Surrogate Receptivity to Participation in Critical Illness Genetic Research

Aligning Research Oversight and Stakeholder Concerns

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BACKGROUND: Collection of genetic biospecimens as part of critical illness investigations is increasingly commonplace. Oversight bodies vary in restrictions imposed on genetic research, introducing inconsistencies in study design, potential for sampling bias, and the possibility of being overly prohibitive of this type of research altogether. We undertook this study to better understand whether restrictions on genetic data collection beyond those governing research on cognitively intact subjects reflect the concerns of surrogates for critically ill patients.

METHODS: We analyzed survey data collected from 1,176 patients in nonurgent settings and 437 surrogates representing critically ill adults. Attitudes pertaining to genetic data (familiarity, perceptions, interest in participation, concerns) and demographic information were examined using univariate and multivariate techniques.

RESULTS: We explored differences among respondents who were receptive (1,333) and nonreceptive (280) to genetic sample collection. Whereas factors positively associated with receptivity to research participation were “complete trust” in health-care providers (OR, 2.091; 95% CI, 1.544-2.833), upper income strata (OR, 2.319; 95% CI, 1.308-4.114), viewing genetic research “very positively” (OR, 3.524; 95% CI, 2.122-5.852), and expressing “no worry at all” regarding disclosure of results (OR, 2.505; 95% CI, 1.436-4.369), black race was negatively associated with research participation (OR, 0.410; 95% CI, 0.288-0.585). We could detect no difference in receptivity to genetic sample collection comparing ambulatory patients and surrogates (OR, 0.738; 95% CI, 0.511-1.066).

CONCLUSIONS: Expressing trust in health-care providers and viewing genetic research favorably were associated with increased willingness for study enrollment, while concern regarding breach of confidentiality and black race had the opposite effect. Study setting had no bearing on willingness to participate.

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ABBREVIATIONS: IRB = institutional review board

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Genetic variation influences disease predisposition and severity.^{1,2} Use of genetic information to aid diagnosis, stratify risk, and guide therapy has potential to impact most facets of medical practice.²⁻⁴ Substantial investment has produced greater understanding of genetic structure and refinement in techniques to facilitate acquisition and analysis of genetic data in a cost-effective fashion.⁵⁻⁷ Genetic biospecimens are commonly collected in observational studies and as adjuncts to therapeutic trials.⁸ Comparable investigations involving acutely ill patients are increasingly commonplace and essential to advancing the field of critical care medicine.^{4,9,10}

Critically ill patients are frequently incapacitated, requiring that informed consent permitting research participation be obtained from surrogate decision-makers (eg, family members, guardians, or domestic partners).¹¹⁻¹⁵ Investigations involving incapacitated subjects are often perceived as entailing greater participant risk relative to studies enrolling cognitively intact individuals.¹¹⁻¹⁸ Several core protections have been proposed to govern research in this context.^{17,18} Among these is an institutional assessment of the risks and benefits of any proposed study.¹⁷⁻¹⁹ Gong et al¹⁹ surveyed institutional review board (IRB) members to understand how this particular protection might be applied. When presented with a hypothetical study involving incapacitated patients in which genetic specimens would be collected, respondents were conflicted as to the risk such a study would pose, with 40% reporting that they would not

permit such a study in the absence of direct patient benefit.¹⁹ Variability in application of research protections has likewise been observed in clinical investigations. In a multicenter, genetic epidemiology, acute stroke trial, Chen et al²⁰ reported that investigators preferentially enrolled less severely affected, cognitively intact participants, because IRBs at 40% of participating institutions would not permit use of decisional surrogates to provide consent in such a study.

