Defining and Achieving Health Equity in Genomic Medicine

Sonya Jooma, MA[1]; Michael J. Hahn, BA[1];
Lucia A. Hindorff, PhD, MPH[1]; Vence L. Bonham, JD[1]

The potential of genomics to improve health comes with the peril that the benefits will not be equitably available to all populations. Existing health disparities can be exacerbated if the implementation of genomic medicine does not intentionally focus on health equity. Defining what health equity means in the context of genomics and outlining how it can be achieved is important for the future of the field. Strategies to improve health equity include addressing underrepresentation of diverse populations in genomic research, investigating how genomic services can be deployed in diverse health care settings and underserved communities, increasing workforce diversity, supporting infrastructure development outside traditional research centers, and engaging communities and health care providers. By employing these strategies, the genomic research community can advance health equity in genomic medicine. *Ethn Dis*. 2019;29(Suppl 1):173-178; doi:10.18865/ed.29.S1.173.

Keywords: Health Equity; Genetic Diversity; Genetic Testing; Genomic Medicine

[1] National Human Genome Research Institute, National Institutes of Health, Bethesda, MD

Address correspondence to Vence L. Bonham, JD; Division of Intramural Research, Social & Behavioral Research Branch & Office of the Director, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD, 20892; bonhamv@nih.gov

Introduction

Genomics has come a long way in the past two decades, with vast improvements in genome sequencing and growing knowledge about how variation in the genome affects human health. Increasingly, health care providers are using genomic testing to screen prenatally for genetic disorders, improve cancer treatment, and diagnose rare disorders. These applications exemplify the promise of genomic medicine and herald a precision medicine era in which prevention and treatment of disease is individually tailored.

However, the field of genomics has failed so far to equitably include diverse populations in the studies that have built the evidence base and translated discoveries to better health. Although this issue is not unique to genomics, diverse populations are underrepresented in the genomic studies that form the foundation for linking genes and disease.[1-4] These groups are at risk of being left behind in the implementation of genomic medicine if efforts are not oriented to address existing gaps.[5] To equitably advance genomics in a way that can improve the health of all populations, the future of genomics must begin by looking at those left behind.

This article aims to define health equity in the context of genomics and describe steps that the field must take so that genomic medicine does not widen health disparities or add to existing inequities. Health equity is broadly defined by *Healthy People 2020* as the "attainment of the highest level of health for all people."[6] Health equity can be a difficult concept to define for genomics because evidence for the clinical utility of genomic testing is still accumulating and thus the translation of research to medicine is still relatively new. Here, we define health equity in genomic medicine

To equitably advance genomics in a way that can improve the health of all populations, the future of genomics must begin by looking at those left behind.

as the global applicability of genomic knowledge, fair and even access to genomic services such as testing and counseling, and unbiased implementation of genomic medicine. Health equity in the context of genomics requires an understanding of how biology influences disease and how disease is influenced by biological and non-biological determinants of health (such as environmental, psychosocial, and socioeconomic factors) in all populations. Thus, successful implementation of genomic medicine will mean that all populations have equal, effective, and affordable access to genomic medicine and that diagnosis, prevention, and treatment strategies can target the bases of disease without bias for or against any group. A commitment to health equity will require funders, researchers, health providers, and other stakeholders to work together to: 1) close existing evidence gaps among diverse and underserved populations; 2) ensure that genomic medicine applications, once implemented, are unbiased and equitably accessible; and 3) build the workforce and infrastructure to make widespread adoption of these strategies possible.

Addressing Gaps in the Evidence Base

Achieving health equity in the application of genomic medicine will first require greater availability of genomic information from diverse populations and dedicated efforts to study the clinical implications of variants in non-European populations. Understanding connections between genomic variants and disease in all populations will enable researchers to develop prevention and treatment strategies that are effective for different populations.[7]

Recent medical applications of genomics research demonstrate the risks of failing to promote equity in genomics. For example, genome-wide polygenic risk scores developed for five common diseases identified individuals at significantly greater risk who could be targeted for prevention efforts. Due to limited available data, these scores were derived from people of mainly European ancestry, reducing the model's predictive power for other ancestries.[8] In another study, genetic tests for hypertrophic cardiomyopathy misclassified some variants as risky, when in fact they were likely to be harmless. These variants were primarily found in Black Americans, who were not included in the studies that led to their classification, which subsequently led to a conflation of what is different and what is harmful and raising the possibility of this occurring for other disorders.[7]

