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DOES DIFFICULTY FUNCTIONING IN THE SURROGATE ROLE EQUATE TO VULNERABILITY IN CRITICAL ILLNESS RESEARCH?:

Use of path analysis to examine the relationship between difficulty providing substituted judgment and receptivity to critical illness research participation

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Abstract

Purpose—Individuals who struggle to provide substitute judgment for the critically ill often find it challenging to engage in decision making for therapeutic interventions. Though essential to the conduct of research, how these individuals respond to requests for clinical trial participation is poorly understood.

Methods—Survey data collected to examine surrogate attitudes towards research provided the conceptual framework to explore influences on decision making. Path analysis was employed to derive the final model (non-latent, fully recursive, one indicator/variable).

Results—Surrogates with list-wise complete records (406) were analyzed. The following variables were not retained in the final model: education, income, religiosity, decision-making experience, discussion of patient's wishes, number of individuals assisting with decision making, trust in care providers, difficulty making decisions, responsibility for decision making. Being Caucasian and having experience making treatment decisions for the patient during the current ICU encounter affected the likelihood the surrogate would permit participation in research positively (parameter estimates 0.281 and 0.06, respectively). No variable reflecting difficulty functioning in the surrogate role was associated with permitting research participation.

Conclusions—We were unable to demonstrate a relationship between perceived difficulty in decision making in the surrogate role and receptivity to clinical trial participation.

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CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

Keywords

path analysis; surrogate decision maker; clinical research; substituted judgment; biospecimen; critical illness

INTRODUCTION

Clinical investigations enrolling acutely ill patients are essential to advancing the practice of critical care medicine(1). These investigations are characterized by logistical and ethical challenges not encountered in studies of non-urgent conditions, such as cancer, hypertension or psychiatric illness(2-5). Conditions prompting intensive care unit (ICU) admission are frequently precipitous and life-threatening and the care provided highly technological(2;6). In addition to immersion in an unfamiliar environment, it is often the case that neither patients nor family members have had opportunity for education regarding the nature of the disease process, expected outcome, or treatment alternatives. Further, ICU patients are frequently incapacitated and unable to provide informed consent permitting medical intervention or research participation(2;3;7-10). Finally, given the rapid tempo of many acute illnesses, e.g., sepsis or myocardial infarction, therapies must be administered quickly following diagnosis. In order to enroll critically ill patients in clinical studies, permission must be obtained – often expediently - from surrogates, many of whom are being confronted with complex and serious medical issues for the first time(2;4;5).

The intellectual, emotional, and physical challenges associated with serving as a decisional surrogate for a critically ill patient are becoming increasingly appreciated(5;11-17). Individuals who struggle in this role may lack confidence in their ability to provide substituted judgement regarding therapeutic interventions and end of life decisions(12). Less completely understood is how individuals who are challenged by decision making as a surrogate respond when permission for patient inclusion in clinical research is requested. Conceivably, these individuals may be less inclined to permit research enrollment due to the additional cognitive demands that such a request might entail, as has been described for surrogate decision makers experiencing significant anxiety(5;13;16). Alternatively, individuals who struggle with surrogate decision making may more readily accede to requests for research participation, motivated by such factors as therapeutic misconception or concern about potentially alienating care providers. Further, to the extent that difficulty in providing substituted judgment impairs the ability of surrogates to process information rationally, decisions made may poorly align with patient preferences. Taken together, these factors may accentuate the vulnerable nature of research conducted in the setting of acute illness(8;18).

Providing substituted judgment is predicated on the surrogate's ability to process information rationally in addition to understanding and acting on the patient's wishes(5). Different strategies for recruitment and consent may be needed for surrogates who perform poorly in this role, such as use of tools which may enable more effective decision making. Further, implementation of additional human subjects' protections may be indicated, e.g., deferring recruitment until the patient is no longer incapacitated(12). Thus, the relationship

between a surrogate's difficulty in providing substituted judgment and their receptivity to permitting study enrollment has implication for the conduct of clinical research in the setting of acute illness. Characterizing this relationship was the purpose of this study.

