

Return of Aggregate Results in Biorepository Research: An Exploratory Study of Participant Perspectives and Preferences

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Abstract

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This thesis reports a preliminary exploration of participant preferences and perspectives on the necessity for, and mode of, returning aggregate (or summary) results of genomic biorepository research. Fifteen semi-structured interviews were conducted with members of the Northwest Institute of Genetic Medicine (NWIGM) cohort. Participants reported a desire for individual results, and expressed a clear preference for allocating funds designated for return of summary results to additional research. In the event that aggregate results were to be returned, the participants of this exploratory study preferred to receive them in the form of emails, letters, or websites rather than in-person interviews or phone calls. The results of this preliminary research suggest that individuals be consulted regarding preferences prior to formation of overarching policy regarding aggregate return, and indicate that further research with larger and more representative cohorts is warranted.

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Introduction

Tissue samples donated for research and stored in biorepositories can be used in many different types of research. Researchers and policy makers recommend returning aggregate (or summary) results from all research using those samples to the research participants (Beskow et al. 2012; Wolf et al. 2012). Those recommendations are founded on a sense that returning results expresses appreciation for participation, confers tangible value on the participants' experiences, and demonstrates respect for participants.

A number of researchers have highlighted the lack of knowledge and consensus on best practices in this emerging area, particularly about how and when to deliver aggregate research results (Fabsitz et al. 2010). It has been suggested that participants' perspectives on such issues would be valuable to incorporate into policy and practice (Dalal and Wingnam 2009; Beskow et al. 2012). In addition, some researchers have questioned the investment of time and expense associated with the return of aggregate research results (Partridge et al. 2003). Despite this recent focus, there have been few explorations of participant perspectives on returning aggregate results. This research has been designed to fill this gap in knowledge by interviewing biorepository participants in order to inform future research practices and policymaking.

Background

Biorepositories are being founded more frequently to further the progress of genetic and genomic research. The establishment of large scale biobanks, or biorepositories, contributes to the efficacy and execution of genome wide association studies (GWAS), which aim to determine links between gene variants and the manifestation and progression of

disease. With a growing collection of whole genomes available for use, researchers are better able to design case-control studies, evaluate drug dosage responses, examine multiple variables and assess the relationship between genetics and population health (Pullman et al. 2011).

Biorepositories as a whole have given rise to a host of ethical questions, mostly pertaining to issues of participant respect, confidentiality, and consent (Hansson, 2009). Since genomic information reveals intimate information about an individual, it is necessary that this information be protected, and that the use of this information be treated with care, and with regard to the wishes of that individual. Given that samples in biorepositories can be used repeatedly for multiple experiments or protocols, investigators and policymakers have been forced to reevaluate standard processes of informed consent. For example, previous research exploring participant perspectives on consent has demonstrated that participants wish to be asked for permission when their samples are used for research not explicitly specified in the original consent (Ludman et al. 2010).

The unique nature of the information stored in biorepositories has led to further discussion of how participant involvement can best be encouraged and respected. While many researchers have called for policymaking to recommend the return of individual results to research participants, there remains little consensus about how, or even whether, returning individual results would be universally beneficial, ethical, or feasible (Beskow et al. 2012).

Returning aggregate results, however, is posited to improve the value of participant experience, encourage repeated participation, and demonstrate gratitude or respect to participants (Beskow et al. 2012; Partridge 2006). It is also suggested that returning aggregate results, in addition to providing participants with a sense of accomplishment, improves trust in

the research institution, and improves the partnership relationship between researchers and participants (Lemke et al. 2010).

Returning aggregate results to participants of biorepository research also has a downside, namely that of cost in time and other resources (Partridge et al. 2002; U.S. Department of Veteran's Affairs 2009). Nonetheless, current assessments of ethical obligations, duties and practices suggest that returning aggregate results be an integral part of research design (Beskow et al. 2012; Partridge et al. 2009), and a matter of practice across all protocols for genetic research (Fabsitz et al. 2010).

Although a growing body of research describes participants' (and prospective participants') attitudes toward involvement in biorepository research, few projects have sought to explore specific participant preferences regarding how extensive that involvement should be, and how it should be mediated (Meulenkamp et al. 2010; Dalal and Wingnam 2009). Many participants in this type of research are motivated by a desire to further the goals of genomic research, and to provide future benefit to others. Those participants are naturally curious about the impact that such research has on scientific progress and development (Lemke et al. 2012).

Study Setting: Northwest Institute of Genetic Medicine

The Northwest Institute of Genetic Medicine (NWIGM) is a biorepository located in Seattle, Washington. The repository is a collaborative project among the University of Washington Medical Center, Seattle Children's Hospital, Group Health Cooperative (GHC), and the Fred Hutchinson Cancer Research Institute. Thus far, blood samples have been collected from over 2000 participants, recruited from among GHC members who have completed the

online Health Risk Appraisal. NWIGM was founded to facilitate translational genomic research for clinical use. NWIGM research focuses on GWAS and the analysis of stored samples for DNA sequencing (www.nwigm.org, 2008).

Tables 1 through 3 below report demographic information for the NWIGM cohort.

Table 1: Reported Race for NWIGM Cohort (N=2073)

Reported Race	%	N
White	80.4	1666
American Indian or Alaska Native	5.26	109
Other	3.52	73
Asian	3.28	68
Black or African American	2.85	59
Don't Know	2.27	47
Mixed	1.11	23
Missing	0.96	20
Native Hawaiian or other Pacific Islander	0.34	7
Refused	0.05	1

Table 2: Reported Ethnicity for NWIGM Cohort (N=2073)

Reported Ethnicity	%	N
Not Hispanic	92.7	1922
Hispanic	4.82	100
Don't Know	1.45	30
Missing	0.96	20
Refused	0.05	1

Table 3: Reported Sex for NWIGM Cohort (N=2073)

Reported Sex	%	N
Female	65.3	1,353
Male	34.7	720

The types of studies conducted by NWIGM can yield two distinct classes of results. *Aggregate results* are summary findings, specifically information based on the research population as a whole. Aggregate results can include research conclusions, findings, discoveries, summary statistics and information about the research population. They do not include information about specific participants, nor are they generally individually medically relevant. *Individual results* pertain to unique participants within the research cohort and may include (but not be limited to) ancestry information, carrier status, potential increased or decreased risk of disease, and paternity.

The NWIGM biorepository consent form (Appendix 1) allows for communication to participants of a narrowly defined subset of individual results, i.e., medically relevant and actionable individual Information, such as predisposition to a preventable disease. There is no mention of the return of aggregate findings in the original consent document, and it is not clear if the meaning of aggregate results or the potential of aggregate return was discussed at the time of study recruitment.

Quantitative and mixed methodological studies have demonstrated that individuals participating in research prefer to be consulted when their data are shared, repurposed or used in another study (Ludman et al. 2010; Trinidad et al. 2010) and that individuals would welcome

regular updates regarding the progress of the research in which they are enrolled (Lemke et al. 2010). There is little exploration into how this involvement as a whole is experienced or conveyed by the participant, or what preferences participants express for the trajectory of the research relationship.

Focus of Research

Future research protocols could be informed by a more comprehensive analysis of how research participants view the experience of research involvement, how those views are influenced by the existing relationships with researchers or other study staff, and how those research roles are themselves reinforced by these discourses. A better understanding of these connections will help to refine how future studies can best be designed to acknowledge and accommodate the participant research experience. This project is designed to fill gaps that remain in our understanding of how and whether research participants would prefer to have aggregate results from biorepository research returned to them.

The primary research question addressed by this research is how current biorepository participants prefer to have aggregate results communicated to them. A secondary aim is to complement our understanding of these preferences with a deeper exploration of how these choices are influenced by participant perceptions of research participation, such as expectations of research results and applications, values surrounding altruism and benefit, and priorities for resource allocation and research agenda.

Methods

This study uses qualitative methods to address two primary questions: 1) Are study participants who have consented to have their genetic material included in a biorepository interested in receiving aggregate results, and, if so, 2) what are participants' preferred methods for receiving those results. The primary aim is to explore what participants wanted and expected from participation in the NWIGM biorepository, and a secondary aim was to supplement that understanding with a more comprehensive look at the factors that influence participant expectations, research participation, and perceptions of research.

Setting and Participants

This project was conducted at the Group Health Research Institute (GHRI), the research arm of GHC, a non-profit health care system based in Seattle, Washington (ghc.org, 2012). All members of the NWIGM biorepository are GHC members and GHRI is a major collaborator in the biorepository research. Four hundred potential participants were identified from an existing database of 2,073 individuals enrolled in the NWIGM biorepository research project, ninety four of whom were invited to participate. The population represented in the biorepository is predominantly comprised of Caucasian females (Tables 1, 2 and 3). Therefore, a purposive sampling technique was used in order to over-select for non-Caucasians and men in order to ensure a more representative sample.

Recruitment

Ninety-four prospective participants were sent a letter of invitation from GHRI (Appendix 2) describing the project and requesting that interested individuals contact the principal investigator (EB) by phone to schedule an interview time. Potential participants were not contacted directly by the principal investigator (PI) or the study coordinator, or solicited by GHC providers, in order to minimize any potential undue influence or coercion in the recruitment process. Rather, interested participants left their names and contact numbers on a GHRI voicemail exclusive to the study, providing dates and times that would be convenient for contact. Seventeen of the 94 contacted indicated an interest in participating. Of these seventeen, fifteen were successfully contacted and enrolled. The PI returned calls within one week and confirmed each appointment. In this way, the study population was self-selected.

Participants were read a summary of the purpose and procedures, and asked for oral consent at the commencement of the interview. Participants were also asked for explicit permission to record and report their responses. Participants were offered \$20 in exchange for participation. A check was sent to each participant after completion of the interview. These procedures were all reviewed and approved by the Group Health Institutional Review Board (approval number 286303)

Development of the Interview Guide

The questions for this study were developed collaboratively by an interdisciplinary group from GHRI (Evette Ludman, PhD, Julie Richards, MPH.) and the University of Washington

(Emmi Bane, MPH, Malia Fullerton, D. Phil, Gail Jarvik, MD PhD), with input from the GHRI IRB.

The questions covered participant preferences and rationale for aggregate result return, participant perceptions of personalized medicine, motivations for research participation, expectations for future research, and perceptions of research roles, responsibilities and rights (Appendix 3).

