Res Ethics. 2010 September ; 5(3): 31–41. doi:10.1525/jer.2010.5.3.31.

Researcher Perspectives on Disclosure of Incidental Findings in Genetic Research

Meredith C. Meacham, **Helene Starks**, **Wylie Burke**, and **Kelly Edwards**
University of Washington

Abstract

Genetic research can produce information that is beyond the aims of the research study yet may be of clinical or personal interest to study participants. We conducted semi-structured interviews with 44 researchers who were asked to describe how they would respond to a hypothetical vignette regarding the disclosure of findings with unanticipated clinical significance to research study participants. Interviews were transcribed and analyzed using content and thematic analyses. Researchers' decision-making processes about whether to disclose incidental findings were governed by potentially conflicting duties in three primary domains: information quality, adherence to rules, and participant welfare. There are several actions researchers can take to prepare for incidental findings, including: adding specific language in informed consent documents to state clearly how investigators will handle disclosure; exploring how prepared participants might be during the consent process to make decisions about how they would like to be approached in the event of incidental findings; developing procedures for appropriately communicating individual results and providing follow-up support based on participant preferences; and, in genetic research, having an awareness of the range of traits expressed by the genes under study.

Keywords

incidental findings; genetic studies; decision-making processes; communication of results; disclosure; qualitative research; vignette study

When research produces unanticipated information of potential clinical or personal interest to study participants, should researchers share this information? Bioethicists differ on whether researchers have an ethical duty to return individual results to participants (Clayton & Ross, 2006; Fernandez, Kodish, & Weijer, 2003; F. Miller et al., 2008; Parker, 2008; Shalowitz & Miller, 2005; Wolf et al. 2008), especially in the context of genetic studies (Cho, 2008; Fernandez & Weijer, 2006; Knoppers et al., 2006; see also Ravitsky & Wilfond, 2006 and associated commentaries). Several national panels have defined a minimum set of factors that should be present before returning research results to individual participants: the findings should have scientific validity, health importance, and be actionable (National Bioethics Advisory Committee, 1999; National Heart, Lung and Blood Institute, 2004; National Human Genome Research Institute, 2003).

Ideally at the start of a study, researchers determine or anticipate what information from the study will be produced that could benefit participants. A plan for returning results can then

Address correspondence to: Kelly Edwards, Department of Bioethics & Humanities, Box 357120, University of Washington, Seattle, WA 98195-7120. Phone: 206-221-6622; Fax: 206-685-7515; edwards@u.washington. edu.

be developed and included in the informed consent process, giving participants the opportunity to choose whether or not they wish to receive this information (Beskow et al., 2001; Parker, 2008). At times, studies may also produce incidental findings, defined as "a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study" (Wolf et al., 2008, p. 219).

In genetic research, incidental findings may take the form of discovering that an individual has a genetic variant for a certain disease or for increased susceptibility to a disease. A more common incidental finding in genetic research is misattributed paternity. Within the larger biomedical research setting, incidental findings have been described more often in radiological research; such situations may present the researcher with similar ethical dilemmas (Illes et al., 2008). Because incidental findings go beyond the original study aims and concern additional variables, they are more difficult to anticipate and plan for: interpretation of these variables may require consultation with clinical experts outside the research team; verification of these findings may require additional procedures; and it must be determined whether the health and other implications for participants are sufficient to override the potential anxiety and burden of disclosure for both participants and researchers (Cho, 2008; Keane, 2008; F. G. Miller et al., 2008; Parker, 2008; Wolf et al., 2008). Researchers may also face questions about return of results when their data acquire new clinical significance during the course of the study, either because the study outcomes exceed initial expectations or because research by other investigators sheds new light on the study finding. Because incidental findings are, by definition, outside the scope of what participants had expected to receive, the national panel guidance on when to return research results may not apply.

To better understand researchers' problem-solving strategies, reasoning processes, and motivations for dealing with this challenge, we asked a group of investigators funded by the National Institutes of Health (NIH) to describe how they would respond to a hypothetical vignette regarding the disclosure of genetic results with unanticipated clinical significance to research study participants.

Methods

This analysis is based on data from the Motivating Research with Human Subjects study, which sought to identify barriers and facilitators to ethical research practices. A sample of NIH-funded investigators was queried about their responses to five ethical challenges described by different hypothetical vignettes. Potential participants were identified by searching the 2004 CRISP database of principal investigators who received federal funding to do human subjects research. We identified researchers in Washington State and Oregon (to allow for the possibility of in-person interviews) whose research was described by at least one of the following types of research involving human subjects: cell and tissue research (including genetics); clinical trials; population research or epidemiology; and social science. This search identified 148 researchers at 14 different research institutions. Letters and response/opt-out cards were sent to all of these researchers; if no response was received, follow-up e-mails were sent. Out of the 148 invited to participate, 10 researchers were ineligible because they did not conduct human subjects research. Of the eligible sample, 13 individuals could not be contacted; of the remaining 125 potential participants, 60 consented to participate. Among the 65 individuals who declined participation, their reasons included no time (n = 21), no interest (n = 3), retired (n = 1), on sabbatical (n = 1), and opt-out postcard returned but no reason given (n = 39). Human subjects approval for the study was granted by the University of Washington institutional review board (IRB).

