



PERSPECTIVE

Vulnerability and the Ethics of Human Germline Genome Editing

Markus K. Labude,¹ Vicki Xafis,¹ Poh San Lai,² and Catherine Mills^{3,*}

Abstract

The concept of vulnerability has played an important role in theoretical bioethics as well as in numerous authoritative guidelines on research ethics. The concept helps to identify situations in which research participants and other individuals may be at a heightened risk of experiencing harm. However, existing guidance documents on the ethics of human germline gene editing largely fail to make any reference to considerations of vulnerability. In this article, we discuss this oversight and we highlight the role that vulnerability can play in ethical debates about human heritable genome editing. Future guidance documents on germline gene editing should pay attention to considerations of vulnerability and reference these appropriately.

Introduction

The concept of vulnerability has been important in theoretical bioethics as well as in numerous guidelines on the ethical conduct of medical research, sometimes in connection to exploitation and gender equality.^{1–7} To be vulnerable means, on a very first and rough attempt, to be at an increased risk of harm. Viewed in this very abstract way, human heritable genome editing (HHGE) may not pose novel problems for vulnerability. However, the concept has not yet been explicitly discussed in the context of the ethics of HHGE.

This omission is particularly surprising given that the first—and to date only—instance of HHGE in practice, the 2018 live births of the gene-edited twins Lulu and Nana, was the result of a medical experiment that was marked by the failure to take into account considerations of vulnerability.⁸ In that experiment, the now-defamed scientist He Jiankui recruited 200 participants, consisting of couples who wanted to have biologically related children but in which the prospective father was HIV-positive. These couples would generally be considered to come from a vulnerable group because they were at greater risk of exploitation.

“Exploitation” here should be understood as one party taking unfair advantage of another party to primarily benefit the first party’s own goals and where the second party

lacks reasonable alternatives.⁹ He recruited participants who lacked alternatives, as viewed against the backdrop of China’s traditionally restrictive *in vitro* fertilization (IVF) policy for HIV-positive parents.¹⁰ Indeed, recruits may have been under the impression that participation in this trial was *necessary* for them to access fertility treatment and, therefore, provided the *only* realistic option for them to have biologically related progeny while avoiding HIV transmission.¹¹ Overseas travel would have been a mere theoretical option, as such travel and medical treatment tends to be prohibitively expensive for many individuals in China.^{10,12}

Taking He Jiankui’s controversial experiment as a point of departure, this article draws attention to several facets of the concept of vulnerability and its implications for the ethics of HHGE, going beyond the specific ways in which vulnerability played a role in He’s trial. The first section discusses the concept of vulnerability and its role in biomedical research ethics. After this, we outline various ways in which the concept is relevant to the ethics of HHGE. We conclude that there ought to be more attention paid to the concept of vulnerability in debates about the ethics of HHGE, since it alerts us to concerns about moral harms such as exploitation and discrimination that are otherwise downplayed in current debates.

¹SHAPES Initiative, Centre for Biomedical Ethics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; ²Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; and ³Monash Bioethics Centre, Faculty of Arts, Monash University, Clayton, Australia.

*Address correspondence to: Catherine Mills, PhD, Monash Bioethics Centre, Faculty of Arts, Monash University, SOPHIS, 20 Chancellors Walk, Monash University, Clayton 3800, Australia, E-mail: catherine.mills@monash.edu

© Markus K. Labude, et al. 2022; Published by Mary Ann Liebert, Inc. This Open Access article is distributed under the terms of the Creative Commons Attribution Noncommercial License [CC-BY-NC] (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and the source are cited.

As a final preliminary remark, it should be noted that recent reports and advisory statements on the application of HHGE have focused on apparently more pressing concerns: these tend to emphasize that the science is not ready yet¹³ or that the alteration of the human germline requires more public dialogue and involvement.¹⁴ However, the existence of these well-discussed issues should not be a deterrent for discussions about the relevance of other important concepts, such as that of vulnerability. Moreover, public dialogue must be informed by relevant bioethical concepts. Vulnerability is one of them.

