CRISPR in Public Health: The Health Equity Implications and Role of Community in Gene-Editing Research and Applications

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CRISPR (clustered regularly interspaced short palindromic repeats) is a Nobel Prize–winning technology that holds significant promise for revolutionizing the prevention and treatment of human disease through gene editing. However, CRISPR's public health implications remain relatively uncertain and underdiscussed because (1) targeting genetic factors alone will have limited influence on population health, and (2) minority populations (racial/ethnic, sexual and gender)—who bear the nation's greatest health burdens—historically suffer unequal benefits from emerging health care innovations and tools.

This article introduces CRISPR and its potential public health benefits (e.g., improving virus surveillance, curing genetic diseases that pose public health problems such as sickle cell anemia) while outlining several major ethical and practical threats to health equity. This includes minorities' grave underrepresentation in genomics research, which may lead to less effective and accepted CRISPR tools and therapies for these groups, and their anticipated unequal access to these tools and therapies in health care.

Informed by the principles of fairness, justice, and equitable access, ensuring gene editing promotes rather than diminishes health equity will require the meaningful centering and engagement of minority patients and populations in gene-editing research using community-based participatory research approaches. (*Am J Public Health*. 2023;113(8):874–882. https://doi.org/10.2105/AJPH.2023.307315)

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The discovery and development of CRISPR (clustered regularly interspaced short palindromic repeats) gene editing over the past decade has sparked considerable excitement in the scientific community for its ability to revolutionize the study, prevention, and treatment of human disease.[1] By making gene editing cheaper, faster, more powerful, and easier to use,[2] CRISPR is expected to significantly advance the field of precision medicine by bringing gene-editing therapies to the forefront of health care. However, at present, CRISPR's ability to advance or hinder health equity remains relatively underdiscussed in the fields of population and public health.

Although there is a corpus of excellent literature discussing the potential influence of genomic technologies on health,[3,4] much of this discussion has been centered (1) in the fields of bioethics, education, and law versus health (where it is arguably most needed), (2) on other forms of genomics research and technology (e.g., genome-wide association studies),[5–7] or (3) on the ethics of gene editing on health broadly with limited targeted focus on issues of health equity and disparities[8,9]—with several notable exceptions.[5,10] Also, across thousands of published CRISPR-based studies, few have detailed the benefits and challenges posed by CRISPR gene editing for bridging the health equity gap for minority patients and populations.[4,10]

In public health and medicine, the concept of health equity is grounded in the principles of justice, ethics, and human rights, wherein all people should be valued equally and have sufficient opportunities to live healthy lives regardless of social characteristics, resources, or

status.[11,12] Thus, nearly every major US health organization, including the American Public Health Association (APHA), the American Medical Association (AMA), the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health (NIH) have called for research and programs to reduce health disparities and promote health equity for all people.

Under this framework, health disparities are defined as group differences in health status resulting from systemic forms of social disadvantage, such as low socioeconomic status, racism, discrimination, and disability, that increase morbidity and mortality in affected groups.[12,13] Importantly, not all health differences constitute disparities, as disparities primarily afflict minority groups (e.g., racial/ethnic minorities, sexual and gender minorities) because they are disproportionately affected by relative social disadvantage in the United States, leading the CDC to note that health disparities "are directly related to the historical and current unequal distribution of social, political, economic, and environmental resources."[14]

Thus, although CRISPR's emergence has generated considerable excitement in the health sciences, it also raises serious health equity concerns because, historically, minority patients and populations have been persistently excluded from clinical research, innovations, and care—contributing to the current health equity gap by suppressing health benefits for groups experiencing the poorest health outcomes. Similarly, minority participants are minimized in genomics health research,[6,15] as most participants in genomic studies are of European ancestry,[6] suggesting a future patterning in which minority populations will fail to benefit equally from CRISPR advances for improving health. Accordingly, given CRISPR's potential rapid progression from the laboratory to frontline care, the health equity implications of introducing CRISPR gene-editing tools and therapies into public health and health care merits focused discussion based in part on the challenging history of both genomics and medicine in attending to the health needs and disparities of minority populations.[16]

GENE EDITING

Human gene editing refers to the process of making targeted alterations to the human genome using technologies that can modify, insert, or delete DNA sequences.[17] To accomplish this, technologies such as CRISPR employ molecular scissor proteins known as "nucleases" to precisely cut DNA at any site targeted by scientists, allowing researchers to functionally manipulate DNA and alter gene-expressed traits and diseases.[18] Thus, should gene editing fulfill its considerable promise, it may achieve numerous health-relevant purposes, including studying the development and expression of human disease risk factors in laboratory settings and preventing, treating, and curing diseases using gene therapies applied either in human adults or embryos before birth.[19]

Gene therapies (which include but are not limited to gene-editing therapies) refer to biological medicinal products that transfer genetic material (e.g., nucleic acids, viruses) into human cells to alter the human genome for diagnostic or therapeutic purposes.[19] There are 2 categories of gene therapies: somatic and germline.[19] Somatic therapies alter all human cells in the body besides reproductive sperm and embryos and are used to treat existing diseases. Because reproductive cells are not involved, genomic changes made by somatic therapies are not transmitted intergenerationally, reducing long-term risk but also limiting their effectiveness, as they may not reach all cells required to completely treat a disease and cannot reverse prior damage.[20] Ethically, somatic therapies are the least controversial gene therapies and are well regulated, with more than 2000 clinical trials completed or in progress.[21] Thus, CRISPR-based somatic therapies are likely to gain similar public and regulatory acceptance.[8,22]

