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A Conditional Case for the Moral Justifiability of Germline Editing for the Prevention of HIV

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Declaration

I Mokgadi Elizabeth Lehong

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am a student registered for **Msc Bioethics and Health Law** in the year **2021.**

I hereby declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above course is my own unaided work except where I have explicitly indicated otherwise.
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Date: 28/06/2020

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Abstract

In "**A Conditional Case for the Moral Justifiability of Germline Editing for the Prevention of HIV**", the morality of human germline editing is divided into issues relating to safety and efficacy and those raised by the potential success of the procedure.

Significant to this moral discussion is the experiment that led to the first gene-edited babies, the 'CRISPR experiment'. Using this experiment as the foundation of my discussion I attempt to answer the question, "Is it morally justifiable to use germline editing to prevent HIV transmission?".

The main defence of the thesis is that using germline editing to prevent HIV transmission would be morally justified provided that (a) the current scientific risks and safety concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven.

Under this argument, reproductive rights and duties associated with the human germline are explored to argue for the existence of transgenerational relationships that binds parents to exercise care and responsibility towards their future children. Furthermore, arguments for germline editing are presented in terms of the principle of procreative beneficence to advocate for promoting the wellbeing interests of prospective generations in reproductive choices.

Countering critics relating to the claims that germline editing violates human dignity, the natural identity of persons, consent and other possible societal concerns (eugenics, discrimination and social justice); I invoke the defence that humans are morally obliged to promote and safeguard the well-being interest of their future generations by pursuing the potential significance of the procedure in advancing human lives through treatment and prevention of diseases.

Following the discussion on possible uses of germline editing, including a comparison with the existing methods of artificial reproduction based on their shortfalls, benefits and purpose in reproductive medicine; I argue for the moral use of germline editing for therapeutic purposes only and further make recommendations based on the proper regulation of the procedure to promote social justice and solidarity.

Key words: germline editing, genetics, CRISPR, HIV transmission, genome editing.

CONTENTS

i. **Cover page**
ii. **Declaration**
iii. **Acknowledgements**
iv. **Abstract**
v. **Acronyms and definitions of terms**

CONTENTS

1. **General Introduction to the study**
    1.1 Background literature analysis
    1.2 Rationale for the study
    1.3 Methodology and contribution to field of study
    1.4 Research aims and objectives.
    1.5 Thesis approach
2. **Germline editing and HIV prevention: the CRISPR'd babies experiment.**
3. **The moral significance of germline editing: procreative beneficence and generational relationships**
4. **The moral controversies of human germline editing**
    4.1 Future child
        4.1.1 human dignity
        4.1.2 consent
        4.1.3 Identity
    4.2 Society and germline editing
        4.2.1 Eugenics, discrimination and social justice
5. **Comparative analysis**
    5.1 Moral difference between germline editing and PGD.
    5.2 Enhancement versus curative germline editing

6. **A way forward**

7. **Final remarks**

8. **References**

9. **Appendices**

   9.1 Ethics waiver

   9.2 Turn-it-in (plagiarism) report.

ACRONYMS AND DEFINITION OF TERMS

Below is a list of abbreviations and meanings of terms used throughout the thesis.

Term /Acronym	Definition
Genome	a set of genetic material or genes (DNA) in a living cell.
Gene/genome editing	DNA is inserted, removed, changed, or improved in a genome of a living organism.
Gametes	Reproductive or germ cells (egg or sperm cell) prior to fertilization.
Genotype	Genetic composition of a person.
DNA	Short for deoxyribonucleic acid. Specific parts of the genes that carry the genetic material of a person.
CCR5	A gene named for the protein it encrypts, which is the 'C-C chemokine receptor type 5'.
Embryo	The product of a fertilised egg by sperm in its early developmental phase.
In vitro	occurring outside the body of a living organism.
Genetic determinism	Dictates that human identity and behaviour are dependent on the genetics of a person.
Enhancement germline therapy	Editing the human genome for non-medical purposes, like increase height, intellect, or other related traits
Curative germline therapy	Genome editing for medical reasons, such as preventing transmittable diseases.
PGD	Short for preimplantation genetic diagnosis; a reproductive technique which allows the screening and selection of embryos through in vitro fertilization (IVF, see below for definition) according to their genomic characteristics.
CRISPR-Cas	Short for clustered regularly interspaced short palindromic repeats CRISPR-associated; a bio-molecular technology that is used by scientists to edit the genome of living organisms.
IVF	Reproductive technique used to fertilize eggs in the laboratory before implanting back to the womb as an embryo. Also known as test-tube fertilization.
HIV	Short for Human Immune Virus; the virus that attacks the white blood cells of a human body, leaving the immune system susceptible to other infections.
Off-target mutations	This occurs when the cell targeting during gene editing goes adrift, resulting in turned off cells, unable to divide normally, or other errors such as mosaicism (see below).
Mosaicism	Result when non-specific gene editing occurs, affecting unexpected genes; at some point, the mutations will appear on some cells and not be on other targeted cells (i.e. partial gene editing).
WHO	Short for World Health Organisation
GGE	Short for germline genome editing. Used in most sources cited in the thesis.
HHGE	Short for Heritable human genome editing. Also used in cited sources.

1. General introduction to the study

The USA-based National Academies of Sciences, Engineering, and Medicine (2017) highlights that human genome editing presents a great potential for "preventing, ameliorating, or eliminating many human diseases and conditions." (The National Academies 2017, p.23) Furthermore, it is cautioned that this great potential and significant power to alter the human genome for these purposes ought to be exercised with the utmost responsibility to ensure morally acceptable use.

The alarming use of germline editing[1] procedures in the 'CRISPR'd babies experiment'[2] revealed the great potential of gene-editing technologies in preventing and curing human diseases. After the methods of germline editing were used to attempt genetic resistance to HIV infection, some people questioned the moral boundaries of these scientific advancements to this possibility.

Amidst these controversies, there is a frequent pattern in the arguments presented. Roughly, the bioethical discourse is divided into two parts, constituted by those who see great potential in the use of germline gene-editing as a reproductive technology; and those who see it as a great threat to humanity (Greely 2019).

Overall, this experiment presents thorny moral questions that cannot be overlooked. Whether we should use germline editing to prevent HIV transmission, and if so, on what conditions would it be morally acceptable to use, are the key questions I attempt to answer in this thesis.

1.1 Background literature analysis and critique

[1] Germline editing is a form of human gene-editing procedure that targets the reproductive cells of humans thereby introducing changes heritable to descendants. A detailed discussion follows in the next section.
[2] This experiment concerned the use of gene editing techniques (CRISPR) to attempt germline editing (heritable genome editing) for reasons of creating genetic resistance to HIV infection. A detailed discussion follows in the next section.

In this part of the thesis, I shortly discuss some of the current literature that is of significance to my research question and which I rely on in my thesis.

Gene-editing[3] refers to a group of scientific techniques used to modify the DNA or genetic material of living cells, by adding, adjusting, or removing specific parts of the targeted genes (Lanphier et al. 2015). Editing the human genome can be achieved in the following ways: (a) through somatic gene editing, which involves altering non-reproductive cells (body cells) of a person, resulting in genetic changes that are limited only to the concerned individual; and (b) using germline editing methods, whereby the reproductive cells (ovules, sperms, or early embryos) of a person are altered, creating a genome that is heritable to the descendants of the particular individual (Schleidgen et al. 2020; National Academies 2017). In this thesis, I limit my focus to human germline editing procedures as potential reproduction technologies used for preventing and treating genetic defects.

Several studies (Liang et al. 2015; Tang et al. 2017) show that it is not yet safe to use the current gene editing technologies to edit the human germline. These studies elevate controversies over the acceptability and effects of human germline editing in recent years by revealing that there are major safety risks associated with the methods. This includes the random side effects that could result from the potential 'on and off-target' mutations and the ineffectiveness of the techniques regarding the high possibility of uncontrollable 'mutations or mosaicism'[4] , which could potentially cause severe health defects (2015, p.364). As a result, an overwhelming majority of bioethicists have proposed a moratorium on germline editing, arguing that it should be banned until all the technical issues have been resolved; and it is guaranteed safe to use on human beings (McCarthy 2015; Lander et al. 2019).

According to the literature on this topic, the concern for possible social harms remains one of the main causes of the ethical controversies of germline editing. There is a strong fear amongst ethicists that editing the germline might lead to exploitation or inhumane uses of the gene editing systems reminiscent of the eugenics programs practiced in the early twentieth century, including

[3]I use editing or modification interchangeably throughout the thesis. Also refer to the acronyms and definitions page above, with relevant abbreviations and meanings of terms used throughout this paper.

[4] Occurs when the cell-targeting during gene editing goes adrift, resulting in turned off cells, unable to divide normally or other errors such as mosaicism. Cell mosaicisms result when non-specific gene editing occurs, affecting unexpected genes; at some point, the mutations will appear on some cells and not be on other targeted cells. See Liang et al. (2015).

that of the Nazi regime in Germany (Rubies and Steger, 2018). The societal impacts of germline editing extend further to issues of social stigmatization and discrimination of people based on their genetic flaws and the creation of different social classes, which might influence inequalities since the rich would most likely have a better advantage of accessing the gene editing resources as compared to the impoverished (Mahoney and Siegal 2018; Rubeis and Steger 2018).

In contrast, and recognising the potential importance and potential effects of germline editing, Hammerstin, Eggel, and Biller-Andorno (2019) and Raposo (2019) point out that germline editing has been misconstrued as a procedure used for creating perfect superior beings, with traits that outmatch normal human beings; while it is merely a reproductive tool that aims to protect and improve the well-being of people. They add to this by highlighting that there are regulatory frameworks that could be used to ensure social justice and solidarity to minimise the harms that may result from immoral uses of the technologies, and related societal issues.

There is also a strong focus in the literature on the potential negative implications of germline editing on future generations. Some scholars argued that editing human germline may be an infringement of the bodily or physical integrity of the child, which is considered to be a pure violation of their 'right to genetic identity' or the right to have a unique identity as natural persons (Hammerstin, Eggel and Biller-Andorno, 2019, p.4). Authors like Henrich (2011) and Harris (2016) question the principles of informed consent regarding germline editing. They argue that the decision to edit is morally problematic as there is no agent to consent to the procedure at the time of inception. In essence, it is argued that there are fair chances that the prospective children may not desire the introduced genetic changes, and by allowing germline editing we are depriving them of the opportunity to an open future, with the possibility of exercising independent decision making regarding their bodies.

Another dominant issue is that of the inherent dignity of the child. It is believed that the human genome is the physical representation of the intrinsic value of human beings, because of this, editing the germline is a violation of this fundamental worth or dignity of the child as a natural being (Malek 2013). However, some scholars (Raposo 2019) have pointed out that if a medical procedure is used to advance a person's health to ensure they get a better life, it promotes care, respect, and value for human lives and should therefore not be considered as an undignified process.