The Concept of Vulnerability

The concept of vulnerability encompasses two broad dimensions.^{15,16} First, it identifies a universal or inherent vulnerability that affects everyone by virtue of the fact that humans are embodied beings. This embodiment, or corporeality, means that we are susceptible to ill-health, disease, injury, and death. In addition, the fact that we necessarily exist in social relationships means that we are vulnerable to the actions of others, perhaps especially to those on whom we depend for care, support, and companionship.^{15,17} Second, vulnerability may refer to a positional or situational vulnerability, where a person's social, political, or economic positioning makes them acutely or especially susceptible to harms and setbacks, including not only morbidity and mortality but also moral wrongs and harms such as exploitation.¹⁸

These two dimensions of vulnerability intermix in various ways, a point often made especially clear in the contexts of health care and biomedical research, where situational characteristics may heighten the susceptibility to corporeal or moral injury, that is, the emotional, psychological, and spiritual turmoil experienced as a result of acts of commission or omission that conflict with core values and moral principles. The case of HHGE is no different in this regard from other instances of invoking vulnerability in health care and biomedical research.

Reference to Vulnerability in Biomedical Research Guidelines

Since it was first invoked in the 1979 Belmont Report,¹ the concept of vulnerability has been integrated into numerous guidelines on the ethical conduct of health care and biomedical research.¹⁹ We can find reference to it, for instance, in the Declaration of Helsinki,² the CIOMS International Ethical Guidelines for Health-related Research Involving Humans,³ the UNESCO Universal Declaration on Bioethics and Human Rights,⁶ the U.S. Code of Federal Regulations (“Common Rule”),⁷ Australia's National Statement,⁵ and Canada's Tri-Council Policy Statement.⁴

These guidelines typically identify groups of people considered to be vulnerable because of situational features that lead to heightened risks of harms, including moral injuries that undermine agency, autonomy, and dignity. Groups that are often mentioned as (situationally) vulnerable include children, pregnant and lactating women, people living in poverty, people with disabilities, prisoners, indigenous or First Nation persons, and the elderly.¹¹

The practical purpose of including vulnerability in these guidelines is to remind the research community to pay particular attention to the needs and interests of groups and individuals that may be at greater risk of harm (including the risk of exploitation). It triggers extra ethical scrutiny by those who are tasked with reviewing research protocols; and it requires researchers to give stronger than usual justification for selecting participants from groups deemed to be vulnerable. It also helps to ensure that vulnerable populations are included only where appropriate, with suitable protections in place to ensure that they also benefit from biomedical research. This may require adequate benefit sharing arrangements, which, in research, could include nonmonetary returns for persons whose genetic material is used.

Even so, the concept has not been without its critics. Some have pointed out that the designation of vulnerable may be an overly crude way of classifying individuals or groups.^{20–22} It may also reinforce deeply ingrained prejudices that place certain people in social categories, often with an underlying assumption that there is something wrong with them.^{23,24} Individuals who are considered vulnerable are further burdened by an epithet that is sometimes seen to describe circumstances that arise from and are part of a group affiliation.²²

Once the label is applied, it leaves little room for a nuanced consideration of personal or group circumstances, cannot easily be escaped, and can have injurious effects for those to whom it is applied.²¹ Describing individuals as vulnerable can, therefore, have a resonance of blaming them for their circumstances, asking them to pull themselves up, or do something themselves to improve their positioning in life. For the purpose of this article, we acknowledge these concerns, the limitations of the concept of vulnerability, as well as the ways in which it may be misused.

Importantly, none of these guidelines advocate for the outright exclusion of vulnerable individuals from participation in biomedical research. Instead, reference to vulnerability draws greater attention to susceptibility for harm or reduced ability to protect oneself from incurring such harm.

