TAKSHASHILA INSTITUTION

Views on Heritable Gene Editing: Survey from India

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Heritable gene editing applications are currently banned in India. This survey seeks to understand views of the Indian public on heritable gene editing. The survey finds that a majority of Indians approve of heritable gene editing to treat or reduce risk of a genetic disease. Based on these results, we recommend the government invest in heritable gene editing research and development to create more affordable indigenous gene therapy products and co-opt religious institutions in increasing awareness about gene editing.

Executive Summary

Heritable gene editing applications are currently banned in India. These applications are also considered unethical in many parts of the world. This survey seeks to understand views of the Indian public on heritable gene editing. The survey finds that a majority of Indians approve of heritable gene editing to treat or reduce risk of a genetic disease. These results are independent of respondents' views on abortion or use of in vitro fertilisation. Prior knowledge of gene editing increases the likelihood of accepting gene editing applications. Religiosity of the respondent appears to play a role in accepting gene editing, with those highly religious less likely to approve gene editing. Finally, exacerbating inequality appears to be the most perceived risk of introducing gene editing in India. Based on these results, we recommend the government invest in heritable gene editing research and development to create more affordable indigenous gene therapy products and co-opt religious institutions in increasing awareness about gene editing.

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1. Introduction

Gene editing technologies have the potential to alleviate disease burden linked to genetic mutations - curing congenital diseases, such as sickle cell anaemia, or reducing risk of diseases, such as BRCA1-associated breast cancer[i]. Repairing harmful mutations in embryos can prevent a lifetime of sickness or premature death and significantly improve quality of life for the individual. However, this form of heritable gene editing (or germline gene editing) is currently banned across the world[ii]. There are three reasons for opposing the use of germline gene editing:

i) The technology is nascent and its impact on the target individual is not comprehensively understood

ii) There are moral concerns associated with changing an embryo's genes[iii]

iii) There may be enhancement applications of gene editing, such as improving intelligence, or muscle strength which are considered controversial[iv]

See Brokowski C for analysis of 61 ethics statements released by the international community between 2015-2018. Position varies from outright ban of gene editing for moral reasons to cautious approach. There is consensus that increased public input and a robust regulatory framework should be used to chart the way forward.

Dewey I and Reintjes C argue that genetic enhancement is immoral because it limits genetic diversity, can give rise to eugenic tendencies and exacerbate inequality.

Safety concerns of using germline gene editing can be resolved as the technology improves. However, moral concerns are difficult to address and are independent of the technology's evolution. These concerns might differ with the application as well. Hence, it is important to understand if the intended audience of a technological application finds it morally acceptable to use.

Heritable gene editing technology has various potential applications. These can be classified as -

i) Therapeutic - treat or reduce the risk of a known illness/disease such as sickle cell anaemia or cancer
ii) Cosmetic - change a physical characteristic without a physical therapeutic effect, such as lightening of skin tone or changing of eye colour
iii) Enhancement - Improve an already existing characteristic such as muscle tone or intelligence

India currently bans the use of germline gene editing and allows research on embryos to be limited to a 14-day period[v,vi]. However, to move forward on creating translational applications of germline gene editing, research in the area has to be allowed. Good public policy can address concerns of off-target mutations, affordability, etc. However, public policy has to consider the ethics of an application to ensure its proper regulation. Bucketing all germline gene editing applications as unethical may preclude its beneficial applications. The ethics of any application is determined by multiple factors - its safety profile, its cost to benefit ratio, its ability to exacerbate inequality and interference with people's beliefs. Personal ethics will drive how an individual will perceive gene editing - whether they will find it acceptable or transgressing nature's laws or their religious beliefs. This survey seeks to understand how Indian citizens feel

The National Ethical Guidelines For Biomedical And Health Research Involving Human Participants 2017 states that "CRISPR-Cas9 needs to be judged for the good of future generations. This needs time and thus, at present, there is a ban on germline manipulations." However, it is unclear how this judgement will be made without research on germline manipulations.

about the use of germline gene editing for various applications to inform policy discussions.

The survey is based on a similar survey performed by the Pew Research group in the US in 2019[vii]. That survey showed that US citizens found the use of gene editing for disease alleviation to be an acceptable use of the technology. Similar surveys across US, Japan, Australia and social media users have also found people generally "accepting the use of heritable gene editing for disease-related genes but concerned about the risks" (Table 1).