From de Melo-Martin's (2005) perspective, genetic determinism, or the idea that a person's genetics constitutes their original identity, as used in viewing the human germline is flawed. The basis of this argument is that genomic growth and development could be impacted by various external factors such as culture or environment, which could, in turn, influence biological changes in a person. In addition to arguing that we should not confine human identity to genetics, Resnik and Vorhaus (2006) point out that identity is more than the genetic composition of a person and that editing the human germline does not change or undermine individual identity. Raposo (2019) criticized one of the commonly held and longstanding attitudes towards germline editing, that the procedure works against nature and is therefore morally wrong. She does this by demonstrating that the everyday practice of medicine, especially in assisted reproduction, completely depends on artificial procedures like PGD, which are used to help people who cannot reproduce naturally because of medical complications.

It was announced at the second international summit on human genome editing in 2018, that a Chinese scientist, He Jiankui[5], had successfully edited the germ cells of human embryos using the CRISPR-Cas9[6] technology, which resulted in the birth of twin babies, commonly known as the 'CRISPR'd babies' (Greely 2019,p.112). According to the reports, the embryos of HIV positive couples were genetically altered *in vitro* and implanted into the womb to make babies with a genome that is immune to HIV infection (Greely 2019). This experiment received widespread condemnation, mainly for the safety issues relating to gene editing technologies, which fueled the existing demand for a moratorium on germline editing (Lander et al. 2019); while other scholars proposed that it must be completely banned all at once to protect the human species (Botkin 2019). Surprisingly, some scholars believed that an experiment of this nature was long overdue scientific progress, similar to the first cloned mammal "Dolly the sheep" in 1996, which significantly paved the way for some of the current scientific advancements in human genetics and reproduction (Greely 2019). Though the experiment was conducted prematurely, with no regard for the wellbeing of the children, it has, nonetheless, motivated many ethical debates to focus on the enormous potential of germline editing, especially for purposes of preventing human diseases, such as HIV infection.

[5] Hereafter referred to as Dr He.
[6] Short for "clustered regularly interspaced short palindromic repeats CRISPR-associated protein 9". This is a biomolecular technology that is used by scientists to edit the human genome (See attached glossary page).

1.2 Rationale for the study

Familiarity with the literature on this topic shows that, apart from the current technical hurdles, germline editing has a goal of potentially creating positive effects that could benefit the health of future generations. The purpose of my study is to show the moral significance of recognizing this enormous potential, particularly with preventing and reducing the risks and burden of diseases in prospective generations. It is, however, one of the key concerns of my study, that there is a substantial amount of discussion in the current literature over germline editing, and much of it holds that germline modifications should be prohibited, even if the technical concerns were resolved.

The birth of the 'CRISPR'd babies' is proof that germline editing is possible; yet many ethical concerns remain. An example of the controversy in the literature is the stark difference in opinion between Meagher et al and Graig Mello. Meagher et al. (2020) contend that using germline editing to prevent HIV transmission is a danger to humanity and that it is unnecessary to expose people to risky procedures while there are more ethical and less intrusive options which can be effectively used to accomplish the same objectives. But Graig Mello (2015) claims that it is unethical to forbid germline editing, in the event where it could be safely used on humans.

There are ethical issues regarding germline modifications that need clarification. But the most significant is the issue of safety, which raises the question of whether it would be morally justified to use the procedure to prevent human diseases, provided the current safety risks could be avoided. It is not enough to rule out germline editing based on its technical shortfalls, bearing in mind the possibility that the issues may be resolved down the line. With the high global prevalence of HIV infection (WHO, data, and statistics 2020), I consider the experiment that led to the birth of the first gene edited babies, the 'CRISPR'd babies' experiment, very crucial to the discussion of my thesis. The possibility of using germline editing to prevent HIV transmission could be a significant procedure that greatly benefits humankind.

Despite it being clear that germline editing currently is not safe to be used for human reproduction, this does not imply that it could not be morally right under conditions where it is

declared safe to use on humans. There is, however, insufficient literature that normatively explores this possibility. This is my intention in this research report.

Therefore, it is imperative to assess the ethical controversies raised by the use of germline editing and to consider its potential future of preventing HIV infection, exclusive of the current technical concerns, which is the principal goal of this study.

1.3 Methodology and contribution to the field of study

This research is a strictly normative study on the moral justifiability of human germline editing for purposes of preventing HIV transmission. I conducted a thorough search of the literature on human germline editing in general and also for specifically preventing HIV transmission. Online databases such as Google Scholar, PubMed, and BMC Medical Ethics were searched for books, journals, articles, and other internet resources relevant to this topic. The following keywords were used: germline editing, germ cells, genome modification, ethics, human genome editing, HIV, prevention and transmission. In defending my thesis, I use the standard methods of philosophical research including careful analysis, making robust arguments, rebutting counterarguments, and clarifying terms and concepts. I draw on the major moral theories, including utilitarianism, deontology, care ethics, virtue ethics and Ubuntu as well as second-order bioethical principles to defend my claims.

I wish to formulate a legitimate academic opinion on the topic of human germline editing for the specific purpose of preventing HIV transmission. I hope that the research will help address the ethical challenges, and possibly guide and inform public policy considerations on this topic.

1.4 Thesis statement, aim and objectives

The aim of my research is to defend the thesis that using germline editing to prevent HIV transmission would be morally justified provided that (a) the current scientific risks and safety

concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven.

In attempting to achieve this aim, I tackle the following question: "Is it morally justifiable to use germline editing to prevent HIV transmission?"

The key objectives of my study are:

a) To give an account of germline editing and its potential significance in reproductive medicine.
b) To identify conditions under which germline editing could be morally justified.
c) To defend the claim that germline editing to prevent HIV transmission can be justified so long as certain conditions are first met.

1.5 Overview of research report

The brief introduction to the study as provided in this **chapter** is followed by **chapter 2 'Germline editing and HIV prevention: the 'CRISPR'd babies experiment'**, which entails thorough discussions and analysis of germline editing that offers urgency to questions regarding how, when and why germline editing should be used for the identified purposes. I devote some attention to the specific case that motivated the discussion at hand, the 'CRISPR'd babies experiment'. I highlight the ethical implications of this experiment, mostly about the potential significance of human germline editing for the specific purpose of preventing HIV transmission. I begin by taking the position as generally maintained by a great majority of ethicists on this topic, that a moratorium should be adopted on human germline editing until it is proven to be safe and adequately effective to use in humans. The starting point of my research report is to point out that the safety and efficacy issues are the *sine qua non*[7] of germline editing. These preconditions recognize one of the dominant objections of germline editing, that it is morally wrong to expose humans to dangerous scientific experiments that could adversely impact their wellbeing. Moreover, there are dissenting arguments, which I address, that oppose the moral

[7] The essential conditions or prerequisites of this research report.

acceptability of germline editing even under the identified conditions, where (a) the current scientific risks and safety concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven.

I address the objection that the existence of alternative methods of assisted fertility treatments for preventing HIV transmission serves as a clear indication that there is no need to consider germline editing because of the effective and less invasive procedures currently used. I argue that this kind of reasoning will only make sense if the methods used to prevent HIV transmission provided a permanent remedy for HIV, that could protect future generations from possible difficulties and sufferings associated with the risk of harm posed by the existing potential of future HIV transmissions. I further attempt to counter this argument by first, pointing out that the objection fails to acknowledge the potential significance of germline editing as a novel method of preventing HIV transmission, with potentially different therapeutic benefits. Second, I argue that germline editing offers protection from potential future risks of exposure to HIV, thereby creating a strong germline that limits its possible transmission from one generation to another, which is a benefit that the existing artificial reproduction technologies lack.

Having established that germline editing is currently not safe and adequately effective to use for human reproduction, in **chapter 3 'The moral significance of germline editing'**, I highlight the potential worth of germline editing by identifying some of the most compelling arguments that could serve as a plausible defense for the moral justifiability of germline modification for the specific purpose of preventing HIV transmission. I propose to consider first the moral rights and duties of humans towards their future children. To justify altering the human germline, I argue that the right to reproductive autonomy of a person works concurrently with the moral duty to protect and safeguard the best interest of the future child. To support this argument, I rely on the work of Rehmann-Sutter (2018) to argue for the existence of 'intergenerational relationships of care and accountability', which I use to show that it is morally justifiable to use germline editing for purposes of improving the quality of life of the future children by minimizing the potential future risks of HIV transmission. Furthermore, I introduce the principle of procreative beneficence as advocated by Savulescu and Kahane (2009), to show that parents have a moral duty to pursue the best possible life for their children by making sure they have a "genetic endowment" that will give them the advantage of having the "most wellbeing" in life. Here, I

attempt to defend the reproductive freedom of parents and the moral obligation they have of protecting future generations from potential risks of HIV transmission with germline editing.

In **Chapter 4 'Moral controversies of human germline editing'**, I challenge the negative arguments raised by those opposed to germline editing, both individual and societal issues. First, I consider the deontological argument that if germline editing procedures promote the best interest of the future children, and not only the reproductive wishes of parents, then the intrinsic worth or dignity of children as natural beings is respected. I use this argument to refute the objection that germline editing entails a violation of inherent human dignity by commodifying human beings or by what some scholars refer to as "creation of perfect babies". Second, I consider the argument relating to lack of consent. The essence of this claim is that prospective children are deprived of the opportunity to have an open future since they are forced to accept permanent physical changes without any choice or option. Similar to these counter-arguments, I argue that the decision to alter the genome for purposes of improving the child's wellbeing is an imperative moral action that ought to be taken by the parent, to improve the child's wellbeing. Lastly, I counter the objection that human germline editing is morally unacceptable because it changes the natural identity of a person without their consent. I rely on the work of Resnik and Vorhaus(2006), and de Melo-Martin(2005) to argue that it is morally unsound to confine human identity to biological assumptions and ideologies of genetic determinism, considering the existence of many factors such as environment or socio-economic conditions, that may influence the biological growth and development of human beings. All this goes to show the weakness of some of the arguments raised against germline editing. Another possible concern is the potential societal impacts of germline editing, which includes causing social stigma for people living with HIV, discrimination, and the potential for abuse or immoral use of the technologies. I consider the views of those who recommend that a regulatory framework could be a possible solution for minimizing or potentially averting the negative social implications of germline editing for purposes of promoting social solidarity and justice. I argue in support of this assertion, that a properly governed system could possibly lead to a safe, peaceful, and morally acceptable use of gene-editing technologies. I expand more on the idea of regulating germline editing in **chapter 6** of the study.

Chapter 5 'Comparative analysis' provides a comparative analysis of germline editing and PGD, and between enhancement and therapeutic germline editing. Following the arguments provided by Hammerstin, Eggel, and Biller-Andorno (2019), and by drawing an analogy with prenatal genetic diagnosis (PGD), I attempt to address some of the objections of germline editing and to argue that the procedure is at least morally justifiable as PGD. In doing this I intend to show that the procedure could be a morally justified method of reproduction, like those currently used. I then extend this defence by arguing for restrictive use of germline editing for curative[8] purposes only and not for enhancement or non-medical reasons. I contend that germline editing can be beneficial to humans only when used to prevent medical diseases or for other medical conditions that affect the quality of life of the child if not prevented. I provide a fundamental distinction between the two methods and reasons why, in my opinion, germline editing for curative purposes is plausible and morally significant than the other.

