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Study Newsletters, Community and Ethics Advisory Boards, and Focus Group Discussions Provide Ongoing Feedback for a Large Biobank

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Abstract

The Personalized Medicine Research Project (PMRP) is a population-based biobank with more than 20,000 adult participants in central Wisconsin. A Community Advisory Group (CAG) and Ethics and Security Advisory Board (ESAB) provide ongoing feedback. In addition, the study newsletter is used as a two-way communication tool with study participants. The aim of this study was to assess and compare feedback received from these communication/consultation strategies with results from focus group discussions in relation to protocol changes.

In summer 2009, enrollee focus groups were held addressing these topics: newsletter format, readability, and content of three articles written to solicit PMRP subject feedback. The CAG and ESAB jointly reviewed focus group results, discussed protocol changes to access residual blood samples, and made recommendations about the general communication approach.

Nearly everyone in three focus groups stated that they wanted more information about PMRP. No focus group participant said that accessing stored samples would have changed their enrollment decision. Most said they wanted to be informed directly about changes affecting their original consent. For minimal-risk PMRP protocol changes, the community, CAG, and ESAB were comfortable with an opt-out model because of the initial broad consent.

The planned duration of the biobank extends for decades; therefore regular, ongoing communication to enrollees is necessary to maintain awareness and trust, especially relating to protocol changes reflecting evolving science. The multi-faceted approach to communication including newsletters, external advisory boards, and focus group discussions has been successful for the PMRP biobank and may be a model for others to consider.

Keywords

Biobank; Community engagement; Ethics; Focus groups; Newsletters

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INTRODUCTION

There is an increase in the development of biobanks for genomics research and a concomitant large and growing body of literature on the ethical, legal, and social issues associated with the development of biobanks [Austin et al., 2003; Clayton, 2003; Caulfield et al., 2008]. Community engagement has been shown to be important in many large-scale genomics projects, including the Marshfield Clinic Personalized Medicine Research Project (PMRP) [Godard et al., 2007; Rotimi et al., 2007; McCarty et al., 2008A]. Community engagement activities for PMRP have included an external Community Advisory Group (CAG), community talks, and focus group discussions. In addition, an Ethics and Security Advisory Board (ESAB) provides guidance on ethical issues, such as communication with the cohort, and protocol and consent form changes.

The PMRP is a population-based biobank in central Wisconsin with more than 20,000 adult participants [McCarty et al., 2005; McCarty et al., 2007A; McCarty et al., 2008B]. Subjects give written informed consent to participate with the understanding that they will not receive personal genetic results, but have the opportunity, if they do not opt out, to receive a study newsletter that is published 2–3 times per year. Initially, the primary purpose of the study newsletters was to provide information about studies using the biobank. Increasingly, the study newsletter has been used to inform study participants about planned protocol changes and to elicit feedback after consultation with the CAG and ESAB. There had been no formal assessment of the use of the newsletters by study participants. Focus group discussions were undertaken to get feedback on the overall communication process, specifically the newsletters, and a joint meeting of the CAG and ESAB was held to review focus group discussion results and consider a proposed protocol change to access residual clinical blood samples prospectively for subjects already enrolled in PMRP.

METHODS

Details of the PMRP have been published previously [McCarty et al., 2008A; McCarty et al., 2005; McCarty et al., 2007A; McCarty et al., 2008B]. Briefly, residents aged 18 years and older living in a 19 Zip-code region in central Wisconsin, where nearly everyone receives their medical care in the Marshfield Clinic system of care, were invited to participate. After signing a written informed consent document that allowed access to the comprehensive Marshfield Clinic medical record, subjects completed a brief questionnaire about demographics, smoking and alcohol intake, and health history. DNA, plasma, and serum samples were extracted and stored from whole blood. All procedures were reviewed and approved by the Marshfield Clinic Institutional Review Board (IRB). A box on the written informed consent document allows subjects to indicate if they prefer not to receive study newsletters. To protect subject confidentiality, newsletters are mailed generically to household residents rather than to specific study subjects.

A random age- and gender-stratified sample of 620 PMRP enrollees was invited to participate in the focus group discussions. Twice as many males as females were invited, assuming that males would be less likely to respond to the invitation letters (they are under-represented in the entire biobank), and the goal was to have age and gender balance in the focus groups. Interested subjects were provided with a form to return for follow-up by an external group so that PMRP staff would not know who had responded. The focus groups were organized and held by an external marketing/research firm. The groups were held at a neutral site, not on the Marshfield Clinic campus. Representatives from PMRP did not observe, but were available for questions after the discussions. One focus group was organized for Marshfield Clinic/St. Joseph’s Hospital employees and two for general PMRP enrollees.