Survey Target Population	Year	Number of respondents	Majority view for Use in disease alleviation	Majority view for Use in enhancement
Global social media users[viii]	2016	12,000	Approve	Reject
U.S. adults[ix]	2017	1,600	Approve	Reject
U.S. adults	2018	2,537	Approve	Reject
Japanese adults[x]	2018	11,925	Approve	-
Australian adults[xi]	2019	1,004	Approve	Reject

Table 1. Overview of select surveys of public perception of germline/heritable gene editing.

2. Methodology

To understand the views of Indian citizens on heritable gene editing, a survey was designed based on the survey conducted by Pew Research Centre in the US. Prior permission was taken from the Centre to adapt questions for use in an Indian context. The survey was disseminated through social media (Twitter, LinkedIn, WhatsApp), in alumni and student networks of the Takshashila Institution and personal networks of the researchers. Efforts were made to reach out to religious organisations of various faiths, since religion has been shown to be an important determinant of acceptance of gene editing technology. The survey looks at the overall association of religiosity and views on gene editing and not at any particular faith. Respondents were asked their views on gene editing for 4 hypothetical conditions – treating disease, reducing the risk of disease, increasing intelligence and lightening skin. The first two conditions represent therapeutic application of gene editing technology. Increasing intelligence is an enhancement application, while lightening skin may be considered as a cosmetic application. Questions were also asked about respondents' views on abortion and in vitro fertilisation (IVF) to understand their association with religious beliefs and views on gene editing.

3. Demographic data

This analysis has been performed on a preliminary sample set of 372 respondents. Of these,

- 58.87% respondents (n=219) were in the 18-30 years age bracket, 33.06% (n=123) were in the 30-50 years age bracket and 8.06% (n=30) were above 50 years of age.
- Nearly 60% of the respondents (n=223) had finished post graduation, 34.17% (n=127) were graduates, 2.42% (n=9) had completed college and 3.49% (n=13) had not completed college.
- 12.63% of respondents (n=47) identified religion to be a very important part of their life, 32.53% (n=121) identified religion to be somewhat important while 54.84% (n=204) said that religion was not too or not at all important in their life.
- 74.13% (n=235) had a science and technology background and
- 87.80% (n=278) of respondents had heard of gene editing before participating in the survey.

4. Findings

Public views on heritable gene editing are application dependent

Indians make a distinction between therapeutic and enhancement applications of the technology and significantly favour the use of heritable gene editing for therapeutic purposes.

Heritable gene editing technology has various potential applications. In our survey, participants discerned between these applications and did not provide a blanket negative or positive response to using heritable gene editing. Participants were more accepting of gene editing when used to TREAT (91.67% positive responses) a serious medical condition at birth and to REDUCE (79.5% positive responses) the risk of a disease that could occur during the lifetime. A majority of participants felt the enhancement (17.53% positive responses) and cosmetic (7% positive responses) applications of gene editing were an inappropriate use of this technology (Figure 1).

These data are similar to those observed in the other public perception surveys (Table 1), which found that a majority of respondents agreed that therapeutic, but not enhancement, applications of gene editing were an appropriate use of medical technology.

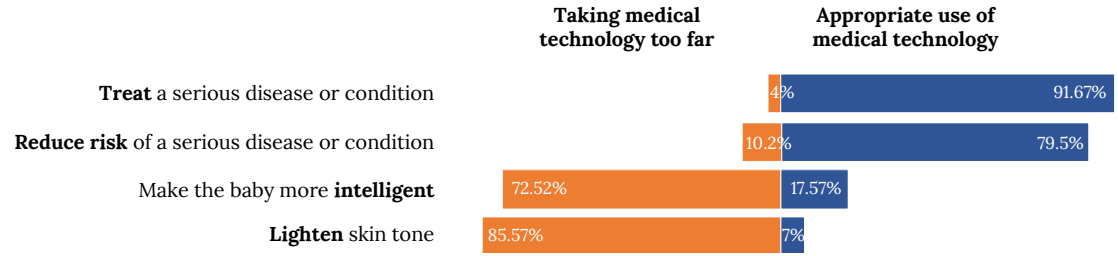

Figure 1: Indians favour the use of heritable gene editing for treating or mitigating risk of disease. Figure shows % response of Indian adults for each application of gene editing. Non-respondents' data is not shown. Results in absolute numbers can be found in Appendix 1.1

These data also reiterate the need to make an application-based governance structure for heritable gene editing. A blanket ban on research/applications or terming the entire technology "unethical" is not in India's national interest, as it will slow progress in this field. India needs to build expertise in the area of gene editing, particularly to create solutions for India-specific diseases. Otherwise we might have to import foreign gene therapy products at exorbitant costs.