Data Collection and Analysis

An experienced interviewer completed semi-structured telephone interviews with the 60 participants to elicit their responses and rationales for their responses for up to five vignettes that were presented in varied order. We set a time limit of an hour for the interview, therefore some participants did not respond to every vignette. Of the 60 participants, 44 responded to the vignette on the return of unexpected results. Table 1 includes the text of the vignette that was given to participants to read before the interview. We used an interview guide to organize the conversation and engage the researchers in further reflection on their reasoning process and rationales, potential conflicts, circumstances in which responses might be different, what the participant's colleagues might do, whether the vignette reflected a common situation, and whether the participants had any direct personal experience or indirect experience through colleagues who had faced a similar scenario. (See Appendix A for the semi-structured interview guide.) The discussion for the incidental findings vignette lasted 10–15 minutes. The interviews were recorded and transcribed verbatim.

We conducted a directed content and thematic analysis (Hsieh & Shannon, 2005; Attride-Stirling, 2001) using Atlas.ti software. The transcripts were independently coded by at least two individuals, using a coding scheme that was developed from the questions in the interview guide and expanded to include additional codes identified during the coding process. The codes were grouped into three broad categories: responses (*how* researchers would respond in this situation), rationales (*why* they would respond in this way, in particular their motivations and reasoning processes), and other (recurring concepts that did not fall into either responses or rationales). We created subcategories within each of the broad categories to differentiate the range of concepts that we identified for each vignette. Coders reviewed and discussed each interview until consensus was reached. After this initial coding was complete, we generated reports of coded quotations, counting how many times a code was used and also analyzing the order of codes within the text (that is, whether the response was top-of-mind or a result of longer deliberation). We then used this information to elucidate the range of responses and rationales and to identify themes that summarize researchers' approaches to the situation depicted in the vignette. We also examined variations in the responses by gender, type of research, or experience as a researcher (dichotomized into "junior" or "senior" based on the number of years they had conducted human subjects research, using seven years as the cutoff). We found no differences in response patterns for any of these variables. Participant demographics are reported in Table 2.

Results

Disclosure

When asked what they would do with the incidental finding presented in the vignette, most researchers (n = 38) said they would disclose. However, they raised questions about what should be disclosed and to whom, and expressed a number of reservations and conditions, as described in more detail below. The six researchers who would not disclose results had two primary reasons: either they were unsure about what to do or felt they must adhere to the informed consent document and their original protocol and study aims.

We identified three key considerations that influenced the researchers' decision-making processes and motivations related to returning results: information quality, participant welfare, and adherence to rules.

Information Quality

High-quality information was a condition of the researchers' decision to disclose: the findings on which they made their decision needed to be verified first as being scientifically valid. In particular, many researchers said their first steps would be to read the articles that substantiated the colorectal cancer risk association and to assess whether the clinical utility of the risk was sufficiently strong to disclose to participants (n = 14). Still, several researchers felt that there would always be uncertainties in interpreting results from genetic studies, as summarized by this senior male social sciences researcher:

> I think the fundamental problem is that it'll be a grey area; without being an oncologist and getting a definitive statement from whomever I go to for advice on the risk of these people and the benefit to these people if I inform them of their risk. … I think [that] could be the biggest single problem of 'am I out of the grey?' Am I into a black and white where it's pretty easy to say you've got to do this or you don't have to do this? … How do you know if you're right? How do you even know if your information is correct, if it's this new a therapy?

A few researchers also acknowledged that they would want the disclosed results to be verified by a Clinical Laboratory Improvement Acts (CLIA)–certified lab or would want to be able to refer participants to a CLIA-certified lab, either because they felt that information from those labs was of better quality or because they felt they were required by law to do so.

Participant Welfare

Minimization of harm to participants was the most common motivation cited for either returning or withholding results (n = 39), followed by providing benefit (n = 25). Although this concern was most often used to justify disclosure of results, it was also used to limit disclosure. Many researchers articulated a duty to convey new information to participants if it was valid and useful, while recognizing that there were both harms and benefits in learning this information as a result of study participation. Potential harms included concerns that participants might not receive sufficient information about risk or have supports or resources to take appropriate follow-up actions. Some also asserted that the participants had a right to know this information. As noted by a junior male clinical trials researcher, the obligation to participants was sometimes expressed as a fundamental obligation one person has to another person:

> I have an obligation to these individuals. … People always assume they're going to get some benefit from participating in research and it's very hard to disavow people of that. So I think my first thought, given all of that, would be that I do have an obligation to them, not as patients or as research participants, but just as human beings.