Each participant was asked the interview questions in the same order, although the type and frequency of follow-up questions varied by participant based on individual responses. Participants were asked directly whether or not they would be interested in receiving aggregate research results or updates on ongoing research conducted using biorepository samples and data. Subsequent questions probed preferences for the method of the return. Participants were given several options, and asked whether or not each would be acceptable (see Results). Then, in a more open-ended fashion, participants were asked to supplement those options with ideas of their own. Participants were then asked to rank their choices, and explain whether and why they objected to any of the choices provided. Other questions were designed to elicit open-ended reflection on issues such as how participants might prioritize funding for genetic research, their thoughts on personalized medicine, and participant expectations and motivations for participation in order to build a more comprehensive understanding of participant perspectives.

Data Collection

The interviews were conducted by telephone, digitally recorded, and subsequently transcribed. During and after each interview, brief field notes were created to record

interesting responses, develop themes, and identify points that could be followed up in subsequent interviews with other participants. All of the interviews were conducted by the PI, to retain consistency in field notes and to help maintain consistency in the follow-up questions. Interview recordings were securely transferred to a password protected file from the audio-recording device, and transcribed by a professional transcriptionist. During transcription, personal identifiers such as names, locations and potentially personal health information were removed by the transcriptionist, and the transcripts identified by a code number. Only coded transcripts were accessed and analyzed.

Data Analysis

For the primary research question, responses to several closed questions were collected and counted using standard methods of content analysis. A conventional content analysis uses data to describe a phenomenon when there is little previous research or exploration. Responses to direct questions regarding preferences were tabulated across interviews, and the top choices ranked from most to least preferable. Responses to semi-structured questions identified key words or concepts that indicated preferences.

The secondary questions, which explored the factors that influenced participation, expectation, and perceptions of research, required multiple reads of each transcript and used directed content analysis (DCA). When employing DCA, pre-determined codes are used to classify information derived from open ended or semi-structured interviews into categories within superordinate themes. Words, phrases and concepts that conform to the pre-determined inclusion criteria are immediately sorted into groups and subgroups within existing

categories. Words and phrases that do not fit immediately into existing categories can be analyzed during a second pass. Often these can be coded into sub-categories, and sometimes these unsorted phrases lead to the generation of new groups or codes. After the data have been sorted, researchers look for convergences in concepts as expressed by participants or repetitions of ideas and themes across transcripts. A theme that is described by two participants is referred to as “convergence” or a point at which two individuals display a consonance of thoughts or experience. Additionally, points at which individuals differ significantly are also of importance, as these differences can enrich the understanding of diversity in a given experience. Analyzing discrepancies can also lead to the development of new theory (Gee 2011).

The first read involved looking for superordinate, or parent themes within a given interview that related to the structured questions. During each interview and immediately after, notes were written about emerging themes and concepts, and about language used, and words that seemed immediately relevant to the primary questions. These notes were utilized during the initial read of the transcripts to confirm and supplement initial impressions. Key words and concepts were noted, and a preliminary codebook was compiled (Appendix 4). On the second read, the codebook was used to identify and code for words and phrases that evoked similar reactions, or which were used in similar contexts to words existing in the codebook. These words were analyzed in context to ensure that the original intention of the speaker was preserved.

Once each transcript had undergone several individual readings, the same process was used to conduct a cross-textual analysis. The cross-textual analysis focused on identifying

converging themes, repeated uses of words, and convergence in concepts. These concepts were organized according to the superordinate themes they represented, and a list of relevant quotes compiled that illustrate these concepts. In keeping with a commitment to reflexivity, a second reader, Dr. Evette Ludman (EL), was engaged to review the themes and codes, and to ensure that the categorization was consonant across reviewers.

Results

Study Sample

Of the 94 potential participants who were sent letters, we enrolled fifteen individuals who participated in a series of semi-structured interviews conducted by telephone. Though this response rate of 16% is fairly low, enrollment was stopped at fifteen as this study was intended as a preliminary exploration due to limited resources.

Respondents were asked a set of previously composed questions to guide the interview. Interviews explored motivations for participation in biorepository research, if and how participants preferred to receive aggregate results of research, and how participants perceived their own roles, expectations and priorities in genetic research. The general demographic characteristics of the study sample are summarized in Table 4 (see next page).

As discussed in the Methods, participants were selected using a purposive sampling method, so as to ensure a more diverse sample. Nevertheless, as shown, respondents were mostly female and identified as white, with an average age of 61.2. This is slightly higher than the average age of the NWIGM cohort overall (57.6), and is a more ethnically and racially diverse sample (see Tables 1-3).

Below, results are organized by primary and secondary research questions. First, initial motivations for participation in biorepository research are explored, followed by a reporting of how participants would prefer to receive results. Following the questions of motivations and preferred methods of receiving results, is an exploration of participant's priorities for future genetic research. Secondary research questions are explored using an analysis of the parent themes "personal benefit", "allocation of resources", and "roles and rights".

Table 4: Demographics of Study Participants (N=15)

Age	Sex	Ethnicity	Race	Participant ID #
62	F	Hispanic	Other	1
65	F	Hispanic	White	2
56	F	Hispanic	Other	3
64	M	Not Hispanic	White	4
58	F	Not Hispanic	Black or African American	5
57	M	Hispanic	White	6
54	F	Hispanic	White	7
63	F	Hispanic	White	8
61	F	Not Hispanic	American Indian Or Alaskan Native	9
57	F	Not Hispanic	White	10
63	F	Not Hispanic	White	11
56	F	Not Hispanic	Asian	12
60	M	Not Hispanic	Black Or African American	13
59	M	Hispanic	Mixed	14
64	M	Hispanic	White	15

Motivations for Participation in Biorepository Research

Preliminary questions about motivations for participation in, expectations for, and perceptions of biorepository research prompted more specific questions regarding the return of results. The interview first asked why participants had chosen to participate in the NWIGM biorepository and whether they had chosen to participate because they felt they might somehow personally benefit.

The question provoked varied responses, touching on key issues in how individuals perceive research and research participation. Most stated that they were motivated to participate because they felt that all research was important and genetic research especially. “I think gene research is very important,” one participant (12) said. “It's something that should be

investigated.” Others said they felt that genetic research was key to the future of population health, and participated out of a desire to further knowledge in that area.

Most (13 of 15 respondents) stated that they felt participation in research in general was a contribution to a greater good, and that they had no expectation of benefitting personally from the research. “I have no fears for my own health, no...the only benefit is part of the larger society,” explained one participant (9). “I don't have any particular issues that I'm concerned about,” said another (12). Another participant explained: “I'm very interested in making improvements for the future. I recognize that they won't necessarily help me, but anything we can do to cut down on, um, diseases would be great... anything we can do to help people in the future, I think it's important to do as a society.” (12)

A number of respondents expressed the belief that they were too old to benefit directly from genetic research. “My genetics have already activated,” said one (2). When asked if any thoughts of personal benefit have helped motivate them to participate, another said, “If I were younger, yes, but at age 67, I don't... for my future, for my child, yes.” (1) “I think I'm kind of old for that at this point,” said another (12). She went on to explain, “If they're not going to come up with anything new in the next 10 or 15 years, I don't think [it] will benefit me. Unless they can make me younger again.” (12)

Preferences Regarding Return of Aggregate Results

After exploring their motivations for participating in the NWIGM biorepository, respondents were asked whether they felt that they, or other biobank participants, would be interested in receiving updates on projects being pursued using their banked specimens and

data. While responses ranged from emphatic to more hesitant, every participant agreed that they would like to be updated. One participant (4) answered yes, but qualified his answer by indicating that he wasn't sure he would be very interested personally, but that overall he thought people would want that option.

Following exploration of general preferences regarding return of research findings, respondents were asked to indicate their preferences with respect to the method of return, consisting either of a letter, an email, a central website, a phone call, a text message, or a Facebook group. Participants were also offered the opportunity to suggest alternative methods of return, though only two participants suggested alternative options, one of which was to broadcast results on the television or radio, or rent advertising space on buses or billboards. One participant mentioned that an in-person interview would be preferable. As each option was read, participants indicated whether or not the option would be acceptable. Next, respondents were asked to identify the three options they considered most preferable, though some chose four (Table 5).

Table 5. Summary of Preferred Methods of Aggregate Return

Mode of Result Return	Number of times ranked in top 3 or 4
Email	14
Letter	12
Website	12
Phone Call	10
Facebook	4
Text	2
Other	2

Participants were generally very thoughtful in their assessment of the options, usually verbally outlining their thought process. Participants made independent evaluations, considering the merits of each choice in light of cost, convenience, and level of intrusion. Of the options provided, few (2 out of 15) of the respondents felt that text messaging was an appropriate vehicle for returning research results, while 14 out of 15 respondents considered email acceptable (Table 5).

The least preferred methods of return proved to be text messages and a Facebook page. Participants were strongly dismissive of texts, saying that there was too much information to be adequately conveyed, or that they did not use text messaging. A Facebook page was also fairly consistently rejected, and often constituted a completely foreign concept. "What is Facebook?" Several participants asked. One participant summarized her objections nicely: "Facebook lacks...what is it they say about presidential candidates? I think it just doesn't have the appropriate *gravitas*." (8) Others agreed with this assessment, saying that they felt Facebook was too informal, insecure, or complicated. Of the most frequently expressed acceptable methods for conveying aggregate results (email, letter, website, phone call), participants indicated that the most preferable of these were email, letter and website. These three options occasioned the most discussion, as well.

When asked about reasons for their preferences, participants tended to express their rationales along distinct lines. Individuals balanced a desire for hard copies of research findings against concerns for reducing environmental impact, the costs of paper mailings, the time required for addressing individual envelopes, and the concerns about the security of internet-based delivery/communication methods.

Participants expressed concerns about finding a balance between potentially intrusive methods of communication, such as phone calls, and approaches that might be too impersonal or require too much self-motivation, such as a website. Some of the opposition to choices such as a Facebook page was occasioned by unfamiliarity with technology in general; several respondents mentioned that they disliked using a computer at home, that they did not use or subscribe to text messaging plans, that email and Facebook raised multiple security concerns, and that they would have difficulty accessing or remembering to check a website.