There is a small but interesting difference between those who believe cosmetic purposes are appropriate uses of gene editing - those in the 18-50 years age group were more acceptable to such use (15.50% positive responses), while 0 participants in the above 50 age group believe it is an appropriate use of technology. However, given the small size of small group (only 30 individuals in the >50 years age group), it is difficult to infer the significance of this result. Further expansion of the survey is required to understand if this trend is representative of the general population.

Participants more aware of gene editing technologies are more likely to find the technology acceptable

Those who have heard about gene editing before responding to the survey were more likely to find the technology acceptable. For treating diseases, 94% of those who had had previously heard about gene editing agreed to its use versus 74% of those who had not heard of gene editing before. Similarly for reducing risk of disease, 81% of those had previously heard about gene editing were okay with its use versus 66% for those who had not heard of gene editing (Figure 2). This suggests that prior knowledge of the benefits and risks of gene editing generates an optimism about using this technology for therapeutic purposes.

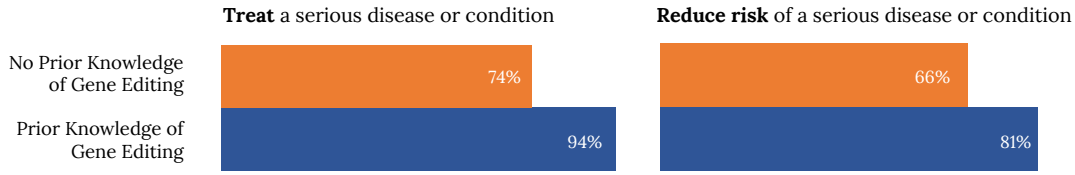

Figure 2: Participants with prior knowledge of gene editing were most likely to find the technology acceptable. Bars indicate number of respondents who found heritable gene editing an acceptable use of technology for each condition.

These data indicate a need for increasing awareness about gene editing and its applications to improve their acceptance. Understanding benefits and risks of the application can help people make informed decision about its adoption/rejection.

Participants who identified religion as very important part of their life were less likely to accept gene editing applications

A comparison of respondents showed that those who identified religion as a very important part of their life were less likely to accept gene editing versus those that felt religion was not at all important. The below figure shows % of respondents who approved of gene editing for each application, based on their identification of the role of religion in their life.

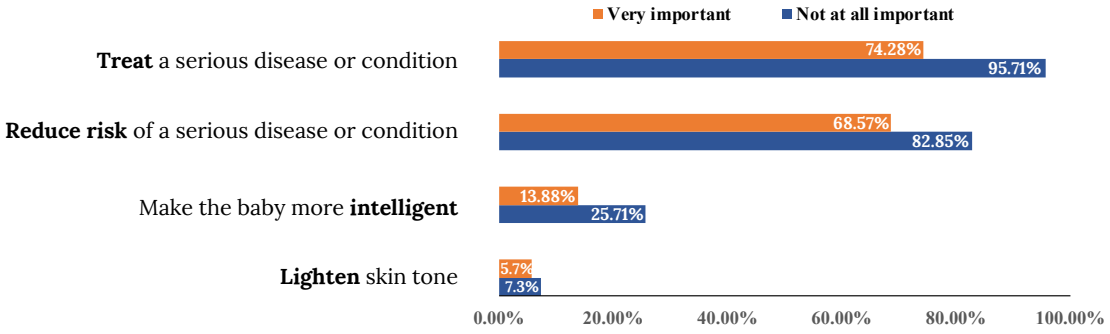

Figure 3: Religious influence seems to be a determinant of acceptance of gene editing technologies. Bars shows % of respondents who approved gene editing for each application, based on whether they felt religion was very important (orange bars) or not at all important (blue bars) in their life.

