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Authors

Klein, William

McBride, Colleen

Allen, Caitlin

et al.

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Optimal Integration of Behavioral Medicine into Clinical Genetics and Genomics

William M.P. Klein,[1,*] Colleen M. McBride,[2,*] Caitlin G. Allen,[2] Elva M. Arredondo,[3] Cinnamon S. Bloss,[4] Kimberly A. Kaphingst,[5] Amy C. Sturm,[6] and Catharine Wang[7]

Clinical genetics and genomics will exert their greatest population impact by leveraging the rich knowledge of human behavior that is central to the discipline of behavioral medicine. We contend that more concerted efforts are needed to integrate these fields synergistically, and accordingly, we consider barriers and potential actions to hasten such integration.

Introduction

> Drugs don't work in patients who don't take them. —C. Everett Koop, MD, US Surgeon General, 1985

In the storied history of medical research and practice, many seminal discoveries have confronted a potent obstacle: the seemingly irrational and unpredictable nature of human behavior. Indeed, Surgeon General Koop's simple and yet profound observation resonates with a rich literature on poor medication compliance.[1] Novel treatments collect dust on shelves if providers and patients do not know about or have access to them, underestimate their potential impact, or acknowledge their benefit but have other reasons not to use them. Vaccinations that could eradicate entire classes of disease might be dismissed because of false information spread through social media. Non-recommended medical practices might be overused because of misinformation or misplaced perceptions of risk (e.g., mammography in young, low-risk women), and alternative treatments might be embraced as more effective despite evidence to the contrary. For example, a recent analysis found that mortality rates were doubled among cancer patients who elected to use alternative, non-pharmacological treatments.[2]

One should also expect the many vicissitudes of human behavior to influence the reach and impact of clinical genetics and genomics—in both research and practice. An active and thriving community of practitioners, scholars, patients, and others has devoted much attention over two decades to the numerous ethical, legal, and social challenges introduced by the availability and provision of genetic information. Yet the relevance of principles of human behavior go well beyond these concerns. Research in areas such as decision making, health behavior change, communication science, social and health inequities, and implementation science has much to contribute and stands to elevate the visibility and impact of genetic discoveries. Such research has been instrumental in undergirding many of the basic principles and approaches of behavioral medicine, a field that utilizes principles of human behavior to address a wide variety of health problems such as obesity, type 2 diabetes, hypertension, HIV, and cancer. We contend that the substantial potential clinical utility and population health impact of clinical genetics and genomics is similarly predicated on an understanding of human behavior.

Consider the current set of options faced by a woman interested in her genetic breast cancer risk. She can be tested for multiple genes linked to breast cancer (and other cancers), enroll in a large sequencing cohort in which *BRCA1* and *BRCA2* results might be provided along with many other results, or ship DNA off to a direct-to-consumer company and learn the *BRCA1* and *BRCA2* results through the mail or on a website. Her choices might be driven by how she processes health information, what her family and health care provider believe she should do, and how she expects to use (and react to) the information. Clearly, a keen understanding of health communication and decision making can shed light on how a woman might engage with these different options. Moreover, an understanding of health inequities and best practices regarding the dissemination of medical advances should assist in maximizing the accessibility of these various options in the populations that need them most.

In general, genetic counselors and other providers are faced with

[1]Behavioral Research Program, Division of Cancer Control and Population Sciences, National Cancer Institute, Bethesda, MD 20892, USA; [2]Department of Behavioral Sciences and Health Education, Rollins School of Public Health, Emory University, Atlanta, GA 30322, USA; [3]Division of Health Promotion and Behavioral Science, School of Public Health, San Diego State University, San Diego, CA 92182, USA; [4]Department of Family Medicine and Public Health, University of California San Diego, San Diego, CA 92039, USA; [5]Department of Communication and Huntsman Cancer Institute, University of Utah, Salt Lake City, UT 84112, USA; [6]Genomic Medicine Institute, Geisinger, Danville, PA 17822, USA; [7]Department of Community Sciences, Boston University School of Public Health, Boston, MA 02118, USA

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*Correspondence: kleinwm@mail.nih.gov (W.M.P.K.), colleen.marie.mcbride@emory.edu (C.M.M.)

