Perceived Risks of Participation in an Epidemiologic Study

by Felicia D. Roberts, Polly A. Newcomb, and Norman Fost

Institutional review boards (IRBs) sometimes limit direct access to patients in recruitment protocols for epidemiologic studies.[1] Ethical and legal concerns for confidentiality may argue against a physician releasing patient information to an investigator without the patient's consent, even for the purpose of contacting that patient to solicit his or her interest in becoming a subject. IRBs may therefore request that patients' personal physicians, or some other provider with legitimate access to their records, contact patients first to determine whether they are willing to have their names released to an investigator. The patient's willingness to be enrolled in a study may be explicitly determined by an "opt-in" or "opt-out" procedure, or inferred by a nonresponse to an opportunity to opt out.[2] While these "card back" (or phone back) protocols may respect confidentiality, they clearly result in both lower participation rates and biased sampling.[3-5] It is not clear, however, whether subjects who are directly contacted by investigators, without having authorized release of their name and medical condition, perceive that their privacy has been invaded, or that the confidentiality of their medical record has been compromised. The purpose of this study was to learn more about patients' views on these issues. We recontacted a sample of women participating in a case-control study of breast and colorectal cancer to evaluate adverse effects of a direct mail contact protocol.

Background

Under Wisconsin State Statute, Chapter 46.73, "Any hospital . . . any physician . . . any laboratory . . . shall report information concerning any person diagnosed as having cancer . . ." Patient consent for such reports is not required, nor need patients be informed that such reports are made. Subsection (3) of the statute explicitly states that all information reported to the registry is confidential and may not be disclosed except to another state or national tumor registry. However, for purposes of epidemiologic studies by researchers outside of the state registry, confidentiality requirements set forth by Wisconsin law are apparently met by having all activities of the project involving access to patient-identifying information performed by individuals who are already employees of the Division of Health (DOH) or those who are on loan to and supervised by the DOH. Furthermore, subjects' physicians, as reported to the Tumor Registry, act as "gatekeepers" for the transfer of patient information to investigators. In this way, a balance can be maintained between the scientific needs of researchers and the privacy of patients.

This protocol was adopted and approved by the Wisconsin Division of Health for an epidemiological study of breast cancer and colon cancer in women. The investigator proposed that physicians of potential subjects evaluate the appropriateness of study participation for each patient and then notify the DOH as to which patients might be contacted. A descriptive letter outlining the study would then be sent to those patients, but *without* an explicit opt-in/opt-out protocol. (A previous registry-based epidemiologic study that included an opt-in protocol resulted in extremely low participation rates.[6]) Although the proposed protocol was considered to be in legal compliance with state statutes, there were ethical concerns on the part of the IRB. It was felt that respondents did not have the fullest opportunity to decline, which was considered particularly worrisome considering the prior unconsented to disclosures of confidential information, first by the physician to the registry, and then by the registry to persons outside the registry. Although subjects were assured of confidentiality in the letter sent to them, one member of the IRB asked, "What does assurance of confidentiality in the [subject] letter mean when a similar assurance in the law [that created] the registry allowed disclosures to investigators outside the registry?"

A compromise was reached between the investigators, the IRB, and the DOH to allow subjects to opt out without providing an explicit card-back mechanism: subject letters contained the phone number and name of the study coordinator so that a subject could call in to accept or decline participation if she so wished, but this was not stated as a requirement in the letter; the phone number of the project coordinator was simply made available. This implicit consent protocol constituted "valid consent," namely "imparting of that information which the patient/subject requires in order to make a responsible decision."[7]

Materials and Methods

All subjects with newly diagnosed breast or colon cancer were identified from Wisconsin's Cancer Reporting System files. Physicians named in the registry reports were sent a letter describing the study and stating that one or more of their patients was eligible for the study. A consent form and a stamped, self-addressed envelope were included to require explicit consent from physicians. After physician approval of patient contact, an introductory letter was addressed to subjects. The contact letter briefly outlined the nature of the study and the source from which the subject's name was drawn. The letter also named the subject's physician as having approved of patient contact. The contact letter invited the subject to participate in a 30-minute telephone interview and informed her that an interviewer would be calling within two weeks to discuss study participation and schedule an interview time at the subject's convenience. The voluntary nature of participation was emphasized in the letter as well as the fact that all information gathered during the interview would be kept strictly confidential. The name and telephone number of the project coordinator were provided for prospective subjects to call if they had questions or wished to refuse to participate. A telephone call was made directly to the subject one week after the letter to discuss the study and enlist participation. If the subject agreed to participate, an interview was scheduled at her convenience. All inter-