IRBs are charged with insuring the protection of research participants in a manner consistent with federal statute and prevailing standards.^{11,18,19} Within this framework, variable application of research subject protections among institutions is problematic insofar as it introduces inconsistencies in recruitment practices and potential for sampling bias.^{21,22} Further, to the extent that protections are applied that do not address concerns of research subjects, they are ineffective. There is growing enthusiasm for the investigative community to engage potential research participants in issues of trial design and human subjects' protection.²³⁻²⁵ We undertook this study to better understand whether restrictions on genetic data collection beyond those governing research on cognitively intact subjects reflect the concerns of surrogates for critically ill patients. Insight into stakeholder preferences holds the potential for achieving greater alignment between research oversight practices and the concerns that those who are directly affected express.²⁴

Materials and Methods

Overview

We sought to determine whether protections beyond those governing research involving cognitively intact participants reflect preferences of those who might be approached with requests to enroll a patient in a critical illness study. To understand these preferences, we examined receptivity to participation in a low-risk study involving genetic sample collection, comparing two populations: ambulatory patients rendering decisions for themselves and surrogates providing substituted judgment for critically ill adults. This was accomplished by aggregating common elements from surveys that had been administered to these two subpopulations.^{26,27} The findings from the ambulatory study have been published previously.²⁶

Data Acquisition

Briefly, the questionnaire to understand attitudes about participation in genetic research was developed with extensive expert review.^{26,27} For the ambulatory study, respondents were enrolled from a convenience sample of adult outpatients at one of five academic health centers (2002 to 2003). For the critical care portion of this study, participants were recruited from surgical and medical ICUs of three tertiary care institutions (March 2010 to December 2012). We sought to interview surrogates actively engaged in the process of providing substituted judgment for critically ill adults. At study initiation, ICU admissions were screened to identify patients who were ≥ 18 years old, who were

mechanically ventilated for ≥ 48 h, and who were expected to require ventilatory support for ≥ 24 additional hours. Excluded patients were those who were prisoners, pregnant, had sustained severe head injury, or who possessed preexisting cognitive dysfunction. Surrogates (ie, family members, guardians, domestic partners, legally appointed individuals) for patients meeting inclusion criteria were approached by research staff and invited to participate. All surveys were conducted by dedicated field interviewers. Participant responses were recorded electronically and submitted in a deidentified fashion to a central repository for coding and analysis (e-Appendix 1).

Analysis

Three authors (B. D. F., K. B., S. C. H.) reviewed the surveys administered in these individual studies to identify common elements that could be pooled for analysis.^{26,27} In addition to demographic variables, these elements included familiarity with genetic research, perception of genetic research, willingness to permit collection of a genetic sample, and concern about unauthorized disclosure of genetic study data (e-Table 1). The approach to analysis was comparable to that previously described.²⁶ Our primary goal was to examine receptivity to genetics research participation, comparing ambulatory patients making decisions for themselves and surrogates providing substituted judgment for critically ill adults. We defined receptivity as follows. Interviewees were asked about the likelihood that they would provide a genetic sample (ambulatory setting) or permit the collection of a genetic sample for an incapacitated patient (critical care setting). The responses "very likely"

and “somewhat likely” were categorized as “receptive”; the responses “not very likely” and “not at all likely” were categorized as “nonreceptive.” The Wald X^2 statistic was used to compare ambulatory and critical care populations and to examine the relationship between dependent (ie, receptivity vs nonreceptivity) and independent variables. Multivariate logistic regression was used to examine the relationship between population (ie, ambulatory, critical care) and variables associated with recep-

tivity to genetic research (SigmaPlot 12.5; Systat Software Inc). Files with missing data elements were excluded from multivariate analysis.

Human Subject Protections

This study was approved by the IRBs of Washington University School of Medicine (201303067) and the National Institutes of Health (02-HG-N237).