Researchers were also concerned about distressing people and about losing participants' trust. When describing a potential drawback of sharing results with participants, one senior female clinical trials researcher stated:

> Scaring people unnecessarily, because then that would undermine our community's trust of us. So that would probably be the largest [concern], from a research perspective. And [my institution]'s perspective. As a trust issue and not wanting to unnecessarily scare people and cause them duress.

On the other hand, another senior female mixed methods researcher was concerned about excessive paternalism. She stated:

> People are just worried about worrying people, but I don't know, it's not my job … to keep people from being worried. … You know, the general idea is to keep them

> healthy. I worry a little bit about the paternalistic attitude that I should save people from worrying.

Several researchers concluded that at the very least participants should be notified that the information existed because they could not know who would or would not want the information. In addition, some, such as this senior female clinical trials researcher, were concerned about whether this communication would be handled delicately and with support structures in place.

> I have a duty, even regardless of the confidentiality thing, I have another feeling that one doesn't just give genetic information out willy-nilly without appropriate types of consent and counseling that go along with it.

Adherence to Rules

Many of the researchers referred explicitly to rules and the imperative to follow them (n = 18). Consulting their institutional review board (IRB) was mentioned by a majority of the researchers (n = 35) and was seen as serving several purposes. Researchers viewed the IRB as a responsibility-assuming authority, a permission-granting authority, or as a consultant. Eleven researchers had an idea of what they wanted to do and why, but weren't entirely sure what was procedurally and ethically appropriate, so they would also seek permission or approval from the IRB before they took action. Eight researchers said they would ultimately defer to the authority of the IRB, regardless of whether they agreed with what the IRB said. As one senior male cell and tissue researcher who planned to follow his IRB's directions stated:

> It's another one of those things where if the IRB at my institution feels strongly that this is what I should do, it's a moral copout for me but I'll say ok, this is what the IRB wants me to do, and I'll do it.

Researchers would ask both the IRB and their colleagues about whether re-contacting participants would violate their original consent document and study protocol, and what the repercussions would be of doing so. For example, a junior female social sciences researcher spoke of whether a protocol revision would be required to share these study results with the participants, and whether doing so could put the study integrity at risk.

> I ultimately think you just can't really do that within the confines of how the study was set up and I think that's sometimes the conflict between wanting to do good for individuals versus the good for the society that's done by conducting ethical research. … It's sort of on the one hand research integrity and sticking to how it is that you set up research, and sort of in a broader sense, knowing that informed consent is there for a reason and you can't just suddenly go against it.

Inherent in these considerations was a need to achieve balance between the goals of research and its purpose of benefiting society, and the role and welfare of individual research participants. More often than not, however, respondents such as this senior female social sciences researcher felt that the participants' welfare overrode specific rules, such as following the consent form as written.

> I think I would be saying ok, we've got what I said in the consent form on the one hand, versus the risk that people are going to die unnecessarily on the other hand. And at some point I definitely think that there are sort of higher principles than following what the consent form says in exact detail.

Consultation

In order to address conflicts and uncertainties, most researchers would consult with their colleagues and their IRBs, in part, as one junior female social sciences researcher said, to share the burden and responsibility of the decision and make it a group decision:

> I would go to my IRB and say, "Here's what I have going on. I feel an ethical responsibility, or an emotional pull, anyway, to get this information to these folks. Help me figure this out." It wouldn't be anything I could do without IRB approval anyway, but I would pull on the collective wisdom of the board. We've [got] a really good IRB and I'd feel really comfortable saying, "Help, I never anticipated being in this position and yet, here I am and I want to do the right thing." … But I don't think I would even decide it on my own, I think I would really make it a more group decision.

Before contacting their IRB, many researchers would consult colleagues on a variety of issues, valuing their advice or realizing that they might be in over their head and needed to speak with others who were more knowledgeable and experienced. Whereas researchers consulted the IRB to seek advice or approval, researchers would consult colleagues for specific expertise and to draw on colleagues' prior experiences. The types of colleagues named included people on their own research team, senior department faculty, and others with relevant expertise such as oncologists, geneticists, and ethicists. Many researchers expressed a great deal of trust in their colleagues, for example referencing how an issue like this would be discussed at lab meetings or how they had a "go-to" person for situations like this.