This result is consistent with the Pew research survey and is likely premised on the hypothesis that gene editing may be viewed as "playing God" or "interfering with the flow of nature."[xii]

Van Dijke I, Bosch L, Bredenoord A, et al.. The ethics of clinical applications of germline genome modification: a systematic review of reasons. *Hum Reprod* 2018;33:1777–1796. DOI: 10.1093/humrep/dey257 highlights concerns over bioscientists "playing God" as an important reason for refusing to engage in germline editing. Locke LG. The Promise of CRISPR for Human Germline Editing and the Perils of "Playing God". CRISPR J. 2020 Feb;3(1):27-31. doi: 10.1089/crispr.2019.0033. PMID: 32091254; PMCID: PMC7047104 reviews literature pertaining to the playing God argument and recommends counter-arguments.

Participants' view on gene editing cannot be correlated with their view on abortion or use of IVF

Abortion, IVF and gene editing in embryos have a common link - they all result in the death of embryos. In abortion, the embryo or foetus being carried by the mother dies; for IVF or gene editing application, any unused or surplus embryos are discarded. These technologies may, therefore, appear unacceptable to those that believe that life begins at conception.

Hence, we sought to see if there were any associations between Indian respondents' views on abortion/IVF and gene editing.

These results suggest that a majority of respondents find the abortion of foetus before 24 weeks of gestation for medical reasons as acceptable (Figure 4). The current legal limit for abortion in India is 24 weeks. Similarly, 75% respondents also approved abortion of foetus after 24 weeks of gestation on medical grounds. The only striking difference of opinion in the respondents was observed for aborting the foetus after 24 weeks of gestation for non-medical grounds. We, therefore, used this data to understand if these respondents felt differently about gene editing applications, i.e., we compared views on gene editing between those who felt abortion after 24 weeks (on non-medical grounds) was appropriate use of technology versus those who felt it was taking medical technology too far.

Germ line genetic engineering with a therapeutic goal in man would in itself be acceptable were it not for the fact that is it is hard to imagine how this could be achieved without disproportionate risks especially in the first experimental stage, such as the huge loss of embryos and the incidence of mishaps, and without the use of reproductive techniques - INTERNATIONAL THEOLOGICAL COMMISSION COMMUNION AND STEWARDSHIP: Human Persons Created in the Image of God

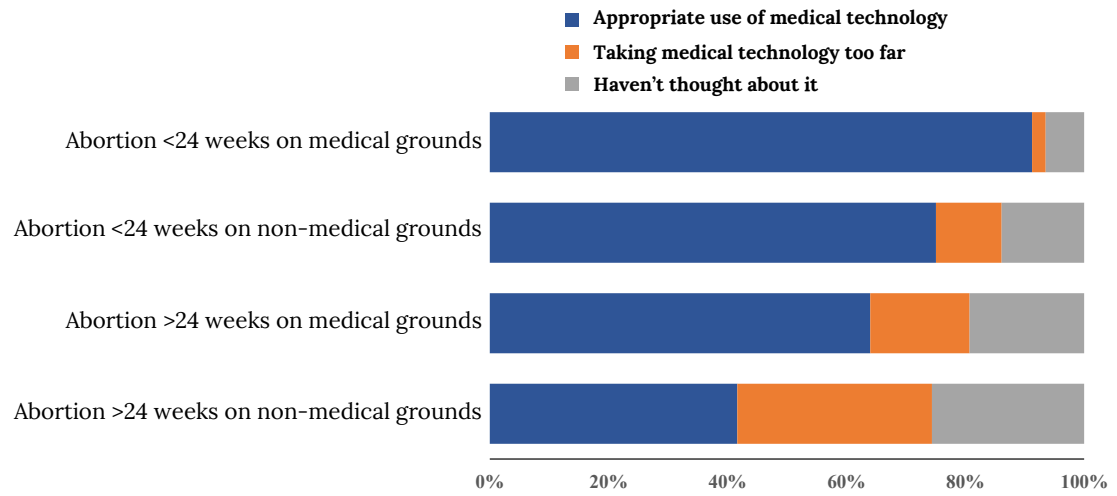

Figure 4: Majority of respondents agree with abortion prior to 24 weeks of gestation; however, there are ambiguity for aborting a foetus post 24 weeks. Bars show % age of respondents who felt abortion was appropriate used of medical technology (blue bars), taking medical technology too far (orange bars) and had not thought about the situation (grey bars) under corresponding conditions. Absolute numbers can be found in Appendix 1.2

We could not find any significant difference in the two groups of respondents when it came to their views on gene editing applications. Thus, in India it appears that abortion by itself is looked on as an acceptable use of medical technology, particularly for medical reasons, and there is no association between views on abortion and gene editing of babies. This is interesting because the association of religiosity and lower approval of gene editing applications (Figure 3) does not appear to stem from the ideology that gene editing would cause death of embryos. Thus, the opposition does not appear to be against the gene editing

protocol, but may be rooted in other moral concerns such as transgressing laws of nature or not taking consent of future generations.

