Published in final edited form as:

J Empir Res Hum Res Ethics. 2013 July ; 8(3): . doi:10.1525/jer.2013.8.3.53.

Critical Illness Research Involving collection of Genomic Data: The Conundrum Posed by Low Levels of Genomic Literacy among Surrogate Decision Makers for Critically Ill Patients

Ellen Iverson,
Children's Hospital Los Angeles

Aaron Celious,
Children's Hospital Los Angeles

Erica Shehane,
Children's Hospital Los Angeles

Mandy Oerke,
University of Texas Southwestern Medical Center

Victoria Warren,
University of Texas Southwestern Medical Center

Alexander Eastman,
University of Texas Southwestern Medical Center

Carie R. Kennedy, and
Washington University School of Medicine

Bradley D. Freeman
Washington University School of Medicine

Abstract

Critical illness clinical trials that entail genomic data collection pose unique challenges. In this qualitative study, we found that surrogate decision makers (SDMs) for critically ill individuals, such as those who would be approached for study participation, appeared to have a limited grasp of genomic principles. We argue that low levels of genomic literacy should neither preclude nor be in conflict with the conduct of ethically rigorous clinical trials.

Keywords

genomic research; critical illness; intensive care unit

While essential to advancing the field of critical care medicine, clinical trials enrolling acutely ill patients are associated with hurdles not encountered in chronic disease studies (Ad Hoc Statement Committee of the American Thoracic Society, 2004). Conditions prompting intensive care unit (ICU) admission are often precipitous and life-threatening, and the care provided highly technological. Most patients and family members lack the opportunity for education regarding the nature of the disease process, expected outcome, or

treatment alternatives. Further, patients in ICUs are frequently incapacitated and unable to provide informed consent permitting research participation. Finally, many therapies must be administered quickly following diagnosis. In order to enroll critically ill patients in clinical studies, permission must be obtained expediently from surrogate decision makers (SDMs), many of whom are being confronted with complex medical issues for the first time. When these studies entail collection of genomic specimens, the complexities are heightened (Freeman et al., 2010; Freeman et al., 2012; Gong et al., 2004; Gong et al., 2010; Chen et al., 2008). We undertook the current investigation to survey understanding of genomic concepts by SDMs for critically ill patients and to consider how the level of genomic literacy might impact the conduct of clinical investigation.

Methods

SDM Sample and Recruitment

Findings presented here are part of an effort to understand SDM attitudes regarding critical illness clinical investigation (Freeman et al., 2012; Iverson et al., 2012; Iverson et al., 2013). Participants were recruited from the surgical and medical ICUs of two academic medical centers: Barnes Jewish Hospital (BJH) in St. Louis, Missouri, and Parkland Hospital (PH) in Dallas, Texas (Iverson et al., 2012; Iverson et al., 2013). Eligible participants were SDMs for adult ICU patients with acute respiratory failure; those agreeing to participate provided informed consent and received a \$50 honorarium.

Data Collection

Data collection occurred over a seven-month period (February–August 2009). Focus groups (FGs) were conducted in conference rooms adjoining the ICUs where the loved ones of the SDMs were receiving care. FG study guides were developed on the basis of themes related to genomic literacy. Two facilitators (AC, ES) moderated all sessions. FGs began by eliciting respondents' initial thoughts when presented with the terms "genes" or "genetics." After this period of free association, the facilitator solicited participants' reactions following a brief overview of basic genetic concepts, current and emerging applications, and commonly held concerns about the use of genomic data. Twenty FGs were conducted (11 at BJH, 9 at PH), enrolling 74 SDMs. Participants (mean [$\pm$ SE] age 48 [$\pm$ 1.7] years) were English-speaking, pre-dominately female (73%), and described long-term relationships with their loved ones (33 [$\pm$ 1.5] years).

Analysis

FGs were audio recorded, transcribed, and analyzed using *Atlas.ti* software (Berlin). The research team reviewed an initial sample of interviews to identify key themes that formed the basis of the project codebook. The codebook was modified and refined as additional themes emerged following review of all transcripts. Inter-coder reliability was assessed through double-coding of approximately 20% of transcripts. Findings reported here are based on analysis of narratives coded for: the meaning of genes/DNA, genes/gene test, experience with genetics, and genetic exceptionalism.

