The Role of Gene Editing in the Future of the Fetus: Circumstances for Wrongful Life

by

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Abstract

Advancements in gene editing and reproductive medicine, particularly through technologies like CRISPR-Cas9, hold the promise of eradicating diseases in fetuses before symptoms arise. While these techniques foreshadow significant social benefits, it also introduces complex ethical and legal responsibilities for the medical community. This thesis examines the emergent moral obligation to employ gene editing for disease prevention in fetuses, exploring the ramifications for existing legislation and medical ethics. The key question is whether a moral duty exists to use gene editing safely to treat severe genetic diseases in fetuses, asserting that failure to do so contravenes the physician's fundamental duty to avoid harm and do good. This could legitimize wrongful life lawsuits against medical professionals for not preventing severe genetic diseases. Moreover, we debate the extension of wrongful life claims to cases of genetic enhancement, arguing that while gene editing should aim to ensure a 'genetic decent minimum,' it must cautiously approach the ethical challenge of enhancing non-disease traits. This thesis contributes to the discussion by assessing these issues while advocating for a balanced approach that prioritizes ethical considerations in the advancement of gene editing.

General Summary

Thanks to recently developed technologies such as CRISPR-Cas9, there is hope that one day diseases could be prevented, and people's overall health could be improved via gene editing. While there is great enthusiasm for anticipating the transition of genome editing into clinics, it is important to consider how to address potential liability issues that might arise due to negligent medical care during gene editing procedures. This paper proposes that a wrongful life lawsuit is an appropriate legal action to address such issues when gene editing is introduced in clinics. This debate raises the question of whether there is a moral obligation to improve individuals beyond disease traits, foreshadowing potential issues that should be addressed in future ethical frameworks governing responsible gene editing technologies.

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BBB	Blood Brain Barrier
CNS	Central Nervous System
CRISPR-Cas9	Clustered Regularly Interspaced Short Palindromic Repeats associated protein 9
DNA	Deoxyribonucleic Acid
EGE	European Group on Ethics in Science and New Technologies
FH	Familial Hypercholesterolemia
HIV	Human Immunodeficiency Virus infection
I.Q.	Intelligence Quotient
GGE	Germline Gene Editing
GMO	Genetically Modified Organisms
IVF	In Vitro Fertilization
LMM	Lipomyelomeningocele
LNP	Lipid Nanoparticles
MAiD	Medical Assistance in Dying
NASEM	National Academies of Sciences, Engineering, and Medicine
PGD	Preimplantation Genetic Diagnosis
PGT	Preimplantation Genetic Testing
PKU	Phenylketonuria
RNA	Ribonucleic Acid
TALENs	Transcription Activator-Like Effector Nucleases
UNESCO	United Nations Educational, Scientific and Cultural Organization
WHO	World Health Organitzation
ZFNs	Zinc Finger Nucleases

Chapter 1

Introduction

Advancements in genetics brought us to a reality where we have a greater ability to precisely manipulate the genome through gene editing techniques. This ability rekindles decades-old discussions regarding what would be considered a responsible use of genetic technologies, particularly in the context of reproductive medicine and the challenges surrounding parental decision-making. In light of the growing understanding of genetic disease transmission and the ongoing refinements in gene editing technologies, it is crucial to reflect about the moral decisions on whether to risk transmitting harm to offspring or to utilize genetic information and technologies for prevention and even for genetic enhancement of non-disease genetic traits.

This thesis explores this premise, particularly in the context of fetal gene editing, reflecting the ethical considerations to employ such technologies to avoid the transmission of severe monogenic diseases and extending this discussion to include a legal remedy known as wrongful life to address physicians' negligence in preventing the transmission of the genetic diseases. The problem explored contemplates a context in which gene editing technologies, specifically fetal gene editing procedures, become more accessible and available in the clinical setting. This scenario raises questions of an ethical and legal nature, respectively, whether there will be a moral obligation to use these technologies exclusively in somatic cells to treat severe monogenic genetic diseases in fetuses, and, if so, what would be the legal remedy to address medical negligence involving fetal gene editing. Moreover, this paper also explores the ethical, social, and legal repercussions of a hypothetical scenario in which there is a moral obligation to enhance non-disease genetic traits in fetuses,

such as intelligence and height. In essence, the ideas postulated in this study include:

a) First, to examine whether when gene editing is deemed safe and efficient for clinical application, there will be a moral obligation to use the technology in somatic cells to treat genetic diseases in fetuses.

b) Secondly, if a physician fails to perform gene editing in a fetus to prevent disease, resulting in the disease's manifestation in the child after birth, such negligence would warrant a wrongful life lawsuit against the doctor or the child's parents as a result of the violation of the physician's moral duty to do no harm and promote good.

c) Thirdly, to discuss whether there could be grounds for a wrongful life lawsuit for failure to enhance non-disease genetic traits.

Before diving into the ethical arguments and legal implications of in utero gene editing, there are key concepts from Genetics and Law domains that must be explained so the main problem and argument may be well supported. To do so, this thesis was organized as follows: Chapter Two provides an overview of the fundamental concepts in gene editing, fetal gene editing and wrongful life lawsuits. Regarding gene editing, we will examine the milestones in DNA manipulation, culminating in the advent of CRISPR-Cas9. Moreover, we will compare gene editing and gene therapy methodologies, emphasizing their relationship, particularly in the context of disease treatment, among with other key terminology. We also examine the concept of fetal gene editing, illustrating its promise in preemptively addressing genetic diseases within the womb, thus providing new frontiers in preventive medicine. This discussion will include the ethical debate on the use of such technologies and the implications of intervening in human genetics at such an early stage of life. Subsequently, we will introduce wrongful life lawsuits, tracing their emergence alongside genetic advancements and their impact on reproductive health, citing landmark cases from diverse jurisdictions. In this chapter, we will emphasize the ethical, legal, and societal ramifications from gene editing's potential applications, ranging from treating hereditary diseases to enhancing human capabilities beyond natural limitations.

Chapter Three will analyze recent research papers associated with the main topics at hand, namely, wrongful life lawsuits in the context of gene editing and the procreative beneficence principle. First, each paper will be categorized into one or more of the following categories: (1) liability within the gene editing landscape, (2)

genetic enhancement, and (3)) other research areas regarding gene editing. The first category will reflect the ideas proposed to address issues of legal compensation in the gene editing context. The second category will focus on the ethical implications of genetic enhancement through gene editing, including a contrast between the use of gene editing tools and preimplantation genetic diagnosis for enhancement goals, and the urge to deter eugenic intentions when applying gene editing technologies. The third category will briefly explore a topic that extends beyond the scope of this thesis, namely, the regulatory challenges involving gene editing technologies. This chapter will outline how this thesis contributes to and builds on the findings drawn from prominent works addressing the ethical and legal dimensions of gene editing.

Chapter Four will explore the legal and ethical dimensions on wrongful life lawsuits. We will set out the criteria of this legal action, encompassing the duty of care, breach of standard, causation, and resultant damages, which combined form the foundation for establishing claims. Subsequently, we will provide an analysis to determine whether physicians have moral responsibilities and owe moral duties to a fetus, particularly within a hypothetical scenario involving fetal gene editing. Then, we will dissect the ethical reasoning that underlie judicial decisions in the landmark wrongful life cases previously described. This will serve to support our advocacy for wrongful life lawsuits as a legal recourse to address harm inflicted in fetuses stemming from negligent gene editing practices. Furthermore, we will demonstrate how fetal gene editing can circumvent the main philosophical objection raised in wrongful life suits, paving the way for the inclusion of ethical arguments in future litigations involving negligently conducted fetal gene editing. In brief, this chapter will clarify the legal and ethical complexities surrounding wrongful life lawsuits, besides providing a legal solution for eventual issues involving children harmed through medical negligence in the context of fetal gene editing.

Chapter Five will examine the ethical, legal, and social implications of genetic enhancement under the lens of the principle of Procreative Beneficence. First, we will describe the principle and its correlation with eugenics ideals. In essence, it holds that prospective parents have a moral obligation to make use of genetic information to select the child with the "best" chance of leading the "best" life. Subsequently, we will conjecture the legal repercussions of utilizing gene editing tools to enhance non-disease traits, followed by a criticism on the Procreative Beneficence principle based on the obsolescence theory and the threat to genetic diversity.

Finally, in Chapter Six, we will offer a conclusive summary, reinforcing the key arguments, claims, and literature references presented throughout this thesis. Each chapter will be summarized to emphasize the important claims made within this work. This concluding chapter serves to encapsulate the essence of our study, providing an overview of the insights garnered and the contributions made in advancing the understanding of the subject matter. This overview will demonstrate that once the technical and safety concerns regarding fetal gene editing are addressed, there will be a moral obligation to utilize gene editing technologies in fetuses' somatic cells to remove severe single-gene diseases. Moreover, we contend that failing to prevent severe single-gene diseases during the fetal stage due to professional negligence will result in wrongful life lawsuits, as it breaches the moral obligation to prevent harm and promote good.

As we stand on the beginning of a new era in genetic medicine, the insights offered in this thesis aim to contribute to a better understanding on how we should deal with the new ethical and legal challenges that emerge within fetal gene editing in the context of wrongful lawsuits.

1.1 Research Questions

The research questions we will address in this thesis are as follows:

1. How have advancements in gene editing technologies, especially CRISPR-Cas9, transformed the possibilities for treating genetic diseases before birth, and what are the ethical implications of such interventions?

2. In the context of wrongful life claims, how would gene editing technologies change the interpretation of such claims and what are the implications for healthcare providers and patients?

3. How does the concept of fetal gene editing challenge existing ethical frameworks in medical practice, particularly regarding the treatment vs. enhancement debate in gene therapy?

4. Given the potential for gene editing to prevent severe genetic diseases in fetuses, to what extent could or should this technology be considered ethically

mandatory, and under what circumstances?

5. How do wrongful life claims related to gene editing technologies reflect and influence societal attitudes towards disability, medical ethics, and the value of life with genetic conditions?

6. What are the potential legal and ethical challenges of integrating gene editing technologies into clinical practice for the purpose of preventing genetic diseases before birth, and how might these challenges be addressed?

Chapter 2

Theoretical and Historical Background

This chapter describes the evolution from early genetic manipulation to the advent of CRISPR-Cas9 technology, while also delving into the distinction between gene editing and gene therapy, describing the ethical considerations of somatic versus germline editing, and examining the implications of using gene editing for treatment versus enhancement. Moreover, we address two central concepts regarding this thesis, namely Fetal Gene Editing applied to somatic cells and Wrongful Life Claims, which will subsequently be interconnected through ethical and legal analysis.

2.1 Gene Editing

This section provides an overview on the historical roots and modern scientific achievements regarding gene editing, highlighting the role of CRISPR-Cas9. Starting from the evolution of DNA manipulation techniques, this overview emphasizes the key milestones that have transformed the emerging understanding of genetic material and the development of techniques to manipulate it into a toolkit for precise genomic alterations.

2.1.1 Evolution of DNA Manipulation: Key Milestones

The goal of this section is to provide a brief historical overview of the most relevant discoveries in Genetics that laid the groundwork for the development of gene editing techniques. The discovery of the DNA as the molecule of heredity will be used as the springboard for this review.

Scientists have being trying to reverse a genetic disease's course for decades by directly intervening in the genome. To make it possible, researchers needed to comprehend the genome's structure, construction, and how it could be manipulated. In 1944, the American molecular biologists Oswald T. Avery, Collin MacLeod, and Maclyn McCarty discovered that the DNA was the chemical basis of heredity, countervailing the common belief of the time that only proteins were associated with the hereditary transmission process. Building on Avery and colleagues' findings in 1950, the Austrian scientist Erwin Chargaff discovered that the DNA molecule has equal amounts of four kinds of bases: adenine, thymine, guanine, and cytosine, which was crucial to understand the DNA's composition. In 1953, thanks to Chargaff's studies, James Watson and Francis Crick were able to uncover the double-helix structure of the DNA, which indicated how the genetic information is transmitted from parent to child (Portin, 2014).

In the 1970s, the first sequencing techniques were created, which enabled scientists to search and discover the underlying genetic origins of the most well-known hereditary diseases at the time, such as Tay-Sachs (Doudna and Sternberg, 2017). As studies advanced in the 1980s and more genetic and DNA information were gathered, the first disease-causing gene was successfully mapped, and sequencing techniques continued to be improved throughout the 1990s, culminating in the Human Genome Project (Portin, 2014).

Despite significant advancements in the study of genetic disorders, genome sequencing is ultimately a diagnostic tool rather than a therapy method. We can now examine how hereditary diseases are encoded in DNA; however, we could not alter that language. Throughout the 70s and 80s, scientists developed and refined a technique involving recombinant DNA to manipulate organisms genetically. This method involved inserting combined DNA segments from different organisms into viruses to obtain desired characteristics in the recipient organism, which later evolved to current methods of gene therapy (Doudna and Sternberg, 2017).

The 1980s was a prosperous period in the history of genetic engineering, marked by the first gene to ever be mapped and the first application of gene transfer in human subjects (Uddin et al., 2020). The 80s also marked the creation of Zinc Finger Nucleases (ZFNs), the first gene editing tool able to make more precise modifications in the genome; however, this tool is highly complex to design and often fails to recognize the desired DNA sequences. Following these achievements, which were not entirely successful but were achievements nevertheless, significant progress occurred in the landscape of genome sequencing after the completion of the Human Genome Project. In 1990, scientists worldwide worked together to sequence the human genome, which was possible due to technological innovations and a massive investment of over three billion dollars. Thirteen years later, the first reference sequence of the entire human genome was achieved, which enabled scientists to advance the whole-genome sequencing process, thus allowing them to identify thousands of genetic mutations that cause diseases (Doudna and Sternberg, 2017).

In 2009, researchers created a new type of gene editing tool called TALEN, which stands for 'transcription activator-like effectors nucleases.' Although it is easier to design, this tool is larger than ZFN, which hinders the delivery of viral vectors. Besides, both ZFN and TALEN are expensive to develop and produce significant off-target effects (Gupta and Musunuru, 2014). Off-target effects are collateral damages that cause unintended mutations that could lead to poor health outcomes, depending on the damage (Carroll, 2019).

In 2012, Science issued a paper that proposed a new methodology that offered significant advances in the process of gene editing of the genome of any living being. Although it did not have an immediate impact, roughly a year later, scientists worldwide were studying the biochemical properties and operational capabilities of the CRISPR-Cas9 system (Doudna and Sternberg, 2017). Eight years later, Jennifer Doudna and Emmanuelle Charpentier, who developed CRISPR-Cas9, were awarded the Nobel prize in Chemistry for revolutionizing the field of genetics (Begley, 2019).

Unlike previous gene editing tools, CRISPR-Cas9 is relatively cheap, more precise and can target many genes simultaneously. Nevertheless, it is not an entirely error-free procedure (Doudna and Sternberg, 2017). Despite its flaws, this genetic tool continues to be improved and has already enabled researchers to remove a few diseases in patients, such as sickle cell disease, beta thalassemia, and amyloidosis, a

rare inheritable disease that causes organ malfunctioning (Stein, R., 2021). More recently, a teenage girl diagnosed with T-cell acute lymphoblastic leukemia was potentially cured in a clinical trial through base editing, a CRISPR-based gene editing tool. After all other treatment options for cancer failed, namely chemotherapy and a bone-marrow transplant, the girl's last resort was experimental medicine with base editing, which was done in May 2022. Six months later, the leukemia is undetected in her system, although she is still being monitored in case the disease returns (Gallagher, 2022). Table 2.1.1 summarizes the timeline of Genetic Research.

Table 2.1: Timeline of Genetic Research and Gene Editing Technologies

Year	**Event**	**Development**
1970s	First sequencing techniques developed	Identification of genetic origins of hereditary diseases like Tay-Sachs.
1990	Initiation of the Human Genome Project	Collaborative effort to sequence the entire human genome.
2003	Completion of the Human Genome Project	First reference sequence of the entire human genome.
2009	Introduction of TALEN (Transcription Activator-Like Effectors Nucleases)	Emerging as a gene editing tool.
2012	Proposal of the CRISPR-Cas9 system for gene editing	Widespread study of its biochemical properties beginning around 2013.
2020	Jennifer Doudna and Emmanuelle Charpentier awarded the Nobel Prize in Chemistry	Development of CRISPR-Cas9.
2022	Successful use of CRISPR-based base editing in a clinical trial	Cure of T-cell acute lymphoblastic leukemia.
Future	Anticipated implementation of gene editing technologies in clinics	Editing genetic conditions in human fetuses.

Gene editing technologies offer the hope to prevent diseases and enhance individuals' overall health. However, given that there are no margins to establish what constitutes ethical or unethical use of gene editing tools, there are concerns about the possible use of this tool to select desirable traits, such as height or intelligence. Currently, the most difficult ethical question regarding this technology is how we should use it to modify the human genome (Zimmer, 2022).

2.1.2 The Concept of Gene Editing

Gene editing is a technique that introduces modifications in specific genes of any living being through DNA repair mechanisms, that is, systems that enable cells to cope with damages to the DNA. While sometimes used interchangeably, genome editing differs from gene editing in terms of scope; while the latter focuses on modifying particular genes, the former aims at altering sequences across the entire genome. Examples of gene editing technologies include ZFNs (zinc finger nucleases), TALENs (transcription activator-like effector nuclease), and CRISPR-Cas9 (clustered regularly interspaced short palindromic repeats) (Khalil, 2020).

2.1.2.1 Gene Editing versus Gene Therapy: Similarities and Limitations

Gene editing and gene therapy are revolutionizing the field of genetics and medicine, sharing similarities in their overarching aim of modifying genetic material to address diseases and disorders. Both approaches hold tremendous potential for treating genetic disorders, inherited diseases, and various other medical conditions.

Gene editing involves altering the genetic material of an organism at specific locations in the genome. Tools like CRISPR-Cas9, TALENs, and ZFNs enable to alter genetic material at particular loci, allowing for the correction of genetic mutations directly within an individual's DNA. On the other hand, gene therapy works by introducing, removing, or altering genetic material within a person's cells to treat or prevent disease. Unlike gene editing, traditional gene therapy does not alter the DNA sequence itself but rather adds a new gene to compensate for a faulty one or to produce a new or missing protein. This is often achieved using vectors to deliver therapeutic genes into the patient's cells (Alhakamy et al., 2021).

In terms of practical applications, genome editing is much broader than gene editing, since it also holds promise, for instance, in agriculture and infectious disease control, besides its main role in human disease correction. In contrast, gene therapy is primarily used to treat specific diseases, focusing on diseases caused by single-gene mutations, such as hemophilia and muscular dystrophy, but also including treatments for some types of cancer and viral infections (Uddin et al., 2020).

As for the risks involving each technique, gene editing can result in permanent changes to the genome, which, if performed on germline cells (sperm, eggs, or

embryos), can be passed down to future generations. This raises significant ethical, societal, and safety concerns, particularly regarding unintended consequences, such as off-target effects. Gene therapy, while also raising ethical questions, primarily concerns the risks associated with the delivery vectors (e.g., viral vectors can integrate an exogenous gene into the genome in unexpected ways, potentially causing harm) and the body's possible immune response (Uddin et al., 2020).

Still regarding the risks, although viruses used have been engineered with focus on safety and efficacy, the presence of viral genetic material is concerning, given that it can trigger an immune response and compromise the efficiency of the technique. Since viral vectors can only carry a certain amount of genetic material and the transgene (i.e., the gene that intends to replace the malfunctioning gene or to be added) needs to be modified to address a specific condition, it sometimes fails to accurately express the gene. Besides, given that the insertion of the modified gene is not always precise, if introduced into the wrong site, it could lead to producing cancerogenous cells (National Academies of Sciences and Medicine, 2017).

In this context, gene editing tools can be utilized for gene therapy purposes by directly correcting the genetic mutation in the genome, thus avoiding introducing a new gene into the genome (Gonçalves and Paiva, 2017). In brief, while both techniques primarily aim to treat or cure diseases, they differ in their approach to modifying the genome, in precision levels, the permanence of their effects, and their ethical implications.

