Will Genomics Alter Risk Assessment Methodology in Health Behavior Research?

R. Morgan Pigg, Jr., HSD, MPH
Michael L. Stellefson, PhD
Samantha R. Paige, MPH

Abstract: Advances in Personal Genome Sequence (PGS) technologies raise provocative questions about the future of health education and health behavior research. Genetic predisposition plays a key role in the adoption of health behaviors, yet health risk appraisal methodologies often underestimate or ignore the strong influence of genetics. Addressing practice-related challenges related to appropriate access to and use of personal genetic information by clinicians, educators, researchers, policy makers, and the public will be important for advancing health behavior research methodologies. Emerging ethical, legal, and social implications of genomics present both an opportunity for growth and challenges for the health education profession.

Keywords: Genomics; risk assessment; health behavior

BACKGROUND
The Human Genome Project (HGP), completed in 2003, mapped the complete genome (genetic sequence of DNA) for humans, marking the beginning of a new era in genomics research. (Collins, Green, Guttmacher, & Guyer, 2003; National Institutes of Health [NIH], 2014). Scientists subsequently identified a Personal Genome Sequence (PGS), also known as a Whole Genome Sequence or a Complete Genome Sequence, which maps the entire personal genomic structure, or “blueprint”, of an individual. An individual's PGS enables scientists to detect associations between specific genes, disease variants, and mutations. Scientists use PGS as a basis to determine an individual's genetic susceptibility to disease (Samani, Tomaszewkis, & Skunkert, 2010; Snyder, Du, & Gerstein, 2010). Genomic Medicine (GM) involves clinical research applications of PGS technology to identify patterns of gene variance indicating susceptibility and predisposition of diseases specific to the individual, including a projected timeline for onset and severity (Feero, Guttmacher, & Collins, 2010; Feero, Guttmacher, & Hudson, 2011). A related field, Pharmacogenomics (PG), predicts how an individual susceptible to a disease or disorder would respond to medications formulated to prevent, delay onset, and reduce effects of the condition. The process includes identifying pharmacotherapies that would work or not work for that person, as well as the predicted response to medication regimens designed to correct or manage the condition. (Johnson, 2003; U.S. National Library of Medicine, 2015)

The principal diagnostic approach in GM, genetic risk assessment and counseling based on individual PGS data, provides a comprehensive genetic screening mechanism to identify genetic markers for disease that detect diseases in progress and predicted diseases, specific to the individual. (Baptista, 2005). Unlike the conventional Health Risk Appraisal (Centers for Disease Control and Prevention [CDC], 2010) genetic risk assessment measures focus on early detection, accurate clinical diagnosis, and clear presentation of preventive and treatment options available to individuals. A formal counseling process with the individual follows the genetic risk assessment to address preventive measures, both clinical and behavioral, as well as preliminary treatments to prevent, slow onset, and reduce severity of illness (National Cancer Institute, 2015).

Definitions and concepts of risk
Negative health behavior includes practices that place an individual at risk for increased morbidity and mortality. For example, the Youth Risk Behavior Surveillance System monitors several negative behaviors of youth: tobacco use; unhealthy dietary behaviors; inadequate physical activity; alcohol and other drug use; sexual behaviors that contribute to unintended pregnancy...
and sexually transmitted diseases, including HIV infection; and behaviors that contribute to unintentional injuries and violence, as well as prevalence of obesity and asthma. (CDC, 2015a; Kann et al., 2014) Likewise, the Behavioral Risk Factor Surveillance System monitors similar behaviors for adults (CDC, 2015b).

Contemporary explanations of risk-taking behavior tend to place emphasis on the influence of social, cultural, and environmental factors, as well as individual psychographic characteristics including outlook on life, or world view. Risk reduction efforts often focus on modifying environmental triggers and reorientation of the individual mindset to change knowledge, attitudes, beliefs, and perceived norms. This approach views risk-taking either as intentional or a response to environmental triggers. However, intriguing research suggests that, in the case of substance abuse, genetic susceptibility plays a key role in an individual’s predisposition to adopt such behaviors (Palmer et al., 2015).