Results

Participant Characteristics

We analyzed data from 1,613 respondents (Table 1, e-Appendix 1). These individuals were predominately middle aged, female (71.9%), and white (74.7%). While the majority (73.7%) categorized themselves collectively as being in “good,” “very good,” or “excellent” health, a substantial number (56.4%) described carrying the diagnosis of a chronic illness. Seventy percent reported completing at least some college course work, and a similar proportion endorsed “complete trust” in their health-care provider. A minority (42.1%) reported being “very religious.” While the 1,176 ambulatory patients and 437 surrogates were comparable with respect to sex, age, race, ethnicity, and degree of trust placed in health-care providers (P was not significant for all), these two groups had notable distinctions. Compared with surrogates, a higher proportion of ambulatory participants reported that they were in fair or poor health and carried the diagnosis of chronic illness ($P < .001$ for both) and were more likely to report that they had previously participated in research ($P < .001$). Finally, while a greater proportion of surrogates described themselves as “very religious,” smaller proportions of these individuals were in the extreme strata of education and income ($P < .05$ for all).

Attitudes About Genetic Research

Interviewees described a general familiarity with genetic research, tended to view this type of research favorably, and reported being “very willing” (52.2%) or “somewhat willing” (30.4%) to permit genetic sample collection (Table 2). Despite the majority of respondents (70.5%) endorsing “complete trust” in their health-care provider, concerns about inadvertent disclosure of genetic results were common, with nearly 60% of individuals stating that this was at least a “moderate worry.” Ambulatory patients and surrogates differed in several key respects. While surrogates were more likely to report that they had “heard a lot about” or “heard a little about” genetic research, they were less likely to view this research positively, to describe willingness to permit genetic data

collection, or to express concerns regarding unauthorized disclosure of results ($P < .001$ for all).

Relationship Between Participant Characteristics, Attitudes About Genetic Research, and Receptivity to Genetic Research Participation

We explored differences among participants who were receptive and nonreceptive to permitting genetic sample collection. Compared with nonreceptive individuals ($n = 280$; 185 ambulatory, 95 surrogates), receptive participants ($n = 1,333$; 991 ambulatory, 342 surrogates) were older, more commonly white, and more likely to report higher annual income. Similarly, these individuals were more likely to carry the diagnosis of chronic illness, to have previously participated in research, and to place trust in health-care providers ($P < .05$ for all) (Table 3). Ambulatory patients appeared more receptive to research participation than surrogates (84.3% vs 78.3%, $P = .006$). In contrast, receptive and nonreceptive participants were similar with respect to sex, ethnicity, religiosity, and education level (P was not significant for all). Receptive and nonreceptive participants differed in their attitudes about genetic research, with receptive individuals more likely to report familiarity with this field and to view it positively, and to be less concerned regarding disclosure of results ($P < .001$ for all) (Table 4).

In multivariate analysis of the pooled sample, reporting “complete” trust in health-care providers, upper income strata, viewing genetic research “very” positively, and expressing “no worry at all” regarding disclosure of results were positively associated with receptivity to research participation, whereas black race was associated with decreased likelihood of participation ($P < .05$ for all). We did not detect an effect of subpopulation (ie, ambulatory patients compared with surrogates for critically ill individuals) on receptivity to enrollment in a genetic study (P was not significant) (Table 5). When analyzed independently, the only variable that differed significantly when comparing ambulatory patients and surrogates was expressing complete trust in the health-care provider (OR, 2.226 [95% CI, 2.290-4.861] vs 1.160 [0.650-2.069]; $P < .05$ for ambulatory patients vs surrogates, respectively) (e-Table 2).

TABLE 1 Demographic Variables Comparing Ambulatory Patients and Surrogates for Critically Ill Individuals