In **Chapter 6 'A way forward',** I discuss the proposal to regulate germline editing, keeping in mind the most important premise of my argument, that germline editing could be morally justifiable given that (a) all the current safety concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven. I consider the idea of regulating human genome editing in detail, particularly for the specific purpose identified in this thesis. The views of several health organisations, such as WHO, are also considered, particularly about implementing a suitable global regulatory framework that encompasses the interests of all members of our societies, including the future generations.

And **chapter 7 'Final remarks and recommendations',** provides a detailed synopsis of the key points of this thesis with recommendations. I stress the moral significance of human germline editing for the specific purpose of preventing HIV infection as defended in the thesis, whilst proposing a way forward in terms of regulation of the procedure.

[8] Includes treatment and prevention of diseases.

2. Germline editing and HIV prevention: the 'CRISPR'd babies experiment'.

I now turn to the specific case which provides the basis for my study, the 'CRISPR'd babies' experiment and the potential future applications of the procedure under the identified *sine qua non* of the thesis. In the preliminary chapter I stated that I intend to use this experiment to highlight the ethical controversies associated with germline editing in general and for the specific purpose of preventing HIV transmission. In the process of doing this, the need for great caution on germline editing is emphasized following the safety considerations associated with the procedure.

Before November 2018 human germline editing was perceived by many as mere science fiction. But reality dawned when the world learned of the research experiment that resulted in the birth of the first-ever genetically altered babies, the 'CRISPR'd babies'. The procedure used, germline editing using CRISPR, is an artificial reproduction method that has the potential to cure disease-causing or defective genes in the human genome.[9] One of the proposed uses of germline editing techniques, as attempted in the 'CRISPR'd babies experiment' is to edit out the gene that is responsible for making the human genome susceptible to HIV infection (Schleidgen et al. 2020; Ebina et al. 2016). As part of the project for HIV prevention research, the lead scientist on this experiment, Dr He, intended to create a genotype with specific resistance to HIV infection by editing the germ cells of human embryos, that were collected and fertilised through IVF for reproduction purposes (Meagher et al. 2020; Greely 2019). In the event where the primary aim of this experiment is achieved, the immune system or body cells of the children would acquire genetic immunity to HIV infection and this genetic trait can be passed on to their descendants. However, it is unknown whether Dr He managed to achieve this purpose despite two healthy babies being born from this experiment, as there are major scientific issues owing to the potential uncertainties associated with germline editing methods that makes it impossible to predict the possible outcome of the experiment[10] (Meagher et al. 2020; Greely 2019). This means that for now we can assume that the genome editing process was partially successful, because the

[9] See the definition of gene editing in the literature review section and on the abbreviations page above.
[10] In the commencing paragraphs, I briefly discuss the basics of these scientific issues mentioned here and the possible effects thereof.

potential long term effects that might come with the unknown risks of the gene editing technology used, CRISPR-Cas9, occur randomly; and may become apparent at any stage of the children's lives.

Questions about genetically transmissible diseases and possible gene therapy increase as the gene editing technologies advance, and as scientists discover more about the human genomics. In concept, the use of germline editing to prevent HIV appears to be straight forward, but it has become apparent from the CRISPR'd babies experiment and other preceding research studies that the procedure is overly complex. The foundational scientific studies (Liang et al. 2015; Tang et al. 2017; Ebina et al. 2016) demonstrate that the current gene editing technologies do not meet the safety and efficacy standards, on which germline editing methods are based. From the early studies in 2015 where non-viable human zygotes were genetically modified "…to investigate the specificity and reliability of the CRISPR/Cas9 system", it was uncovered that the current gene editing methods have unpredictable scientific risks[11] that can be detrimental to human beings (Liang et al. 2015, p.366). As explained in chapter1, the consequences of germline editing include "off-target effects, unintended base changes, mosaicism and double-stranded breaks" which show the ineffectiveness of the procedure and the potential harm that may arise if used in human beings (2015, p.366). These risks were identified to have a high possibility of causing abnormalities on the normal growth and development of humans, including physical deformities and most likely, cancer, which could potentially result from the unexpected cell mutations (Ormond et al. 2017; Schleidgen et al. 2020). Another study further revealed that there is a possibility that editing the germline for HIV resistance using the current methods may damage the immune system by causing the human genome to be weak and ultimately susceptible to other infections such as 'West Nile Virus Infection' (Xiao, Guo and Chen 2019). Similar to the CRISPR experiment, many scientists and ethicists have expressed great concern for the health and wellbeing of the children as there is a high possibility that they might experience medical complications down the road (lander et al. 2019; Meager et al.,2020). Considering the possibility of physical harm or severe medical problems to prospective generations, it is not for the benefit of the human species to use germline editing as it currently stands. The CRISPR'd babies have been subjected to a potentially dangerous inescapable fate, bearing in mind the possible

[11] One of the primary shortfalls of human germline editing is the unexpected off-target mutations that may result from "mosaic mutations, and double-stranded break errors" (Liang et al., 2015). see chapter1, literature review.

unpredictable effects of the gene editing methods used. Essentially, this overzealous use of germline editing, if continued, may threaten the general wellbeing and survival of the present and future generations, considering the possible aforementioned consequences.

By conducting this experiment, Dr He has violated two of the most significant principles of biomedical ethics, namely non-maleficence (avoiding harm) and beneficence (furtherance of the wellbeing of others)[12]. According to these two principles, in any scientific study involving human participants the best interest of the participants ought to be promoted or given due regard, as beneficence dictates. In terms of non-maleficence, no intentional harm or any risk of harm that a reasonable researcher would have anticipated and therefore avoided or at least minimised, should be suffered by the participants (Beauchamp and Childress 2013). This experiment has therefore demonstrated that it is currently premature and unethical to consider using germline editing for the stated reasons, given their potential risks. Whether or not the experiment followed the relevant ethical or procedural requirements is not relevant to my study. I merely intend to signify the moral conflict caused by this experiment in relation to the two key points of the study, which I discuss below.

In this connection, two points deserve emphasis. The first relates to the limitations of germline editing procedures due to safety concerns. The general position maintained in this thesis is that at this point, human beings should not be exposed or subjected to germline editing procedures until it is proven to be safe and adequately effective to use for the intended purposes. One of the primary risks of germline editing is that the consequences of the procedure are beyond that of the existing artificial reproductive technologies and its application does not guarantee that the desired outcome will be achieved. As highlighted above, it is not worthwhile to risk condoning a procedure that poses a potential threat to the wellbeing of humans. This issue is one of the most expressed fears amongst bioethicists that inspired the immense support for a temporary prohibition on heritable gene editing until it is guaranteed safe to use on human beings. As Lander et al. (2019) asserts,

[12]All of the four principles including respect for autonomy and justice will be discussed depending on the relevant moral issues in conflict. In the next chapters I attempt to address ethical issues aside from those related to safety and efficacy of germline editing. However, in this section, I only invoke beneficence and non-maleficence because they relate to both parts of my discussion, which is for the safety and efficacy, and potential use of germline editing for the identified reasons.

> "…proposed moratorium does not apply to germline editing for research uses, provided that these studies do not involve the transfer of an embryo to a person's uterus. A global moratorium and framework are therefore necessary to ensure proper consideration of the relevant issues surrounding clinical uses of germline editing…for germline editing to even be considered for clinical application, its safety and efficacy must be sufficient, taking into account the unmet medical need, the risks and potential benefits." (2019, p.166).

As noted above germline editing is valuable only as a research tool for the present time; dependent on the fact that it has enormous potential for various clinical applications, including the one specified in this thesis, preventing HIV infection. The paragraph cited above from Lander et al. (2019) successfully addresses the question of 'how far should we go in pursuit of germline editing?' From a scientific standpoint, there are unknown risks associated with the use of human germline editing, that inspired the introduced thesis statement of my research report, which is that germline editing would be morally justified provided that (a) the current scientific risks and safety concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven. In essence, the first point highlights the paramountcy of the identified thesis of my study in the debate for the moral justifiability of germline editing, because all the modifications made with germline editing are permanent and heritable, the procedure ought to be accurate and adequately effective for the particular purpose it is intended for. So, I maintain the position that once the safety and efficacy issues have been resolved gene editing procedures would potentially have the ability to successfully edit the human genome; and ultimately result in profound effects that could improve the wellbeing of humans, such as genetic resistance to HIV infection.

In a few years from now, we may be able to use germline editing to prevent HIV transmission. Many scientists and bioethicists have questioned the purpose of the CRISPR experiment, mostly concerning this possibility. Germane to these questions are issues about the safety and effectiveness of the procedure which have been represented as one of the greatest controversies in reproductive medicine. As noted above many authors, including Lander et al. (2019) and McCarthy (2015) have maintained a cautionary approach towards these issues by emphasising the need for safer and sufficiently effective gene editing technologies. Some consider germline editing to be a futile process for preventing HIV transmission because the virus can be managed

and treated through the existing methods of assisted fertility treatments, which involves sperm washing, antiretroviral drug therapy, and other well-tested methods currently used(Xiao, Guo and Chen 2019; Meager et al. 2020). Nonetheless, the fact remains that millions of people in the world are infected with HIV and that despite a highly active drug treatment in place, no permanent cure exists, and there are still many deaths owed to this disease (WHO, data, and statistics 2020). It is also noteworthy that much money is spent on various HIV treatment programs to reduce its effect on mortality, which is a difficult situation especially in disadvantaged societies, which have poverty and poor sanitation, amongst other issues. The financial support for HIV treatment could be used for other needs, such as those mentioned above, which could immensely improve the lives of humans. Another important factor is the novel possibilities that germline editing methods have that broaden the scope and options for reproductive medicine, particularly with preventing HIV infection, one of the biggest threats to public health. Human germline editing has proposed more than what the current methods have offered so far with preventing or permanently curing HIV infection. The current antiretroviral treatment strategy only weakens the virus by making it undetectable but does not remove the "latent viral reservoirs in HIV patients"[13] (Ebina et al. 2016). The treatment supresses the virus to prevent it from multiplying and ultimately defeating the immune system; but it does not completely remove it, and therefore the virus may reappear anytime. Though germline editing technologies are still a work in progress, the procedures have several potential advantages over the existing methods of artificial reproduction, which makes the pursuit for clinical use in humans quite appealing. These arguments are properly addressed in chapter 5, where I compare the current methods of selection in PGD and germline editing.