Practical Considerations

Twenty researchers also discussed *how* they would recontact the participants; for many this issue was the primary question that defined the dilemma. Their concern stemmed from an acknowledgment that participants had both the right to know or not to know their results, which led to needing to find an approach that would leave the decision to participants, since ultimately, only the participants could decide the harms and benefits of this information for themselves. Most researchers thought that mailing a letter to the participants (instead of a telephone call or newsletter) was the most appropriate approach. Some researchers, such as this junior female cell and tissue researcher, even articulated specific wording for communicating with participants:

> I guess it would be to … draft a letter saying … "Some of you may have heard that this particular enzyme that we were studying, in the study you participated in, may be an important risk factor for the development of colon cancer. This enzyme was tested in your case. If you should desire to have these results made available to you, [here is who] you can call or contact."

Several researchers also considered whether to re-contact the whole cohort or only the 10% who were at increased risk due to the genetic variant and decided that it would be better to re-contact everyone so as not to single out the affected population. One researcher also thought about what would happen if they did not receive a response from participants, questioning how much trouble they should go through to seek them out if their contact information was not up to date and how many times to follow up, particularly for the participants with the genetic variant.

Determining who would be responsible for the resources required to carry out their decision was another issue raised by 13 researchers. They discussed the considerable time, energy, and personnel necessary for re-contacting and re-consenting participants and wondered about where they would get the funds for the mailings, additional sequencing, or provision

of clinical consultation and genetic counselors, none of which was presumably included in the original study budget. Additional worries included whether participants might not be able to follow up with appropriate screening and preventive measures if they did not have adequate health insurance, or if the researchers would be obligated to pay for prophylaxis or treatment. These researchers felt that the absence of such resources could limit the actionability of the information.

Another practical consideration was the potential for adverse consequences of disclosure or non-disclosure on researchers' careers. One junior male population researcher discussed this concern in the context of being subject to legal liability should participants feel sufficiently aggrieved by the result disclosure or non-disclosure.

> If it was alarming enough to them, would I be the target of a lawsuit for breaching their confidentiality and contacting them, or would that be an assault, I guess, had I assaulted them by giving them information that they did not consent to receive? I suspect that such a lawsuit would not stand up, but it could be a big hassle.

Dynamic Problem Solving

Individual researchers addressed different combinations of the above considerations and discussed them in varying order. Common initial reactions were to verify the validity of the information, to bring the dilemma to the IRB or colleagues, and if their immediate decision was to disclose, to figure out the logistics of communicating this information. Researchers often brought up concerns about possible harm to participants, violation of their informed consent document or study protocol, and possible legal or career repercussions in response to a probe about competing interests.

In some interviews, we could observe the evolution of the participant's thinking about the problem, sometimes resulting in a change of position about returning the result. The following example shows the process used by one junior male cell and tissue researcher and how he deliberated, using elements of all three themes in his response. At first, he was dubious about the quality of the information regarding the association between the variant and the risk for colon cancer.

> Well, that's a tough one. … If I put my clinical hat on … I'd have to know how big of a risk it is, in these several other publications that show that it's directly linked to an increased risk. If it's a very slight increased risk vs. a very huge increased risk, in what population is it a risk? I know that 10% of my population has the gene variant, but do all those 10%—did they fit in the specific population that was reported? I don't know.

He was still doubtful he would disclose individual results even if the association was strong, valid, and generalizable because this possibility was not included in the informed consent document. He proposed instead that he could send the published articles to the participants, but remained concerned about adhering to the rules.

> Yes, send the articles to my patients. They can go out and get themselves tested if they want. Obviously labs are offering it as a clinical service. I could do that. … What I think would be going through my mind is, these 10% of people are higher risk but this test is in my hands, it's something that wasn't the point of what I was looking at, and I wasn't going to notify them of any underlying genetic problems. … I've read IRBs and I know that's one of the questions, "Could you find something in the course of the study that might show disease susceptibility?" So it's a dilemma, but I think that the rules are the rules, and it's written in there, I'll leave it at that.

His initial response was not to disclose. Yet when asked about competing interests, he expressed concern about the welfare of the participants.

> The welfare of the patient is the most important. Welfare of the participant is probably the main competing interest, to notify him or her that— again, assuming that the multiple publications showed a significantly higher risk—is a real cause for alarm. There are all these things that come out and get published in our medical and scientific journals that show a significant increase in risk of that, but it's not something that people go out and change their behavior because of. And so, I'd have to see the data, but, again, assuming that it's something remarkable, then the competing interest would be the patients' welfare.

At the end of the discussion, this researcher has talked through and thought more about the impact on the participants. He came up with a way to work with the IRB within the bounds of established rules to try to re-contact the participants:

> The only problem is a purely personal thing, knowing in the back of my mind that these people are, by my study, by my findings, possibly at higher risk. That's the problem. And also for the patients, I mean, that's their problem. The only other thing one could think about doing would be to—yeah, that would be very difficult … to propose a modification in the study to the IRB to be able to tell patients, things like that.