By contrast, germline therapies target reproductive cells and create heritable gene edits across offspring. Consequently, germline therapies have raised profound safety and ethical concerns with no global consensus reached[8] because (1) any consequences and problems caused by editing may be compounded across generations because every cell in offspring will carry the edits, and (2) these therapies may be used unscrupulously for the purpose of eugenics or enhancing children for advantageous and favorable traits, furthering inequalities.[22,23]

CRISPR

CRISPR refers to short, repeated segments of DNA in bacteria that provide the foundation for bacteria's adaptive immune system against viruses. Specifically, when a virus invades a bacteria, it injects its DNA into the cell, reprogramming the cell to create virus copies until the cell ruptures and releases the replicated virus.[24] If the bacteria survives the attack, its CRISPR system will splice pieces of the viral DNA into the bacteria's chromosome (as short, repeated DNA segments that code for the virus) to create a type of bacterial immunity record.

After a bacteria's CRISPR immune system has encoded a virus into its

chromosome, whenever that virus invades the bacteria, the CRISPR system will direct programmable enzymes such as the Cas9 "scissors" enzyme—which can precisely cut DNA at any site like scissors[24]—to locate the virus using specific RNA guides (guideRNA) coded to that viruses' unique genetic signature. Once the Cas9 enzyme locates the virus with the help of the guideRNA, it will bind to and disable the virus by unwinding and cutting its DNA. What makes the Cas9 enzyme remarkable is that the scissors can be easily programmed using different guideRNAs to cut DNA sequences at any gene site. Thus, by combining the Cas9 enzyme with laboratory-designed guideRNAs—creating CRISPR-Cas9 complexes—scientists can edit any DNA sequence in the human body. Impressively, multiple guideRNAs can be employed in 1 Cas enzyme, allowing the simultaneous or multiplexed targeting of numerous genes.

Before CRISPR, gene-editing technologies, such as zinc finger nucleases and transcription activator-like effector nucleases, relied on specially coded proteins to recognize key DNA sequences, requiring complex, labor-intensive development processes that created roadblocks in terms of time, cost, and efficiency (e.g., limited specificity and target recognition, off-target effects).[18] By contrast, by cleverly repurposing the CRISPR system and Cas proteins to cut genes at any desired DNA sequence, scientists can easily target, edit, regulate, and modify the human genome.[25] Through these mechanisms, disease-causing genes can be turned on or off or replaced by inserting donor DNA into CRISPR-Cas9 complexes—allowing researchers to cure human diseases linked to our genetic code.

CRISPR CLINICAL BENEFITS

Because CRISPR can target genetic architectures more precisely than previous gene-editing tools, CRISPR breakthroughs have quickly advanced the health sciences. For example, CRISPR has accelerated the study of genetic models of human diseases by allowing scientists to efficiently induce genetic changes in animal models and study their effects. Through this process, scientists have successfully elucidated genetic pathways for diseases by introducing disease-causing mutations (e.g., cancers) into nonhuman animals, allowing scientists to model human diseases in the laboratory with speed and precision.[1]

Additionally, CRISPR can allow scientists to develop gene therapies to correct point mutations in the genome to treat or cure single-cell hereditary diseases such as sickle cell anemia (SCA), which has received intense research focus as a proof-of-concept application of CRISPR's therapeutic potential.[26] Caused by a single point mutation in the B-globin gene, SCA affects 100 000 people nationally[27] who are primarily of African ancestry or Central and South American descent. Millions of people are also affected by SCA worldwide in Africa, India, the Mediterranean, and the Arabian Peninsula,[28] with available cures involving high-risk stem-cell or bone marrow transplants.[29] Yet, human experiments indicate CRISPR may effectively treat SCA in patients.[30–32] This success provides promising evidence of CRISPR's potential to cure genetic disorders, while also highlighting longstanding disparities in the development of treatment options for minority populations[33] as SCA has historically received limited research and clinical funding[28] compared with genetic conditions that are more prevalent in European ancestry populations.

For instance, despite hemophilia and cystic fibrosis being less prevalent than SCA, large US networks of hemophilia and cystic fibrosis treatment centers provide high-quality specialty care to most individuals with these disorders, whereas only a minority of individuals with SCA receive specialty care[34] owing to limited US funding for SCA networks and centers.[35] Early investments in SCA gene-editing research also raise significant concerns around targeting African American populations in the first CRISPR human trials considering the safety risks associated with previous gene-editing trials[19] as well as concerns involving fairness in application should these trials lead to viable cures given the legacy of discrimination against the SCA community (e.g., denial of education, work, and health care opportunities).[33]

CRISPR PUBLIC HEALTH BENEFITS

The potential public health benefits of CRISPR are murkier as the technology's capacity to influence most major causes of disability and death remain unclear.[2] First, because genes and environment play an intertwined role in many chronic diseases (e.g., asthma, cardiovascular disease), it is questionable whether technologies targeting genetic factors alone can have a measurable effect on health equity, as genes do not appear to be the primary driving factor for many health disparities. Second, because CRISPR therapies operate at the individual rather than population level, any improvements in health outcomes will be limited to a single patient at a time. Yet, despite these issues, CRISPR innovations in disease surveillance, diagnosis, and

treatment may someday yield public health benefits if appropriately attuned to minority populations, who bear the heaviest US disease burdens.