MATERIALS AND METHODS

Data collection

We used path analysis to explore the potentially biasing effects related to challenge in providing substituted judgment relative to demographic and contextual factors(19). This analytic approach was applied to data which had been obtained to examine attitudes and experiences regarding collection of genetic biospecimens in the context of critical illness research. The survey instrument developed for this purpose has been previously described(20). Briefly, our questionnaire, modified from Hull *et al*, records attitudes and perceptions related to the conduct of critical care research(20;21). Information collected included familiarity with research (non-genetic, genetic), perceptions as to usefulness of research, likelihood of allowing a patient to participate in research (non-genetic, genetic), and demographic variables. Prior to fielding the final survey instrument, cognitive interviews were conducted to assess the clarity of the questions, uniformity in comprehension, and respondent comfort with the content(20).

English-speaking participants were recruited from the surgical and medical ICU's of three tertiary care institutions (Barnes Jewish Hospital, St. Louis, MO, St. Louis University Hospital, St. Louis, MO and Parkland Hospital, University of Texas-Southwestern Medical Center, Dallas, TX) over 34-month period (March 2010-December 2012). These study sites were chosen because of the demographic and ethnic diversity afforded. Our selection criteria have previously been reported(14;22). Briefly, we sought to interview individuals identified to serve as surrogate decision makers for critically ill adults. At the time of study initiation, admissions to participating ICUs were screened to identify patients who were 18-years of age, intubated and mechanically ventilated for 48 hours, and expected to require ventilatory support for 24 additional hours. We excluded patients who were freedom-impaired, pregnant, had sustained severe head injury, or who possessed pre-existing cognitive dysfunction (which would preclude interview participation). As the study evolved, 2 minor modifications were made to the inclusion criteria in an effort to increase enrollment. The requirement for mechanical ventilation was first decreased to 24 hours and then subsequently eliminated. Surrogates (i.e., family members, guardians, domestic partners, legally-appointed individuals) for patients meeting inclusion criteria were approached by research staff and invited to participate. Those agreeing provided informed consent and completed an in-person on-site computer assisted interview conducted by dedicated field staff. Participant responses were recorded electronically and submitted in a de-identified fashion to a central repository (located at the Center for Survey Research, University of Massachusetts, Boston, MA) for coding and analysis.

Analytic approach

We first constructed a conceptual model incorporating 3 clusters of independent variables (*background, decision making and mediating*) and 1 cluster of dependent variables (**Figure**

1). *Background* variables included age, gender, race, highest educational level achieved, annual income and self-reported religiosity. These variables have performed well historically as proxies for social background in a variety of settings and have been thoroughly tested in prior research(21). Because these variables are either ascribed at birth or logically determined prior to the ICU encounter, we have placed them temporally first in our scheme. *Decision making* variables were intended to reflect the surrogate's experience with this task, and included whether the surrogate had engaged in conversation with the patient regarding decision making in the event of incapacitation, whether the surrogate had provided substituted judgment previously, whether the surrogate had been called upon to provide substituted judgment during the current episode of illness, and the number of individuals assisting the surrogate in providing substituted judgment. Prior experience providing substituted judgment and conversation between surrogates and patients regarding this task have been previously reported to affect confidence in functioning in the surrogate role(12). *Mediating variables* (confidence and trust placed in care providers, the proportion of responsibility the surrogate feels for providing judgment, the perceived difficulty of decision making, attitudes regarding the utility of research) were included as factors potentially influencing decision making for clinical trial participation. We have positioned *mediating* variables temporally between *decision making* and *outcome* variables. We made no assumptions about causal ordering among the variables within the *background*, *decision making* and *mediating* clusters, allowing the variables within these clusters to freely interact with one another. In contrast, the variables contained in the *outcome* cluster have a defined temporal sequence. In constructing our survey instrument, we assumed that attitudes regarding permitting patient participation in clinical research would be influenced by the surrogate's own personal inclination toward research. Thus, before asking the surrogates about their willingness to allow the patient to participate in research, we asked them about their own willingness to participate. We also asked about their willingness to provide genetic biospecimens for research purposes. Only after recording their responses to these questions did we ask them if, in their role as surrogate decision-makers, they would be willing to allow the patient to participate as a research subject, and whether they would permit collection of a genetic biospecimen from the patient. Our assumption regarding these outcome variables was that the two responses the surrogate provided for themselves precede those regarding their approval for the patient's participation in research. We also assumed that the surrogates' thoughts about genetic research were formed temporally later than their thoughts about non-genetic research. This temporal ordering was reflected in the specification of our model.

