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Recruitment Approaches for Family Studies:

Attitudes of Index Patients and Their Relatives

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Background

A significant amount of health-related epidemiological, behavioral, and genetic research requires the participation not only of persons with a medical condition but also their family members. Inclusion of family members in research facilitates the ability to understand the complex role of familial relationships in disease—from examining pathways of familial communication to the collection of DNA samples for genetic linkage analysis. The success of family research is heavily dependent on the recruitment process, which is complicated by factors such as family size, dynamics, and attitudes about the condition under study. A growing body of scholarship has focused on approaches to maximize the participation of family members in research,¹ acknowledging both the logistical and ethical challenges of adequate recruitment.

Although the initial participants in family research (often referred to as “probands” or “index patients”) can be identified and recruited through a variety of mechanisms including physicians, disease registries, and support groups, access to their family members often can be gained only through information reported by the probands themselves. In order to determine which family members are eligible for study participation, researchers often must ask probands to provide family history information including the relationship and disease status of multiple family members. This dependence on the proband for access to family members can be a rate-limiting step for the research process and raises questions about the

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appropriate approach to be used in making an initial contact with a family member. A standard approach involves researchers personally contacting family members after receiving names and contact information (and, often, personal health information) from probands. Alternatively, some have argued that the initial contact ought to be made by a person who has an existing relationship to the recruitee, i.e., “proband-initiated contact,”² to protect family members’ privacy. However, depending on the family dynamic, proband-initiated recruitment might place inappropriate pressure upon relatives to participate.³

Researchers and institutional review boards (IRBs) are routinely faced with the question of how to balance the effectiveness of recruitment approaches with minimizing unwelcome intrusions and undue influences upon patients and family members who are potential subjects of research. Empirical data regarding how welcome or unwelcome probands and family members consider different recruitment approaches may play a role in addressing this normative concern of IRBs and researchers. The few studies that have addressed aspects of this issue suggest a preference for proband-initiated approaches over researcher-initiated approaches,⁴ although additional research is needed to understand the factors that are associated with these preferences.

Different approaches to the recruitment of family members may have important methodological implications. Specifically, if some approaches lead to reduced response rates or to selection bias related to probands’ subjective determinations about which family members to approach, the validity of conclusions drawn from these samples may be compromised. The methodological impact of different recruitment approaches has not been well characterized. While one study found no difference in response rates between different recruitment approaches,⁵ several studies have found that different recruitment approaches generated different response rates according to specific contextual factors such as ethnicity of the participants⁶ and degree of stigmatization associated with the disease being studied.⁷

To date, no research has focused on the attitudes of both probands and family members who have already been contacted to participate in family research about different approaches to recruitment, or on whether there are differences between people who agree to participate in family research and those who refuse to participate. Understanding the attitudes of people who have been approached to participate in research is meaningful because their perspective is informed by having directly faced the issue of recruitment. Our survey of people who were recruited to participate in the Colon Cancer Risk Counseling (CCRC) study addresses this gap in the literature.

Methods

Study Context and Sample

This survey was conducted as a follow-up to the CCRC study. The CCRC study was a randomized trial of a culturally sensitive counseling intervention that aimed to improve adherence to guidelines for early detection of colorectal cancer (CRC), comprehension of personal CRC risk, and psychological adaptation to familial cancer. Eligible subjects were siblings and children, aged 40 and over, with a positive history of CRC in one first-degree

relative. In the CCRC study, first-degree relatives were randomly assigned to receive either Colon Cancer Risk Counseling or a General Health Counseling control intervention.

For this survey, respondents included both index patients (IPs) and first-degree relatives (FDRs) who were invited to take part in the CCRC study (n = 892 IPs and 346 FDRs). The IPs were people ages 25–90 that were identified by the Hawaii Tumor Registry as having been diagnosed with colon cancer between the years 1995 and 2000. The FDRs were siblings and children age 40 and older.