2.1.2.2 Somatic vs. Germline Applications

Before delving into the central point of this paper, it is important to highlight two significant areas of concern regarding gene editing technologies (Johnston, 2020). First is the possibility of making permanent and heritable changes to the human genome, depending on which cells are targeted. This issue revolves around the somatic-germline cell distinction, often used in the literature to differentiate what constitutes a morally permissible or impermissible genetic application (Buchanan et al., 2000). While this issue is particularly relevant, it is not fundamental for the discussion around fetal gene editing, given that the focus of this study is on somatic cell gene editing rather than germline gene editing. For this reason, the somatic-germline distinction will be acknowledged but not thoroughly discussed.

Secondly, these technologies raise concerns about underlying eugenic intentions behind attempts to modify human DNA. This fear stems from a debate on genetic interventions for either treatment or enhancement purposes, which have also been used to establish a moral line regarding the responsible use of gene editing technologies. While using these technologies to eliminate diseases is ethically acceptable, enhancing non-disease traits could be considered unethical (Evans, 2020).

In what follows, an overview will be presented on what is morally relevant and different about somatic/germline genetic interventions besides the moral purpose of the treatment/enhancement barrier. Clarifying these concepts is fundamental for understanding this thesis' proposal of an eventual moral obligation to use gene editing to eliminate genetic diseases and conditions and for potential wrongful life lawsuits when gene editing moves into clinics.

Determining what types of cells to target has been the subject of many academic, policy, and industry discussions regarding genetic interventions (Howard et al., 2018). As previously discussed, genome editing involves the delivery of a genetic tool capable of repairing genes directly in the genome of any living organism (Doudna and Sternberg, 2017). These modifications can be done to the DNA in somatic cells (all body cells, such as the brain, blood, heart, and skin cells) or to the DNA in germ cells (eggs and sperm) or early-stage embryos (Baylis, 2019)

If used in conjunction with IVF to establish a pregnancy, alterations to germ cells or early-stage embryos can be inherited by subsequent generations. Targeting somatic cells, ethically speaking, is less challenging than targeting germ cells or early-stage embryos. Not all editing done to the embryo will be heritable; if gene editing is performed on a later-stage embryo or a fetus, it is possible only to select its somatic cells (Greely, 2019). Genetic alterations to the DNA in somatic cells will be confined to that individual; thus, the modifications cannot be passed down to that individual's offspring (Johnston, 2020). While germline gene editing is far from being introduced in clinics soon, somatic genome editing is much closer. For instance, in 2019, Victoria Gray, a patient with sickle-cell disease, became the first person to be successfully treated with CRISPR-Cas9 ("The evolving promise and potential of gene therapy", 2021).

One of the promises of CRISPR-Cas9 is the potential to cure monogenic diseases (those caused by a single genetic mutation, such as sickle-cell disease) (Doudna and

Sternberg, 2017). Once the safety and efficacy concerns are addressed, somatic genome editing will likely be introduced in clinics as a feasible technique to treat and cure certain single-gene diseases (Howard et al., 2018). Thus, the potential benefits of somatic gene editing for patients experiencing life-threatening diseases are significant, and many are excited about the potential outcomes of this gene therapy. Furthermore, it could be possible to employ somatic gene editing in fetuses to prevent the development of debilitating genetic diseases (Baylis, 2019).

2.1.2.3 Treatment vs. Enhancement

As previously indicated, gene editing technologies are considered key players for future treatment and disease prevention at the genomic level. When the use of the technology is aimed at eliminating diseases or disabilities, it is generally considered 'treatment' (Johnston, 2020). Beyond this purpose, these could also be used for what is commonly referred to as 'enhancement,' in other words, to improve beyond the ordinary functioning of a genetic trait, resulting in 'gifted individuals' (*Human Genome Editing: Science, Ethics and Governance*, 2017).

For decades, scholars have employed the treatment-enhancement distinction to suggest that the first would be a morally acceptable goal, but the second would not. This distinction has been used as a demarcation line between obligatory and nonobligatory services to provide to others, such as in the health insurance context (Buchanan et al., 2000). However, this does not help provide moral boundaries between the ethical and unethical use of genetic technologies, as it reveals blurry lines between these notions. Dr. Françoise Baylis provides an illustrative example regarding this issue, discussing the case of using somatic cell human genome editing to increase the height of young boys. Whether the short stature is due to a hormonal deficiency or genetic factors inherited from his parents, the ethical evaluation of using gene editing as a treatment or an enhancement could be debated. While correcting a hormonal deficiency through gene editing might be seen as an ethically permissible treatment, using it to address inherited short stature might not be as acceptable, highlighting the ethical issues on the use of gene editing (Baylis, 2019).

Why is it only questionable to use gene editing to enhance the inherited short stature? In both scenarios, the boy's stature results from the genetic lottery, which could lead to this individual be subjected to prejudice and bullying in life. Suppose

it is possible to remedy the boy's short stature with gene editing or growth hormones, for instance, and reduce the boy's burden. In that case, both situations are either equally ethically permissible or impermissible. The intervention could be considered a "treatment" because it addresses the boy's hormonal deficiency. On the other hand, it could also be considered an "enhancement" because it improves a non-disease trait (Baylis, 2019).

Non-disease traits do not always relate to traits such as intelligence or height; for instance, one could use gene editing to confer supranormal amounts of protein or to enhance the immune system against viral infections, which could also be considered a "treatment" (*Human Genome Editing: Science, Ethics and Governance*, 2017). Inasmuch as prevalent social and cultural norms determine the desirability of genetic traits, there is no objective way of knowing which ones are the "best," as it is differently interpreted in each society (Baylis, 2019).

In a different example, Baylis suggests that it would be ethically questionable (or unacceptable) to use gene editing to increase the height of an individual already considered tall according to society's standards. In this situation, what is ethically problematic is not the chosen genetic trait to be edited but the effects that this type of intervention could engender, namely an increase in social inequality (Baylis, 2019). There is, however, a grey area in the 'enhancement' discussion: if gene editing could be performed in a fetus to confer enhanced immunity to infectious diseases, such as avian influenza or a covid variant, would it be ethically justified to do so? This kind of health-related enhancement could become morally mandatory if gene editing in utero is deemed safe. In this manner, it seems arbitrary to keep the treatment-enhancement distinction (Buchanan et al., 2000).

A request to increase one's height (or another non-disease trait, such as memory) when this individual is already tall or of ordinary to above-average intelligence is just not a morally compelling justification for gene editing. Besides issues of inequality, it is possible that enhancing non-disease traits in human fetuses could further accentuate parental focus on the intellectual and financial potential of children (Kaposy, 2018). This intention, in turn, could result in a toxic relationship between parents and children across generations since children could be regarded as products of their parent's design (Sandel, 2007).

Consider an individual born with sickle-cell disease (or another single-gene disease)

in a different scenario. Sickle-cell disease occurs in a child when both parents have sickle-cell genes. People who suffer from this disease experience severe pain episodes because sickled cells block the blood flow. As it prevents blood and oxygen flow, it can harm the organs, potentially leading to death (Tatiana Lanzieri et al., 2020). In this case, using gene editing to treat this disease, or prevent it if detected early in a fetus, can be justified and morally obligatory depending on circumstances.

People carrying single-gene diseases, such as sickle-cell, are strong candidates for somatic gene editing applications (Shanahan et al., 2021). When safety and efficacy issues are addressed, human fetuses afflicted with devastating single-gene diseases should also be a priority. The benefits of eliminating diseases in utero could be tremendous. For the individual who receives gene editing at the fetal stage, they would avoid the pain and suffering caused by such disease. Depending on how accessible somatic gene editing becomes, it could reduce the prevalence of several diseases, such as Tay-Sachs and Huntington's disease (Tatiana Lanzieri et al., 2020).

As genome editing technologies are continuously refined, the incidence of off-target effects should be reduced. Irrespective of how well-developed these technologies may get, errors could still occur and have catastrophic consequences for individuals. Since genetic modifications to the DNA are irreversible, individuals harmed by a negligently performed gene editing procedure could seek legal redress to obtain financial compensation. In this manner, wrongful life lawsuits could be a means to seek justice in this context.

2.1.3 Latest Achievements in Gene Editing

The last decades have demonstrated fascinating improvements in medicine's ability to predict various genetic conditions and even control some of them through gene editing. In 2018, a Chinese scientist, Dr. He Jiankui, announced the birth of the first gene-edited babies, Lulu and Nana. Using IVF to create the embryos, their genomes were altered with the gene editing tool CRISPR-Cas9, which aimed at making them resistant to HIV infection (Foong, 2021). The experiment has largely been met with outrage from the scientific community due to his irresponsible attempt to create gene-edited humans before the scientific community agreed it was safe to do so. Dr. He's seemingly reckless application of this emerging and unregulated technology culminated in the scientist's imprisonment. Nevertheless,

Dr. He's actions represent a substantial step in human germline editing history once he achieved something that before was just hypothetical (Marx, 2021).

After Dr. He Jiankui's announcement of his "achievement" with the gene-edited babies, several fertility clinics around the world contacted the Chinese scientist inquiring if he could help them deliver gene editing in embryos to their patients. There is an undeniable commercial potential in providing gene editing services and individuals eager enough to buy them, such as prospective parents at risk of transmitting genetic diseases to their offspring (Begley, 2019).

This case raises the hope that one day gene editing may be safely applied in humans to remove diseases prematurely. Rather than merely being morally acceptable, gene editing technologies could eventually be deemed ethically mandatory if the individual carries a severe genetic disease and gene editing is deemed safe and effective. Furthermore, depending on the circumstances, after the introduction of gene editing technologies, individuals born with severe genetic disease or condition that might have been addressed in utero could have a legitimate compensation claim.

2.2 Fetal Gene Editing

In this section, we detail the possibilities of gene editing during fetal development, covering various facets of this emerging field. First, we cover the concept of Fetal Gene Editing in subsection 2.2.1, introducing it as a transformative approach to correcting single-gene genetic disorders in utero. We emphasize its potential to modify DNA in developing fetuses using technologies like CRISPR-Cas9, highlighting both the ethical debates and the promise it holds for treating diseases before birth. Moreover, in section 2.2.2, we categorize genetic diseases and conditions that could potentially benefit from fetal gene editing. This classification ranges from severe monogenic diseases, to less severe monogenic conditions and non-disease genetic traits. The final section 2.2.3 discusses the first fetal gene therapy case, which sets a precedent for treating genetic disorders before birth. For the purposes of this study, prenatal genome editing or fetal gene editing refers to the application of CRISPR-Cas9 and other tools to fetuses (Peddi et al., 2022).

2.2.1 The Concept of Fetal Gene Editing

Fetal gene editing represents a cutting-edge frontier in genetic medicine, harnessing molecular tools like CRISPR-Cas9 to modify the DNA of developing fetuses. Traditionally, gene therapy has aimed at replacing or introducing genes in cells to rectify genetic anomalies (Peranteau and Flake, 2020). In contrast, fetal gene editing operates in utero, targeting single-gene mutations responsible for diseases. As this technology evolves, ethical and moral considerations emerge alongside the potential to correct diseases in fetuses. This discussion explores the stages of human development at which gene editing can be applied, emphasizing the potential benefits of in utero interventions ("Gene Therapy and other Medical Advances", 2022).

At the preconception stage, gene editing on early-stage embryos and gametes raises ethical concerns due to unknown and irreversible effects on future generations. However, targeting later-stage embryos or fetuses allows interventions confined to the individual, avoiding potential germline consequences. In contrast, in utero gene editing, specifically during mid-to-late gestation, emerges as a feasible approach to address monogenic diseases without affecting future generations (Mattar et al., 2021).

Researchers highlight the physiological advantages of fetal gene editing. In general, the timing of in utero interventions is crucial, with fetal immune tolerance occurring between 11 to 14 weeks of gestation. For instance, in 2021, researchers Rohan Palanki and Michael J. Mitchell and fetal surgeon William H. Peranteau published a paper outlining the advantages of therapeutic gene editing delivery during the fetal stage of development. In their study, they point out some of the benefits of fetal gene therapy compared to post-birth gene therapy, such as the fetus' small size and the early stage of the fetal immune system that prevents an immune response to the introduction of external genetic material and delivery vector (Palanki et al., 2021). Other studies also support these findings (Shanahan et al., 2021); (Mattar et al., 2021). Despite promising outcomes, challenges such as vector delivery methods and potential risks, including genotoxicity and disruption of normal fetal development, must be addressed before widespread clinical applications.

In brief, fetal gene editing represents a paradigm shift, offering potential therapeutic solutions for previously untreatable conditions. While successful cases and preclinical studies demonstrate promise, the ethical, safety, and legal implications

necessitate thorough examination. As technology advances, the scientific community must collaborate to balance between the potential of in utero gene editing and the responsibility to navigate it responsibly.

2.2.2 Categories of Genetic Diseases and Conditions

This section is set out to describe what genetic diseases or conditions should be ideal candidates for fetal gene editing according to two reports: one published by the National Academies of Sciences, Engineering, and Medicine in 2017 and the other by the National Academy of Medicine, National Academy of Sciences, and the Royal Society in 2020. The 2017 report presents considerations on both somatic and germline gene editing approaches and the 2020 report focuses on heritable genome editing (National Academies of Sciences and Medicine, 2017). While the focus of this thesis is on somatic gene editing, both reports present examples of prime target severe single-gene diseases that could be addressed by gene editing applications on either somatic or germ cells. The 2020 report (focused on germline gene editing) outlines categories of genetic diseases in more detail compared to the 2017 report and for this reason it is used as a resource in this section, given that a subset of those categories apply to the context of in utero gene editing. For the purposes of this study, only the severe genetic diseases from Categories A and B (below) will be referred to throughout the thesis, as they are prime targets for somatic gene editing applications, as well as the most likely to appear in litigation involving wrongful life.

2.2.2.1 Category A: Cases of Serious Monogenic Diseases in Which All Children Would Inherit the Disease Genotype

Before delving into this category, it is important to clarify the classification of the genetic diseases in this category. All diseases have genetic components which play a role in regulating a person's susceptibility to various conditions. The development of diseases occurs through a multifaceted combination of interactions between genes and the environment. However, there are rare instances where all of the offspring would inherit the disease-causing genotype. This phenomenon is exemplified in Category A severe monogenic diseases (National Academy of Medicine et al., 2020).

Category A addresses severe monogenic disorders that are characterized by high

penetrance, which emphasizes the need for genome editing interventions. The primary aim is to modify well-defined pathogenic variants into non-pathogenic sequences. This category pertains to couples facing the likelihood that all their offspring would inherit the disease-causing genotype.

Although it is rare, this situation can happen in certain circumstances. For instance, in autosomal dominant diseases, if one parent possesses two disease-causing alleles, resulting in an affected homozygote, all offspring would inherit the genotype and consequently the disease. Similarly, in autosomal recessive diseases, if both parents carry two disease-causing alleles, all children would inherit the disease-causing genotype. Examples include autosomal dominant diseases such as Huntington's disease, as well as autosomal recessive conditions such as cystic fibrosis, sickle cell anemia, and beta-thalassemia. For X-linked recessive diseases, if the prospective female parent is an affected homozygote and the male parent carries a disease-causing allele on his only X-chromosome, all offspring would be affected by the disease. For prospective parents falling within this category, conventional prenatal diagnosis and Preimplantation Genetic Testing (PGT) lack efficacy in identifying genetically unaffected embryos. Therefore, individuals within this category have more reason to pursue somatic fetal gene editing.

2.2.2.2 Category B: Serious Monogenic Diseases in Which Some, but Not All, of a Couple's Children Would Inherit the Disease-Causing Genotype

Category B involves serious monogenic diseases where only some of a couple's children would inherit the disease-causing genotype. The purpose of genome editing in this category is to modify a well-characterized pathogenic variant to a common, non-disease-causing DNA sequence. Examples of diseases falling into this category include familial adenomatous polyposis, and the circumstances typically revolve around couples where only a subset of their offspring would be affected. Unlike Category A, which deals with severe monogenic disorders with high penetrance, Category B couples are more prevalent and diverse. This is due to statistical and medical factors, as Category B often includes individuals carrying one disease-causing variant, increasing the likelihood of occurrence, and encompasses a wider range of diseases, including serious recessive conditions where parents may be

unaffected carriers. Estimates suggest that 1 percent of global births involve a monogenic disease falling into Category B. However, not all instances of monogenic diseases fit this category, as some may not meet the severity criteria, and others may result from new mutations rather than inherited ones, making prospective identification in parents impossible.

2.2.2.3 Category C: Other Monogenic Conditions with Less Serious Impacts Than Those in Categories A and B

Category C encompasses monogenic conditions with less severe impacts compared to Categories A and B. These conditions may still necessitate genome editing to replace pathogenic variants with non-disease or non-disability-causing sequences. This category involves prospective parents whose naturally conceived children may inherit the genotype causing the condition. Examples include familial hypercholesterolemia (FH), where heterozygous FH can be managed with medications, significantly reducing the risk of heart disease, while homozygous FH poses greater challenges and leads to life-shortening heart disease. While Categories B and C both comprise monogenic disorders, Category C conditions have less severe morbidity and may benefit from simple medical or lifestyle interventions to mitigate the risk of premature death.

2.2.2.4 Category D: Polygenic Diseases

Category D focuses on polygenic diseases influenced by numerous genetic variants and environmental factors, where genome editing would aim to modify multiple genetic variants associated with disease risk to alternative common variants with lower risk. Such diseases, such as type 2 diabetes mellitus and heart disease, are influenced by hundreds of genetic variants with small effects on disease risk. Unlike Category A's severe monogenic disorders, altering single genetic variants associated with polygenic diseases is unlikely to prevent the condition and may have undesired effects due to their involvement in other biological functions and interactions with the environment, suggesting potentially better options for disease prevention.

2.2.2.5 Category E: Other Applications

Category E encompasses genetic alterations unrelated to heritable diseases, aiming for various objectives that may or may not be health-related and could involve introducing new genetic sequences. These changes can range from genetic variants to the introduction or disabling of genes, with applications including attempts to confer resistance to infectious diseases like HIV by editing genes such as CCR5, enhancing abilities like endurance through gene activation, modifying complex traits like height or cognitive ability, and conferring new abilities for situations like extended spaceflight. However, the impacts of such interventions remain uncertain, as altering genes for specific traits could have unforeseen consequences, raising ethical and social concerns.

Table 2.2: Categories of Genetic Disorders/Conditions Amenable to Correction Through Gene Editing

Cat.	**Disease Type**	**Purpose of Editing**	**Circumstances / Examples of Diseases**
A	Severe monogenic disorder with high penetrance.	Modify pathogenic variant to prevalent non-pathogenic sequence.	Couples with all children inheriting disease genotype / Huntington's disease, cystic fibrosis.
B	Serious monogenic disease with high penetrance.	Change pathogenic variant to common non-disease sequence.	Some children inherit disease genotype / Familial adenomatous polyposis, Huntington's disease, cystic fibrosis.
C	Monogenic condition with less serious impacts.	Modify pathogenic variant to common non-disease sequence.	Some or all children inherit genotype causing condition / Familial hypercholesterolemia (FH).
D	Polygenic diseases.	Change genetic variants associated with higher risk.	Risk influenced by many genetic variants / Type 2 diabetes, heart disease, schizophrenia.
E	Other Applications.	Genetic changes beyond heritable diseases.	Varied objectives / Modifying traits like height or cognitive ability.

2.2.3 Advantages of Fetal Gene Editing

The concept of Fetal Gene Editing encompasses three key stages in human development for addressing single-gene diseases. At the preconception stage, gene editing technologies can be applied to early-stage embryos and gametes, introducing potential unknown and irreversible effects transmitted to future generations (Mattar et al., 2021). While certain countries and international treaties exclude such practices during intended pregnancies, research is allowed on embryos created for reproductive purposes but never used. Modifications to the somatic cells of later-stage embryos or fetuses' DNA can be confined to the individual, offering the possibility to target monogenic diseases prenatally without affecting future generations (Vidalis, 2022).

For effective fetal gene editing, interventions should occur in utero during mid-to-late gestation, ensuring genome alterations without impacting the germline. This involves the application of CRISPR-Cas9 and other gene editing tools to fetuses, providing a focused approach to genetic corrections ("Fetal Development: Stages of Growth", 2020). The distinction between preimplantation embryo editing and fetal gene editing lies in the timing and in vivo application, with implications for the mother considered in the latter (Peddi et al., 2022).