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numerous (and evolving) communication, decision-making, and implementation challenges. How, for example, should providers communicate multiple results, secondary findings, and variants of uncertain significance to their patients? Recipients of personalized genetic information have a variety of choices to make about what from their complex suite of results to share with their providers and families. Policymakers also must decide whether and how to implement population-level genetic screening efforts for genetic predispositions (such as Lynch syndrome, *BRCA1* or *BRCA2*, and familial hypercholesterolemia (FH)) that have strong evidence bases, and they must do so in a way that does not exacerbate disparities arising from long-standing inequities in access to healthcare, limited health personnel, and funding shortages. Tackling these questions is essential if genomics-informed innovation is to have public health impact, particularly given that population-level genetic screening can be perceived as competing with other essential public-health priorities.[3]

The field of behavioral medicine and related work in the communication, behavioral, and social sciences—as well as implementation science—is well equipped to help address these challenges. Decision science, for example, has produced abundant evidence that human decision making is not as unpredictable as it might look but rather is driven by several core principles, such as the desire to satisfice when faced with complex choices. Moreover, people bring a raft of emotions and motivations to contexts where they are making sense of or making decisions regarding health information. In one genomic-sequencing cohort study, participants who expected to become distraught in response to unwelcome genetic feedback were in turn less likely to seek those results, but this pattern did not occur among the individuals who tended to focus on personal values and strengths in the context of threat.[4] Findings such as these only scratch the surface of understanding the panoply of psychological constructs driving a person's engagement with genetic information.

One central question is the extent to which access to genetic information might influence behavior—particularly behaviors (e.g., consenting to screening, making lifestyle changes, and adhering to treatments) that reduce the effects of genetic risk. So far, the evidence of such an effect across a range of behaviors has been mixed; one meta-analysis suggested little to no effect,[5] and another provided more promising evidence.[6] In general, this literature is only in its infancy and is based largely on the communication of single gene results in mostly homogeneous populations. Whether genetic risk information influences behavior and decision making is also only part of the story—behavioral medicine can help us understand how, when, and why it might have such an effect.[7]

Moving from the individual to the population, the promises of precision medicine and population health rely squarely on the ability to enable broad and sustainable access within complex health systems to genomics-informed innovation. Implementation science frameworks offer a roadmap for interdisciplinary considerations of the important technical and contextual factors required to shape dissemination accordingly. Consider that principles of implementation science that were applied to organizational practices and practitioner behavior regarding cardiac resuscitation guidelines essentially eliminated disparities in survival among whites and blacks during a ten-year period.[8] Similar approaches could greatly enhance the effective implementation and dissemination of genomic innovation.[9]

Identifying Barriers and Strategies

Although one might expect expertise from behavioral medicine to be well represented in genetics and genomics research, we have the capacity for much more growth and opportunity. There has never been a better time to promote such integration. Some concerns have been expressed, for example, that emerging large sequencing projects might have much more of a basic science focus rather than a clinical-translational or behavioral focus. Behavioral medicine research can play a role in many ways, not the least of which is identifying genetic determinants of consequential health behaviors such as tobacco use.

The authorship of this commentary constitutes a Society of Behavioral Medicine (SBM) working group charged by the organization's president with the important and potentially daunting task of considering how to better integrate behavioral medicine into genetics and genomics practice and science. The group began with the observation that there were major gaps between advances in genetic and genomic science and the application of this research to clinical and population health goals. Over a two-year period, we have scoured the literature, conducted focus groups, engaged with SBM leadership, and reflected extensively on the current state of the field and how we could move forward. We engaged with colleagues in the field of behavioral medicine who themselves had a wide range of views, from enthusiasm to skepticism. We also reached out to junior scientists, whose perspectives were considered to be essential given their seemingly greater comfort with breaking down antiquated intellectual barriers.