His thought process began by considering the quality of information of the findings. Assuming the quality was high enough he felt that he must adhere to the rules of the IRB and study protocol. Ultimately, his consideration of and obligations to the participants' welfare are what compelled him to think about how he could act within the bounds of the rules.

Discussion

Researchers presented with a hypothetical vignette of a research finding with unanticipated clinical significance responded with a variety of approaches and considerations, with decisions converging in favor of disclosure of the result. They were motivated in large part by concern for their participants' welfare, and would want to be assured of the quality and usefulness of the findings before taking action. They were also concerned about whether their actions were in concordance with applicable rules and procedures. In considering this scenario, they also identified many unanswered questions with respect to how best to return results and what resources would be needed.

The competing duties revealed in our data are consistent with recent bioethics discourse on return of research results. Even though they were not always explicitly named, researchers often appealed to the ethical principles of beneficence, respect for persons, and justice, highlighted in the Belmont Report (Department of Health and Human Services, 1979). The relative weight of these principles and their application to returning research results have been evaluated in detail in a target article and open peer commentaries in the *American Journal of Bioethics* (Ravitsky & Wilfond, 2006). In our study, beneficence was cited by the researchers most often, in the form of concern for the participants' welfare, specifically to minimize the harms of cancer and/or of disclosure. Respect for persons was represented by comments from researchers who thought participants should have access to clinically relevant information but should also have a choice regarding whether they wanted to learn this information. Justice was invoked when researchers considered balancing their duties to participants and to society, the equitable use of limited resources, and reciprocating the assistance and contributions of participants. The researchers in our study also recognized the conflicts inherent in the application of these principles to the situation under discussion.

Researchers emphasized the importance of the quality and clinical value of information as factors in the decision about disclosure, in keeping with several commentaries and expert panels (Beskow, 2006; National Bioethics Advisory Committee, 1999; National Heart, Lung and Blood Institute, 2004; National Human Genome Research Institute, 2003; Parker, 2008; Sharp & Foster, 2006). Their narratives displayed a healthy skepticism regarding reports of genetic associations and an awareness of the challenge of confirming genetic associations (Fryer-Edwards & Fullerton, 2006; Facio, 2006). There was no discussion of non-clinical personal meaning (such as ancestry) for research participants, but many implicitly acknowledged, as Lavieri and Garner (2006) argue, that individual participants may have a different assessment of utility than that of the researchers.

Despite the existence of advisory panels and recommendations on this issue, the only regulatory authorities noted by our respondents were the institutional review board and CLIA regulations. Some researchers questioned whether they could disclose results generated in a lab that was not CLIA-certified, and nearly all noted the importance of adhering to the informed consent document and study protocol and the importance of IRB review prior to implementing any return of results.

Although the nature of the researcher-participant relationship was not explicitly discussed, researchers noted responsibilities to participants, either as responsibilities between individuals or as the need to maintain the participants' trust of the researchers as trained experts. Trust of the researchers by the participants and responsibility as a trained expert were alluded to several times, reflecting the defining aspects, respectively, of the partial entrustment model (Richardson & Belsky, 2004) and the professional duty of beneficence (F.G. Miller et al., 2008).

The concerns of the researchers in this study are in keeping with the issues raised by Ravitsky and Wilfond's results-evaluation approach (2006) to return of results and by recommendations for handling incidental findings outlined by Wolf et al. (2008). Nevertheless, unlike these two approaches, which feature decision trees that direct the action of the researcher based on context of the study and the quality of the information, researchers in our study came into the decision-making process at a variety of different points, sometimes returning to an earlier node in the decision tree, and often deferring the decision-making process to the IRB.

Similar to Ravitsky and Wilfond's results-evaluation approach, researchers were keen to ensure the clinical utility and analytic validity of the information, and they considered the capabilities of the investigator to disclose this information, the alternative access by participants to the information, and what researchers might owe the participant based on their relationship. There was, however, no discussion of how the duration or intensity of the relationship might temper this obligation.

Although the hypothetical scenario in our study assumed that the researchers did not adequately plan for and anticipate incidental findings, as recommended by Wolf et al. (2008), the researchers in our study did identify the subsequent recommended actions of verifying the incidental finding, consulting with experts, and considering how possible benefits and harms contributed to the net benefit of disclosing the finding. Wolf et al. (2008) described the finding of an allele associated with hereditary non-polyposis colorectal cancer (HNPCC) as an example of a "strong net benefit" and thus would mandate disclosure to willing study participants. Yet researchers in our study seemed more likely to consider this hypothetical finding of an increased rate of colorectal cancer as a "possible net benefit" and so disclosure to participants would be more discretionary, perhaps because the level of increased risk for developing colorectal cancer was not specified.