At the focus group discussion, participants were provided with copies of the past study newsletters and the written informed consent document and were given time to read the documents. The discussions included questions about the newsletters and feedback on three newsletter articles written to solicit feedback from participants regarding the following: 1) sharing of data into central repositories; 2) access to stored pathology samples; and 3) access to residual clinical blood samples. The Marshfield Clinic IRB reviewed the protocol and determined that the focus group project met the requirements for exemption set forth in CFR 46.101 (b) (2). Common themes and trends were summarized, as well as differences, specifically between the employee and general enrollee groups.

A joint meeting of the CAG and ESAB was held where the results of the focus groups were presented. Logistics for changing the protocol to allow for access to residual clinical blood samples were discussed, and recommendations for moving forward were provided.

RESULTS

Focus groups

Approximately 620 letters were mailed, and 173 PMRP enrollees returned forms expressing interest in participating in the focus groups. The focus groups were filled by subjects in the order in which they were contacted. The two general population groups comprised 11 and 12 participants, respectively, and the employee group had 9 participants. There was representation across all age decades through 70+. Twelve of the 19 Zip codes in the sampling frame for the biobank were represented. Occupations of the focus group members included: retired, laborer, electrician, sales representative, project manager, registered nurse, teaching assistant, guidance counselor, homemaker, teacher, elected official, unemployed, accountant, janitor, law enforcement, research scientist, computer programmer, and technician.

Unaided recall of PMRP was very low; however, those who did remember being enrolled had positive perceptions. Most non-employee focus group participants were either unsure whether they had enrolled in PMRP or had completely forgotten enrolling, while all but one of the employees recalled enrolling in PMRP. Reasons for low recall included: 1) most people said they enrolled more than five years previously (the first 17,500 subjects were enrolled between Sept 2002 and April 2004); 2) fewer than half of the non-employee participants thought they received the study newsletter (Table 1); and 3) a marketing campaign for Marshfield Clinic health care system also uses the term “personalized medicine” and this caused confusion regarding information about Marshfield Clinic Research Foundation and PMRP.

Nearly everyone stated that they would like more information about PMRP. After reviewing the newsletter in the focus groups, most who previously opted out stated that they would like to receive the newsletter.

After reviewing the PMRP newsletter article about data sharing with dbGaP, the majority of focus group participants said that it would not have changed their decision to participate in the biobank. Positive reasons they cited to share data included, “to help” people who had similar health problems and “to contribute” to advancements in medicine. The majority said that the perceived risk of loss of confidentiality would not have changed their decision to enroll. Two or three enrollees who said that data sharing would or might change their decision to enroll mentioned data and privacy concerns.

After reviewing the newsletter item about access to stored pathology samples, none of the focus group subjects said that the protocol change would have altered their decision to

participate in PMRP. Many stated that they assumed pathology samples were already accessible to PMRP as part of their medical record. Sample comments included “if someone can learn from my samples that’s good,” and “I have kidney cancer. If they could find out anything…that could make a person tolerate the medications…terrific”. Focus group participants found this newsletter article easier to read than an earlier article because it included fewer acronyms.

The third newsletter article reviewed by focus group participants was a draft item about a potential protocol change to allow access to residual clinical blood samples for subjects already enrolled in PMRP. All participants said this protocol change would not have affected their decision to participate in PMPR, with comments such as “a good use of the blood,” “practical and economical,” “Why wouldn’t they use it?” and “If I am not using it, I don’t care if someone else uses it.” Questions about the implementation of this protocol change included: “How will the lab know whose blood to include in PMRP?”; “Will enrollees have to have another blood draw?”; and a question about how the changes in the protocol are approved.

Focus group participants unanimously agreed that they wanted to be informed about protocol changes through a personal letter and a card facilitating withdrawal from the study if desired. They wanted more information about the function of the IRB and other review boards. For general news about PMRP, they preferred a newsletter format, but suggested a name change from “Personalized Medicine” so that they could connect it with the research project. They suggested that the newsletter come out more often, preferably four times a year, and on a more regular schedule. They suggested reminding people in every newsletter that they are receiving it because they have enrolled in PMRP. Suggestions for newsletter content included: 1) provide timelines for the research projects; 2) explain how research results might change health care for patients in the future; and 3) explain how PMRP research studies fit into the national and global research picture.