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viewers were blinded as to the disease status of subjects. Overall participation rates were very high: only 2.6 percent (125 of 4,755) of contacted breast cancer cases and 4.6 percent (44 of 940) of colorectal cancer cases refused to participate. The study interview included a complete history of reproduction and lactation, use of oral contraceptive and replacement hormones, age-specific alcohol consumption, physical activity level, family and medical history, and cancer screening utilization.

Six months after the original telephone interview we sampled 113 subjects to evaluate concerns regarding study participation. The sub-study participants were randomly selected from a list of all case subjects having completed the interview during June and July of 1991. All sub-study interviews were completed during the first two weeks of October 1991. We contacted the subjects by telephone and invited them to participate in a brief survey regarding the original interview. Eight close-ended questions were designed to ascertain respondent concerns over matters of confidentiality regarding both selection for the study and the conduct and content of the original study interview. For example, participants were asked, "After you received our letter, but before we contacted you to complete the interview, did you have any concerns about how or why you were selected for the study?" This was followed by an inquiry about the degree of concern: "Would you say you were slightly concerned, moderately concerned, or seriously concerned?" One final open-ended question allowed the respondent to offer specific objections to particular questions or content areas.

TABLE 1: SUBJECT CHARACTERISTICS (BY CANCER TYPE)

	BREAST (n=56)	COLON (n=52)
AGE (mean # yrs)	56.6	65.3
RACE		
White	56 (100%)	49 (94.2%)
Black	0	3 (5.7%)
EDUCATION		
<12 yrs.	5 (8.9%)	11 (21.1%)
High School	22 (39.2%)	28 (53.8%)
1-4 yrs. College	22 (39.2%)	12 (23.0%)
Graduate Degree	15 (26.7%)	1 (1.9%)
MARITAL STATUS*		
Married	36 (72.0%)	38 (74.5%)
Divorced	4 (8.0%)	1 (1.9%)
Widowed	10 (20.0%)	12 (23.5%)

* BASED ON N=50 (BREAST CANCER) AND N=51 (COLORECTAL CANCER)

TABLE 2: SUMMARY RESPONSES TO QUESTIONNAIRE

	n=108	% of TOTAL
CONCERN ABOUT SELECTION METHODOLOGY (PRIOR TO PHONE CONTACT)		
No concern	88	(81.7)
Slight concern	11	(10.1)
Moderate concern	7	(6.4)
Serious concern	2	(1.8)
DISCUSSED PARTICIPATION WITH M.D.		
Yes	3	(2.7)
No	105	(97.2)
CONTENT TOO SENSITIVE		
Yes	2	(1.8)
No	106	(98.2)
RESERVATIONS REGARDING CONFIDENTIALITY		
None	99	(91.7)
Slight	5	(4.6)
Moderate	4	(3.7)
Serious	1	(0.9)
APPROPRIATENESS OF THIS APPROACH TO STUDY HEALTH		
Not appropriate	0	(0)
Slightly appropriate		(0)
Moderately appropriate	0	(0)
Appropriate	108	(100)

Results

The response rates for this sub-study were excellent. Of the 113 subjects contacted by phone for the survey, 108 (95.5%) agreed to complete the telephone interview. Three subjects (2.6%) refused participation, one was deceased, and one subject could no longer be located. The study group included 56 women with breast cancer and 52 women with colon cancer. The characteristics of respondents were very similar to participants in the epidemiologic study: respondents were primarily white (97.2%) and the mean age was 61.0 years (56.6 years for the breast cancer cases and 65.3 for colon cancer cases). The subjects were similar in terms of their current marital status and mean number of years of education (Table 1).

Responses to the questionnaire are summarized in Table 2. Overall, while 20 subjects (18.5%) expressed some concern *prior* to interview about either how or why they were selected for study, the level of concern was modest: 9.2 percent were slightly concerned, 7.4 percent were moderately concerned, and only 1.8 percent were seriously concerned. The respondents did not differ in their response to this question by cancer type. We did not ask whether subjects felt concerned about being selected for the study *after* having completed the interview; indeed subjects commented that if they had been concerned over their selection for the study they had discussed it with the interviewer at the outset and then felt comfortable to proceed.