Thus, in determining risk potential, one’s desire to change a given risk behavior may no longer suffice for researchers actually knowing the genetically determined parameters that allow an individual to change a risk behavior. In the future, self-reported intention or desire to change a behavior may no longer predict behavior change with the same level of accuracy as the potential precision of knowledge about biological limitations that truly dictate one’s actual opportunity and options for successful behavior change.

**Effectiveness of current interventions**

In addressing risk behaviors, we prepare interventions designed to elicit positive cognitive and affective responses, and ultimately, behavior change or reinforcement of positive behaviors. If the intervention does not succeed, researchers often assume the intervention proved ineffective, and they seek to modify the intervention based on identified or perceived deficiencies. We believe that, if we persist, we can find the right combination, or at least a better combination of methods, measures, and active ingredients to reach and impact the subjects. However, current research designs may actually underestimate effectiveness of behavioral interventions due to lack of controlling for genetic information about individual subject susceptibility. Smoking cessation provides an example that illustrates this potential underestimation of intervention effectiveness.

National smoking rates typically remain at approximately 20% (CDC, 2015c). When we conduct smoking cessation interventions, we accept that smoking cessation often requires multiple serious attempts and relapses before a smoker succeeds in quitting. We assume personal motivation plays a key role in success or failure. However, genomics research suggests that individuals, particularly adolescents, who engage in risk behaviors such as tobacco use, possess a level of genetic predisposition to nicotine dependence with the strength of the dependence unique to the individual. (Dobbs, 2011; Palmer et al., 2015). Thus, if we can accept that some people can quit smoking relatively easily, while others simply cannot quit smoking due to a strong individual genetic predisposition to dependence on nicotine, then we understand that failure to quit, or relapse after quitting, reflects genetic reality for that individual and not necessarily failure of the intervention. If subjects possess a strong predisposition and susceptibility to dependence on nicotine, adoption of the smoking behavior provides the mechanism that triggers genetic dependence (Bierut et al., 2007; Drgon et al., 2009; Uhl et al., 2008). If we remove these individuals who cannot change the behavior for genetic reasons from the treatment group, the smoking cessation success rate in the treatment group should increase among individuals with a realistic potential to quit smoking based on their genetic makeup.

**Implications for research design and analysis**

Advances in genomics raise provocative questions about the future of health risk behavior research. How should we modify hypotheses and research questions? Given individual genetic variability, how will we define “random” in the subject selection process? Can we continue to assume a common neutrality among control group participants? Can we ensure homogeneity of a group or population sample, and validity throughout the measurement process? What criteria will establish causation? What outcome measures will determine success or failure of interventions?

Health Education research designs often rely on methods such as interviews, observations, case studies, and survey research based on individual observations and population demographics. Emergence of the ability to quantify genetic risk potential for each individual will limit the usefulness of some methods for scientific inquiry such as cross-sectional designs and self-report data, unless we complement these methods with genetic screening and risk assessment data at baseline for each subject. At a minimum, methods for considering an individual’s genetic predisposition to risk behavior must be adopted when evaluating associations between risk factors and behaviors. Absent these advances in research methodology, risk analyses based on estimated and extrapolated data will diminish in usefulness.

Furthermore, we cannot conduct research or plan effective interventions for individual risk
behaviors, such as smoking cessation, unless we understand the genetic parameters in which the individual behavior occurs. Because each individual possesses a discrete PGS, individuals no longer can be randomly assigned to intervention and control conditions. Stratified randomization based on personal and population demographics – even if done perfectly – will not account for the known (and potentially unknown) genetic realities and dispositions of each individual in that population. Consequently, research subjects no longer can be placed in a treatment group with the assumption of equal potential for change. Behavioral outcomes from data analysis of intervention trials will make sense only if interpreted within the context of confirmed genetic susceptibility of individual subjects to disease. Consequently, can we best assess change in subjects on a case-by-case basis, or do we continue to evaluate change in groups of individuals who share common genetic traits linked to risk behavior susceptibility? How will the decision affect the relative emphasis on individual versus group-level interventions? Can we assess effectiveness of a risk behavior intervention without possessing information on genetic predisposition and relative quantified risk for each subject?

