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Risk Terminology in Biobanking and Genetic Research: What's in a name?

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Abstract

It is well established that the general public has varying interpretations of the term “risk” and the qualifiers associated with it, such as low, moderate, or high. What is less well known is how definition and application of this term impacts recruitment of individuals, particularly for biomedical and behavioral research designed to improve knowledge of and access to innovations in cancer genetics. This Commentary discusses the nomenclature used in bio-behavioral research and the potential for confusion due to divergent meanings of risk and its associated categorizations. We discuss both our experience with recruitment of familial cancer families for a study on perceptions of biobanking as well as lessons learned from published examples where divergent understanding of risk levels, genetic research processes, and interpretation of results between community members and researchers result in misunderstandings for both parties. Ultimately, a critical challenge remains to ensure that accurate and mutually relevant risk terms are used in recruiting research participants and providing genetic results. Achieving this goal requires that regulations, policy, education and practice change in step with rapid discoveries in genetic research to reduce misinterpretations resulting from lack of common understanding and specificity in risk terminology.

Keywords

risk communication; ethics; biobanking; bioethics

INTRODUCTION

The rapidly advancing science of genetic research provides a fortuitous opportunity, and even a duty, we argue, for social science researchers to assess a host of ethical issues associated with the concept of “risk”. As the call intensifies to improve the public’s participation in cancer genetics and genomics research, researchers must be attuned to divergent interpretations of “risk” and how definitions and their qualifiers (e.g., low, moderate, high) impact recruitment of individuals to cancer prevention research. Indeed, risk has a multitude of meanings in the research context. For example, there is the risk associated with one’s disease or family history and, separately, the risk associated with participating in medical research. The public’s perception of “risk” in both of these contexts has

implications for researchers. This article focuses on the risk associated with research participation.

In recent years, behavioral and biomedical researchers have reported ethical challenges with recruiting human subjects, often due to language of “risk.” The success of large scale genomic based initiatives implies there is no shortage of research participants; however, the difficulties in recruiting or educating the public are rarely reported and are often discussed anecdotally. This may create a false sense of reassurance, particularly in the context of varying risk levels, likely due to the many issues that go unreported. This Commentary discusses the nomenclature used in bio-behavioral research and the potential for confusion in the case of divergent meanings of risk between researchers and the public. Of note, we do not focus on the public’s ability to understand their own risk for a specific disease (numerical literacy), or healthcare decision-making based on this risk, as these topics have already been addressed in numerous publications [Bates et al., 2003; Emery et al., 1998; Lanie et al., 2004; Slovic, 1987; Yoon et al., 2002]. While individual understanding of risk is important to personal decision making, that understanding of risk comes from communication with one’s health care provider. It can be equally impacted by emotional and affective factors as well as the weight (e.g., relevance) and value ascribed to previous experiences.

Challenges in Previous Research

The impetus for this Commentary comes from our own recruitment challenges. In developing an educational program to increase biomedical and behavioral researchers’ understanding of the ethical issues in consenting families with hereditary cancer (i.e., families who have an increased risk of cancer due to known hereditary or germ line pathogenic variants [PV]), the potential consequences of misunderstandings about “risk” became clear. Our goal was to identify concerns limiting participation in genetic and biospecimen research among families who were currently affected by a known PV, and to relay these concerns in the form of a focused training program to cancer biomedical and behavioral researchers. Our intention was to include first- and second-degree relatives with a broad array of hereditary cancer types (e.g. breast, colon, and prostate). However, this design posed a series of challenges, in that the definition of risk within the kindred varies according to mutation type, as well as the level of risk associated with one or more potential cancers. Although these definitions and the naming of the risk type as “high risk” or other terminology referring to the groups’ pre-disposed risk to particular genetically linked cancers are highly relevant in the clinical setting, it is often less important to unaffected or unaware family members. In another example, we attempted to recruit participants from the Cancer Genetics Network (CGN) for a study to identify bioethical concerns about biobanking and willingness to become a biospecimen donor.[Massachusetts General Hospital Biostatistics Center, 2010] The CGN database regroups individuals who are known to have a genetic predisposition to various cancer types. Developing a proposal for recruiting individuals from this database was difficult since the terminology for using the term “risk” became an obstacle with CGN’s steering committee. The committee did not approve the recruitment of individuals termed “at risk” or “high risk,” a categorical designation identifying their confirmed elevated risk or pre-disposition for certain cancer types based on their genetic make up. Each of these terms had different definitions, depending on the PV. Thus, we had to significantly modify our recruitment terms to include people who “ever had a genetic test for hereditary cancer” in order to receive approval from the CGN committee and eliminate concern to potential respondents.