As shown by the current state of genomic databases, recruiting underrepresented participants for research has generally been of lower priority than using convenience samples or incentivizing overall recruitment goals, which tend to favor European ancestry populations. Funding agencies can play a key role in advancing equity in genomic research by emphasizing higher levels of inclusion of underserved populations in the study design and review criteria for funding opportunities, and actively monitoring and supporting researchers in reaching recruitment targets.[5,9] Additionally, the need for increased funding of diversity-related research should span a range of research, from basic to applied. Ethical, Legal, and Social Implications (ELSI) research should not be neglected. Understanding how issues such as genomic literacy, informed consent, responsible return of results, biobanking, data sharing, and recontact of research participants affect minority and other underrepresented groups, and how implementation of genomic medicine can be more culturally competent is key to increasing participation.[10,11] Researchers should design and implement studies with measurable target goals for recruitment and retention of underrepresented populations and investigate research questions of special interest to diverse populations.

To increase diversity, genomic medicine research programs, funded by the National Human Genome Research Institute, have prioritized recruiting a high percentage of participants from minority and underserved populations.[5] Pilot implementation studies are developing models and frameworks that can be used and adapted in the future. Two of these programs, the Clinical Sequencing Evidence-Generating Research (CSER) program and the Implementing Genomics in Practice (IGNITE) program, have been able to successfully conduct projects in diverse clinical settings.[12,13] The CSER program aims to generate evidence for the utility of genome sequencing and identify barriers to incorporating genomic data into health care. Notably, funded clinical sites have committed to recruit a 60% minimum of patients of non-European

ancestry, medically underserved populations, or populations who experience poorer health outcomes.[12]

The IGNITE program piloted implementation projects in genomic medicine with an emphasis on those conducted in diverse clinical settings rather than solely academic medical centers. Diverse settings could include community hospitals, primary care practices, military or Veterans' Administration hospitals, and facilities treating underserved populations. These efforts reinforce the early implementation of genomic medicine in diverse settings, building an evidence base that can be modeled and adapted for other underserved areas.

As others have pointed out, it is not enough to mandate higher percentages of inclusion; investigators need adequate resources and time to engage with communities, promote trust, and modify studies based on community feedback. This community engagement strengthens study participation and facilitates outcomes that are aligned with community values.[11] For example, in the study, "Genetics of Asthma in Latino Americans (GALA)," researchers were on the ground at each site including Mexico and Puerto Rico, far beyond the San Francisco Bay Area in which they were located. They engaged local community groups and leaders, investigators who had experience working with diverse groups, and multilingual clinical coordinators.[14] While recruitment of underrepresented populations may be more resource- and time-intensive, investigators can draw from such existing models of success when designing studies.

Reducing Disparities in Access to Genomic Services

Improving the genomic evidence base will allow for genetic tests that are more applicable to diverse populations. However, high costs and variable insurance coverage for those tests, uncertain availability of technology in low-resourced areas, the need for more provider knowledge about genomics, and a shortage of genetic counselors indicate that access to genomic services is still a significant barrier. Currently, reimbursement policies for genomic testing are not well-established, and insurers are grappling with the high volume of genomic tests that are entering the market.[15,16] The genomics community must engage in active, concerted collaborations with insurers to chart a path forward. This will involve continuing to build the evidence base for not just the accuracy, but also the cost-effectiveness and clinical utility of different genomic tests, including tests for variants and disorders that disproportionately affect minority groups. This evidence base is likely to include randomized and observational data. For example, IGNITE began building a structured evidence base without initially relying on a clinical trial design[17]; in its subsequent phase, IGNITE is adopting a pragmatic clinical trial design.[18] Insurers must also communicate the evidence that they would need to see before providing coverage for the tests. Policymakers have a unique role in ensuring access to genomic testing, in an evidence-based manner, and monitoring for equitable distribution of resources. Medicaid policies, which are managed state-by-state, may be one way to provide underserved groups with access to genomic services. One proposed bill advances a plan to amend Medicaid to allow states to offer coverage for genome sequencing for children with undiagnosed conditions, an area in which the likelihood of diagnosis is promising. So far, there have been limited instances of coverage for genomic sequencing through Medicare and Medicaid outside of specific applications (eg, advanced stage cancer), and policymakers must work with relevant stakeholders to find the best way forward to enable access for genomic testing for underserved groups.