Similarly, when we asked people about their views on IVF, the majority agreed that IVF should be allowed for everyone, particularly for couples who are having difficulties conceiving, or whose babies may have genetic predisposition to diseases.

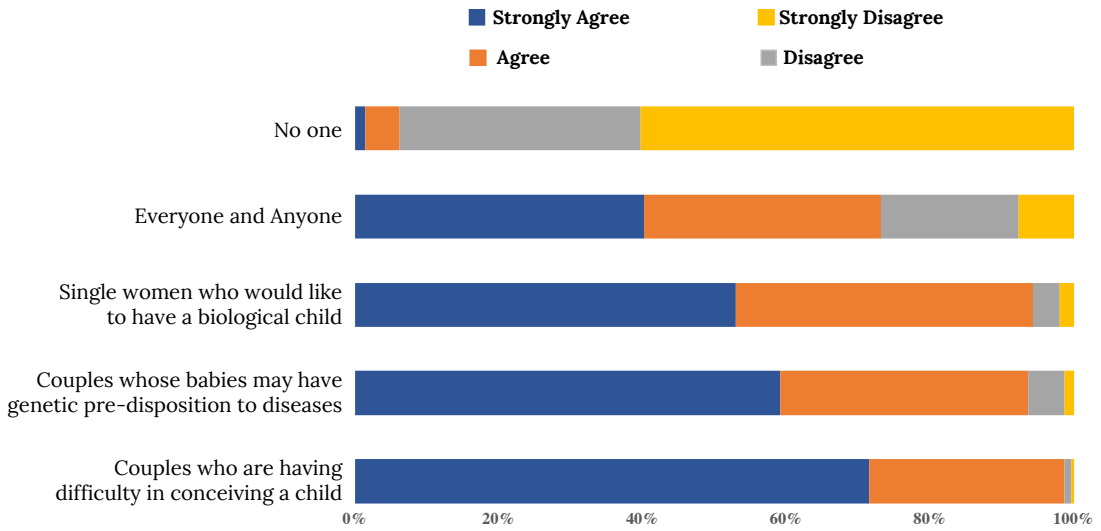

Figure 5: Acceptance of IVF is also application dependent. Bars show % respondent who strongly agreed (blue bars), agreed (orange bars), disagreed (grey bars) or strongly disagreed (yellow bars) to the use of IVF under corresponding situations. Absolute numbers can be found in Appendix 1.3

This is an important parameter, because current techniques that can potentially be used for gene editing embryos, will require IVF to be performed. These data

suggest that respondents find selection of healthier embryos as an acceptable use of medical technology.

However, since we did not find any disparity between respondents on the use of IVF, we could not assess whether views on IVF could be correlated with views on gene editing.

People perceive inequality as the most likely negative impact of gene editing technologies

When asked “How likely, if at all, do you think each of the following would occur if gene editing to change a baby’s genetic characteristics becomes widely available?”, a majority of respondents (73.08%) said that inequality would increase because gene editing would be available only for the wealthy (Figure 6 and Appendix 1.4).

The second most perceived risk was the application of gene editing for morally unacceptable purposes and the third most perceived risk for premature use of the technology.