Vulnerability in HHGE

Although vulnerability has a significant role in general research ethics guidelines, its place in discussions of the ethical permissibility of (research involving) alteration to the human germline has been considerably smaller. A helpful collection of 61 ethics reports and statements on HHGE²⁵ suggests that only four make reference to vulnerability. Three of them (The Australian Council of Learned Academies' Report on *The Future of Precision Medicine in Australia*, the National Academies' Report on *Human Genome Editing: Science, Ethics, and Governance*, and a Report by the Public and Professional Policy Committee of the European Society of Human Genetics) address specifically the care that must be taken when vulnerable individuals are recruited for genetic research.

They do not, however, address some of the more specific issues of vulnerability that arise in research involving genetic modification, generally, or HHGE, specifically. More recently published guidance documents, such as a Report by the National Academy of Sciences and the National Academy of Medicine,¹³ and a Position Paper by the World Health Organization (WHO),²⁶ likewise fail to acknowledge the role that the concept of vulnerability can play in the debate.

In the narrow frame of HHGE research, such as He's experiment, three groups of individuals stand out as being especially (situationally) vulnerable: the prospective parents, women who participate in such research, and the future children. First, prospective parents might be particularly vulnerable because participation in such experiments could be the only realistic way of achieving biological progeny. In He Jiankui's experiment, this was the case because of the (perceived) lack of IVF treatment for HIV-positive individuals.

However, we can imagine such situations in other contexts as well, such as when prospective parents are carriers of a genetic disease, seek IVF, but then generate only embryos that carry a disposition for developing a potentially lethal disease (e.g., Cystic Fibrosis or Huntington's disease). They can be viewed as "desperate" patients perhaps resembling the participants in He's experiment.^{27–29} Their desire for "healthy" genetically related offspring makes them especially dependent on the researchers who, in turn, would stand to gain from the success of any such research. We acknowledge the blurring in research participants' perceptions (and perhaps, more worryingly, also in researchers' perceptions) of the aims of research and the aims of medicine but will not focus on it further in this article.

Some might argue that the use of HHGE does not differ from the general use of IVF, since even the use of IVF

(without HHGE) may sometimes be the only realistic option for individuals to have a "healthy" genetically related child. This, it might be argued, places prospective users of IVF in a similar situation of desperation and renders them vulnerable to exploitation. According to this analogy-based argument, we should then not object to HHGE on grounds of vulnerability, since we also do not object to IVF on grounds of vulnerability.

However, this argument fails to appreciate some relevant differences between HHGE and IVF. What generates vulnerability in the case of HHGE is, in part, that it is in the early stages of research, with clinical researchers having much to gain from its development. IVF, in comparison, is tried and tested. It has become part of clinical practice and is governed by clinical practice guidelines. Hence, it is less likely that professional gain associated with scientific firsts would prompt the exploitation of IVF patients and create a situation of vulnerability. A comparison of HHGE and IVF would perhaps gain traction if IVF were also a technique in its early development; and here it is, indeed, worth consulting the bioethical debate on early IVF research and the ethical issues it gave rise to.³⁰

It may also be suggested that HHGE does not exemplify an instance of the parents' vulnerability but, on the contrary, that the parents' autonomy is enhanced or better respected by offering the intervention. In He's experiment this was, of course, not the case because the intervention was characterized by gross deception, with prospective parents having been told they would participate in a vaccine trial.³¹ In addition, He's experiment was marked by a disregard for the health, well-being, and safety of the resulting children and parents' wishes, desires, expectations, and interests. However, abstracting away from the specifics of He's experiment, it is difficult to defend the notion of "enhanced parental autonomy" when the science is premature and its application is potentially unsafe.