Survey Elements ^a	All Respondents	Ambulatory Patients	Surrogates	P Value
Female sex (1,638)	1,174 (71.7)	839 (70.3)	335 (75.3)	.055
Age, median (IQR), y (1,638)	52 (42-63)	52 (41-63.5)	51 (42-60)	.126
Current health status (1,633)				<.001
Excellent	234 (14.3)	159 (13.4)	75 (16.9)	
Very good	510 (31.1)	333 (28.0)	177 (40.4)	
Good	460 (28.1)	334 (28.1)	126 (28.4)	
Fair	276 (16.8)	217 (18.2)	59 (13.3)	
Poor	153 (9.3)	147 (12.4)	6 (1.3)	
Serious or chronic medical illness (1,632)	920 (56.2)	729 (61.3)	191 (43.2)	<.001
Ever participated in research study? (1,623)	581 (35.5)	519 (43.9)	62 (14.0)	<.001
Hispanic or Latino (1,630)	79 (4.8)	57 (4.8)	22 (5.0)	.974
Race (1,603)				.265
Black/American	278 (17.0)	192 (19.6)	86 (16.2)	
White	1,223 (74.7)	903 (76.0)	320 (72.9)	
Other ^b	126 (7.7)	93 (7.8)	33 (7.5)	
Education (1,634)				<.001
Did not complete high school	128 (7.8)	98 (8.2)	30 (6.8)	
High school graduate or equivalent	363 (22.2)	234 (19.7)	129 (29.0)	
Some college	464 (28.3)	332 (27.9)	132 (29.7)	
College graduate	305 (18.8)	223 (18.7)	82 (18.5)	
Some graduate school	86 (5.2)	69 (5.8)	17 (3.8)	
Graduate degree	288 (17.6)	234 (14.3)	54 (12.2)	
Annual income, \$ (1,492)				.043
<20,000	283 (17.3)	218 (20.1)	65 (16.0)	
20,001-40,000	346 (21.1)	260 (24.0)	86 (21.1)	
40,001-60,000	311 (19.0)	216 (19.9)	95 (23.3)	
60,001-80,000	181 (11.0)	119 (11.0)	62 (15.2)	
80,001-100,000	311 (19.0)	272 (25.1)	39 (24.3)	
Religiosity (1,623)				<.001
Not religious	186 (11.3)	164 (13.8)	22 (5.0)	
Somewhat religious	745 (45.5)	560 (47.1)	185 (42.4)	
Very religious	693 (42.3)	464 (39.0)	229 (52.5)	
Trust your doctor (1,550)				.148
Completely	1,155 (75.3)	835 (75.3)	320 (75.6)	
Somewhat	347 (22.6)	236 (21.3)	111 (25.2)	
A little/not at all	32 (2.1)	38 (3.4)	10 (2.3)	

Data are presented as No. (%) unless otherwise indicated. IQR = interquartile range.

^aNumbers in parentheses refer to participants analyzed for survey element.

^bIncludes Asian, American Indian, and other races.

Discussion

We sought to identify factors affecting receptivity to participation in genetic research and found that expressing trust in health-care providers and viewing this type of research favorably were associated with increased

willingness for enrollment. In contrast, concern regarding breach of confidentiality and black race had the opposite effect. Reassuring potential research subjects as to the confidentiality of research data, as well as describing the safeguards in place to maintain this confidentiality,

TABLE 2] Survey Responses Related to Attitudes Concerning Genetic Research Comparing Ambulatory Patients and Surrogates for Critically Ill Individuals

Survey Elements ^a	All Respondents	Ambulatory Patients	Surrogates	P Value
How much have you heard about health-related genetic research? (1,515)				< .001
Heard a lot about it	411 (25.1)	321 (26.9)	90 (27.9)	
Heard a little about it	968 (59.1)	748 (62.7)	220 (68.3)	
Heard almost nothing about it	136 (8.3)	124 (10.4)	12 (3.7)	
How positive or negative about genetic research? (1,386)				< .001
Very positive	604 (36.9)	506 (47.5)	98 (30.5)	
Somewhat positive	615 (37.5)	453 (42.5)	162 (50.5)	
Neither positive or negative	119 (7.3)	67 (6.3)	52 (16.2)	
Somewhat negative	37 (2.2)	29 (2.7)	8 (2.5)	
Very negative	11 (0.1)	10 (0.9)	1 (0.3)	
How willing to permit genetic sample collection? (1,613)				< .001
Very willing	843 (52.2)	681 (57.9)	162 (37.1)	
Moderately willing	490 (30.4)	310 (26.4)	180 (41.2)	
Not very willing	187 (11.6)	135 (11.5)	52 (11.9)	
Not willing at all	93 (5.8)	50 (4.2)	43 (9.8)	
How concerned about disclosure? (1,551)				< .001
Big worry	445 (27.2)	354 (31.9)	91 (20.5)	
Moderate worry	471 (28.7)	352 (31.7)	119 (26.9)	
Small worry	399 (24.3)	282 (25.4)	117 (26.5)	
No worry at all	236 (14.4)	121 (10.9)	115 (26.0)	

Data are presented as No. (%) unless otherwise indicated.