For instance, CRISPR may allow clinicians to identify, regulate, and correct certain genetic contributors to chronic diseases (e.g., diabetes, cancer, heart disease) that interact with sources of disadvantage and stress in the environment (e.g., poverty, pollution) to perpetuate health disparities. This includes using CRISPR tools to correct key asthma-linked polymorphisms that increase asthma risk among individuals repeatedly exposed to heavy air pollution[36]—a common environmental hazard disproportionately affecting minority communities.

CRISPR may also enhance public health by strengthening virus surveillance. This is especially true for many low-income minority communities, which often suffer disproportionate rates of infectious diseases caused by viruses such as human papillomavirus, HIV, mpox, and SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) owing to structural inequities in the social and built environment (e.g., racial segregation, stigma, lack of access to clean air and water, limited health care access). As these viruses are challenging and expensive to track on a population scale using current testing approaches, scientists have developed novel CRISPR-based surveillance platforms such as CARMEN-Cas13: a multiplexed CRISPR-based assay capable of diagnosing hundreds of viruses per sample at low cost.[37] Using CARMEN-Cas13 may allow professionals to efficiently screen people in communities for viruses, facilitating rapid public health responses to mitigate future community outbreaks.

Finally, CRISPR-based tools can be used to address other possible drivers of health disparities, such as poor vector-borne disease control. For example, CRISPR may reduce infectious disease transmission from vectors (living organisms), which cause 17% of all infectious diseases and 700 000 deaths annually worldwide.[38] This ability is illustrated by recent advances in CRISPR gene drives, which can knock out genes in entire populations of disease-causing organisms, allowing genetic modification of vectors at the population level.[24,39] This technology has already been shown in the laboratory to effectively block mosquitoes from transmitting malaria parasites,[40] potentially reducing the spread of malarial diseases that affect hundreds of millions of people worldwide.

Under ideal circumstances, CRISPR may also play a role in combating food insecurity in minority communities and developing nations through the development of CRISPR-Cas9–modified crops (e.g., pest-resistant fruits, high-yield soy and wheat)[41] and livestock (e.g., disease-resistant farm animals).[42] However, given the complex scientific, business, regulatory, and ethical issues surrounding CRISPR-based agriculture,[43] a more fulsome discussion is warranted[42–46] than this article can provide.

CRISPR AND HEALTH EQUITY

From a health equity perspective, although CRISPR may significantly advance science and health care, gene-editing technologies concurrently raise serious concerns about fairness, justice, and access for minority populations. The first concern is rooted in fundamental cause theory,[47] a well-established theory in the public health canon that states that health disparities persist in part because major advances in medicine and treatment overwhelmingly benefit society's advantaged over its disadvantaged.[47] Thus, when novel interventions emerge to reduce sickness or mortality (e.g., COVID-19 testing, vaccines, and therapeutics), individuals with higher social status—who possess greater resources to protect their health (e.g., money, power, knowledge)—have more access to these interventions than do those with minority status, who are often blocked from obtaining equal health-protective resources.[48,49]

Far from being a theoretical concern, many non-CRISPR gene therapies cost between $450 000 to $2 million per treatment,[50,51] with the gene therapies Hemgenix and Zolgensma costing $3.5 million and $2.1 million, respectively, per 1-time treatment.[52,53] These extraordinary costs place gene therapies primarily within the reach of society's most advantaged while excluding much of the population—including many individuals from historically disadvantaged groups who are traditionally denied access to essential social, economic, and health care institutions owing to their minoritized status.[54] Consequently, as novel CRISPR therapies enter the health care marketplace, current inequities in gene therapy access and benefits are likely to worsen because research has linked extreme medication pricing to (1) discriminatory insurance coverage,[55] (2) onerous reimbursement payee issues,[56] and (3) severe copay burdens that create high rates of medication noninitiation and abandonment.[57–59] For example, exa-cel—a CRISPR therapy for SCA expected to receive Food and Drug Administration approval in 2023[60]—is speculated to potentially exceed Hemgenix's pricing because of the $4 to $6 million cost of lifetime treatment for severe SCA.[61]

Beyond cost barriers, minority patients are also less likely to live in communities where cutting-edge CRISPR therapies will be accessible—in part owing to racial

segregation—and may have limited knowledge and awareness of these therapies upon their availability. Many of these differences in access, knowledge, and health are heavily rooted in structural racism,[16] which is regularly reinforced in health care through systemic actions such as racially biased doctoring and medical practices,[62] medical abuse in research (e.g., Tuskegee syphilis study),[16] and inadequate or biased distribution of health care resources.[63] Consequently, mirroring calls by scholars at the National Human Genome Research Institute,[5] it is critical that the equitable application of gene editing serve as the bedrock for all research seeking to move CRISPR research into human applications.[5]

Yet, achieving this goal requires addressing a second pressing concern—minorities' glaring underrepresentation in genomics and gene-editing research.[3] This gap is illustrated by a 2016 analysis that found that only 4% of participants in genome-wide association studies were of African, Hispanic/Latino, or Indigenous ancestry.[64] Although recent initiatives such as the NIH's All of Us study have set promising diversity targets, including 50% minority participation, these efforts have received strong criticism for their limited investment in providing meaningful benefits to minority groups for their participation.[65] Accordingly, without meaningfully engaging minorities across all stages of gene-editing research, CRISPR's entry into health care may create numerous health equity challenges.