Protection of Human Subjects

This study was approved by the Human Studies Committees of Washington University School of Medicine, University of Texas Southwestern Medical Center, and Childrens' Hospital Los Angeles (HRPO 06-0637).

Results

Basic Understanding of Genomic Concepts

Most participants reported that issues pertaining to genomic technology were “not on their radar” and displayed a rudimentary understanding of the topics presented. For example, several respondents had difficulty understanding the connection between “DNA” and “genes”:

Well actually I didn't know the word, but I did hear of DNA and actually I didn't know they were pretty much the same.

Participants shared that mass media represented their primary information source about the topics discussed:

That's pretty much what I know ... what I've seen on TV ... other than that ... I don't know very much about it.

Participants commonly understood that “DNA” could be used for forensic applications and paternal attribution. Most SDMs were able to make the link between “genes” and shared familial traits (e.g., eye color or hair color) and diseases that “run in families”:

Well, when you put it like that ... that it runs in the family ... that makes sense. My grandson has a pinhole in his heart ... just like his father.

Several female participants were able to discuss genomic analysis as a component of prenatal screening. Individuals who reported a family member with specific diseases with well-described Mendelian patterns of inheritance, such as cystic fibrosis or sickle cell anemia, were able to describe this association to the group. Several individuals reported a family member with breast cancer who had participated in research examining the genetic predisposition to this illness. These discussions stimulated other participants to consider how genomic concepts might underlie other familial characteristics, such as multiple twin births within a family pedigree:

There are two sets of twins in my mother's family and my uncle has two sets of identical twins ... maybe a gene runs through the family that is responsible for producing twins.

Many expressed insight into what genomic data might imply about ancestry and race:

We're made up of a lot of different people and some of us have secrets in our background. They might look white and be black or they may look black and actually be white or somebody else's child...they may have a fear of discovering this.

Perceptions of Potential Medical Applications of Genomic Technology

Most participants perceived that genomic technology had the potential to lead to the discovery of new treatments, envisioning some form of gene therapy:

I guess in the future, we'll know a little bit more and can use genes in a different way ... if somebody's ill, somebody else in the family's DNA may be used to correct it.

Or

I think you could use genes and DNA to help a person if they have a sickness. You know how they say somebody's got a bad disease and they can't fix it. They can get a relative's DNA and fix it.

One respondent speculated that a genetic test could determine an individual's generalized robustness or disease susceptibility:

I'm sure they probably would test us to see how powerful the genetics are. They might take the test to say "oh man you got some good genetics" ...

Finally, some respondents had a general appreciation that genomic testing could provide information beyond that provided by current routine clinical testing:

DNA tells us everything about a human because it encompasses your history. Where you came from, what you are and what you're made up of. It's the basis of fundamentals of life.

Discussion

We assessed genomic literacy among family members actively engaged in decision making for critically ill patients. FG participants were predominately female, described long relationships with the patients represented, and were both ethnically and economically diverse. Consistent with the findings of other investigators, these individuals displayed a rudimentary grasp of even the most fundamental genomic concepts (Bates et al., 2005; Christensen et al., 2010).

We speculated that given the psychological duress confronting these individuals, low levels of genomic literacy might pose a significant barrier to study participation. However, we previously found that participants tended to view the concept of genomic data collection as relatively low risk, and were generally receptive to study participation (Iverson et al., 2012; Iverson et al., 2013). Thus it appears that factors other than detailed knowledge and understanding of the specific technology being investigated ultimately affect the decision to permit enrollment. We found that among these factors was a sense of altruism, a sentiment that appeared accentuated by the current ICU experience (Iverson et al., 2012).

In addition, participants distinguished among various types of trial designs, expressing a preference for observational studies (perceived as lower risk) as opposed to interventional studies (perceived as entailing higher risk) (Iverson et al., 2012). Further, participants reported that trust in the physicians and nurses providing care as well as in the entity that would be conducting the research were important (ibid.). In addition, some participants described therapeutic misperception—i.e., if the SDM was being approached for research participation, the situation must be dire, and study participation might confer some benefit (ibid.). Finally, SDMs did not seem to distinguish between genomic and nongenomic data collection, tending to view the risk of genomic data collection as the risk associated with sample acquisition, i.e., requiring sampling of blood or body fluid as opposed to an invasive procedure (Iverson et al., 2013).