Many participants worked through their initial impulse to choose a letter over an email, deciding ultimately that email was both cheaper, and better for the environment. "I could just print the email, then [if I needed the hard copy for records]," one participant (15) said. Another mentioned that he was elderly, southern, and old-fashioned, and often had to ask himself, "Man, am I just wasting paper and resources?" (13) before ultimately deciding that an email was probably a better option. Most participants felt that email was a good balance between a phone call and a website; one would be unable to control the timing of a phone call, but a website would leave too much to the initiative of the participant alone. One participant said, "[an email is] the least intrusive. I mean, you know, it doesn't require answering a phone or anything. And if you want to read it, you can read it, if you don't want to read it, you can delete it. You can file it... um, it's just the most convenient way of getting the information." (12)

Participants expressed additional concerns about screening and missing calls, being unable to remember the content of phone calls, and being charged for text messages or phone minutes. Most respondents had a very negative reaction to receiving information via text

message, though one participant ruefully acknowledged that the major drawback was the difficulty he had reading print on the tiny screen.

Many decisions were driven by expressed concerns related to memory and permanence of information, stating that the letter would last longer than an email or a text, and could be filed for repeated reference. Several participants expressed a distrust of security parameters behind web-based communication. However, the most common factor was the desire to have, or have access to, a physical, hard-copy reminder of the information received.

Priorities for Genomic Research

Several subsequent questions focused on what participants viewed as funding priorities for genomic research. Participants were asked to imagine that they headed the National Institutes of Health (NIH), and to identify which areas from a list of options should receive funding for genetic research. Participants were encouraged to agree or disagree with each option presented. After the options had all been considered, participants were provided with the short list of options they had agreed with, and were asked to choose the top three. A few had difficulty limiting their choices to fewer than 4. Some options required explanation, and several participants seemed confused about distinguishing features among the options. Where appropriate, each option was clarified with examples, and participant questions were addressed as each option was presented.

Participants were given eight options, with the opportunity to provide additional suggestions. The eight options offered were: reproductive health, cancer research, preventive care, diagnostics, information privacy, protection from stigma or discrimination, public

education, and clinical applications. The options identified by each participant as a top priority are shown below (Table 6). The “Other” category represents a single participant’s suggestion of further exploration of gene-environment interactions.

Participants indicated a clear preference for the options that people characterized as most practical and utilitarian. The positive response to these options is discussed in part directly below, and further in the presentation of dominant themes, as many of the responses related more directly to participant perceptions of the role of genomics in current and future clinical care.

Table 6. Top Three Priority Areas for Research Funding.

Priorities for Genetic research	Ranked in top 3 or 4
Clinical Applications	11
Cancer Research	9
Diagnostics	9
Preventive Care	8
Public Education	5
Protection against Stigma and Discrimination	1
Information Privacy	1
Reproductive Health	1
Other	1

Clinical Applications (This category represents ways in which genetic information might be directly incorporated into medical care, for example, by helping to determine the type or amount of medication): Participants were the most enthusiastic about this category, and claimed that it could be the most useful to people in general. Most people were very taken with the idea of genes helping to determine the type or amount of medication, and the concept of “personalizing medicine.” One participant characterized his preference in terms of utility. “Well,

I see less waste in the medical system, more pinpointed diagnostics, and hopefully more effective treatments.” (8)

Cancer Research (This category was described as use of genomics to further exploration into causes, diagnosis and treatment of cancers): Many participants shared that they had lost loved ones to cancer, and mentioned that many people are affected by the disease. This seemed to be the category that participants related to most personally, and that many felt would have the greatest impact.

Diagnostics (This category represents the use of genomics in narrowing the scope of diagnosis): Many felt that “diagnostics” was a reasonable choice because narrowing the scope of diagnosis and helping to limit the diagnostic odyssey would save time and money, and would, in the long run, be most effective in helping doctors treat patients.

Public Education (The category was described as outreach and education efforts for the general public about uses and applications of genomics and genomics research): There was some disagreement among those interviewed regarding funding for public education. Many participants felt that scientists and researchers do not have the obligation, let alone the time and resources, to be responsible for educating populations about genetics or genetics research. When asked who should, in that case, shoulder that responsibility, responses varied. Some asserted that people should look it up themselves, though others claimed that research organizations should be responsible for disseminating results, though not the researchers themselves. “The Media!” was also a popular response to this question.

Protection Against Stigma/Discrimination (This category refers to efforts to protect individuals against potential stigma or discrimination arising from genetic information):

Notably, with only a single exception, every participant mentioned concerns about insurance discrimination. When informed that the federal Genetic Information Non-Discrimination Act (Pub.L. 110-233, 122 Stat. 881 , known as GINA) explicitly prevents health insurers from discriminating against individuals based on genetic information, participants revised their initial decision to prioritize this option.

One respondent felt that protection against stigma and discrimination was an important element of future research. “I think it could become an issue. Particularly in the areas of, uh, gender. ...And...you know, issues of LGBTQ [lesbian, gay, bisexual, transgender, queer] populations....I think it could be used against them...in the sense that...if they find that there is a genetic predisposition to your gender orientation...maybe it could be used against you...because there’s so many different ways that people can be discriminated against.” (5)

However, most seemed to feel that concerns about stigma and discrimination were not areas in which additional funding was needed. The lack of concern may have resulted from confusion regarding the question’s scope. Some responses suggested that participant assessments of priorities were concentrated more locally than nationally. One individual, who expressed the opinion that stigma and discrimination were non-issues, stated in response to a request for clarification that stigma and discrimination were not really potential problems in the Pacific Northwest, because people are more accepting of differences. “...I feel as though we live in the part of the country where, uh, we're more liberal...We’re more accepting of variety and types of people...here, in the Pacific Northwest, we’re more accepting people. There may be parts of the country where it’s not that way.” (12)

In response to probing, many respondents specified that stigma and discrimination were certainly problems elsewhere, but not, they felt, issues needing attention at Group Health specifically. When questioned about lack of concern about stigma or discrimination, one participant said that she had, "No worries about that at Group Health!" (5) but that in general, it might be an issue other places.

Reproductive Health (This category refers to the use of genomics to further reproductive technology such as pre-implantation genetic diagnosis and fertility treatments): "Reproductive Health" garnered little support. Many respondents simply felt that enough money was funneled into reproductive research already, while others noted that they were well past the years in which such research could be useful to them personally. Many respondents felt strongly that it just wasn't as immediate a research funding priority as other, more urgent areas, such as cancer research.

Information Privacy (This category refers to efforts to maintain confidentiality and unlicensed data sharing): One participant expressed his support of additional funding for privacy measures in light of his perceived erosion of privacy standards in general. "Well, you may not get this job because you have bad credit scores," or, "You may not get this job because you're a homosexual," or "You may not get this... Because of the way that society is going now, um, you know, employers now want your Facebook account! So, it could just harm you in, I think... the less they know about me, the better. You know, better my chances. I just don't want all of my stuff aired out there in the public." (13)

It is worth noting that aside from this participant, very few individuals prioritized funding for the prevention of stigma or discrimination, or protecting the privacy of information.

Given the concerns expressed in previous responses with regard to the security of email and expressing concerns about how information is shared, this was surprising. However, participants, when queried, supplied interesting explanations for this apparent discrepancy. For example, while many participants admitted that they felt privacy was important, they also felt that privacy protections were not issues that needed research, nor did they feel that research funding should be redirected from competing projects to fund research on information privacy.

This is in keeping with the tone of most of the responses regarding return of results; the cohort seemed most immediately concerned with husbanding resources to promote health research, rather than exploring participant protections. As one participant noted, “I just feel that It’s important to have the information in the hands of the researchers and the clinicians...Um, We need protections, but I think those should be statutory things...I just think that we’re worrying too much about privacy when, uh, the information sharing and interactions of different, uh, programs and research and clinical studies is...is so important, that we need to share the information as much as we can, while protecting individuals.” (4) Others mentioned that they felt there were sufficient protections in place already.

One respondent noted, for example, that “keeping people healthy, and finding ways to keep people healthy in the future, I think is most important...privacy’s certainly important, but it’s not, to me, as much of a priority as people’s health.” (9) Other participants expressed the belief that while privacy protections were the responsibility of the research institution, those protections were more of an executive function than a research priority: “[privacy protections don’t] seem like so much of a scientific study as an administrative or procedural one...I wouldn’t put that for research purposes...It just wouldn’t be high. I don’t think that’s where the funding

should come from..." (8) Nonetheless, one savvy individual said, "It's pretty important [that genetic information remains private.] Otherwise, you might get fewer people to volunteer [for research]." (3)

Future Uses of Genetic Information

The most popular selections above, i.e., cancer research, preventive care, diagnostics, and clinical applications, were often chosen in light of what people felt would be the most useful application of genomic data. Most responses centered around the importance of aiding diagnosis, preventing illnesses, or determining the best treatment for a condition or disease. After the above options had been discussed and ranked, participants were asked whether or not they were familiar with the term "personalized medicine." As many had not heard the term before, a brief description was provided by the interviewer: "We often use this term to describe the tailoring of an individual's medical care based on personal information, including genetic information."

Participants were also asked if they could think of any benefits to having their genetic information available to their primary care practitioner. Most people felt that the primary use of genetic information in health care would be preventive, or predictive. In the future we could "Use my genetic history to help forecast my health future, and figure out ways to treat problems as they arise, or prevent them from arising." (9) When asked if they could think of some ways genetics could be of use to them specifically, or to their families, one individual said, "Yes, if you know there's [sic] genes in your family, or that would cause a propensity toward something, the individual can take action to prevent it in their early life." (1) Another said "...

you know, what kind of vitamins would be best for me, versus, genetically, I'm a woman over 50, and so therefore you should take a particular type of vitamin." (12)

Many individuals were adamant about the need for integration into clinical care. "I think it's the future of medicine. The things you talked about, you know, finding out which medications are best with which genotypes, I think that's a big...a future out there," one participant (11) explained. Another agreed, "I think it's very important that [genetic information] be a part of medical care, once...it has known medical significance." (8) This implied caveat was supplied more than once, "I think it's an important and practical thing to be involved in medical care, as these kinds of connections get better understood." (8) As one individual said, "[genetics] has import in it for all of us, I mean, if we didn't have genetic information, we wouldn't have genetics, and we probably wouldn't be here." (15)

Others had clearly given the question of how genetic information could be used in primary care some thought prior to the interview. One participant stated that he and his family often discuss the possible future of medicine, although, he warned that they also read a lot of science fiction. "It may not be too far off in the future that we actually all might have an implanted chip which would have all of our records right there, which would make it easy for a physician any place to, you know, to access records and treatments and things like that," he said (6).