The researchers' concerns regarding this scenario in genetic research also overlapped with some practical guidelines for addressing incidental findings in brain imaging research. In particular, Illes et al. (2008) emphasize the need for a transparent pathway for managing the incidental findings, the potential need for expert review and consultation outside the research team, and the importance of timely and straightforward communication with study participants. Illes et al. (2008) also strongly urge that researchers anticipate the possibility of incidental findings during the experimental design, subject recruitment, and informed consent process.

Finally, only some researchers also recognized the right of participants to not know their results and so wanted to disseminate information in a way that would leave it up to participants to decide whether they want to receive their specific results. These responses point to the need to emphasize this right not to know in future guidelines and to raise its visibility to researchers and to IRBs. This analysis also indicates that resources and procedures for appropriately communicating individual results and providing follow-up support need to be finessed and disseminated, with clear delineation of duties for researchers, funding sources, IRBs, and participants.

Our findings must be considered within the limitations of the study design. Researchers' decisions and rationales were based on a hypothetical vignette that was designed to align with recommendations in favor of disclosure of results (strong association, health implications, clinical utility). Thus, their responses may not capture their own experiences or their responses to ethical dilemmas arising with less straightforward findings. Still, most (though not all) researchers viewed this as an ethical dilemma and, in order to resolve this dilemma, identified three conditions that influenced their response: quality of information, adherence to rules, and participant welfare.

Best Practices

Our study results point to two practices that will help researchers navigate the dilemma of disclosing incidental findings. The first practice is to anticipate potential incidental findings and have a plan for how to respond to their occurrence; the second practice is to seek advice and collaboration with peers and IRB members throughout the duration of the study. In the study planning process, researchers should work through actions to take in the event of incidental findings, especially by examining the wording of the informed consent documents for potentially ambiguous statements, allocating resources, and having an awareness of the range of traits expressed by the genes under study. Researchers should also keep in mind that the clinical utility or personal meaning of medical or genetic information may be assessed differently by the participant than by the research team.

Collaboration and communication between researchers, with the IRB, and with participants are also essential. Knowledge and experience of colleagues can be invaluable in the planning stages or when ethical dilemmas arise. IRBs will be expected to provide counsel and have an awareness of the relevant guidelines and bioethics discourse. In this study, researchers relied on their colleagues and the IRB to help them address their uncertainties about what to do. The strong reliance on colleagues demonstrates the importance of teamwork when dealing with ethical dilemmas in research. The strong reliance on the IRB implies that IRBs will be expected to provide counsel and have an awareness of the relevant guidelines and bioethics discourse, and the ability to apply these to specific situations. Given considerable uncertainty about the appropriate way to resolve questions about returning incidental or unexpected research results (Wolf et al., 2008), this topic may be an important one for deliberation among groups that include experts in research regulation, ethics, clinical care, and research.

Research Agenda

Researchers were equally concerned with both *if* and *how* they would disclose results and their concerns point to the lack of guidance and support for the resource-intensive process of results disclosure and follow-up. Areas of future research should address both researcher responses to incidental findings and participant preferences in receiving study results. Returning findings from research studies requires funding and support that may not be in place at both fund granting and academic institutions (Fernandez et al., 2004). In particular, unresolved issues include the funding of professional genetic counselors and the appropriate strategies and resources for the return of genetic results that were initially generated in non-CLIA-certified laboratories. Regarding participant preferences, focus groups with people who have participated in studies and interviews with people who have received results back from studies may provide further guidance. Previous research suggests that most participants may be interested in receiving results (Murphy et al., 2008), but less is known about their preferences for how those results are to be returned or how prepared participants might be during the consent process to make such decisions. These preferences may largely depend on the type of study and diseases and on participant understanding, but such further research may help determine how to better anticipate concerns.

Educational Implications

This study confirms the need to raise awareness about the possibility of incidental findings in biomedical research and highlights domains of concern facing researchers (e.g., quality of information, adherence to rules, participant welfare). In the context of genetic studies, this study also points to a need for a better understanding of genetic information on the part of researchers, the media, and the public—in particular, the concept of genetic pleiotropy and that both harms and benefits may arise from sharing and acquiring personal genetic information. The dynamic decision-making of the researcher- participants in this study also demonstrates how discussion of these issues, even if hypothetical, may assist researchers in converging on the best ethical practices.

Acknowledgments

This work was supported by grants from the Office of Research Integrity (R01 NS-44486, W. Burke & K. Edwards, co-PIs) and the National Human Genome Research Institute (P50 HG 3374, W. Burke, PI). We would like to extend our thanks to Elizabeth Hopley for her interviewing skills and to Nicole Deming and Heather Linn Culley for their assistance with data coding and analysis.

Biographies

Meredith C. Meacham is a graduate of the University of Washington's Institute for Public Health Genetics Master of Public Health program. She analyzed the coded transcripts and drafted this manuscript from her master's thesis on the topic.