When considered in the broader context of the ICU environment, the apparent disconnect between low levels of genomic literacy and permissive attitudes toward genomic data collection seems consistent with other aspects of care. It is often the case that SDMs and family members have had very little prior experience with ICU care. Even the physical environment of most ICUs is very different from those encountered in other healthcare settings. For instance, ICU rooms offer little privacy and are abundantly equipped with life support and monitoring devices. Similarly, the tempo of disease and of the care provided is often fast paced, and typified by dramatic changes in clinical status.

An additional layer of complexity is the frequent involvement of one or more consultants, potentially complicating lines of communication between the team providing care and the SDMs. These and other features may render it difficult for SDMs and their families to gain

independent information about the nature of the disease, recommended treatment, and expected outcome. Ultimately, SDMs and their family members may come to place a great deal of trust in the care providers, and follow their recommendations about treatments and interventions without necessarily possessing a detailed understanding of the issues involved. Thus, approaching individuals in this environment about potential genomic study participation might simply be viewed by SDMs as part of this continuum.

Limitations

Our study had a number of limitations. By their nature, our FG sessions presented concepts in abstract terms. We do not know the extent to which the views expressed might translate into an actual willingness or disinclination to permit study participation. Stated differently, while an SDM may be receptive to allowing participation in a hypothetical circumstance, when confronted with the realities of an actual study, interest in participation may diminish. In addition, while the qualitative methods we employed allowed us to explore the range of views held by participants, this approach does not allow us to understand the determinants or correlates of particular viewpoints (e.g., education level, religiosity, severity of illness, time elapsing between onset of critical illness and FG participation, and so forth). Additionally, we solicited opinions about clinical research from those agreeing to participate in our study. Such attitudes may differ significantly from those declining our invitation. Finally, we interviewed SDMs who were actively involved in clinical decision making, but did not interview patients, and do not know the extent to which the views of SDMs and patients align.

Best Practices

Many concerns voiced about genomic data collection are not unique to this technology (e.g., whether data is identifiable, whether it will be shared with other investigators, or whether it will have future uses) (Iverson et al., 2013). Independent of the specific aspects of a given study, these types of details can be discussed with the patient (and their representatives) in a sufficiently transparent fashion so as to understand and honor participant preferences.

Research Agenda

Variability exists in the manner in which IRB's view the risk of gene variation research involving incapacitated patients. Gong et al. (2010) reported that when presented with a hypothetical genetic epidemiology study in this setting, most IRB members reported that such a study would represent greater than minimal risk and 40% would not allow such a study to proceed in the absence of direct patient benefit. Similarly, in a multicenter genetic epidemiology acute stroke study, Chen et al. (2008) reported that investigators preferentially enrolled less severely affected, cognitively intact participants because IRBs at 40% of participating institutions would not permit use of SDMs to provide consent in this context. In contrast, we previously reported that SDMs would be receptive to genomic sample collection, and endorsed that such data collection in some circumstances would be acceptable without explicit consent, analogous to the creation of data repositories in non-acute settings (Iverson et al., 2013; Pulley et al., 2010; Roden et al., 2008). Taken together, these findings emphasize the need for IRBs to develop a consistent approach to patient protection in the critical care setting.

Educational Implications

SDMs appear interested in learning about opportunities for critical illness research (Iverson et al., 2012). The critical care community should cultivate this curiosity by providing information in a readily accessible form, such as placing posters and brochures in highly

visible locations of ICU waiting rooms and corridors, and referring SDMs, patients, and family members to appropriate online resources. Such practices would not only be of benefit by driving recruitment, but would also educate the public as to the nature of critical care research.

Acknowledgments

The authors are indebted to the nurses, physicians, patients, family members, and personnel of the medical and surgical ICUs of Barnes Jewish and Parkland Hospitals, whose generous cooperation and support made this study possible. This work was supported by National Institutes of General Medical Sciences (GM080591).