However, participants also expressed some concerns regarding the use of genomics in primary care. Participants were asked if they could think of some downsides to including genetic information in routine clinical care. As mentioned above, all but one participant mentioned, unsolicited, fear of insurance discrimination. "...Are you going to lose your

insurance? ...Or [learning you might have] Alzheimer's. What's the price of knowing that ahead of time?" (11)

Another respondent concurred. "[A downside?] Certainly. Using genetic information to exclude certain classes of people from health insurance, for one thing, or charging them different rates...if you have a combination of genes, you're charged, or denied health insurance, or charged a much higher rate. That, I feel, would be very unfair. That would be abusive." (9)

Others expressed varying concerns, including social discrimination labeling and individual distress resulting from alarming knowledge. "You could think, 'oh, I don't think I'll marry you,'" one woman (11) said, laughing.

Some participants addressed the issue of ambiguous test findings as a major drawback. "...To what extent does the genetic information throw you into a gray zone that doesn't really tell you what's going to happen to you. That's going to be hard to deal with." (11) Another response echoed this concern, saying, "It could tell you things you don't want to know, but it's better to know than not know." (8)

Some participants felt that genetic information could be misleading, or cause practitioners to overlook other explanations. Some felt that distracting practitioners from other issues could lead to a less productive and potentially harmful emphasis on potential problems as opposed to current concerns. As one said, "...Sometimes you can know too much. And if you use that information in the wrong way, it's kind of...like an amniocentesis thing?...It's like you're looking for something to go wrong." (3)

Several participants expressed concern about third party access to genetic information, such as pharmaceutical researchers or the government. One participant expressed concerns

about how confidentiality of health information might be affected by routine integration of genomic information. "...If law enforcement was able to get genetic information directly from medical providers, I think, uh, that would, um, present some search and seizure questions for me." (4)

Others displayed more imagination in their prognostications, painting an alarming, if unlikely future, one in which genetic information became a part of the underpinnings of daily life at a younger age:

"[One could say,] 'Ah, Look at that genetic [sic] over there! I don't want my kid in school with him because they're going to get some disease,' or something like that. ...you know, when it comes to genetics, you know, ... maybe I watch too much TV, you know, in my life, but people messing around, experimenting with genetics? ...personally, I'd kind of like to know what they're doing.... you know, I don't stay awake at night worrying about it. But yeah... I think you have to be careful about... um... who has information and what they might be doing with it." (15)

An additional aspect of these interviews that bears mention is the confusion and misconception regarding future uses of genomic data. While the exploration of this particular concern was, by necessity, curtailed in these interviews so as not to alarm participants, it was clear that many of those interviewed were unaware of the potential for future research using their contributed samples, and by extension, seemingly unaware of the fundamental purpose of a biorepository.

Several individuals seemed confused about the purpose of the original research protocol, which was to facilitate translational genomic research, and many harbored the mistaken belief that they would learn about their ancestry or individual disease risk as a result of their participation. Others needed repeated clarification of the distinction between summary and individual results. When asked whether or not he might be interested in receiving summary results of research he participated in, one man replied, “If it’s good news, yes. If it’s bad news, no.” (12)

While discussing participant rights with one woman, she was asked if she felt a need to know what researchers were doing with her genetic data in the future. She said, “[if I sign] something that says you’re going to be using [genomic data] for educational [or] research purposes, I don’t necessarily need to know what those are, except for if...like, I don’t know, because then it gets kind of into a moral issue, if you’re using blood samples from babies...I would want to know that my blood is not being used for that.” (3) When asked if she minded her if her samples were used beyond the original research protocol, she replied, “After that, then, no. I don’t care.” For many of the participants, their perception of their participation ended after they contributed a sample.

Discussion of Dominant Themes

Throughout these interviews, participants expressed their preferences and perspectives on the research experience. The following section discusses the prominent emergent themes identified in these conversations, and explores how these themes themselves contribute to the

overall experience of the participant, and how these experiences inform participant preferences regarding aggregate result return.

Altruism, Personal Benefit and Allocation of Resources

As discussed above, one of the emergent themes throughout these interviews was that of the question of personal benefit versus altruism, and the need to maximize the applications of genetic research. This theme was evident in discussions regarding motivation for participation, the value of participation, and expectations for personal benefit, as well as discussions of how limited resources were best allocated to ensure that the research itself was meaningful. Most participants said they participated in research explicitly to help others, and agreed that the research agenda should be prioritized above the return of aggregate results. However, many mentioned that aggregate results would be of no direct utility, but would be primarily useful in lending a sense of purpose to their contributions.

Many felt that receiving updates or aggregate results would help to provide some meaning to their participation. “If there... if there was something... if there was something available, just um... it's like if you donate to a charity or something, you just kind of like to know where your money went, maybe into a pool or something.” (15) Most agreed that aggregate results would give them a sense of accomplishment, and help them to feel that their contribution was valuable. “it makes you feel like you're, um, what you've done is helpful and meaningful.” (12)

However, most respondents stated that lending an air of legitimacy to their participation was really the extent of how useful aggregate results would be to them, since

aggregate results could do very little in the way of individual benefit, and would not mean much to them personally. Most mentioned that individual results would be much more helpful or interesting. When asked if she would be interested in receiving aggregate results, one woman asked, "What might be there that might be specific to me?" (15) One participant mentioned that aside from health information, it might be interesting to receive some data about his ancestry. "... I know that some people like to get genetic tests to, kind of assist in finding their ancestral lines and where they might have come from, the general area of the world, especially since most Americans have ancestors that came from someplace else than North America...." (15)

Several mentioned their desire for learning something about themselves, though they were careful to draw the distinction between what they felt was a right and what they felt was a courtesy. When asked about expectations for personal benefit, one participant was specific. "I didn't have that expectation," she said, laughing. "You could say I had the wish." (11)

Some people said they would have no use for or interest in study updates if there was no personal application. "Unless there's something critical that they find that's related to me, I don't have a need to find out how they're using study information," said one man (7).

Others felt that research itself was simply more important than informing participants of the findings. "If you had to inform everyone who contributed a bit of...uh...physical fluid or bodily parts, then you would never get any research done. It just doesn't seem practical," said one (8). "I didn't join this project just so I could be updated about what you're doing. I joined this project so that research, real research, could be done." (9)

When asked if they would be comfortable receiving results less often or not at all if it meant more research could be done, most participants said yes. However, some clarified that while “less often” was acceptable, especially given the limited funds available, they would not be comfortable with never hearing from researchers.

Throughout these interviews, participants expressed a commitment to working through the question of limited resources versus participant protections, such as privacy and confidentiality, and participant benefit. Most of those interviewed felt that research was of ultimate importance. In response to queries about why he would be willing to forgo updates to facilitate further genetic analyses, one participant responded, “Because I think it’s important that, um, genetic analyses get done, and I understand what budget crunches are like.” (5) When the same respondent was asked if he felt that a participant would have the right to know what was being done with their information, he responded, “Um, I feel like they...we do, but I also, at the same time, realize that, um, we can’t always get all of the information all of the time.” (5)

Some evidenced a rational understanding of the research process. “I realize it takes a huge interval of time to do analyses on... on something. Especially if you're... person's taking a drug, and you have a control group taking a placebo, and you have to get all the information back again. It does take a while.” (1) Another participant said that genomic research sounded extremely complicated and lengthy, and said simply, “I don't anticipate they'll have a lot of time to keep me up-to-date on all of it.” (10)

Many felt that availability of research results was important, but that it should be the purview of participants rather than researchers to access them. These participants expressed a belief that research partnership indicated that participants themselves had certain

responsibilities for keeping themselves informed. “Well, if the information [is available] then the participants can go and ahead and look if they want to. If it’s not that important to them to look, you shouldn’t be tracking them down, or chasing them down, to give them the information. You’ve got more important things to do,” said one (9).

Many acknowledged the need for parsimony in a time of limited budgets, and mentioned that while receiving updates might be considered a right, in light of current need for constraint, they felt like it was more responsible to waive it. “... you know, if I obey the speed limit, then the police aren't spending their time giving me a ticket, they're spending their time looking for bad guys. And that's how I think about my health. If anything would help me to be healthy, gives doctors more time to help people that really... really have some needs. So that's the way I kind of look at health.” (15)

Roles and Rights

A second major theme focused on participant conceptions of research and clinical roles. This category was mainly represented by the words participants chose when describing their experiences with genomics research, their relationship with researchers, clinicians, and their opinions regarding rights and respect. This theme explored how participants viewed their own role in these relationships, and focused on perceptions of what characterized that role, such as respect, rights, protections, and inclusion in future related research projects, and extends to both clinical and research obligations.

Most individuals seemed not to draw a distinction between being a research “subject” and being a research “participant,” as the terms were frequently used interchangeably in the

interviews. Additionally, expectations for updates and on-going communication were low, with several individuals expressing surprise at the possibility of receiving aggregate results. A few individuals mentioned that they had had previous experience as a research subject, and that those experiences had informed their approach to research as a biorepository participant. “I’ve done medical research, so...there wasn’t any expectation [of return of results or ongoing communication] with the kind of things that I researched.” (11) “If I’m participating, I’m participating,” said another (1), negating the possibility that his participation might be contingent on additional factors such as type of experiment or return of results. Another participant drew a distinction between what might be due to a research partner as opposed to a subject, “No, [one is not entitled to results of a study] because they *volunteered*.” (7) Others, however, felt that participant rights entitled them to that information. Interestingly, many of those who expressed that they felt they had a right to research results also explicitly stated that they were willing to waive that right in order to prioritize research. “I’m not particularly concerned with my own information, no...I mean, theoretically, I have a right to know, but I’m not particularly concerned with what that information develops from” said one (9). “Oh, I suppose I have the right to know,” said another,” but do I *demand* to know? No.” (1)

Language around participant expectations was also interesting, as most of those centered around a desire for what the return of results might represent in terms of respect rather than information. “I don’t think it’s a right,” said one (12), “I think it’s a nicety.” Others mentioned that it would be “respectful,” “interesting” or “valuable.” As one participant put it, “I just feel, the person, if they participate in a study, they must have some, uh, commitment to

it in some feel like they're vested in it, and if you're vested in something, you'd like to know an outcome.” (1)

Other participants felt that responsibility for accessing results should be the participant's rather than the researchers. Many people noted that they would be happy to find and learn more about aggregate results themselves, if they were merely made aware of where they could look for such things. “Yeah, when [information is] not at all [accessible], then I don't really... I'm kind of out of touch. Because I don't... I mean... yeah, because I don't have any way to get the kind of information I might be seeking,” said one (13). Another expressed himself in terms of priorities. “Well, if the information is there, then the participants can go and ahead and look if they want to. If it's not that important to them to look, you shouldn't be tracking them down, or chasing them down, to give them the information. You've got more important things to do,” he said (9).