The second point relates to ethical issues concerning the possible success of human germline editing. Beyond the position discussed above are the views of those who advise against flattening the moral debates on heritable genome editing to the issues of safety and efficacy (Jasanoff and Hurlbut 2018; Botkin 2019). The 'CRISPR'd babies experiment' has invited many controversies into the recent normative debates on human germline editing which mostly relate to the arguments that strongly suggest that the procedure should be completely banned and not be

[13] 'existence of dormant viral reservoirs in the immune system of an infected person that enables the virus to stay in the body even when the antiretroviral drugs have killed all of the active viruses.'

allowed, even under the proposed 'adequately safe scenario'[14]. The main contention here is that the ethical assessment of germline editing should not be limited to the possible technical issues of the methods used (Saha et al. 2018). An issue that warrants consideration is whether it would be morally justifiable to use germline editing once the safety and efficacy issues have been eliminated. I attempt to address this question in the subsequent chapters. The essence of these moral claims is that they contend the use of germline editing even under the identified preconditions of this thesis, which essentially demonstrate the validity of the moral conflict in this discussion. My sole intention in attempting to address these dismissive claims is to clarify the ethical position concerning the validity of the moral issues presented by the CRISPR'd babies experiment by making a justifiable case for germline editing for the stated purpose.

In this chapter, I have divided the moral assessment of germline editing into two parts: (1) the possible defects of the gene editing technologies (safety and efficacy), and (2) the potential success of the procedure to edit the human germline once the technical flaws have been eliminated[15]. This brief introduction to germline editing and the events surrounding the specific incident of the CRISPR'd babies experiment shows that most of the bioethical debates revolve around the issue of safety of the gene editing technologies, as a legitimate concern for the wellbeing of humans.

[14] This is in reference to the most important premise of my argument, which is that germline editing could be morally justifiable given that (a) all the current safety concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven. As discussed above, the same position has been maintained by the advocates for a temporary moratorium on germline editing (Lander et al. 2019).
[15] This point is chapter 3-6 of the thesis.

3. The moral significance of germline editing: procreative beneficence and intergenerational relationships.

Before addressing the main criticisms of the procedure, I first have to answer the question of whether the parental decision to edit the human germline for reasons of preventing HIV transmission has a necessary connection with the possible chances of advancing the well-being of prospective children.[16] To justify the moral significance of germline editing to this end, the standard parental obligations towards future generations are discussed following the principle of procreative beneficence and the possible intergenerational effects of the procedure.

The development of gene-editing technologies for reproduction has heightened debates about the moral significance of parental rights and responsibilities in procreation. Having identified that germline editing could potentially be used to introduce irreversible genetic changes that are heritable to the entire progeny of a person, it may be difficult to defend the moral justifiability of the procedure, particularly parental control over reproductive decisions.[17]

When considering the moral rights and duties of parents towards their future children a key factor is a prevalent belief that parents, as representatives and surrogate decision-makers ought to promote the interests and values ideal for the welfare of their children. The basis of this general assumption rests on the principle of procreative beneficence as defended by Savulescu (2007). Procreative beneficence identifies the inherent intuitive nature of humans towards their children. In his formulation of this principle, Savulescu (2007) supports the claim that parents have a 'prima facie' obligation to choose a child with the 'best prospects in life'(2007, pp.521-22). He further points out that this obligation is inferred from 'common sense morality' which entails the 'intuitive response' of parents when making decisions that concern their prospective children (2007, pp.521-22). It is assumed that the choices that parents make typically reflect their best intentions for the welfare of their children. Judging from the daily interactions of humans, parents make decisions on behalf of their children, decisions that greatly impact on their development and survival. This includes health choices, education, to name a few.

[16] This is the 'wellbeing argument', one of the arguments I invoke to refute objections against germline editing.
[17] Most of these difficulties are expressed in the objections against the procedure of which I address in the next chapter.

In 2009 Julian Savulescu and Guy Kahane published an article titled ‘The moral obligation to create children with the best chance of the best life’. In it, the authors remark that procreative beneficence morally obligates parents to ensure that the ‘genetic endowment’ inherited by their children is beneficial and desirable for purposes of offering them the opportunity of living the ‘best life possible’ (Savulescu and Kahane, 2009, pp.277-278).

The main argument of the authors in the above interpretations of the principle is that parents have a moral obligation to exhaust possible procreative choices available in reproductive medicine that could better the survival of their prospective children, and thereby ensuring that their children get the ‘most wellbeing’ in life or the ‘best life possible’.

However, some scholars, particularly those who are anti-human germline editing, have expressed the concern that giving parents control over procreation could lead to ‘a culture of procreative perfectionism’ (Furger and Fukunyama, 2007, p.120). The basis of this argument is that parents will most likely procreate children in their perfect image, overlooking the moral significance of the procedure and most importantly, the best interests of the children. Rebecca Bennet (2014) also adds that creating standards for the best life possible implies that those who are born with the genetic flaws are ‘unworthy’ or have lives that are not valuable.

One of the controversies of using this principle relate to the process of defining what encompasses 'the best possible' or ‘a life worth living’ as used by the authors. To address these objections, it is therefore essential that I define what ‘the best life’ possible entails as used to formulate the principle of procreative beneficence.

In one of his earliest works titled ‘Deaf lesbians, designer disability, and the future of medicine’, Julian Savulescu asserts that:

> “reproduction should be about having children who have the best prospects. But to discover what are the prospects, we must give individual couples the freedom to act on their own value judgement of what constitutes a life of prospect. ‘Experiments in reproduction’ are as important as ‘experiments in living’ as long as they don’t harm the children who are produced” (Savulescu, 2002, p.772)

The aim of procreative beneficence, as defended by Savulescu and Kahane (2009), is to give parents the reproductive liberty to choose, where the choice exists, the 'best' but not 'perfect' life for their future children (2009, p.275). The key point here is 'the best but not perfect life'. This point is very essential for purposes of providing clarity to what comprises the 'best possible life' or what Savulescu (2002) describes as a 'life of prospect' for the future children; and most importantly, why the argument for this thesis of using germline editing to prevent HIV transmission best fits the category.

As noted above, Savulescu (2007) emphasizes that humans, parents in particular, have a 'common moral intuition' of what constitutes a 'good or best life' for their prospective children, and hence they are morally expected to pursue the best procreative choices for their children. Thus, it is only reasonable to infer from this position that the 'best life possible or a life of prospect' is primarily based on the quality of life or the best level of wellbeing attainable for future children.

In a feminist approach to human reproduction, Laura Purdy (1996) defends the use of women's reproductive technologies for procreation as the creation of "a life worth living" (1996, pp.68-69). She further argues that the 'best possible life' for our future generations or a 'life worth living' is one that is sustainable and free from diseases. In essence, the objective of using artificial reproduction technologies is not to reach the state of perfection, but to improve the human species for the ultimate survival of our future children. Therefore, the reasonable answer to this question is that the 'best possible life' is a life free from reasonably avoidable risk of harm, suffering or any preventable issues that can be remedied by humans.

With the understanding of what constitutes procreative beneficence and its prominence as a principle that promotes the advancement of human life through reproduction and having defended the reproductive autonomy of parents to use germline editing, it is important to stress that there are expected standards of parental rights and duties that relate to how the current generation should provide for the needs and preferences of their descendants.

Savulescu and Kahane (2009) recognize the concept of 'preventing harm' as a significant part of procreative beneficence. They argue that it is the moral duty of parents to ensure that their future children '…experience the least suffering or limited opportunity or serious loss of happiness or good' (2009, p.281). Preventing diseases using reproductive technologies can potentially

increase the chances for a better life, considering the possible minimal exposure to diseases and prevention of sufferings associated with the risks of harm. In this connection and drawing from Beauchamp and Childress's approach of principlism, the process of safeguarding the best interest or wellbeing of prospective generations also involves protecting them from harm or minimizing the risk of harm, where reasonably possible.[18]

Savulescu et al (2015) also argue that the act of refraining from participating in 'life-saving medical interventions is to be morally responsible for predictable and preventable deaths' (2015, p.476). It is the responsibility of prospective parents to consider procreative choices that will be advantageous to the lives of future children, and to ensure that the choices will not be detrimental to the wellbeing of their children.

Christopher Rehmann-Sutter (2018) argues that the human germline represents a relationship between parents and their prospective children that should be understood in terms of transgenerational 'relations of care and responsibility' (2018, p.15). He points out that the human germline is more than just a mere genetic lineage between generations that it represents a moral connection that exists within family relations (Rehmann-Sutter, 2018, p. 9). The significance of these generational relations is that they bind the current generations to be responsible and protective when dealing with issues that impact on the well-being of future generations.

What is significant about Rehmann-Sutter's approach is that he recognizes the existence and importance of intergenerational relationships and the moral duties that arise thereof, which closely resonates with procreative beneficence. But his overall position on the moral justifiability of germline editing contradicts the argument of my thesis. He contends that germline editing involves the recreation of a new embryo, which ultimately tempers with the normal parent-child relations that exist within families. The basis of this argument is that the act of editing the human germline changes the natural order of things in terms of 'relationality' between generations because new responsibilities are formed to accommodate the genetically altered aspects of the genome. I agree with his philosophy to a certain extent. The parent-child relationship may be different because the genetically altered children have acquired a new genetic trait that makes them better suited for survival. So, the parent-child relationship is likely to be different from that

[18] Principle of non-maleficence.

of a child without a modified germline because of the newly assumed responsibilities associated with the genetic changes. But, it makes no sense to say that editing the germline 'damages' the generational relationships between the parent and child because in introducing these genetic changes, it is assumed from, as per procreative beneficence that the parents have the sole intention of ensuring that their children are better suited for survival, which shows 'responsibility, care and accountability' for future generations. From this viewpoint I do not see how a different genetic composition can damage the generational relations between parents and children, even if the responsibilities towards the children change, it does not mean that parents do not have any responsibilities towards them because they are responsible for the reproductive decisions and therefore have to be accountable for the actions.[19]

Unlike the other critics, Billy Saunders (2015) gives an interesting critique of the principle. He argues that Savulescu's formulation of the principle is a downplay, the reason being that he failed to show that procreative beneficence is a moral obligation, not just moral reasoning based on the intuition of the parents. In essence, he argues that even in circumstances where parents have the opportunity to give their children the 'best possible life', they could choose not to, since they are not obligated, which he contends to be a weakness of the principle (2015, p.454). He proposes that the principle should be an absolute obligation, that binds all parents to pursue the 'best possible life' for their children, where reasonably possible (2015, p.455).

It is difficult to envision the future of reproductive medicine where every prospective parent is morally bound to exercise or use gene editing methods. In certain circumstances, such as preventing serious genetic diseases, it would be to the benefit of humans. But when it comes to the case for genetic enhancements, the situation is tricky, and better as a decision of each parent.[20] Hence, I invoked procreative beneficence, as defended by Savulescu and Kahane(2009), to argue for a liberal approach, one that allows parents to have the reproductive autonomy of freely deciding on their children's future, as they normally do or are expected to as representatives of the children. As emphasised earlier these are *prima facie* reproductive

[19] I expand further on this argument in the next chapter, specifically when refuting the claim that germline editing deprives the future child of their true identity as natural persons.
[20] This discussion continues in chapter 5 (distinction between enhancement and curative germline editing).

obligations, to decide to edit their children's germline depending on whether they see the procedure as morally suitable for giving their future children the 'best possible life'.

This discussion postulates that parents have procreative autonomy as reproducers that entitles them to make reproductive decisions that will positively contribute to the best or at least better life chances for their children. But these reproductive decisions do not represent a moral ought or absolute obligation, they are the moral choices that individual parents make to safeguard the prospective welfare interests of their children.