On the contrary, it is such circumstances that highlight the advantages gained by the researcher, particularly in an environment where HHGE is perceived as a science race. The promise of scientific fame and immense grant-funding in a multibillion-dollar industry is a huge reward for scientists developing this technology.³²

Moreover, even if parental autonomy is enhanced by offering an intervention such as HHGE, that does not render vulnerability irrelevant. Autonomy and vulnerability are not conceptually opposed. We can see this clearly in the debate about the permissibility of kidney sales, for example. Even if it were true, as some argue, that permitting individuals to sell their kidneys in a well-regulated market enhances their autonomy,^{33,34} this is compatible with the view that such an arrangement also increases vulnerability (to exploitation, illness, etc.).

The second group of vulnerable individuals are the women who will gestate the fetus. Women are central to the process of reproductive innovation, both in terms of supplying biological materials, such as oocytes, and insofar as their participation in experimentation is essential. So long as we require pregnancy for the full reproductive realization of HHGE, the burden of innovation is going to fall on women. The necessary involvement of women in this type of research stands in contrast to the fact that pregnant women have often been excluded from clinical trials because of a perception of their vulnerability.^{35,36} The burdens of HHGE may disproportionately fall on women in other ways too that go beyond any immediate bodily intervention to include burdens of caregiving.

This will be particularly true in societies where the burdens of informal care continue to be distributed unevenly in families, with women disproportionately providing care, including for children with disabilities.^{37,38} In such cases, we may conjecture that if HHGE has unintended effects that ultimately cause disability, the burden of care for that offspring is likely to fall on women.^{39–41}

Our point here then is clearly not that women in general should be categorized as vulnerable. Moreover, science and medical intervention by themselves cannot be expected to remedy these burdens, as mitigating or eliminating them requires larger shifts in social structures and practices. Rather, the point is that the bioethical literature and guidelines, as well as the societal debate on the ethics of HHGE need to recognize how these additional burdens in reproduction and family may give rise to particular forms of situational vulnerability, often related to cultural factors.

The third group consists of prospective children themselves. Children are often seen as quintessentially vulnerable—they are highly susceptible to and often unable to defend themselves against physical harms as well as moral harms such as exploitation.⁴² In the context of HHGE this is even more pronounced because decisions that are made about these children will carry beyond just one generation of children.

This would seem to suggest that vulnerability may be a useful lens through which to explore the potential moral harms for future children who come about as a result of HHGE. At the same time, if HHGE proves safe and effective, it is also children created through HHGE that stand to gain the most, along with their offspring. Hence, questions about vulnerability would have to be weighed up alongside recognition of the potential benefits.

Vulnerability from a Wider Perspective

The aforementioned discussion suggests that vulnerability should play a role in deliberations about HHGE insofar as vulnerable individuals are themselves to be

recruited or involved in the research. There are, however, other dimensions of vulnerability that arise beyond the immediate experimental context.

A first concern is that use of this technology, without appropriate safeguards, has the potential to contribute to greater vulnerability of individuals with disabilities. HHGE may increase already marginalized groups' vulnerabilities, in a way similar to concerns that established prenatal screening technologies lead to the marginalization of individuals with disabilities.^{43–46}

The Nuffield Council's Report on Genome Editing and Human Reproduction cautions that HHGE may contribute to greater social marginalization of and discrimination against people living with disabilities.^{43,45,47} One way in which this can come about is that a technology to prevent a disease or disability can turn certain genetic conditions into "conditions that have been chosen" and, consequently, making it a "lifestyle choice" or an instance of what philosophers have come to call "expensive tastes"⁴⁸ of the parents themselves.

Furthermore, concerns have been raised that reducing the number of individuals with a particular genetic condition could reduce the societal will to provide consideration in policy planning.^{47,49,50} It has, for instance, been argued that the wide availability of prenatal screening options has reduced the incidence of Down syndrome⁵¹ with news reports indicating that this condition could be at the brink of being eliminated.^{52,53} This itself may lead to an increase in situational vulnerability.