A preponderance of participants seemed bemused when asked to assign responsibility for public outreach and education. While many maintained that it should be the responsibility of the research institution to keep the population informed about current research, many suggested that this is a role better suited to the media.

Summary of Results

The interviews suggest that participants in this cohort felt strongly that research was an important priority, and genetics research in particular. Most individuals participated in biorepository research primarily out of altruism, though some expressed some curiosity about their own genetic information. All participants said they would be interested in aggregate

results, or that participants as a whole would want to have that option. However, while participants were interested in receiving aggregate results, the majority of participants felt that returning aggregate results was penultimate in priority to the conduct of research. They were less interested in receiving summary or composite results than they were in receiving results personal to themselves.

Discussion

This study explores in greater detail participant preferences regarding the need for, and method of return of, aggregate results. To this end, 15 qualitative interviews explored the perceptions and preferences of individuals purposively selected from the NWIGM biorepository research project. It was determined that participants felt aggregate results would be both interesting and encouraging, and that they would prefer to receive those results in a non-intrusive, easily retainable manner, such as a letter or an email. Although participants agreed that returning aggregate results was, as one participant noted, “a nicety,” a significant number of respondents stated explicitly that they would prefer that resources be conserved and dedicated to additional research conduct, such as genetic analyses. Moreover, most (all?) participants reported that individual results would have more meaning to them than aggregate results.

Based on the consensus expressed in the literature for return of aggregate research results it was expected that the majority of individuals would express a desire to learn aggregate research results, and that most would be anxious to remain informed of developments as the research progressed. What was unexpected was how many participants stated explicitly that, given a choice, they would prefer that funds be allocated to research. However, given this perspective, it is unsurprising that so many participants would choose methods of return that did not immediately appeal to them in deference to budgetary and temporal constraints although it was expected, and supported by the research, that participants would prefer written communications such as letters to more automated updates

like text messages or emails. Previous research related to themes of participant preferences, expectations and motivation will be contrasted with the results of this study.

Participant Interest in Research Results

These findings can be laid alongside previous research relevant to the return of results to participants. However, more has been written previously about return of aggregate findings in clinical research settings than in biorepository research. While there are numerous similarities between participants in clinical trials and participants in biorepository research, namely the personal and relevant nature of study outcomes, there are some notable differences. Clinical trials have a far more specialized and immediate outcome, whereas genomic research is often broader, with results that may vary in relevance over time. These differences may explain, in part, differences relative to the findings described here.

The current study found that while all respondents expressed interest in receiving aggregate results, most felt that resources were better prioritized towards further research, and that individual results would be more meaningful to them than summary results. This is consistent with previous published findings related to clinical trials. In 2005, Partridge et al. conducted a quantitative survey of clinical trial participants. Of all respondents, 88% said they would want to be informed of aggregate results, as compared to the 93% who opted to receive individual results. Consistently, individuals regarded aggregate results as a measure of the value of their contribution, and most noted that they would prefer to receive individual results. This study suggested that receiving results by mail was the most acceptable option for participants, which underscores the more immediate reaction of most participants in our protocol.

It was also surprising to learn how strongly participants in this study felt about the superior importance of the research itself. Given that several respondents stated that they believed that access to research outcomes and further research protocols was a right of participants, it was unexpected that the majority (12 of 15) of participants stated explicitly that they either were willing to waive that right, or felt strongly that those rights were subsumed by the need to conduct more research.

Partridge and Winer(2002) and Fernandez et al. (2009) argue that both individual and aggregate results are essential to return to research participants, as the majority of participants in clinical research view access to results as a right. While this is inconsistent with the findings reported here, this paper encourages researchers to explore the question of how results to should be returned, as opposed to whether or not they should be. The authors assert that a clear plan to return results should be included in the original research design, with the inclusion of an option for participants to opt out. This approach is a slightly different take on the traditional argument, which proposes that individuals opt in to a program to receive information regarding summary and individual results. This paper takes the approach that receipt of this information should be considered a right of participants, and assumes that participants will welcome these results, although they do acknowledge that not everyone will want to receive individual results.

Partridge and Winer (2002) propose that results should be returned by “Mail, internet, telephone call, or in person meeting,” and that “optimally, flexibility should be built into the process to allow patients with different learning styles and potentially different trial experiences to receive the results in the manner that is best for them individually.” This

proposal does not allow for the obvious obstacles to this approach, which are namely money, time, and overall feasibility. Moreover, this proposal does not consider that participants may wish to waive their newly acquired right to results in favor of reallocating the resources required to research. Dalal and Wingnam (2009) also explored participant preferences in how results are communicated, specifically aggregate results using a quantitative survey.

The Dalal and Wingnam study, while not specific to genomic research, explored how participants of research trials initially preferred to access information, and followed up to determine how each given method of return was viewed by participants. The researchers determined that patients did want aggregate results of studies they had participated in, and the preferred method of return was by letter or email. While Dalal and Wingnam initially state that returning results in clinical trials is uncommon in the UK and in general, they do refer to the burgeoning debate regarding aggregate results as “. . . [a] moral obligation to inform participants of the results as a matter of human dignity and to avoid treating people simply as a means to an end in scientific research.”

Dalal and Wingnam (2009) also noted that not all participants elect to receive aggregate results: while 90% of the participants in this specific study requested return, a previous study focusing on antibiotic use and early delivery found that less than 20% of participants opted to receive aggregate information. However, Dalal’s research had a much higher response rate (86%) which can be partially explained by the fact that the 2009 cohort was self-selected at the time of the initial trial, while previous research had relied on random recruitment from trial participants.

The findings of the current research are generally in accordance with those reported by Dalal and Wingnam (2009), though there was some discrepancy in the demographics. The cohort in the 2009 study was made up of a preponderance of men, whereas the participants in our protocol were mostly female. They found that their male participants preferred to be informed of aggregate results in a meeting, and that most women were opposed to receiving results electronically and preferred a letter. These distinctions were not borne out by the results of the current study, although it may be that in larger cohorts, gender-based differences would be more apparent. It is also possible that these differences are attributable to age, level of trust in the research institution, and familiarity with technology. Additionally, Dalal and Wingnam (2009) did not explore the reasons behind individual preferences, simply offering a basic survey format for participant choices. Their study found that participants experienced a high level of satisfaction with the results returned, and with the method of return chosen, though again, there was little explanation for why this method was satisfying or preferred.

The authors note that a further qualitative study aimed at exploring the rationale behind participant choices would be highly beneficial. The reasoning that participants in the current protocol advanced for their preferences may, despite the particular nature of the cohort, be useful in helping researchers craft more relevant and appropriate policies in regard to aggregate return.

Dixon-Woods et al. (2006) also pursued the question of how individuals prefer to access aggregate study results. While their study was again specific to clinical trial participants, there were also some significant differences between the cohort involved in that research and those involved the present study. In stark contrast to the participants in the current study, less than

one-fifth of participants in the 2005 trial indicated that they wished to receive summary information about the trial.

However, some strong similarities were evident between the participants of Dixon-Woods et al.'s (2006) protocol and those who participated in the current protocol. As with the cohort interviewed in the current protocol, participants were far more interested in results as they applied specifically to themselves. For example, participants in the Dixon-Woods et al. cohort wanted to know whether they had been assigned to a control group or an experimental group, and whether their participation had affected them in any way. Additionally, most participants viewed the receipt of aggregate results as a legitimization of their own participation. As with those in the current protocol, aggregate results were regarded as most useful in providing value and worth to the individuals' participation.

The Value of Participation

Participants in this study overall attached far less value to aggregate results than personal results. A common statement expressed was that the primary value of access to or return of aggregate results lay in the fact that seeing progress underscored the value of their own contributions and participation in research.

Previous research is consistent with these observations. Snowden et al. (1998) offered both aggregate and individual results to 24 sets of parents whose children had been enrolled in a clinical trial, and assessed the impact. While much of this study focused on the import of individual result return, and the necessity of being sensitive to potentially distressing information, this study also highlighted the importance of results to participants in lending

value to participation and increasing satisfaction with participation. Snowdon et al. (1998) demonstrate that participants need to feel their contribution was valuable, and that this element is key in continuing to attract participants to further research. These authors, as well as others (Trinidad et al. 2010; Lemke et al. 2010; Beskow et. al 2012) suggest that returning results (especially aggregate results) can provide participants with a sense of accomplishment, and that results play an important role in crafting and maintaining a relationship with participants characterized by transparency and inclusion.

Maintaining Trust in Research Relationships

A wide spectrum of diverse responses arose when participants were questioned as to their expectations regarding the research experience. Many of the responses indicated an explicit trust in GHC and GHRI to behave considerately and respectfully towards research participants, some drawing a very firm differentiation between their confidence in Group Health as opposed to elsewhere. This is in accordance with the findings of Lemke et al. (2010), who noted that research participation was heavily motivated by the reputation of the institution, and the nature of the relationship between the participant and the researchers.

Beskow et al. (2012) argue that return of aggregate results ultimately strengthens and promotes the research agenda. They state that returning aggregate results can reinforce the conception of partnership in research, and can strengthen trust and enhance the reputation of research institutions in the community. The authors observe that biorepositories as research institutions will require additional trust building within communities, as they give rise to several inherent concerns about continuous data use, future applications of genomic

information, and potential misuse of that information. Beskow et al. also discuss the potential for confusion or personalization of these results, which suggests that although returning aggregate results may be a moral responsibility, it may also be beneficial to ensure that these results are not misconstrued or misapplied. For example, it is possible that individuals may perceive aggregate results to be personal, or ascribe personal meaning to summary information or risk factors. This could be distressing, and require additional intervention and/or education in order to correct these misconceptions. As Snowden et al. (1998) note, determining the level of education of individual participants in order to determine what information to provide is a problem of varying complexity.