Researchers emphasize the advantages of therapeutic gene editing during the fetal stage, highlighting the fetus's small size and an early-stage immune system that prevents adverse responses. Fetal gene therapy presents distinct benefits compared to post-birth interventions, providing a unique window for effective corrections.

As gene editing technologies advance, their potential application in clinical settings, particularly in utero, becomes increasingly conceivable. Nevertheless, the risk of errors persists, considering the reality that physicians may not consistently remain informed about the latest technological developments. To deter the potential for medical negligence in the field of fetal gene editing, the subsequent discussion will explore a lawsuit aimed at addressing such situations.

2.3 Wrongful Life Claims

In this section we explore the legal, ethical, and societal implications of wrongful life litigation, a complex area of law that has emerged alongside advances in genetic technology and prenatal diagnostics. First, we analyze the historical precendents on wrongful life cases in section 2.3.1, tracing the main cases across different jurisdictions. Moreover, in section (2.3.2), we present the definition of wrongful life claims, distinguishing them from wrongful birth and wrongful pregnancy lawsuits, while also exploring the contentious issue of quantifying damages and the moral implications of valuing life with disability or diseases. Finally, in section 2.3.3, we examine the societal, technological, and legal trends that have contributed to the emergence of wrongful life litigation, including the development of genetic counseling, advances in prenatal diagnostics, changes in reproductive rights, and evolving notions of patient autonomy and informed consent. This analysis contextualizes wrongful life claims within the trajectory of medical ethics and legal standards concerning reproductive technologies and genetic medicine.

2.3.1 Historical Context of Wrongful Life Cases

In what follows, a historical review of landmark cases involving 'wrongful life' claims is provided. Although not every case involves a genetic condition per se, even the non-genetic cases provide insight into the ethical issues and how the courts have legally addressed them. It is important to emphasize that the following are a disparate group of cases from different countries (mostly United States) based on a range of fact situations such as genetic, non-genetic, pre-conception, post-conception.

2.3.1.1 Zepeda v. Zepeda (1963)

The term "Wrongful Life" first appeared in the Illinois Court of Appeals' decision in the case of Zepeda vs. Zepeda (Botkin, 1988). In this case, a child sued his father for the harm of being born in adultery. Although the plaintiff did not claim a disability or disease, he claimed to live a wrongful life and sought damages. The latter persuaded the plaintiff's mother to have sexual intercourse by promising to marry her. Since the promise was not kept, the plaintiff was born as an illegitimate

child, forced to live with social stigma, and deprived of certain rights, such as inheritance (Zepeda vs. Zepeda). Although the court recognized that the plaintiff had suffered an injury, it dismissed the claim out of fear that a wave of lawsuits would emerge from other individuals in a similar situation (Antunes de Souza, 2014)

2.3.1.2 Gleitman v. Cosgrove (1967)

This was the first wrongful life case that involved a child born with a disability. The plaintiff's mother, Mrs. Gleitman, had been diagnosed with rubella during gestation. In consultation with the defendant's doctors when she was pregnant, the doctors erroneously informed her that rubella would not affect her child. Subsequently, her son was born blind and deaf due to his congenital rubella (Botkin, 1988). Hence, the child and his parents brought a wrongful life and a wrongful birth suit, respectively, claiming that had the parents been adequately informed, they would have decided to terminate the pregnancy. Although the Supreme Court of New Jersey acknowledged the child's right to sue for prenatal injuries, their case did not succeed. The court concluded that the physicians did not cause the child's condition, and there was no way they could have prevented it. Besides, since abortion was prohibited at the time, Mrs. Gleitman would not have the right to access it under the law; for this reason, the wrongful birth claim was denied ("Gleitman v. Cosgrove", 1967).

2.3.1.3 Park v. Chessin (1977)

This was the first successful wrongful life suit after the Roe v. Wade decision in 1973. In this case, Mrs. Park and her husband were aware that they carried one copy of a mutated gene that caused polycystic kidney disease, which is fatal. After losing their first child to this disease, they consulted Dr. Chessin to investigate the risks of having another child with the same condition; if it were the same, the mother would choose to terminate the pregnancy. The doctor incorrectly informed them that the chances of having another child with polycystic kidney disease were meager, which encouraged the couple to conceive again. In 1970, Mrs. Park gave birth to a girl who passed away two years later due to polycystic kidney disease. The Parks filed a wrongful life suit on behalf of their late daughter against Dr. Chessin for failing to inform them about risks in an eventual pregnancy. The New York Court of Appeals recognized that the plaintiffs had indeed suffered due to medical

negligence and granted damages from the doctor's wrongful act (Zhang, 2012).

2.3.1.4 McKay v. Essex Area Health Authority (1982)

In 1975, a pregnant Mrs. McKay suspected that she had been infected with rubella, so she consulted with her doctor, who took blood samples. However, due to the doctor's and the hospital's testing service's negligence, they concluded that she had not been infected. As a result, Mrs. McKay gave birth to a child with severe aftereffects of rubella, which led her to file a wrongful life suit on behalf of her son against the doctor and the hospital (Weir, 1982).

The child raised two complaints: First, if not for the doctor's negligence in identifying the disease in the mother, she would have been given a rubella vaccine; as a consequence of the doctor's mistake, his injuries were worse than they would otherwise have been. Second, he contended that by failing to inform Mrs. McKay about her infection, her physician failed to give her the option of abortion. Although the court of appeal recognized the medical negligence, the wrongful life claim was denied. The court reasoned that "life - whether experienced with or without a major physical handicap - is more precious than non-life" (Liu, 1987). Besides, the court claimed that it would be impossible to assess the damages once it would be necessary to compare the plaintiff's life with nonexistence (Antunes de Souza, 2014).

2.3.1.5 Turpin v. Soritini (1982)

In 1976, James and Donna Turpin consulted Dr. Soritini out of concern for their daughter's hearing condition. After examining, the doctor informed that her hearing was fine, and the couple decided to have another child. However, when the second child was born, specialists detected a hereditary disorder that caused deafness in the first child, which was also passed on to the younger sibling (Zhang, 2012).

In 1978 the Turpins brought a wrongful life suit on behalf of their second child against Dr. Soritini ("Turpin v. Soritini", 1982). The California Supreme Court acknowledged that the physician's negligence deprived the second child of the opportunity to be free of the hereditary condition. Due to the difficulty in assessing the damages by comparing living with a disability and nonexistence, the damages awarded were measured according to all medical expenses needed by the child

throughout her life (Antunes de Souza, 2014)

Deafness is no longer considered a disease but a disability that does not impede individuals from thriving in life. In the context of gene editing, there is an international consensus that the technique should be limited to a severe and incurable diseases, which does not include deafness (Scully and Burke, 2019). In the future, wrongful life should not contemplate cases involving negligence claims to "correct" the deafness gene in an individual through gene editing.

2.3.1.6 The Affaire Perruche (2000)

This case happened in France and became a well-known controversy for establishing the 'right not to be born.' Due to the absence of wrongful life precedents in Europe at the time, this case's judgment has been quoted in subsequent lawsuits in several European countries (Antunes de Souza, 2014). In 1982, Mrs. Perruche suspected that she had rubella and told her doctor that if that were the case, she would have an abortion to prevent the birth of a child with severe conditions. Mrs. Perruche underwent a blood exam that did not detect rubella; unconvinced, she retook the exam, and this time the result was positive for the disease. Instead of investigating the contradiction, her doctor told her to disregard the second result and advised her to go through gestation (Spriggs and Savulescu, 2002).

In 1983, her son Nicolas Perruche was born deaf and blind, with a brain malformation and heart problems. His health conditions were dire and required a caretaker and medical equipment to treat him. At two years old, Mrs. Perruche suffered a nervous breakdown that required psychiatric care, followed by divorce. The Perruche family brought a wrongful birth suit in 1988 and claimed they would not have to bear such a heavy burden if not for the doctor and the laboratory's negligence. Besides, they also filed a wrongful life suit on behalf of their son, contending that Nicolas had been harmed by medical negligence (Lysaught, 2002).

Mrs. Perruche and her ex-husband were awarded compensation for their wrongful birth lawsuit in 1997. However, the wrongful life suit had its decisions reversed in appeals in the course of twelve years until it reached the Cour de Cassation, France's highest court (Lysaught, 2002). At last, the court upheld the compensation in Nicolas' favor, which caused an uproar among physicians, jurists, and disability

advocacy groups who saw the decision as encouraging eugenics ideals (Daley, 2002).

2.3.1.7 Johnson v. California Cryobank (2000)

In 1988, Mrs. and Mr. Johnson consulted California Cryobank, a sperm bank, about a potential donor. The fertility doctors falsely claimed that the donor's sperm had been tested and screened for genetically transmissible diseases. That sperm was used to conceive Mrs. And Mr. Johnson's daughter. A few years later, she was diagnosed with Autosomal Dominant Polycystic Kidney Disease, a serious genetic illness that causes hypertension and neurological disorders (Cohen, 2014). This disease is characterized by "gross enlargement of the kidneys and progressive renal failure" (Skolnik, 2003). As neither of the Johnsons had a family history of the disease, it was clear that the anonymous donor transmitted the disease to the couple's daughter - a fact later confirmed during the trial (Cohen, 2014).

In 1999, the Johnsons and their minor daughter filed a lawsuit against California Cryobank, claiming damages for their daughter's pain and suffering caused by professional negligence, fraud, and breach of contract. The couple claimed the defendant sold the faulty sperm while aware that it came from a donor with a family history of Autosomal Dominant Polycystic Kidney Disease (Skolnik, 2003). Notwithstanding the professional negligence in informing the Johnsons about the disease and the direct connection between the negligent conduct and the child's condition, the court stated that their claim characterized wrongful life action and denied the plaintiffs' claim (Billauer, 2020).

In this case, the child, represented by their parents, did not claim the right not to be born but rather the right to have had their genes carefully selected when screening the sperm that contributed to their existence. Autosomal Dominant Polycystic Kidney Disease is a common monogenic disease that is incurable. Theoretically, gene editing technologies such as CRISPR-Cas9 could be applied to correct the somatic cells from kidneys that inherited such disease (Lau et al., 2018). Suppose the case above involved medical negligence in detecting and correcting the disease using gene editing technologies. In that case, there could be grounds for a wrongful life lawsuit, such as in Park v. Chessin (1977). Whether the court would accept it is a different matter and would depend on the legal, cultural, and social context.

2.3.1.8 Toombes v. Mitchell (2021)

This case is currently the most recent and successful wrongful life suit. In February 2001, Caroline Toombes consulted Dr. Mitchell about her intention to conceive. However, the physician failed to inform her about the importance of ingesting folic acid before her conception, which is necessary for developing the neural tube ("Toombes v. Mitchell", 2021). In November 2001, Mrs. Toombes gave birth to her daughter, Evie Toombes, who was diagnosed with a lipomyelomeningocele ("LMM"), a form of neural tube defect. According to the judgment records, she experienced difficulty with mobility to the extent that she occasionally relied on a wheelchair or Zimmer frame for support. Additionally, Evie had to manage a neuropathic bladder, which necessitated the use of catheters at times, leading to repeated urinary tract infections. Beyond these, Evie also endured bowel incontinence and constipation, along with a related gastrointestinal disorder that resulted in vomiting and nausea.

Evie Toombes filed a wrongful life lawsuit against Dr. Mitchell, claiming that she would not have been conceived if not for his negligence in informing Mrs. Toombes about the importance of folic acid. Instead, her mother would have delayed conception, and a genetically different sibling would be born later without spina bifida". After examining all the evidence, the High Court understood that a later conception would have generated a healthy individual, although genetically different. It concluded that the defendant was liable, and the claimant was entitled to be awarded damages for being born in her condition ("Toombes v. Mitchell", 2021).

2.3.1.9 Florence v. Benzaquen (2021)

The case took place in Ontario, Canada. Dana Florence, a 25-year-old woman, began taking Serophene, a fertility drug, in July 2007, and became pregnant with triplets soon after. However, due to premature birth, the triplets suffered serious disabilities. In 2011, Dana and her husband, along with the triplets, sued Dana's gynecologist, Dr. Benzaquen, for negligence. They claimed that Dana wasn't adequately informed about the risks of Serophene, including the possibility of conceiving multiples and associated neurological and developmental issues. They argued that Dr. Benzaquen prescribed Serophene despite indications that it was unreasonable in Dana's circumstances. The lawsuit asserted that the doctor owed a duty of care not only to

Dana but also to the triplets. However, the doctor argued that physicians don't owe a duty of care to future children for negligence pre-conception ("Florence v. Benzaquen", 2021). The court upheld the decision to dismiss the triplets' claims, citing settled law and the correct application of precedent by the motion judge. Table 2.3 summarizes the historical context of Wrongful Life Cases in this section.

Table 2.3: Historical Context of Wrongful Life Cases

Year	**Case**	**Country**	**Significance**
1963	Zepeda v. Zepeda	USA	First use of "Wrongful Life" term
1967	Gleitman v. Cosgrove	USA	First case involving disability
1977	Park v. Chessin	USA	First successful Wrongful Life suit post Roe v. Wade
1982	McKay v. Essex Area Health Authority	UK	Wrongful Life claim denied despite medical negligence
1982	Turpin v. Soritini	USA	Damages measured according to medical expenses
2000	The Affaire Perruche	France	Controversial case establishing the 'right not to be born'
2000	Johnson v. California Cryobank	USA	Wrongful Life claim denied, focusing on professional negligence
2021	Toombes v. Mitchell	UK	Most recent Wrongful Life suit in the UK
2021	Florence v. Benzaquen	Canada	Most recent Wrongful Life suit in Canada

2.3.2 The Concept of Wrongful Life

In the early 1960s, the development of prenatal diagnosis and the establishment of rights to contraception and abortion led to the emergence of the legal concepts of (1) wrongful pregnancy, (2) wrongful birth, and (3) wrongful life malpractice actions (Botkin, 1988). (1) Wrongful pregnancy (or conception) describes a lawsuit in which the parents sue the prenatal physician who, out of negligence, caused them an unwanted pregnancy (for instance, due to a failed sterilization procedure). (2) Wrongful birth refers to a lawsuit in which the parents sue the prenatal physician for negligent action that led to the birth of a child with a disease or disability. In this case, the physician's negligence in informing the parents about the child's condition removed the right of the parents to make an informed decision about continuing the pregnancy (Antunes de Souza, 2014). (3) Wrongful life malpractice actions involve legal claims where individuals assert that they were born with a serious genetic or congenital condition due to a healthcare provider's negligence, arguing that they would have preferred not to have been born if informed during pregnancy.

While wrongful conception and wrongful birth lawsuits have been generally accepted as actionable worldwide, the claim of wrongful life is more controversial and often rejected. Although wrongful life suits involve the birth of a child with a disease or

Table 2.4: Concepts of Wrongful Pregnancy, Wrongful Birth and Wrongful Life

Concept	Description	Key Elements
Wrongful Pregnancy (Botkin, 1988)	Lawsuit where parents sue a prenatal physician for negligence leading to an unwanted pregnancy, such as a failed sterilization procedure.	Negligent actions causing unintended conception; often involves contraceptive or sterilization failure.
Wrongful Birth (Antunes de Souza, 2014)	Lawsuit where parents sue a prenatal physician for negligence resulting in the birth of a child with a disease or disability, with the physician's failure to inform removing the parents' right to make an informed decision.	Physician's negligence in informing parents about a child's condition; deprivation of the right to make an informed decision.
Wrongful Life (Botkin, 1988)	Legal claims where individuals assert being born with a serious genetic or congenital condition due to healthcare provider negligence, arguing they would have preferred not to have been born if informed during pregnancy.	Allegations of serious genetic or congenital conditions due to healthcare provider negligence; preference not to be born if informed about the condition.

disability, this action is brought by the child, not the parents. Strictly speaking, the main argument in a wrongful life suit is that the plaintiff has been harmed by having been brought into existence with their genetic condition, which would not have occurred if not for the physician's negligent conduct. This situation typically involves a physician who, although they did not cause the child's harmful condition, failed to detect and warn the parents about their child's risk of developing a severe and genetically transmitted disease or condition (Buchanan et al., 2000).

For clarity, wrongful life is a lawsuit brought by a child who claims that he was harmed for having been born with a severe genetic disease or condition. On the other hand, wrongful birth is a lawsuit brought by a parent who seeks compensation for the physician's negligence in failing to detect and inform the parents about their child's genetic disease or condition. The difference is in who brings up the claim; If by the child or if the parents bring it on behalf of the child, it is a wrongful life lawsuit; if the parent brings it up, it is a wrongful birth lawsuit (Billauer, 2020).

The notable aspect of wrongful life suits that distinguishes them from standard negligence claims is that the child's disease or condition is so intolerable that it makes the child wish he was never born. According to William Duncan, unlike the usual medical malpractice scenarios where a patient's injury or condition directly results from a healthcare provider's error, such as the accidental loss of a limb or the contraction of a disease, wrongful life and birth cases do not accuse the doctor of causing the child's disability. Instead, these cases center on the very existence of the

child with a disability as the alleged harm. This perspective necessitates that both the claimant and the legal system view the state of being born with a disability as an injury in itself (Duncan, 2004). Furthermore, the genetic diseases or conditions that usually appear in wrongful life cases are incurable, and the only way to prevent them is by terminating the pregnancy. Generally, courts worldwide find this claim offensive and often dismiss such actions because it is assumed that any life, regardless of its conditions, is better than nonexistence (Buchanan et al., 2000).

In this context, the Superior Court of Quebec declared the criterion of "reasonable foreseeable death" unconstitutional to request medical assistance in dying (MAiD) in the recent decision of Truchon v. Canada ("Legislative Background: Bill C-7: Government of Canada's Legislative Response to the Superior Court of Québec Truchon Decision", 2021). Part of this ruling stated that it is a matter of personal decision for each individual to judge whether or not life, as they experience it, is worth living (Shingler, 2019). The same reasoning could be applied to wrongful life cases, as it also involves an individual's claim that living with a debilitating illness is worse than never being born (Buchanan et al., 2000).

2.3.3 Contextual Factors that Gave Rise to the Creation of Wrongful Life Suits

Several contextual factors were fundamental to the emergence of wrongful life lawsuits. In the twentieth century, the establishment of informed consent, the sexual liberation movement, refinements to tort law, and the professionalization of medical genetics all played a crucial role in the trajectory of wrongful life actions nowadays (Haqq, 2020). Moreover, an overview of the contextual forces that gave rise to the notion of wrongful life suits will be provided to better understand the circumstances behind the legal precedents that will be reviewed in the following sections.

2.3.3.1 Genetic Counseling

Genetic counseling currently plays a vital role in wrongful life claims. Genetic counseling consists of providing information, addressing concerns about how a genetic condition could affect an individual, and estimating the risk of transmitting such a trait (*International Summit on Human Gene Editing: A Global Discussion*,

2015). For this reason, it has become an important option for individuals with a potential genetic condition in their family background who wish to conceive or are already in the early stages of pregnancy. As such, genetic counseling can be understood as a process undergone at the preconception or prenatal phase that aims to interpret genetic information associated with genetic diseases or conditions to avoid their transmission to future offspring (Antunes de Souza, 2014).

Since the early decades of the twentieth century, genetic counseling has been practiced (under different names) when the eugenics movement was prevalent. However, in the attempt to disassociate the practice from discredited eugenic notions, it was only described as genetic counseling in 1947 by the geneticist Sheldon Reed. As other geneticists and doctors were trying to separate the field of genetics more generally from its association with eugenics "science," Reed's description formalized the incorporation of genetics in clinical care. This led to a significant increase in medical genetics clinics in the 1960s, especially in the United States, where the expression 'wrongful life' was first coined in the 1963 case of Zepeda vs. Zepeda (Botkin, 1988). The details of this case are outlined later in this chapter.

In wrongful life lawsuits, the plaintiff is a child born with a disease or a disability who seeks damages from either their parents or their parent's doctor for allowing the child to be born with that condition. Due to a lapse in genetic counseling, physicians might provide a false negative diagnosis, resulting in failing to identify a genetic disease or disability. Therefore, in a wrongful life suit, the plaintiff claims that if not for the doctor's negligence in informing the parents about the child's genetic condition, they would have opted for ending the pregnancy (Botkin, 1988).