However, there are insufficient data to prove that such screenings also erode respect for individuals with Down syndrome. Countries such as Iceland or Denmark where prenatal screenings are widely and freely accessible have also stipulated in government statements that the availability of this technology should exist in an environment where disabled individuals continue to be valued and respected as part of human diversity.⁵⁴ Such statements express a commitment to implementing safeguards.

Moreover, the case of screening for Down Syndrome may not be easily transferable to that of HHGE. One reason is that there will likely be disparate access to HHGE in many countries, which would limit the number of prospective parents with access to these technologies. Although limited access points to another dimension of vulnerability (addressed hereunder), the point is that the limited use of HHGE may (at least in the short term) prevent society-wide marginalization of individuals with disabilities resulting from the use of this technology.

Another consideration is that the number of prospective parents for whom HHGE is the only available path to having genetically related children is relatively

small.⁵⁵ A restrictive policy that limits the use of HHGE to only rare cases could address concerns about a general marginalization of individuals with disabilities.

A second concern related to vulnerability from a wider perspective relates to the allocation of research funding. From a global perspective, the benefits of HHGE are not likely to reach populations or groups of people who are most situationally vulnerable. For example, HHGE is unlikely to bring significant benefits to the poorest populations of the world because it would remain prohibitively costly and would not address their urgent health priorities. It might be objected that although most medical innovations (new therapies or medicines) are initially expensive, they tend to become cheaper over time. Moreover, HHGE itself is a comparatively easy and inexpensive procedure.

However, HHGE requires IVF, which will remain an essentially labor-intensive clinical procedure. This makes cost reduction to the point of widespread accessibility unlikely now or in the near future.^{56,57} This concern is in line with a recent WHO Report, which draws attention to the centrality of values such as fairness, social justice, equal moral worth, and global health justice in decision-making.²⁶

Conclusion

The concept of vulnerability helps to highlight important ethical concerns in biomedical and clinical research on HHGE. In particular, it highlights concerns around exploitation, discrimination, and the potential for increasing situational vulnerability for some groups.

To be sure, none of the vulnerability concerns raised in this article should be taken as decisive arguments against the use of HHGE. Indeed, in some instances, we have indicated how concerns about vulnerability could be addressed: for instance, worries about increased discrimination of individuals with disabilities could be addressed with explicit policy commitments. Moreover, a policy of thoroughly reviewing and monitoring the ethical conduct of research would be able to address many of the issues that were raised in He's experiment. Nonetheless, we believe that current discussions of the ethics of HHGE would do well to focus more attention on vulnerability and related concerns.

Acknowledgments

This study is part of the SHAPES Gene Modifying Technologies (GMT) Project, which is one of the projects approved under the SHAPES Initiative. The GMT Working Group was chaired by Prof. Ruth Chadwick and Assoc. Prof. Poh San Lai. We are most grateful to the following members of the broader SHAPES Gene Modifying Technologies Working Group: Ruth Chadwick, Soren Holm, Terry Kaan, Benjamin Capps, Simona

Giordano, Roger Foo, G. Owen Schaefer, Citra Nurfarah binte Zaini Mattar, and Hallam Stevens. We also warmly thank Capucine Barcellona for her comments and assistance.

Authors' Contributions

M.K.L., V.X., and C.M. conceptualized the article. M.K.L. drafted an initial version of the article. All authors contributed to subsequent revisions of the article and the arguments.

Author Disclosure Statement

No competing financial interests exist.

Funding Information

This study was supported by the Singapore Ministry of Health's National Medical Research Council under its NMRC Funding Initiative grant (NMRC/CBME/2016). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the article.