The participants interviewed for this study constitute a cohort that exhibits a strong dedication to involvement in their own health care and applicable research protocols. Most participants mentioned conducting independent research about their conditions, their lab results, and their medications. Consequently, the desire to remain involved in the research reflects less of a misguided belief that individual results were guaranteed, and instead seems to be more of a product of interest and curiosity.

Individuals expressed a desire to access aggregate results in order to explore the effect of their contribution more thoroughly, but did note that since these results were not expected to benefit them personally, they were less invested in being kept apprised and more invested in ensuring that projects in which they participated produced actionable, legitimate results. The question of how aggregate findings might influence expectations and/or understandings of individual results was not explored directly in these interviews.

Many of those interviewed for this study were careful to delineate between expectations and desires, noting that while they did not *expect* to be notified of study results, they did have a *desire* to be notified. Several clarified further, explaining that they would prefer to be given personal results.

This particular cohort is comprised of involved, self-directed individuals who did not expect or require momentous efforts on the part of the research institution to keep them involved. A familiar refrain became that of access to information – participants did not expect researchers to make contact directly and discuss aggregate results but they were willing to explore the outcomes themselves. The exploration of how to best direct individuals to responsible, peer reviewed information may also be grounds for further research, as reliable access to clear and accurate information may be directly related to how likely individuals are to seek this information on their own. Given the number of misconceptions that surfaced throughout those conversations, it might be prudent to also evaluate alternative methods of presenting peer reviewed results.

In summary, while nearly every participant questioned in this study expressed interest in receiving information regarding aggregate results, most professed themselves less interested in those results than in information that might have more personal application. Additionally, nearly all agreed that returning aggregate results was not nearly as important as conducting the research itself, and thus resources were better allocated to conduct of research. In light of these findings, some form of return of results is indicated, but it may be best to devise a strategy during the initial consent process by which participants could themselves determine degree to which information is shared.

Recommendations for Future Research

Future research might well focus on obtaining further insight into the value that participants ascribe to return of results, and the meaning that aggregate results might hold for different subsets of NWIGM participants. Moreover, assessing the need for re-consent when using stored samples, and assessing participant's understanding of informed consent paperwork, particularly when determining whether or not returning results is stipulated in the original consent, may help to clarify how a desire for results is influenced by participant expectations. While research is evolving on the nature and content of informed consent, a more interactive process is needed when biorepositories conduct multiple research protocols with the same population. While this study focused primarily on the return of aggregate results, participant comments indicated fundamental misconceptions surrounding sample use in biorepositories, namely that samples would be used for a single research protocol only. Further research may be needed regarding the management of initial and continual uses of samples.

While most participants in this study displayed at least a rudimentary understanding of genomics, the study also revealed several interesting misconceptions regarding personal benefit and the original informed consent. When assessing how well participants understood the stipulations of the original informed consent form for research participation, it may be relevant to explore how these misconceptions might influence individual participation.

Many of the above studies noted that participants expressed frustration with a lack of individual results (Dixon-Woods et al. 2006; Dalal and Wingnam 2009). Dixon-Woods et al. noted that many participants wanted a more concrete summary indicating specifically success or failure of a given experiment or protocol, while many expressed dismay with the amount of

time that lapsed between participation and return of results. Dixon-Woods et al. discuss the importance of cultivating reasonable expectations of research in participants, and highlight the need for a better balance between comprehensive information and resource allocation, and most importantly participant education. In response to the confusion generated by a lack of comprehension regarding trial results, the authors note that “Providing results to participants in research studies is not straightforward; it constitutes an intervention in its own right and requires more rigorous evaluation than it has previously received.” The authors also argue that we cannot assume that any result provided to participants will be clear and direct, and that measures should be taken to evaluate the potential for necessary ancillary support provision (Dixon-Woods et al. 2006).

One potential cause for concern illustrated through some of the respondent’s language is the belief that research participation will offer personal benefit. It has been argued that the concept of the “therapeutic misconception” is more nebulous in genetic research than it is in other disciplines, given that personal benefit is possible under certain circumstances (Halverson & Friedman-Ross 2012). Indeed, the original consent form for the NWIGM biorepository stipulated that directly relevant health information, if found, would be returned. Nevertheless, a few participants mentioned that they expected to receive personal results as a consequence of participation, or that they were motivated to participate through curiosity regarding ancestry or hereditary conditions.

Additionally, most participants seemed unaware of the potential for future uses of tissues stored in a biorepository, and so assumed that aggregate results, if any, would be returned only once. Several mentioned that they had participated because they believed

strongly in the focus of the particular project, but did not indicate that they were aware that there was potential for future research using the same specimens. While this was notable, it was not a line of questioning pursued, out of concern for alarming participants and encouraging speculation and distrust. However, given that many felt strongly about moral agreement with research they participated in, that issue may bear further examination as it is relevant to the process of re-consent and ongoing engagement.

Recommendations for NWIGM Return Policy

Beskow et al. suggest that provisions for aggregate result return should be explicitly included in the original consent forms, and explained comprehensively as a part of the consent process. Additionally, the authors suggest that results with limited significance be made passively available, for example, on a website as opposed to in a letter, so as to minimize the possibility of participants receiving distressing or unwanted information. The results of the present study support this recommendation, and further suggest that those provisions should be made voluntary; participants should be presented with the option to waive receipt of aggregate results. After reviewing levels of interest and participant concern regarding certain methods of return, the following course of action is proposed as both respectful and non-invasive, as these criteria were the most significant in guiding participant preferences for modes of aggregate return (see Results).

Recommendations should consider limited resources, the consistent positive response to mailing (electronic and traditional), and the acknowledgment that the predominant obstacle to the universal appeal of a website was cited as requiring too much effort on the part of the

participant. With that context, the recommended course of action in response to the emerging question of how to return aggregate results to this specific cohort would be to establish a central website, with an automated listserv that would notify participants when the website was updated with a link included. Such an approach addresses the preferences reflected in participant interviews that the responsibility for checking a website not be placed entirely on research participants, while still respecting participant preferences for a non-intrusive method of communication. Further, it minimizes the time and resources necessary to initiate individual contact with research participants to apprise each of them of aggregate results.

The current practice of existing biorepositories is to return general or aggregate findings as they become available via either a newsletter or a website (Zawati & Rioux 2011). The findings of this study suggest that a more practical method might be a combination of these two approaches; while most participants felt that a letter or email would be the preferred method of return, given the time and resources necessary to write a newsletter in contrast to the ability to update isolated sections of a website, and given participant preference for the prioritization of research, it might be more appropriate to create a listserv to notify participants en masse when the website has been updated with new information.

Organizing results on a website would allow for more options, clearer categories, and better explanations of the results in question. It would also allow participants to access optional built-in explanations of each finding, creating a tiered presentation of information which could be displayed or explored at the discretion of the participant. A newsletter would not allow for this method of optional access, making the amount of information conveyed in an email or letter potentially overwhelming or confusing. However, an email notification summarizing new

developments with direct links would address participant preference for an existing reference, while still allowing for further information should the participant choose to access it. This combination also resolves the issue of responsibility – many respondents mentioned that a website alone would place too much burden on participants to remember to check it, or to memorize the website address.

The potential for misunderstanding aggregate results, or the provisions of the initial informed consent agreement, raises the question of whether or not resources should be made available for clarification and education when aggregate results are offered. While the general consensus is that aggregate results are, in and of themselves, not harmful and can be returned without concern, and while many argue that these summary results are a right adjunct on participation in research (Fernandez et al. 2003) and that researchers have an obligation to provide them, it should also be considered that confusion about the purpose or relevance of these results could cause alarm or distress to participants (Lemke et al. 2012). The potential for misunderstanding demonstrated within our own research suggests that at the very least steps should be taken to explicitly clarify the nature of the results that are being returned whenever the possibility of return is discussed.

While the responses outlined here are in many ways indicative of the cohort interviewed, it seems likely that similar policies might be implemented with success elsewhere. Although many of the responses may have been influenced heavily by age, geographic location and affiliation (for example, it is unlikely that one might encounter analogous loyalty and trust to health cooperatives universally) the tensions created by autonomy and paternalism, paucity of resources and access to information might well be comparable in more diverse populations.

Limitations

The current study is subject to several significant limitations. Some limitations derive from to the size and composition of the cohort from which the sample was recruited. The original mailing of 94 yielded a 16% response rate, which can be attributed in part to the nature of recruitment: the burden of contact was placed entirely on the potential participants. Moreover, because enrollment was stopped after fifteen interviews, there is an inherent bias towards those individuals who responded more quickly, and hence were more positively inclined to discuss specifics of biorepository research. It is possible that had individuals been identified and contacted by random telephone recruitment procedures, the response rate would have been much higher. Given the low response rate, it is possible that results of this study are biased towards those who have a more significant interest in research and research results, and as such, cannot be confidently generalized to the NWIGM cohort or other populations.

A sample size of fifteen is not large enough to justify drawing concrete conclusions. Moreover, the sample itself, while purposively selected to compensate for the original cohort's homogeneity, was composed predominantly of Caucasian females, and therefore these results may not be generalizable to other races or ethnicities. The age range of this cohort (54-64) was also limited, which suggests that the results and conclusions may not extend well to other age groups. It is also likely that several of the outcomes of this protocol are influenced by the age of the participant, which may inform results regarding how participants prefer to receive results, namely factors such as familiarity with technology, previous participation in research, prioritization of genetic research, and motivations for participation in research.

Several avenues of investigation were heavily circumscribed in order to avoid alarming participants, or drawing attention to inconsistencies between their beliefs and the tenets of the original consent form. Consequentially, it was often impossible to pursue questions surrounding therapeutic misconception, repeated use of samples, or potential breaches of confidentiality. These topics may have had implications for the outcomes reported here, and might have provided alternative explanations or interpretations of these data. However, since even hypothetical references to these subjects may have proved distressing, they were not pursued.

Additionally, the GHC is exceptional in its relationship with patients and research participants; these data may have been heavily influenced by the nature of that relationship, as not all institutions can be expected to foster the same sense of trust and affiliation. Moreover, since this cohort was self-selected, it is likely that these individuals feel a more significant sense of loyalty and affinity for the Cooperative.

