Ethics and Economics of Genome Editing

Srija Chaudhuri
Upper Dublin High School

Abstract
Somatic and germline modifications are the two types of genetic modifications that can be performed on human cells. Somatic modifications have earned ethical approval and are being implemented in healthcare as gene therapy, treating conditions such as sickle cell disease. Germline modifications have not earned the same approval and are highly regulated in the research sector of some countries with multiple countries banning the modification type altogether. Germline editing is criticized for being unsafe, not allowing patients to give informed consent, and promoting ableism. Moreover, if germline editing procedures become available but are not affordable for everyone, having a genetic disease could become an indication of a lower financial status. Regardless, the modification type can offer individuals with incurable genetic diseases a way to eliminate the suffering their future generations may endure. Consistent regulation of germline editing between countries, including outlining the difference between disease treatment and trait enhancement, is critical to avoid the abuse of the treatment through jurisdictional arbitrage. In this review, countries were analyzed based on their number of common monogenic diseases of high occurrence and their GDP per capita to determine which nations may become centers of germline editing exploitation for clinical testing and economic beneficiaries of performing germline editing procedures.

Introduction
New genetic modification techniques allow for the rise of new types of medical treatments. These treatments include modifying both somatic (non-reproductive) and germline (reproductive) human cells. While these treatments are regulated differently and still require testing in terms of their safety and effectiveness, other aspects of using genetic modifications as treatments to consider are if changing a human's genes or genome is ethical and how inconsistencies of genetic modification regulation between countries will affect the international healthcare industry.

Somatic and Germline Genetic Modifications
There are two types of genetic modifications that can be performed

directly on human cells, somatic and germline modifications. Somatic modifications, also known as gene therapy, are used to edit genes of specific non-reproductive cell types (Bergman, 2019). This method can be used to silence, replace, or introduce genes to a patient's cells, allowing for the targeting of the root cause of the disease (Cleveland Clinic, 2023). Gene therapy can be conducted in vivo or ex vivo. In vivo is when a gene is delivered to a patient's cells within their body, while ex vivo is when a patient's cells are genetically modified outside of the body and then returned to the body (Children's Hospital of Philadelphia, 2024). Gene changes resulting from somatic modifications are not passed onto the offspring of the patient, which means the patient's child can inherit their parent's genetic condition (Bergman, 2019). The price of therapy depends on the disease being treated, with the average one-time treatment costing close to $2.3 million (Buntz, 2024). Currently, gene therapies are used to treat genetic diseases such as sickle cell disease, spinal muscular atrophy, and inherited retinal dystrophies (Food and Drug Administration, 2024). Therapies are also used to treat some cancers and HIV/AIDS (*Is Gene Therapy Available to Treat My Disorder?: MedlinePlus Genetics*, 2022). By 2035, 1.09 million patients are anticipated to have received gene therapy (Wong et al., 2021).

Gene therapy regulation varies between countries, with most nations highly regulating it. For example, in the United States, the modification method is highly regulated, with 40 therapies approved by the U.S. Food and Drug Administration and hundreds more therapies in the clinical trial stage (Food and Drug Administration, 2024; Genetic Literacy Project, 2020). Gene therapies utilizing the newer, more precise CRISPR-Cas system are especially regulated compared to viral vector-based therapies (Broad Institute, 2018).

Germline modifications, or germline editing, involve editing the genes of sperm or egg cells or early embryos. As a result, the genetic changes made to these cells are replicated in all of the new cells of the organism. Since genetic changes resulting from germline editing are passed onto future generations of the patient, these modifications can be used to correct mutations in a person's genome and therefore permanently remove genetic diseases for the person's posterity (Bergman, 2019).

Germline editing regulation, like gene therapy regulation, also varies between nations. Some countries, such as Canada and Sweden, have banned germline editing completely. Other countries, such as the United States, United Kingdom, and China, highly regulate the modification method, limiting its use solely to research purposes. Many countries prohibit reproductive germline editing and do not have relevant information on non-reproductive germline editing. Factors that affect whether or not a country permits germline editing include the country's laws, the availability of funding, and access to equipment for

such research. In the United States, research is allowed if it is privately funded but not publicly funded. Similar research is permitted in the United Kingdom given researchers obtain a license from the Human Fertilisation and Embryology Authority. In China, researchers must obtain approval from an ethics committee prior to conducting research (Baylis et al., 2020).

Risks of Genetic Modifications

Similar to traditional medical treatments, somatic and germline modifications carry risks, such as being unsuccessful or having side effects. With the two types of treatments being new and germline editing having limited research, the long-term effects are unknown. Since genetic modifications involve introducing foreign material to the body, the new material may trigger an immune response (Cleveland Clinic, 2023).