Initially, CRISPR therapeutics designed without the active research involvement of minority populations may be unlikely to be maximally feasible or effective with minority patients. For example, the Population Architecture Using Genomics and Epidemiology study of 49 839 non-European individuals identified a number of health-relevant complex traits and risk alleles in minority individuals that were previously missed in Eurocentric genome-wide association studies.[7] This poses a concern because genetic architectures in minority and European ancestry populations potentially differ and so may reduce the efficacy of, or increase side effects for, minority patients treated with gene-editing therapies derived mainly from European ancestry samples[7]—thus introducing treatment risks and outcomes that could exacerbate health disparities and intensify mistrust.

Next, given minority populations' warranted cultural mistrust stemming from their historical underrepresentation and unethical treatment in health care and medical research, excluding these groups from meaningful inclusion in research is likely to reduce public acceptance and use of resulting CRISPR tools and therapies. This distrust will likely be especially powerful for DNA-altering technologies such as CRISPR owing to racism's enduring legacy in health care, as demonstrated by many African American communities' strong initial hesitancy toward mRNA vaccines, which triggered antivaccine beliefs and biology-related misinformation (e.g., vaccines cause biological changes affecting fertility and pregnancy).[66,67]

To increase CRISPR acceptance, researchers must therefore cultivate trust in gene editing through transparency and communication, making information accessible, relatable, and culturally relevant for minority groups.[10] However, this leads to a third challenge caused by minorities' limited inclusion in gene-editing research: communicating the benefits of, and combating misinformation about, novel CRISPR tools and therapies to minority patients, who often experience lower health literacy because of language barriers or lack of culturally appropriate health care messaging. To counteract this, health communication research must be firmly situated in the CRISPR research agenda to facilitate minority acceptance[10,68] and establish transparency and trust by identifying (1) their preferred communications strategies and formats (e.g., narratives, community endorsements); (2) culturally responsive and linguistically appropriate images, graphics, and language; and (3) cultural and structural barriers to using CRISPR tools and therapies.[69]

Unfortunately, even when minority groups are included in genomics research, history indicates their contributions can be exploited. In a notorious case, blood samples donated by members of the Havasupai Tribe for a study on diabetes risk were used without their consent by Arizona State University researchers to publish multiple genetic studies on tribal migration, mental disorders, alcoholism, and inbreeding.[70] As these topics were culturally taboo and several findings violated core tribal beliefs and myths, tribal members sued the university, winning a hefty financial settlement to address the harms caused by researchers' misuse of their genetic data.[71] As this case reveals, increasing minority representation alone is unlikely to prevent CRISPR-driven health equity problems from emerging unless researchers engage minority groups as informed power brokers and decision-makers through community-based participatory research (CBPR).

COMMUNITY-BASED PARTICIPATORY RESEARCH

CBPR is a widely accepted collaborative research approach that works to protect public health by equitably involving

all partners in the research process—bridging the gap between science and practice through community engagement and social action to promote health equity.[72] According to the NIH, community stakeholders should be fully involved in each research stage from conception to design, analysis, and dissemination, with stakeholders possessing equal voice, power, and decision-making capacity in all project aspects. Through this process, CBPR provides an avenue to reduce exploitation and ensure that minority groups benefit from their participation in gene-editing research, as minority communities are often interested in engaging in ethical research to address their health needs and problems, provided their concerns and voices are attended to in the research process.[15]

Integrating CBPR into gene-editing research carries several key scientific benefits. First, obtaining community involvement can lead to scientifically sounder research by facilitating the recruitment of hard-to-reach or hesitant minority populations into gene-editing studies and by generating findings and data with improved ecological validity. Second, giving minority communities a genuine voice in gene-editing research allows evidence generated through CBPR to be fed back to, vetted, and shaped by community members to tailor and design effective, community-accepted interventions for these groups,[73] increasing the likelihood of intervention feasibility and success. Third, CBPR builds greater trust and respect by stimulating active, participatory dialogue between CRISPR researchers and stakeholders, strengthening long-term research access, collaborations, and direct translation of interventions to minority communities.[5]

To provide a theoretical example of infusing CBPR into gene-editing research, CRISPR researchers studying SCA could engage minority communities as partners and stakeholders in several ways. First, they should approach institutions and organizations in these communities (e.g., churches, cultural organizations, historically Black colleges and universities) to serve as community partners and develop advisory boards consisting of patients with SCA, community leaders, and local clinicians to ensure that community needs and concerns are represented in the research agenda. Second, they should engage these partners and boards in providing feedback and insights on the research design (e.g., hypotheses, sampling and recruitment, analytic plan), coleading data collection activities, reviewing and interpreting results from a community and cultural perspective, and facilitating data dissemination efforts to participants, policymakers, and communities. Third, they should work with partners and boards to develop communication materials containing culturally responsive messaging (e.g., images, terms, narratives) to enhance community acceptance and uptake of ensuing CRISPR products. Although potentially requiring additional time and costs to complete, these efforts are justified by the increased likelihood that CRISPR tools and therapies shaped by CBPR will be more feasible for, accepted by, and effective in minority communities.