Conclusions

The most prominent theme emergent in these interviews was the prioritization of research over adjuvant issues, such as privacy or return of results. Throughout each area of discussion, participants consistently demonstrated an explicit preference for outcomes or decisions that conserved funds for research conduct.

This research demonstrated that while individuals in this cohort expressed interest in receiving aggregate results, most preferred that resources be allocated to further research, and felt that personal results would have more value to them as acknowledgement for their participation. Participants preferred to receive aggregate results in ways that they perceived as less intrusive, such as via email or letter, rather than receiving them over the phone or text message. This preference, however, may be attributable more to the aggregate and impersonal nature of the results; these expressed preferences are not extendable to personalized, individual results. The interviews demonstrated that participants of genetic research are interested in the issues of privacy, confidentiality and participant respect, although these issues are of secondary importance when contrasted with the conduct of research and the development of more targeted clinical applications, and participants would prefer that resources be concentrated on furthering research rather than participant protections.

While the current consensus among researchers and policymakers is that returning aggregate results to study participants is ethically indicated, demonstrates respect, and gives meaning and relevance to participation, the results of this study suggest that participants may prefer to be presented with all information, including the potential consequences of limiting resources, and given a choice as to how they would prefer those resources be allocated. While

this information could potentially be considered coercive, it can also be argued that asking participants to make a decision based on insufficient data, or making that decision on behalf of participants, could be an undue exercise in paternalism. If the stated goal is to demonstrate respect for participants, involve participants in research, and enhance the value of participation, it can be argued that involving participants in the process of crafting the research agenda and the prioritization of diverse interests ultimately fulfills these objectives more comprehensively than the provision of aggregate results with little personal application.

The question of how to best involve and respect research participants is an evolving question, and one that gains relevance when applied to biorepository research, which is of itself an evolving field. These issues are likely to affect more and more people as the use of genetic information becomes more commonplace and more practical. With the uses and potential applications of genetic information growing, and with them the prevalence of biorepositories, this is the time to begin examining the obligations and perspectives that inform our policies, and to ensure that the preferences and expectations of participants are a primary consideration.

An interesting aspect of these interviews en masse was hearing individuals work through the process of resource allocation, personal investment, and population benefit. It was both unexpected and inspiring to be a part of this process; the deliberations and the complexity of the responses were what made these results as rich and as detailed as they are. Overall, the participants in this study were thoughtful, and spent time working through the intricacies and implications of each question. While some were more ponderous than others, and others

downright glib, each one of the individuals I spoke with contributed insightful, valuable and provocative material, and often suggested unforeseen connections and complications.

As one participant said, “Well, you know, genetics is so intimate to us.” He laughed. “I mean, it's who we are.” (15)

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Appendix 1: Letter of Invitation to Participate In Research



January 9, 2012

Participant Name
Street Address
City, State, Zip code

Dear PARTICIPANT,

Would you like someone to pay you for your opinions about participating in genetics research?

If the answer to this question is yes – keep reading.

Researchers at Group Health and the University of Washington want to know how to communicate better with participants in genetic research projects.

We are contacting you because you participated in the Northwest Institute of Genetic Medicine project. We want to know more about your thoughts about participating in this project and genetics research in general. The interview will be done over the phone and will take about 20 minutes. We will pay you \$20 for your time.

(We have included an information sheet that has more details about this project and about being a research participant.)

Interested in learning more or joining this study?

Call us at 206.287.2827 to leave your name and phone number on our confidential voicemail and we will call you back.

If we have not heard from you within about 7 days, we may call you to see if you are interested. If you do not wish to be called, please leave a message at the phone number above.

We look forward to talking with you!

Sincerely,

A handwritten signature in black ink, appearing to read "Evette Ludman".

Evette Ludman, PhD

Lead Investigator, Group Health Research Institute

PS - Being in this study is voluntary. Your decision won't affect your care or your benefits at Group Health, and none of the information we collect will be shared with your doctor or added to your medical record.

Appendix 2: NWIGM Consent Form

CONSENT TO PARTICIPATE IN A RESEARCH STUDY Northwest Institute of Genetic Medicine [NWIGM]

Please read this entire document before agreeing to join this study. If you have any questions about the study, you may contact the study coordinator at Group Health at 1-866-458-5467. You may also contact the researchers listed below.

Researchers

Eric B. Larson, MD, MPH, Group Health 206-287-2900
1730 Minor Ave Suite 1600, Seattle, WA 98101

Gail Jarvik, MD, PhD, University of Washington 206-685-9069
University of Washington Medical Center, Box 357720, Seattle, WA 98195

Michael Bamshad, MD, University of Washington 206-221-4131
University of Washington Medical Center, Box 356320 Seattle, WA 98195-6320

What is the purpose of this study?

The purpose of this study is to create a research database and sample bank to learn more about how genes can affect health or disease. Genes are small portions of DNA found in your cells. They carry information about traits that run in families, like whether you will have brown eyes or blue eyes. They may also partly explain why some people are more likely to get diseases like diabetes, asthma and dementia. Understanding more about the relationship between genes and health may help to develop new ways to prevent and treat some of these diseases.

Who is funding the study?

The Washington State Life Sciences Discovery Fund is funding this project.

What will happen if I take part in this research?

We will ask you to provide a blood sample so we can store your genetic information for future research. We will also store your answers to the questions we asked you before sending you the blood draw kit. In the future, we may also look at additional information in your Group Health medical record, like:

- Your medical history, from both the past and in the future, including sensitive topics like mental health disorders, alcohol and substance use, and sexually transmitted diseases
- Medicines you have been prescribed
- Lab and other test results
- Behavioral information, for example, whether or not you have ever smoked.

We will then compare your information with other participants to try to understand the differences between people. This could help researchers in the future answer questions, like:

What genetic features may be important for developing vascular (blood vessel) diseases? Or what are the best medications to lower an individual person's cholesterol (also called "personalized medicine")?

Future research using your medical record information (described above) and blood specimen may be conducted by researchers who are not affiliated with Group Health. We may also send a part of your sample to other research partners to do genetic tests in their labs. We will not give your name, Group

Health number, or contact information to research partners; all your information will be labeled only with a code number.

Future researchers may want to contact you to ask you to additional questions or to participate in additional research studies. If this happens, Group Health staff will contact you to tell you about this research and/or ask for permission to release your contact information. You may refuse any request asked of you, if you wish.

How do I give a blood sample?

Detailed directions are included in the blood draw kit. Briefly, here is what will happen:

- ❖ We will mail you a package that contains items needed to draw a small sample of your blood.
- ❖ You will take this package to your local Group Health Cooperative lab.
- ❖ Give the package and enclosed directions to the staff at the lab.
- ❖ The staff will draw a small amount of blood, about 4 tablespoons. This visit may take 10-30 minutes, depending on the wait time at your clinic.
- ❖ The lab staff will package your blood sample and ship it to a lab at the University of Washington.
- ❖ If we do not receive your completed consent form or returned package within two weeks of sending them to you, the Group Health study staff will contact you to make sure that you received them.
- ❖ There is no charge to you for the blood draw or for mailing the package. To thank you for your participation, Group Health researchers will send you \$50 when they receive the package.
- ❖ If your sample is not useable when it is received at the University of Washington, you may be asked to provide a second sample. If you agree to do this, you will receive a second \$50 after your blood sample is received at the University of Washington.

What will be done with my blood?

- ❖ To protect your confidentiality, we will label your blood sample with a number only, not your name. Only select study staff at the Group Health Research Institute will be able to link your number with your name.
- ❖ We will conduct studies on the genetic material called DNA and RNA taken from the cells in your blood.
- ❖ We will compare your genetic information with information from your Group Health medical record and additional information you provide to us. Also, to help us understand the differences between people, we will compare your genetic and health information with the information from other participants.
- ❖ Your samples will be stored indefinitely in a secure lab at the University of Washington. The samples will not be destroyed unless you ask us to do so (see below). We will use these samples for future research related to understanding the relationship between genes and disease.
- ❖ Information from your stored genetic sample at the University of Washington, as well as health information from your Group Health medical record (including sensitive information, as described on page 1 of this form) may be shared with the United States National Institutes of Health databank for genetic related information, called dbGaP (database for Genetic and Phenotype). These data in the databank are used in future research to further knowledge in the interaction of diseases and genes, and will be kept indefinitely. Qualified researchers that receive permission to access and share these data may be from universities or from commercial companies. Your name, contact information, or any other information that could easily identify you will never be released to the databank.

- ❖ The results of this test will not be used to diagnose illness or disease. Since they will not be useful to your medical care, we will not give the results to you or your doctor.

What happens if you find out I have a medical condition I don't know about?

- ❖ Since your DNA will be used for future research, there is the possibility we may discover you have a medical condition or disease you don't know about.
- ❖ If this happens and it could affect your medical care, please indicate below if you want to be contacted. This means we may need to try to contact you many years in the future.

<p>Please initial one of the options below:</p> <p>_____ *Yes, please attempt to contact me about this information</p> <p>_____ No, do not contact me with this information.</p> <p><i>*Please notify us if your contact information changes. To do this you may call the NWIGM coordinator or any of the researchers listed on the front page.</i></p>

Why might I want to be in this study?

- ❖ The information you give us could help us to better understand how genes and health are related. This information could one day help us find new ways to prevent or treat diseases.
- ❖ There is no direct benefit to you for being in this study, but some people feel good when they help with research like this.

What are the risks?

- ❖ Future research may find that some genetic differences appear more often in people from certain groups. These differences might also be more common in people with a certain disease. This could result in people from that group being treated differently.
- ❖ Another risk is possible loss of confidentiality. If your samples are stolen or mistakenly released outside the research setting, it is possible that people not working on this project could learn your identity and that your information may be misused. Nobody can tell just by looking at your blood or tissue sample that it came from you. But, because your genetic information is unique to you, there is a small chance that someone could trace the information back to you. We will take many precautions to make sure this risk is small and there are laws to prevent discrimination by health insurers or employers (like the Genetic Information Nondiscrimination Act of 2008), but these laws don't cover all forms of discrimination.
- ❖ There may also be some discomfort associated with having your blood drawn. You may feel a small needle prick when the blood is drawn. Some people may get a slight bruise that will go away within a day or two. Occasionally people feel lightheaded or faint. If you have any problems from the blood draw, you can see your Group Health provider under your usual insurance coverage.