Another important aspect of guaranteeing access to genomic medicine is ensuring that health care providers are equipped to interpret, communicate, and respond to results. Although genetic testing for ancestry and other direct-to-consumer genomic services are offered outside traditional research and clinical care, here we focus on those generated during the clinical encounter. Genomic literacy is still generally low among primary health care providers, and many providers may lack knowledge or confidence in interpreting or using genomic information for patient care.[13,19] Implicit bias among health care providers has also been associated with poorer communication with non-White participants.[20] These concerns will be increasingly relevant to non-genomics providers as disclosure of genomic findings becomes more common in primary care settings. Barriers to accessing

genetic counseling services include challenges in payer reimbursement and projected workforce shortages of genetic counselors.[21,22] A greater understanding among all providers of how genomic variants contribute differentially to the health of individuals can result in the more precise application of genomic medicine to advance equity.

Because of this, research institutions and medical centers should invest resources and make it routine for health care providers, including physicians, nurses, and pharmacists, to learn about the application of genomics to patient care. These efforts should include medical school curricula as well as resources for practicing providers, such as continuing medical education classes, educational opportunities built into the electronic health record, point of care resources, or maintenance of certification credits for genomics.[23] CSER and IGNITE have both developed resources for non-genetics providers as a first step toward making genomic resources widely available (CSER Toolkit [http://www.ashg.org/education/csertoolkit/index.html], SPARK Toolbox [https://ignite-genomics.org/spark-toolbox/]), but these resources and others must be effectively disseminated to medical communities.

Health care institutions must also create ways to incorporate diversity in implementing genomic medicine at the health system level. Research into best practices for implementing genomic medicine with minority and underserved groups and in a broad range of clinical and public health settings is limited,[24] and continued implementation science studies into the best methods of conveying genetic-testing information are needed to determine what methods are most effective and beneficial for each population. These studies are needed to develop effective approaches to integrating and using genomic and non-genomic information from diverse populations into existing systems, and to develop tailored approaches to communicating genomic results. Alternatives to traditional in-person visits could include telemedicine, online-based genetic counseling, and increased availability of educational resources to support patient understanding of genomic findings.

Building Stronger Infrastructure Outside Traditional Academic Medical Centers

Access is also dependent on technology dissemination into diverse health care settings, a key reason that generating strong scientific evidence in environments outside of academic medical centers is important for health equity. Preparing for delivery of genomic services beyond academic medical centers and other quaternary care providers is also crucial. Researchers can learn how to successfully implement genomic technologies into settings with different needs, though there is still the challenge of how to efficiently distribute new technologies across different settings.

Additionally, funders should prioritize supporting infrastructure and workforce development in institutions with low levels of research funding, especially minority-serving institutions. The benefits of doing so include building a diverse scientific workforce, increasing recruitment and retention of underrepresented groups, and improving access and engagement with genomic medicine.

Infrastructure investment has been a successful strategy for international efforts in genomics. The Human Heredity and Health in Africa (H3Africa) Consortium supports African-led genomic research and has resulted in scientific and community gains by building a network of African scientists and funding for both training and equipment in African institutions.[25] This work has increased the ancestral diversity of genomic databases and led to key discoveries about genomic contributors to health and disease. The impact has also extended beyond the initial scientific goals, such as the development of a consensus framework for ethical genomics in Africa, providing international researchers a roadmap for future research.[26]

Like H3Africa, US-based institutions with close ties to the surrounding community, including community hospitals, minority serving institutions and federally qualified health centers, coupled with a more diverse scientific workforce, have the potential to facilitate community engagement and participation by minority, rural, underserved, or under-resourced populations. Investing in local institutions and training researchers in these communities while partnering with well-established research centers can advance short-term research goals, while building long-term capacity.