Data Collection

Potential respondents were sent a mailing that included a cover letter explaining the study and a survey. A complimentary video rental coupon (valued at \$5.00) was included with the letter and survey. Respondents were asked to mail back the survey in pre-addressed, postage paid envelopes. The survey included a box to check if they did not wish to participate (active refusal). If a survey was not received within two weeks, a second similar mailing was sent. If there was no response after two weeks of the second mailing, project staff made a follow-up phone call. The institutional review boards at the University of Hawaii and the National Human Genome Research Institute approved the study protocol.

Measures

The survey was a five-page self-administered questionnaire formatted for optical scanning. Items included background information (ethnicity, education, religion, self-rated health, and previous research participation); questions about respondents' attitudes about recruitment approaches for themselves and their relatives; and attitudes about health research and family communication. Because there are few data regarding how welcome or unwelcome people (including cancer patients/survivors) consider various approaches of researchers to themselves and their families, most of the questionnaire items were developed by the investigators specifically for this survey. Some items had been previously developed for a study by SCH and BW (still in progress) on patient attitudes about the collection, storage, and use of tissue samples for genetic research. The survey was pretested and pilot-tested among non-eligible adults for clarity and wording. (A copy of the survey is available from the authors on request.)

In addition to items on the survey, researchers had access to selected relevant data from the original CCRC study: gender, age, IP/FDR status, and CCRC study participation status (refusal, ineligible, or participant).

Data Analysis

All data preparation and analyses were conducted using SAS Statistical Software. Screening and recruitment information from the CCRC study such as respondent type (IP or FDR), gender, age, and participation status was first linked to the survey data. Next, frequencies were generated for all survey items. Likert-scale items were measured on a 4-point scale and reduced to dichotomous outcomes based on either the positive/negative wording of the response anchors or the distribution, as was the case for the benefits of various types of research that had very few negative responses. We compared the dichotomized survey

responses across demographic variables, respondent type, and CCRC participation using chi-square and Fisher's Exact tests.

Findings

Study Participant Characteristics and Response Rates

Of 1238 people who had been approached to participate in the CCRC, this survey was mailed successfully to 1119 people; 119 were not reachable or were deceased. A total of 498 respondents completed the survey, with an overall response rate of 45%. However, the response rate varied greatly according to history of participation in the CCRC (Table 1). Response rate was 74% for CCRC participants and 30% among those who were approached but refused participation in the CCRC. Forty-three percent of respondents were CCRC participants, and 57% had not participated in the CCRC for a variety of reasons including refusal to participate and ineligibility. The majority of respondents were identified as index patients in the CCRC (64%), while the remaining respondents were first-degree relatives (36%) including sisters (12%), daughters (10%), brothers (7%), sons (7%), and mothers (<1%).

Of the 498 respondents, forty-five percent were Japanese, 25% white, 14% Hawaiian, 7% Chinese, 6% Filipino, and 3% other/mixed, representative of the approximate ethnic distribution of CRC in Hawaii (Table 2). The population was evenly distributed between males and females and was highly educated with 42% being college graduates or beyond. The dominant religious background of participants was Protestant (40%).

Attitudes About Research

Attitudes about research were generally positive, with the majority of respondents believing that various types of research are beneficial to society as a whole. Respondents believed that "research about how people think, feel, and act" (i.e., social and behavioral research) was less beneficial than other types of research, including genetic research (Table 3). Respondents who participated in the CCRC were more likely to say they felt genetic research and cancer research are extremely beneficial than those who refused participation ($p < .05$ for these comparisons).

Over half (55%) of respondents reported having participated in some kind of medical research study in the past. Seventy-nine percent believed it is fairly or very important for them to participate in medical research. A majority of respondents would be willing to participate in four types of research activities (Table 3), indicating the greatest willingness to complete a mail survey (89%), and the least willingness to participate in a telephone interview (53%). Respondents who participated in the CCRC were significantly more willing to participate in all four research activities than those who refused CCRC participation ($p < .001$ for these comparisons). In addition, respondents with more education were more willing to participate in mailed surveys, telephone interviews, and cancer educational programs ($p < .05$ for these comparisons).

Attitudes About Recruitment Approaches

A majority of respondents would mind if their names were given to researchers by their doctors (64%) or relatives (66%) without their permission. However, respondents generally would be willing to grant permission to their doctors (85%) and relatives (75%) for their names to be given to a researcher if asked (Table 4).