References

- 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]
- Bates BR, Lynch JA, Bevan JL, Condit CM. Warranted concerns, warranted outlooks: A focus group study of public understandings of genetic research. *Social Science and Medicine*. 2005; 60(2):331–344. [PubMed: 15522489]
- Chen DT, Meschia JF, Brott TG, Brown RD, Worrall BB. Siblings with Ischemia Stroke Study Investigators. Stroke genetic research and adults with impaired decision-making capacity: A survey of IRB and investigator practices. *Stroke*. 2008; 39(10):2732–2735. [PubMed: 18658034]
- Christensen KD, Jayaratne TE, Roberts JS, Kardina SL, Petty EM. Understandings of basic genetics in the United States: Results from a national survey of black and white men and women. *Public Health Genomics*. 2010; 13(7–8):467–476. [PubMed: 20203477]
- Freeman BD, Kennedy CR, Frankel HL, Clarridge B, Bolcic-Jankovic D, Iverson E, et al. Ethical considerations in the collection of genetic data from critically ill patients: What do published studies reveal about potential directions in empirical research? *Pharmacogenomics Journal*. 2010; 10(2):77–85. [PubMed: 19997084]
- 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.
- Gong MN, Wei Z, Xu LL, Miller DP, Thompson BT, Christiani DC. Polymorphisms in the surfactant Protein-B gene, gender, and the risk of direct pulmonary injury and ARDS. *Chest*. 2004; 125(1):203–211. [PubMed: 14718442]
- Gong MN, Winkel G, Rhodes R, Richardson LD, Silverstein JH. Surrogate consent for research involving adults with impaired decision making: Survey of institutional review board practices. *Critical Care Medicine*. 2010; 38(11):2146–2154. [PubMed: 20802325]
- 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]
- Iverson E, Celious A, Kennedy CR, Shehane E, Eastman AE, Warren V, Freeman BD. Perspectives of surrogate decision makers for critically ill patients regarding gene variation research. *Genetics in Medicine*. 2013; 15(5):368–373. [PubMed: 23154525]
- Pulley J, Clayton E, Bernard GR, Roden DM, Masys DR. Principles of human subjects protections applied in an opt-out, de-identified biobank. *Clinical and Translational Science*. 2010; 3(1):42–48. [PubMed: 20443953]
- Roden DM, Pulley JM, Basford MA, Bernard GR, Clayton EW, Balser JR, Masys DR. Development of a large-scale de-identified DNA biobank to enable personalized medicine. *Clinical Pharmacology and Therapeutics*. 2008; 84(3):362–369. [PubMed: 18500243]

Biographies

Ellen Iverson has expertise in the conduct of qualitative and quantitative research, particularly in vulnerable populations, and is a collaborator on this multidisciplinary effort.

She directed the conduct of the focus groups, participated in data analysis, and was the primary author of this manuscript.

Aaron Celious has expertise in the conduct of qualitative and quantitative research, particularly in vulnerable populations, and is a collaborator on this multidisciplinary effort. He helped conduct the focus groups, participated in data analysis, and assisted with manuscript preparation.

Erica Shehane has expertise in the conduct of qualitative and quantitative research, particularly in vulnerable populations, and is a collaborator on this multidisciplinary effort. She helped conduct the focus groups, participated in data analysis, and assisted with manuscript preparation.

Carie R. Kennedy is a clinical research nurse with expertise in conducting patient-oriented research in the critical care setting. She assisted with subject recruitment, data analysis, and manuscript preparation.

Mandy Oerke is a clinical research nurse with expertise in conducting patient-oriented research in the critical care setting. She assisted with subject recruitment, data analysis, and manuscript preparation.

Victoria Warren is a clinical research nurse with expertise in conducting patient-oriented research in the critical care setting. She assisted with subject recruitment, data analysis, and manuscript preparation.

Alexander Eastman is a critical care physician and researcher, and a collaborator on this multidisciplinary, multi-institutional effort. He assisted with subject recruitment, data analysis, and manuscript preparation.

Bradley D. Freeman is a critical care physician, researcher, and serves as the principal investigator on this multidisciplinary, multi-institutional effort to explore attitudes and perceptions of patients and surrogate decision makers regarding genetic data collection in the ICU environment. He assisted with data analysis and manuscript preparation.