CAG/ESAB meetings

The CAG and ESAB met separately several times to discuss the potential protocol change of accessing residual clinical blood samples for subjects already enrolled in PMRP. The CAG was unanimously in favor of this change, for the same reasons cited by the focus group participants. They suggested handling the change by informing subjects through the newsletter, and then applying for a waiver of written informed consent if there was no or very little objection to the newsletter item.

The ESAB discussed the potential protocol change during several teleconferences and could not reach a consensus. The group split on the fundamental issue of whether the change constituted a meaningful change that substantially increased risk to subjects and should therefore require active reconsent of all subjects.

The CAG and ESAB met together and had the results of the focus group discussions presented to them. The Chair of the Marshfield Clinic IRB attended this meeting. The ESAB members posed questions to the CAG members about the issue of increased risk and what protocol change would be great enough that they would want to be actively reconsented and might consider withdrawal from the study. The responses from the CAG members included, “We trust the Marshfield Clinic” and “a change in the way the data are protected” would be great enough to warrant reconsenting or possible withdrawal. A couple of CAG members thought that it would be a waste of resources that could be better used for research to reconsent all subjects.

After hearing the focus group results and speaking with the CAG, the ESAB reached a consensus on issues related to study communication and protocol changes with the following recommendations:

1. Prepare a regular update for all PMRP subjects to remind them of the study, projects that are ongoing, and remind them of the option to withdraw at any time. Allow the option to opt-in to the study newsletter and to receive it by email.
2. In a separate mailing to study subjects, inform study subjects of the potential protocol change to access residual clinical blood samples and include a card to opt-out of that protocol change or drop out of the study entirely.
3. Remove the opt-out option form the consent form related to receiving the study newsletter.

The ESAB members also discussed a potential later empirical study of whether subjects recalled seeing and reading the information that they receive.

As of September 30, 2010, 19976 subjects had enrolled in PMRP and 1084 (5.48%) had died. On advice from the ESAB, two-page letters were mailed to 18,970 living participants with known addresses to remind them about their participation, to inform them about the approved changes in the protocol since their enrollment and to mention the open-ended time frame for the study and the potential to access residual clinical blood samples in the future. They were reminded that they could withdraw from the study. Postage paid post cards were included to inform study staff of their wish to withdraw from the study, to request newsletters if they had initially opted out of receiving the newsletter and to provide email addresses if they chose to receive the newsletter electronically. One-hundred twenty subjects (0.6% of letters mailed) elected to withdraw from the study after receiving the information letter (Table 2). The most common reason given for withdrawing, similar to the initial reasons for refusal was “no reason” (n=73, 60.8%). A relatively small number of people were unhappy with the protocol changes (n=13, 10.8%).

DISCUSSION

There is little information in the medical literature about ongoing communication with participants enrolled in long-term prospective studies. The results of these focus groups and ongoing consultation with the external CAG and ESAB highlight the need for ongoing consultation with the study population. All groups highlighted the importance of community trust in the Marshfield Clinic and how detrimental it would be to the study to lose that trust. High levels of confidence in the organization conducting the research was found in a study in England to be important in decisions about taking part in a genetic epidemiology study, despite misunderstandings of some of the key concepts of the study [Dixon-Woods et al., 2007].

Two recent empirical studies found strong subject desire for research results from genetic studies [Beskow et al., 2008; Kaufman et al., 2008]. In a study of forty subjects in North Carolina where subjects were asked to review a consent form document, researchers found that more than half thought it would be very important to receive general news about studies being done through a biorepository, and several thought it would constitute fair exchange for having volunteered in the study[Beskow et al., 2008]. Nearly two-thirds were not concerned about not receiving personal genetic results. An on-line study of adults across the US assessing opinions about a potential national genetics study found that 3 in 4 people would be less likely to participate in such a study without return of research results [Kaufman et al., 2008]. These results are similar to several findings related to sharing of research results that we have documented in our PMRP cohort. We found previously, in a 10% random sample

of the PMRP cohort, that 61% of participants were unsure or thought that they would learn, as a result of participating, which conditions/diseases they would develop, despite the fact that the written informed consent document states that they will not receive any personal genetic information from the study [McCarty et al., 2007B]. From this current focus group study and the feedback we have received from our CAG, it is clear that we need to find a way to provide study information to all study subjects, regardless of whether they opted out of the study newsletter in the initial consent process. Prospectively, we have removed the opt-out from the consent form, because ongoing communication with study subjects in an open-ended biobank study is essential.