To better understand attitudes regarding recruitment approaches, we asked about respondents' ongoing discussions of health issues with their family members. Seventy-one percent of respondents reported that they often or sometimes talk to close relatives about serious concerns or problems, such as a major illness. Thirty percent of respondents had 2 or fewer family members with whom they could talk about serious health events; 42% had between 3 and 5 family members, and 28% had 6 or more such family members. Factors associated with greater willingness to grant permission to doctors and relatives to give their names to a researcher included CCRC participation, having more education, and having more family members with whom respondents could talk about serious health events ($p < .001$ for these comparisons).

Willingness to Assist Researchers

With respect to helping researchers recruit family members, respondents were least willing to give relatives' names to researchers without first asking their relatives' permission (41%), preferring instead approaches that involved their own initial contact with their relatives such as first checking with the relative (79%), telling their relatives about the study and giving them the researcher's phone number (78%), or forwarding a letter to their relatives on behalf of the researcher (67%) (Table 4). Factors associated with a greater willingness to engage in each of these four recruitment approaches included participation in the CCRC ($p < .001$) and having more family members with whom respondents can talk about serious health events ($p < .05$). First-degree relatives and women were significantly more willing to engage all of the approaches except giving relatives' names to researchers without first getting permission ($p < .05$ for these comparisons). There was no clear pattern of differences in attitudes toward these recruitment approaches by respondents' ethnicity, education levels, religion, or age.

In addition to asking about the acceptability of each recruitment approach, respondents were also asked to indicate their single preferred approach. The recruitment approach that was ranked as preferable by the most respondents in our study was to give relatives' names to the researcher, after first checking with the relatives (Table 5).

Discussion

We found that two thirds of the respondents in this study prefer that their names and contact information be given to researchers only with their permission, and indicate they would not provide this information about their relatives without first checking with the relatives in some manner. Index patients, who are perhaps more engaged in the health care system due to their cancer diagnosis, were less likely to mind doctors giving out their information to researchers than were first-degree relatives. Similarly, participants in the parent CCRC study were less likely to mind than non-participants. While most participants felt that their

permission should be sought before researchers contact them, they reported being likely to grant such permission. Indeed, at least three-quarters of respondents in our study would allow their doctor or relatives to pass their information along to a researcher if asked. Although seeking permission from potential research subjects is an additional step in the logistics of recruitment, our data indicating that such permission is likely to be granted suggests that this step may not be a significant barrier in the recruitment process.

In addition, our findings indicate that most respondents would be willing to do a number of different things to help researchers recruit family members, as long as the initial contact was made by them rather than by the researcher. These activities would require incrementally higher degrees of effort on the part of respondents, from contacting relatives to get their permission, to distributing letters on behalf of researchers, to having a conversation with relatives about the study and providing them with the researchers' contact information. Each approach affords protection to the privacy of family members, requiring their authorization and/or active response in order for researchers to acquire their contact and health information.

Worrall and colleagues have argued that asking probands to distribute letters to relatives on behalf of researchers is an ethically-preferable recruitment strategy, more respectful of privacy than conventional researcher-initiated approaches of contacting family members directly.⁸ Our data suggest that there might be even simpler ways to accomplish the goals of "proband-initiated" contact that are satisfactory to both subjects and researchers. While respondents in our study are generally willing to distribute letters to relatives on behalf of researchers, this is not the most preferred approach. Instead, respondents are most willing simply to ask their relatives' permission to give contact information to the researcher, an approach that places fewer burdens on the respondent but still ensures that researchers are not getting unauthorized information about family members. One might reasonably expect this less burdensome and more preferred approach of recruitment to yield a higher response rate than other approaches that require additional effort on the part of respondents. At the same time, it limits researchers from obtaining private, identifiable information without the knowledge and authorization of family members.