References

1. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Bethesda, MD: U.S. Department of Health and Human Services. 1979. <https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html>
2. World Medical Association. Declaration of Helsinki: Ethical principles for medical research involving human subjects. *JAMA*. 2013;310:2191–2194. DOI: 10.1001/jama.2013.281053.
3. CIOMS. International ethical guidelines for health-related research involving humans. Geneva. 2016. <https://cioms.ch/wp-content/uploads/2017/01/WEB-CIOMSEthicalGuidelines.pdf>
4. Canadian Institutes of Health Research Natural Sciences and Engineering Research Council of Canada, Council S5aHR. Tri-council policy statement: Ethical conduct for research involving humans. 2018. <https://ethics.gc.ca/eng/documents/tcps2-2018-en-interactive-final.pdf>
5. National Health and Medical Research Council. National Statement on Ethical Conduct in Human Research. 2018. <https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018> (last accessed April 28, 2022).
6. UNESCO. Universal declaration on bioethics and human rights. Paris, France. 2005. <https://unesdoc.unesco.org/ark:/48223/pf0000146180> (last accessed April 28, 2022).
7. Code of Federal Regulations. 2009. Title 45 Public Welfare Part 46 Protection of Human Subjects. <https://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/ohrpregulations.pdf> (last accessed April 28, 2022).
8. Sample I. Chinese scientist who edited babies' genes jailed for three years. *The Guardian*. 2019. <https://www.theguardian.com/world/2019/dec/30/gene-editing-chinese-scientist-hejiankui-jailed-three-years>
9. Resnik DB. Exploitation in biomedical research. *Theor Med Bioeth*. 2003;24:233–259. DOI: 10.1023/a:1024811830049.
10. Zhang H. Chinese 'gene-editing' scientist raises eyebrows by promoting sperm washing for HIV-positive couples. *Global Times*. 2018. <https://www.globaltimes.cn/page/201812/1132670.shtml> (last accessed April 28, 2022).
11. Kipnis K. Vulnerability in research subjects: A bioethical taxonomy. In: *Ethical and Policy Issues in Research Involving Human Participants*.