The coding scheme for the variables used in this analysis is presented in **Table 1**. In analyzing our data, the Kolmogorov-Smirnov test was used to determine normality of distribution for continuous variables, with these variables reported as mean ($\pm$ standard deviation ($\pm$ SD)) or median with interquartile range (IQR), as appropriate. Beginning with a saturated model, all paths were tested for significance, with the residuals from the fit of each path calculated to include any unaccounted-for variance. The saturated model was fully recursive and included one indicator per variable with no latency. To move toward the best-fitting, most parsimonious model, variables were tested for significance and non-significant variables were removed in a backward stepwise fashion(19). Given the exploratory nature of

our study, we assumed our data to be homoscedastic, both because regression modeling is typically robust with respect to departure from equality of variance and because we felt that this approach would provide an unbiased estimate of the influences represented in our conceptual model. All analyses were performed using *R*-statistical software(23).

Human Subjects Protections

This study was approved by the Human Studies Committees of Washington University School of Medicine (HRPO 06-0637) in addition to all sites participating in this effort, and adheres to the ethical standards promulgated by the 1964 Declaration of Helsinki and its later amendments.

RESULTS

Description of participants

Selected findings from the survey on which this path analysis is based have been reported previously(24-26). Briefly, 568 surrogates were invited to participate. Of these, 63 were excluded due to withdrawal of consent or inability to meet with the field interviewer, and 60 were excluded because their corresponding patient had died or had been discharged prior to the interview taking place. The remaining 445 surrogates completed the interview for a cooperation rate of 87.6%. (**Table 1**) These individuals (most commonly spouses/domestic partners (45.1%) and parents (25.7%)) were predominately middle-aged, female (75.3%) and Caucasian (71.9%). More than one-half described themselves as ‘very religious’ and a minority (34.3%) had completed a college education. More than one-half of respondents (52.3%) described prior experience providing substituted judgement, most (61.3%) reported that they had previously engaged in discussions about decision making with the patient in the event of incapacitation, and the majority (73.3%) had engaged in decision making during the current critical illness episode. Surrogates frequently reported that other family members or social contacts participated in the decision making process (median (IQR) number of individuals assisting, 2.0 (1.0-3.5)). However, two-thirds of the individuals we interviewed reported being responsible for ‘all’ (34.2%) or ‘most’ (33.7%) of the decision making, respectively, and viewed this process as moderately difficult (median (IQR) 5.0 (2.0-8.0) on an 11-point scale (0-least difficult, 10-most difficult)). Surrogates had an overall favorable view of care providers, with a majority (71.9%) expressing complete trust in clinicians to place the patient’s interest above all other considerations. Similarly, most surrogates (66.7%) were very confident that physicians were providing them with all the necessary information to make informed decisions. In the same way, surrogates held generally favorable attitudes regarding research. Half of all surrogates interviewed viewed all or most research as useful, and nearly 60% were either ‘very’ or ‘somewhat’ positive about genetic research. Finally, nearly 80% of surrogates reported that they would be ‘very’ or ‘somewhat’ likely to allow the patient they were representing to participate in research, including studies entailing collection of genetic biospecimens.