To understand the ultimate purpose of artificial reproduction technologies, particularly germline editing methods, one has to understand the moral significance of reproducing a healthy baby with no defects or prospective risk of harm. This purpose also comes in the form of generational relations between predecessors and prospective generations.

All in all, the point that I wish to drive home is that creating humans with better genetic endowments, such as heritable resistance to HIV infection can potentially give them a greater chance of living a good life; and that parents, as predecessors should have reproductive freedom to decide for their children, to symbolize care and responsibility.

4. Moral controversies of human germline editing

I have argued that the main reason why at this present time it is morally right to reject human germline editing is that the procedure is not yet safe to use on humans. But, to some authors, particularly proponents of germline editing, this is not the case; the current safety concerns associated with the procedure is just one amongst other moral arguments that reject its use. It is, therefore, clear that the one question that seeks clarity is why, even under conditions where the human germline can be safely edited, there are claims that the procedure is not morally permissible. To address this question, I criticise and contest some of the dominant objections identified in the literature that relates to the violation of human dignity, undermining natural genetic identity, lack of consent for the future child, and pertinent social concerns relating to enforced eugenics, discrimination and social justice.

4.1 The future child

4.1.1 Human dignity

Amongst the many objections to human germline editing is the argument that altering the genetic composition of humans is an affront to dignity and that it infringes upon the inherent value of humans as natural beings. The basis of this claim is that editing the human germline is a form of monetization of human beings and that it ultimately undermines the natural worth of humans (Malek 2013).

Before discussing this claim in detail, it is important to first consider the question of what constitutes human dignity and whether there is a clear meaning to it.

One of the well-known definitions of human dignity is that which is formulated by German philosopher Emmanuel Kant, who described the concept as the 'intrinsic worth' of humans as rational beings (Shell, 2008, p. 335).[21]

Sulmasy (2008), Andorno (2009), Raposo (2019), Schulman, Davis, Dennett, et al. (2008), embrace the idea that human beings have an inherent value in themselves, that they possess by virtue of being human and that the concept of dignity is all about respecting humanity by protecting this fundamental worth of humans. It seems that most of the exiting ideologies of dignity have been inspired by Kant's philosophy of dignity to some extent. Some scholars hold that the concept of dignity primarily relates to embracing the autonomous decision-making ability of humans, which encompasses respect for self-rule (Shell 2008). Thus, endorsing the 'rationality' aspect of Kant's philosophy.[22]

African philosophers, on the other hand, have also proposed an interesting conception of dignity, one that is rooted in communality. According to Metz (2011), the African conception of dignity is that "…human beings emanates from the network of relationships, from being in community" (2011, p.543). It rejects the western conception based on the argument that dignity "…cannot be reduced to a unique, competitive and free personal ego" (2011, p.543). Still, in a way, this conception also resonates with the Kantian version of dignity in the sense that it promotes the essence of 'respect for human beings' but the difference is that it is derived from a collective perspective.

However, I do not go into the depth of these contrasting conceptions but wish to show that the concept is diverse, which makes its application vague. It is also noteworthy to point out that some scholars argue against using the concept in medical ethics, on the basis that it is 'useless' and unfounded (Macklin, 2003, p.1420).[23]

With these different conceptions in mind, Lucy Michael (2014) maintains that:

[21] For purposes of this thesis, I do not enter into the debate of whether the human embryo at the time of editing possesses rational thought or moral status relating to 'personhood'. I am, rather, interested in the effects of the procreative decisions on prospective generations, once born.

[22] Even though in this section I do not engage in the issues relating to the autonomy of the future child, It is, however, important to note that according to Kant it is through rationality that humans can possess this intrinsic worth.

[23] Ruth Macklin(2003) argues that dignity is worthless and that it merely exists as ' vague statements …or mere slogans…conveyed in the principle of respect for autonomy'(2003, p.1420).

> "Dignity cannot be reduced to a single definition; rather the concept's core meaning is established by a network of ideas related to worth and value, providing a 'sense of dignity'. This 'sense of dignity' represents a universal understanding that all people have value which places obligations on each of us to treat others well. " (2014, p.33)

Endorsing this approach could be a solution. I recognise much of Kant's philosophy in these interpretations, showing that, despite different conceptions, there is a general agreement that the idea of dignity, as suggested by Michael (2014), involves treating humans with integrity and respect to show acknowledgment of their fundamental value as natural beings.

Having in mind the above different interpretations it is apparent that reliance on human dignity to counter the moral permissibility of germline editing is complicated. The idea or the concept of dignity itself is vague and its application to the moral dilemma at hand is tricky.

But to make my case for germline editing, I adopt the most commonly endorsed Kantian conception of dignity that associate with honouring and respecting the inherent value of human beings.[24] Kant's moral philosophy is based on the idea that humans as rational beings ought to be treated equally with respect; and further forbids using a person as a mere tool or means of fulfilling one's ends (Kant,1997: xxii; Shell, 2008, p. 335). The most significant part of Kant's account of human dignity in this discussion is his strong condemnation of the 'instrumentalization' of human beings, which essentially means that it is demeaning and disrespectful to use other humans as tools for pursuing personal gains.

I have argued in the preceding chapter that when arguing for the parental rights and obligations to edit the human germline, parents have the best interest for the future well-being of their prospective children at the forefront. In making this argument I am assuming that parents will not use their children as instruments for satisfying personal reproductive interests but that they will promote the future welfare of their children. This shows that in pursuing germline editing parents are not undermining the value of the children's lives as future natural beings but advancing their lives so they can give them a better life.[25] On a similar note, Raposo(2019)

[24] As argued, Many authors have adopted his idea of human dignity, this includes Raposo(2019),Hammerstin, Eggel, and Biller-Andorno's (2019) and in most of the essays presented in "Human Dignity and Bioethics: Essays Commissioned by the President's Council on Bioethics" by Schulman, Davis, Dennett, et al. (2008) which comprises several journals on human dignity and bioethics.

[25] Chapter 3, procreative beneficence and the wellbeing argument.

asserts that "…as vague as human dignity is, it is necessary to embrace measures that promote human relief from pain and sickness, and it cannot be invoked to prevent measures aimed to that purpose" (2019, p.253). From these arguments, the claims that germline modifications serve as means of manipulating humans for undignified reasons appear morally unsound.

The concept of human dignity is used with hesitance owing to its vague nature. But most of these different conceptions seem to be rooted in the same idea of the Kantian philosophy of 'respect for the inherent nature of humans as rational beings'. Based on this common conception, it is argued that permitting germline editing for the identified reason of this thesis would not violate or undermine the inherent dignity of the future children because it could potentially give them an opportunity of living a better life, one with minimum risk or possibly no risk at all of HIV transmission.

4.1.2 Consent

The principle of consent forms part of the basic ethical principles of biomedical sciences and its application is very significant to the bioethical discourse at hand. The main reason for relying on this principle is that it protects the autonomous choices of humans, giving them the liberty of exercising free will or independent decision-making.

Consent is defined as "…a person's autonomous permission to medical interventions or participation in health research." (Ebbesen et al., 2015, p.4).

Bernabe et al. (2016) indicate that consent is primarily associated with the individual autonomy of a person and the right to self-determination, which encompasses having an open future or control over future decisions. According to Beauchamp and Childress (2013), an autonomous being is a person who is competent to make the decision voluntarily and has 'sufficient comprehension' of the information about the choice they are making (2013, p.107).

The argument for consent is tricky because a human zygote or embryo cannot give consent or participate in the decision-making process. As a result, I address the issue of consent from future child perspective, where the child is a rational being capable of consent. It is also not beneficial to the argument I wish to relay here to go in-depth on the requirements for valid consent. [26]

The moral dilemma presented here is that the personal autonomy of the future children and their prospective wishes may contrast with the procreative decisions of their parents, as surrogate decision-makers. The basis of this issue is that the autonomy of the child may be violated since the chances of exploring possible future choices relating to the introduced genomic changes have been exhausted without their consent (Henrich 2011; Mameli 2007). The basic implication of this objection is that using germline editing in artificial reproduction deprives prospective children of the opportunity to have an open future, with the liberty to independently make informed decisions regarding their bodies.

Vital to this discussion is the question concerning the child's best interest in terms of having decisions regarding their bodies taken on behalf of them; and whether it is just not to have the future option of deciding on their own, independently and unassisted, as to whether or not they

[26] Informed consent can be broken down into three important preconditions which are: "information, comprehension and voluntariness" (Bernabe et al. 2016). But the list is not exhaustive.

wish to edit their genome. Part of this question has been addressed earlier in the discussion about the moral rights and duties of parents towards their future children. Relying on procreative beneficence and the existence of intergenerational obligations of accountability and care, I argued that parents have the moral duty to make procreative choices that will be desirable to the basic interests of their prospective children; and that parents ought to exercise these rights responsibly.

As noted in chapter 3, these duties stem from a 'common moral sense' of parents as the surrogate decision-makers, and which enables them to make reproductive choices that best suit the interests of their prospective children.[27] I have also argued that it is part of a parent's everyday duties to make choices for their children that will possibly shape their future for the better. A common example is that parents normally decide on important issues relating to their children's health, education, environment, etc. These are morally significant decisions that potentially serve a vital role in the child's life.

By representing the interest of their prospective children, parents have to make decisions that will best advance the children's health and wellbeing, as dictated by procreative beneficence. An action of this nature justifies the use of parental reproductive autonomy over the consent of the future child.

[27] The remedial assumption of germline editing is that the person born will be in favour of the procedure and in turn be cured of a certain genetic defect, which in this regard is a genetic weakness to HIV infection.

4.1.3 Genetic identity

I now turn to the contra nature arguments. These are critics based on the 'unnaturalness' of gene-editing procedures, regarding the claim that they deprive humans of their unique identity as natural beings.

Many authors (Botkin 2019; Rubies and Steger 2018; Meagher et al. 2020), rely on this claim to oppose the moral justifiability of germline editing. They argue that prospective children have a right to inherit a natural genetic identity that is not artificially manipulated by human beings.

The moral basis of this argument is partly built on religious beliefs expressed in the well-known biblical verses, that describe humans as representations of God or natural creatures made in the " image of God" (Li and Zhang 2019).[28] Based on this argument, it is morally wrong to attempt to alter the natural creation of life through artificial reproduction methods, such as those identified in this thesis. On similar views, and also rejecting the use of genetic interventions for reproduction, Sandel (2007) maintains that children are a blessing from God and that the use of artificial reproduction procedures fails to acknowledge the essence of this gift of life.

The reality of this discussion is that we need artificial procedures to advance the health of humans. Arguing that the procedure is anti-nature and therefore immoral to use on humans, appears to be illogical relative to this reality. On this note, Raposo (2019) contends that there are significant artificial procedures, that are used in everyday life for the development and survival of humans, some as medical interventions employed for helping with health-related issues in reproduction or for promoting the general wellbeing of people. Emphasising this point further, Hammerstin, Eggel, and Biller-Andorno (2019) assert that "…in today's medicine there is no line between 'natural and unnatural' therapy" (2019, p.10). A clear example is the current methods of PGD, used in artificial reproduction to select healthy embryos through IVF, as an attempt to avert prospective children from inheriting severe, life-threatening genetic diseases.