- (National Bioethics Advisory Commission; ed). Rockville, MD: Volume II: Commissioned Papers. 2001; pp. G1–G13.
12. Rana P. How a Chinese scientist broke the rules to create the first gene-edited babies; Dr. He Jiankui, seeking glory for his nation and justice for HIV-positive parents, kept his experiment secret, ignored peers' warnings and faked a test. *Wall Street J (Online)*. 2019. <https://www.wsj.com/articles/how-a-chinese-scientist-broke-the-rules-to-create-the-first-gene-edited-babies-11557506697> (last accessed April 28, 2022).
 13. National Academy of Medicine, National Academy of Sciences. Heritable human genome editing. Washington, DC: The National Academies Press. 2020.
 14. Baylis F. Human germline genome editing and broad societal consensus. *Nat Hum Behav*. 2017;1:0103. DOI: 10.1038/s41562-017-0103.
 15. Rogers W, Mackenzie C, Dodds S. Why bioethics needs a concept of vulnerability. *Int J Feminist Approaches Bioethics*. 2012;5:11–38. DOI: 10.2979/intjfemappbio.5.2.11.
 16. O'Neill O. Towards justice and virtue. Cambridge: Cambridge University Press. 1996.
 17. Butler J. Precarious life—The powers of mourning and violence. London, United Kingdom: Verso. 2008.
 18. Hurst SA. Vulnerability in research and health care; describing the elephant in the room? *Bioethics*. 2008;22:191–202. DOI: 10.1111/j.467–8519.2008.00631.x.
 19. Bracken-Roche D, Bell E, Macdonald ME, et al. The concept of 'vulnerability' in research ethics: An in-depth analysis of policies and guidelines. *Health Res Policy Syst*. 2017;15:8. DOI: 10.1186/s12961-016-0164-6.
 20. Luna F. Elucidating the concept of vulnerability: layers not labels. *Int J Feminist Approaches Bioethics*. 2009;2:121–139. DOI: 10.3138/ijfab.2.1.121.
 21. Luna F. Identifying and evaluating layers of vulnerability—A way forward. *Dev World Bioeth*. 2019;19:86–95. DOI: 10.1111/dewb.12206.
 22. Levine C, Faden R, Grady C, et al. The limitations of "vulnerability" as a protection for human research participants. *Am J Bioeth*. 2004;4:44–49. DOI: 10.1080/15265160490497083.
 23. ten Have H. Respect for human vulnerability: The emergence of a new principle in bioethics. *J Bioeth Inq*. 2015;12:395–408. DOI: 10.1007/s11673-015-9641-9.
 24. Walker AK, Fox EL. Why marginalization, not vulnerability, can best identify people in need of special medical and nutrition care. *AMA J Ethics*. 2018;20:E941–E947. DOI: 10.1001/amajethics.2018.941.
 25. Brokowski C. Do CRISPR germline ethics statements cut it? *CRISPR J*. 2018;1:115–125. DOI: 10.1089/crispr.2017.0024.
 26. WHO Expert Advisory Committee on Developing Global Standards for Governance and Oversight of Human Genome Editing. Human genome editing: A framework for governance. Geneva: World Health Organization. 2021. <https://www.who.int/publications/i/item/9789240030060> (last accessed April 28, 2022).
 27. Patel A, Sharma PSVN, Kumar P. "In cycles of dreams, despair, and desperation:" Research perspectives on infertility specific distress in patients undergoing fertility treatments. *J Hum Reprod Sci*. 2018;11:320–328. DOI: 10.4103/jhrs.JHRS_42_18.
 28. Kirksey E. The mutant project—Inside the global race to genetically modify humans. New York: St. Martin's Press. 2020.
 29. Greely HT. CRISPR people—The science and ethics of editing humans. Cambridge, MA: MIT Press. 2021.
 30. Bender L. Feminism & bioethics: Beyond reproduction. *J Law Med Ethics*. 1997;58–61. DOI: 10.1111/j.748–720x.997.tb01397.x.
 31. Stein R. Facing backlash, Chinese scientist defends gene-editing research on babies. 2018. <https://www.npr.org/sections/health-shots/2018/11/28/671375070/facing-backlash-chinese-scientist-defends-gene-editing-research-on-babies>
 32. Jiang L, Rosemann A. Human embryo gene editing in China: The uncertain legal status of the embryo. *BioSocieties*. 2019;14:46–66. DOI: 10.1057/s41292-018-0116-1.
 33. Taylor JS. Autonomy, constraining options, and organ sales. *J Appl Philos*. 2002;19:273–285.
 34. Taylor JS. Autonomy and organ sales, revisited. *J Med Philos*. 2009;34:632–648. DOI: 10.1093/jmp/jhp044.
 35. Ballantyne A, Rogers W. Pregnancy, vulnerability, and the risk of exploitation in clinical research. In: *Clinical Research Involving Pregnant Women Research Ethics Forum*. (Baylis F, Ballantyne A; eds). Cham: Springer. 2016.