Path model development

All surrogates with list-wise complete records (406) were included in our analysis. We tested the saturated model and removed all non-significant paths while allowing within-

group covariation for social background, decision making, and mediating variables to remain unconstrained ($X^2=322.8$, $df=129$, $GFI=.93$, $AGFI=.89$). To foster parsimony, we removed all independent variables which did not have significant direct or indirect paths affecting the outcomes. These variables included education, income, religiosity, decision-making experience, prior discussion of patient's explicit wishes, number of individuals assisting with the decision making process, trust in care providers, self-reported difficulty in making decisions, and degree of responsibility for decision making. (**Figure 2**, $X^2=109.3$, $df=32$, $GFI=.95$, $AGFI=.91$). Little difference exists comparing the explanatory power of the initial and parsimonious models, with the final model accounting for more than one-third of the variance (38.7%) in likelihood the surrogate will allow the patient to participate in research, and more than one-half the variance (53.1%) in the likelihood of allowing the patient to participate in genetic research.

Direct and indirect paths

Six variables contained in the *background*, *decision making*, and *mediating* clusters had direct influences on the *outcome* variables in our most parsimonious model. (**Table 2**, **Figure 2**) Being Caucasian and having made treatment decisions for the patient during the current ICU encounter affected the likelihood the surrogate would participate in research positively (parameter estimates 0.324 and 0.141, respectively) as well as the likelihood the surrogate would permit the patient to participate in research (0.281 and 0.060, respectively). Similarly, confidence that care providers were disclosing all information necessary to inform decision-making also influenced the likelihood of the surrogate permitting research participation positively (0.095). Perceiving medical research as useful affected the likelihood the surrogate would participate in research (0.215), while how positively or negatively the surrogate perceived genetic research affected likelihood of participating in genetic research (0.207). Finally, age influenced the likelihood the surrogate would participate in genetic research negatively (-0.095).

We also sought direct influences amongst the *outcome* variables. Likelihood of surrogate participation in research influenced both the likelihood of surrogate participation in genetic research (0.506), and of permitting the patient to participate in research (0.364). Similarly, the likelihood of the surrogate participating in genetic research influenced the likelihood of permitting the patient to participate in research (0.127) including studies entailing collection of genetic specimens (0.489). Finally, how likely the surrogate was to permit participation in research influenced permission to participate in genetic research (0.383).

A number of variables had indirect effects in our model. (**Table 2**) Among the dominant indirect effects was Caucasian race, which influenced how likely the surrogate was to participate in genetic research (0.222) as well as how likely the surrogate was to permit participation in both non-genetic (0.173) and genetic (0.282) research. Perceptions of usefulness of research influenced likelihood of surrogate participating in genetic research (0.109). How positive or negative surrogates viewed genetic research and how likely the surrogate was to participate in research influenced the likelihood of permitting participation in genetic research (0.111, 0.411, respectively). The remaining indirect effects were relatively small in magnitude.

DISCUSSION

We undertook this study to understand which surrogate characteristics and experiences affect decision making for clinical trial participation. Most individuals completing our survey viewed the surrogate role as challenging, reported prior experience serving in this capacity, and described having conversations with the patient regarding their wishes in the event they might become incapacitated. We used path analysis to examine how these factors in conjunction with demographic characteristics and mediating influences might affect the decision to permit enrollment in a critical illness study. In our model, whether or not the family member had provided substituted judgment during the current ICU admission was the only variable related to surrogate experience found to produce a small indirect effect on this outcome. In contrast, decision making for or against clinical trial participation seemed to be independent of the perceived difficulty of the decision making process.

Our inability to demonstrate a relationship between perceived difficulty in decision making and receptivity to clinical trial participation seems counterintuitive and may be related to several factors. While we examined a number of variables which may both reflect and influence how an individual might function as a surrogate, potentially important components were lacking from our model. These include emotional duress and acuity of patient illness. Further, comfort in the surrogate role may evolve during a patient's ICU stay; we did not control for such time-dependence in our analysis. Finally, we elicited the opinions of individuals who agreed to participate in a survey, who generally viewed research and care providers favorably, and who appeared receptive to allowing patients to participate in research. Our sampled population may express views which don't generally reflect those of most individuals called upon to serve as surrogates(27). Our findings are nonetheless consistent with previous qualitative and quantitative research. Surrogates participating in focus groups reported that though emotionally burdened, they felt nonetheless capable of providing informed consent for purposes of clinical research(14). Similarly, receptivity to providing genetic biospecimens was similar comparing patients in ambulatory settings and surrogates for critically ill adults, suggesting that context does not substantially influencing decision making for study participation(25).