Table 1. Strategies to achieve health equity in genomic medicine

Increase representation of underrepresented groups
Researchers
Prioritize recruitment of underrepresented participants over quickly reaching recruitment goals
Investigate research questions of special interest to diverse and underserved populations
Conduct clinical genomic studies in diverse healthcare settings
Increase community engagement to build relationships, garner trust, and address local concerns
Funders
Encourage higher levels of inclusion in study design and review criteria for funding opportunities
Provide investigators adequate time and resources to engage communities
Actively monitor and support researchers in reaching recruitment targets
Facilitate equal access to genomic services
Researchers
Build on evidence base for cost-effectiveness and clinical utility of genomic tests
Engage payers to promote evidence-based coverage of genomic services
Payers
Communicate what evidence is needed to make coverage decisions about tests and genetic counseling services
Policymakers
Explore ways to promote access to testing for underserved groups, such as through state Medicaid policies
Research institutions, medical centers, and medical schools
Invest resources and make it routine for health care providers to learn about genomics
Incorporate genomics into medical school curricula, continuing medical education courses, and point of care resources, among others
Conduct implementation science studies to learn how to effectively integrate genomics into the clinical care of diverse groups
Build infrastructure outside traditional settings
Funders and institutions
Support research that strengthens infrastructure outside traditional settings
Recruit and train minority investigators

Conclusions

As genomics continues to progress from understanding the structure and biology of genomes to the translation and implementation of genomic medicine, the principles of health equity are critical for success. Table 1 presents a summary of principles related to genomics along with strategies for key stakeholders that have been outlined within this article. As genomics becomes an increasingly integral part of clinical practice, the field runs the risk of widening existing health disparities if we do not make a commitment to conducting research that will ensure its applicability to populations of all ancestral, socioeconomic, and geographic backgrounds.

When planning for the next decade, we must be particularly mindful of health equity in the goals and milestones that will guide the future of genomics. The scientific community must align its priorities so that inclusion of diverse populations and targeted research are no longer afterthoughts but instead primary and urgent goals across the spectrum of research and translation. Genomic medicine will have its greatest chance at success when the whole field advocates for equitable access. It is time for researchers, administrators, funders, and policymakers to use the momentum of genomics to drive toward greater health equity and make personalized medicine a reality for all persons.

Conflict of Interest

No conflicts of interest to report.

Author Contributions

Research concept and design: Hahn, Bonham; Data analysis and interpretation: Jooma, Hindorff, Bonham; Manuscript draft: Jooma, Hahn, Hindorff, Bonham; Administrative: Jooma, Hahn, Hindorff, Bonham; Supervision: Bonham

References

1. Bustamante CD, Burchard EG, De la Vega FM. Genomics for the world. *Nature*. 2011;475(7355):163-165. https://doi.org/10.1038/475163a PMID:21753830
2. Popejoy AB, Fullerton SM. Genomics is failing on diversity. *Nature*. 2016;538(7624):161-164. https://doi.org/10.1038/538161a PMID:27734877
3. Spratt DE, Chan T, Waldron L, et al. Racial/ethnic disparities in genomic sequencing. *JAMA Oncol*. 2016;2(8):1070-1074. https://doi.org/10.1001/jamaoncol.2016.1854 PMID:27366979
4. Landry LG, Ali N, Williams DR, Rehm HL, Bonham VL. Lack of diversity in genomic databases is a barrier to translating