Helene Starks is Assistant Professor in the Department of Bioethics and Humanities at the University of Washington. She is a mixed-methods researcher who teaches qualitative methods and research ethics, and co-investigator and Director of Training for the Center for Genomics and Healthcare Equality (CGHE), a NHGRI-funded Center of Excellence in ELSI research. She participated in coding the original transcripts and analyzing this vignette, and contributed to editing the manuscript.

Wylie Burke is Professor and Chair of the Department of Bioethics and Humanities at the University of Washington. She was co-principal investigator (PI) of the Motivating Research with Human Subjects study and is PI of the CGHE. Her research interests focus on

the ethical, legal, social, and policy implications of genetics research for researchers, regulators, community partners, and participants. She secured funding for the project and contributed to editing the manuscript.

Kelly Edwards is Associate Professor in the Department of Bioethics and Humanities at the University of Washington. She was co-principal investigator (PI) of the Motivating Research with Human Subjects study, provided oversight and management of both the study and Meredith's master's thesis, coded the original transcripts, and contributed to editing the manuscript.

References

Attride-Stirling J. Thematic networks: An analytic tool for qualitative research. Qualitative Research. 2001; 1(3):385–405.

Beskow LM. Considering the nature of individual research results. American Journal of Bioethics. 2006; 6(6):38–40. [PubMed: 17085406]

Beskow LM, Burke W, Merz JF, Barr PA, Terry S, Penchaszadeh VB, Gostin LO, Gwinn M, Khoury MJ. Informed consent for population-based research involving genetics. Journal of the American Medical Association. 2001; 286(18):2315–2321. [PubMed: 11710898]

Cho MK. Understanding incidental findings in the context of genetics and genomics. Journal of Law Medicine & Ethics. 2008; 36(2):208–212.

Clayton EW, Ross LF. Implications of disclosing individual results of clinical research. Journal of the American Medical Association. 2006; 295(1):37. [PubMed: 16391213]

Department of Health and Human Services. [Retrieved July 14, 2009] The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects Research. 1979. from http://ohsr.od.nih.gov/guidelines/belmont.html.

Facio FM. One size does not fit all. American Journal of Bioethics. 2006; 6(6):40–42. [PubMed: 17085407]

Fernandez CV, Kodish E, Weijer C. Informing study participants of research results: An ethical imperative. IRB. 2003; 25(3):12–19. [PubMed: 14569989]

Fernandez CV, Skedgel C, Weijer C. Considerations and costs of disclosing study findings to research participants. Canadian Medical Association Journal. 2004; 170(9):1417–1419. [PubMed: 15111476]

Fernandez CV, Weijer C. Obligations in offering to disclose genetic research results. American Journal of Bioethics. 2006; 6(6):44–46. [PubMed: 17085409]

Fryer-Edwards K, Fullerton SM. Relationships with test-tubes: Where's the reciprocity? American Journal of Bioethics. 2006; 6(6):36–38. [PubMed: 17085405]

Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qualitative Health Research. 2005; 15(9):1277–1288. [PubMed: 16204405]

Illes J, Kirschen MP, Edwards E, Bandettini P, Cho MK, Ford PJ, Glover GH, Kulynych J, Macklin R, Michael DB, Wolf SM, Grabowski T, Seto B. Practical approaches to incidental findings in brain imaging research. Neurology. 2008; 70(5):384–390. [PubMed: 18227420]

Keane MA. Institutional review board approaches to the incidental findings problem. Journal of Law Medicine & Ethics. 2008; 36(2):352–355.

Knoppers BM, Joly Y, Simard J, Durocher F. The emergence of an ethical duty to disclose genetic research results: International perspectives. European Journal of Human Genetics. 2006; 14(11): 1170–1178. [PubMed: 16868560]

Lavieri RR, Garner SA. Ethical considerations in the communication of unexpected information with clinical implications. American Journal of Bioethics. 2006; 6(6):46–48. [PubMed: 17085410]

Miller FA, Christiansen R, Giacomini M, Robert JS. Duty to disclose what? Querying the putative obligation to return research results to participants. Journal of Medical Ethics. 2008; 34(3):210–213. [PubMed: 18316466]

Miller FG, Mello MM, Joffe S. Incidental findings in human subjects research: What do investigators owe research participants? Journal of Law Medicine & Ethics. 2008; 36(2):271–279.

Murphy J, Scott J, Kaufman D, Geller G, LeRoy L, Hudson K. Public expectations for return of results from large-cohort genetic research. American Journal of Bioethics. 2008; 8(11):36–43. [PubMed: 19061108]

National Bioethics Advisory Committee (NBAC). Research Involving Human Biological Materials: Ethical Issues and Policy Guidance. Rockville, MD: NBAC; 1999.