Among variables included in our model, race was the most influential. Relative to other subgroups, Caucasian surrogates were more likely to both participate in research and permit patient enrollment. Further, race exerted indirect influence through effects on confidence in care providers, views concerning genetic research, and likelihood of having made a decision as a surrogate. We controlled for several factors which potentially confound the influence of race on decision-making including education, income, religiosity, and trust in care providers. While our study was not designed to determine the reasons for lower potential rates of trial participation among non-Caucasians, it is consistent with a large body of literature describing this phenomenon in the non-acute setting(28;29). Combined with other factors such as the inability to locate surrogates during recruitment efforts, racially-associated reluctance to participate in a clinical study presents a significant hurdle to achieving broad demographic inclusion in critical care research(30;31).

To our knowledge, this manuscript reports the first application of path analysis to the examination of factors influencing decision making in the ICU setting. Our use of this approach was associated with a number of limitations. We developed a conceptual model which was based on a plausible set of assumptions and which imposed a particular temporal ordering. The relationships among the variables retained in our final model are consistent with what we proposed initially, with the paths relating these variables being positive and of the appropriate magnitude. While this ‘best fit’ model conforms to our data, it only explains one-third of observed variance in decision-making for patient participation in clinical research and one-half of the observed variance in decision-making for participation in genetic research. There appear to be many other influences - some of which may relate to function in the surrogate role – which were not captured by our methodology. In addition, our analysis was based on opinions elicited from individuals recruited from academic medical centers. While much critical care research occurs in this environment, the demographic makeup, types of illnesses treated, care delivery models, and nature of encounters experienced by surrogates might differ substantially from non-academic settings, limiting the applicability of our findings. Finally, the focus of our study was clinical research. Our findings may not be relevant to other facets of decision making that occurs in ICUs, such as that pertaining to acceptability of specific treatments or end of life care.

CONCLUSIONS

We were unable to demonstrate a relationship between perceived difficulty of decision making in the surrogate role and receptivity to clinical trial participation. In contrast, racial background and attitudes about research strongly influenced surrogate interest in study enrollment. These findings suggest that some characteristics which may substantially affect whether or not surrogates will permit participation in a critical illness investigation are determined prior to hospital admission. Individualized approaches to recruitment which target surrogates who struggle to make decisions may have effects on other aspects of the consent process (such as transparency), but may not influence likelihood of participation. Finally, factors which influence decision making for clinical trial participation may not necessarily correspond to those which influence decision making for therapeutic interventions or end of life care. Greater insight into these influences may be of value in assisting surrogates as they navigate the ICU environment.

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REFERENCES

1. Coopersmith CM, Wunsch H, Fink MP, Linde-Zwirble WT, Olsen K, Sommers MS, et al. A comparison of critical care research funding and the financial burden of critical illness in the United States. *Critical Care Medicine*. 2012; 40:1072–1079. [PubMed: 22202712]