Our findings differ somewhat from those of a recent study examining the uptake of genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC),⁹ in which probands with HNPCC mutations were asked to choose from among three different approaches to help recruit their eligible first-degree relatives: (1) contacting relatives to describe the study and provide them with the researcher's contact information, (2) sending the relative a letter (provided by the study) informing them of the identification of an HNPCC mutation within the family and providing them information about the study, or (3) providing relatives' contact information to the researchers so that the researchers could contact relatives via telephone following notice by the proband. All probands in the HNPCC study selected the first approach. In contrast, our study found the highest preference for the third option. The difference in study samples may account for this variation: the Hadley et al., study queried probands identified to be at high risk who had already undergone genetic testing, while the CCRC study focused on intermediate-risk probands and their relatives.

While personally informing relatives about the study was the recruitment approach of choice among probands in the HNPCC study, it is not clear that this approach generated an acceptable response rate: of 111 relatives who were deemed to be eligible, only 51% chose to participate in the study. It is not known whether non-participating family members were simply never approached by the proband, or whether they had specific reasons to decline participation. Our data do not address this important concern: whether more involved recruitment approaches will lead to lower rates of recruitment. A number of contextual factors might bear on the appropriate recruitment approach to use in different studies. For example, it seems inappropriate to ask probands to distribute letters to their spouses or family members living within their household, particularly if these individuals might be known in some capacity to the researcher. It may be difficult for probands to contact family members with whom they have a strained or no pre-existing relationship. Conversely, it might be preferable to involve probands in initiating contact with family members for research on more sensitive or private types of issues.

Although a majority of participants in this study felt that permission should be sought from potential subjects of research before their names and contact information are provided to researchers, approximately one-third of the respondents would not mind this occurring without their permission. To the extent that participants' views are reflective of what is ethically appropriate to do, it might be acceptable for researchers to initiate contact with those family members who would not mind their information being given to the researcher without their permission,¹⁰ while obtaining permission from those family members who would mind. Practically speaking, this would require researchers to ask probands to make a judgment regarding which approaches would be acceptable to their relatives. A single study, then, might offer probands a variety of approaches for contacting family members from which they could make considered choices based on their understanding of their family members' preferences as well as their own willingness to become engaged in the recruitment process. Respecting participants' variable preferences in this manner may maximize the response rate, contributing to both ethically and scientifically desirable outcomes.

These data also show that a majority of the people in this study who had declined CCRC participation were nonetheless willing to grant permission for their doctors and relatives to give their names to researchers. This suggests that people distinguish between recruitment and enrollment and may decline to participate in research even though they do not mind being asked. Although certain recruitment approaches may help protect the privacy of family members, it is important not to equate recruitment—which is preparatory to conducting research—with the consent process that provides people with the opportunity to make a voluntary decision whether to participate in the research. While some people may prefer not to be contacted directly by researchers, ensuring their ability to voluntarily decline to enroll in the research is perhaps an even more important consideration that may also help mitigate some of the concerns regarding recruitment.

This study has several important limitations. First, selection bias within the study population may have resulted from a lower than ideal response rate among those people who had declined to participate in the original CCRC study. However, given that these are people who are inclined not to participate in research and therefore challenging to obtain data from, it is

still valuable to have even limited data on their attitudes about recruitment. Second, the study sample, while representative of the Hawaiian population of colorectal cancer patients from which it was drawn, does not reflect the overall ethnic and racial distribution of the United States population. Although no significant differences were seen in attitudes about recruitment based on race or ethnicity, additional research to assess the applicability of our findings to other research populations would be useful. Although one might question whether these findings can be generalized to other populations and research contexts, our key observation—that there is interest in a wide variety of recruitment approaches—is likely to hold true across different contexts. Accordingly, our conclusions, which are based on the presence of *any* variability in attitudes about recruitment, will still hold. Third, this study focuses on stated willingness to participate in various recruitment activities but does not track actual behaviors regarding participation in the recruitment process. However, since these subjects already had the experience of being asked to make similar decisions in the context of the CCRC, their attitudes may be more grounded.