Additionally, both genetic modification methods may result in off-target edits or off-target impacts, which are risks specific to modifying cells as opposed to any other type of treatment (*What Are the Ethical Concerns of Genome Editing?*, 2017). Off-target edits are when the incorrect gene is modified, resulting in unintended genetic mutations. Scientists have recently developed and are currently working on methods to reduce the chances of an off-target edit (Asmamaw Mengstie et al., 2024). Off-target impacts may include the alteration of one gene causing a problem in another gene. A risk particular to germline editing is mosaicism, which is when not all copies of a gene are successfully modified. As a result, the organism will have some cells with the modified gene and some cells without it. Such an issue could occur if an early embryo is modified as opposed to if a germline cell is modified (Bergman, 2019). Although the severity of the effects of mosaicism depends on which gene is inconsistent between the organism's cells, mosaicism could result in developmental abnormalities (Mehravar et al., 2019). More research needs to be done to better understand the extent of the risks of genetic modifications.

Ethics of Genetic Modifications

Aside from these risks, an important concern is if modifying one's genes, whether the modified cells are somatic or germline, is ethical.

Most scientists consider gene therapy as ethical, which is why the U.S. Food and Drug Administration approved the treatment and supports further research into it (University of Missouri School of Medicine, 2019). Gene therapy provides patients with incurable genetic diseases a potentially effective treatment option. Despite the risks of this practice, gene therapy can provide patients and doctors with an optimistic treatment outlook (Cleveland Clinic, 2023).

On the other hand, germline editing has not garnered the same support. In 2018, a Chinese scientist was imprisoned for three years

after using the CRISPR-Cas system to genetically modify embryos to give them HIV immunity. Even today, the same procedure would not be permitted in any country (Sadeghi, 2023).

Those against germline editing are concerned with the permanence of the modification, since the genetic change is not reversible and will be passed onto future generations. Modifying a person's genome for more desirable traits can reduce the gene pool, decreasing genetic diversity and lessening humans' ability to evolve (Joseph et al., 2022). Additionally, germline editing is performed on sperm or egg cells or embryos, so critics of this modification type contend that those who undergo the modification are unable to give informed consent and therefore are not given the freedom of choice (Joseph et al., 2022; *What Are the Ethical Concerns of Genome Editing?*, 2017).

Supporters of germline editing argue that the purpose of such a procedure is to remove genetic diseases, so the modification's permanence would be beneficial to the patient and future generations. In this way, the patient and future generations would avoid the suffering and financial burdens that result from an incurable genetic disease. Moreover, the parents who are opting to have their gamete cells or embryos modified are giving informed consent for their future child, similar to how a surrogate would make a decision for a patient who is unable to make decisions for themself.

While germline editing can offer a generational cure, such a procedure will not be affordable to everyone (Bergman, 2019). All treatments come with a cost, and those who are unable to pay for their treatment must continue to endure the suffering that results from their condition. In the case of germline editing, parents may not be able to afford the germline modification to cure the genetic disease that their future child will have. As a result, the child will be born with the genetic disease, and their disease may be an indication of their and their parents' economic situation. In other words, in the availability of a germline editing procedure, having a genetic disease could become a sign of a lower financial status (*What Are the Ethical Concerns of Genome Editing?*, 2017).

Additionally, by making germline editing possible, those who exhibit traits of "bad genes" could face more social inequality, such as in the form of ableism (Sufian & Garland-Thomson, 2021). Such discrimination used to occur during the employment process, where employers would refuse to hire those with a family history of genetic conditions or required potential employees to pass a genetic test before being hired (Slaughter, 2008). As recently as 2009, government organizations, such as the Equal Employment Opportunity Commission in the United States, outlawed discrimination based on genetic information in the workplace (U.S. Equal Employment Opportunity Commission, 2009). If germline editing is portrayed as a cure for genetic disorders, social views against genetic disorders could be

intensified and result in a surge in discrimination against those with them.

A more extreme version of this discrimination involves promoting eugenics. Eugenics movements held global influence in the 20th century, when selective breeding of humans was used to prevent individuals of certain races or with disabilities from passing on their traits (National Human Genome Research Institute, 2022). Germline editing, a form of selective breeding, could bring back similar sentiments on which traits are suitable to be passed down. By genetically modifying humans so they do not have undesirable traits, which includes removing genetic disorders, the genetics of the human race might be considered "improved" (University of Missouri School of Medicine, 2019).

Another major ethical consideration with germline editing is the extent to which the modification of a person's genome is considered disease treatment as opposed to trait enhancement (Bergman, 2019). Using germline editing to cure a genetic disorder like sickle cell disease may seem obvious, but using germline editing to cure a genetic disorder like color blindness may not be approved since color blindness does not affect a person's daily life as severely. In other words, curing color blindness could be considered trait (vision) enhancement.

Furthermore, as scientists are able to identify the places on the genome that code for each gene, it may become possible to alter a person's genes to make them more intelligent or more athletic. The term "designer baby" will be taken to a level of trait enhancement beyond ensuring that a child does not have genes associated with disease (Veit, 2018). If only wealthy individuals can afford genetic enhancements, a society where the rich have superior traits could worsen social divides. Additionally, designer babies will result in a decline in human diversity and the acceptance of such diversity. Germline editing can be a vital tool to reduce the suffering and costs those with genetic diseases face, but strict regulation is crucial upon the approval of this powerful practice. Without sufficient regulation between countries, a societal divide could be catalyzed by taking advantage of inconsistencies between countries.