2. Ad Hoc Statement Committee of the American Thoracic Society. The ethical conduct of clinical research involving critically ill patients in the United States and Canada. *American Journal of Respiratory and Critical Care Medicine*. 2004; 170:1375–1384. [PubMed: 15590885]
3. Burns KEA, Zubrinich C, Tan W, Raptis S, Xiong W, Smith O, et al. Research recruitment practices and critically ill patients. A multicenter, cross-sectional study (The Consent Study). *American Journal of Respiratory and Critical Care Medicine*. 2013; 187:1212–1218. [PubMed: 23525935]
4. Report from the National Human Research Protections Advisory Committee on Informed Consent and the Decisionally Impaired. 2002. www.hhs.gov/ohrp/archive/nhrpac/documents/nhrpac10.pdf; accessed May 4th, 2015
5. Barrett KA, Scales DC. Considering the vulnerabilities of surrogate decision-makers when obtaining consent for critical care research. *Intensive Care Medicine*. 2012; 38:4–6. [PubMed: 22120772]
6. Freeman BD, Danner RL, Banks S, Natanson C. Safeguarding patients in clinical trials with high mortality rates. *American Journal of Respiratory and Critical Care Medicine*. 2001; 164:190–192. [PubMed: 11463585]
7. Davis N, Pohlman A, Gehlbach B, Kress JP, McAtee J, Herlitz J, et al. Improving the process of informed consent in the critically ill. *Journal of the American Medical Association*. 2003; 289:1963–1968. [PubMed: 12697799]
8. Luce JM. Research ethics and consent in the intensive care unit. *Current Opinion in Critical Care*. 2003; 9:540–544. [PubMed: 14639076]
9. Silverman HJ, Luce JM, Schwartz J. Protecting subjects with decisional impairment in research: the need for a multifaceted approach. *American Journal of Respiratory and Critical Care Medicine*. 2004; 169:10–14. [PubMed: 14695105]
10. Luce JM. Is the concept of informed consent applicable to clinical research involving critically ill patients? *Critical Care Medicine*. 2003; 31(3 (Suppl)):S153–S160. [PubMed: 12626961]
11. Pochard F, Azoulay E, Chevret S, Lemaire F, Hubert P, Canoui P, et al. Symptoms of anxiety and depression in family members of intensive care unit patients: ethical hypothesis regarding decision-making capacity. *Critical Care Medicine*. 2001; 29:1983–1987. [PubMed: 11588467]
12. Majesko A, Hong SY, Weissfeld L, White DB. Identifying family members who may struggle in the role of surrogate decision maker. *Critical Care Medicine*. 2012; 40:2281–2286. [PubMed: 22809903]
13. Mehta S, Pelletier FQ, Brown M, Ethier C, Wells D, Burry L, et al. Why substitute decision makers provide or decline consent for ICU research studies: a questionnaire study. *Intensive Care Medicine*. 2012; 38:4754–54.
14. Iverson E, Celious A, Kennedy CR, Shehane E, Eastman AE, Warren V, et al. Real-time perspectives of surrogate decision makers regarding critical illness research - findings of focus group participants. *Chest*. 2012; 142(6):1433–1439. [PubMed: 22677349]
15. Azoulay E, Pochard F, Kentish-Barnes N, Chevret S, Aboab J, Adrie C, et al. Risk of post-traumatic stress symptoms in family members of intensive care unit patients. *American Journal of Respiratory and Critical Care Medicine*. 2005; 171:987–994. [PubMed: 15665319]
16. Menon K, Ward RE, Gaboury I, Thomas M, Joffe A, Burns K, et al. Factors affecting consent in pediatric critical care research. *Intensive Care Medicine*. 2012; 38:153–159. [PubMed: 22120768]
17. Wendler D, Rid A. Systematic review: The effect on surrogates of making treatment decisions for others. *Annals of Internal Medicine*. 2011; 154:336–346. [PubMed: 21357911]
18. Luce JM. Is the concept of informed consent applicable to clinical research involving critically ill patients? *Critical Care Medicine*. 2003; 31(3 (Suppl)):S153–S160. [PubMed: 12626961]
19. Streiner DL. Finding our way: an introduction to path analysis. *Canadian Journal of Psychiatry*. 2005; 50:115–122.
20. Freeman BD, Kennedy CR, Bolcic-Jankovic D, Eastman AE, Iverson E, Shehane E, et al. Considerations in the construction of an instrument to assess attitudes regarding critical illness gene variation research. *Journal of Empirical Research on Human Research Ethics*. 2012; 7(1):58–70.
21. Hull SC, Sharp RR, Botkin JR, Brown M, Hughes M, Sugarman J, et al. Patients' views on identifiability of samples and informed consent for genetic research. *American Journal of Bioethics*. 2008; 8(10):62–70. [PubMed: 19003716]

