Leveraging Implementation Science to Address Health Disparities in Genomic Medicine: Examples from the Field

Megan C. Roberts, PhD; George A. Mensah, MD; Muin J. Khoury, MD, PhD

The integration of genomic data into screening, prevention, diagnosis, and treatment for clinical and public health practices has been slow and challenging. Implementation science can be applied in tackling the barriers and challenges as well as exploring opportunities and best practices for integrating genomic data into routine clinical and public health practice. In this article, we define the state of disparities in genomic medicine and focus predominantly on late-stage research findings. We use case studies from genetic testing for cardiovascular diseases (familial hypercholesterolemia) and cancer (Lynch syndrome and hereditary breast and ovarian cancer syndrome) in high-risk populations to consider current disparities and related barriers in turning genomic advances into population health impact to advance health equity. Finally, we address how implementation science can address these translational barriers and we discuss the strategic importance of collaborative multi-stakeholder approaches that engage public health agencies, professional societies, academic health and research centers, community clinics, and patients and their families to work collectively to improve population health and reduce or eliminate health inequities. Ethn Dis. 2019;29(Suppl 1):187-192; doi:10.18865/ed.29.S1.187.

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INTRODUCTION

In the era of precision medicine, genomic discoveries are slowly being translated to improve clinical care and population health. However, the rate (and quality) of translation has lagged relative to the rate of genomic discovery.1 Translational genomic research can be differentiated into four phases from initial discovery to population health impact.2 While phase one (T1) research includes pre-clinical research, phase two (T2) focuses on evidence-based evaluation leading to practice guidelines.3 Subsequent phases of translational research include research that moves evidence-based guidelines into practice (T3) and evaluates real world outcomes of a genomic application into practice and population health impact (T4).3 Three genomic applications have been identified by the Centers for Disease Control and Prevention (CDC) as being ready for implementation; these applications have significant potential to improve public health based on existing clinical guidelines and recommendations.4 These applications include genetic testing for hereditary breast and ovarian cancer syndrome (HBOC), Lynch Syndrome (LS), and familial hypercholesterolemia (FH) among individuals at high risk of these genetic conditions. In this article, we use these applications to illustrate principles of implementation science, especially in relation to health disparities.

These three genetic disorders (HBOC, LS, and FH) significantly increase risk of: breast, ovarian, and other cancers; colorectal, endometrial and other cancers; and cardiovascular disease, respectively. It is estimated that approximately two million people in the United States are affected by these genetic conditions.4 Identification of individuals with these hereditary syndromes through genetic testing is important; evidence-based guidelines have been developed for the management of these high-risk individuals and thus, reduce morbidity and mortality.5,7

However, implementation of these genomic applications in high-risk populations has been suboptimal.1 Due to multiple factors, including low rates of early detection through genetic counseling and testing uptake, a large proportion of affected individuals remain...
unaware that they carry genetic mutations. These rates are even lower among medically underserved populations\(^8\)\(^{-11}\) that historically have inadequate access to, or reduced utilization of, high-quality health care.\(^12\) These populations include racial/ethnic minority populations, socioeconomically disadvantaged populations, underserved rural populations, and sexual and gender minorities.\(^12\) Disparities in uptake of evidence-based guidelines for HBOC\(^9\)\(^{,10}\) and FH\(^8\)\(^{-11}\) have been documented and demonstrate a critical challenge in the implementation of genomic medicine.

In this article, we: 1) describe the state of disparities in genomic medicine using examples from the literature on cancer (HBOC and LS) and cardiovascular diseases (FH) genetic testing; 2) address the importance of implementation research in addressing these disparities; and 3) discuss the strategic importance of collaborative multi-stakeholder approaches to work collectively to improve population health and reduce health inequities.