Current Biobanking Initiatives

We argue that examining the nomenclature of risk terminology is timely and relevant. There is a new urgency to anticipate potentially problematic ethical issues in relation to rapidly developing emerging technologies, especially as they relate to genetics. The Human Genome Project has contributed vast amounts of knowledge with the aim of developing improved technologies to diagnose, treat and even prevent a number of diseases like cancer. However, a significant body of ethical and legal literature indicate the general public is unaware of the purpose of the project [Cunningham-Burley, 2001; Manolio, 2005; Smerecnik et al., 2008] misunderstands the purpose [2012; Hayden, 2012; Manolio, 2005; Rosenberg, 1995], or perceives it will have negative effects for them personally [Alaszewski and Horlick-Jones, 2003; Berry, 2004].

In addition to the Human Genome Project, there are other federal initiatives that focus on the collection and storage of biospecimens, from which DNA may be extracted. It is imperative that populations who are approached as donors have accurate perceptions about the purpose and scope of the research, as well as distinctions between average risk participants vs populations with increased levels of risk. One such project is the NIH Biobanking Initiative, which seeks to expand the libraries of DNA evidence from healthy individuals to serve as healthy controls for case control studies [Collins and McKusick, 2001; Wallace and Kent, 2011]. This initiative is also charged with outreach and recruitment of a wide range of racial and ethnic minorities as well as national geographic representation. However, the initiative has faced several challenges with recruitment. The likely causes of these challenges includes: lack of common risk nomenclature, poor communication between behavioral and basic researchers, and reduced attention on recruitment issues in research efforts regarding the need for racially-ethnically diverse samples in cancer genetics research [Collins and McKusick, 2001; McGuire et al., 2008].

Perceptions of Risk: Social, Cultural, and Legal Factors

It is neither new nor surprising that there are varying interpretations of the term “risk” and the diverse qualifiers associated with it, nor that these interpretations diverge from clinical or epidemiological understandings of the term [Lupton, 1999]. Risk terminology must be understood within a historical and social context [Rosenberg, 1995]. There is a large body of social science literature that attempts to explain how and why people identify, process, and respond to risks, which can be generally divided into cognitive science and socio-cultural approaches [Berry, 2004; Lupton, 1999]. Cognitive science approaches tend to explain perceptions and decision-making from a rationalistic, objective, and individualistic orientation. However, research has shown that “objective” perceptions of risk are often limited, with slight changes to wording, order of questions, or the range of values significantly altering the way that people estimate risks [Taylor-Gooby and Zinn, 2006]. Additionally, emotional and affective issues factor into risk decisions, as well as the weight (e.g., relevance) and value (e.g., positive or negative) that people ascribe to previous experiences. People often embed risk statements within personal illness experiences, drawing from their own disease history, or consider risks to social relationships alongside biological risks. In other words, while “risks” are perceived as objective, independent phenomena, individuals’ reactions to these phenomena are seen as subjective and dependent [Lupton, 1999]. In order to “correct” lay perceptions, researchers and health educators often advocate education for the public—and occasionally, practitioners—to reduce what is seen as “irrational” interpretations. However scientific knowledge often has an insignificant effect [Alaszewski and Horlick-Jones, 2003] and even thorough understanding of risk constructs is not always complete among clinical practitioners [Hunt et al., 2006].

Social and cultural factors play a significant role in how people identify, perceive, and respond to risks. Because risks are culturally constructed, they are perceived differently among individuals who identify with particular social worlds [Lupton, 1999]. Thus, risk perceptions are not limited to the individual, because they are, to some extent, products of shared meanings, experiences, and understandings. What remains to some degree unclear, however, is what people understand as a risk and how meaningful various types of risk are to their lives. Furthermore, the relative importance of the scientifically understood risk appraisal may have little relevance for some persons [Hobson-West, 2003; Hunt et al., 2006]. While the risk appraisal is absolutely essential to scientific, medical, and public health understandings of the relative merits of biobanking, there is less reason to assume participants use the same process to consider the relative merits of participating in studies. The challenge then, for study recruitment of healthy participants becomes understanding and then tailoring efforts so that they are relevant to participants.