Promisingly, some of this work has already begun. In 2017, Persaud et al. engaged diverse SCA stakeholders (patients, parents, hematologists) in research to capture their perspectives toward participating in CRISPR clinical trials.[69] Stakeholders identified multiple barriers that researchers should address to engage patients in CRISPR trials, including fears involving possible complications from trial participation (e.g., infertility, increased disease severity, permanent genomic alterations), the high burdens of trial participation, and whether SCA therapies will equitably benefit their communities.[69] Stakeholders also provided pragmatic recommendations for promoting meaningful research engagement, including engaging SCA stakeholders in designing CRISPR trials; enacting transparency and open access to information about trial protocols, risks, and limitations; having greater community outreach and engagement including partnering with community-trusted brokers (e.g., family physicians); and creating and disseminating patient-centered communications through community-preferred channels (e.g., social media, news channels).[69] Through this work, researchers obtained essential information for promoting CRISPR clinical trial engagement in the SCA community.

Overall, to conduct effective CRISPR-CBPR work, researchers should engage community partners at the start to discuss the purpose, goals, and intended products of the desired research, and develop formal agreements as needed on issues of informed consent, recruitment, data ownership, dissemination, and equitable access to research products. Several Indigenous communities have already developed effective research guidelines, policies, and boards, providing community-supported pathways for engaging these communities—and their valuable genetic participation and data—in CRISPR research.[70,74] Claw et al.[15] have further proposed a framework containing key principles for engaging Indigenous populations in ethical genomics research that includes 4 CBPR principles recommended here that CRISPR researchers implement to perform ethical research

with minority groups: cultural competency, transparency, capacity building, and dissemination.

CONCLUSIONS

Given our incomplete knowledge about the long-term effects of CRISPR on health equity and the human body,[4] researchers and funders must carefully consider the ethical and real-world implications of allowing these technologies to be implemented at scale in public health and medicine.[4] If health equity is an essential value underpinning health care and public health, CRISPR research must be made equitable by engaging minority groups as informed stakeholders and decision-makers to ensure that resulting CRISPR tools and therapies are relevant and accessible for populations experiencing health disparities. This includes deciding who gets access to treatments and which diseases are targeted (i.e., selection of investment). However, without appropriate guideposts and mandates from funders and organizations (e.g., NIH, APHA) to center health equity in gene-editing research,[10] it is unclear whether CRISPR developers will focus their investments on treating high-impact genetic diseases that carry the greatest public health impact or merely the most profitable ones.[50]

Unfortunately, neither the APHA's Health Equity Fact Sheets[75] nor the AMA's Health Equity Strategic Plan[76] presently address issues of equity and inclusion in genomic medicine. More positively, the recent Third International Summit on Human Genome Editing[77] encouraged gene-editing equity and access for underserved populations and countries, urging global commitments to advance "equitable, financially sustainable, and accessible treatments" and research that "includes more genetically diverse populations and expanding the range of those who conceive and conduct the research."[78]

Consequently, researchers and community stakeholders should collaboratively develop frameworks and processes to guide CRISPR researchers in promoting health equity through inclusion, community engagement, ethical oversight, and transparency, as it is unlikely health equity will be advanced without strong commitments by all partners to the ideals of justice, fairness, and equitable access in gene editing. However, because the field of equitable genomics remains in its infancy,[5] without meaningful inclusion of minority communities and clear guidelines and principles to assist researchers and health professionals in conducting ethical, community-partnered gene-editing research, innovative CRISPR tools and therapies are likely to result in inequitable access to precision medicine for minority populations—reifying existing health disparities for those suffering society's highest burden of disease.[7] AJPH

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REFERENCES

1. Doudna JA. Genomic engineering and the future of medicine. *JAMA.* 2015;313(8):791. https://doi.org/10.1001/jama.2015.287
2. JAMA Network. Gene Editing Using CRISPR. Why the Excitement? August 29, 2017. Available at: https://jamanetwork.com/journals/jama/article-abstract/2646800?casa_token=pakCcJ9lAjkAAAAA:TK7IHrBDoM3FxtLXDrLWFFKRNq7jL9h5l_oZJ_ftloFW42EBW63THK1_gQlgH7rIUS7HOC1gf94. Accessed December 24, 2022.
3. Hildebrandt CC, Marron JM. Justice in CRISPR/Cas9 research and clinical applications. *AMA J Ethics.* 2018;20(9):826–833. https://doi.org/10.1001/amajethics.2018.826
4. Baylis F. *Altered Inheritance: CRISPR and the Ethics of Human Genome Editing.* Cambridge, MA: Harvard University Press; 2019. https://doi.org/10.4159/9780674241954
5. Jooma S, Hahn MJ, Hindorff LA, Bonham VL. Defining and achieving health equity in genomic medicine. *Ethn Dis.* 2019;29(suppl 1):173–178. https://doi.org/10.18865/ed.29.S1.173
6. Clyde D. Making the case for more inclusive GWAS. *Nat Rev Genet.* 2019;20(9):500–501. https://doi.org/10.1038/s41576-019-0160-0
7. Wojcik GL, Graff M, Nishimura KK, et al. Genetic analyses of diverse populations improves discovery for complex traits. *Nature.* 2019;570(7762):514–518. https://doi.org/10.1038/s41586-019-1310-4
8. Coller BS. Ethics of human genome editing. *Annu Rev Med.* 2019;70:289–305. https://doi.org/10.1146/annurev-med-112717-094629
9. Committee on Human Gene Editing. *Human Genome Editing: Science, Ethics, and Governance.* Washington, DC: National Academies Press; 2017. https://doi.org/10.17226/24623
10. Feliú-Mójer MI. Gene editing communication must center marginalized communities. *Environ Commun.* 2020;14(7):877–880. https://doi.org/10.1080/17524032.2020.1812274
11. Braveman PA, Kumanyika S, Fielding J, et al. Health disparities and health equity: the issue is justice. *Am J Public Health.* 2011;101(suppl 1):S149–S155. https://doi.org/10.2105/AJPH.2010.300062
12. Braveman P. What are health disparities and health equity? We need to be clear. *Public Health Rep.* 2014;129(1, suppl 2):5–8. https://doi.org/10.1177/00333549141291S203
13. American Public Health Association. Creating the healthiest nation: advancing health equity. 2017. Available at: https://www.apha.org/-/media/files/pdf/factsheets/advancing_health_equity.ashx. Accessed March 6, 2020.
14. Centers for Disease Control and Prevention. Health disparities. October 4, 2022. Available at: https://www.cdc.gov/healthyyouth/disparities/index.htm. Accessed December 22, 2022.
15. Claw KG, Anderson MZ, Begay RL, Tsosie KS, Fox K, Garrison NA. A framework for enhancing