Some scholars link the genomic identity of humans to the idea of genetic determinism. According to this ideology, the human genotype is a special genomic design of a person that represents their uniqueness and identity. The philosophy behind this idea is that the human

[28] The scripture (Genesis 1:27) says that all humans are "made in the image of God" (Gelernter, 2008, p.399).

genome symbolises the heritage or true origin of a person and that introducing artificial changes to it deprives humans of their natural, unique identification (Botkin 2019; Resnik and Vorhaus 2006). This means that humans only get their distinct identity from their genes, and as a result, the act of modifying the human germline is associated with creating designer beings with no sense of 'unique' belonging.

In utter difference with the argument presented above, some authors contend that the ideology behind genetic determinism lacks logic. What is considered to be most problematic about genetic determinism is that it does not correspond with the natural development or growth of human beings. De Melo-Martin (2005) warns bioethicists to be careful when interpreting and discussing the role of genes in the development of humans or the causal link between a human's genes and their uniqueness. This is because many approaches to the moral issue in question seem to be leaning towards genetic determinism, thereby proposing that human genomic composition signifies a person's true individual identity, which he contends to be incorrect. His critique of this ideology is that:

> "…there is no empirical foundation for the belief that genes alone determine most human traits and behaviors. This is not to say that genes play no role at all, nor to reject the claim that sometimes genes might provide the best explanation for the genesis of a trait." (de Melo-Martin, 2005, p.526)

He further asserts that these basic traits and behaviours (physical and psychological qualities) that humans develop come about as a result of influences from a variety of internal and external factors to which humans are exposed as they grow (2005, pp.526-527). This includes the environment they grow in, their cultures or way of living, and socio-economic factors. In essence, both the genetic and external factors play a significant role in the genomic growth of humans and no genomic traits can be entirely determined by one in the absence of the other.

On similar views, Resnik and Vorhaus (2006) argue that it is morally unsound to assume that the human genotype is the only fundamental source of identity of humans. The authors further substantiate their argument with the example of identical twins, born with similar genotypes. They argue that the mere fact that the twins possess the same genotype does not allude to that they will have the same personal identity or develop a similar phenotype (physical and behavioural qualities).

According to a psychological study conducted by Knox (2004), human beings get their life skills and a sense of identification from various environmental influences that they get exposed to as they grow. Emphasising this point and further endorsing de Melo-Martin's (2005) argument, Mameli (2006) maintains that:

> "By ensuring that their children experience certain environments, parents can raise the probability that their children acquire certain desired genetic traits. Similarly, by ensuring that their children have certain genes, parents can-at least in principle, assuming that genetic science becomes sufficiently advanced-increase their children's chances of developing certain desired traits. But different developmental factors, whether genetic or environmental, affect development in different ways." (Mameli, 2006, p.88)

In light of this, it is clear that even though we are natural beings, we are nonetheless exposed to different forces, whether they be environmental conditions, different medical interventions that help improve our health or to cure illnesses, or different socio-economic conditions that shape our way of developing as humans. Because of all these interactions, we grow and develop into unique natural beings. This essentially goes to show that being born through artificial reproduction methods of germline editing does not mean that a new human being, with a different identity, is recreated but it means that a person's genome has been altered so that they can be best suited for life on earth and the person will further grow and develop, depending on the environment they grow in and other factors they get exposed to.

On the whole, I have argued that the deterministic assumptions about the unnaturalness of the procedure to the natural distinctiveness of humans are flawed and therefore morally unsound. It is therefore emphasised that the individual growth and development of humans should not be confined to genetics only.

4.2 Society and germline editing

4.2.1 Eugenics, discrimination and social justice

The biggest concern about gene editing technologies is that they could be used to the detriment of society. This issue dominates most, if not all of the bioethical debates on this topic. The feared consequences of using germline editing include issues of unequal access to health resources, discrimination, social justice and the potential use of the procedure for evils of scientific eugenics. Against these concerns, a discussion about the possible societal responses to these problems is also necessary.

Given the tragic history of eugenics, it is reasonable that the possibility of artificially altering the human germline for reproduction, as attempted in the CRISPR'd babies experiment, has sparked great fear within humans.[29] The main concern amongst people is that permitting the use of germline modification procedures may lead to immoral uses of the technologies, and possibly result in a new form of imposed eugenics where human lives could be endangered (Sandel 2009; Li and Zhang 2019). These concerns have been invoked by many scholars to defend the argument that germline editing should, because of the potential threat to humans, be considered as a form of dehumanisation and therefore be criminalised (Annas 2002; Botkin 2019). The harsh reality is that there is a high possibility that some people may use the procedures for recreational purposes, with the sole intention of creating perfect children with traits desirable for their ends. This is not to say that using germline editing for other purposes aside from traditional methods of treating and preventing diseases is morally wrong, only that the possible undesirable consequences that may result from such practices are mostly detrimental to humans.[30] And also, as pointed out in the former chapter, it is morally wrong in terms of the theory of deontology to use human beings as mere tools for furthering personal fulfilments. Overall, this is a valid concern that deserves to be given due regard so we can maintain morally acceptable use of germline editing technologies in our societies.

[29]Eugenics programs implemented during the early twentieth century resulted in 'mass involuntary sterilizations and mass murders', see Mahoney and Siegal (2018, pp. 209-210) for more details on the incidents. Eugenics refers to reproduction-related studies that implement selection procedures, to target selection of the desirable traits in humans, while the bad or undesirable traits are removed.

[30] A proper engagement on the curative-enhancement therapy distinction is provided in the next chapter.

However, using the procedures for morally acceptable reasons, such as those identified in this thesis does not resemble the dark eugenics practices. In the earlier chapters, I argued that the purpose of germline editing is not to achieve genetic perfection but to better the prospective children's chances of survival by ensuring that they have the best possible life; and in this way, the procedure does not pose a threat to humans. On the same note, Mahoney and Siegal (2018) clarify that:

> "What those who invoke the specter of eugenics fail to recognize is that human germline modification is its opposite, not its heir. At the core of support for eugenics was the conviction that-for the benefit of society-certain individuals should not reproduce. The alleged good of the collective trumped the rights of individuals, and government force took centre stage in determining the genetic profile of the generations to come. By contrast, a chief goal of heritable genome editing would be to expand the options available to individuals while leaving sensitive decisions about family life up to them. If this technology fulfils its promise, then many with well-founded anxieties about the genetic makeup of their descendants who in the past would have hesitated to have children will have access to viable treatments." (2018, p.209)

Supporting this view, and recognising the potential of germline editing in reproduction, I have argued in the previous chapters that these technologies could someday serve as an alternative to the current methods and most importantly, provide a remedy where the current methods lack.[31]

From a healthcare standpoint, there are several concerns for the possible socio-economic inequalities that may result from the use of gene-editing technologies in our societies. This concern is corroborated by the argument that the underprivileged members of the society stand to be deprived of the opportunity to enjoy the benefits and opportunities associated with the techniques (Botkin 2019; Meagher et al. 2020; Rubies and Steger 2018). To avert these potential injustices, strict measures must be put in place to ensure equitable access to the resources, and to avoid serving only the health interest of the wealthy members of the societies. In essence, the argument here is that it would be unfair to have a form of elitist medicine, accessible only to a certain class of people. Hence, in the next chapters, I support the idea of regulating the procedures to ensure social solidarity and justice.[32]

[31] This point is explored further in the next chapter, where I compare the current methods of selection in PGD to germline editing techniques.
[32] Chapter 6 of the study.

Another major societal concern of germline editing is the possible stigmatisation of people based on their genotypes, which may lead to unjust social norms that promote social division and discrimination of humans based on their genomic capabilities (Prainsack and Buyx 2017). Simply put, those who are not genetically modified may feel less valuable or outshined by those who possess the desirable traits or possibly the other way around.

The dark past of eugenics is certainly one of the reasons germline editing is being subjected to grave scrutiny. But this does not mean that the procedures are a threat to humanity. Using germline editing to prevent HIV infection promotes the welfare of future children. It is also apparent that having this genetic trait does not make one person perfect, better, or superior to the other, only that it aims to advances their prospective chances of survival.

4.3 Summary

In this chapter, I hope to have shown the weakness of the arguments contesting the moral justifiability of germline editing, and why it is morally unsound to rely on them for purposes of nullifying the procedure. Also, it has been briefly proposed that the societal concerns related to germline editing technologies could be managed through regulation of the procedure, which I engage in the next chapters.

5. Comparative analysis

The essence of this chapter is to compare germline editing to the current methods of selection in pre-implantation genetic diagnosis (PGD), and to defend it as a potentially viable and novel alternative reproduction technique. Furthermore, the restrictive use of germline editing for curative purposes (treatment and prevention) is justified, based on an attempt to prevent exploitation of the procedures for immoral uses.

5.1 The moral difference between germline editing and PGD.

Earlier on I highlighted the position of the opposition in this moral debate, which is that the existing methods of artificial reproductive technologies including genetic selection in PGD suffice in preventing genomic diseases and that the use of germline editing procedures for reproductive is unnecessary.[33] But, taking a closer look at the currently used reproductive technologies, PGD in particular, many shortfalls have been identified which ultimately raise doubts on whether the potential use of germline editing techniques in the future should be prohibited or further pursued.

During the early years of its introduction as reproductive technology, PGD has also been subjected to grave moral scrutiny. This includes moral issues relating to the unnaturalness of the procedure or societal concerns associated with the possible use of the procedures for trivial reasons (Gyngell et al. 2017). But, for the past two decades or so the procedure has become to be considered one of the most significant procedures, used in reproduction medicine for several functions including the process of preventing disease-causing genotypes from being passed on to prospective generations. I do not imply that we should ignore the concerns raised based on the fact that every technology normally faces such moral scrutiny. I am, rather, arguing that not

[33] As highlighted in the thesis, one of the main motives behind this is that unlike the current reproduction techniques, germline editing is not adequately effective and safe for the stated functions.

every scientific development will lead to the detriment of the human species, and given the chance, germline editing could also prove to be useful in advancing artificial reproduction.

In the following, the moral significance of germline editing is explored in comparison to PGD. In the process of making this distinction, the question of whether germline editing has any essential advantages over the current methods of PGD is answered as an attempt to show that in some instances the gene-editing procedures may be the only possible avenue for curing and preventing genetic diseases.

In this chapter, I am not particularly concerned with arguing for the specific purpose of this study, justifying the use of germline editing to prevent HIV. Rather, I aim to show that one of the most significant procedures in artificial reproduction, PGD, is not an 'all-disease remedy' process and that germline editing techniques could potentially supplement where it technically lacks.

According to the selection process used in PGD, *in vitro* fertilised embryos with no disease-causing genotypes are identified and examined for disease purposes before being implanted back to the womb (Ranisch 2019).