Risk perception and risk appraisal are often rooted in ethical, cultural and legal foundations particularly among racial/ethnic minority communities with histories of prior research transgressions. The majority of these instances were related to genetic terminology or lack of full disclosure during recruitment for genetic studies where cultural and ethical values clashed with research. In 2010, the Havasu 'Baaja (Havasupai) tribe research participants successfully sued for their samples to be returned to them and for restitution to be made when they discovered their DNA samples were used not only for the studies on diabetes to which they consented, but also for admixture studies [Americans, 2010; Harmon, 2010a; Harmon, 2010b]. While admixture studies may be part of standard procedure for genetic-based studies, especially those focused on risk assessment, the general public lacks knowledge of them. [Americans, 2010; Caplan and Moreno, 2011; Mello and Wolf, 2010]. Researchers have since been banned from setting foot on the reservation - perhaps the worst possible outcome for projects seeking greater participation and inclusion of minority communities. The chaos of this situation might have been avoided had there been better shared understanding of genetic study procedures, nomenclature, and the cultural interpretations of risk and ancestry.

The Havasupai lawsuit implied that the rights of research subjects can be violated when they are not fully informed about how their DNA might be used. In addition, concerns have emerged about participants' rights to "incidental findings." The emergence of high-throughput genomics, with its ability to catalogue vast amounts of information about current and future health status, has prompted researchers to rethink the convention of not revealing "incidental findings" to participants [Hayden, 2012]. A recent National Institutes of Health (NIH) working group concluded that biobanks "shoulder significant responsibility" for addressing how to deal with "incidental findings" — those research results that could have medical consequences for the donors of genetic material [Wolf et al., 2012]. Historically, researchers have withheld individual results in order to keep participants from expecting to benefit personally from the study ("therapeutic misconception"), and there are also logistical challenges to communicating such results. However, many geneticists now suggest that participants have a right to know of any unwelcome surprises in their genome, a position which the NIH report supports. There are fundamental differences in what the general public understands about such results. For instance, many results are not returned due to questionable clinical significance, also reflecting divergent meanings because there are various levels of risk conferred by these incidental findings. During this process the question arises regarding who should be responsible for returning or communicating such results.

Other potential misunderstandings occur through recruitment practices focused on perceptions of genetic risk. [Quinn et al., 2011]) reported on an experience in recruiting a diverse group of Hispanic women for a behavioral study on knowledge of hereditary breast

and ovarian cancer syndrome. The goal of the research was to identify women of Cuban, Puerto Rican, and Mexican origin with a first degree relative who had had breast cancer before age 50 or ovarian cancer at any age. Recruitment targeted these sub-groups and requested interested women call a study hotline to establish if they met the inclusion criteria for the study. It quickly became clear that some Mexican women, more so than either of the other two sub-ethnic groups, were unable to qualify for the study because they knew their mother or sister had a gynecological cancer but could not specify if it was ovarian. Many stated that this was because cancer health history was not openly discussed in their families. In addition, Hispanic women *not* part of the target group (e.g., of Columbian or Venezuelan origin) who wished to be part of the study but were excluded because they were not part of the target group, mistakenly believed they were not at risk for these cancer since their sub-ethnic groups were excluded from the study.. This reinforces the need for researchers to be sensitive to various perspectives and understandings of the public and prompts the need for researchers to be better attuned to these misperceptions.

Finally, another group of stakeholders interpreting the nomenclature of genetic risk is the insurance industry. While the Genetic Information Nondiscrimination Act (GINA) of 2008 proclaims it illegal to deny coverage or refuse employment opportunities to non-military individuals based on genetic predisposition to disease, this law is less known to the general public [Van Hoyweghen and Horstman, 2008] and not trusted among families with hereditary disease concerns [Malorye, 2008; Wallace and Kent, 2011]. The genetic professional community has called for a restructuring of terms and a cautious interpretation of “true risk” as clinically important genetic predispositions are discovered, for the public, families at risk, and the insurance industry. However, these changes have been slow in emerging.

CONCLUSION

The rapidly advancing science of genetic research and public perceptions of this research provides a fortuitous opportunity and duty for social science researchers to assess a host of ethical issues among researchers and the general public. As the Human Genome Project and NIH Biobanking Initiatives progress, researchers must examine the longitudinal effects of biobanking for individuals, communities and sub-populations. It is now well recognized that advancements in genetic and genomic research produce new challenges in risk communication within the risk community and with individuals, families, and communities affected. However, much remains to be accomplished to ensure that the lessons learned from experiences such as the GINA legislation and the Havasupai incident are swiftly, thoughtfully, meaningfully and timely translated into effective and understandable policy and practices that benefit both scientists and research participants. There remains a multitude of unknowns for current and future donors and the need to inform with knowledge that is ethically, legally, and culturally relevant is the only path to informed decision making. We propose an education curriculum is necessary and would serve as an example of responsive programs. The lessons learned from the research summarized here are instructive for other bio-behavioral and basic researchers regarding significant IRB and ethical challenges in attempting to thoughtfully and sensitively recruit at-risk populations.

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