^aNumbers in parentheses refer to participants analyzed for survey element.

would appear to be a modifiable variable that might favorably impact recruitment.

This study was based on the premise that human subjects' protections should mirror the concerns expressed by those directly affected (ie, the research subjects themselves).²³⁻²⁵ We reasoned that application of research restrictions based on setting would be reflected in willingness of individuals approached in these contexts to participate. Scenarios presented to ambulatory patients and surrogates described low-risk studies. Among possible outcomes from this comparison, we speculated that surrogates, when confronted with the exigencies of the ICU environment, might have heightened concerns about research participation and be less willing to permit genetic sample collection relative to patients in the ambulatory setting.²⁸⁻³⁰ Alternatively, relative to the risks associated with conditions prompting ICU admission and with procedures necessary to provide care, we reasoned that surrogates might perceive the risks associated with research as trivial and be more permissive with respect to enrollment. Either outcome would suggest potential vulnerability on the part of surrogates and

would argue for greater stringency in research subjects' protections for genetic research conducted in the critical care environment. However, in multivariate analysis, we found that ambulatory patients and surrogates were indistinguishable with respect to their willingness to participate in genetic research. One interpretation of this finding is that human subjects' protections should likewise be comparable in these two settings; imposition of additional protections would not appear to match concerns held by surrogates approached for research participation.

To our knowledge, this is the first study to directly compare attitudes about clinical research among individuals in ambulatory and critical care settings. Important differences existed between these subpopulations. Reflecting that ambulatory participants were recruited from outpatient clinics, these individuals more commonly described poor chronic health relative to surrogates. Similarly, because one ambulatory enrollment site recruited patients who had previously participated in an epidemiologic investigation, these individuals were more likely to report previous research experience.

TABLE 3] Demographic Variables Comparing Participants Receptive and Not Receptive to Genetic Sample Collection

Survey Elements ^a	Genetic Sample Collection		P Value
	Receptive	Nonreceptive	
Female sex (1,613)	950 (71.3)	210 (75.0)	.234
Age, median (IQR), y (1,613)	52 (43-63)	50 (37-60)	<.001
Current health status			.023
Excellent	179 (13.4)	49 (17.6)	
Very good	414 (31.1)	90 (32.2)	
Good	367 (27.6)	86 (30.8)	
Fair	233 (17.5)	39 (14.0)	
Poor	137 (10.3)	15 (5.4)	
Serious or chronic medical illness (1,609)	780 (58.6)	128 (45.9)	<.001
Ever participated in research study? (1,600)	498 (37.6)	71 (25.6)	<.001
Hispanic or Latino (1,607)	62 (4.7)	16 (5.7)	.234
Race (1,579)			<.001
Black/American	183 (13.7)	90 (32.7)	
White	1,046 (78.8)	159 (57.8)	
Other ^b	99 (7.4)	26 (9.4)	
Education (1,610)			.078
Did not complete high school	100 (7.5)	25 (9.0)	
High school graduate or equivalent	296 (22.2)	62 (22.2)	
Some college	367 (27.6)	95 (34.0)	
College graduate	262 (19.7)	39 (14.0)	
Some graduate school	67 (5.0)	17 (6.1)	
Graduate degree	239 (18.0)	41 (14.7)	
Annual income, \$ (1,471)			.007
<20,000	221 (18.8)	57 (24.2)	
20,001-40,000	280 (23.8)	65 (27.5)	
40,001-60,000	249 (21.2)	58 (24.6)	
60,001-80,000	161 (13.7)	19 (8.0)	
80,001-100,000	265 (22.5)	37 (15.7)	
Religiosity (1,601)			.610
Not religious	153 (11.6)	27 (9.7)	
Somewhat religious	610 (46.1)	127 (45.7)	
Very religious	560 (42.3)	124 (44.6)	
Trust your doctor (1,529)			<.001
Completely	992 (76.9)	148 (66.4)	
Somewhat	279 (21.6)	62 (27.8)	
A little/not at all	19 (1.5)	13 (5.8)	
Subpopulation (1,613)			.006
Ambulatory	991 (84.3)	185 (15.7)	
Surrogate decision-maker	342 (78.3)	95 (21.7)	