Thus, the most important implication for risk behavior research involves the potential to use individual genetic risk assessment data to scientifically quantify risk and predict health outcomes for diseases and disorders based on an individual’s genetic predisposition and susceptibility risk to behaviors. Consequently, contemporary sociological and psychological methods and models that rely substantially on cognitions, motivations, and environment to explain risk behavior will require revision to accurately estimate risk or explain behavior (Hernandez & Blazer, 2006). We cannot operate on the premise that anyone can change a health risk behavior. We must understand the genetic parameters in which individual health behavior occurs. Health Educators will need to develop and test theories of health behavior that view risk in the context of individual genetic predisposition to adopt or cease a given behavior. We must establish realistic model criteria based on genetic predisposition to predict the realistic potential for an individual to change a behavior.

**Ethics in research and evaluation**

Amid these changes, our view of research ethics will evolve as well. To conduct valid assessments of individual risk behavior, Health Educators will need access to genetic screening data, either through direct access to subjects’ screening results or through referral of subjects’ summary data from other health professionals qualified to collect and interpret such personalized data. Also, to establish a true baseline status for each subject, Health Education researchers will need information on individual subject predisposition and susceptibility to disease or dependence. Ethics related to managing genetic screening data will require Health Educators to master new competencies and obtain appropriate credentials to legitimately access such data (Chen & Goodson, 2007; National Coalition for Health Professional Education in Genetics, n.d.). Ethics related to managing individual PGS and genetic screening data will require reassessment of how we address principles concerning informed consent, voluntary participation, anonymity, confidentiality, privacy, and avoiding physical and psychological harm, as well as anticipating unintended consequences such as inadvertent discrimination (Genetic Information Nondiscrimination Act of 2008).

**Ethical, Legal, and Social Implications, a formal component of HGP, addresses policy and practice issues related to appropriate access to and use of personal genetic information by clinicians, educators, researchers, policy makers, and the public (U.S. Department of Energy, 2014). Issues include mechanisms for dissemination of genetic information; procedures to ensure legislation and legal protection for individuals and institutions; credentialing processes that enable appropriate access for individuals with a confirmed “need to know”; and attention to the needs of specific populations with sensitivity to factors such as race, ethnicity, and socioeconomic status (Badzek, Henaghan, Turner, & Monsen, 2013).**

**Challenge and opportunities**

As the science underlying genomics research continues to evolve, Health Education researchers must compete for access to genetic screening information with a number of professionals such as physicians, nurses, psychiatrists, genetic counselors, and other health professionals (Guttmacher, Jenkins, & Uhlman, 2011; Kardia & Wang, 2005; Phimister, Feero, & Guttmacher, 2012; Wang, Bowen, & Kardia, 2005). What discipline will emerge to lead in communicating and disseminating genomic health information, research, and interventions to the public? What unique role among the many healthcare disciplines will Health Education play in this competitive and evolving environment? What combination of scientific training and professional experience will justify our legitimate use of personalized genetic information for health education research and practice? Will funding sources continue to support population-based research based primarily on methods of inquiry that do not formally address quantified risk of individual subjects as determined by genetic risk assessment and genetic
screening?

Though precise scientific measurement of individual genetic susceptibility to risk behaviors will require years to perfect, the process has begun. As the capacity to detect individual predisposition and susceptibility to diseases and disorders increase in accuracy, scope, and specificity, PGS and genetic screening data will drive decisions in medical practice and public policy. This PGS technology increasingly will form the basis for medical decision-making affecting both quality and length of life. Will Genomic Medicine eventually predict onset of individual risk-taking behaviors before they occur? Will gene therapy eventually eliminate some risk behaviors entirely? For example, according to NIH Director James Collins, “...obesity and associated diseases are the end result of a complex interplay between our genes, diets, lifestyles, and microbiomes. And, yet, despite this daunting level of complexity, they raise the intriguing possibility that people might one day be able to visit their health-care providers, receive a blood or urine test, and leave with precise, individualized information regarding their risk for a wide range of health consequences” (2015). Thus, advances in genomics research present both a unique opportunity for growth and a challenge to the continued viability of the Health Education profession.

References