 36. Macklin R. Enrolling pregnant women in biomedical research. *Lancet*. 2010;375:632–633. DOI: 10.1016/S0140-6736(10)60257-7.
 37. Carlson JM, Miller PA. Family burden, child disability, and the adjustment of mothers caring for children with epilepsy: Role of social support and coping. *Epilepsy Behav*. 2017;68:168–173. DOI: 10.1016/j.yebeh.2017.01.013.
 38. Sharma N, Chakrabarti S, Grover S. Gender differences in caregiving among family—Caregivers of people with mental illnesses. *World J Psychiatry*. 2016;6:7–17. DOI: 0.5498/wjp.v6.i1.7.
 39. Bucher-Koenen T, Farbmacher H, Guber R, et al. Double trouble: The burden of child-rearing and working on maternal mortality. *Demography*. 2020;57:559–576. DOI: 10.1007/s13524-020-00868-6.
 40. Väänänen A, Kevin MV, Ala-Mursula L, et al. The double burden of and negative spillover between paid and domestic work: Associations with health among men and women. *Women Health*. 2005;40:1–18. DOI: 0.1300/J013v40n03_01.
 41. Brookes A. Women's voices: Prenatal diagnosis and care for the disabled. *Health Care Anal*. 2001;9:133–150. DOI: 10.1023/A:1011369917884.
 42. OECD. 2019. Changing the odds for vulnerable children: Building Opportunities and Resilience. Paris, OECD Publishing, <https://doi.org/10.1787/a2e8796c-en> (last accessed April 28, 2022).
 43. Parens E, Asch A. Prenatal testing and disability rights. Washington, DC: Georgetown University Press. 2000.
 44. Thomas GM, Rothman BK. Keeping the backdoor to eugenics ajar?: Disability and the future of prenatal screening. *AMA J Ethics*. 2016;18:406–415. DOI: 10.1001/journalofethics.2016.18.4.stas1-1604.
 45. Asch A. Disability equality and prenatal testing: contradictory or compatible? *Fla State Univ Law Rev*. 2003;30:315–342. <https://ir.law.fsu.edu/lr/vol30/iss2/7>.
 46. Burke L. Hostile environments? Down's syndrome and genetic screening in contemporary culture. *Med Humanities*. 2021;47:193–200. DOI: 10.1136/medhum-2020-0120.
 47. Nuffield Council on Bioethics. Genome Editing and Human Reproduction: Social and ethical issues. London: Nuffield Council on Bioethics. 2018. <https://www.nuffieldbioethics.org/publications/genome-editing-and-human-reproduction> (last accessed April 28, 2022).
 48. Keller S. Expensive tastes and distributive justice. *Social Theory Pract*. 2002;28:529–552. DOI: 10.5840/soctheorpract200228426.
 49. Nov-Klaiman T, Raz AE, Hashiloni-Dolev Y. Attitudes of Israeli parents of children with Down syndrome toward non-invasive prenatal screening and the scope of prenatal testing. *J Genet Couns*. 2019;28:1119–1129. DOI: 10.002/jgc4.62.
 50. Buchanan A, Brock DW, Daniels N, et al. From chance to choice: Genetics and justice. Cambridge: Cambridge University Press. 2000.
 51. de Graaf G, Buckley F, Skotko BG. Estimation of the number of people with Down syndrome in Europe. *Eur J Hum Genet*. 2021;29:402–410. DOI: 10.1038/s41431-020-00748-y.
 52. Quinones J, Lajka A. "What kind of society do you want to live in?": Inside the country where Down syndrome is disappearing. CBS News. 2017. <https://www.cbsnews.com/news/down-syndrome-iceland/>
 53. Zhang S. The last children of down syndrome—Prenatal testing is changing who gets born and who doesn't. This is just the beginning. *The Atlantic*. 2020. <https://www.theatlantic.com/magazine/archive/2020/12/the-last-children-of-downsyndrome/616928/>
 54. Government of Iceland. Facts about Down's syndrome and pre-natal screening in Iceland London. 2018. <https://www.government.is/diplomatic-missions/embassy-article/2018/03/26/Facts-about-Downs-syndrome-and-pre-natal-screening-in-Iceland/>
 55. Gyngell C, Douglas T, Savulescu J. The ethics of germline gene editing. *J Appl Philos*. 2017;34:498–513. DOI: 10.1111/japp.12249.
 56. Collins J. An international survey of the health economics of IVF and ICSI. *Hum Reprod Update*. 2002;8:265–277. DOI: 10.1093/humupd/8.3.265.
 57. Mor-Yosef S. Cost effectiveness of in vitro fertilization. *J Assist Reprod Genet*. 1995;12:524–530. DOI: 10.1007/bf02212915.

Received: April 27, 2021

Accepted: April 3, 2022

Online Publication Date: May 6, 2022

Issue Publication: June 20, 2022