precision medicine research into practice. *Health Aff (Millwood)*. 2018;37(5):780-785. https://doi.org/10.1377/hlthaff.2017.1595 PMID:29733732
5. Hindorff LA, Bonham VL, Brody LC, et al. Prioritizing diversity in human genomics research. *Nat Rev Genet*. 2018;19(3):175-185. https://doi.org/10.1038/nrg.2017.89 PMID:29151588
6. US Department of Health and Human Services. *Disparities*. 2018. Last accessed December 17, 2018 from https://www.healthypeople.gov/2020/about/foundation-health-measures/Disparities.
7. Manrai AK, Funke BH, Rehm HL, et al. Genetic misdiagnoses and the potential for health disparities. *N Engl J Med*. 2016;375(7):655-665. https://doi.org/10.1056/NEJMsa1507092 PMID:27532831
8. Khera AV, Chaffin M, Aragam KG, et al. Genome-wide polygenic scores for common diseases identify individuals with risk equivalent to monogenic mutations. *Nat Genet*. 2018;50(9):1219-1224. https://doi.org/10.1038/s41588-018-0183-z PMID:30104762
9. Oh SS, Galanter J, Thakur N, et al. Diversity in clinical and biomedical research: a promise yet to be fulfilled. *PLoS Med*. 2015;12(12):e1001918. https://doi.org/10.1371/journal.pmed.1001918 PMID:26671224
10. Williams JR, Yeh VM, Bruce MA, et al. Precision medicine: familiarity, perceived health drivers, and genetic testing considerations across health literacy levels in a diverse sample. *J Genet Couns*. 2018. https://doi.org/10.1007/s10897-018-0291-z PMID:30105426
11. George S, Duran N, Norris K. A systematic review of barriers and facilitators to minority research participation among African Americans, Latinos, Asian Americans, and Pacific Islanders. *Am J Public Health*. 2014;104(2):e16-e31. https://doi.org/10.2105/AJPH.2013.301706 PMID:24328648
12. Amendola LM, Berg JS, Horowitz CR, et al; CSER consortium. The Clinical Sequencing Evidence-Generating Research Consortium: Integrating Genomic Sequencing in Diverse and Medically Underserved Populations. *Am J Hum Genet*. 2018;103(3):319-327. https://doi.org/10.1016/j.ajhg.2018.08.007 PMID:30193136
13. Sperber NR, Carpenter JS, Cavallari LH, et al. Challenges and strategies for implementing genomic services in diverse settings: experiences from the Implementing GeNomics In pracTicE (IGNITE) network. *BMC Med Genomics*. 2017;10(1):35. https://doi.org/10.1186/s12920-017-0273-2 PMID:28532511
14. Burchard EG. Medical research: missing patients. *Nature*. 2014;513(7518):301-302. https://doi.org/10.1038/513301a PMID:25230631
15. Burns J. Health insurers struggle to manage number, cost of genetic tests. *Manag Care*. 2016;25(4):20-23. PMID:27265964
16. Phillips KA, Deverka PA, Hooker GW, Douglas MP. Genetic test availability and spending: where are we now? where are we going? *Health Aff (Millwood)*. 2018;37(5):710-716. https://doi.org/10.1377/hlthaff.2017.1427 PMID:29733704
17. Orlando LA, Sperber NR, Voils C, et al. Developing a common framework for evaluating the implementation of genomic medicine interventions in clinical care: the IGNITE Network's Common Measures Working Group. *Genet Med*. 2018;20(6):655-663. https://doi.org/10.1038/gim.2017.144 PMID:28914267
18. National Human Genome Research Institute. *Implementing Genomics in Practice (IGNITE) II: Pragmatic Clinical Trials Network.* 2018. Last accessed December 17, 2018 from https://www.genome.gov/27572183/implementing-genomics-in-practice-ignite-ii-pragmatic-clinical-trials-network/
19. Guttmacher AE, Porteous ME, McInerney JD. Educating health-care professionals about genetics and genomics. *Nat Rev Genet*. 2007;8(2):151-157. https://doi.org/10.1038/nrg2007 PMID:17230201
20. Schaa KL, Roter DL, Biesecker BB, Cooper LA, Erby LH. Genetic counselors' implicit racial attitudes and their relationship to communication. *Health Psychology.* 2015;34(2):111-119.
21. Doyle N, Cirino A, Trivedi A, Flynn M. Exploring barriers to payer utilization of genetic counselors. *J Genet Couns*. 2015;24(1):122-133. https://doi.org/10.1007/s10897-014-9745-0 PMID:25138080
22. Hoskovec JM, Bennett RL, Carey ME, et al. Projecting the Supply and Demand for Certified Genetic Counselors: a Workforce Study. *J Genet Couns*. 2018;27(1):16-20. https://doi.org/10.1007/s10897-017-0158-8 PMID:29052810
23. Murray MF. Educating physicians in the era of genomic medicine. *Genome Med*. 2014;6(6):45-45. https://doi.org/10.1186/gm564 PMID:25031626
24. Roberts MC, Kennedy AE, Chambers DA, Khoury MJ. The current state of implementation science in genomic medicine: opportunities for improvement. *Genet Med*. 2017;19(8):858-863. https://doi.org/10.1038/gim.2016.210 PMID:28079898
25. Peprah E, Wiley K, Sampson U, Narula J. A New age for african-driven genomics research: Human Heredity and Health in Africa (H3Africa). *Glob Heart*. 2017;12(2):67-68. https://doi.org/10.1016/j.gheart.2017.05.003 PMID:28867289
26. Yakubu A, Tindana P, Matimba A, et al. Model framework for governance of genomic research and biobanking in Africa? *AAS Open Research.* 2018;1(13).