**Current Barriers and Disparities Identified in T3 and T4 Genomic Research**

Disparities in genomic medicine have been documented.\(^8\)\(^{-11}\) For example, African American women with breast cancer\(^10\) and family history of breast or ovarian cancer\(^13\) are less likely than White women to receive related genetic testing. Such disparities likely originate from socioeconomic and cultural factors that are associated with health care disparities more broadly.\(^14\) However, unique social, ethical and legal issues associated with genetic testing in underserved populations may compound challenges in the translation of genomic applications, calling for tailoring based on the socio-cultural context of each population.\(^15\)\(^{-16}\) Disparities in access to and use of genetic testing are exacerbated by differential participation in translational research, in which we find lower inclusion of racial/ethnic minority populations in pre-clinical and clinical genomic research (T1-T2), calling into question the utility of genetic testing and the effectiveness of implementation in these populations.\(^14\)\(^{-17}\) Moving forward, the inclusion of diverse populations is needed across preclinical, clinical and public health research settings in order to promote health equity.

Reported barriers to the implementation of genetic testing include low patient awareness and knowledge,\(^18\)\(^{-20}\) stigma,\(^21\) concerns about cost,\(^15\)\(^{-22}\) fear and distress,\(^23\) patient education level,\(^24\) family concerns,\(^21\) medical mistrust (including fear of misuse of genetic test results\(^18\)\(^{-20}\)), lack of a provider recommendation,\(^24\) low provider knowledge,\(^22\) and limited access to genetic services (eg, rural geography).\(^14\) Among others. A recent review\(^16\) demonstrated low awareness and knowledge about genetic testing for hereditary cancer among ethnic minority groups, despite generally positive attitudes and perceived benefits of testing, including test results’ positive implications for personal and family health.\(^16\) However, concerns about confidentiality, stigma, and discrimination were noted in the review, and in some cases these concerns were more common among ethnic minority groups.\(^16\)\(^{-20}\)\(^{-21}\) For example, in a population-based sample of African Americans, one third expressed concern that genetic testing for colon cancer risk could lead to discrimination.\(^25\) Of note, Olaya et al found that among those who received genetic counseling, African American women were as likely as Whites to move forward with genetic testing for HBOC,\(^26\) suggesting that research to reduce access issues may do well focusing on access to genetic counseling as an important outcome of interest. Another recent review\(^27\) identified major barriers to identifying and testing relevant family members (ie, cascade screening) once an individual is diagnosed with a genetic condition. State variation in genetic privacy laws, family communication, and geography were noted as major barriers to cascade screening, and a paucity of T4 research was identified that focused on disparities or that included underserved study populations.\(^27\)

Not only is variation in knowledge, attitudes, and benefits notable between racial/ethnic groups, but also within minority populations. Among studies in racial/ethnic minority populations, knowledge about genetic testing varied by sub-ethnic group,\(^28\)\(^{-29}\) acculturation,\(^28\) nativity,\(^29\) education,\(^28\) and language skills.\(^28\)\(^{-29}\) For example, in one study, increasing acculturation was associated with being more familiar with genetic tests for cancer risk, being more likely to cite perceived benefits of testing, and being less likely to cite perceived barriers among Latinos.\(^30\) Another study found that ethnic identity was positively associated with perceived benefits of genetic testing for cancer risk among African American women.\(^21\) Of note, many of the current studies have focused on HBOC, and while barriers and facilitators may
generalize to LS and FH, unique barriers to these hereditary conditions warrant additional research in relation to equitable implementation of genetic testing. Additional studies that seek to understand barriers for men, who have demonstrated lower rates of genetic testing, will also be important.