While the expansion of genetic counseling practices represented an essential step for reproductive freedom and wrongful life claims, other events also laid the foundations for this kind of litigation. For instance, in the first half of the twentieth century, a social transition occurred from childbirth by midwives to obstetricians in hospital settings, enabling situations of medical liability (Haqq, 2020). However, in the United States, it was the landmark decision in Roe v. Wade (1973) that, by declaring abortion a right, enabled the birth of wrongful life actions, since its fundamental claim is that the plaintiff's parents would have chosen to terminate the pregnancy if it wasn't for the negligence of the prenatal doctor.

After Roe v. Wade, other social movements gained strength from this decision, such

as the movement in support of equality of genders in employment; the right to contraception and abortion provided women greater control over their career prospects and family planning. As medical knowledge and prenatal technologies improved in detecting and treating congenital diseases, women could choose to terminate the pregnancy if a genetic condition was detected (Haqq, 2020).

Although prenatal torts existed before the Supreme Court's decision in Roe v. Wade, it was after that landmark case that wrongful life actions began to flourish. Conventional prenatal tort actions emerged in the early 1900s, but little attention was paid to them because they were uncommon, and there were no successful cases. Most states in the United States only began to recognize this kind of tort in the 1960s, when the first federal court acknowledged it. It is noteworthy that standard prenatal torts emerged during this time due to spikes in newborns' malformations due to the use of thalidomide. The new variants of prenatal torts, wrongful conception, wrongful birth, and wrongful life appeared in the mid-1960s, a time in which the literature on the ethics and legal aspects of the interests of the unborn and creating and avoiding harm to future generations was blooming (Haqq, 2020).

In the late 1960s, Congenital Rubella Syndrome was the most frequently litigated injury in wrongful life and wrongful birth lawsuits (Gleitman v. Cosgrove; Procanik v. Cillo; (Haqq, 2020). This syndrome results from maternal infection with rubella during pregnancy and afflicts infants. Severe consequences of this illness include heart disease, deafness, and delayed neurologic development (Tatiana Lanzieri et al., 2020). Although Congenital Rubella Syndrome is caused by a virus and not transmissible through genes, wrongful life cases involving this condition help pave the way for wrongful life litigations, including genetic diseases.

Throughout the 1980s and 1990s, as more genetic conditions were identified, other often alleged conditions – especially in wrongful life suits – were Down Syndrome ("Kassama v. Magat", 2001), Tay Sach's disease ("Howard v. Lecher", 1976), Sickle Cell anemia ("Williams v. Rosner", 2016), among others (Haqq, 2020). While some wrongful life suits provide parents some financial compensation for children with unexpected conditions, disability groups, and scholars have contested that this kind of lawsuit devalues life with a disability, which is the case for Down Syndrome litigation in wrongful life and birth suits (Rinaldi, 2009).

2.3.3.2 Challenges with Discrimination and Disabilities

Efforts to fight discrimination against people with disabilities highlighted the need to differentiate diseases from disabilities, which is pertinent to the discussion around wrongful life actions and the context of gene editing. Besides the expansion of genetic information provided by preimplantation and prenatal diagnosis of the embryo and fetus, gene editing is likely to enter clinics within the next 25 years. The possibility of modifying the human genome will impose new moral challenges to prospective parents and new liability issues on physicians, which is why it is crucial to examine the background of wrongful life lawsuits. Gene editing moves the discussion of wrongful life beyond its focus on harm prevention to potential liability around failure to provide genetic advantages to an individual (i.e., height, athletic traits, better memory, etc.) (Peebles, 2022).

2.4 Chapter Summary

This chapter has highlighted the historical development of gene editing, its main concepts, the transformative potential of CRISPR-Cas9, and the ethical and legal challenges presented by fetal gene editing and wrongful life claims. This chapter paved the way for understanding gene editing's implications, and prepares the reader for deeper discussions on the ethical, legal, and societal dimensions in the following chapters. In section 2.1, we summarized the main historical roots and modern scientific achievements and key milestones regarding gene editing. In section 2.2, we covered the concept of Fetal Gene Editing, emphasizing the role of CRISPR-Cas9 and categorized genetic diseases and conditions that could potentially benefit from fetal gene editing. In section 2.3, we analyzed the historical landmarks on wrongful life cases, defined wrongful life claims, distinguishing them from other concepts while examining the legal trends that contributed to wrongful life litigation, including the development of genetic counseling and other notions within medical ethics and genetic medicine.

Chapter 3

Related Work

This chapter serves to lay out where our thesis stands in relation to some of the most recent work of experts like Billauer, Roa, Ishii, Araujo, Ranisch, and Friedmann on the debates on legal aspects of gene editing and enhancing genetic traits. By comparing our positions with those authors, we aim to carve out a space for our contributions within this narrative, expressing where we converge and diverge, while offering a fresh perspective on the future of gene editing.

3.1 Ethical Perspectives on Lawsuits in the Gene Editing Context

The works of Billauer (Billauer, 2020), Roa (Roa, 2021), and Ishii (Ishii, 2021) each highlights different aspects of the ethical debate on genetic manipulation. Billauer's paper, "Wrongful Life in the Age of CRISPR-CAS: Using the Legal Fiction of 'The Conceptual Being' to Redress Wrongful Gamete Manipulation," introduces a novel legal construct, the "conceptual being," to address the gap in wrongful life claims and provide a pathway for compensation for individuals born with genetic modifications. Similarly, Roa's "Designing Children: Tort Liability for Medical Providers in the Era of CRISPR/CAS-9 Genetic Editing" explores the potential for tort liability for medical providers, emphasizing the need for a clear legal framework to address the consequences of genetic editing errors. On a different perspective, Ishii's "Assignment of responsibility for creating persons using germline

genome-editing" shifts the focus to the ethical responsibility and the challenges of consent of germline genome editing. The following lines will detail each of the contributions listed above contrasting with our position towards the ethical perspectives on lawsuits in the context of gene editing.

3.1.1 Wrongful Life in the Age of CRISPR-CAS: Using the Legal Fiction of 'The Conceptual Being' to Redress Wrongful Gamete Manipulation

The paper "Wrongful Life in the Age of CRISPR-CAS: Using the Legal Fiction of 'The Conceptual Being' to Redress Wrongful Gamete Manipulation" by Barbara Pfeffer Billauer (Billauer, 2020) discusses how traditional law struggles to handle problems from new reproductive technologies, which could result in the birth of children with a disease or disability. She anticipates the resurgence of wrongful life actions as a legal avenue to obtain compensation for injuries. In light of the courts' reluctance to accept wrongful life claims, a stance generally grounded on the argument of the sanctity of life, the author suggests a reformulated version of wrongful life named Wrongful Gamete Manipulation, an action brought by a fictional individual – the conceptual being – where a child born with genetic defects as a direct result of faulty genetic manipulation would be able to sue the negligent physician for the harm. By reformulating its name, the author intends to distance this legal action from the pre-conceived erroneous interpretations that courts have regarding wrongful life lawsuits.

The issues raised by the author are similar to the ones presented in this thesis, as we are also concerned in addressing medical negligence in the context of fetal gene editing. We agree with Billauer's position regarding the need to establish just means to seek compensation for a harm inflicted on a child before birth, however, with a different approach. While we specifically address injuries caused by negligently performed gene editing in fetuses' somatic cells, Billauer focuses on gene editing applied in embryos, which would likely result in modifications to the germline. In this context, the author anticipates scenarios in which genetic defects generated by faulty gene editing could be passed down from generation to generation but argues that it would be a difficult endeavor to claim this kind of harm in a wrongful gamete

manipulation action due to the issue of assigning blame. We acknowledge the consequences of gene editing in the germline, however, because it is not possible to predict how these alterations would impact future generations or how to assign culpability were a legal action to be initiated in this context, we are not concerning ourselves with germline gene editing here. Instead, our argument is focused on individuals directly harmed by somatic cell gene editing in utero. In this context, both the specific embryo whose genes are manipulated as well as the particular clinician involved in conducting the genetic therapy can be clearly identified. As such the potential for a successful wrongful life suit is heightened. Hence, somatic cell editing in utero is the focus of this thesis.

3.1.2 Designing Children: Tort Liability for Medical Providers in the Era of CRISPR/CAS-9 Genetic Editing

"Designing Children: Tort Liability for Medical Providers in the Era of CRISPR/CAS-9 Genetic Editing" by Sarah Roa (Roa, 2021), examines the legal implications of CRISPR/Cas-9 gene editing technology in the context of tort law. The paper describes the scientific background of CRISPR/Cas-9, discussing its therapeutic potential while also noting the ethical and legal challenges posed in two scenarios: A) when a physician performs gene editing with CRISPR-Cas9 to result in a healthy child, but the child is directly harmed by off-target effects, here understood as unexpected genetic mutations that might lead to undesired physical appearance, cell death or diseases; and B) when parents request a physician to intentionally select genetic defects with the goal of producing a child with a harm (the author did not specify if the harm would be a disease or a disability). In light of the absence of a lawsuit to claim compensation in either scenario, Roa discusses the adequacy of wrongful life lawsuits to address both issues; however, given that courts often reject such claims, the author renames the lawsuit to "mistaken manipulation". In scenario A, the author argues that the genetically-modified child injured by off-target effects would have a claim on medical negligence grounds. In contrast, scenario B invokes a battery claim, given that the physician's harmful actions were intentional. It concludes by advocating for legal remedies that recognize the rights of children affected by CRISPR/Cas-9 editing, moving beyond

traditional wrongful life arguments.

Roa explores how current legal frameworks might grapple with the consequences of CRISPR-Cas9 technology, especially when off-target effects or other unintended outcomes result in harm. Building on the theme, Billauer introduces the concept of "the conceptual being" as a means to address the legal gap in wrongful life actions. This aims to expand the class of damages recoverable by children born with serious harms due to genetic editing, offering a pathway to compensation for pain and suffering, emotional injury, and even unjust enrichment. Billauer's proposition is a significant departure from traditional legal remedies, reflecting the challenges posed by CRISPR-Cas9 and the limitations of existing legal frameworks to compensate for such harms.

Regarding this thesis, the proposed idea is similar. Like Roa, we discuss the ethical and legal implications of gene editing applied before birth, as well as its therapeutic capabilities. In addition, like Roa, we examine wrongful life claims arising in the gene editing context; however, Roa's scenario A is more congruent with this thesis' objectives than scenario B. Besides, the thesis provides a broader scope, encompassing a wider overview of the ethical implications of gene editing applied in utero, while Roa's article is mostly focused in tort law. In conclusion, Roa and this thesis present complementary ideas that will further reflect on the implications of gene editing.

3.1.3 Assignment of responsibility for creating persons using germline genome-editing

Ishii's work entitled: "Assignment of responsibility for creating persons using germline genome-editing" (Ishii, 2021) explores the assignment of responsibility associated with using germline genome-editing (GGE) in embryos, focusing on the risks and potential harms. The study refers to the controversial 2018 announcement of gene-edited children in China and discusses the difficulties in proving the absence of harmful off-target mutations because the precision of genome sequencing relies on the DNA samples. Given that GGE comprises the whole genome, it means that an off-target mutation could be overlooked. In essence, the paper emphasizes the responsibility of practitioners and parents for the safety of genome-edited offspring.

Furthermore, it examines the ethical implications of GGE and the challenges of follow-up for individuals born through it. The uncertainty in assigning responsibility is discussed in the context of potential legal claims by offspring harmed by unsafe GGE, with the authors suggesting that societal attitudes toward the risks and benefits of GGE may influence policies, leading to either its prohibition due to unacceptable risks or its acceptance based on a tolerable balance.

The core of Ishii's argument is on the responsibility towards individuals born via GGE and the broader societal implications of altering human genomes. Ishii also highlights the lack of international consensus on the safety and ethical acceptability of GGE, raising concerns about off-target mutations and the long-term health impacts on individuals. In contrast, Billauer's work does not directly tackle the broader ethical implications of CRISPR-Cas9, instead, it addresses the specific legal issue of wrongful life actions in the context of genetic editing, focusing on the legal mechanisms through which harmed individuals could seek redress. While ethical considerations are her basis, the paper is concerned with the practical side of legal theories to address the outcomes of faulty genetic manipulation.

Ishii's and Roa's papers converge on the themes of responsibility and consent, although from different angles. Ishii questions the ethical responsibility of practitioners and parents in the GGE process, highlighting the complexities on consent when the individuals most affected by the decisions—those born via GGE—cannot participate in the decision-making process. Roa, meanwhile, considers that in the informed consent is not relevant since medical negligence is related to whether the physicians involved engaged in their stated area of expertise with an adequate level of competence.

Comparing to our work in this thesis, Ishii's article strengthens our argument regarding the kinds of cells that should be targeted in gene editing procedures, once it clarifies the risks of germline genome editing. The article briefly mentions that if an individual harmed as a result of unintended mutations of GGE wanted to sue the physician or their parents through a wrongful life lawsuit, the individual would likely be unsuccessful. The author explains the difficult task of demonstrating whether their health condition was caused by an off-target effect or not, once it is recognized that mutations that can occur naturally during the embryo's development could hinder this process. Furthermore, it would become more difficult to obtain the proof

after the genetic mutations are passed down from generation to generation.

3.1.4 Summary of Ethical, Legal and Consent Topics in Gene Editing

Table 3.1 summarizes the comparison between this thesis and the works from Billauer, Roa and Ishii regarding the main topics discussed in these works, namely: "Ethical Considerations and Societal Impacts", "Legal Challenges and Liability", "Responsibility, Consent, and Regulation". Further development of the topics addressed in this section and explanations about their direct relevance to the topic of this thesis are provided in Chapter 4.

Table 3.1: Ethical, Legal Liability and Consent Work Comparison

Source	**Ethical Considerations**	**Legal Challenges and Liability**	**Responsibility, Consent, and Regulation**
Billauer, 2020	Indirectly touches on ethical implications through legal theories.	Proposes "the conceptual being" to address legal gaps in wrongful life actions, offering a new form for compensation.	n/A
Roa, 2021	n/A	n/A	Highlights the critical role of informed consent as a defense against liability, pointing to the need for robust consent processes.
Ishii, 2021	Emphasizes the ethical challenges of GGE, including risks and the societal implications of altering human genomes.	n/A	Questions the ethical responsibility of practitioners and the consent process, given the impact on individuals unable to consent.
This Thesis	Explores the ethical reasoning of courts' decisions in rejecting wrongful life claims.	Examines if physicians can be sued for gene editing failures or for not performing it.	n/A

3.2 Ethical Perspectives on Enhancement of Genetic Traits

In this section, we discuss the perspectives of Araujo (de Araujo, 2020), Ranisch (Ranisch, 2020), and Friedmann (Friedmann, 2019) on the enhancement of genetic traits. Araujo's work, "The Ethics of Genetic Cognitive Enhancement: Gene Editing or Embryo Selection?", evaluates how we approach the moral considerations of genetically enhancing humans, particularly through CRISPR and embryo selection. Similarly, Ranisch's discussion in "Germline genome editing versus preimplantation genetic diagnosis: Is there a case in favour of germline interventions?" contrasts the ethical implications of germline genome editing (GGE) with those of existing reproductive technologies, probing the justifiability of GGE over preimplantation genetic diagnosis (PGD) from both clinical and ethical standpoints. Furthermore, Friedmann's editorial, "Genetic therapies, human genetic enhancement and ... eugenics?", raises additional concerns about gene therapies to the ethically controversial field of human genetic enhancement, highlighting the dangers of reviving eugenic ideologies. We compare these scholars' insights with our thesis's stance on the dilemmas posed by genetic enhancement, highlighting where our views align or diverge.

3.2.1 The Ethics of Genetic Cognitive Enhancement: Gene Editing or Embryo Selection?

The work "The Ethics of Genetic Cognitive Enhancement: Gene Editing or Embryo Selection?" (de Araujo, 2020) explores how an innovative discussion on the morality of genetically enhancing humans has been prompted by current research with human embryos conducted in many regions of the world. The author observes that while the focus has been on gene editing technologies, particularly CRISPR, there has been less discussion of the possibility of pursuing human enhancement through IVF in combination with in vitro gametogenesis, genome-wide association studies, and embryo selection. As a result, he looks at the moral ramifications of the pursuit of cognitive enhancement through embryo selection and gene editing, respectively. He contends that public perceptions of human genomes and enhancement research have

to be taken into account in the philosophical discussion of the ethics of enhancement.

Despite the different scope between Araujo's article and the thesis, there are multiple similarities among both. For instance, Araujo raises the question of whether genetic enhancement through gene editing and embryo selection is morally acceptable. Although the thesis focuses mostly on gene editing, the same question is raised regarding the potential use of the technique to enhance non-disease genetic traits. The author also touches on one of the main aspects of this thesis, that is, whether the child gene-edited prior to birth would be entitled to sue their doctor in case they failed to enhance their non-disease traits (Araujo uses cognitive enhancement as his main example). In addition, Araujo touches on the aspect of parental responsibility, stating that if prospective parents are aware that they will bring a child affected with a disease into the world and have access to technologies that could potentially relieve the child from the condition, the parents would be morally accountable if they failed to use the technology. This argument is in line with the idea proposed in this thesis regarding a moral obligation to use fetal gene editing to remove severe single-gene diseases.

3.2.2 Germline genome editing versus preimplantation genetic diagnosis: Is there a case in favour of germline interventions?

The author Robert Ranisch that wrote "Germline genome editing versus preimplantation genetic diagnosis: Is there a case in favour of germline interventions?" (Ranisch, 2020), explores the ethical implications on germline genome editing (GGE) in comparison to existing reproductive technologies like preimplantation genetic diagnosis (PGD). He examines whether GGE presents any significant advantages over PGD from both clinical and ethical perspectives. Ranisch argues that while GGE may offer unique opportunities in specific scenarios where PGD cannot ensure the birth of a healthy child, the ethical justification for GGE is complex, which includes the problem of consent, and societal implications such as exacerbating social inequalities and the prospect of designer babies.

Although the author focuses on reasons in favor of GGE applications, some of them can be used to support the argument in the thesis. For instance, Ranisch argues

that GGE would be a preferable alternative to PGD in circumstances where one or both prospective parents are carriers or suffer of a genetic disorder and desire to have a genetically-related child free of this condition. Although PGD can occasionally increase the likelihood that intended parents will have healthy children, it is not always a successful tactic. In certain cases, such as when both parents are homozygous for an autosomal recessive genetic disorder (e.g. cystic fibrosis) PGD will be of little benefit at all, or the likelihood that selective reproduction may assist intended parents in producing a child devoid of the mutation is extremely low. In light of the risks presented by GGE, we contend that such argument is applicable in the case of in utero gene editing applied to somatic cells.

3.2.3 Genetic therapies, human genetic enhancement and ... eugenics?

Theodore Friedmann's editorial in Gene Therapy, "Genetic therapies, human genetic enhancement and ... eugenics?" (Friedmann, 2019), highlights the evolution from therapeutic applications aimed at treating genetic diseases to the potential for genetic enhancements. He differentiates between medically justifiable gene therapies and genome editing for disease treatment and the ethically fraught territory of enhancing human traits, advocating for a ethically grounded approach to genetic research, and emphasizing the need to prevent the revival of eugenic ideologies.

Although not an innovative argument, the article articulates concerns about harmful applications of gene editing technologies, alerting to the potential discriminatory use to select "desirable" genetic traits. This discussion is intimately related to the thesis' discussion, as we also contend the moral wrongness of fetal gene editing to enhance non-disease genetic traits.

3.2.4 Summary of Ethical Concerns, Clinical and Societal Implications of Fetal Gene Editing Technologies

Regarding the Ethical Concerns, the papers mentioned thus far express deep concern about the potential for genetic technologies to be used with eugenic intentions, which would ultimately devalue the lives of people with disabilities. Overall, they

emphasize the importance of establishing limits to the applications of gene editing before birth, and that the most beneficial use should be directed towards disease prevention. While similar views are presented, each paper achieved their goal through different approaches. As an example, Friedmann's paper cautions the use of gene editing technologies for enhancement purposes by referencing former social programs adopted in the early twentieth century. Those programs encouraged reproduction among individuals with "desirable traits" while enforcing extreme measures to prevent the birth of those associated with disabilities. In contrast, Ranisch focuses more on the specific ethical dilemmas presented by GGE and PGD, analyzing them through the lens of contemporary ethical theories without delving as deeply into the historical context.