Regulation of Germline Editing

Despite all of the safety and ethical considerations of germline editing, the practice is not entirely banned everywhere. While the treatment is not ready to be implemented, governments of some countries permit research on germline editing. Furthermore, governments of different countries have different levels of regulation on the practice. The use of germline editing will not be avoidable in the future, and the companies currently conducting research on the practice will have an economic advantage when the treatment is approved for clinical use. This economic advantage will be a result of jurisdictional arbitrage.

Jurisdictional arbitrage involves taking advantage of more favorable policies in another jurisdiction (*Jurisdictional Arbitrage*, 2024). For instance, if a certain medical treatment is banned in one country but legal or unregulated in another, companies can administer the treatment in the country where it is legal or unregulated. As a result, those who need the procedure and can afford it will travel to the country where the treatment is legal or unregulated to receive it. The economic advantage comes from companies conducting research on the treatment and eventually profiting from administering it in the countries where it is legal or unregulated. In the case of germline editing, companies will research and perform germline modifications in nations that have more lenient regulations. Even though people may have to travel to another country to have their future child genetically modified, many will likely take advantage of this practice, allowing the countries with more flexible regulations to profit. Countries with no policies regarding germline editing in place may also become centers where these modifications are conducted on humans. Examples of such countries are Peru, South Africa, and Vietnam (Baylis et al., 2020). The limited regulation in these countries will allow companies and patients to perform and receive human embryo modifications.

Similarly, even if multiple countries approve the germline editing treatment, there may not be a consensus of what is considered disease treatment and what is considered trait enhancement. An inconsistency between regulations will result in those who are unable to get a certain modification in one country traveling to another country where they can get that modification.

Demographics of Most Common Monogenic Diseases and Potential Germline Editing Involvement of Countries

Genetic diseases can be classified as monogenic, polygenic, or chromosomal. Monogenic diseases are caused by a single gene mutation, and polygenic diseases are caused by multiple gene mutations. Chromosomal diseases are a result of abnormal chromosome arrangements during early development (Cram & Zhou, 2016). Nearly 10,000 genetic diseases are monogenic. These monogenic diseases, although considered rare, affect 1 out of every 100 people. Some of the most common monogenic diseases include Achondroplasia, Beta-thalassemia, Cystic Fibrosis, Huntington's Disease, Sickle Cell Disease, and Hemophilia (Genehome, 2021).

To evaluate the potential market for germline editing treatments, the prevalence of the six listed monogenetic diseases and gross domestic product (GDP) per capita in U.S. dollars (USD) were evaluated by country. The prevalence of the diseases indicates the demand for germline editing treatments, while the GDP per capita indicates the average person’s ability to afford a germline editing treatment. Countries with a larger number of monogenic diseases and a

lower GDP per capita were identified as being at risk of germline editing exploitation for clinical testing since they have a high demand for germline editing treatments and a lesser ability to enforce clinical testing regulations. Countries with a larger number of monogenic diseases and a higher GDP per capita were identified as having a higher economic opportunity of performing germline editing treatments since they have a high demand for such treatments and the ability to afford them.