**ADDRESSING HEALTH DISPARITIES THROUGH IMPLEMENTATION SCIENCE**

The current body of literature demonstrates the complex, multilevel (eg, patient, provider, policy levels) array of barriers that contribute to disparities in the implementation of guidelines recommended for genetic testing of HBOC, LS, and FH. However, we need more T3 and T4 research to optimize the equitable translation of these lifesaving genomic applications into clinical care and public health practice. Implementation science (IS) is the study of methods to promote the translation of evidence-based practices into routine health care and public health practice. IS may provide the frameworks needed for reducing/eliminating existing disparities in access to genomic medicine as well as emerging disparities in genomic medicine. IS can identify barriers to effective implementation of practices, measure important outcomes related to translation, and test strategies to optimize or adapt implementation within a given clinical or public health context. IS frameworks highlight multilevel constructs that impact the implementation of evidence-based care, such as the Consolidated Framework for Implementation Research, which highlights constructs related to the intervention, the individual, inner (eg, clinic level), and outer settings, as well as processes that influence implementation. In other words, IS frameworks acknowledge the importance of patient (eg, knowledge), interpersonal (eg, family or provider communication), organizational (eg, health systems), community (eg, geographic access to genetic services), policy (eg, genetic privacy laws), and socio-cultural (eg, mistrust of medical system) levels, which influence disparities and are critical to implementation of genetic testing, and genomic medicine more broadly.

Indeed, others have called for the use of IS to reduce health disparities and increase the impact of health research. The Centers for Population Health and Health Disparities program included implementation research as a requisite skill for researchers in cardiovascular disease and cancer in order to address the complexity of observed disparities. Within public health genomics, the Genomics and Public Health Action Collaborative has identified objectives and metrics for HBOC and LS that include an IS framework and implementation outcome measures. Moreover, systematic reviews of the literature and an National Institutes of Health research portfolio have demonstrated an ongoing need to incorporate implementation science into genomic medicine research. Efforts such as Implementing Genomics in Practice (IGNITE), Clinical Sequencing Evidence-Generating Research (CSER), and other funding announcements attempt to facilitate this movement.

In the current health disparities literature, implementation science frameworks have been used to address disparities in underserved populations. This work could be extended to T3 and T4 genomic research to help researchers and practitioners systematically measure disparities in genetic services use, evaluate interventions to reduce disparities, adapt interventions to the unique socio-cultural needs of racial/ethnic minority populations, and measure population impact of evidence-based genomic medicine. For example, researchers in a 2015 study examined the implementation of a screening tool to identify underserved women at high risk for HBOC within a community-based hereditary cancer screening program. The study used mixed methods to measure the acceptability and utilization of this tool among non-genetic clinicians in the community. From this, an education module was developed to improve clinician knowledge of cancer genetics and self-efficacy for connecting clients to genetic counseling and testing for HBOC; this module was then implemented and evaluated. In the end, the education module was effective in improving knowledge and confidence among clinicians. Using implementation frameworks, strategies and measures will further strengthen health disparities research in genomics, by providing standardized metrics and strategies for assessing use of genomic medicine across clinical and public health settings.

However, the use of implementation research to reduce health disparities in genomic medicine, specifically, remains a major gap in the current literature. A review of implementation research in translational genomics found that study populations were primarily White, non-Hispanic, and often authors did not report race or ethnicity. Findings were similar
in a review of the NIH portfolio in implementation science in genomic medicine research.\textsuperscript{41} Taken together, these findings demonstrate limited research within racially/ethnically diverse populations in this area, which has implications for our understanding of disparities in implementation of genomics as well as the generalizability of study findings to diverse populations.

**Collaborative Multi-stakeholder Approaches to Address Health Disparities**

As researchers engage in work that falls at the intersection of health disparities, implementation science, and genomic research, the use of collaborative, multi-stakeholder approaches will be imperative. Inherent in IS approaches, researchers must account for multilevel factors by incorporating stakeholders across multiple levels, including patients, family members, patient advocates, providers, health administrators, community leaders, industry leaders, and policy makers (Table 1).\textsuperscript{51} Without consideration of all levels, implementation may fail. For example, even if patients and providers have bought into the importance of genomic medicine to their health, patients, particularly those who are underserved, may still not have access to genetic services due to policies (eg, insurance coverage of follow up care for Tier 1 applications) or geography (eg, low access to genetic counselors) despite individual level buy-in. Given the complexity of implementing genomics, multiple perspectives across these levels (Table 1) will be needed to address disparities in translation.