Considering the clinical implications of genetic technologies, such as the benefits of GGE, in preventing or curing genetic diseases are acknowledged across the papers. They recognize the transformative potential these technologies hold for addressing conditions that are currently untreatable, although they allude to germline gene editing, and not somatic gene editing. For instance, Ranisch provides an analysis of scenarios where GGE could offer clinical advantages over PGD, particularly in cases where PGD cannot select disease-free embryos due to genetic constraints of the parents. He examines the clinical and moral rationale for pursuing GGE in these contexts, which include the avoidance of discarding affected embryos when undertaking PGD, given that gene editing can in theory correct the genetic mutations that cause diseases. Conversely, Friedmann remains more concerned with the broader ethical implications and potential misuse of genetic technologies for enhancement, rather than dissecting specific clinical scenarios where gene editing techniques could be more advantageous than other technologies.

In terms of the societal implications of genetic technologies, a common denominator among the papers is the need for careful consideration and regulation of genetic technologies to prevent potential misuse and ensure ethical deployment. The documents highlight the importance of societal debate and ethical oversight in guiding the development and application of these technologies. Friedmann discusses the societal implications of genetic enhancements in a broad sense, cautioning against the pursuit of eugenic goals under the guise of enhancement. He calls for a societal consensus on the ethical boundaries of genetic technologies, which he believes should be limited to therapeutic applications. Ranisch, while acknowledging

similar concerns, is more focused on articulating a nuanced ethical framework for evaluating when GGE might be ethically justifiable, especially in comparison to PGD, emphasizing the conditions under which GGE could be pursued ethically.

Table 3.2 summarizes the above comparison among the works presented in this section. These key insights summarized here will be further explored in Chapter 5.

Table 3.2: Ethical Frameworks, Clinical and Societal Implications Work Comparison

Source	**Ethical Frameworks**	**Clinical Implications**	**Societal Implications**
de Araujo, 2020	Discusses the morality of genetic enhancement via gene editing and embryo selection.	Focuses on cognitive enhancement, questioning the ethics and potential responsibility of gene editing before birth.	Considers the societal impact and ethical implications of human genome enhancement research.
Ranisch, 2020	Explores ethical justifications for GGE over PGD, focusing on consent and societal impact.	Analyzes GGE's clinical benefits over PGD, especially in scenarios where PGD fails to ensure the birth of a disease-free child.	Highlights potential social inequalities and the emergence of designer babies due to GGE
Friedmann, 2019	Differentiates between therapeutic gene therapies and ethically contentious human enhancements. Warns against eugenics and the discriminatory selection of traits.	Critiques the potential misuse of gene editing for enhancement instead of focusing on specific clinical scenarios.	Discusses the need for societal consensus on ethical limits of genetic technologies, primarily to therapeutic uses.
This Thesis	Aligns with discussed sources by questioning the moral obligation to use gene editing for disease prevention and addressing wrongful life claims.	Considers the implications of wrongful life lawsuits for gene editing failures or omissions, particularly in non-disease trait enhancement.	Touches on parental responsibility and the societal debate on ethical applications of gene editing, focusing on preventing misuse and ensuring ethical deployment.

3.3 Other Research Topics Related to Ethical Aspects of Gene Editing

From a research perspective, the topics previously discussed represent the foremost areas of interest within Ethics in Gene Editing. Nonetheless, other research topics have emerged, including "Ethical Perspectives on Gene Editing Regulations". While

it is not the focus of this thesis, we have provided an overview of the latest contributions as follows.

A regulatory framework for gene editing faces multiple challenges, including the number of applications ranging from somatic cell therapies to germline edits. Consequently, each area demands unique regulatory approaches, encompassing everything from individual consent to the wider societal and environmental consequences. Moreover, national regulatory stances can differ, due to the diverse cultural, ethical, and legal viewpoints regarding gene editing. While some nations have embraced the research on the topic, others have prohibited it on specific practices, such as germline editing. The study titled "Experiments that led to the first gene-edited babies: the ethical failings and the urgent need for better governance" is among the few that afford considerable focus ethical aspects of regulation in this field (Li et al., 2019). The argument is built on top of a recent achievement from Chinese scientists who claimed to have gene-edited the first baby to be naturally immune to the human immunodeficiency virus (HIV).

3.4 Chapter Summary

This chapter encapsulates the central arguments and contributions of this thesis by comparing its views to those of some of the most recent papers on the ethical and legal aspects of gene editing. First, in Section 3.1 we commented on the legal frameworks for wrongful life claims and medical liability, discussing the proposals and analyses offered by the scholars Billauer, Roa, and Ishii to address the unique challenges posed by gene editing. Then, in section 3.2 we emphasized the ethical considerations surrounding the enhancement of genetic traits through gene editing through the works by Araujo, Ranisch, and Friedmann. This section highlighted the moral debates on cognitive enhancement, the comparison between germline genome editing and preimplantation genetic diagnosis, and the caution against eugenic practices. Lastly, in section 3.3 we acknowledge other relevant fields of research that were not addressed in the thesis, such as regulatory challenges. The section called for a careful and ethically informed approach to gene editing research, highlighting the balance needed between advancing scientific knowledge and upholding moral responsibilities.

Chapter 4

Ethical Perspective of Wrongful Life and Fetal Gene Editing

This chapter dissects the legal criteria of wrongful life, such as duty of care, breach of standard, causation, and damage, alongside examining the ethical nature of the doctor-patient relationship concerning fetal gene editing. It delves into the advantages fetal gene editing holds over traditional methods, balancing the moral obligations, potential benefits and risks. Furthermore, it examines how fetal gene editing could reframe the philosophical foundations of wrongful life suits, introducing ethical discussions centered on the prevention of genetic diseases and the obligations to prevent harm and to ensure a "genetic decent minimum".

4.1 Legal and Ethical Aspects of Wrongful Life

The intersection between bioethics and law is mostly evident in situations involving medical malpractice. When patients' health is harmed by negligent medical conduct, it is considered unjust and requires reparation through legal means. In this section, we contend that if a child is harmed due to a negligently performed fetal gene editing or due to negligence with regard to failing to offer in utero gene editing when the child was still a fetus in the first place, they are entitled to sue the physician through a wrongful life lawsuit.

4.1.1 Criteria for Wrongful Life

To ascertain why wrongful life is the appropriate legal action to address situations involving medical negligence in fetal gene editing, it is necessary to lay out the criteria for this lawsuit and verify if all the requirements are fulfilled. A wrongful life lawsuit is a type of medical malpractice, specifically a prenatal negligence lawsuit, due to when negligent conduct that resulted in injury occurred (Burns, 2003). As such, a plaintiff in a wrongful life must prove the basic elements of malpractice: duty of care, breach of the standard of care, causation, and injury (Solomon, 2006).

4.1.1.1 Duty of Care

The first element, the duty of care, is established when there is a doctor-patient relationship. Typically, this relationship arises when a person seeks care in a clinical setting and a physician attends to their medical needs. In a wrongful life suit involving fetal gene editing, the plaintiff (a child born with a severe disease) must prove that the physician owed them a duty of care when they were a fetus. Although fetal gene editing can only be sought by the pregnant person and not the fetus itself, this procedure is aimed at treating the fetus; therefore, the fetus can be considered a patient, and the physician has a direct duty of care toward them (Powell, 2017).

4.1.1.2 Breach of Standard

The second element is a breach of standard of care, which occurs when a physician fails to provide medical services with the same care and diligence expected from a reasonable physician who treats a patient with the same or comparable clinical presentation and in similar circumstances (Solomon, 2006). For instance, in Park v. Chessin, due to the physician's failure to inform a couple of patients about the risks of transmitting a fatal condition to their offspring, the couple conceived a child affected by the feared disease (Zhang, 2012).

4.1.1.3 Causation

The third element, causation, is the key factor that distinguishes a standard medical negligence action from a wrongful life lawsuit. Causation is the causal connection

between the physician's negligent conduct (breach of duty of care) and the alleged damage to the plaintiff (Solomon, 2006). In a standard medical negligence lawsuit, courts usually apply the "but for" test to establish a causal nexus; that is, they ask, "But for the defendant's negligence, would the plaintiff have been injured?" If the answer is affirmative, it can be treated as an ordinary medical negligence lawsuit (Lovell, 2018). In a wrongful life lawsuit, however, the plaintiff does not claim that the doctor caused their disease but that had the professional not been negligent, the child would not have been born with a severe and debilitating disease (Frasca, 2006).

4.1.1.4 Damage

The fourth element, damage, is the most important aspect of wrongful life actions and also the reason why courts are reluctant to uphold such claims. In this case, the harm alleged by a plaintiff is having been born with a severe disease that, although preexistent to the physician's misconduct, was not remedied or alleviated by the professional. Nevertheless, most courts have interpreted wrongful life claims as the right not to be born because the alternative to being born with a severe condition would never to have been born at all (Billauer, 2020). Table 4.1.1.4 summarizes the Wrongful Life elements.

Table 4.1: Elements of Wrongful Life Lawsuit

Element	**Description**	**Example/Reference**
Duty of Care	Doctor-patient relationship in clinical setting; fetus considered a patient in gene editing.	Fetal gene editing and duty of care.
Breach of Standard	Physician's failure to meet expected care; deviation from standard leading to harmful outcomes.	Failure to inform patients, resulting in a child with a fatal condition.
Causation	Connection between physician's negligence and plaintiff's harm; in wrongful life, not causing but preventing severe disease.	Application of "but for" test in medical negligence vs. wrongful life.
Damage	Alleged harm: born with burdensome disease not alleviated by the professional; courts reluctant due to misinterpretation.	Misinterpretation of wrongful life claims and the alleged harm.

With the arrival of fetal gene editing in clinics, such interpretation is likely to

change. In this context, since the negligently performed act proposed in this study is the failure to properly remove a genetic disease in a fetus with gene editing, the resulting harm – a child with a preexisting debilitating disease – will not be measured against nonexistence but against the outcome in which a correctly performed fetal gene editing would have resulted in a child free of a severe disease.

In light of the four basic elements explained above, for a claim to be characterized as a wrongful life claim, its fundamental argument must derive from the damage of living a wrongful life. As proposed in this thesis, the negligent act performed by the physician happens when the plaintiff is in the fetal stage, which falls under the prenatal torts category and not standard medical negligence. The doctor also does not cause the plaintiff's disease in this hypothetical scenario, unlike in routine medical malpractice, but is responsible for not eliminating the devastating condition. It can be concluded that a wrongful life lawsuit is the most adequate legal avenue to address issues arising from negligent fetal gene editing.

4.1.2 The Doctor-Patient Relationship in the Context of Fetal Gene Editing

Mistakes can occur with the increasing availability of prenatal services and the eventual implementation of gene editing techniques in clinics. Miscalculations when modifying one's DNA might cause severe problems if that fetus becomes a person in the future. Therefore, it is necessary to establish just means for individuals injured as fetuses through a negligently performed gene editing process or through negligence by omission of the opportunity to have had undergone the procedure while the child was still a fetus.

Although children injured before birth can seek damages in certain jurisdictions, the courts that recognize such claims do so by broadly interpreting the physician's duty to the patient. For instance, in cases in which a physician negligently performed surgery on a woman's uterus and a child conceived later suffers the consequences of the doctor's actions, some courts have recognized a preconception tort by seeing the child as a third beneficiary of the doctor-patient relationship (Powell, 2017). This kind of interpretation might also be applied in the context of gene editing human fetuses. In fertility services, only the pregnant person is considered a patient;

however, due to the presence of a fetus in the patient's uterus, the physician also has a beneficence-based obligation to the fetus (Powell, 2017). Thus, in the event of negligent gene editing, the future individual could have grounds to seek damages.

Because of this unique point in the life of the future individual when gene editing occurs, the traditional doctor-patient relationship must be reviewed. Since gene editing will be performed on a fetus in a person's uterus, it is reasonable to attach to it certain duties owed by the responsible physician. This would not mean that physicians would owe duties to a hypothetical future person, but the same beneficence-based duty owed to a fetus in a person's uterus (Powell, 2017). As such, this ensures that the welfare of the future individual is safeguarded without extending obligations to hypothetical future entities, thereby maintaining a balance between medical innovation and ethical medical practice.

4.1.3 Ethical Perspective of Wrongful Life Cases

Wrongful life claims are charged with complex ethical questions, such as whether individuals with severe health conditions would be better off having never been brought into existence. Beyond legal reasoning, courts often reject such claims on ethical grounds. In this section, we analyze how the introduction of fetal gene editing in clinics could change courts' objections to wrongful life suits.

The underlying ethical arguments in courts' reasoning to object to wrongful life claims can be gathered from two perspectives. Both approaches pertain to what constitutes harm in these claims, as the unique feature of a wrongful life suit is that "life itself is an injury and that the defendant's negligence caused the birth and thus the injury" (Liu, 1987). The cases outlined earlier illustrate some of the key ethical perspectives that have informed the courts in the past and which will no doubt influence subsequent wrongful life decisions.

The first ethical perspective is the high regard for the sanctity of life. For instance, in Gleitman v. Cosgrove (1967), in which a child was born with congenital disease due to the prenatal doctor's negligence in informing the mother about the risks of contracting rubella during pregnancy, the plaintiff claimed his right not to be born with such a devastating condition. The court, however, decided that such a claim "would be precluded by the countervailing public policy supporting the preciousness

of human life" and therefore rejected the claim ("Gleitman v. Cosgrove", 1967).

This notion is no longer as strong as it was during Gleitman v. Cosgrove. Currently, this reasoning is balanced against the respect for the quality of life, thus weakening the notion that life, whether experienced with or without diseases/disabilities, is always a great good (Billauer, 2020). For a specific category of people experiencing diseases such as Huntington's disease, living with this condition is so challenging that the sanctity of life position is challenging to maintain (Buchanan et al., 2000).

The second ethical perspective is the interpretation that wrongful life encourages the idea that the birth of a child with disabilities could constitute harm. This thorny concern rekindles eugenic threats, which several disability rights advocacy groups have also voiced against recognizing wrongful life claims and the use of reproductive assisted technologies such as prenatal genetic testing (Billauer, 2020); (Parens and Asch, 1999). This is indeed a legitimate concern, given there is a general ableist assumption that people with disabilities are in a constant state of pain and suffering. Having a disability does not impede an individual from enjoying a worthwhile life. Thus, it should not be ethically or legally justified to accept a claim that nonexistence is preferable to living with a disability (Sulfian, 2021).

People with disabilities battled for their rights to be treated equally and with respect after years of segregation, euthanasia programs, and forced sterilization. Advocates for disability rights have made strides in educating the public about prejudice and the value of persons with disabilities lives. Still, they continue to encounter antidisability prejudice, notably in the provision of reproductive medicine (Kaposy, 2019). When the diagnosis of prenatal genetic testing shows a positive result for disabilities, such as Down syndrome, it generally culminates in the termination of pregnancy. As such, disability rights advocates have raised concerns about human gene editing, given that it enables the selection of traits and might promote more discrimination (Genetics and Society, 2019).

Given that there is a category of genetic diseases that are so severe that they might result in the affected individual having a life not worth living, as in the cases previously described, wrongful life claims should not be rejected in courts in such circumstances (Buchanan et al., 2000). According to Billauer (2020), "the importance of the wrongful life claim is that it incorporates the child's life-long damages for pain, suffering, fear, and related emotional angst, along with economic

loss—claims which together typically generate higher awards" (p. 455).

4.2 Ethical Considerations of Fetal Gene Editing

This section examines the ethical debate that emerge from the potential to modify the genetic makeup of fetuses to prevent severe hereditary diseases, exploring the balance between the risks and benefits of preventing genetic disorders before birth and the ethical responsibilities entailed in making such decisions. By analyzing the advantages of fetal gene editing in comparison to embryo gene editing and the moral obligations tied to the prevention of genetically transmitted diseases, this section highlights the ethical considerations that must guide the application of gene editing technologies and sets the stage for an exploration of the ethical dilemmas, potential benefits, and moral questions regarding fetal gene editing.

4.2.1 Advantages of Fetal Gene Editing Over Embryo Gene Editing

There are three stages in human development at which single-gene diseases can be targeted. First, at the preconception stage, gene editing technologies can be applied to gametes (Mattar et al., 2021). Genomic modifications carried out at early embryonic development stage or even pre-implantation embryos would result in effects that are both unknown and irreversible; in addition, these alterations would be inherited by future generations. Due to uncertainty about the potential effects of genetic alterations on human reproductive material (such as eggs, sperm, or embryos), several countries and international agreements prohibit these practices when they are intended to be used during pregnancy. This approach demonstrates a precautionary attitude in regulating technologies like gene editing to prevent potential harm or unintended consequences (Vidalis, 2022).

While modifications on early-stage embryos would transmit genetic changes to future offspring, alterations to later-stage embryos' or fetuses' DNA can be confined to the future individual. As such, it is possible to target monogenic diseases prenatally and avoid safety concerns of consequences for future generations. To edit the genome of an embryo without affecting its germline, gene editing should be applied in utero at

a mid-to-late gestation stage. From the moment of conception until the eighth week of pregnancy, the conceptus is considered an embryo; after this threshold, until birth, it is deemed a fetus ("Fetal Development: Stages of Growth", 2020).

Preimplantation embryo editing requires the genetic mutation to be identified and corrected before uterine implantation. In fetal gene editing (or in utero genome editing), however, the technology could be applied to address genetic mutations diagnosed later in pregnancy. On the one hand, while preimplantation embryo gene editing is performed ex vivo (i.e., outside the body of the mother), the mother has minimal chances of being affected by it. In utero gene editing, on the other hand, is conducted in vivo (i.e., gene editing is performed directly into the body), and thus implications to the mother must be taken into account (Peranteau and Flake, 2020).

Previously, prenatal interventions were limited by a lack of technologies to make timely and reliable molecular diagnoses. Beyond diagnostic hurdles, there was no way to precisely target genetic mutations responsible for genetic diseases in utero. However, thanks to refinements in genomic sequencing technologies, even small-scale structural genetic mutations that cause disorders can now be detected within a few hours or days. With the advent of gene editing technologies such as CRISPR-Cas9, precise genomic intervention to correct underlying pathogenic mutations before birth is now a realistic goal. However, more studies are needed before gene editing arrives in clinics (Shanahan et al., 2021). More details on the delivery of in utero gene editing can be found in Appendix A.

4.2.2 Ethical Considerations in Fetal Gene Editing: Balancing Risks, Benefits, and Moral Obligations

Following the discussion on the legal and ethical dimensions of wrongful life and the broader ethical implications of fetal gene editing, this section examines the moral obligations of medical practitioners and the ethical responsibilities toward both the unborn child and society. Besides, it also anticipates the societal implications, thereby preparing the ground for wrongful life claims in the context of gene editing.

Despite the promising results in preclinical studies involving fetal gene editing procedures with animal models for diseases like Hemophilia A and B, fetal gene editing has critical hazards that must be addressed prior to moving into clinics. The

most pressing risks of fetal gene therapy using gene editing include the risk of disrupting normal development, the risk of affecting the germline with genetic alterations, and the risk of genotoxicity or oncogenesis, which can be translated into damages to the DNA that may lead to cancer (Peddi et al., 2022). Given the promise and concomitant benefits of gene editing technologies, we can anticipate that they will eventually make their way to the clinic. However, given the risks and other unknown adverse effects we should also anticipate the possibility of future wrongful life litigation related to the clinical applications of these technologies.

Beyond technical issues that impede immediate clinical applications of gene editing in utero, ethical concerns must also be taken into consideration. Gene editing applications have unique risks, such as unintended effects and mosaicism which occurs when only a few cells are genetically modified, and others are not. Currently, in light of positive results yielded from in utero gene editing in animal studies, fetal gene editing is more likely to be moved into clinics than embryo genome editing, given that it avoids germline modifications (Mattar et al., 2021).