Our data show the greatest support for the least complex proband-initiated strategy: giving researchers' familial contact information after first checking with family members. This should be reassuring to researchers who might be concerned about recruitment approaches that rely on probands to initiate contact with relatives. While it is important to balance concerns for privacy against the need for efficient recruitment, it is not a given that the more involved recruitment approaches will result in lower response rates in all research contexts. Respecting probands' preferences among a range of possible recruitment approaches—which would enable probands to determine how involved they want to be in recruitment as well as what their family members are likely to prefer—may result in greater levels of cooperation on the part of probands and their relatives.

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6.
See ref. 1, Preloran et al. 2001.
7.
See ref. 1, Bonvicini 1998.
8.
See ref. 2, Worrall et al. 2001.
9.
See ref. 4, Hadley et al. 2003.
10.
This would require an IRB determination that such approaches are acceptable under the Common Rule at 45 CFR part 46 and the Privacy Rule at 45 CFR parts 160 and 164.

Table 1**Response Rate and Participation in the Colon Cancer Risk Counseling (CCRC) Study**

	Refused to participate in CCRC	Ineligible to participate in CCRC	Participated in CCRC	Total
Index patients	133 (29%)	94 (45%)	92 (72%)	319 (40%)
First-degree relatives	48 (32%)	8 (89%)	123 (75%)	179 (55%)
Total	181 (30%)	102 (47%)	215 (74%)	498 (45%)

¹ Percentages reflect the number of respondents in each category over the total number of CCRC participants in that category who received the survey. (For example, among index patients who refused to participate in the CCRC, only 29% responded to this study.)

² The denominator (n=1119) does not include CCRC participants who were not reachable.

Table 2

Respondent Demographics (n=498)

Characteristic	Percentage ^I
Ethnicity	
Japanese	45
White/Caucasian	25
Hawaiian	14
Other/Mixed	16
Religion	
Protestant	40
Catholic	24
Buddhist	17
None	15
Other	5
Sex	
Female	49
Male	51
Education	
12th grade or less	27
Some college	31
College graduate	26
Graduate/professional school	16
Self-rated health status	
Fair/poor	26
Good	39
Very good/excellent	34

^IPercentages may not add up to 100 due to rounding.

Table 3

Respondents' Attitudes About Research

	Total
Believe that type of research is "extremely beneficial"	
Cancer research	86% *
Medical research	75%
Epidemiological research ("about the kinds of diseases that people get")	75%
Laboratory research	74%
Genetic research	70% *
Behavioral and social science research ("about how people think, feel, and act")	43%
Would be (somewhat or very) willing to:	
Complete a mail survey	89% **
Participate in an education program about cancer	74% **
Give blood for genetics research	74% **
Participate in a telephone interview	53% **

* Significant differences between CCRC participants and refusers ($p < .05$).

**
 $p < .001$

Table 4

Attitudes about Recruitment Approaches

	Index Patient	First-Degree Relative ¹	Participated in CCRC	Refused Participation ²	Total
Would not mind/would be pleased if your name was given to a researcher without being asked first ...					
by your doctor	41%	25% **	36%	31%	36%
by a relative	32%	37%	41%	24% **	34%
Would be (somewhat or very) likely to agree to give your permission to give your name to a researcher ...					
by your doctor	84%	86%	94%	73% *	85%
by a relative	70%	85% **	89%	62% *	75%
Would be (somewhat or very) willing to ...					
give relatives' names to researcher, after checking with relatives	75%	87% *	91%	67% **	79%
tell relatives about study and give researcher's phone number	74%	85% *	85%	68% **	78%
forward letter to relatives on behalf of researcher	63%	72% *	75%	53% **	67%
give relatives' names to researcher	41%	40%	49%	33% **	41%

¹ Reflects comparison between index patients and first degree relatives² Reflects comparison between those who participate vs. refused participation in the Colon Cancer Risk Counseling study

* p< .05

** p< .001

Table 5

Preferred Contact Approach

	Total^I
To give relatives' names to researcher, after checking with relatives	198 (42%)
To forward letter to relatives on behalf of researcher	134 (29%)
To tell relatives about study and give researchers phone #	121 (26%)
To give relatives' names to researcher	17 (4%)
Total	470

^I Percentages may not add up to 100 due to rounding.