Monogenic Germline Editing Exploitation and Economic Opportunity

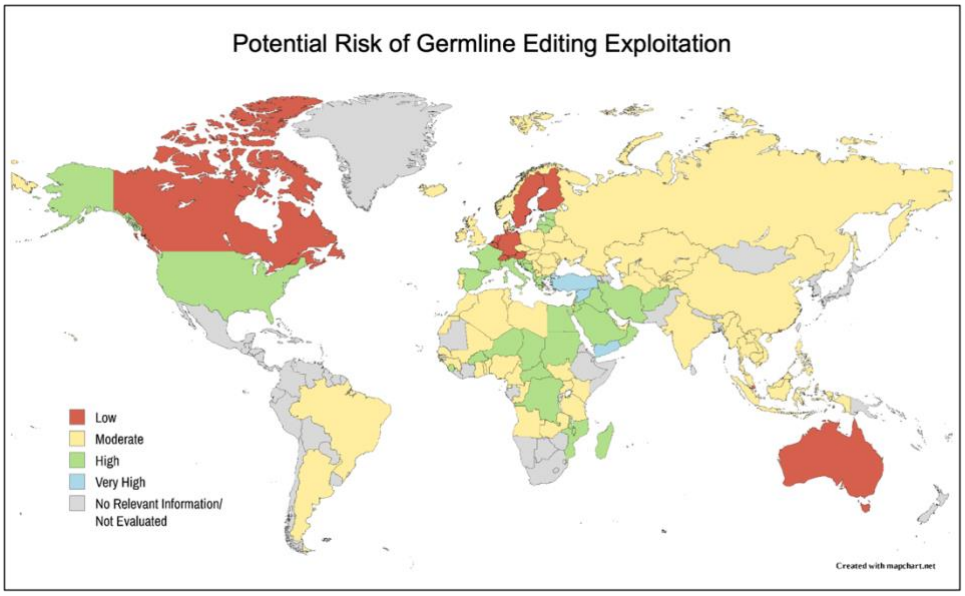

FIGURE 1. Map of countries colored by potential risk of germline editing exploitation for clinical testing. A country's risk increases as the country has a larger number of common monogenic diseases of high occurrence and as the country's GDP per capita decreases. A larger number of monogenic diseases indicates a greater demand for germline editing treatments, and a lower GDP per capita indicates a lesser ability to enforce clinical testing regulations.

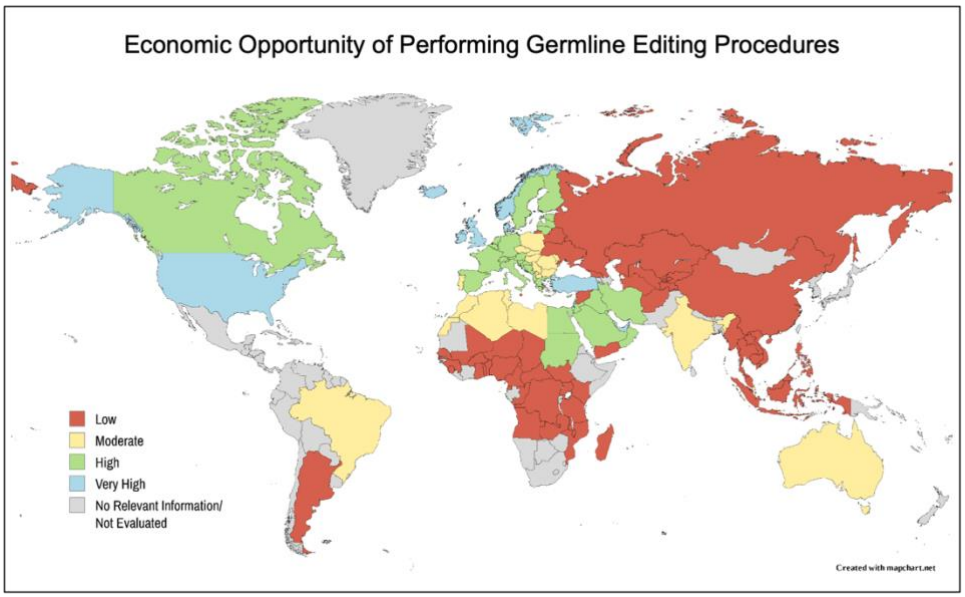

FIGURE 2. Map of countries colored by economic opportunity of performing germline editing treatments. A country's opportunity increases as the country has a larger number of common monogenic diseases of high occurrence and as the country's GDP per capita increases. A larger number of monogenic diseases indicates a greater demand for germline editing treatments, and a higher GDP per capita indicates the ability to research and afford such treatments.

Countries with a low GDP per capita have minimal economic opportunity in the germline editing field compared to their richer counterparts. These countries, however, are at risk of being exploited, or being used for unauthorized germline editing clinical testing. On the other hand, countries with a high GDP per capita are less likely to be exploited during the clinical testing process with the exception of countries with a high occurrence of more than three of the common monogenic diseases. High income countries with two or more of the common monogenic diseases have high or very high economic opportunity of performing germline editing treatments. For countries with a medium GDP per capita, the potential risk of germline editing exploitation and economic opportunity of performing germline editing treatments depends on the number of common monogenic diseases that are of high occurrence in the country.

Since only six monogenic diseases were used for this analysis, the data may slightly vary if other less common monogenic diseases were assessed in addition to the assessed diseases. Additionally, not all genetic diseases are monogenic, so the data may also vary if polygenic diseases were assessed. Polygenic diseases are a result of multiple gene mutations, which means that the results of a polygenic disease analysis may be more extreme because such a treatment would require even more testing and funding.

Alternatives to Germline Editing

Even though the recent growth in genetics research increases the chances of germline editing eventually being administered clinically, the potential genetic disease cure has alternatives. These alternatives are disease-dependent and none of them are passed down to patients' offspring. For example, sickle cell disease can be treated with blood transfusions, pain-relieving medications, and gene therapy (National Heart, Lung, and Blood Institute, 2022). In comparison, spinal muscular atrophy can be treated with medications that increase protein synthesis, physical therapy, and gene therapy (National Institute of Neurological Disorders and Stroke, 2023). The gene therapy treatments for both, which each cost over $2 million for one dose, have high initial success rates (Buntz, 2024). Since these treatments are relatively new, their long-term success rates in disease management are yet to be determined.