In utero gene editing also has particular ethical concerns that do not arise with embryo gene editing or postnatal gene editing, as in the former case, there are two patients – the fetus and the mother (Peddi et al., 2022). In this procedure, only the fetus might benefit directly from it, but not the mother; although the prospective mother has the right to refuse treatment, this may lead to situations in which a mother feels pressured to consent to the procedure or feels judged and guilty for opting not to undertake this intervention. Even though the mother's autonomy overrides fetal beneficence, this may not preclude ethical and legal ramifications (Mattar et al., 2021). Another ethical concern revolves around the purpose of in utero gene editing. Given that gene editing technologies can modify any genetic trait, some individuals may wish to use these technologies beyond disease-prevention to enhance non-disease traits in the future child.

Once the practical and ethical concerns regarding in utero gene editing are addressed and deemed effective in targeting diseases, experts believe it will significantly improve individuals' overall quality of life (Peddi et al., 2022). However, errors could still occur even when therapeutic effectiveness and safety are achieved for in utero gene editing; in other words, this intervention might not achieve the desired outcome and could result in the birth of a child with disabilities or at risk of

developing tumors due to the procedure not properly addressing the issues it was expected to (Mattar et al., 2021). As such, if a physician negligently performs a gene editing procedure in an embryo or fetus and causes a profound negative impact on its health, such conduct could warrant a wrongful life lawsuit.

4.3 Wrongful Life in the Context of Fetal Gene Editing: Challenges and Perspectives

The development of fetal gene editing will change how classic discussions about wrongful life have been framed. This section examines the issues of wrongful life claims in the context of fetal gene editing, emphasizing the balance between technological potential and ethical duties, looking at how society, law, and medicine can overcome these challenges while protecting people's wellbeing.

4.3.1 Reframing the Philosophical Objection in Wrongful Life Suits with the Emergence of Fetal Gene Editing

Traditionally, wrongful life claims arise when a physician fails to tell the parents about their child's genetic condition, leading to the birth of a child with severe disease or disability. However, current advances in assisted reproductive technologies, particularly the expanding availability of gene editing techniques, could impact the nature and prevalence of these types of lawsuits. Before explaining how the technique might impact wrongful life claims, it is necessary to explain how it will be used and for what purpose once it is safe and effective.

The development of gene editing techniques rekindled the interest in rewriting the human genome. While its application has proved effective in curing certain genetic diseases, much attention has been focused on its possible use to make "better" humans, otherwise understood as giving them genetic traits beyond health. In this context, futurists spurred considerable philosophical interest in imagining a dramatic, science fiction scenario of the future of humankind in which altering people's DNA to improve their minds and bodies would make a better society. Supporters of this view are known as transhumanists, as they believe incorporating

gene editing and artificial intelligence will raise a new state of human beings (*Human Genome Editing: Science, Ethics and Governance*, 2017).

Although it is an exciting topic for discussion, this dystopian scenario is not widely accepted. Studies conducted throughout Europe, Russia, the Americas, and the Asia-Pacific region show that the global public is far more interested in the use of gene editing for unmet health needs rather than human enhancement, mainly if meant to treat diseases in babies (Funk et al., 2020). However, there are a few scientists who have stated intentions to pursue genetic enhancement, such as a Russian scientist who claimed he will use gene editing to eliminate one of the genes that cause deafness in children (Cohen, 2019).

Realistically speaking, it is more likely that gene editing will be exclusively used in a negative eugenics sense, that is, to remove a disease-causing genetic mutation. In this sense, gene editing is considered a potential reproductive technique to avoid the birth of children affected by genetic conditions (UK, 2016). Many clinics that provide fertility services, such as preimplantation genetic diagnosis – which allows the selecting of embryos carrying certain traits – have indicated an interest in specializing in embryo editing (Morrison and de Saille, 2019). Given that most heritable, single-gene diseases with high recurrence risks and high morbidity and mortality rates have no cure, it is reasonable to assume that there will be a great demand for gene editing once the technique is deemed safe (Bick et al., 2021).

However, technical limitations still impede full access to clinical applications of gene editing. The first issue refers to how precise the technology is and how widely it might be applied. In 2012, a gene editing tool called CRISPR-Cas9 made the news for its ability to target and modify the genes of any living being precisely. It uses the RNA as a guide to the desired target and the Cas9 protein as a "Swiss knife" to slice the targeted DNA sequence. By slicing it, CRISPR-Cas9 alerts the cell to fix the damage the scientist might control. Due to its potential to repair genes, that is, to delete or insert DNA letters in an organism, CRISPR-Cas9 raised the hope that all genetic diseases (at least, every disease for which the underlying genetic mutation is known) might become treatable (Doudna and Sternberg, 2017).

Despite its gene editing prowess, CRISPR-Cas9 has proven more efficient at deactivating genes than repairing them. That is because although it can precisely target a genetic sequence, the cell's process of repairing the cut made in the genomic

sequence cannot be guaranteed (Eisenstein, 2022). For a successful repair, the cell must ensure that the sliced pieces of DNA have clean ends before gluing them back together, which might involve deleting or inserting a few letters of DNA (Doudna and Sternberg, 2017). These insertions or deletions often confuse the cell in the repair process and are why it usually fails (Eisenstein, 2022).

Alternative CRISPR-based technologies were created to overcome the obstacles faced by CRISPR-Cas9. In 2016, scientists David Liu and Alexis Komor developed base editing, a gene editing tool that acts like a "genetic pencil" by chemically rewriting a single letter of the DNA without breaking its strands (Chaudhry, 2021). The advantages of base editing consist of higher precision and efficiency (compared to CRISPR-Cas9) and fewer errors (Antoniou et al., 2021).

Three years after the development of base editing, the same inventors created prime editing, an even more refined gene editing tool. Prime editing offers complementary strengths to base editing, such as the ability to precisely edit a more extensive scope of genetic variants that cause diseases. Together, it is estimated that they could correct up to 89% of known genetic mutations associated with human diseases, thus raising a remarkable potential as a gene therapy tool (Kantor et al., 2020).

While ensuring the safety and efficacy of the gene editing procedure is a paramount challenge for successful gene therapy, another critical factor is enabling access to these therapies. Regarding economic costs, the price of human gene editing therapies currently ranges between $373,000 and $2.1 million, which results from massive investments that pharmaceutical companies make in research and development. In addition, patents also contribute to the high-cost so as to guarantee market exclusivity of the drug or therapy, which results in less competition and drives prices up, thus limiting patient access to treatment (Muigai, 2022).

However, a change in the business model could bring prices down and expand patient access to gene editing therapies (Muigai, 2022). For instance, when the Human Genome Project was concluded, the cost of whole-genome sequencing was estimated at 150 million dollars. However, advances in sequencing technologies and methodologies began lowering the cost of genome sequencing. Currently, DNA sequencing costs just a few hundred dollars, thanks to the rise of commercial companies offering genome-sequencing services (National Human Genome Research Institute, 2021). According to Dr. Jennifer Doudna, one of the creators of

CRISPR-Cas9, as gene editing tools and techniques improve and scientists can target a broader range of genetic diseases, the cost to access the technology will need to be reduced (Thomas, 2021).

The arrival of gene editing in clinics will create new responsibilities for physicians, which implies new liability issues. A child born as a result of genetic intervention in the fetal phase might have a legally cognizable injury if their DNA was modified in a way that causes the child harm (Rabe Smolensky, 2008). Article 8 of the Universal Declaration on the Human Genome and Human Rights recognizes compensation for damages of such nature (*Universal Declaration on the Human Genome and Human Rights*, 1997): "Article 8 - Every individual shall have the right, according to international and national law, to just reparation for any damage sustained as a direct and determining result of an intervention affecting his or her genome."

However, to date, no country has specific regulations on liability for damages caused by gene editing of reproductive cells, embryos, or fetuses (Krekora-Zajaz, 2020) In the absence of special regulations in this matter, legal precedents involving wrongful life lawsuits might be the way to claim compensation for a failed gene editing procedure on a fetus. However, as noted previously, such lawsuits are complex and are generally rejected by courts worldwide due to their understanding that the plaintiff claims that nonexistence is preferable to living with their condition.

This thesis focuses not on strictly legal challenges for wrongful life lawsuits but on the underlying ethical ones. In this scenario, a physician could be held liable if they negligently performed the procedure that failed to remove or correct the disease from a fetus. In this case, the plaintiff does not claim that nonexistence is preferable to living with the condition but that the physician failed to rectify it. Since courts would no longer understand the claim as a comparison between life and nonexistence, the main controversial objection to wrongful life suits is avoided (Caulfield, 2001).

4.3.2 Fetal Gene Editing and Abortion

In this section, we challenge the following objection: if a person found out that their fetus has an incurable genetic disease, would there be an obligation to remove it with gene editing that takes priority over a decision to terminate the pregnancy instead? The answer is that there is a limited moral obligation to use fetal gene

editing in this case. It is a limited moral duty because fetal gene editing is not meant to compel women to give birth and rule out abortion or adoption but to allow them to carry on gestation if pregnancy is desired and if their fetus is diagnosed with an incurable and debilitating disease.

The moral rationale used to answer such objection, which is intimately related to the following moral arguments of harm prevention and a 'genetic decent minimum,' is based on the respect for the individual's reproductive autonomy and on the parental moral responsibility to ensure a reasonably good start in life for their children. It is important to highlight that such parental moral duty should be understood as making sure that the child's life is reasonably good from the point of view of the child's own good, not the parents' or society's. By "reasonably good," we mean that children should at least start life free of severe conditions that would otherwise hinder their self-fulfillment and future.

One could object to the "reasonably good start in life" notion by claiming that parents should be compelled to do everything in their power, including genetic interventions, to guarantee that their children will have the best possible life. However, such a position imposes controversially high standards, given that it raises eugenic ideals of perfection. Furthermore, the notion of what is "best" varies among individuals from different generations, circumstances, and cultures, which makes it impossible to determine a single set of "perfect" genetic traits that could guide parental decision-making. It restricts reproductive autonomy by forbidding prospective parents to produce and raise children according to their interests.

An obvious objection to fetal gene editing is that if a fetus is diagnosed with a severe genetic disease, abortion is a reasonable alternative to giving birth to an affected child. However, many families decide against termination of pregnancy even though it means they will have to care for a child with a debilitating health condition. In a different context, many conservative countries forbid abortion, thus narrowing down even more safe options for parents at risk of having an affected baby: to give birth to the child, resort to unsafe and illegal abortion, or travel abroad to terminate the pregnancy, if they can afford to safely. When a pregnancy is desired but the fetus is diagnosed with a severe health condition that could be genetically corrected, fetal gene editing will provide a chance of having a disease-free child, whether abortion is legal or not in a country (Coutelle, 2008).

At present, the options for people at risk of giving birth to a child with a severe genetic disease are either abortion or caring for a child with an incurable and condition. Fetal gene editing offers a third option: to treat the fetus and allow a desired pregnancy to continue. Suppose a person chooses to carry out gestation regardless of the fetus' condition. In that case, I argue that they have a limited moral obligation to use fetal gene editing to prevent the disease because when you have a task as important as bringing someone into existence, you should ensure they will not be subject to so much pain and suffering.

4.3.3 Incorporating Potential Ethical Arguments in Wrongful Life Claims

Emerging fetal gene editing technologies introduce new considerations that challenge traditional legal frameworks and ethical norms. This transition emphasizes the necessity to adapt the courts' ethical reasoning and legal arguments to accommodate the implications of these technologies. As we explore the potential ethical arguments that could be incorporated in wrongful life claims, this section highlights the complexity of these discussions and the need for a nuanced approach to address the ethical dilemmas they present.

4.3.3.1 Prevention of genetically transmitted severe diseases

In this section, I contend that preventing genetically transmitted harm is a strong moral argument in favor of using gene editing in utero to prevent diseases in fetuses. The rationale used to justify this position is based on the principle of nonmaleficence (Buchanan et al., 2000). This reasoning includes the comparison between the ethical cost of deciding to carry a pregnancy to term while knowing that the child will develop a severe disease and the ethical cost of preventing severe diseases based on a limited moral obligation to use fetal gene editing in such cases.

This discussion raises the question of when would individuals be morally required to undergo genetic testing to avoid transmitting harm to their offspring. In general, no one who desires to procreate is morally compelled to undergo genetic testing. However, today we have more access to our health information, whether obtained during routine medical examinations, knowledge about family history, or through

results provided by genome sequencing companies. So if prospective parents are aware of the possibility of transmitting a severe genetic disease to their children, it would be morally responsible for them to undergo genetic testing to confirm such likelihood of transmitting harm.

Beyond mere responsibility, there are exceptions in which prospective parents would be subject to a moral obligation to undergo genetic testing. Prior to fetal gene editing, genetic testing must be done to ascertain the presence of the disease in order to carry out the procedure. Genetic testing could be morally mandatory under the following circumstances: 1) when one or both prospective parents are aware that they have a severe genetic condition and want to have a genetically related child; 2) they are aware of the risks of having a child affected by a severe genetic disease; 3) they have access to clinics where fetal gene editing can be provided; and 4) the disease in question is on the list of candidate diseases for fetal gene editing.

From the child's well-being standpoint, being born free of severe diseases would be better, as they could lead a better life. Such a benefit outweighs the ethical cost of minimally restricting parents' reproductive autonomy, as they would be under a moral obligation to use fetal gene editing to prevent the transmission of disease. On the other hand, lifting such moral obligation and letting parents intentionally transmit a debilitating disease would result in a severely affected child, which could be considered a case of child abuse or neglect. Harm to health caused by negligent conduct is considered unjust, and justice requires reparation; therefore, such actions could later on result in a wrongful life lawsuit,

Before CRISPR-Cas9, questions were raised about when there is a strong moral obligation to prevent genetically transmitted harm to the offspring. While creating another being is a personal and intimate decision, some scholars defend that this kind of obligation is present at least in one instance. That is when parents decide to bring into existence children who suffer so much pain and distress from a genetic disease that it would be reasonable to assume, on the child's behalf, that nonexistence would be preferable (Sparrow, 2014). For instance, a child born with Tay-Sachs or other devastating conditions could have been brought into existence through medical or parental neglect. In such a case, it seems justified to bring a wrongful life lawsuit against the negligent person (Nussbaum, 2000); Buchanan et al., 2000). After the introduction of gene editing technologies in clinics, assuming

that a reasonable number of individuals could access them, the moral obligation to prevent such harm in fetuses is even more vital.

However, deciding what constitutes harm so severe that it should be prevented is challenging. It is relevant mentioning that numerous debates about the governance of human germline editing call attention to the 'serious' nature of the genetic condition as a parameter in establishing what conditions should be targeted by gene editing technologies (Kleiderman et al., 2019). This consideration could also be used in the context of wrongful life lawsuits. Although it focuses on human germline modification, the discussed purpose for which the technology should be used (as a therapeutic tool) is the same as in the case of somatic cell genome editing.

In their 2021 report, the European Group on Ethics in Science and New Technologies (EGE) listed the following as a threshold to be met for the use of genome editing in humans (*Human Genome Editing: Science, Ethics and Governance*, 2017): "The EGE asks the European Commission to engage in a global mechanism to guarantee that heritable human genome editing is not prematurely clinically applied and is not applied for purposes other than against serious diseases that cannot be prevented otherwise" (European Commission, Directorate-General for Research and Innovation, 2021, p. 86). Similarly, in 2017 the National Academies of Sciences, Engineering, and Medicine (NASEM) included as one of the conditions for heritable human genome editing "restriction to preventing a serious disease or condition" and "reliable oversight mechanisms to prevent extension to uses other than preventing a serious disease or condition" (pp. 8-9).

The "serious" criterion for advancing heritable human gene editing is not shared by all. In response to Kleiderman, Ravitsky, and Knoppers, Iñigo De Miguel Beriain argued against their position by questioning why gene editing should be restricted only to "serious" conditions instead of being offered to all diseases. The argument made by the three authors departs from the premise that gene editing will be safe and effective in the future; if that is the case, De Miguel Beriain wonders why it should not be allowed to cure all diseases (De Miguel Beriain, 2020).

This section does not aim to create an exhaustive list of serious diseases that could be potential candidates for fetal gene editing, as it appears to be a difficult task even for experienced prominent scholars. Still, drawing a line on which genetic mutations can be considered harmful or not would help establish a difference between what

constitutes a disease, a disorder, or a disability, thus avoiding discriminatory decision-making in eventual fetal gene editing procedures. To ascertain if there is a moral obligation to use gene editing in utero to prevent harm, it would be necessary to select and examine cases in which the genetically transmitted disease or condition is so acute and intolerable as to make the individual's life, from their perspective, not worth living. This duty would be contingent on the severity of the genetic disease and if fetal gene editing can rectify it (Buchanan et al., 2000).

4.3.3.2 A moral obligation to ensure a "genetic decent minimum"

In the previous sections, we argued that after the introduction of gene editing technologies in clinics, if a fetus presents a severe genetic disease that could be prevented by editing its genome, it would be morally wrong not to do so. I further discuss this position by contending that fetal gene editing should be used to prevent severe diseases to ensure that the child will at least be able to have a reasonably good start in life or a "genetic decent minimum." The rationale used to defend a limited moral obligation to use fetal gene editing arises from the principles of beneficence, nonmaleficence, and equality of opportunity.

Here, we claim that certain diseases constitute a harm so severe as to make it possible to conjecture that such a condition would be incompatible with a worthwhile life from the child's standpoint, but not comprise genetic enhancement in the sense that it promotes unfair social advantages. In addition, failing to genetically intervene in utero, in this case, would be contrary to the obligation to prevent harm. While harm prevention is a source of moral obligations, such obligations might also be grounded in appeals to justice (Buchanan et al., 2000).

In this section, we subscribe to a similar version of the 'genetic decent minimum' concept proposed by Allen Buchanan (Buchanan et al., 2000) as a moral obligation for using gene editing technologies. However, our account of a "genetic decent minimum" only considers severe diseases as harms to be prevented, not disabilities. For Buchanan et al., this concept suggests that genetic interventions should prevent or alleviate diseases and disabilities that limit people's opportunities. They argue that genetic knowledge should be used to "level the playing field" of core human abilities to enable human flourishing (Buchanan et al., 2000).

There are many health conditions that children could be expected to live with reasonably well, such as the heterozygous form of familial hypercholesterolemia (FH), where a person inherits one normal gene and one faulty gene related to cholesterol regulation. People with this condition are more likely to develop cardiovascular problems and have a higher risk of experiencing early morbidity and mortality due to elevated levels of LDL cholesterol. However, LDL levels can be controlled with medications, a healthy diet, and physical activities (Evans, 2020). In such cases, it would not be morally obligatory to prevent this condition through genetic editing because because this condition would not completely hinder the individual's development and could be reasonably managed through readily available therapies. However, there are diseases known to cause so much pain and suffering that it would make a person consider they are worse off for existing with that condition than they would have been if they had not been brought into existence. In such cases, it would be morally wrong of a parent to have a child afflicted by a severe disease that could have been prevented through in utero gene editing, provided that the parent could have accessed the procedure.

While prospective parents at risk of transmitting a severe disease could have a child through other ways, such as adoption, surrogacy, or gamete donation, many individuals would rather not forego their desire to have a genetic bond. Suppose individuals decide to conceive a child in spite of the risk of passing down a burdensome disease. In that case, under the principles of beneficence and nonmaleficence, there is a moral duty to use in utero gene editing to prevent harm (the transmission of disease) and promote good (to eliminate or relieve the symptoms of such disease) (Clarkeburn, 2000).

The moral principle of equality of opportunity also engenders a moral duty to prevent serious diseases through genetic intervention. To justify why that is true, the notion of harm must be regarded as the setback of someone's wellbeing as a result of deliberate or accidental actions on the part of another person. According to Clarkeburn (Clarkeburn, 2000) (p. 400), "Some interests, often called "welfare interests", are more basic than the others in a sense that when they are severely set back, no other interests in a person's interest-network can advance." The transmission of a severe and debilitating genetic disease is an excellent example of an occurrence that causes a harm so severe as to hinder one's potential to start life with healthy steps. The moral obligation to use in utero gene editing then serves

equality of opportunity in helping mitigate unfair genetic disadvantages that would prevent individuals from living a fulfilled life – at least, from the start.

