



Review Article

Moral Boundaries of Germline Gene Editing: A Reappraisal After CRISPR-Based Clinical Trials

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ABSTRACT

The 2018 announcement that a researcher had edited and implanted human embryos using CRISPR-Cas9, resulting in the birth of twins with an altered germline, forced bioethics to confront heritable genome editing as an urgent rather than speculative question.

This review reappraises the moral boundaries around germline editing several years after that scandal and roughly two years after the first CRISPR-based somatic therapies reached patients through conventional regulatory approval.

It surveys the institutional aftermath of the He Jiankui affair, the major governance frameworks issued since, from the National Academies and Royal Society, the World Health Organization, and the Nuffield Council on Bioethics, and the underlying disagreement in the literature over whether the objection to heritable editing is fundamentally about safety or about something safety data cannot resolve.

It then contrasts this unsettled germline debate with the comparatively rapid and successful translation of somatic gene-editing therapy for sickle cell disease, which raises its own distinct questions about global access and honest description of benefit rather than intergenerational consent.

We conclude that governance instruments issued since 2018 have converged on shared procedural safeguards without resolving the deeper normative disagreement about whether heritable editing should ever be permitted, leaving that question for future clinical and regulatory decisions to confront directly.

Keywords: germline gene editing; CRISPR; genome editing governance; reproductive ethics; bioethics

Citation: Radcliffe W, Greco M and Silva K (2023) Moral Boundaries of Germline Gene Editing: A Reappraisal After CRISPR-Based Clinical Trials. *Bioethics*. 1(1):01-05.

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Article History: Received 27 December 2022 | Accepted 20 March 2023 | Published 25 June 2023

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INTRODUCTION

Late in 2018, a Chinese researcher announced that he

had edited the genomes of two embryos using CRISPR-Cas9 and implanted them, resulting in the birth of twin girls whose germline had been

permanently altered before anyone could assess whether the edit was safe, whether it did what it was supposed to do, or whether the parents fully understood what they had consented to [1]. The scientific community's reaction was close to unanimous condemnation, and the affair remains the only confirmed instance of heritable human genome editing performed outside a regulated clinical framework [2]. What makes the episode worth revisiting several years on is not the shock value, which has faded, but what came after: a wave of somatic gene-editing therapies has since reached actual patients through conventional regulatory pathways, forcing bioethicists to draw a line between somatic and germline editing with more precision than the field previously required.

That line matters because the two forms of editing are technically related but ethically distinct in almost every respect that bears on permissibility. A somatic edit changes the genome of a treated patient and dies with that patient; a germline edit is transmitted to every subsequent generation, none of whom will have had any opportunity to consent to the intervention performed on their ancestor's embryo [3]. This review reappraises where the moral boundaries around germline editing now sit, five years after the scandal that first tested them and roughly two years after the first CRISPR-based somatic therapies received regulatory approval, changing the landscape those boundaries have to operate in. Even proponents of eventually permitting therapeutic germline editing for serious monogenic disease have acknowledged that any future clinical trial would face ethical demands, on consent, on long-term follow-up across generations, on defining which conditions justify the intervention, that ordinary somatic trials simply do not encounter [4].

THE HE JIANKUI AFFAIR AND ITS INSTITUTIONAL AFTERSHOCKS

The immediate scientific response to the 2018 announcement was procedural: an international summit condemned the experiment as irresponsible, the researcher was investigated, fined, and briefly imprisoned, and the hospital and university associated with the work moved quickly to distance themselves from it [5]. The deeper and more consequential response was regulatory. Chinese authorities, embarrassed by an episode that had drawn global scrutiny to gaps in their own oversight system, used the affair to justify a substantial tightening of the legal framework governing human genetic research, including new criminal liability provisions that did not previously exist [6].

What is less often discussed is how quickly, and how quietly, related research resumed. Commentators have described a "double-pacing problem" in which formal governance instruments move slowly and deliberately while the underlying science, embryo-editing techniques, preimplantation genetic tools, and

reproductive technology more broadly, continues to advance largely unconstrained by that governance, creating recurring windows in which a determined actor could plausibly repeat something close to the 2018 experiment [7]. This asymmetry between the speed of technical progress and the speed of institutional response is, on this reading, the structural condition that made the He Jiankui affair possible in the first place, and it has not been resolved simply by punishing the individual responsible.

BUILDING INTERNATIONAL GOVERNANCE AFTER THE SCANDAL

The most substantial institutional response came from two parallel efforts. The U.S. National Academies of Sciences, Engineering, and Medicine, together with the U.K.'s Royal Society, convened an international commission that in 2020 concluded heritable human genome editing should not proceed at present for any application, and set out a detailed translational pathway, covering preclinical evidence standards, oversight mechanisms, and long-term follow-up, that would need to be satisfied before any country could responsibly consider a clinical use [8]. The World Health Organization followed with its own governance framework, emphasizing registries, transparency, and a mechanism for whistleblowers to report noncompliant research, explicitly designed to close the kind of oversight gap that allowed the 2018 experiment to occur outside institutional view [9]. A companion WHO expert advisory committee statement recommended that no state currently possesses the regulatory maturity to permit heritable editing responsibly, and called for a coordinated international registry of all human genome editing research regardless of jurisdiction [10].