Conclusion

In the end, somatic and germline cell modifications offer new treatments and cures to numerous medical conditions. Although both types of modifications come with risks, they can transform the lives of those with chronic and severe conditions. As with all new types of practices, the ethics and economics of the treatments, specifically the ethics and economics of the germline editing treatment, must be considered. Nations with a higher occurrence of genetic diseases and higher income will have greater economic opportunity, while countries with a higher occurrence of genetic diseases and lower income may be more prone to germline editing exploitation for clinical testing. Countries must collaborate in outlining which specific germline modifications are permitted and compromise on which modifications are considered disease treatment as opposed to trait enhancement. Global organizations, such as the World Health Organization, must enact these standards into laws similar to the International Health Regulations, which are policies used to manage global health events (World Health Organization, 2024). With consistent regulations between countries, the world can see the appropriate implementation of germline editing and the resulting improvement in human health.

Disclosure

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Country/ Region	High occurrence of Achondro-plasia	High occurrence of Beta-thalassemia	High occurrence of Cystic Fibrosis	High occurrence of Huntington's Disease	High occurrence of Sickle Cell Disease	High occurrence of Hemophilia	# of common monogenic diseases of high occurrence	GDP per capita in USD	Potential risk of germline editing exploitation	Economic opportunity of performing germline editing treatments
Afghanistan		✓					1	Low	High	Low
Albania		✓		✓		✓	3	Medium	High	High
Algeria	✓	✓					2	Medium	Moderate	Moderate
Andorra		✓		✓		✓	3	Medium	High	High
Angola					✓		1	Medium	Moderate	Low
Argentina				✓			1	Medium	Moderate	Low
Australia				✓			1	High	Low	Moderate
Austria				✓		✓	2	High	Low	High
Bahrain	✓	✓				✓	3	Medium	High	High
Belarus				✓			1	Medium	Moderate	Low

Country/ Region	High occurrence of Achondro-plasia	High occurrence of Beta-thalassemia	High occurrence of Cystic Fibrosis	High occurrence of Huntington's Disease	High occurrence of Sickle Cell Disease	High occurrence of Hemophilia	# of common monogenic diseases of high occurrence	GDP per capita in USD	Potential risk of germline editing exploitation	Economic opportunity of performing germline editing treatments
Belgium				✓		✓	2	High	Low	High
Benin					✓		1	Medium	Moderate	Low
Bosnia and Herzegovina		✓		✓		✓	3	Medium	High	High
Brazil				✓	✓		2	Medium	Moderate	Moderate
Bulgaria				✓		✓	2	Medium	Moderate	Moderate
Burkina Faso					✓		1	Low	High	Low
Cambodia		✓					1	Medium	Moderate	Low
Cameroon					✓		1	Medium	Moderate	Low
Canada				✓		✓	2	High	Low	High
Central African Republic					✓		1	Low	High	Low
Chad					✓		1	Low	High	Low

Country/ Region	High occurrence of Achondro-plasia	High occurrence of Beta-thalassemia	High occurrence of Cystic Fibrosis	High occurrence of Huntingt on's Disease	High occurrence of Sickle Cell Disease	High occurrence of Hemophilia	# of common monogenic diseases of high occurrence	GDP per capita in USD	Potential risk of germline editing exploitation	Economic opportunity of performing germline editing treatments
China						✓	1	Medium	Moderate	Low
Congo					✓		1	Medium	Moderate	Low
Croatia		✓		✓		✓	3	Medium	High	High
Cyprus	✓	✓				✓	3	Medium	High	High
Czechia				✓		✓	2	Medium	Moderate	Moderate
Denmark			✓	✓		✓	3	High	Moderate	Very High
DR Congo					✓		1	Low	High	Low
Egypt	✓	✓			✓		3	Medium	High	High
Equatorial Guinea					✓		1	Medium	Moderate	Low
Estonia			✓	✓		✓	3	Medium	High	High
Finland			✓			✓	2	High	Low	High
France		✓		✓		✓	3	Medium	High	High

Country/ Region	High occurrence of Achondro-plasia	High occurrence of Beta-thalassemia	High occurrence of Cystic Fibrosis	High occurrence of Huntington's Disease	High occurrence of Sickle Cell Disease	High occurrence of Hemophilia	# of common monogenic diseases of high occurrence	GDP per capita in USD	Potential risk of germline editing exploitation	Economic opportunity of performing germline editing treatments
Georgia				✓			1	Medium	Moderate	Low
Germany				✓		✓	2	High	Low	High
Ghana					✓		1	Medium	Moderate	Low
Greece		✓		✓		✓	3	Medium	High	High
Guinea					✓		1	Medium	Moderate	Low
Hong Kong						✓	1	High	Low	Moderate
Hungary				✓		✓	2	Medium	Moderate	Moderate
Iceland			✓	✓		✓	3	High	Moderate	Very High
India		✓			✓		2	Medium	Moderate	Moderate
Indonesia		✓					1	Medium	Moderate	Low

