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Inequitable Access to Gene Therapy Treatments

What is Gene Therapy? A Brief History of the Technology Leading to the Current Equity Conundrum

Gene therapy refers to the process of modifying a gene for therapeutic purposes, i.e., to treat certain diseases. The modification is achieved through inserting a healthy version of the gene, known as the therapeutic gene, into human cells where a genetic disease exists. An agent, or vector, most commonly a virus, is used to insert the therapeutic gene, as viruses are naturally programmed to break into cells and alter their genetic content [1][2]. The viral vectors are modified to have their harmful genetic encodings removed. Gene therapy can treat many diseases that result from defective genes, such as cystic fibrosis, hemophilia, combined immunodeficiency syndromes, and many forms of cancer [1]. However, some of these treatments remain under development.

The first human application of gene therapy was administered in 1990 to a patient with severe immunodeficiency. A viral vector injected a functional copy of the faulty gene into the patient's immune cells. The effectiveness of gene therapy was obvious as the patient, initially not expected to survive to adulthood, went on to live a relatively normal life [3]. As of 2019, two thousand gene therapy trials had been conducted worldwide and twenty gene therapy products had been approved [3]. Gene therapy is a fast-emerging technology that has great potential for treating many otherwise incurable diseases. As with most other new technologies, gene therapy is extremely expensive – current treatment costs range from around $300,000 USD to $2.1M USD [4]. The high cost of treatment leaves few that can afford it, leading to a clear inequitable access issue [5][6]. However, many argue that the technology is wroth the cost since it is extremely effective, and often the only cure to some diseases. Policymakers should find solutions to address the affordability conundrum.

Theoretical Background - What is Equity in the Health Sector?

In the context of public health, equity can be equated with equality of access to treatments [7]. Variations in the equality of access arise for multiple reasons, including

1. Availability: certain treatments may be unavailable to a portion of the population;
2. Difference in the quality of treatments;
3. Difference in the affordability of the treatments among different population groups;
4. Different access to service information, due to language, cultural, and/or technological barriers.

Research also indicates that inequity can often be difficult to measure in the context of public health due to the lack of a clear theoretical framework [7]. Therefore, clearly defining equity in the context of gene therapy is important to assess the issue. For our technology, point 3 –

difference in affordability - will be the most significant cause of inequity. As a result, the terms "equity" and "affordability" will be used interchangeably in this report.

Gene Therapy and the Equity Crisis - Inequitable Access due to Cost

Gene therapy, a relatively new technology, is expensive and unaffordable. The American Society of Gene and Cell Therapy (ASGCT) set "[C]ontribution to improved patient access to gene therapy in low- to middle-income countries" as one of their priorities for 2021 policies [8]. In fact, an average gene therapy treatment costs 30 times the U.S. median household income [9]. From available studies of the gene therapy affordability problem, there is a lack of consensus on how to approach the issue, and a variety of solutions have been proposed. The bottom line is that the equity issues relating to gene therapy are non-trivial. Almost all researchers agree that this is an issue we must address [4][5][10][11][12].

Key Stakeholders of the Gene Therapy Technology

Many groups affect or are affected by the gene therapy technology. These include:

- **Scientists that develop the technology**. They have the power to improve the technology, making it more efficient, effective, and/or affordable.
- **Pharmaceutical companies** – those delivering and charging for the technology
- **Patients** of all income classes. This is a diverse group of stakeholders, but they would receive the same benefit from the technology. The difference among those in this group is in their financial ability to receive the treatment.
- **Government and policymakers**. The government has tremendous control over the cost and distribution of the technology. Governmental agencies, such as the FDA for the U.S., have the power to reject gene therapy trials on the grounds of safety. Furthermore, the government can regulate the price of treatment, which would directly impact the equity issue.
- **Ethics researchers** seeking to address the gene therapy equity issue. This stakeholder group is also diverse, in that they have a variety of opinions and proposals regarding the issue. The diversity in stances is further discussed in the next section.

Varying Perspectives between and within Different Stakeholder Groups

Scientists: the major objective of researchers is to develop the most effective treatment possible.

The pharmaceutical industry must charge high prices for gene therapy treatments since the research and development of such treatments is costly and it cannot be widely applied to a large percent of the population.

Government: a benevolent government's priority should be to optimize their country's healthcare system. Objectives should include being accessible, treating as many diseases as possible, and being ethical. The government should seek to provide the best treatment for a disease.

Patients receiving gene therapy treatment want the most effective and affordable treatment. However, the definition of affordability will depend on the individual. This will be the key to our analysis of the issue and final recommendation.

