

National Council on Disability  
Topic: Germline editing, fetal medicine, and their impact on people with disabilities  
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Public Comment

Commenter:

Susan Klugman, MD, FACMG, FACOG, President, American College of Medical Genetics and Genomics (ACMG)

ACMG Public Comment:

On behalf of the American College of Medical Genetics and Genomics, or ACMG, I thank you for the opportunity to provide comments on germline editing and its impact on people with disabilities.

The ACMG is a prominent authority in the field of medical genetics and genomics and the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics. ACMG represents the full spectrum of medical genetics disciplines in the United States and provides education, resources, and a voice for more than 2,600 clinical and laboratory geneticists, genetic counselors, and other healthcare professionals. ACMG's mission is to improve health through the clinical and laboratory practice of medical genetics as well as through advocacy, education, and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health.

The ACMG is committed to ensuring that medical genetics principles are addressed appropriately and with equity in our policies, procedures, and guidelines that inform the field of medical genetics. Medical geneticists provide diagnosis, counseling, management, and treatment for individuals and families affected by genetic disorders. Advances in genome editing technologies could offer significant changes to the way we alleviate the pathology of genetic conditions. Further, high-risk pregnancies and miscarriage disproportionately affect disabled and chronically ill people, challenges for which genome editing may offer solutions.

However, limitations, such as off-target effects, must be addressed prior to clinical application. This requires the ability to demonstrate that the desired change can be made without introduction of aberrant genetic variations. This is especially concerning when it comes to germline editing as potential adverse effects could have far-reaching consequences that could take years or even decades to recognize and could impact future generations. Further, the consequences of editing a pathogenic variant may have unknown epigenetic effects that may alter normal patterns of gene expression in some tissues.

We also must recognize the wide array of genetic conditions with varying pathologies that range from mild to devastating effects on health and well-being of individuals. The decision as to which specific genetic variants should be subject to genome editing needs further discussion at a societal level, including adequate representation from the disability community. Some variants that are associated with highly penetrant disorders with major adverse effects on health and quality of life might seem like compelling candidates for therapeutic editing. It is inevitable, however, that consideration will also be

given to editing variants associated with phenotypes that are not fully penetrant and for which effects on quality of life are less clear.

In 2017, the ACMG published a statement on genome editing and clinical genetics that highlighted these concerns. It remains current that the risks associated with gene editing must be balanced with the potential benefits of alleviating severe pathologies associated with a condition. As technologies for editing the human genome continue to rapidly advance, there will undoubtedly be pressure to apply it clinically. The significance and potential impact of this should not be underestimated, and the ACMG continues to encourage broad public debate regarding the clinical application of genome editing. We also must be cognizant of and learn from history to ensure that genetic and genomic technologies are applied ethically and in such a way that does not contribute to eugenics, racism, inequities, or discrimination, the history of which was recently reviewed in a detailed statement from the American Society of Human Genetics, the professional association representing genetics in research.

The ACMG appreciates the Council's attention to this topic and looks forward to further engagement on the topic of clinical applications of genome editing. For additional information or questions, please contact Dr. Michelle McClure, ACMG Director of Public Policy, at [mmcclure@acmg.net](mailto:mmcclure@acmg.net).