ethical genomic research with Indigenous communities. *Nat Commun.* 2018;9(1):2957. https://doi.org/10.1038/s41467-018-05188-3

16. Bhopal R. Spectre of racism in health and health care: lessons from history and the United States. *BMJ.* 1998;316(7149):1970–1973. https://doi.org/10.1136/bmj.316.7149.1970
17. Hsu PD, Lander ES, Zhang F. Development and applications of CRISPR-Cas9 for genome engineering. *Cell.* 2014;157(6):1262–1278. https://doi.org/10.1016/j.cell.2014.05.010
18. Waryah CB, Moses C, Arooj M, Blancafort P. Zinc fingers, TALEs, and CRISPR systems: a comparison of tools for epigenome editing. In: Jeltsch A, Rots MG, eds. *Epigenome Editing: Methods and Protocols.* New York: NY: Springer; 2018:19–63. https://doi.org/10.1007/978-1-4939-7774-1_2
19. Wirth T, Parker N, Ylä-Herttuala S. History of gene therapy. *Gene.* 2013;525(2):162–169. https://doi.org/10.1016/j.gene.2013.03.137
20. Turocy J, Adashi EY, Egli D. Heritable human genome editing: research progress, ethical considerations, and hurdles to clinical practice. *Cell.* 2021;184(6):1561–1574. https://doi.org/10.1016/j.cell.2021.02.036
21. Ginn SL, Amaya AK, Alexander IE, Edelstein M, Abedi MR. Gene therapy clinical trials worldwide to 2017: an update. *J Gene Med.* 2018;20(5):e3015. https://doi.org/10.1002/jgm.3015
22. Marchant GE. Global governance of human genome editing: what are the rules? *Annu Rev Genomics Hum Genet.* 2021;22:385–405. https://doi.org/10.1146/annurev-genom-111320-091930
23. Stein R. Experts weigh medical advances in gene-editing with ethical dilemmas. March 6, 2023. Available at: https://www.npr.org/sections/health-shots/2023/03/06/1158705095/genome-summit-gene-editing-ethics-crspr. Accessed April 4, 2023.
24. Wollert D. The fascinating & controversial new science of CRISPR. *Am Biol Teach.* 2020;82(5):279–288. https://doi.org/10.1525/abt.2020.82.5.279
25. Doudna JA, Charpentier E. The new frontier of genome engineering with CRISPR-Cas9. *Science.* 2014;346(6213):1258096. https://doi.org/10.1126/science.1258096
26. Park SH, Lee CM, Deshmukh H, Bao G. Therapeutic Crispr/Cas9 genome editing for treating sickle cell disease. December 2, 2016. Available at: https://ashpublications.org/blood/article/128/22/4703/101474/Therapeutic-Crispr-Cas9-Genome-Editing-for. Accessed December 16, 2020.
27. Centers for Disease Control and Prevention. Data & statistics on sickle cell disease. May 2, 2022. Available at: https://www.cdc.gov/ncbddd/sicklecell/data.html. Accessed March 3, 2023.
28. Baffoe-Bonnie MS. A justice-based argument for including sickle cell disease in CRISPR/Cas9 clinical research. *Bioethics.* 2019;33(6):661–668. https://doi.org/10.1111/bioe.12589
29. National Institutes of Health. Stem cell transplant reverses sickle cell disease in adults. May 14, 2015. Available at: https://www.nih.gov/news-events/nih-research-matters/stem-cell-transplant-reverses-sickle-cell-disease-adults. Accessed March 3, 2023.
30. Kaiser J. Tweaking genes with CRISPR or viruses fixes blood disorders. *Science.* 2020;370(6522):1254–1255. https://doi.org/10.1126/science.370.6522.1254
31. Frangoul H, Altshuler D, Cappellini MD, et al. CRISPR-Cas9 gene editing for sickle cell disease and β-thalassemia. *N Engl J Med.* 2021;384(3):252–260. https://doi.org/10.1056/NEJMoa2031054
32. Locatelli F, Lang P, Li A, et al. Efficacy and safety of a single dose of exagamglogene autotemcel for transfusion-dependent β-thalassemia. *Blood.* 2020;140(suppl 1):4899–4901.
33. Bonham VL, Smilan LE. Somatic genome editing in sickle cell disease: rewriting a more just future. *North Carol Law Rev.* 2018;97:1093.
34. Smith LA, Oyeku SO, Homer C, Zuckerman B. Sickle cell disease: a question of equity and quality. *Pediatrics.* 2006;117(5):1763–1770. https://doi.org/10.1542/peds.2005-1611
35. Grosse SD, Schechter MS, Kulkarni R, Lloyd-Puryear MA, Strickland B, Trevathan E. Models of comprehensive multidisciplinary care for individuals in the United States with genetic disorders. *Pediatrics.* 2009;123(1):407–412. https://doi.org/10.1542/peds.2007-2875
36. Yang IA, Fong KM, Zimmerman PV, Holgate ST, Holloway JW. Genetic susceptibility to the respiratory effects of air pollution. *Thorax.* 2008;63(6):555–563. https://doi.org/10.1136/thx.2007.079426
37. Storch GA. CRISPR tool scales up to interrogate a huge line-up of viral suspects. *Nature.* 2020;582(7811):188–189. https://doi.org/10.1038/d41586-020-01447-w
38. World Health Organization. Vector-borne diseases. March 2, 2020. Available at: https://www.who.int/news-room/fact-sheets/detail/vector-borne-diseases. Accessed July 20, 2021.
39. Vigliotti VS, Martinez I. Public health applications of CRISPR: how children's health can benefit. *Semin Perinatol.* 2018;42(8):531–536. https://doi.org/10.1053/j.semperi.2018.09.017