Recently, the National Heart, Blood, and Lung Institute convened a think tank meeting and recommended collaborative research to reduce health inequities.\textsuperscript{38} By including stakeholders (such as community organizations) in translational genomic research, research teams can bring understanding to the complexity of reducing disparities and enhance the reach of genomic medicine by engaging the key stakeholders who are ultimately the end users of genomic medicine. In addition, capacity building will be important for health systems to effectively implement evidence-based genomic medicine.\textsuperscript{52}

Provider training and resources will be

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<tr>
<th>Level/stakeholder</th>
<th>Examples of factors</th>
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<tbody>
<tr>
<td>Persons with HBOC, LS, FH</td>
<td>Knowledge about genetic conditions and genetic testing; family dynamics; communication with providers and relatives; access to genetic services; medical mistrust; cultural beliefs</td>
</tr>
<tr>
<td>Relatives of HBOC, LS, FH patients</td>
<td>Knowledge about genetic conditions and genetic testing; family dynamics; communication with providers and relatives; access to genetic services; medical mistrust; cultural beliefs</td>
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<tr>
<td>Providers</td>
<td>Knowledge about FH, HBOC, LS screening recommendations; communication about genetic conditions with patients and relatives; reimbursement for diagnosing and reporting genetic conditions; reimbursement of initiating contact with relatives of patients; competing demands in a clinic visit; knowledge of genetics and genetic counseling referral patterns; ability to interpret genetic findings and recommend appropriate care (eg, variants of unknown significance)</td>
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<td>Laboratories</td>
<td>Different methods and approaches for screening for genetic conditions (eg, in LS, microsatellite instability and IHC as well as DNA sequencing); different laboratory systems (eg, centralized versus local) to undertake screening</td>
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<tr>
<td>Health care organizations</td>
<td>Coordination between various specialties (primary care, oncology/cardiology; genetics); policies and standard practices for screening cases and returning results; integration of genetic information into electronic health records; presence of decision support tools for genetic testing and subsequent guideline recommendations; standardized informed consent for genetic testing; training, tools and resources related to genetic testing for providers and patients</td>
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<tr>
<td>Community/state leaders</td>
<td>Socio-cultural contexts of genetic screening; insurance coverage and reimbursement; existence of state guidelines for recording genetic data; state efforts to promote adoption of guidelines; state certification policies for laboratories/personnel; state laws about genetic privacy; state public health programs to improve access to genetic testing</td>
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<tr>
<td>National health policymakers</td>
<td>Medicare and Medicaid benefits for genetic testing; national policies and regulation of laboratories and genetic testing; professional societies standards; public health efforts to address disparities in implementation of genetic testing and cascade screening</td>
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needed for practitioners to keep up with the rapid pace of translational genomic research. Incorporating infrastructure for research will allow health systems to learn from implementation successes and failures; a core function of this learning health care system could be assessing, monitoring and addressing disparities in the use of genetics services.

As the era of precision medicine marches forward, it is imperative that we address disparities in genomic research and genomic medicine. By using implementation science and incorporating key stakeholders in T3 and T4 research, we can begin to address existing disparities in genomics. Through this transdisciplinary research, investigators open the opportunity to develop and implement precision public health to improve population health and reduce disparities. Strategic collaborative engagement of all stakeholders across multiple sectors in approaches that place the patient and family at the center of genomic medicine implementation will be critical for success.

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Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Roberts, Mensah, Khoury; Manuscript draft: Roberts, Mensah, Khoury

References

1. Manolio TA, Chisholm RL, Ozenberger B, et al. Implementing genomic medicine in the clinic:

   PMID:23360799

   PMID:20051673

geart.2014.12.002
   PMID:25754560


   PMID:19125126

   PMID:21600525

   PMID:28908546

ygyno.2018.07.023
   PMID:30077346

   PMID:2135836

   PMID:28701632


   PMID:15827311

   PMID:16682739

   PMID:24253862

   PMID:28545429

   PMID:29733732

   PMID:19752639

   PMID:21691939