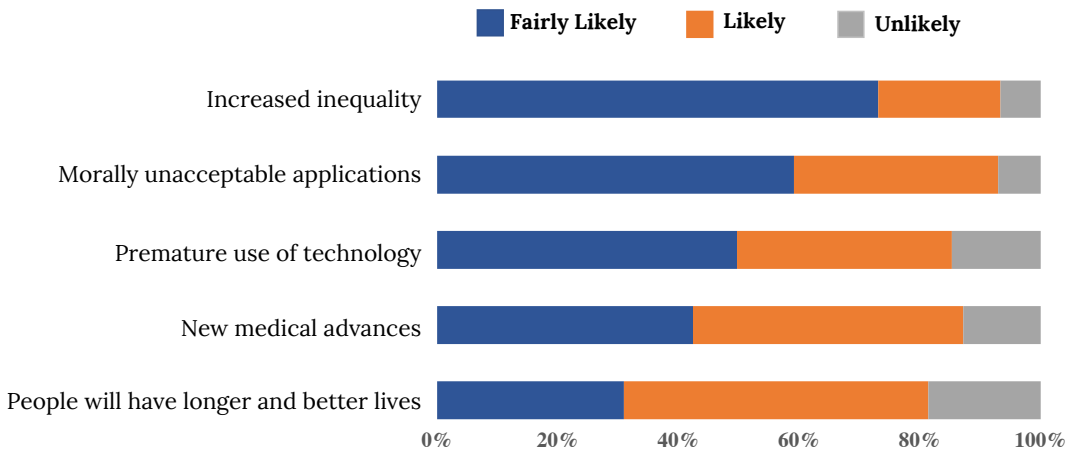

Figure 6: People anticipate risks of gene editing as more likely than benefits. Bars show whether respondents viewed corresponding outcome of gene editing technology as fairly likely (blue bars), likely (orange bars) and unlikely (grey bars).

Overall respondents anticipated risks of introducing gene editing technologies over benefits. While this does not appear to impact respondents' acceptance of gene editing applications as demonstrated in Figure 1, further education on the benefits of gene editing may help people make informed decisions.

5. Conclusion and Recommendations

The preliminary analyses of a dataset of 372 surveyed Indians suggests that Indians are acceptable of certain applications of heritable gene editing. Thus, any governance of gene editing in India should allow research and development of these applications. The results suggest that those with previous knowledge of gene editing are more accepting of its applications. Therefore, increased awareness of these applications through government programmes or inclusion within educational programmes would help increase adoption of gene editing when the technology is ready. Further, IVF, which may be essential to germline gene editing, also seems to be acceptable to a majority of respondents. Religious respondents were less likely to approve of gene editing applications; hence, co-opting religious leaders to explain the utility of these technologies may help increase their acceptability. Finally, inequality to access appears to be the biggest fear of respondents. Most new medical technologies are expensive at the onset, and prices eventually become affordable. Governmental policies could subsidise gene editing applications for certain key applications that are relevant to public health. More importantly, investment in research leading to indigenous development of applications would reduce dependence on expensive foreign gene editing therapies. Thus, the government should focus on investing more on germline gene editing research and co-development of awareness programmes to increase adoption of these applications once they become available.

6. Future Work

These analyses are based on a small cohort of 371 respondents. Expansion of this survey to 10,000 or more respondents would yield better insights into Indian views on germline gene editing. Further, understanding these views based on socio-economic factors may also yield factors that could be addressed through policy.

Further work needs to be done to understand people's views on cosmetic use of gene editing, such as skin tone. While skin tone remains a controversial topic, it can be used to cause mental harassment in an Indian context. In such cases, the question on whether skin change could provide therapeutic benefits for mental health remains to be addressed. Therapeutic benefits of treating physical diseases with well-understood genetic origins are a low-hanging fruit of gene editing applications. But these therapies may also provide a new lens to understand and alleviate issues related to mental health.

7. Appendix

Appendix 1.1

–	AN APPROPRIATE USE OF MEDICAL TECHNOLOGY –	TAKING MEDICAL TECHNOLOGY TOO FAR –	HAVEN'T THOUGHT ABOUT IT –	TOTAL –
Changing a baby's genetic characteristics to make the baby more intelligent	17.57% n=55	72.52% n=227	9.90% n=31	313
Changing a baby's genetic characteristics to lighten the baby's skin tone	6.89% n=21	85.57% n=261	7.54% n=23	305
Changing a baby's genetic characteristics to TREAT a serious disease or condition the baby would have at birth	91.67% n=286	3.53% n=11	4.81% n=15	312
Changing a baby's genetic characteristics to REDUCE THE RISK of a serious disease or condition that could occur over the course of his or her lifetime	79.49% n=248	10.26% n=32	10.26% n=32	312

Appendix 1.1 Table showing the breakdown of respondent data for each gene editing application.