These deliberations were particularly helpful in identifying key areas to address when fostering cross-disciplinary discussions and fruitful collaborations. We contend that several steps can be taken by scientific leadership—journal editors, officers of professional associations, university administrators, funders, and others with comparable impact—to foster a more synergistic science. Of note, our conclusions align well with principles suggested by Brown and colleagues in fostering interdisciplinary collaboration.[10] Perhaps most importantly, successful interdisciplinary collaboration requires mutual understanding and

empathy for differing disciplinary norms. A key principle that galvanizes productive conversations is a shared mission. Brown and colleagues also describe the need for constructive dialog that, over time, prioritizes both breadth and depth. These discussions are conducted with assumptions of mutual respect in safe co-learning environments, where plain language is given precedence over jargon. Over time, the constructive dialog moves away from disciplinary dominance and narrows into shared listening that fosters creativity. These concepts resonate with the emerging "science of team science."

Some of our discussants expressed worry that genomic innovation could inadvertently increase health disparities or that established collaborations with primary care and community partners would be imperiled, given that these potential partners would not regard genetic applications disseminable in the populations they serve. Thus, a mission that might be of interest to both genomic scientists and behavioral researchers is to address the enduring problem of health disparities. Opportunities for cross-discipline discussions of how genomics and behavioral medicine might work together to foster appropriate dissemination could be particularly fruitful.

Our discussions also noted the importance of publication and manuscript review, along with the observations that interdisciplinary research often struggles to find a home in prestigious journals and that grant reviewers often lack interdisciplinary expertise. Behavioral medicine researchers, like genetics and genomics researchers, often publish in discipline-specific journals and attend discipline-specific conferences such as the SBM annual meeting, reducing opportunities for interaction and collaboration. Junior researchers worry about the lack of appreciation of interdisciplinary research in tenure standards. Making proactive efforts to foster interactions across the disciplines was strongly suggested in our discussions.

We arrived at several specific steps that could address these barriers; they are as follows:

1. Provide longer-term collaboration opportunities to foster cross-talk among behavioral-medicine researchers and genomic scientists (as well as public health practitioners). A long-term view would enable each to gain familiarity with and expertise in the other disciplines. The seeds for these collaborations might be sown through development of conferences and workshops supported by professional organizations such as ASHG and SBM.
2. Design symposia and other conference events that are co-sponsored by professional organizations in these areas, and perhaps combine these with attempts to cross-fertilize across the annual meetings of those organizations. Recent collaborations between ASHG and the National Society of Genetic Counselors (NSGC) could serve as one possible model. ASHG hosted a joint ASHG-NSGC "Genetic Counselors Forum" at its 2018 annual meeting, and there are plans to mount reciprocal educational programs at ASHG and NSGC conferences annually. ASHG also had a guest blog post, written by two genetic counselors about their roles in research, that ASHG promoted on the 2nd Annual GC Awareness Day in late 2018. At present, our SBM committee is working to establish collaborations between SBM and ASHG.
3. Introduce incentives for collaboration both within and across institutions to allow for the formation of strong interdisciplinary teams that possess genetic, behavioral, population health, and implementation expertise. Such incentives would need to complement existing promotion expectations and reward structures.
4. Consider and highlight special sections, special series, invited articles, and other publication venues that illustrate the value of the type of interdisciplinary research for which we advocate.
5. Ensure that peer reviewers at the interface of behavioral and genomic medicine are well versed in both disciplines.
6. Leverage the rapidly emergent knowledge base on the "science of team science" to maximize the team-based research that will result from integration.

We point to success in other areas of disciplinary integration as evidence that this vision is achievable. The integration of basic neuroscience research and conventional behavioral research has cast new light on our understanding of brain disorders, learning trajectories, and interpersonal communication. Cardiovascular medicine research has been buttressed by the systematic integration of behavioral research on stress and the implementation of evidence-based guidelines. An integration of research on kinesiology and behavioral medicine has propelled our understanding of the best ways to promote health-enhancing physical activity. And research on behavioral economics and social psychology has demonstrated how defaults, tweaks to the physical environment, and other behavioral strategies can have nontrivial effects on public health outcomes. Surgeon General Koop was on target in noting the obvious—that medical advances mean little if people do not engage with them. Were he able to witness the full scope of the genomics revolution, we are certain he would have considered genetics and genomics research a perfect example of a medical advancement ripe for the application of research on human behavior.

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