How will you protect my confidentiality?

Your health information will be de-identified. This means it won't include your name, Group Health number, or other information that is usually used to identify you. We will label your information only with a code number. We will keep the link between your name and your code number at Group Health and will not share it with other researchers, unless you give us permission. We also have a Certificate of Confidentiality from the NIH. This lets us refuse to share any information that might identify you, even if we are asked to by a court of law. It's not likely that we would ever be asked to give out your identity. But

because we are sharing some of your information outside of Group Health, we got the Certificate as extra protection. The Certificate doesn't stop study records from being reviewed by some federal agencies. In addition, Group Health and the funding agency may audit study records as part of study oversight. The Certificate also doesn't stop you from sharing information about yourself or your part in this research. We will not share your name or other identifying information without your consent. The one exception is your genetic information, which is unique to you. At this time it would be very difficult for someone to identify you only from your genetic information, though new advances in science could increase this risk in the future.

What else do I need to know?

- ❖ Your health information is protected by a federal privacy law that applies to Group Health doctors, researchers and staff. This privacy law may not apply to researchers or others outside of Group Health. However, there may be other laws or privacy protections that do apply.
- ❖ If you agree to join this study, your health information may be shared with the researchers named above and their staff at the University of Washington and Group Health Cooperative.
- ❖ We may share information in this bank with other qualified research partners, like researchers from universities, non-profit organizations, and commercial organizations, such as drug or device companies. This information will not include your name or information, such as your consumer number or birth date, which would easily allow someone to know who you are, but may include your genetic information, which is unique to you.
- ❖ A group called an Institutional Review Board (IRB) protects the rights of people in research studies. Only researchers who receive permission from the IRB and the researchers in charge of this sample bank will be allowed access to this information. The IRB may require these researchers to contact you for permission to use your sample.
- ❖ Research using your samples may lead to the development of commercial products. There are no plans to provide financial compensation to you if this occurs.
- ❖ No publications or reports from this study will ever identify you. Your confidentiality will be protected as provided by law.
- ❖ Unless you take back your permission, this authorization/consent to use your health information from this study will not expire.
- ❖ We will give you information on any important new findings that may change your decision to be part of the Northwest Institute of Genetic Medicine.
- ❖ If you have any questions about your rights as a research subject, please contact the Group Health Human Subjects Office at 206.287.2919.

What if I don't want to sign this consent?

You do not have to join this study. Whether or not you join (or change your mind) will not affect your medical care or benefits at Group Health Cooperative and there will be no penalty or loss of benefits to which you are otherwise entitled.

What if I decide to drop out after I join this study?

If you decide to be part of this study and later change your mind, you can drop out by:

- ❖ Writing one of the investigators listed at the top of this consent
- ❖ Calling the study toll-free number and leaving a message with your contact information: 1-866-458-5467.

If you ask us to do so, we will destroy your DNA sample and information we have collected from you and remove your information from the dbGaP National Genetic databank. If researchers have already used

your sample, they will still use information learned from tests done on your sample. If you drop out, we may ask you a few questions to help us understand your reasons for not participating.

If you agree to participate in this study, please read the following statement and sign below:

Participant's Statement

I have read the information on this form and agree to participate in this study. I do not have any questions or I have contacted the study staff above and they have answered all of my questions regarding this study.

I have been informed of the following:

- ❖ Taking part in this research study is voluntary and I can withdraw at any time.
- ❖ If I have questions about giving the blood sample, I can contact the study staff at Group Health.
- ❖ My confidentiality will be maintained as provided by law.
- ❖ The study staff may collect information from my Group Health medical record in the future, which may be linked to information from my blood sample. This might include information on mental health disorders, alcohol, and substance abuse, and sexually transmitted diseases. This information may be shared with the other researchers named above and with other researchers in the future.

Sign full name

_____ **Date**

▶ **Did you initial one of the options on Page 2?**

▶ **You must sign and return this form to join this study. A postage-paid envelope is included for your convenience.**

Appendix 3: Interview Guide

NWIGM Qualitative Interview Guide

<Introduction>

Hello, this is _____ calling from the Group Health Research Institute calling to speak to _____ (person who called in or returned reply form).

You recently contacted us to say you were interested in giving us your responses about some questions we have about genetics research. <if necessary go into more detail>

Is now a good time to tell you about it?

Yes, <continue>

No <schedule call back.>

The interview includes some general questions about your feelings and thoughts about participating in genetics research and some more specifically about your participation in the Northwest Institute of Genetic Medicine, or NWIGM sample bank research project. The interview will take approximately 20 minutes and we'll send you \$20 for your participation.

None of the answers that you give me today will be included in your medical record, as they will only be used for this research. Participating is completely voluntary. Whether or not you decide to participate will not affect your care at Group Health in any way. Your answers will remain private. You are free to refuse to answer any question you wish. Just say "please move on to the next question" if you would rather not answer a question.

Would you like to continue?

Yes, <continue>

No <Thank and end call>

Just a reminder that purpose of NWIGM is to create a research database and sample bank to learn more about how genes can affect health or disease. Genes are small portions of DNA found in your cells. They carry information about traits that run in families, like whether you will have brown eyes or blue eyes. They may also partly explain why some people are more likely to get diseases like diabetes, asthma and dementia. Understanding more about the relationship between genes and health may help to develop new ways to prevent and treat some of these diseases.

When you joined NWIGM you gave a blood sample and signed a consent form that said researchers could use information in your medical records. The goal of this project, and other projects like this one, are to help researchers try to understand what role people's genes play in their health and to answer genetic questions like: What genetic features may lead to susceptibility to vascular (blood vessel) diseases or infections? Or, what are the best medications to lower an individual person's cholesterol, given their genetic make-up?

NWIGM collected samples from Group Health enrollees 50-65 years old and currently over 2,000 people have participated. We are starting to genotype the samples (meaning, we look at some of the specific gene variations NWIGM participants may have). Currently we only have enough funding to look at some

of the samples (about 300) and we are looking for funding opportunities (research grants from the National Institutes of Health, or NIH) to allow us to continue building sample bank and do more genetic analyses.

Before I get started asking you questions are there any other questions you have about the NWIGM sample bank? *(Note any questions and refer to NWIGM project manager if you don't know the answer). Please remember, we are trying to get at what research volunteers' true feelings and opinions are, so please be as candid as possible. Please also remember your answers are private and your name will never be used with any of your responses.*

Let's get started...

1. Why did you decide to take part in the NWIGM study? What were your reasons for participation? Did you participate because you thought you might somehow personally benefit from the project or because you wanted to make a more general contribution to science?
2. Right now we do not have new information to share with the participants in this particular study, but hypothetically if we did have general information to share about what kinds of projects we are doing and how we are using the data we've collected, do you think research volunteers would like to receive such information?

If yes, how would you like this information communicated? I'm going to read you a list of options, let me know which of the following would be acceptable. You can say yes or no to each option, and at the end, I will read your YES responses and I'd like you to rank your top 3 priorities.

- Letter
- Email
- Website
- Phone call
- Text message
- Facebook site
- Any other ideas

3. Now I'll ask the question again, but this time a little differently. In the age of shrinking budgets, scientists conducting any kind of health research often have to make their dollars stretch a lot further to get the work done. Considering the personnel time and other resources required to reach out and update NWIGM sample bank participants with new information to share, and that doing this kind of work might mean not being able to pay for "scientific work" (like genetic analyses. Questions are sometimes asked how researchers can and should find the right balance between sharing information with their study participants and doing the bench work. Would you be willing to receive updates less frequently or even not at all if it meant that more genetic analyses could be done? Why or why not do you feel that way?
4. Now an even more hypothetical question; If you were made the director of the National Institute of Health, which funds much of the medical research done in the United States, what would you consider to be a high priority for giving out grants for genetic research? I'll read you a list of possible options. You can say yes or no to each option, and at the end, I will read your yes responses and I'd like you to rank your top 3 priorities.
 - reproductive health
 - cancer research
 - preventative care

- diagnostics
- information privacy
- protection against stigma or discrimination
- public education
- clinical applications
- Is there anything I left out that you think is important?

Next I'd like to ask some more general questions about your thoughts about linking genetic information to people's medical records. As a reminder, since it may have been awhile since you signed the study consent, we do NOT plan to include any genetic information we may learn about you in the future through your participation in this study in your Group Health medical record. These questions are purely hypothetical. However, the things we learn through our research may influence what genetic information becomes used as a routine part of medical care.

5. How would you feel about the routine use of genetic information in medical care? For example, would you like to have your genetic information available to help you and your doctor choose the type or amount of medication?
6. Can you think of any other benefits the routine use of genetic information might bring to you personally? Would there be benefits for your family?
7. Can you think of any concerns about the routine use of genetic information in medical care? For example, would you be concerned that your genetic information could be used against you in any way
8. The phrase 'personalized medicine' is used to describe tailoring an individual's medical care based on their personal information, including genetic information. Have you heard this term before? What is your vision of personalized medicine

Thank you so much for sharing your opinions with me today. We really appreciate your time! <Confirm address for mailing thank you letter with incentive.

Appendix 4: Code Book

Superordinate Themes	Subthemes
Personal Benefit/ Altruism	<ul style="list-style-type: none"> • Personal Utility • Altruism • Personal Involvement • Memory • Permanence • Agreement with Principles of Research • Convenience • Meaning of Contribution • Sense of Achievement • Benefit • Value of Participation
Language Describing Research Roles	<ul style="list-style-type: none"> • Donation • Participation • Expectations • Desires
Duty, Obligation, Rights and Privileges	<ul style="list-style-type: none"> • Responsibility • Education • Public Outreach • Responsibility • Media • Duty • Obligation • Right to Know

	<ul style="list-style-type: none"> • Privacy • Applications of Genomic Information • Clinical Obligation
Allocation of Resources	<ul style="list-style-type: none"> • Importance of research • Priorities • Resources • Resources in Print • Save Time • Save Money
Misconceptions/Conceptions	<ul style="list-style-type: none"> • Insurance Discrimination • Use of Information • Moral Agreement with Use of Tissue/Sample • Group Health vs. Elsewhere • Genomics as the Future • Confidentiality • Stigma • Discrimination • Misuse of Information • Misconceptions