40. Adolfi A, Gantz VM, Jasinskiene N, et al. Efficient population modification gene-drive rescue system in the malaria mosquito *Anopheles stephensi*. *Nat Commun.* 2020;11(1):5553. https://doi.org/10.1038/s41467-020-19426-0
41. Molteni M. CRISPR can help solve our looming food crisis—here's how. *Wired*. August 8, 2019. Available at: https://www.wired.com/story/gene-editing-food-climate-change. Accessed July 20, 2021.
42. Singh P, Ali SA. Impact of CRISPR-Cas9-based genome engineering in farm animals. *Vet Sci.* 2021;8(7):122. https://doi.org/10.3390/vetsci8070122
43. Menchaca A, dos Santos-Neto PC, Mulet AP, Crispo M. CRISPR in livestock: from editing to printing. *Theriogenology.* 2020;150:247–254. https://doi.org/10.1016/j.theriogenology.2020.01.063
44. Chen K, Wang Y, Zhang R, Zhang H, Gao C. CRISPR/Cas genome editing and precision plant breeding in agriculture. *Annu Rev Plant Biol.* 2019;70:667–697. https://doi.org/10.1146/annurev-arplant-050718-100049
45. Zhu H, Li C, Gao C. Applications of CRISPR–Cas in agriculture and plant biotechnology. *Nat Rev Mol Cell Biol.* 2020;21(11):661–677. https://doi.org/10.1038/s41580-020-00288-9
46. Lamas-Toranzo I, Guerrero-Sánchez J, Miralles-Bover H, Alegre-Cid G, Pericuesta E, Bermejo-Álvarez P. CRISPR is knocking on barn door. *Reprod Domest Anim.* 2017;52(suppl 4):39–47. https://doi.org/10.1111/rda.13047
47. Link BG, Phelan J. Social conditions as fundamental causes of disease. *J Health Soc Behav.* 1995;Spec no.:80–94. https://doi.org/10.2307/2626958
48. Saegert S, Fields D, Libman K. Mortgage foreclosure and health disparities: serial displacement as asset extraction in African American populations. *J Urban Health.* 2011;88(3):390–402. https://doi.org/10.1007/s11524-011-9584-3
49. Phelan JC, Link BG, Tehranifar P. Social conditions as fundamental causes of health inequalities: theory, evidence, and policy implications. *J Health Soc Behav.* 2010;51(1, suppl):S28–S40. https://doi.org/10.1177/0022146510383498
50. Sherkow JS. CRISPR, patents, and the public health. *Yale J Biol Med.* 2017;90(4):667–672.
51. Wilson RC, Carroll D. The daunting economics of therapeutic genome editing. *CRISPR J.* 2019;2(5):280–284. https://doi.org/10.1089/crispr.2019.0052
52. Tanne JH. FDA approves $3.5m gene therapy for adults with haemophilia B. *BMJ.* 2022;379:o2858. https://doi.org/10.1136/bmj.o2858
53. Wertheimer AI. The world's priciest medicine. *J Pharm Health Serv Res.* 2019;10(3):269–270. https://doi.org/10.1111/jphs.12318
54. Subica AM, Link BG. Cultural trauma as a fundamental cause of health disparities. *Soc Sci Med.* 2022;292:114574. https://doi.org/10.1016/j.socscimed.2021.114574
55. Gruber J. The genetic revolution highlights the importance of nondiscriminatory and comprehensive health insurance coverage. *Am J Bioeth.* 2019;19(10):10–11. https://doi.org/10.1080/15265161.2019.1644822
56. Naveed A, Calderon H. Onasemnogene abeparvovec (AVXS-101) for the treatment of spinal muscular atrophy. *J Pediatr Pharmacol Ther.* 2021;26(5):437–444. https://doi.org/10.5863/1551-6776-26.5.437
57. Gleason P, Starner CI, Gunderson BW, Schafer JA, Sarran HS. Association of prescription abandonment with cost share for high-cost specialty pharmacy medications. *J Manag Care Pharm.* 2009;15(8):648–658. https://doi.org/10.18553/jmcp.2009.15.8.648
58. Dusetzina SB, Huskamp HA, Rothman RL, et al. Many Medicare beneficiaries do not fill high-price specialty drug prescriptions. *Health Aff (Millwood).* 2022;41(4):487–496. https://doi.org/10.1377/hlthaff.2021.01742
59. Doshi JA, Li P, Huo H, Pettit AR, Armstrong KA. Association of patient out-of-pocket costs with prescription abandonment and delay in fills of novel oral anticancer agents. *J Clin Oncol.* 2018;36(5):476–482. https://doi.org/10.1200/JCO.2017.74.5091
60. Stein R. Sickle cell patient's success with gene editing raises hopes and questions. March 16, 2023. Available at: https://www.npr.org/sections/health-shots/2023/03/16/1163104822/crispr-gene-editing-sickle-cell-success-cost-ethics. Accessed April 4, 2023.
61. Liu A. Vertex teases launch plans for first CRISPR gene editing therapy ahead of FDA decision. February 8, 2023. Available at: https://www.fiercepharma.com/marketing/vertex-teases-launch-plan-first-crispr-gene-editing-therapy-ahead-fda-decision. Accessed April 4, 2023.
62. Matthew DB. Just medicine: a cure for racial inequality in American health care. 2015. Available at: https://www.jstor.org/stable/j.ctt15zc6c8. Accessed December 27, 2022.
63. Douglas JA, Subica AM. COVID-19 treatment resource disparities and social disadvantage in New York City. *Prev Med.* 2020;141:106282. https://doi.org/10.1016/j.ypmed.2020.106282
64. Popejoy AB, Fullerton SM. Genomics is failing on diversity. *Nature.* 2016;538(7624):161–164. https://doi.org/10.1038/538161a