The Nuffield Council on Bioethics took a more permissive long-run position, arguing in a joint statement that heritable genome editing could in principle become ethically acceptable for some future applications provided it served the welfare of the resulting child and did not increase disadvantage or discrimination, a position notably less categorical than the National Academies/Royal Society commission's near-term moratorium [11]. This divergence between an outright "not yet, and not by this pathway" position and a conditional "not yet, but potentially someday" position is not merely rhetorical; it reflects a real disagreement in the literature about whether the objection to germline editing is to the technology's current immaturity or to something more fundamental about heritable modification itself [12].

Table 1 summarizes how the major governance instruments issued since the scandal compare on this question, and on how they treat the harder issue of eventual clinical translation. A comparative review of these documents notes that despite genuine convergence on process, transparent oversight, international coordination, robust preclinical evidence,

none of the major reports actually agree on the substantive question of whether heritable editing should ever be permitted, leaving that question for national regulators to answer independently of the international consensus on process [13]. More recent work canvassing scientists and governance professionals directly finds a similar split in expert opinion: near-universal agreement that current oversight is inadequate, alongside real disagreement about what an adequate system would eventually permit [14].

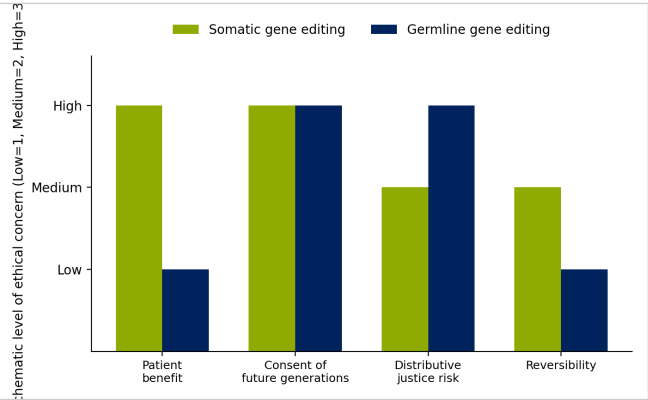
Table 1. Major governance instruments issued after the He Jiankui affair, compared on process recommendations and their substantive position on eventual clinical translation.

Instrument	Process recommendations	Position on eventual clinical use	Enforcement mechanism
NAS/Royal Society commission (2020)	Detailed translational pathway; preclinical evidence standards; long-term follow-up	Not now for any application; conditional future pathway defined but not endorsed	Advisory; relies on national regulators
WHO governance framework (2021)	International registry; whistleblower reporting mechanism; transparency	Defers to member states; focuses on process not substance	Advisory; voluntary registry participation
Nuffield Council joint statement (2018)	Welfare-of-child and non-discrimination criteria	Potentially acceptable in future for some applications if criteria met	Advisory only
China's post-scandal legal reforms	New institutional review and reporting requirements	Prohibited pending reform of oversight system	Criminal liability introduced

WHAT THE ETHICAL DEBATE IS ACTUALLY ABOUT

A recurring frustration in this literature is that "safety" has become a placeholder that lets participants in the debate avoid stating their actual disagreement. A systematic mapping of the ethical debate on heritable genome editing found that safety concerns, while real, are doing less argumentative work than they appear to: many commentators who cite safety as their objection are, on closer reading, actually objecting to something that would remain true even if the technology were made perfectly safe, namely that heritable editing removes a choice from people who do not yet exist and cannot consent to having their genome permanently altered [15]. Framing the debate as fundamentally about safety, on this account, has let the field defer harder normative questions by treating them as temporary technical problems awaiting a solution.

Figure 1. Schematic comparison of how core ethical considerations weigh for somatic versus germline gene editing (illustrative summary of themes in the literature discussed, not derived from a single empirical study or quantitative index).



One useful way historians of the debate have approached this is to ask how an intervention once treated as an obvious moral red line came to be discussed, within roughly two decades, as a plausible future clinical option pending safety data. Tracing this shift, one analysis argues that changes in how germline editing was described, from irreversible tampering with the human species to a precision medical intervention comparable to other reproductive technologies, did real argumentative work independent of any actual change in the risk profile of the underlying techniques [16]. Disability rights scholars have pushed back hardest against this reframing, arguing that heritable editing programs aimed at eliminating heritable conditions risk expressing a judgment about the value of disabled lives that the framing of "reducing suffering" does not adequately acknowledge or answer [17]. A separate strand of the literature focuses specifically on enhancement rather than disease prevention, treating the harder case, editing embryos not to avoid a disease but to confer an advantage, as the one that best exposes disagreements about justice, since access to any approved enhancement technology would almost certainly track existing patterns of wealth and privilege rather than medical need [18].