22. Freeman BD, Kennedy CR, Coopersmith CM, Zehnbauser BA, Buchman TG. Genetic testing and research in critical care: surrogates' perspective. *Critical Care Medicine*. 2006; 34(4):986–994. [PubMed: 16484903]
23. The R project for statistical computing. www.r-project.org/; accessed May 4th, 2015
24. Bolcic-Jankovic D, Clarridge B, LeBlanc J, Mahmood R, Freeman DH. Determinants of surrogate decision making confidence: an example from the ICU. *Journal of Empirical Research on Human Research Ethics*. Oct; 2014 9(4):476–85.
25. Freeman BD, Butler K, Bolcic-Jankovic D, Clarridge B, Kennedy C, LeBlanc J, et al. Receptivity to genetic variation research participation comparing ambulatory patients and surrogate decision makers for the critical ill. *Chest*. 2014 doi:10.1378/chest.14-0797.
26. Freeman BD, Bolcic-Jankovic D, Kennedy C, LeBlanc J, Eastman AE, Barillas J, et al. Perspectives of decisional surrogates and patients regarding critical illness genetic research. *American Journal of Bioethics-Empirical Bioethics*. In Press.
27. Johnson TP, Wislar JS. Response rates and nonresponse errors in surveys. *Journal of the American Medical Association*. 2012; 307(17):1805–1806. [PubMed: 22550194]
28. Corbie-Smith G, Thomas SB, Williams MV, Moody-Ayers S. Attitudes and beliefs of African Americans toward participation in medical research. *Journal of General Internal Medicine*. 1999; 14:537–546. [PubMed: 10491242]
29. Shavers VL, Lynch CF, Burmeister LF. Racial differences in factors that influence the willingness to participate in medical research studies. *Annals of Epidemiology*. 2002; 12:248–256. [PubMed: 11988413]
30. Glassberg AE, Luce JM, Matthay MA. Reasons for nonenrollment in a clinical trial of acute lung injury. *Chest*. 2008; 134:719–723. [PubMed: 18689583]
31. Soto GJ, Martin GS, Gong MN. Healthcare disparities in critical illness. *Critical Care Medicine*. 2013; 41:2784–2793. [PubMed: 24121467]

Figure 1.
Initial Path Model

Figure 2.
Final Path Model

Table 1

Distribution of responses for survey elements used in path analysis

Survey Variables	Surrogates (n=445)	Variable Coding for Path Analysis
Background		
Race		
White or Caucasian	320 (71.9)	1
Other	119 (26.7)	0
NA or Missing	6 (1.3)	
Age		
Mean ($\pm$ SD)	50.9 ($\pm$ 12.7)	Recorded Value
NA or Missing	2	
Gender		
Male	110 (24.7)	1
Female	335 (75.3)	0
Education		
Did not complete high school	30 (6.7)	1
High school graduate or equivalent	129 (29.0)	2
Some College	132 (29.7)	3
College Graduate	82 (18.4)	4
Some Graduate School	17 (3.8)	5
Graduate Degree	54 (12.1)	6
NA or Missing	1 (0.2)	
Religiosity		
Not religious	22 (4.9)	1
Somewhat religious	185 (41.6)	2
Very religious	229 (51.5)	3
NA or Missing	9 (2.0)	
Annual Income		
< \$20,000	67 (14.6)	1
\$20,001 - \$40,000	94 (19.3)	2
\$40,001 - \$60,000	114 (21.3)	3
\$60,001 - \$80,000	68 (13.9)	4
\$80,001 - \$100,000	40 (8.8)	5
>\$100,000	62 (13.5)	6
Decision Making		
Made treatment decisions for patient while in ICU?		
Yes	373 (73.7)	1
No	128 (28.8)	0
Had discussion with patient about making decisions?		