65. Fox K. The illusion of inclusion—the "All of Us" research program and Indigenous Peoples' DNA. *N Engl J Med.* 2020;383(5):411–413. https://doi.org/10.1056/NEJMp1915987
66. Hsu AL, Johnson T, Phillips L, Nelson TB. Sources of vaccine hesitancy: pregnancy, infertility, minority concerns, and general skepticism. *Open Forum Infect Dis.* 2022;9(3):ofab433. https://doi.org/10.1093/ofid/ofab433
67. Frisco ML, Van Hook J, Thomas KJA. Racial/ethnic and nativity disparities in US COVID-19 vaccination hesitancy during vaccine rollout and factors that explain them. *Soc Sci Med.* 2022;307:115183. https://doi.org/10.1016/j.socscimed.2022.115183
68. Murphy ST, Frank LB, Chatterjee JS, et al. Comparing the relative efficacy of narrative vs nonnarrative health messages in reducing health disparities using a randomized trial. *Am J Public Health.* 2015;105(10):2117–2123. https://doi.org/10.2105/AJPH.2014.302332
69. Persaud A, Desine S, Blizinsky K, Bonham VL. A CRISPR focus on attitudes and beliefs toward somatic genome editing from stakeholders within the sickle cell disease community. *Genet Med.* 2019;21(8):1726–1734. https://doi.org/10.1038/s41436-018-0409-6
70. Garrison NA. Genomic justice for Native Americans: impact of the Havasupai case on genetic research. *Sci Technol Human Values.* 2013;38(2):201–223. https://doi.org/10.1177/0162243912470009
71. Sterling RL. Genetic research among the Havasupai: a cautionary tale. *AMA J Ethics.* 2011;13(2):113–117. https://doi.org/10.1001/virtualmentor.2011.13.2.hlaw1-1102
72. Viswanathan M, Ammerman A, Eng E, et al. Community-based participatory research: assessing the evidence: summary. 2004. Available at: https://www.ncbi.nlm.nih.gov/sites/books/NBK11852. Accessed July 30, 2022.
73. Subica AM, Brown BJ. Addressing health disparities through deliberative methods: citizens' panels for health equity. *Am J Public Health.* 2020;110(2):166–173. https://doi.org/10.2105/AJPH.2019.305450
74. Hudson M, Garrison NA, Sterling R, et al. Rights, interests and expectations: Indigenous perspectives on unrestricted access to genomic data. *Nat Rev Genet.* 2020;21(6):377–384. https://doi.org/10.1038/s41576-020-0228-x
75. American Public Health Association. Health equity. Available at: https://www.apha.org/topics-and-issues/health-equity. Accessed July 20, 2021.
76. American Medical Association. The AMA's strategic plan to embed racial justice and advance health equity. Available at: https://www.ama-assn.org/about/leadership/ama-s-strategic-plan-embed-racial-justice-and-advance-health-equity. Accessed July 20, 2021.
77. Royal Society. Third International Summit on Human Genome Editing. March 2023. Available at: https://royalsociety.org/science-events-and-lectures/2023/03/2023-human-genome-editing-summit. Accessed April 4, 2023.
78. Royal Society. Statement from the Organising Committee of the Third International Summit on Human Genome Editing. March 2023. Available at: https://royalsociety.org/news/2023/03/statement-third-international-summit-human-genome-editing. Accessed April 4, 2023.