Iran	✓	✓				✓	3	Medium	High	High
Iraq	✓	✓				✓	3	Medium	High	High
Ireland			✓	✓		✓	3	High	Moderate	Very High
Country/ Region	**High occurrence of Achondro-plasia**	**High occurrence of Beta-thalassemia**	**High occurrence of Cystic Fibrosis**	**High occurrence of Huntingt on's Disease**	**High occurrence of Sickle Cell Disease**	**High occurrence of Hemophilia**	**# of common monogenic diseases of high occurrence**	**GDP per capita in USD**	**Potential risk of germline editing exploitation**	**Economic opportunity of performing germline editing treatments**
Israel	✓	✓				✓	3	High	Moderate	Very High
Italy		✓		✓		✓	3	Medium	High	High
Jordan	✓	✓				✓	3	Medium	High	High
Kazakhstan		✓					1	Medium	Moderate	Low
Kenya					✓		1	Medium	Moderate	Low
Kosovo				✓		✓	2	Medium	Moderate	Moderate
Kuwait	✓	✓				✓	3	Medium	High	High
Kyrgyzstan		✓					1	Medium	Moderate	Low
Laos		✓					1	Medium	Moderate	Low
Latvia			✓	✓		✓	3	Medium	High	High
Lebanon	✓	✓				✓	3	Medium	High	High
Libya	✓	✓					2	Medium	Moderate	Moderate
Liechtenstein				✓		✓	2	High	Low	High
Country/ Region	**High occurrence of Achondro-plasia**	**High occurrence of Beta-thalassemia**	**High occurrence of Cystic Fibrosis**	**High occurrence of Huntingt on's Disease**	**High occurrence of Sickle Cell Disease**	**High occurrence of Hemophilia**	**# of common monogenic diseases of high occurrence**	**GDP per capita in USD**	**Potential risk of germline editing exploitation**	**Economic opportunity of performing germline editing treatments**
Lithuania			✓	✓		✓	3	Medium	High	High
Luxembourg				✓		✓	2	High	Low	High
Madagascar					✓		1	Low	High	Low
Malawi					✓		1	Low	High	Low
Malaysia		✓					1	Medium	Moderate	Low
Mali					✓		1	Medium	Moderate	Low
Malta		✓					1	Medium	Moderate	Low

Moldova				✓		✓	2	Medium	Moderate	Moderate
Monaco		✓		✓		✓	3	High	Moderate	Very High
Montenegro		✓		✓		✓	3	Medium	High	High
Morocco	✓	✓					2	Medium	Moderate	Moderate
Mozambique					✓		1	Low	High	Low
Myanmar		✓					1	Medium	Moderate	Low
Country/ Region	**High occurrence of Achondro-plasia**	**High occurrence of Beta-thalassemia**	**High occurrence of Cystic Fibrosis**	**High occurrence of Huntingt on's Disease**	**High occurrence of Sickle Cell Disease**	**High occurrence of Hemophilia**	**# of common monogenic diseases of high occurrence**	**GDP per capita in USD**	**Potential risk of germline editing exploitation**	**Economic opportunity of performing germline editing treatments**
Netherlands				✓		✓	2	High	Low	High
Niger					✓		1	Low	High	Low
Nigeria					✓		1	Medium	Moderate	Low
North Macedonia				✓		✓	2	Medium	Moderate	Moderate
Norway			✓	✓		✓	3	High	Moderate	Very High
Oman	✓	✓				✓	3	Medium	High	High
Palestine	✓	✓				✓	3	Medium	High	High
Philippines		✓					1	Medium	Moderate	Low
Poland				✓		✓	2	Medium	Moderate	Moderate
Portugal				✓		✓	2	Medium	Moderate	Moderate
Qatar	✓	✓				✓	3	High	Moderate	Very High
Romania				✓		✓	2	Medium	Moderate	Moderate
Russia				✓			1	Medium	Moderate	Low
Country/ Region	**High occurrence of Achondro-plasia**	**High occurrence of Beta-thalassemia**	**High occurrence of Cystic Fibrosis**	**High occurrence of Huntingt on's Disease**	**High occurrence of Sickle Cell Disease**	**High occurrence of Hemophilia**	**# of common monogenic diseases of high occurrence**	**GDP per capita in USD**	**Potential risk of germline editing exploitation**	**Economic opportunity of performing germline editing treatments**
Saudi Arabia	✓	✓				✓	3	Medium	High	High
Senegal					✓		1	Medium	Moderate	Low
Serbia				✓		✓	2	Medium	Moderate	Moderate

Sierra Leone					✓		1	Low	High	Low
Singapore		✓					1	High	Low	Moderate
Slovakia				✓		✓	2	Medium	Moderate	Moderate
Slovenia		✓		✓		✓	3	Medium	High	High
South Sudan					✓		1	Medium	Moderate	Low
Spain		✓		✓		✓	3	Medium	High	High
Sudan	✓	✓			✓		3	Medium	High	High
Sweden			✓			✓	2	High	Low	High
Switzerland				✓		✓	2	High	Low	High