Data are presented as No. (%) unless otherwise indicated. See Table 1 legend for expansion of abbreviation.

^aNumbers in parentheses refer to participants analyzed for survey element.

^bIncludes Asian, American Indian, and other races.

TABLE 4] Survey Responses Related to Willingness to Provide a Genetic Sample for Research Comparing Interviewees Receptive and Not Receptive to Genetic Sample Collection

Survey Elements ^a	Genetic Sample Collection		P Value
	Receptive	Not Receptive	
How much have you heard about health-related genetic research? (1,490)			< .001
Heard a lot about it	352 (28.2)	51 (21.2)	
Heard a little about it	805 (64.4)	147 (61.2)	
Heard almost nothing about it	93 (7.4)	42 (17.5)	
How positive or negative about genetic research? (1,362)			< .001
Very positive	547 (47.1)	43 (21.5)	
Somewhat positive	496 (42.7)	111 (55.5)	
Neither positive or negative	89 (7.7)	28 (14.0)	
Somewhat negative	24 (2.1)	13 (6.5)	
Very negative	6 (0.5)	5 (2.5)	
How concerned about disclosure? (1,531)			< .001
Big worry	341 (26.1)	94 (41.8)	
Moderate worry	395 (30.2)	71 (31.6)	
Small worry	357 (27.3)	39 (17.3)	
No worry at all	213 (16.3)	21 (9.3)	

Data are presented as No. (%) unless otherwise indicated.

^aNumbers in parentheses refer to participants analyzed for survey element.

Finally, while surrogates reported greater familiarity with genetic research, they were less likely to view this technology positively.

A number of investigators have examined the relationship between race and clinical trial participation.³¹⁻³⁴ While our methodology did not allow us to explore the reasons for less receptivity to clinical research among blacks, this finding did not appear explained by education, income, religiosity, or trust. Coupled with other factors common in underrepresented populations, racially associated reluctance to enroll in critical care research presents a significant hurdle to achieving broad demographic inclusion and for rectifying racial disparities in critical care.^{33,35,36} Further, these findings suggest that motivations for participation in clinical investigation may largely be formed prior to the ICU experience. Understanding the concerns of underrepresented groups and determining how best to surmount these concerns might be further pursued using qualitative methodology.

Our study had several limitations. Individuals might execute the surrogate role in one of several ways, such as providing substituted judgment (reflecting what the incapacitated patient would wish for themselves) or engaging in decision making based on what the surrogate perceives is in the patient's best interest. We did

not provide guidance as to what framework participants should adopt in responding to our survey and cannot exclude the possibility that providing this background might have altered their responses. In addition, acquisition of data from the two surveys analyzed differed in time. Attitudes might have been affected by portrayal of genetic technology in the mass media, as well as reporting of legislative initiatives such as the Genetic Information Nondiscrimination Act.³⁷ Further, while we intended the concept of trust as used in our survey instruments to measure confidence in health-care providers, this term is open to variable interpretation, which may have affected our findings.³⁸ Similarly, due to sampling bias and exclusion of incomplete surveys, the opinions we report may not be representative of the broader population, further limiting the generalizability of our results.^{39,40} Finally, we solicited attitudes about participation in a hypothetical low-risk study. We may have detected a divergence in interest in participation among the groups sampled if we had included scenarios of variable risk.⁴¹ Similarly, opinions we recorded may not reflect an individual's consideration if approached about an actual clinical study. Nonetheless, our findings are consistent with those reported by Smart et al,⁹ who found that the majority of surrogates granting permission for participation in clinical trials coordinated through the Acute Respiratory Distress Syndrome