John H. Evans further supports a "genetic decent minimum" goal under the lens of fairness. According to Evans, fairness in the context of gene editing contains two requirements: First, genetic modifications to the genome should be used by individuals whose genetic traits put them at a disadvantage, for instance, individuals at a disadvantage due to a severe disease or condition could be given a chance to attain an "equal opportunity" by bringing them up to a genetic decent minimum". This concept, however, does not hold that all individuals should be equally genetically able but that genetic diseases or conditions that significantly hinder individuals' opportunities to enjoy the simple things in life should be prevented. The second requirement is that genetic interventions should not be aimed at obtaining social advantages, such as conferring higher I.Q. to an individual who already possesses a reasonable I.Q (Evans, 2020).

Although this concept is in line with the international consensus on the goals of genome editing ("WHO issues new recommendations on human genome editing for the advancement of public health", 2021), Buchanan et al. (Buchanan et al., 2000) define "genetic decent minimum" as follows: "In practice, this would mean a strong societal commitment to use advances in genetic intervention to prevent or ameliorate the most serious disabilities that limit individuals' opportunities across a wide range of cooperative frameworks." (p. 82). The authors also mention that, in a pluralistic society, it is challenging to form a rational agreement on what counts as genetically influenced harm, given that there is still so much discrimination toward certain genetic traits that cause differences among people (Buchanan et al., 2000). Therefore, adopting a 'genetic decent minimum' stance must be cautious in avoiding what might be considered discriminatory attempts to eliminate genetic diversity.

Some genetic diseases or conditions are considered severe obstacles to the opportunity to enjoy life, such as Tay-Sachs and phenylketonuria (PKU), a metabolic condition that, when untreated, often results in intellectual and developmental disabilities ("Recommended Uniform Screening Panel", 2022). To the extent that genetic mutations that contribute to these barriers can be accurately identified and safely removed, there is a strong prima facie obligation to do so (Buchanan et al., 2000). In light of the complexities brought about by the value of

genetic diversity and respect for people's differences, the next chapter presents wrongful life precedents. They provide strong cases that involve severe diseases and conditions that virtually everyone would agree could be potential candidates for eventual genome editing procedures.

4.4 Chapter Summary

The chapter has highlighted the ethical challenge of balancing the benefits and risks associated with fetal gene editing, particularly in the prevention of severe genetic diseases. The discussion reframed some philosophical objections to wrongful life suits in the light of advancements in fetal gene editing, including the ethical implications of using fetal gene editing to prevent genetic diseases and the moral considerations surrounding the termination of pregnancies based on genetic information. The arguments thus far in the chapter are that there are reasons to determine a moral obligation to prevent single-gene diseases in fetuses through somatic gene editing. The present discussion supports the view that once gene editing becomes a safe and effective technique, the best way to employ this technology is to remove serious diseases or conditions that, in light of current data, are known to cause suffering in individuals who experience them. In the gene editing era, we argue that failing to prevent severe diseases in individuals during the fetal stage will lead to wrongful life lawsuits due to violating a moral obligation to prevent harm and promote good. It has been argued here that we are moving into an era in which it may be both possible and hence morally obligatory to ensure that every child born begins life with a 'genetic decent minimum'. Beyond this goal, this thesis also addresses the ethical complexities before genome editing technologies are introduced in clinics, such as whether or not to consider enhancing non-disease traits in fetuses.

Chapter 5

Procreative Beneficence and Gene Editing: Optimizing Genetic Traits

This chapter addresses Savulescu's "Principle of Procreative Beneficence" (PPB) that postulates that prospective parents should select the child with highest probability of leading the "best life" based on the available genetic information (Savulescu, 2001). We then present a counterargument, which was conjectured according to what we believe Julian Savulescu would argue if he had read the present thesis. Savulescu's hypothetical argument would be as follows: if fetal gene editing is eventually provided in clinics, parents (or physicians) should be held negligent if they do not take advantage of the technique to improve the genome of their future children. Put otherwise, Savulescu's work suggests there could also be grounds for a wrongful life lawsuit in favor because of a failure to meet an obligation to enhance. In what follows, we analyze Savulescu's proposal and anticipate possible scenarios that could take place if gene editing applications for non-disease trait enhancement became a moral obligation and its implications on wrongful life lawsuits. My counterargument includes ethical statements on genome editing by international institutions, namely, the World Medical Association and the International Bioethics Committee. In addition, the argument encompasses Robert Sparrow's theory of social obsolescence, which underscores societal and emotional challenges that could stem from an obligation to genetically enhance.

5.1 Beyond Disease Removal: The Risks of Genetic Enhancement

Advancements in genome editing techniques provide us with hope and a predicament. The hope is that it will be soon introduced in clinics to prevent severe single-gene genetic diseases; the predicament is that it could be used to manipulate non-disease genetic traits, such as height and eye color, which aligns with the notion of genetic enhancement. This section explores the moral wrongness of genetic enhancement under the lens of the Procreative Beneficence principle and anticipates potential scenarios of its implications.

5.1.1 Genetic Technologies and the Potential for Eugenic Concerns

It is frequently argued that using CRISPR and other gene editing tools in reproduction could eradicate several genetic conditions. However, these technologies could also enable the elimination of genetic differences that cause disability, which rekindles eugenic fears. Even though the eugenics theory has been discredited, it is still practiced in the form of genetic selection through assisted reproductive technologies, which raises the question of whether it would be immoral not to use gene editing to alter non-disease traits in fetuses (Sheppard, 2022).

Preimplantation Genetic Testing for Polygenic Risk (PGT-P), for instance, is a diagnostic test used in IVF that allows prospective parents to choose the embryo with the most favorable gene pool based on a variety of polygenic risk factors. This involves assessing the risk of a specific condition by considering the combined influence of numerous genetic variants (Black, 2022).

It is noted that the United Kingdom allows the screening of embryos for 400 conditions, including intellectual disability and primordial dwarfism, through Preimplantation Genetic Testing (PGT). This aligns with the argument that the goal of gene editing aligns closely with the outcomes achievable through PGT. In practical terms, the ongoing debate on editing embryos appears to be more theoretical than practically applicable. The limited instances where PGT, a well-established and secure technology, might supersede gene editing provoke a

reconsideration of the ethical and practical implications of the application of gene editing for modifying non-disease traits in fetuses (Sheppard, 2022).

However, there are situations in which both prospective parents are carriers for a single-gene genetic disease in which there is a high likelihood of disease transmission to their future offspring. In these situations, PGT would not allow them to select unaffected embryos; gene editing, on the other hand, would be the ideal solution to fulfill their desire of having a genetically related child. Even though these circumstances are uncommon, they still highlight the need for ethical consideration of the risks of the use of genome editing to improve non-disease traits.

5.1.2 The Procreative Beneficence Principle and Expanded Genetic Selection

Savelescu argues that prospective parents have a *prima facie* moral obligation to select the child with the best chance of having the "best life" based on the available genetic information. He maintains that if in vitro fertilization and preimplantation genetic diagnosis are available to prospective parents, the embryo selection should be based on the available genetic information, particularly non-disease genes. This concept forms the core of the Procreative Beneficence principle, as formulated by Savulescu, which is designed to provide guidance in parental decision-making regarding the selection of children to bring into existence (Savulescu, 2001).

Preimplantation genetic diagnosis (PGD) is employed on early-stage embryos to detect any chromosome abnormality (a potential alteration in the structure or number of chromosomes). This procedure identifies whether an embryo has a single-gene disorder or a chromosome abnormality that could lead to pregnancy issues or the birth of a child with a disease or disability. With this information, prospective parents can choose which embryos should be implanted in the uterus (Stern, 2014). In theory, PGD could also detect any other genetic trait, such as skin tone or eye color, otherwise known as a non-medical trait. Many jurisdictions forbid using PGD for non-disease traits (Savulescu and Singer, 2019). However, with the possible introduction of gene editing in clinics, selecting genetic traits in fetuses could be a reality, and it is a matter of concern.

Although gene editing with CRISPR-Cas9 was not a reality when Savulescu

published his work on the Principle of Procreative Beneficence, he defended the principle's application for gene editing purposes in later papers. In other words, he argues that there is a moral imperative to use gene editing to select genetic traits that are most likely to increase the child's chances of achieving the "best most well-being" (Gyngell et al., 2019).

Savulescu extends his argument to advocate for the utilization of assisted reproductive technologies, including Preimplantation Genetic Diagnosis (PGD) and gene editing tools, beyond merely preventing diseases. He emphasizes the importance of using those to select favorable non-disease traits, distinguishing between disease genes and non-disease genes. Disease genes, according to Savulescu, are those that cause a genetic disorder or predispose to disease. Non-disease genes are those that influence non-disease traits, such as height, intelligence, or character (Savulescu, 2001).

Savulescu uses intelligence as an example of a non-disease genetic trait that should be enhanced through gene editing. Although many environmental factors contribute to intelligence development, studies show that this trait is 50% influenced by genetic factors (Gyngell et al., 2019). In particular, intelligence is linked to gaining knowledge and developing rich social relations (Savulescu, 2001). Hence, Savulescu proposes that an individual's level of well-being is a function of their intellectual capacities. According to its genetic information, the point of selecting the embryo with the highest capacities is that such embryo is transferred to the uterus, and the eventual child can hope to enjoy "the most well-being" (Kaposy, 2018).

5.2 Implications of the Procreative Beneficence Principle and Gene Editing in Wrongful Life Suits

In theory, gene editing technologies offer an opportunity to intervene in one's genome to select "desirable" traits. Despite advancements in the field of Genetics, this sort of use, which has traditionally been called "enhancement," is still not ready to be implemented due to a lack of knowledge about genotype and phenotype interactions in humans (Sparrow, 2019). For instance, given that intelligence is

strongly influenced by the environment and not just genes, to enhance this trait, it would be necessary to target several genes in order to have a meaningful results (Schaefer, 2019). However, in the interest of anticipating some potential implications of human genetic enhancement in wrongful life suits, we will proceed as if it is already possible to make this attempt.

For my counterargument to the Procreative Beneficence principle in the gene editing context, this section aims to raise concerns and anticipate scenarios about the implications of genetic enhancement based on the ethical stance summarized under Robert Sparrow's theory of genetic obsolescence. To do so, it is assumed that gene editing could enhance genetic traits (Sparrow, 2019). In this scenario, after the introduction of gene editing in clinics to eliminate serious diseases, individuals could question whether other non-disease traits might be enhanced through gene editing. A possible argument would be: "if there was a chance of improving my capabilities through genetic intervention, such as increasing my I.Q. or concentration levels, why didn't scientists do it?" As a result, they could claim that the lack of genetic enhancement of non-disease traits constitutes, beyond a disadvantage, a "life-invalidating harm" (Benston, 2019)

Although it might seem too farfetched to imagine that wrongful life lawsuits could rise in the gene editing era due to individuals' dissatisfaction with "undesirable" non-disease genetic traits, there are strong reasons to believe it could be possible. The profit motive, for instance, could be stimulated through marketing strategies that could encourage parental demand for the technology to be used to enhance non-disease traits in fetuses (Buchanan et al., 2000).

Alternatively, some historical precedents chronicled in the previous chapter demonstrate that it is a possible scenario. For instance, the plaintiff brought a wrongful life lawsuit against their doctor for failing to inform the parents that their child would be deaf ("Turpin v. Soritini", 1982). Still today, unfortunately, deafness is seen by some as a condition that diminishes an individual's quality of life, and some scientists have already announced their intention to eliminate the the genes that cause deafness through gene editing in human embryos (Cyranoski, 2019). As such, in the gene editing era, if genetic interventions for non-disease trait enhancement are permitted, deaf children (or children with other genetic differences) could argue, in a wrongful life suit, that they could have been genetically

"enhanced" in the fetal stage, but due to parental or medical negligence they will have to live with a "genetic disadvantage."

However, my argument so far regarding the responsible use of gene editing technologies is that they should aim at removing serious diseases from fetuses to prevent pain and suffering but not to threaten genetic diversity. After all, many individuals with serious genetic diseases face challenges related to access to adequate diagnosis and treatment and receive coordinated care, as well as obstacles to employment, education, social life, and health care.

5.2.1 Ethical Considerations and Recommendations

Issues related to genetic enhancement and its potential ethical concerns are not new in the field of Genetics. In fact, several international documents and committee reports support the stance that genetic enhancement of non-disease traits should not be pursued. For instance, the World Medical Association, which developed the Declaration of Helsinki in 1964, updated its statement on human genome editing, expressing concerns regarding non-therapeutic and enhancement purposes that could potentially lead to eugenic practices. In their statement, the association declared their support to the efforts of germline genome editing for therapeutic applications (World Medical Association, 2020).

Likewise, the International Bioethics Committee's report on reflection on the Human Genome and Human Rights raised concerns over the goals of human genome editing. In their report, the committee elaborated a number of recommendations, among which particular attention to genetic enhancement was pointed out. They articulated that the objective of enhancing individuals and the human species by manipulating genes associated with certain characteristics should be distinguished from the discredited projects of eugenics. While not advocating for the elimination of individuals deemed 'imperfect,' genetic enhancement raises concerns about the principle of respecting human dignity. It also challenges the notion that the differences among human beings, irrespective of their inherent capabilities, form the basis for recognizing and preserving their equality and furthermore, that there is a potential risk of introducing new forms of stigmatization against those unable to afford such enhancements or those who opt not to pursue them "Report of the IBC on Updating its Reflection on the Human Genome and Human Rights", 2015.

Similar concerns about potential genetic discriminatory threats were expressed when gene splicing, a technique that paved the way for genome editing, was created in the 1970s (Science History Institute, 2017). In 1982, the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research elaborated a report on social an ethical concerns regarding genetic engineering applications in human beings (of Ethical Problems in Medicine et al., 1982). Some of the ethical issues raised were the following: (1) Genetic engineering techniques are already showcasing significant potential for enhancing human well-being and encouraging these is ethically justified due to the potential aid they may offer in alleviating human suffering. (2) Many human applications of genetic engineering resemble accepted forms of diagnosis and treatment utilizing other techniques. The novelty of gene splicing should not automatically hinder its use but prompt thoughtful analysis. (3) Distinguishing between 'medical treatment' and 'nonmedical enhancement' is subjective, and the difficulty of drawing a line suggests the risk of drifting toward attempts to 'perfect' human beings once 'enhancement' is explored (of Ethical Problems in Medicine et al., 1982).

In 2015, during the first International Summit on gene editing, another ethical statement was issued. The organizing committee listed six concerns over human genome editing, one among which noted, in terms of justice: "the possibility that permanent genetic 'enhancements' to subsets of the population could exacerbate social inequities" Johnston, 2020. This concern is related to both issues of equitable access and the ethical use of genome editing in humans for therapeutic purposes. Françoise Baylis, one of the members of the organizing committee, observed that "considerations of social justice demand that discrimination and oppression be addressed in preventing disease and promoting health" (*International Summit on Human Gene Editing: A Global Discussion*, 2015).

In the 2017 National Academies report on the ethics of human gene editing, the committee reported ten recommendations within four categories of ethical areas of concern regarding the responsible use of gene editing technologies and governance. Among the major areas of concern, the "potential use of genome editing for enhancement" was listed, and the committee concluded that there is a public discomfort regarding the application of genome editing for enhancements, which is rooted in fears of exacerbating social inequities and the creation of societal pressures that might drive unnecessary technological adoption. Emphasizing the significance

of public discussion in exploring both genuine and perceived social impacts, particularly in the formulation of governance policies, the committee firmly advocated against the progression of somatic genome editing for purposes other than treating or preventing diseases and disabilities (*Human Genome Editing: Science, Ethics and Governance*, 2017).

The ethical concerns on the perils of genetically enhancing non-disease traits in human beings expressed in the recommendations above are recurrent in debates about genome editing. Even though the distinction between "treatment" and "enhancement" remains blurry, certain conditions are clearly serious diseases that cause pain and suffering to thousands of people. As such, the documents emphasize that gene editing technologies should prioritize unmet medical needs rather than unnecessary interventions to attempt to create the "best" child possible. Thus, there is a strong objection to enhancing non-disease genetic traits based on the possibility that it would accentuate social inequality, such as unequal access to the technology. This is the focus of recent work by Sparrow (2019), which is key for the argument that the Principle of Procreative Beneficence should not be considered a moral guide in parental decision-making (Sparrow, 2019). We turn to that argument now.

5.2.2 Genetic Obsolescence and Wrongful Life Lawsuits

In the genetic enhancement context, Sparrow states that "significant progress in genomics and in molecular and developmental biology, as well as in relevant technologies, would need to occur" (Sparrow, 2019); so, for the purposes of his paper, he accepts this assumption to be true. Sparrow also claims, "If the genetic enhancements available to parents to choose for their children improve every year, then the enhancements provided to children in any given year will quickly become obsolete" (2019, p.8). As such, the author argues that if gene editing technologies and genetic knowledge quickly improve, this will naturally make individuals with unenhanced genes feel and be seen as less suited for purpose and, eventually, obsolete. In other words, each cohort of genetically enhanced individuals would probably feel technologically and socially outcompeted by the following gene-edited generation if gene editing technologies improve fast and are widely accessible.

In 2012, CRISPR-Cas9 was reported as the most efficient and accurate gene editing tool; four years later, scientists developed base editing, a more refined gene editing

tool. Only three years later, an even more sophisticated gene editing tool, prime editing, was created (Diotte, 2020). Considering the speed at which gene editing technologies advance, each gene editing procedure will likely be surpassed in terms of accuracy, efficiency, and even new knowledge on how genes interact with each other. This could mean that if genetic enhancement improves at such a rate and becomes commonly used in fetuses, as they grow, each generation could feel obsolete compared to the next one (Schaefer, 2019).

Sparrow states that obsolete genes should not be confused with "bad genes" but rather as no longer desirable due to technological progress (Sparrow, 2019). Ultimately, Sparrow worries about the social effects of previous versions of genetic enhancement on individuals' sense of self-worth and well-being, which could be impacted by socialdiscrimination. For instance, parents that choose to enhance their future child's non-disease traits to allow them to live "the best life" might resent their child when comparing them to the next generation of genetically enhanced children (Sparrow, 2019).

In the employment context, according to Sparrow, "While enhancement technology continues to improve, young people will be highly desirable employees for a few short years before a new generation, with better enhancements, enters the job market." (Sparrow, 2019). In this regard, individuals born with the previous enhancement version and individuals not gene-edited at the embryonic stage could argue that "they were doomed to the harm of leading a life intrinsically inferior to the lives of all born after them" (Benston, 2019).

5.2.3 Social Implications and Wrongful Life Lawsuits

Assume that the new standard of life becomes the idea that a life deprived of genetic enhancement is not worthwhile. In this case, both unedited individuals and individuals with 'obsolete' genes could seek legal compensation for the suffering inherent to their existence (Benston, 2019). In this context, a wave of wrongful life lawsuits could be raised to address this new issue. As previously discussed, traditional wrongful life suits involve a child born with a disease or disability so devastating that they seek compensation for the burden of existence in that condition. In the hypothetical context of individuals unsatisfied with a life devoid of genetic enhancement, they could claim financial compensation for the obstacles

engendered by the increasing standard of enhancement (Benston, 2019).

Shauna Benston (2019) suggests a shift in the criteria for these claims. Instead of relying on the standard of a life free from pain and financial distress, plaintiffs might ground their cases on an increasing standard of enhancement. The focus would shift from proving debilitating disabilities to demonstrating that an unenhanced existence itself constitutes a life not worth living. This implies that the threshold for defining a life-impairing "impairment" leading to compensable damages would decrease compared to the standards applied in previous wrongful life cases (Benston, 2019).

Wrongful life lawsuits appear as an adequate legal action to address the obsolescence issue in the genetic enhancement context. This lawsuit forces society to reflect on whether it can be harmful to bring a child with certain conditions into life. As gene editing advances and moves closer to being integrated into assisted reproductive technologies offered in clinics, prospective parents may find themselves compelled to weigh the implications of choosing the traits of their future offspring. Consequently, with individuals perceiving their genes at risk of becoming obsolete, there is a foreseeable surge in wrongful life suits. This could result in courts receiving numerous claims from individuals dissatisfied with their genetic and social status, potentially acting as a significant obstacle toward utilizing gene editing not only for disease prevention but also for the enhancement of non-disease traits.