National Heart, Lung, and Blood Institute. Bethesda, MD: 2004 Jul 12. NHLBI Working Group on Reporting Genetic Results in Research Studies. from http://www.nhlbi.nih.gov/meetings/workshops/gene-results.htm

National Human Genome Research Institute. [Retrieved July 13, 2009] Federal Policy Recommendations Including HIPAA. 2003. from http://www.genome.gov/11510216.

Parker LS. The future of incidental findings: Should they be viewed as benefits? Journal of Law Medicine & Ethics. 2008; 36(2):341–351.

Ravitsky V, Wilfond BS. Disclosing individual genetic results to research participants. American Journal of Bioethics. 2006; 6(6):8–17. 8–17. See also the associated commentaries, pp. 18–46. [PubMed: 17085395]

Richardson HS, Belsky L. The ancillary-care responsibilities of medical researchers: An ethical framework for thinking about the clinical care that researchers owe their subjects. The Hastings Center Report. 2004; 34(1):25–33. [PubMed: 15098404]

Shalowitz DI, Miller FG. Disclosing individual results of clinical research: Implications of respect for participants. Journal of the American Medical Association. 2005; 294(6):737–740. [PubMed: 16091577]

Sharp RR, Foster MW. Clinical utility and full disclosure of genetic results to research participants. American Journal of Bioethics. 2006; 6(6):42–44. [PubMed: 17085408]

Wolf SM, Lawrenz FP, Nelson CA, Kahn JP, Cho MK, Clayton EW, Fletcher JG, Georgieff MK, et al. Managing incidental findings in human subjects research: Analysis and recommendations. Journal of Law Medicine & Ethics. 2008; 36(2):219–248.

Appendix A

Semi-Structured Interview Guide

Interview Guide for Incidental Finding Vignette

Interviewer Introduction—Thank you for talking with me today. We are interested in learning how researchers think through dilemmas that arise in the course of their research work. I will be asking you to consider a few hypothetical scenarios in which decisions must be made. I would like you to walk me through how you think the decisions should be approached and why. We are not looking for “right” or “wrong” answers, but rather want to understand how researchers approach challenging situations. You may request that we turn off the tape recorder at any time, or request that we not transcribe any portion of the tape. Do you have any questions for me before we begin?

1. I will read you a vignette that poses a dilemma. I will ask you to respond to the dilemma as if you were the researcher involved. Again, just to remind you, we are not looking for “right” or “wrong” answers, but rather want to understand how researchers approach challenging situations.

Vignette—You are the PI on a study that is investigating genetic differences in metabolizing enzymes. During the course of the study, several research groups across the country simultaneously publish papers linking variations in one of the genes you have studied to a high risk of developing colorectal cancer. You were not anticipating that your results would have clinical significance, but apparently 10% of your study population has this gene variant. You are concerned that many of these individuals might need additional screening for colorectal cancer. Labs around the country have already started offering genetic testing for this variant as a clinical service. Since you did not know that your results

would have clinical significance for the participants, you did not include in the study consent form the possibility that study subjects would be notified of results. However, you do keep current contact information for your participants and it would be possible to reach them.

2 Sequential probes:

- **a.** What would be going through your mind if you were faced with such a situation?
- **b.** [If it doesn't come out with first probe] How would you describe the dilemma you are facing?
- **c.** What are the competing interests that you would have to weigh in making a decision about what to do next?
- **d.** What would you do in this situation?
  - **i** Why?
- **e.** What problems do you foresee in taking these next steps (to resolve the dilemma)?
- **f.** Could you justify moving forward in any other way?
- **g.** How do you imagine your peers/colleagues would respond if faced with the same dilemma?
- **h.** Does this scenario represent a common type of problem researchers face?

TABLE 1

Return of Results Vignette.

You are the PI on a study that is investigating genetic differences in metabolizing enzymes. During the course of the study, several research groups across the country simultaneously publish papers linking variations in one of the genes you have studied to a high risk of developing colorectal cancer. You were not anticipating that your results would have clinical significance, but apparently 10% of your study population has this gene variant. You are concerned that many of these individuals might need additional screening for colorectal cancer. Labs around the country have already started offering genetic testing for this variant as a clinical service. Since you did not know that your results would have clinical significance for the participants, you did not include in the study consent form the possibility that study subjects would be notified of results. However, you do keep current contact information for your participants and it would be possible to reach them.

TABLE 2

Demographics of Study Participants.

	Number (n = 44)	Percent
Gender		
Male	22	50%
Female	22	50%
Experience		
Junior (≤7 years of experience)	11	25%
Senior (>7 years of experience)	33	75%
Self-Identified Research Field		
Cell and Tissue Biology (including Genetics)	6	14%
Clinical Trials	12	27%
Population Research/Epidemiology	10	23%
Social Sciences	10	23%
More than One Field	6	14%