Professional medical ethics bodies have generally tried to hold two positions simultaneously: that heritable editing research should continue cautiously in the laboratory because it may eventually offer real benefit to families with severe heritable disease, and that clinical translation should remain off the table until governance, not just laboratory safety data, catches up [19]. Reactions to the National Academies/Royal Society report itself illustrate how contested even this middle position is: critics on one side argued the commission's translational pathway was too permissive in principle, effectively normalizing an eventual clinical use it claimed to be deferring, while critics on the other side argued it was needlessly restrictive given the narrow set of monogenic conditions where germline editing might actually

outperform existing alternatives like preimplantation genetic testing [20].

Figure 1 offers a schematic comparison of how the debate's core considerations, patient benefit, consent of future generations, distributive justice, and reversibility, weigh differently for somatic versus germline applications, illustrating why arguments that are largely settled for one category remain genuinely open for the other.

SOMATIC GENE EDITING AS THE FIELD'S ACTUAL FRONTIER

While the germline debate has continued largely at the level of principle, somatic gene editing has moved from bench to bedside. The 2023 regulatory approvals of CRISPR-based therapies for sickle cell disease marked the first time a genome-editing treatment reached patients through a conventional approval pathway, and the clinical and ethical literature it has generated offers an instructive contrast to the germline debate [21]. Because the edit is confined to the treated patient's own hematopoietic cells and is not transmitted to offspring, the deepest objections to germline editing, intergenerational consent and irreversible modification of the species' gene pool, simply do not apply, which is part of why these therapies proceeded to approval far faster than heritable editing ever could.

That does not mean the somatic pathway is free of ethical difficulty. Commentators addressing the African context, where sickle cell disease has its highest global burden but where the infrastructure and cost required for CRISPR-based treatment are least available, have argued that a therapy developed with international CRISPR research capacity but priced and distributed through wealthy-country health systems risks reproducing a familiar global health injustice: the population most affected by the disease is the population least likely to benefit from the treatment it inspired [22]. A related ethical critique concerns how these therapies are described to patients. Framing a gene-edited therapy for sickle cell disease as a "cure" understates the genuine uncertainty that remains about very long-term outcomes and risks overselling a treatment whose full risk-benefit profile will only be known after years of post-approval follow-up, language that matters directly for the informed consent patients are asked to give [23]. The broader lesson bioethicists have drawn from the somatic pathway's relative success is that clear, categorical distinctions between disease-treatment and enhancement, and between somatic and heritable modification, have done more to make responsible translation possible than any single safety threshold has.

WHERE THE GOVERNANCE CONSENSUS ACTUALLY STANDS NOW

Cataloguing efforts have tried to track every jurisdiction's regulatory posture on heritable editing in one place, and the resulting picture is one of

near-universal prohibition or moratorium alongside considerable variation in enforcement mechanism and legal form, criminal statute in some countries, professional self-regulation in others, and an absence of any explicit rule at all in a smaller number of jurisdictions that have simply not legislated on the question [24]. A retrospective assessment of the three major post-scandal governance reports, the National Academies/Royal Society commission, the WHO framework, and the Nuffield Council statement, concludes that their most durable effect has been procedural rather than substantive: national regulators now have a shared vocabulary and a shared set of oversight mechanisms to draw on, even though the reports themselves never resolved the underlying disagreement about whether heritable editing should eventually be permitted at all [25].

CONCLUSION

The moral boundary around germline gene editing has not moved as far as the He Jiankui affair once threatened it might, but it has not stayed static either. What has changed is less the substantive ethical consensus, which remains genuinely divided between an outright and a conditional prohibition, than the field's institutional capacity to prevent a repeat of 2018: transparent registries, international coordination mechanisms, and criminal liability in the jurisdiction where the original violation occurred. Meanwhile, the somatic gene-editing pathway has demonstrated that CRISPR-based therapy can reach real patients responsibly when the intergenerational and consent objections that make germline editing hard simply do not arise, and the justice concerns that pathway has surfaced, around global access and honest description of benefit, are arguably now the more urgent unresolved questions in the field. Any future reconsideration of germline editing's moral boundaries will have to reckon honestly with the fact that "safety" was never really the whole of the objection, and that the harder questions, about consent across generations, about the meaning of eliminating heritable conditions, and about who gets to benefit from genomic medicine at all, remain exactly where they were before the scandal that briefly made them impossible to ignore.

DECLARATIONS

Acknowledgements

The authors are grateful to colleagues at their respective bioethics centres for helpful conversations that shaped the scope and structure of this review.

Funding

This review received no external funding.

Conflict of Interest

The authors declare no conflicts of interest relevant to this work.

Author Contributions

Wolfgang Radcliffe conceived the review, drafted the sections on the He Jiankui affair and international governance, and coordinated the manuscript. Markus Greco developed the analysis of the underlying ethical debate and the somatic-germline comparison and critically revised the manuscript. Karolien Silva contributed the section on somatic gene editing and global justice and prepared the final manuscript for submission. All authors read and approved the final version.

Ethics Statement

As a literature review synthesizing previously published research and policy documents, this article did not involve new data collection from human or animal subjects and did not require institutional ethics committee approval.

Data Availability

No new data were generated or analyzed in the preparation of this review. All sources discussed are cited in the reference list and are publicly available through their respective publishers.

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