5.3 The Ethical Cost of Going Beyond the "Genetic Decent Minimum"

Numerous scholars have criticized the Procreative Beneficence Principle for several reasons (e.g., Kaposy, 2018; Bennett, 2009; Holland, 2016; Sparrow, 2007; Parker, 2007). It has been argued, for instance, that selecting an embryo based on a high level of capacities that many consider valuable does not always entail excellent levels of well-being (Kaposy, 2018). Others object to the principle by arguing that it embodies eugenics notions, places a low moral value on people with disabilities, and the purported moral duty to bring the "best child" into existence hinders reproductive autonomy (Bennett, 2009).

My views on the Procreative Beneficence Principle are similar to these critiques, and

some of them will be the point of departure for my objection to this principle. I begin by exploring the argument that the Procreative Beneficence Principle promotes eugenics, followed by how this principle devalues the life of individuals with disabilities. I believe that these arguments are strong enough to prove that the ethical cost of incorporating the Procreative Beneficence Principle in health policies involving gene editing could be hazardous to society, as it could engender the obsolescence effect predicted by Robert Sparrow, which could ultimately lead to a wave of wrongful life lawsuits.

Investigating the ethical cost of surpassing the "genetic decent minimum" reveals a future fraught with societal ramifications. This reflection is not merely restricted to the academic circle, since it propels us to contemplate what is the best way to harness gene editing technologies. The potential for widening socioeconomic gaps becomes a critical concern when we consider enhancing genetic traits beyond necessary health benefits, thus requiring a cautious and morally sound approach.

According to Savulescu (Savulescu, 2001): "Eugenics is selective breeding to produce a better population." A public interest justification for interfering in reproduction differs from Procreative Beneficence, which aims to produce the best child, of the possible children, a couple could have" (p. 424). Although Savulescu denies any association between the Procreative Beneficence Principle and eugenics, whether it comes from public enforcement or private enterprise, both concepts attempt to impose an obligation on parents to avoid bringing certain lives into existence (negative eugenics) as well as to give birth only to the "best child" (positive eugenics) (Sparrow, 2007). Negative eugenics aims at improving the population's health by directly preventing reproduction between members of a given community with disabilities or health conditions, often through forced sterilization. The goal of positive eugenics, on the other hand, is to encourage reproduction between individuals with "good traits and capabilities" to produce healthy and "high-performing" individuals (Buchanan et al., 2000).

Even though Savulescu advocates for this principle as a matter of individual freedom and not state intervention, pursuing the latter is no less morally condemnable than the former. According to Rebecca Bennett (Bennett, 2009), "If the morally right thing to do is to create only the best children possible, then publicizing this moral obligation and allowing it to influence policy to enable its

fulfillment would seem to be perfectly acceptable, even if such policy could then technically be termed eugenic" (p. 272). Given how such a policy would pressure parents to choose only the "best" progeny according to this policy, then it would not be so different than the old eugenics. In this context, the ethical boundaries between individual freedom and state intervention become blurred, prompting reflection on the potential consequences of policies aimed at guiding reproductive decisions in the pursuit of morally defined ideals.

Furthermore, Savulescu argues that the Procreative Beneficence Principle does not entail that the lives of people with disabilities are less valuable than those who do not have disabilities (Savulescu, 2001). However, in postulating a moral obligation to select the genetic traits that make the "best child" possible, the Procreative Beneficence Principle seems to favor discriminatory choices against oppressed groups, given that the prospects of one's well-being are primarily influenced by social factors (Sparrow, 2007). Given how systemic societal oppression dictates life opportunities, such as jobs, if prospective parents embrace Procreative Beneficence, they would have to select "the best child" according to physical, emotional, psychological, and intellectual standards that fit in an unjust society's demands.

In alignment with this perspective, Savulescu and Kahane assert the following (Savulescu and Kahane, 2011): "According to our account, some state of a person's biology or psychology is a disability if that state makes it more likely that a person's life will get worse, in terms of his or her well-being, in a given set of social and environmental circumstances" (p. 45). In claiming that an individual's well-being is reduced in the presence of a disability and that it would be morally preferable to avoid bringing such life into existence, it is clear that supporters of the Procreative Beneficence Principle place a lower moral value on an individual with disabilities than other lives (Bennett, 2009). According to Robert Sparrow (Sparrow, 2007), "Best" is not an idea which allows room for pluralism" (p. 54). Adopting the Procreative Beneficence Principle would significantly reduce genetic diversity in society, thus intensifying injustice.

In brief, the debate on the Procreative Beneficence Principle raises ethical questions regarding individual freedom, state intervention, and the potential implications of selecting the "best possible child." Despite Savulescu's assertion that the principle does not devalue lives with disabilities, the moral obligation it posits seems to

endorse discriminatory choices, influenced by societal factors. This perspective, coupled with the other assertions of this author, suggests a potential lower moral value placed on individuals with disabilities, and the adoption of such a principle could diminish genetic diversity, intensifying societal injustice. Therefore, to apply such a principle, it is necessary to rank potential lives as "better" or "worse," which is impossible to determine (Parker, 2007). A moral obligation to select the "best possible child" according to notions of racism, ableism, sexism, and other forms of discrimination is unethical, going against all the progress made by several social movements. However, it is different to suggest that a severe genetic disease should be eliminated from the embryo through gene editing. In this case, the intention is to prevent the individual's pain and suffering that would otherwise stem from that particular disease and thus allow them to attain a "genetic decent minimum."

5.4 Chapter Summary

This chapter examined the ethical, legal, and social implications of using gene editing for genetic enhancements beyond disease prevention, especially in the context of wrongful life lawsuits. Section 5.1 highlighted the fears of a new form of eugenics, emphasizing the ethical dilemmas posed by modifying non-disease traits and examined the moral considerations in selecting embryos based on genetic desirability, addressing the complexity of defining "optimal" genetic traits through "The Procreative Beneficence Principle". Moreover, Section 5.2, discussed the link between genetic enhancement and wrongful life suits, considering how evolving gene editing technologies might influence legal actions brought by children who were not genetically enhanced. Lastly, Section 5.3 analyzed the ethical considerations of surpassing the "genetic decent minimum" through genetic enhancements. In particular, it evaluated the moral obligation to prevent serious disabilities while cautioning against attempts to eliminate all forms of genetic diversity, emphasizing the need for a balanced approach to gene editing.

Chapter 6

Conclusion

Gene editing technologies present the possibility to intervene in fetuses and eradicate diseases before symptoms manifest. Although such interventions hold promise for significant societal benefits, they also entail more responsibilities for the medical profession. New knowledge implies a duty of responsibility, and failure to fulfill it generates potential liability. Thus, gene editing raises a potential moral obligation to prevent genetic diseases before birth and warrants a greater understanding of legal and ethical duties in the medical field. This chapter concludes this thesis by offering considerations and highlighting its contribution to the field.

6.1 Final Considerations

The introduction of gene editing in clinics to address severe single-gene diseases in fetuses engenders a moral and legal obligation to utilize the technology prudently. Failure to employ gene editing where it could prevent life-threatening conditions could be considered negligent, potentially warranting compensation for the affected individuals through wrongful life lawsuits. This thesis argues for a focused application of gene editing technologies on the somatic cells of fetuses to eradicate severe single-gene diseases, avoiding the ethically fraught territory of germline editing due to its irreversible consequences and potential harm to descendants. Furthermore, this argument emphasizes the ethical benefits and costs of employing gene editing for treating serious monogenic diseases to achieve a "genetic decent

minimum" versus enhancing non-disease traits.

The genetic enhancement of traits is critiqued for numerous ethical reasons, which includes the potential of increasing social inequity and discrimination, thus urging caution against utilizing gene editing to create a "gifted" class of individuals. In light of the ethical and social risks raised by genetic enhancement, we contend that the fair and responsible purpose of gene editing should be to confer a "genetic decent minimum". Our account of a "genetic decent minimum" consists in utilizing gene editing to eliminate a life-threatening single-gene disease in a fetus and not to confer any genetic advantages beyond the ordinary functions of genes.

Moreover, we have advocated that there could be grounds for a wrongful life claim if a physician fails to use gene editing to remove a severe monogenic genetic disease. In this case, failing to treat a fetus would contravene the obligation to prevent harm and the principle of justice. To be able to contemplate possible moral obligations and liability issues regarding genetically altering fetuses, we first conjectured what circumstances could engender them. In the following years, gene editing will probably be utilized to edit out monogenic disorders in utero. Despite the possibility of using gene editing tools to improve people's health, when a technology evolves rapidly, clinicians' knowledge base and practical skills can briskly become obsolete, resulting in practice with insufficient expertise. When a healthcare professional fails to provide the standard duty of care to a patient (e.g., misinterpretation of genetic screening, performing an incorrect kind of surgery) causing injury to a patient, there can be grounds for a malpractice action for medical negligence.

6.1.1 Comments on the Ethical Perspective of Wrongful Life and Fetal Gene Editing

In the context of fetal gene editing, we have argued that wrongful life lawsuits are the appropriate legal avenue to address negligence issues since the claim corresponds to the criteria of this kind of lawsuit. For many decades, wrongful life lawsuits have been rejected by courts due to the controversial nature of their claims. Two approaches were used to analyze the underlying ethical considerations to reject claims of wrongful life, both address what constitutes harm, which is a distinguishing feature of a wrongful life suit. The first was the high regard for the

sanctity of life, which was observed in some of the legal precedents narrated in chapter two. This notion is no longer prevalent in light of the respect for the quality of life, which results in the idea that living with a disease is not always better than nonexistence. The second, is that wrongful life promotes the notion that the birth of a child with disabilities could be harmful. This contentious issue rekindles eugenic threats, which several disability rights advocacy groups have raised in opposition to recognizing wrongful life claims. This is a valid concern, given the ableist assumption that people with disabilities are constantly in a state of suffering. We have argued that disabilities do not prevent a person from living a meaningful life. As a result, accepting a wrongful life claim that nonexistence is preferable to living with a disability should not be ethically or legally justified.

In our analysis of the underlying ethical reasoning behind each court decision in the landmark wrongful life cases, we have remarked an interesting juxtaposition between both ethical perspectives. Thanks to the promotion of personal autonomy, the concept of quality of life gained strength in clinical decision-making, which mitigated the effects of the sanctity of life. This topic repeatedly surfaces in the context of MAiD, especially in Canada, where legislation is expanding its role. When patients face a severe and irreversible disease that causes physical or mental suffering, they may choose to abbreviate their life in light of their declining quality of life (Government of Canada, 2022). Given how Canadian law (and other countries where MAiD is legal) supports the notion that living with a disease is not always preferable to not living at all, the concept of the sanctity of life will likely lose even more strength, thus favoring our argument.

There is a societal shift towards valuing life, particularly for individuals with disabilities, following years of advocacy for equality and dignity. Despite progress, discrimination persists, especially in reproductive healthcare, where assisted reproduction technologies such as PGD can lead to selective abortion based on genetic traits. With gene editing enabling the selection of genetic traits, disability rights advocates fear it may lead to the devaluation of disabled lives. This tension between valuing quality of life and respecting the lives of people with disabilities is crucial in the context of gene editing and potential wrongful life lawsuits. The lack of clear distinction between disease and disability raises concerns about discriminatory gene editing applications and the possibility of legal action for medical negligence resulting in a health condition.

While grappling with the comparison between living with a disease and nonexistence remains complex in legal proceedings, fetal gene editing offers a potential resolution to this philosophical dilemma. Rather than juxtaposing life with a serious disease against nonexistence, it reframes the comparison to a life free of that disease, which avoids the primary contentious aspect of such lawsuits. However, given the challenge in distinguishing between diseases and disabilities and their impact on wellbeing, and considering which types of conditions can be targeted with gene editing, we have determined that only severe, single-gene disorders warrant a moral obligation to avoid the transmission of harm and a potential wrongful life lawsuit.

6.1.2 Comments on the Procreative Beneficence and Gene Editing: Optimizing Genetic Traits

We have also investigated whether the failure to enhance non-disease genetic traits could result in a wrongful life lawsuit. This idea was inspired by Julian Savulescu's principle of Procreative Beneficence, which proposes that prospective parents are morally obligated to select the child with the best chances of leading the "best life" based on available genetic information. Savulescu advocates for the use of assisted reproductive technologies, such as PGD and gene editing tools, not only for disease prevention but also for selecting or enhancing non-disease traits such as intelligence, height, and memory. By selecting the fetus with the greatest potential according to its genetic information, the aim is to maximize the eventual child's wellbeing.

The application of gene editing to enhance non-disease traits is still not possible at this point. Taking this into consideration, the Procreative Beneficence argument in the context of gene editing might seem more hypothetical than realistic at this stage, but still possible. Thus, we have contemplated the possible outcomes in a theoretical scenario where genetic enhancement of non-disease traits through gene editing are feasible. In this context, following the integration of genome editing into clinical practice, individuals—both those who have undergone genetic enhancements and those who have not—may experience discontentment with their genetic status.

With gene editing capable of targeting any gene, questions may arise as to why certain traits such as intelligence or physical abilities were not genetically enhanced. Simultaneously, those without access to gene editing or whose parents opted against

it may perceive themselves at a disadvantage compared to edited individuals. If a new standard emerges identifying a life without genetic enhancement as inferior, both unedited individuals and those with "obsolete" genes could pursue legal recourse for the suffering stemming from their genetic disadvantages. Hence, the introduction of gene editing can worsen emotional and psychological issues, potentially leading to an increase in wrongful life lawsuits. Before fetal gene editing is introduced in clinics, we suggest a study similar to this one should be carried out to update the list of severe monogenic diseases that can be considered serious to an individual's health and, incidentally, cognizable harm in a wrongful life lawsuit.

6.2 Contributions

The contributions of this thesis to the field are enumerated as follows:

1. Reviewed the literature regarding potential moral obligations resulting from gene editing applications, particularly before birth, emphasizing the need for ethical decision-making and potential legal ramifications for negligence.

2. Advocated for the application of gene editing techniques specifically on somatic cells of a fetus rather than on germ cells to avoid the risks associated with germline editing and its irreversible consequences.

3. Contended that gene editing should be applied to eradicate serious monogenic genetic diseases in order to achieve a "genetic decent minimum" rather than used to enhance non-disease traits. This stance was taken in response to concerns about the eugenic intentions and potential increase in social inequity, discrimination, and for creating a divisive class system based on genetic traits.

4. Analyzed the legal implications of failing to utilize gene editing to prevent severe single-gene diseases, suggesting that wrongful life lawsuits could serve as a legitimate legal avenue for compensation in cases of medical negligence.

5. Discussed the ethical considerations on court decisions in landmark wrongful life cases, contrasting the sanctity of life with the quality of life arguments, and addressed the issue of living with disabilities versus nonexistence.

6. Examined the societal emphasis on the value of life and the challenges faced by individuals with disabilities within the context of gene editing and reproductive technologies, advocating for careful ethical consideration to avoid discriminatory practices.

7. Critiqued the Procreative Beneficence principle for its social and ethical implications, including a potential to regress into eugenic practices, urging for a responsible approach to gene editing that respects dignity and societal values.

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Appendix A

Administration of In Utero Gene Editing

In 2021, researchers Rohan Palanki and Michael J. Mitchell and fetal surgeon William H. Peranteau published a paper outlining the advantages of therapeutic gene editing delivery during the fetal stage of development. In their study, they point out some of the benefits of fetal gene therapy compared to post-birth gene therapy, such as the fetus' small size and the early stage of the fetal immune system that prevents an immune response to the introduction of external genetic material and delivery vector (Palanki et al., 2021). Other studies also support these findings (Shanahan et al., 2021). According to the authors (2021):

> The delivery of genetic material to target cells in a developing fetus has several physiologic advantages (. . .). The small size of the fetus (100 g at 14–16 weeks) compared to a postnatal recipient (e.g., 3.5 kg newborn, 60 kg adult) maximizes delivery vector titer per weight of recipient, which facilitates efficient gene transduction (. . .). In addition, small recipient weight minimizes large-scale manufacturing constraints of delivery vectors (. . .). The immunologic immaturity of the fetus allows for introduction of antigens (e.g., vector materials, transgenes) without a limiting immune response and with the induction of antigen-specific immune tolerance (. . .). (p. 53)
>
> (. . .) For target diseases that require serial doses of therapeutic vector, tolerance to gene therapy components is also favorable, since it avoids diminishing returns due to a gradual immune blockade. (p. 53)
>
> (. . .) The fetus also has a highly accessible and abundant population of stem and/or progenitor cells, which are ideal targets for long-term

> therapeutic genetic correction given their enhanced potential for expansion with propagation of the genetic correction, migration, and distribution in the fetal microenvironment (. . .). (p. 53)
>
> (. . .) Fetal permeability of the blood-brain barrier (BBB) permits potential treatment of central nervous system(CNS) disorders with gene therapy via systemic delivery, which is a difficult endeavor postnatally. (p. 54)

To circumvent difficulties in transporting gene editing technologies in utero due to the large size of its components, multiple platforms were developed to deliver gene editing tools in vivo, such as CRISPR-Cas9. Adenoviral vectors, for instance, are one option researchers adopt. According to Palanki et al. (Palanki et al., 2021), "(. . .), researchers have turned to adenoviral vectors for delivery of genome editing technology due to their larger carrying capacity and efficient transduction of multiple cell types" (p. 56). However, viral vectors such as adenovirus vectors carry risks of immunogenicity, i.e., the chance of provoking an immune response of the cells, thus blocking the gene editing delivery (Palanki et al., 2021).

Other studies have found that non-viral vectors are better candidates to deliver gene editing technologies in utero. According to Peddi et al. (Peddi et al., 2022):

> Viral vectors have a large packaging ability but carry the risks of immunogenicity and tumorigenesis (. . .). Non-viral gene delivery platforms are less immunogenic and are important in in utero gene transfer for gene editing. Non-viral vectors are also more versatile and less expensive to produce on a large scale" (p. 3).

Examples of non-viral vectors include electroporation, which is a physical genetic manipulation method that uses an electric field to destabilize the cell membrane to introduce nucleic acids into cells. Although it is an efficient method, electroporation is limited for human applications in light of the high voltage that it requires (Palanki et al., 2021). Other options include nanoparticles, LNPs (lipid nanoparticles), and a recently developed nanotechnology called CRISPR-Gold, which according to Palanki et al. is: "A clinically translatable recent innovation [which entails] a gold nanoparticle conjugated with DNA and complexed with donor DNA, Cas9 ribonucleoprotein, and an endosomal disruptive polymer (. . .)" (p. 58). Although none of these technologies are ready yet for clinical translation, studies suggest that LNPs, in particular, are strong candidates to deliver CRISPR-Cas9 in utero due to their ability to carry a modified gene to the target cell without causing unintended genetic mutations or germline effects (Palanki et al., 2021).

The route of vector delivery of gene editing in utero plays a key role in terms of efficiency and safety. According to Peddi et al. (Peddi et al., 2022), gene editing can be therapeutically administered in the following ways:

> Intravenous: Intravenous access to the umbilical vein can be obtained through ultrasound guidance. The umbilical vein also acts as a pathway for the systemic route. Umbilical vein injections can be used to target the liver, which is one of the sites of hematopoiesis in the fetus (...).
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> Intra-amniotic: The distribution of transduction by intra-amniotic injection is influenced by changes in epithelial differentiation (. . .). After the formation of the periderm, this route offers limited access to progenitor cells. It also offers increased distribution of transgenes, which is facilitated by fetal breathing and swallowing movements (. . .). However, a high dose of transfection is needed due to the dilution of genes in the amniotic cavity, which can be addressed by intratracheal injections (. . .).
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> Intracardiac: This route is highly specific but associated with an increased risk of the procedure. Other routes of administration include intramuscular, intraperitoneal under ultrasound guidance and intraparenchymal injections to target the lungs (. . .). (pp. 3-4)

Besides the route of administration and delivery vector, the timing in gestation in which therapeutic in utero gene editing is performed also plays a key role in its successful application. According to Shanahan et al. (Shanahan et al., 2021): “Fetal immune tolerance occurs between 11 to 14 weeks of gestation, and fetal gene therapy should ideally be done near the beginning of this window to influence the postnatal immune repertoire” (p. 14).