Country/ Region	High occurrence of Achondro-plasia	High occurrence of Beta-thalassemia	High occurrence of Cystic Fibrosis	High occurrence of Huntingt on's Disease	High occurrence of Sickle Cell Disease	High occurrence of Hemophilia	# of common monogenic diseases of high occurrence	GDP per capita in USD	Potential risk of germline editing exploitation	Economic opportunity of performing germline editing treatments
Syria	✓	✓				✓	3	Low	Very High	Low
Tajikistan		✓					1	Medium	Moderate	Low
Tanzania					✓		1	Medium	Moderate	Low
Thailand		✓					1	Medium	Moderate	Low
Togo					✓		1	Medium	Moderate	Low
Tunisia	✓	✓					2	Medium	Moderate	Moderate
Türkiye	✓	✓		✓		✓	4	Medium	Very High	Very High
Turkmenistan		✓					1	Medium	Moderate	Low
Uganda					✓		1	Medium	Moderate	Low
Ukraine				✓			1	Medium	Moderate	Low
United Arab Emirates	✓	✓				✓	3	High	Moderate	Very High
United Kingdom			✓	✓		✓	3	High	Moderate	Very High
Country/ Region	**High occurrence of Achondro-plasia**	**High occurrence of Beta-thalassemia**	**High occurrence of Cystic Fibrosis**	**High occurrence of Huntingt on's Disease**	**High occurrence of Sickle Cell Disease**	**High occurrence of Hemophilia**	**# of common monogenic diseases of high occurrence**	**GDP per capita in USD**	**Potential risk of germline editing exploitation**	**Economic opportunity of performing germline editing treatments**
United States of			✓	✓	✓	✓	4	High	High	Very High

America										
Uzbekistan		✓					1	Medium	Moderate	Low
Vietnam		✓					1	Medium	Moderate	Low
Western Sahara	✓	✓					2	Medium	Moderate	Moderate
Yemen	✓	✓				✓	3	Low	Very High	Low
Zambia					✓		1	Medium	Moderate	Low

References

Adigwe, O. P., Onoja, S. O., & Onavbavba, G. (2023). A Critical Review of Sickle Cell Disease Burden and Challenges in Sub-Saharan Africa. *Journal of blood medicine*, *14*, 367–376. https://doi.org/10.2147/JBM.S406196.

Asmamaw Mengstie, M., Teshome Azezew, M., Asmamaw Dejenie, T., Teshome, A. A., Tadele Admasu, F., Behaile Teklemariam, A., Tilahun Mulu, A., Mekonnen Agidew, M., Adugna, D. G., Geremew, H., & Abebe, E. C. (2024). Recent Advancements in Reducing the Off-Target Effect of CRISPR-Cas9 Genome Editing. *Biologics: Targets and Therapy*, *18*(1), 21–28. https://doi.org/10.2147/BTT.S429411.

Baylis, F., Darnovsky, M., Hasson, K., & Krahn, T. M. (2020). Human Germline and Heritable Genome Editing: The Global Policy Landscape. *The CRISPR Journal*, *3*(5), 365–377. https://doi.org/10.1089/crispr.2020.0082.

Bergman, M. T. (2019, January 9). *Perspectives on Gene Editing*. The Harvard Gazette; Harvard University. https://news.harvard.edu/gazette/story/2019/01/perspectives-on-gene-editing/.

Broad Institute. (2018). *Questions And Answers About CRISPR*. Broad Institute. https://www.broadinstitute.org/what-broad/areas-focus/project-spotlight/questions-and-answers-about-crispr.

Buntz, B. (2024, March 25). *With costs up to $4.5M, cell and gene therapies redefine norms*. Drug Discovery and Development. https://www.drugdiscoverytrends.com/how-price-safety-and-efficacy-shape-the-cell-and-gene-therapy-landscape/.

Children's Hospital of Philadelphia. (2024, February 9). *What is ex vivo gene therapy?* Www.chop.edu. https://www.chop.edu/centers-programs/cellular-therapy-and-transplant-section/what-ex-vivo-gene-therapy.

Children's Hospital of Pittsburgh. (2019). *Cystic Fibrosis Symptoms & Treatment | Children's Pittsburgh*. Children's Hospital of Pittsburgh. https://www.chp.edu/our-services/transplant/liver/education/liver-disease-states/cystic-fibrosis.

Cleveland Clinic. (2023, April 12). *Gene Therapy*. Cleveland Clinic; Cleveland Clinic. https://my.clevelandclinic.org/health/treatments/17984-gene-therapy.

Cram, D. S., & Zhou, D. (2016). Next generation sequencing: Coping with rare genetic diseases in China. *Intractable & Rare Diseases Research*, *5*(3), 140–144. https://doi.org/10.5582/irdr.2016.01020.