In the current focus group and advisory group discussions, the majority of participants and members felt that information about minimal risk protocol changes to enrolled subjects with the option for an opt-out would be sufficient to then apply for a waiver of written informed consent from the IRB. In additional to being impractical to attempt active reconsent for a biobank of 20,000 subjects, anecdotally it was felt that a requirement for an opt-in instead of an opt-out would significantly impact participation in the protocol change. A cross-sectional study of 177 older patients pre- and post-waiver of written informed consent and Health Insurance Portability and Accountability Act (HIPAA) authorization found that there was a substantial increase in participation rates post-waiver for a minimal risk study [Krousel-Wood et al., 2006]. Protocol changes involving more than minimal risk would require a different process for informing subjects of the change and may require active reconsent; they were not considered as part of this study and process.

The results of a series of focus groups across the US addressing public opinion on informed consent and privacy concerns for biobanking were reported recently [Kaufman et al., 2009; Murphy et al., 2009]. Greater than 75% of these participants in focus groups from larger cities across the US felt that they would have more trust in the study and would feel more respected and involved if researchers had to get their permission to use their hypothetical samples in a biobank before each new project [Murphy et al., 2009]. Twenty-seven percent felt that it would be a waste of time and money, and 265 felt that they would be bothered by this process. Ninety percent of participants expressed concern about privacy, and 60% said that they would participate in a biobank despite these concerns [Kaufman et al., 2009]. Ninety-two percent would allow sharing of data with academic researchers, and 75% would allow sharing with industry. The participants were nearly equally divided on whether they would prefer to give a one-time only consent with oversight review or would want to provide consent for each project separately. The level of concern expressed by these focus group participants is somewhat higher than expressed by the PMRP focus groups and CAG members. There are likely two reasons for these differences. First, the PMRP focus groups were conducted with biobank participants, while the national sample was conducted with people in hypothetical situations. Participation in the PMRP biobank is slightly less than 50%, and it is likely that people who had levels of concern about privacy and data sharing as outlined in the PMRP informed consent document elected not to participate in the biobank. Those who chose to participate, although they have privacy concerns as expressed in the focus groups, ultimately felt that the potential scientific good outweighed the potential for a privacy breach. The second possible reason for the observed difference is the relationship of the Marshfield Clinic to the community from which people were recruited. As expressed by both the PMRP focus groups members and the CAG, they trust the Marshfield Clinic, and this trust led them to participate in the biobank. In contrast to the national focus groups, respondents were considering an entity whom they knew rather than a hypothetical situation. Consistent across the earlier PMRP focus groups and the recent focus groups was the need for regular communication about studies using the biobank.

The limitations of our approach lie in the generalizability of the results and the fact that a qualitative approach can be difficult to replicate. The effectiveness of advisory boards is very much dependent on the membership. Half of all working age adults in Marshfield are employed by either Marshfield Clinic or St. Joseph's Hospital so the medical campus is very much a part of the community. Feelings towards health care institutions and the research being conducted there might differ in large metropolitan areas where people seek their health care at different institutions and may not feel the same allegiance that they do in a small community. Nevertheless, we feel that this approach to community engagement and feedback for large scale biobanks may be applicable in other settings.

In summary, ongoing communication with study participants is essential to maintain the trust of the community, especially where study duration is long, with evolving scientific and ethical issues. For the particular issue under consideration, because of the broad consent given initially, the focus group participants, CAG, and ESAB were comfortable with an opt-out model for protocol changes that are minimal risk, such as accessing residual blood samples. Given the duration of the biobank, communication at regular intervals is necessary for all study participants, particularly those who initially elected not to receive study newsletters. This multi-faceted approach to stakeholder communication has been successful for the PMRP biobank and may be a potential model for others to consider.

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TABLE 1

Close-ended focus group questions and response tallies about PMRP study information

Question	Responses
As an enrollee of the PMRP, how would you describe your level of interest in information about PMRP?	0 no interest
	19 somewhat interested
	12 very interested
After you enrolled, have you been satisfied or dissatisfied with information that you receive or have access to about PMRP?	21 satisfied
	9 dissatisfied
	2 no answer
Do you receive the *Personalized Medicine* newsletter at home?	17 yes
	12 no
	4 no answer/don't know

PMRP=Personalized Medicine Research Project

TABLE 2

Reasons given for withdrawal

Reason	Number (%)
No reason, doesn't want to be in the study anymore	73 (60.8%)
Does not agree with protocol changes	13 (10.8%)
No longer lives in the area or gets care at Marshfield Clinic	12 (10.0%)
Power of attorney doesn't want participant enrolled any longer	8 (6.7%)
Doesn't remember enrolling	6 (5.0%)
Other	8 (6.7%)
Total	120 (100%)