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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. CHEST 2015; 147(4):979-988

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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 al[19] 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 al[20] 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 a 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"