Food and Drug Administration. (2024, April 26). *Approved Cellular and Gene Therapy Products.* U.S. Food and Drug Administration. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-

therapy-products/approved-cellular-and-gene-therapy-products.
Foreman, P. K., Kessel, F., Hoorn, R., Bosch, J., Shediac, R., & Landis, S. (2020). Birth prevalence of achondroplasia: A systematic literature review and meta-analysis. *American Journal of Medical Genetics Part A*, *182*(10), 2297–2316. https://doi.org/10.1002/ajmg.a.61787.
Genehome. (2021). *The Impact of Genetic Diseases*. Gene Therapy. https://www.thegenehome.com/basics-of-genetics/disease-examples.
Genetic Literacy Project. (2020). *Global Gene Editing Regulation Tracker*. Global Gene Editing Regulation Tracker. https://crispr-gene-editing-regs-tracker.geneticliteracyproject.org/.
Is Gene Therapy Available to Treat My Disorder?: MedlinePlus Genetics. (2022). Medlineplus.gov. https://medlineplus.gov/genetics/understanding/therapy/availability/.
Joseph, A. M., Karas, M., Ramadan, Y., Joubran, E., & Jacobs, R. J. (2022). Ethical Perspectives of Therapeutic Human Genome Editing from Multiple and Diverse Viewpoints: a Scoping Review. *Cureus*, *14*(11). National Library of Medicine. https://doi.org/10.7759/cureus.31927.
Jurisdictional Arbitrage. (2024). TheFreeDictionary.com. https://financial-dictionary.thefreedictionary.com/Jurisdictional+Arbitrage.
Medline Plus. (2020, August 18). *Sickle cell disease: MedlinePlus Genetics*. Medlineplus.gov. https://medlineplus.gov/genetics/condition/sickle-cell-disease/.
Mehravar, M., Shirazi, A., Nazari, M., & Banan, M. (2019). Mosaicism in CRISPR/Cas9-mediated genome editing. *Developmental Biology*, *445*(2), 156–162. https://doi.org/10.1016/j.ydbio.2018.10.008.
National Heart, Lung, and Blood Institute. (2022). *Sickle Cell Disease - Treatment* . National Heart, Lung, and Blood Institute. https://www.nhlbi.nih.gov/health/sickle-cell-disease/treatment.
National Human Genome Research Institute. (2022, May 18). *Eugenics and Scientific Racism*. National Human Genome Research Institute. https://www.genome.gov/about-genomics/fact-sheets/Eugenics-and-Scientific-Racism.
National Institute of Neurological Disorders and Stroke. (2023, January 23). *Spinal Muscular Atrophy | National Institute of Neurological Disorders and Stroke*. Www.ninds.nih.gov. https://www.ninds.nih.gov/health-information/disorders/spinal-muscular-atrophy.
Sadeghi, M. R. (2023). Technical Problems and Ethical Concerns Regarding Gene Editing in Human Germlines and Embryos. *Journal of Reproduction & Infertility*, *24*(3), 145–146.

https://doi.org/10.18502/jri.v24i3.13270.

Slaughter, L. M. (2008). The Genetic Information Nondiscrimination Act: Why Your Personal Genetics are Still Vulnerable to Discrimination. *Surgical Clinics of North America*, *88*(4), 723–738. https://doi.org/10.1016/j.suc.2008.04.004.

Sufian, S., & Garland-Thomson, R. (2021, February 16). *The Dark Side of CRISPR*. Scientific American. https://www.scientificamerican.com/article/the-dark-side-of-crispr/.

University of Missouri School of Medicine. (2019). *Gene Therapy and Genetic Engineering*. Missouri.edu; University of Missouri. https://medicine.missouri.edu/centers-institutes-labs/health-ethics/faq/gene-therapy.

U.S. Equal Employment Opportunity Commission. (2009). *Genetic Information Discrimination | U.S. Equal Employment Opportunity Commission*. www.eeoc.gov. https://www.eeoc.gov/genetic-information-discrimination.

Veit, W. (2018). Procreative Beneficence and Genetic Enhancement. 10.13140/RG.2.2.11026.89289.

What are the Ethical Concerns of Genome Editing? (2017, August 3). National Human Genome Research Institute; National Institutes of Health. https://www.genome.gov/about-genomics/policy-issues/Genome-Editing/ethical-concerns.

Wong, C. H., Li, D., Wang, N., Gruber, J., Conti, R. M., & Lo, A. W. (2021, April). *Estimating the Financial Impact of Gene Therapy in the U.S.* https://www.nber.org/system/files/working_papers/w28628/w28628.pdf.

World Bank Group. (2023). *GDP per capita (current US$)*. Worldbank.org. https://data.worldbank.org/indicator/NY.GDP.PCAP.CD.

World Health Organization. (2024). *International Health Regulations*. www.who.int. https://www.who.int/health-topics/international-health-regulations#tab=tab_1.

World Hemophilia Day 2023 I Cromos Pharma. (2023, April 17). https://cromospharma.com/world-hemophilia-day-2023/.