Hammerstin, Eggel, and Biller-Andorno (2019) compared germline editing to PGD, regarding its function and purpose as a potential technique for reproduction. The comparative analysis conclusively shows that the two methods are not as different as has been supposed and that germline editing has the potential of achieving the same aim, and potentially more, as PGD, which is to produce 'healthy and genetically related children' (2019, p.11). Selection reproduction using PGD offers people with heritable defects an opportunity to reproduce healthy, genetically related children, but the procedure is not always successful.

Ranisch (2019) points out that there are some instances where germline editing is applicable that PGD is unable to produce a healthy and genetically related child. Under these circumstances, the chances of reproducing a child who is not genetically affected using selection methods are very low to an extent that the process becomes ineffective for achieving the desired outcome. One of the common examples is when,

> "…parent is homozygous for an autosomal-dominant disease (e.g. Huntington´s disease or Marfan syndrome) or where both parents are homozygous for an autosomal-recessive disease (e.g. cystic fibrosis). In such cases, it is impossible not to pass on a mutated allele to any future offspring." (Ranisch, 2019, p.4)

Also, in terms of individuals who carry the gene for dominant diseases, they only have a 50% chance of reproducing disease-free children through the selection procedures in PGD, which makes the reproduction process problematic in some instances (Hammerstin, Eggel, and Biller-Andorno 2019).

Concerning the aforementioned, it is apparent that germline editing has more to offer reproduction medicine than the current methods of selection have to offer. Given a scenario similar to that described above, with 'homozygous carriers of a recessive transmitted disease', PGD cannot be used because all the embryos created would still be affected by the disease.

Another distinction between the two methods is that, instead of selecting the good embryos and discarding the defective, as used in selection reproduction, germline editing, protects the embryos.

On the issue of curing genetic defects, Gyngell et al. (2017) point out that:

> "Genetic selection substitutes one individual with a disease with a healthy individual. It does not benefit those with disease. […] germline modifications on the other hand could provide benefits to persons who would otherwise be born with genetic conditions – it could cure their disorders" (2017, p.501)

Two issues arise from this distinction. One relates to the potential ability of germline editing to fix or cure the genetic defect. The second is that with gene-editing the possibility of fixing the embryos means that instead of discarding defective embryos we can opt to remedy the defects and therefore creating more viable embryos for reproduction.[34]

Another issue worth raising relates to the act of destroying or discarding defective embryos once the selection of the healthy ones is completed. In some religions and cultures, the human embryo is afforded the same moral status as that of a person (Altaany et al. 2019; Ginsburg and Rapp

[34] In the first chapter, I have described how gene-editing works, that a defective gene in the embryo is deleted, removed, or altered using gene editing methods like CRISPR.

2020; Knoppers, Bordet and Isasi 2006). In terms of these beliefs, embryo selection in PGD is considered an immoral practice used to destroy and undermine human life. This ultimately shows that some people may prefer not to have their embryos wasted away, even if they have genetic defects. In support of this point, Ranisch (2019) argues that germline interventions "…might seem an attractive option for some intended parents because it could avoid the destruction of embryos after PGD and offer a direct fix for affected embryos" (2019, p.11).

The future possibility of using germline editing in reproduction becomes even more interesting in cases where the current techniques are limited or cannot provide the solution. This goes to show that there may be a time in the future where the human species may need these techniques to cure diseases.[35] . It is imperative to recognize the potential significance and role of the emerging genetic technologies, with novel possibilities for advancing reproductive medicine.

[35] Again, I am not implying that the human species cannot live without these procedures, I am merely highlighting the point that I raised earlier that there may be genetic diseases that only germline editing can cure. In this particular instance germline editing could possibly save many lives.

5.2 Enhancement versus curative germline editing

I now consider the question of what constitutes justifiable use of germline editing procedures. I have stated before that one of the major societal concerns of germline editing is that the procedure may end up being used for non-medical (enhancement) reasons which could lead to a variety of societal disasters associated with the possible immoral uses of the technologies on humans. One question that has been the centre of debates regarding this concern is whether genetic enhancements should also be permitted in healthcare for reproductive purposes.

In support of germline editing, Harris (2015) asserts that the procedure should also be used for genetic enhancements, to introduce advanced genetic traits that further enhance normal human capacities to function above the ordinary level. Even though the primary aim of my thesis is to defend the moral justifiability of germline editing, I, however, do not support the argument that germline editing should be extended to enhancement purposes as suggested, for the reasons discussed below.

The moral significance of having the enhancement-curative germline editing distinction is not explored only for reasons of drawing the moral difference between the two methods but also to show the importance and necessity of the procedures in terms of their potential role and purpose in reproductive medicine. However, creating a moral line between the two methods is difficult. There are multiple approaches to this distinction, some of which I touch on in this discussion, that create controversy about the grounds on which the fundamental difference between the procedures should be drawn.

The distinction presented here primarily rests on the purpose of the gene-editing therapies, which makes it necessary that I first provide clarity as to what distinguishes one from another.

One way to look at this distinction could be through the different types of eugenics, as proposed by Vilaca and Marques (2015). The authors argue that:

> "in virtue of the biotechnological advances and the successes of genetic therapy, it is important to separate the negative eugenics from the positive eugenics, that is, between what is therapy – the prevention of evils, such as diseases and deficiencies, which are seen as deviations or lack of normal organizational functioning, typical of the species, – and what genetic enhancement, which refers to

> interventions as exploitative and tecnicized of human nature, in that they would be affected by a mere programming guided by the egotistical preference of a third." (2015, p. 267)

On the same note, and further clarifying the purpose of this distinction, Kleiderman et al. (2019) provides that:

> "The rationale behind GGE for the treatment of severe diseases is therapeutic, i.e. to cure a disease to generate health. The use of GGE for non-medical purposes is, as the name implies, non-therapeutic in nature, i.e. it is an enhancement and/or change of a "non-disease" phenotype, e.g. increased height or change of hair color, respectively"(2019, p.8)

In essence, the basic and most commonly invoked differentiation of the procedures is that curative germline editing encompasses 'medical' genetic interventions, associated with treatment and prevention of diseases, while genetic enhancements are 'non-medical' interventions, primarily used to advance normal human qualities or traits.

French Anderson (1990) argues that the only morally legitimate forms of genetic interventions are those that are only used for the traditional medical tasks of preventing and treating diseases. He further cautions that to fulfil the main purpose of medicine, which is to cure, prevent and ultimately provide relief from diseases, the moral line dividing enhancement and curative therapy should never be crossed (1990, pp.22-23.).

In terms of this approach curative germline editing is recognized as an inherently more significant form of editing than the other methods of genetic enhancements, thereby leading to the assumption that editing for enhancement purposes is inherently wrong. However, critics (Kleiderman et al. 2019; Rubies 2019) argue that this is not a reasonable approach to this distinction.

Before going into the controversies, it is essential to highlight that I do not intend to argue that the genetic enhancements are inherently wrong; only that, allowing the use of germline editing procedures for this purpose may not be ideal considering the potential moral concerns associated

with its use.[36] Hence I suggest that it may be best to take precautions and use the procedures for curative purposes only.[37]

In connection to the identified flaws of this distinction, Kleiderman et al. (2019) highlight that there is no definite description of what constitutes 'medical-purposes' or 'serious genetic disease'. Moreover, and also still emphasising this point, the authors remark that the evolving qualification of these concepts depends on:

> "… elements that are constant and objective (e.g., morbidity/mortality), as well as elements that are flexible and evolving (e.g., disability as impacted by social arrangements or treatability as impacted by effectiveness and cost of treatment). […] concepts such as 'health-related' and 'disease' should not be defined without considering the adaptation of an individual to a given environment" (2019, p.512).

Scholar David Resnik (2000) makes a similar point about the distinction. He contends that to assess the acceptability of any gene-editing procedure, one must consider the unique facts of the case and the pertinent moral principles (2000, p.365).

On the same note, Rubies (2019) also state that:

> "Whether a medical intervention is to be considered as treatment or enhancement depends on the specific circumstances of the case. Each case where GGE is applied would have to be evaluated by an ethics committee, since there is no overall criterion to separate treatment from enhancement. This would have to be a case-to-case decision" (2019, p.6)

The above-cited authors agree that it is significant for every genetic intervention to be conducted with the prime aim of advancing the health needs of people. As noted above, this "intention to improve the health or wellbeing of humans" could be achieved through a flexible approach, that deals with the issues on a case-by-case basis. Adopting this approach does not ultimately conclude that the curative-enhancement distinction is insignificant. It is essential to acknowledge what discerns curative germline editing from genetic enhancements for purposes of understanding moral issues raised by these procedures.

[36] Going back to chapter 4, I have argued that genetic enhancements are most likely to lead to social destruction, owing to possible harmful eugenics amongst other issues.
[37] This argument unfolds with the discussion.

The main idea here is that there is no particular genetic intervention that is inherently immoral. The question that should be asked about the distinction is not whether the type of gene-editing is an enhancement or curative germline editing, but rather if the procedures, in general, pose any threat to humans (individually and, or collectively), and whether it infringes upon the inherent rights of people or whether it promotes justice, and so on.

I have identified that the basic difference between the two methods is that one is used for medical purposes and the other for non-medical reasons. I have also argued that the moral assessment of each genetic intervention depends on its role and purposes in reproductive medicine which is judged based on the unique circumstances of each case to determine if the procedure is morally justifiable.

The general position maintained in this moral distinction debate is that neither of the two methods is inherently wrong. But, if we were to accept the use of germline editing procedures for reproduction, it would be wise and responsible not to allow the procedure to be extended to genetic enhancements. And again, this is suggested out of pure concern for society and all its stakeholders.

The overall argument is that it would be less destructive to use germline editing procedures for curative reasons only, owing to the concern that genetic enhancements would be much more than we can handle as humans, and history dictates that it can easily get out of hand.[38]

In this chapter, I have considered different arguments that support the idea that no particular genetic intervention is fundamentally more important than the other, which goes to show that the moral assessment of every germline editing procedures should be an open enquiry. The main concern with enhancement is not that they do not conform to the traditional[39] methods of medicine, but the possible undesirable consequences associated with the procedures.

[38] Here, I am referring to the history of eugenics, as discussed in the previous chapter.
[39] Treating and preventing diseases.

6. A way forward

So far, I have mainly been concerned with defending germline editing against some of the dominant critiques, which includes moral justifications based on comparative analysis to other methods of artificial reproduction. Another key theme of my thesis, that I am predominantly concerned with here involves providing an answer to the question of how germline editing should be properly adopted or implemented into our societies as a possible system for artificial reproduction, once proven to be safe and adequately effective for the proposed uses. Like many other bioethicists (Rubies 2019; Brokowski 2018; Raposo 2019), I propose that the regulation of gene-editing practices could be the possible answer to this question.