TABLE 5] ORs and 95% CIs for Relationship Between Survey Elements and Receptivity to Providing Genetic Sample for Research^a

Survey Element	OR (95% CI)
Sex	
Female	0.958 (0.690-1.329)
Male (reference)	1.000
Age	1.001 (0.994-1.009)
Current Health Status	
Excellent	0.754 (0.474-1.198)
Very good	1.045 (0.723-1.512)
Good (reference)	1.000
Fair	1.439 (0.909-2.278)
Poor	1.795 (0.943-3.418)
Serious or chronic medical illness?	
Yes	1.218 (0.885-1.675)
No (reference)	1.000
Ever participated in research study?	
Yes	1.277 (0.942-1.733)
No (reference)	1.000
Ethnicity (Hispanic/Latino)	
Yes	0.975 (0.494-1.923)
No (reference)	1.000
Race	
Black	0.410 (0.288-0.585)
White (reference)	1.000
Other	0.636 (0.373-1.085)
Education	
Did not graduate high school	1.212 (0.621-2.367)
High school/General Educational Development test	1.163 (0.706-1.917)
Some college	0.703 (0.449-1.101)
College graduate (reference)	1.000
Some graduate school	0.554 (0.279-1.100)
Graduate degree	0.822 (0.493-1.371)
Annual income, \$	
<20,000	1.192 (0.770-1.844)
20,001-40,000	1.210 (0.818-1.788)
40,001-60,000 (reference)	1.000
60,001-80,000	2.347 (1.322-4.167)
>80,000	1.512 (0.987-2.314)
Religiosity	
Not religious	0.839 (0.512-1.375)

(Continued)

TABLE 5] (continued)

Survey Element	OR (95% CI)
Somewhat religious (reference)	1.000
Very religious	1.132 (0.833-1.538)
How much do you trust your doctor?	
Completely	2.091 (1.544-2.833)
Somewhat (reference)	1.000
A little/not at all	1.165 (0.568-2.390)
How much have you heard about health related genetic research?	
Heard a lot about it	0.899 (0.610-1.324)
Heard a little about it (reference)	1.000
Heard almost nothing about it	0.718 (0.416-1.238)
How positive or negative about genetic research?	
Very positive	3.524 (2.122-5.852)
Somewhat positive	1.480 (0.989-2.215)
Neither positive or negative (reference)	1.000
Somewhat negative	0.619 (0.279-1.373)
Very negative	0.415 (0.105-1.638)
How concerned about disclosure?	
Big worry	0.948 (0.658-1.368)
Moderate worry	1.335 (0.922-1.933)
Small worry (reference)	1.000
No worry at all	2.505 (1.436-4.369)
Subpopulation	
Surrogates for critically ill individuals	0.738 (0.511-1.066)
Ambulatory patients (reference)	1.000

^aHosmer-Lemeshow statistic: 7.732 ($P = .460$).

Network likewise permitted genetic specimen collection, and that patients largely affirmed participation when given the opportunity for reconsent.

Conclusions

Receptivity to participation in genetic research was similar comparing ambulatory patients and surrogates for critically ill adults. These findings suggest that restrictions imposed by IRBs on genetic research involving incapacitated individuals, beyond those governing research for cognitively intact participants, may impede valuable investigations without conferring any meaningful and

offsetting human subjects' protections. Achieving greater alignment between stakeholder preferences and research subjects' protections may be one strategy for minimizing interinstitutional variation in IRB behavior.

While this study focused on a specific field of inquiry, we feel that this approach is applicable to other domains where ambiguity exists as to the manner in which research subject protections might be optimally applied.

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Additional information: The e-Appendix and e-Tables can be found in the Supplemental Materials section of the online article.

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