Ethics researchers: as with most contemporary issues, there is no consensus on how to approach the issue of inequitable access to gene therapy among ethics or public health researchers, or even whether addressing this issue is necessary. Some argue that the inequitable access to the new technology is inevitable, comparable to how the low- and middle-income individuals could not afford antibiotics when it was first developed. The author of a 2007 study argued that unequal access should not be the reason to discourage the advancement of a new technology that could save people's lives [3]. However, this viewpoint is in the minority, and most researchers agree on the need for some framework to ensure gene therapy treatments are more accessible. A variety of solutions were proposed, including outcome-based pricing, multiple payments, and price-volume agreement [10][12]. Another popular proposal is a complete shift in the way we think about novel treatments like gene therapy. For example, Pfizer's Biopharmaceuticals executive Angela Hwang argued that the "pay by bill" model "is a poor fit in a world of costly one-treatment cures" [4]. Of course, there exists some bias to this claim as Pfizer develops many of these "one-treatment cures", so it would like the consumers to put more value to them. Hwang's argument is grounded on the "outcome-based pricing" solution to the affordability crisis, where the treatment cost should be a function of observable improvements to the patient's well-being [12]. Some even argue that this approach to gene therapy is inevitable [4]. Some of these proposals, although correctly identifying the current issue with the technology, fail to address the affordability crisis at its root – shifting our perspective on gene therapy will not make the technology more affordable, it merely hides the issue under a cover for it to be overlooked.

Two Recommendations for Canada - one Short-Term and one Long-Term Solution

The previous section made it clear that there are many approaches to addressing the accessibility issue surrounding gene therapy. In fact, policymakers should implement multiple measures that will have immediate and long-term impacts. Overall, gene therapy as a technology should continue to be pursued by researchers and drug companies, because it has proven potential to save lives and significantly improve patients' living conditions [14]. More concretely, I propose one short-term and one long-term solution to the crisis.

1. As a long-term approach, the government should encourage gene therapy research. Accessibility and equity issues aside, the gene therapy technology can greatly improve and save lives. Also, more research contributes to cheaper, more effective, and more efficient treatment methods, which would lower the cost. A tangible means to encourage research is to provide funding to programs focusing on gene therapy. Another benefit of encouraging more groups to develop the technology is to prevent monopolies. More competition means that the price will be lowered, reducing the price of the treatment.
2. A more immediate solution that makes gene therapy more affordable is to implement a subsidy system where the amount that the patient pays is inversely proportional to their household income. Lower income individuals should have a significant portion of their

therapy paid for by the government, especially live-saving treatments. Furthermore, patients should have to option to pay over an extended period to increase affordability. The specific amount of subsidy will require further research and calibration by social science professionals and is beyond the scope of this report.

Metrics to Judge the Recommendations' Effectiveness

The primary objective of the proposal is to improve the affordability of gene therapy. Two major metrics have been developed to judge the effectiveness of any solution to this equity crisis:

1. Feasibility: recommendation that are more realistic are better. One can judge a solution's feasibility based on how likely it is to be implemented, given the existing government structure and other stakeholder interests.
2. Effectiveness, measured by the difference between the average income of those receiving the treatment compared to the average income of the general population, before and after policy implementations. For an equitable distribution of the treatment, assuming those requiring the treatment is evenly distributed through all income classes, the average income for those receiving the treatment should be close to the average income of the entire population. This metric is a good indication of how effective the policy changes were in addressing in equity issues regarding access to treatment.

Assessment of and Potential Limitations to the Recommendations

The recommendations satisfy the feasibility metric. Despite the high costs for each treatment, few treatments are administered every year so the net cost in the Canadian government's perspective would be relatively low (estimated to be under $200 million CAD), as it is only a fraction of the health care budget (over $300 billion CAD) [15]. The taxpayers would also likely approve of a partially publicly funded gene therapy program, since, based on research in Canada and Europe, society tends to favour "spending on relatively high-cost drugs in cases where diseases are severe and lack alternative treatments" [16]. As the technology becomes more ubiquitous, one should also expect the cost of treatment to decrease, thus keeping the government's spending relatively constant.

Metric 2 directly assesses the tangible impacts of the policy changes. Unfortunately, this metric is very difficult to assess without patients' income data after implementing the policies. I predict that complete equality will not be possible to achieve for the given recommendation for multiple reasons. First, a potential limitation to the recommendation pertains to the fourth point discussed in the *Theoretical Background* section: different demographic groups have different access to information, and therefore will not receive available resources equally. A recent example of effect was observed during the COVID-19 vaccine distribution in Canada: even though vaccines were offered for free, not all population groups had equal access. Minorities and lower income neigbhourhoods had much lower vaccination rates than the average [17]. Second, those with higher income are often at positions of power, and they tend to manipulate any system to their advantage, including a possible implementation of the progressive-funding proposal. Put simply, those that can afford the treatment would still try to use the government funding by taking

advantage of loopholes in the system, such as how income is assessed. This limitation is not a pessimistic view on society, but rather a reasonable assumption given an inequity in power.

Conclusion

Inserting healthy genes into a patient's body for therapeutic purposes, a process known as gene therapy, is a novel and costly technology. However, it has a promising medical future of permanently curing genetic diseases and saving lives. For this reason, we must make gene therapy more affordable. This issue had been subject to extensive research, with a variety of proposals ranging from price-volume agreement to a shift in the way we value one-time cure treatments. However, to address the root of the affordability issue, I recommend a policy where the government pays for a portion of the treatment cost, whose amount is inversely proportional to the patient's income. The government should also prioritize the funding for gene therapy research due to its great potentials. Although accessibility inequalities are expected to continue to exist, these progressive policies would nonetheless aid low- and middle-income individuals in dire need of the treatment.

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