A few months after the news of the CRISPR experiment broke, the World Health Organization (WHO 2020) established an advisory committee to look into various issues concerning the controversial uses of germline editing for reproduction. Most importantly, it should formulate global standards that could potentially serve as guidelines for addressing issues pertinent to possible future uses of the procedures. The committee advised that in the interim, any clinical applications associated with the use of procedure on humans should be put on hold until a safer path is found. No proper global guidelines have yet been proposed in this regard.[40]

In their recent report, the 'International Commission on the Clinical Use of Human Germline Genome Editing, National Academy of Medicine, National Academy of Sciences and The Royal Society'[41] attempts to define what a responsible pathway for the clinical application of human germline editing should be, including the ideal structure and processes for governing the procedure. This report, together with the unofficial guidelines from the WHO serve as the most relevant sources for this discussion. But, for the purposes of this study, I do not go into depth on what the actual rules, guidelines or standards say, I merely discuss what has been proposed so far in terms of creating a suitable global framework for promoting the morally justifiable application of the procedure. [42]

[40] The document from WHO that I rely on is a 'draft framework for governance', issued 3 July 2020. It is also emphasised by the organization that this document is not a finished product but a mere work in progress.
[41] Hereafter referred to as the National Academy of Sciences (2020).
[42] The scope for the proposed regulation of gene-editing technologies, from WHO guidelines, National Academies and other international organizations are very broad. And therefore, a comprehensive and in-depth exploration of these issues goes beyond the scope of my thesis. However, the interested reader can refer to the recent report from the National Academies (2020) and WHO draft guidelines. See reference list for full citations.

Governance[43] is described as "… structures and processes that are designed to ensure accountability, transparency, responsiveness, rule of law, stability, equity and inclusiveness, empowerment, and broad-based participation" (UNESCO)[44]. In basic terms, to govern is to control or administer a certain process by creating rules or standards that serve as prerequisites for practicing something.

Writing about the significance of regulating human genome editing, and the need to progress in reproductive medicine, de Miguel Beriain (2017) points out that the new rules governing the use of biotechnologies should be put in place to inform the existing laws so that the new gene-editing technologies such as CRISPR could be properly accommodated.

However, the idea of regulating human germline editing becomes challenging when considering the different domestic laws of each country, worldwide. The difficulty becomes how to ensure that each country's national regulations adhere to or incorporates the global standards on germline editing so that there can be a universal regulatory framework that ultimately promotes social justice and solidarity within the entire global community.

Since the initiation of the WHO advisory committee in 2019, many countries have been actively engaged in voluntary discussions relating to the proposed prohibitions on the procedure and the essential conditions [45] that ought to be considered to promote the interest of the individuals and the society at large (WHO, 2020, p.18). While some countries have temporarily banned germline editing practices, some have remained vague in their national laws regarding the issue in discussion (Brokowski 2018).[46] In essence, once clear guidelines have been formulated, the governments and the relevant policymakers must decide whether to follow the guidance of the proposed international regulations when creating laws on this matter.

According to the recommendations of the National Academies (2020), for global governance of human germline modifications to be effective "…national decision-making should be informed

[43] For purposes of my argument here, the process of regulating and governing are considered synonymous, and therefore applied interchangeably throughout. But in terms of the actual definitions, governing is much broader and a bit more complex than regulation.
[44] Cited directly from the website 'http://www.ibe.unesco.org/en/geqaf/technical-notes/concept-governance'.
[45] Conditions relating to safety and efficacy, refer to chapter 2 of this paper.
[46]For instance, some nations are party to the Oviedo Convention (1997), an international treaty that prohibits any form of human germline genome modifications. See Council of Europe Convention on Human Rights and Biomedicine (the Oviedo Convention), Chapter IV, Article 13.

by transparent international discussions before any country's regulatory authorities can make major threshold decisions on uses of heritable gene-modifications" (2020, p.15). The report further advises that:

> "…all countries in which heritable human genome editing (HHGE) is being researched or conducted would need to have mechanisms in place to oversee translational progress toward potential clinical use of HHGE, to prevent unapproved uses, and to sanction any misconduct. It is recognized that not all countries necessarily have the scientific expertise and regulatory and societal engagement mechanisms to meet the requirements listed below. Nonetheless, if a country is not able to meet all these conditions, no clinical use of HHGE should occur in that country." (National Academy of Sciences, 2020, p.14)[47]

International regulations would assist in guiding the national policy formulations for germline editing by creating global standards that could be considered as guidelines for implementing proper governance of the procedure. The only way to reach a proper global consensus on regulating germline editing is to ensure that every state is committed to the proposed mechanism of governance and that they participate in the discussions and all the relevant decision-making processes involved.

I am unable in this short discussion to thoroughly engage on how these regulations would work, from a global spectrum and the relevant processes. Hence, in the afore arguments I simply highlight the basis of this idea and how it could be incorporated into global standards for governing the procedure in the future.

The WHO (2020) emphasizes a global regulatory framework that integrates societal values into policy considerations. This includes incorporating all parts of our international community, including our diverse cultures, religions, and the relevant socio-economic factors applicable to this process.

As mentioned in the preceding chapter, some of the dominant societal concerns relating to germline editing include the potential socio-economic inequalities, discrimination and social stigmatization that could arise from its use on humans. It is important for the relevant legislative bodies to priorities the needs of the global poor by making sure that there is affordable access to

[47] HHGE stands for "Heritable human genome editing". Another way to say germline editing.

gene-editing technologies and also to encourage worldwide healthcare equity (WHO 2020).[48] This includes making sure that public healthcare facilities, worldwide, have sufficient resources that enable everyone, irrespective of social status, access to proper healthcare services.

Regulating the use of germline editing in our societies requires utmost responsibility. It is the ultimate argument of my thesis that a morally justifiable use is one where safety and effectiveness of the procedures can be guaranteed. To ensure that these procedures do not lead to the detriment of the society and its people, we must, upon implementing the regulatory frameworks, ensure that every nation will be able to properly adopt the recommended measures to ensure that the purpose behind governing this procedure is fulfilled.

Another problematic issue arises from the challenges associated with creating clear limits between curative germline editing and genetic enhancements. In the previous chapter, I argued that to avoid the potential misuse of gene-editing technologies for inhumane reasons, the procedure should be limited to treatment purposes only, which encompasses preventing and treating diseases.[49] I therefore in this regard, emphasise that it should be part of the substantive prerequisites for regulating germline editing techniques that its application be restricted to treating and preventing disease and not for non-medical purposes. As defended in the previous chapter, the argument that germline editing should not go beyond prevention and treatment of diseases could minimise the potential exploitation of the procedure for immoral practices.

Another essential requirement that I have overly emphasized as the *sine qua non* of my thesis is that there should be no risk associated with the genetic intervention in question. The procedure must be declared adequately safe and effective for the proposed uses. Hence, I have highlighted earlier that clinical research on germline editing should be continued so that the technologies can be advanced and possibly eliminate the scientific hurdles associated with the procedure.

When it comes to the procedure that has to be followed or put in place to ensure that the immoral uses of the technologies are averted or at least reduced to the possible minimum, I first briefly

[48] See also the National Academies (2020, p.149).

[49] In the previous chapter, I have argued that genetic enhancement is when a typical or perfectly adequate trait is altered. I have further argued that this does not mean that genetic enhancements are inherently immoral, only that they are more likely to lead to the unwanted path.

discuss decision making. Who decides on these standards or rules and what should be considered when making these decisions?

The best way to develop policies for regulating germline editing procedures should be through an open process, where public participation is promoted. The decision-making process requires all the affected parties to be involved, from government, scientific community and most importantly, the society (WHO, 2020). Similarly, the National Academies (2020) propose that before any clinical application of gene-editing procedures "…there must be widespread societal engagement and approval, and the establishment of national and international frameworks for responsible uses." (2020, p.7). The individual and collective interests of the people must be given the utmost attention in this process because all these changes and advancements in biotechnologies have a great impact on them.

However, despite arguing that society should be involved in the decision-making process, I do not imply that the decisions should be made by the people per se, but rather that, the qualified regulatory body should keep in mind the needs and interests of the society when making the relevant policy decisions. One of the main ethical controversies of germline editing procedures, as identified in this thesis, is that the procedure has scientific issues that pose a risk to human life; and these issues could be eliminated through scientific knowledge and practices, which common people lack. In connection to this, the National Academies (2020) recommends that:

> "…an International Scientific Advisory Panel (ISAP) should be established with clear roles and responsibilities before any clinical use of heritable human genome editing (HHGE). The ISAP should have a diverse, multidisciplinary membership and should include independent experts who can assess scientific evidence of safety and efficacy of both genome editing and associated assisted reproductive technologies." (2020, p.4)

In essence, the constituents of the responsible governing body, as proposed in the report, should be people with adequate knowledge and experience on the matter in question, so they can make reasonable and properly informed decisions that could potentially benefit the interest of all stakeholders. I agree with the National Academies that, aside from the current regulatory bodies, assessing the social and ethico-legal issues, there must be a special panel of scientific

professionals who oversee the issues of safety and efficacy relating to the technologies. This is essential for purpose of ensuring that the recognized prerequisites of my thesis are met.

The success of governing germline editing is affected by knowledge of the rules, which entail creating awareness and involvement in the policy-making discussions and choices; and approachability of the regulations (will the impacted find the rules accessible or properly developed to cater for their needs ?) What is of essence is that proper global guidelines, that adequately accommodate the interests of everyone, should be established to avert scenarios where there is a black market for underground medical activities relating to germline editing.

In this chapter, I have sought to argue for proper governance of the gene-editing technologies, one that could prompt the global community to implement adequate precautionary measures essential for considering all the relevant aspects including the legal, scientific, and societal issues associated with germline editing. I have therefore argued for the ethico-legal assessment of germline editing in two ways. The first part involves the substantive questions which relate to the moral position of the technologies and the pertinent issues that could result from their use. The second part is about how the procedures should be governed and who should make these decisions.

7. Final remarks

One thing that signifies the moral essence of germline editing, is the potential to improve human lives through artificial reproduction methods used for preventing and treating diseases. But we have learned from the CRISPR'd babies experiment that the pursuit of this end does not trump the responsibility of safeguarding the welfare interests of humans. My central argument is that using germline editing to prevent HIV transmission would be morally justified provided that (a) the current scientific risks and safety concerns associated with its use were resolved, and (b) an effective method of using germline editing for this purpose were proven. Under the current scientific state of the gene-editing techniques, it is only safe to continue the use of germline editing strictly for research purposes to ensure scientific progress and a chance to possibly achieve the envisioned future.

Procreative beneficence and generational relations defend giving parents reproductive autonomy over the decision to edit the human germline. As such, the procreative decision that parents make should be exercised responsibly, with the sole purpose of giving the future child the 'best life possible'. The 'best life possible' simply encompasses the best quality of life, with no suffering due to preventable diseases or the risk of being susceptible to avoidable harm. This shows respect, care, and responsibility toward the prospective wellbeing of the child. To have functional use of this procedure it must be pursued for morally acceptable uses to avoid potential social disasters. One of the possible approaches to achieving this end is through a regulatory system. Limiting the procedure for curative germline editing could be one way to possibly ensure that the procedure does not lead to inhumane practices. The relevant authorities, also must take precautionary measures necessary for ensuring that the germline gene-editing technologies, once in use, are properly governed to ensure morally acceptable use that adequately serves the interests of the society, government, and the scientific community.

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8. References

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