Appendix 1.2

–	AN APPROPRIATE USE OF MEDICAL TECHNOLOGY –	TAKING MEDICAL TECHNOLOGY TOO FAR –	HAVEN'T THOUGHT ABOUT IT –	TOTAL –
– Aborting a foetus before 24 weeks of gestation on medical grounds (potential harm to baby or mother)	91.15% n=278	2.30% n=7	6.56% n=20	305
– Aborting a foetus after 24 weeks of gestation on medical grounds (potential harm to baby or mother)	75.08% n=226	10.96% n=33	13.95% n=42	301
– Aborting a foetus before 24 weeks of gestation for non-medical reasons	64.00% n=192	16.67% n=50	19.33% n=58	300
– Aborting a foetus after 24 weeks of gestation for non-medical reasons	41.67% n=125	32.67% n=98	25.67% n=77	300

Appendix 1.2 Table showing views of respondents per various conditions for abortion

Appendix 1.3

–	STRONGLY AGREE –	AGREE –	DISAGREE –	STRONGLY DISAGREE –	TOTAL –
– Everyone and Anyone	40.27% n=120	32.89% n=98	19.13% n=57	7.72% n=23	298
– Single women who would like to have a biological child	53.02% n=158	41.28% n=123	3.69% n=11	2.01% n=6	298
– Couples who are having difficulty in conceiving a child	71.57% n=214	27.09% n=81	1.00% n=3	0.33% n=1	299
– Couples whose babies may have genetic pre-disposition to diseases	59.20% n=177	34.45% n=103	5.02% n=15	1.34% n=4	299
– No one	1.46% n=4	4.74% n=13	33.58% n=92	60.22% n=165	274

Appendix 1.3 Table showing views of respondents per various conditions for IVF

Appendix 1.4

–	VERY LIKELY–	FAIRLY LIKELY–	NOT TOO LIKELY–	TOTAL–
Even if gene editing is used appropriately in some cases, others will use these techniques in ways that are morally unacceptable	59.11% 185	33.87% 106	7.03% 22	313
These techniques will help people live longer and better quality lives	30.87% 96	50.48% 157	18.65% 58	311
We will use these techniques before we fully understand how they affect people's health	49.68% 155	35.58% 111	14.74% 46	312
Inequality will increase because this option will be available only for the wealthy	73.08% 228	20.19% 63	6.73% 21	312
Development of these techniques will pave the way for new medical advances that benefit society as a whole	42.31% 132	44.87% 140	12.82% 40	312

Appendix 1.4 Table showing views of respondents for various risks and benefits of using germline gene editing.

[i] Doudna, J.A. The promise and challenge of therapeutic genome editing. Nature. 2020 February ; 578(7794): 229–236. doi:10.1038/s41586-020-1978-5.

ii Botkin, J.R. The case for banning heritable genome editing. Genet Med 22, 487–489 (2020). https://doi.org/10.1038/s41436-019-0696-6

iii Brokowski, C. Do CRISPR Germline Ethics Statements Cut it? The CRISPR Journal. 2018 DOI: 10.1089/crispr.2017.0024

iv Dewey I and Reintjes C. A Bioethical Analysis of Gene Editing. Sciential. 2020 March

v National Guidelines for Gene Therapy Product Development and Clinical Trials 2019.

vi National Guidelines For Stem Cell Research 2017.

vii https://www.pewresearch.org/science/2018/07/26/public-views-of-gene-editing-for-babies-depend-on-how-it-would-be-used/

viii McCaughey T., et al A Global Social Media Survey of Attitudes to Human Genome Editing. Cell Stem Cell. 2016 18(5) 569-572. https://doi.org/10.1016/j.stem.2016.04.011

ix Scheufele A.D., et al U.S. attitudes on human genome editing. Science. 2017 357(6351), 553-554/ https://www.science.org/doi/10.1126/science.aan3708

x Uchiyama, M., Nagai, A. & Muto, K. Survey on the perception of germline genome editing among the general public in Japan. J Hum Genet 63, 745–748 (2018). https://doi.org/10.1038/s10038-018-0430-2

xi Critchley C., et al Predicting Public Attitudes Toward Gene Editing of Germlines: The Impact of Moral and Hereditary Concern in Human and Animal Applications. Frontiers in Genetics. 2018 9 DOI=10.3389/fgene.2018.00704

xii Delhove J, Osenk I, Prichard I, Donnelley M. Public acceptability of gene therapy and gene editing for human use: a systematic review. Hum Gene Ther. 2020;31:20–46. doi: 10.1089/hum.2019.19719