Survey Variables	Surrogates (n=445)	Variable Coding for Path Analysis
Yes	273 (61.3)	1
No	172 (38.6)	0
Others helping make decisions for patient? (Median (IQR))	2.0 (1.0-3.5)	Recorded Value
Previous experience as a decisional surrogate?		
Yes	233 (52.4)	1
No	212 (47.6)	0
Mediating		
How much of medical research is useful?		
Almost all of it	69 (15.5)	4
Most of it	153 (34.4)	3
Some of it	187 (42.0)	2
Almost none of it	34 (7.6)	1
NA or Missing	2 (0.4)	
How positive or negative about genetic research?		
Very positive	98 (22.0)	5
Somewhat positive	162 (36.4)	4
Neither positive or negative	175 (39.3)	3
Somewhat negative	8 (1.8)	2
Very negative	1 (0.2)	1
NA or Missing	1 (0.2)	
Confident doctors telling everything		
Very confident	297 (66.7)	4
Somewhat confident	139 (31.2)	3
Not confident	1 (1.6)	2
Not at all confident	1 (0.2)	1
NA or Missing	1 (0.2)	
Difficulty of making decisions (0-10 scale) Median (IQR)	5.0 (2.0-8.0)	Recorded Value
Missing or NA	3	
Trust doctors and nurses		
Completely	320 (71.9)	4
Somewhat	111 (24.9)	3
A little	9 (2.0)	2
Not at all	1 (0.2)	1
NA or Missing	4 (0.9)	
Surrogate responsibility for making decisions		
All of it	152 (34.2)	4
Most of it	150 (33.7)	3
About half of it	81 (18.2)	2

Survey Variables	Surrogates (n=445)	Variable Coding for Path Analysis
Less than half of it	62 (13.9)	1
Outcome		
How likely is surrogate to participate in research?		
Very likely	198 (44.5)	4
Somewhat likely	188 (42.2)	3
Not very likely	36 (8.1)	2
Not at all likely	18 (4.0)	1
NA or Missing	5 (1.1)	
How likely is surrogate to participate in genetic research?		
Very likely	229 (51.5)	4
Somewhat likely	180 (40.5)	3
Not very likely	52 (11.7)	2
Not at all likely	20 (4.5)	1
NA or Missing	8 (1.8)	
How likely is surrogate to permit patient to participate in research?		
Very likely	174 (39.1)	4
Somewhat likely	169 (38.0)	3
Not very likely	59 (13.3)	2
Not at all likely	37 (8.3)	1
NA or Missing	6 (1.3)	
How likely is surrogate to permit patient to participate in genetic research?		
Very likely	162 (36.4)	4
Somewhat likely	180 (40.4)	3
Not very likely	52 (11.7)	2
Not at all likely	43 (9.7)	1
NA or Missing	8 (1.8)	

Table 2

Direct and indirect effects of independent variables on outcome variables in final path model

		Dependent Variables							
Independent Variables		How likely is surrogate to participate in research?		How likely is surrogate to participate in genetic research?		How likely is surrogate to permit patient to participate in research?		How likely is surrogate to permit patient to participate in genetic research?	
		Direct	Indirect	Direct	Indirect	Direct	Indirect	Direct	Indirect
Background	Race	0.324	0.018		0.222	0.281	0.173		0.282
	Age			-0.095			-0.012		-0.051
	Gender		-0.024		-0.012		0.003		-0.005
	Education								
	Religiosity								
	Annual Income								
Decision Making	Had discussion with patient about making decisions?								
	Made treatment decisions for patient while in ICU?	0.141			0.072	0.06			0.058
	Others helping make decisions for patient?								
	Previous experience as a decisional surrogate?								
Mediating	Trust doctors and nurses								
	Confident doctors telling everything					0.095			0.036
	Surrogate responsibility for making decisions								
	Difficulty of making decisions								
	How much of medical research is useful?	0.215			0.109		0.092		0.089
	How positive or negative about genetic research?			0.207			0.026		0.111
Outcome	How likely is surrogate to participate in research?			0.506		0.364	0.064		0.411
	How likely is					0.127		0.489	0.049

		Dependent Variables							
Independent Variables		How likely is surrogate to participate in research?		How likely is surrogate to participate in genetic research?		How likely is surrogate to permit patient to participate in research?		How likely is surrogate to permit patient to participate in genetic research?	
		Direct	Indirect	Direct	Indirect	Direct	Indirect	Direct	Indirect
	surrogate to participate in genetic research?								
	How likely is surrogate to permit patient to participate in research?							0.383	
	How likely is surrogate to permit patient to participate in genetic research?								