Although we gained physician approval to contact each of the case subjects for the original study, and mentioned that fact in the contact letter, we asked subjects if they felt the need to discuss study participation in more detail with their doctor prior to interview. Only 2 percent of participants responded that they felt the need to do so.

Concern that study information would not be kept confidential was

expressed by 9.2 percent of the subjects; 4.6 percent of these subjects felt "slightly concerned," 3.7 percent felt "moderately concerned," and only 0.9 percent felt "seriously concerned." Only two respondents felt that the questions were "too personal." The sensitive question identified by one respondent was age; the other mentioned no specific question or area of inquiry that she perceived as "too personal."

Finally, all subjects stated that health studies such as the one we conducted with them were important and appropriate, provided that strict confidentiality was maintained.

Discussion

Participation rates for our breast and colon cancer studies indicate that the direct mail protocol being tested was extremely successful in recruiting a high proportion of eligible subjects. The results from our sub-study corroborate that the respondents were overwhelmingly in support of the research effort and expressed very little concern that confidentiality would not be respected. Although subjects were approached directly, that is without an explicit "opt-out" mechanism available to them, there was little risk of engaging an unwilling participant. Respondents could refuse prior to contact (upon receipt of the introductory study letter) or at the time the interviewer first called. Nonetheless, few subjects elected to refuse participation when the study protocol was described to them both through the contact letter and later, as needed, over the telephone with the interviewer.

The encouraging results of the sub-study may not be surprising, since the cohort interviewed for it consisted exclusively of patients who were willing participants in the original study. The responses of those who declined to participate in the original study may have been different. However, considering that so few prospective subjects declined to participate under the original study protocol, the benefit of recontacting them did not seem to outweigh the cost of impinging on their privacy once again for the sub-study, particularly since their refusals were occasionally due to ill health. Therefore, those who refused to participate in the original study were not recontacted for this sub-study.

The results from this study support positive outcomes from similar research. Funch concluded that the majority of breast cancer case subjects were "glad" that their physicians gave permission to contact them and that they actually felt that they received some benefit from participating.[8] Taylor and Savitz report similar responses from women participating in studies of cervical cancer.[9,10] In the current study, however, some differences were noted in the two case groups. Breast cancer subjects responded more negatively to the question about confidentiality than did colon cancer cases. This could be due to the younger age of the breast cancer subjects, their somewhat higher educational attainment, or some factor related to a differential emotional response to the disease itself.

The results of this study should be reassuring to epidemiologists and IRB members involved in similar investigations. Overall, this survey indicates that the risks of participation in the original study protocol—loss of privacy, free choice, and/or volunteerism—were judged to be minimal by participants. The difficult ethical and policy question is whether the small number of patients who do object to unconsented disclosure of their condition to investigators constitute a sufficient reason to require consent for such disclosures. In this research, the potential societal benefits of the research were considered sufficient to balance the minor infringements on the rights of subjects deemed necessary to ensure scientific validity. As with all studies, this balancing included considerations of the design of the study as well its social importance. Were there little likelihood of societal benefit, the IRB might have concluded that the small number of aggrieved patients would have been sufficient to outweigh the investigator's interests. In general, it is rare for participants in epidemiologic research to accrue personal benefit. In the absence of this benefit, studies including the risk of psychosocial harm, perhaps through invasive assessment, may consider a more conservative recruitment protocol.

For those in the current study who did strongly object to the protocol, it may be efficient (and ethically preferable) to identify them prior to the study by informing individuals of the use of existing registries (or records) for epidemiologic studies at the time of entry into the source population (e.g., at the time of admission to the hospital or primary care practice). In this way, potential subjects would be invited to opt out of future studies. The cost of such an approach would be a potential biasing of sample populations that could seriously compromise study integrity. However, based upon our experience with this study population, few individuals would actively refuse.

Although the six-month lag between the original study contact and this sub-study may have modified participant opinion regarding the original study protocol, we feel confident that this approach was appropriate to the study population. Further investigation of subject response to study protocols is needed, not just in terms of methodologies that produce high response rates, but also in terms of the costs to participants as measured by their evaluation of the invasiveness of various recruitment protocols.

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