



OPEN LETTER

REVISED **Making sense of it all: Ethical reflections on the conditions surrounding the first genome-edited babies****[version 2; peer review: 2 approved]**Qi Chen¹, Yonghui Ma ¹, Markus Labude², G Owen Schaefer², Vicki Xafis ², Peter Mills ³¹Centre for Bioethics, Medical School, Xiamen University, Xiamen, 361102, China²Centre for Biomedical Ethics, National University of Singapore, Singapore, 117597, Singapore³Nuffield Council on Bioethics, London, WC1B 3JS, UK**v2** First published: 16 Sep 2020, 5:216
<https://doi.org/10.12688/wellcomeopenres.16295.1>
Latest published: 23 Jun 2021, 5:216
<https://doi.org/10.12688/wellcomeopenres.16295.2>**Abstract**

In November 2018 the birth of the first genome-edited human beings was announced by Chinese scientist, He Jiankui. The ensuing ethical controversy, institutional investigations and legal proceedings led to the revision of standards, rules and procedures at many levels. Arguably, however, these developments have not fundamentally changed the conditions or the culture that nourished He Jiankui's vaulting ambition in the first place and enabled it to find expression. In this paper we explore the clinical, regulatory and societal circumstances of the 'gene-edited baby' case, the political, cultural and economic conditions that created a radical and dangerous climate for biotechnology innovation, and the responsibilities of the international research community, many of whose members were apprised of Dr He's intentions. The aim is not to heap anathemas on the heads of implicated individuals but to draw attention to the need for different communities (researchers, authorities and domestic publics) to play a part actively in the governance of biomedical innovation and for research to be bridled by human values.

Keywords

He Jiankui, Human germline genome editing, CRISPR-Cas9, HIV, Gene editing, Twins/genetics, Research ethics, Research governance

Open Peer Review**Reviewer Status**

Invited Reviewers

1

2

version 2(revision)
23 Jun 2021

report



report

**version 1**

16 Sep 2020



report



report

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Any reports and responses or comments on the article can be found at the end of the article.

This article is included in the **GFBR: Genome editing for human benefit: ethics, engagement and governance** collection.



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Competing interests: No competing interests were disclosed.

Grant information: This work was supported by the Wellcome Trust through funding to the Global Forum on Bioethics in Research (GFBR). GFBR funding is provided by The Wellcome Trust, the Bill & Melinda Gates Foundation [OPP1151904], the National Institutes of Health and the UK Medical Research Council. Additionally, YM received funding from the President's Foundation project 2019 of Xiamen University on 'Ethical and governance considerations in human genome editing'. This work was also supported by the Singapore Ministry of Health's National Medical Research Council under its NMRC Funding Initiative grant (NMRC/CBME/2016) in relation to the involvement of OS, VX, and ML.

The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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How to cite this article: Chen Q, Ma Y, Labude M *et al.* **Making sense of it all: Ethical reflections on the conditions surrounding the first genome-edited babies [version 2; peer review: 2 approved]** Wellcome Open Research 2021, 5:216 <https://doi.org/10.12688/wellcomeopenres.16295.2>

First published: 16 Sep 2020, 5:216 <https://doi.org/10.12688/wellcomeopenres.16295.1>

REVISED Amendments from Version 1

This version responds to the helpful comments of reviewers on the initial version. In particular: the aims of the paper are clarified; material in the section on 'Clinical, regulatory and societal conditions' is clarified; legal information is added to the section on 'Political, cultural and economic conditions'; clarifications have been made to improve the balance of the section on 'silence and complicity'; editorial improvements have been made and additional references have been supplied throughout. Additionally, minor amendments have been made to the order in which the authors are listed and the acknowledgements.

Any further responses from the reviewers can be found at the end of the article

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Introduction

The facts of the case, though they were initially met with incredulity, are now more or less established: Dr He Jiankui, a biotechnology entrepreneur and researcher at the Southern University of Science and Technology in Shenzhen, China, recruited a number of couples to a project that led to the birth, in 2018, of the first babies from embryos that had their DNA deliberately modified using the genome editing tool CRISPR-Cas9¹. The objective of these procedures was not connected with the avoidance of an imminent risk to the future children but to confer to them the advantage of inherent resistance to HIV, with which the male partner of each couple was infected. These treatments, described at the Second International Summit on Human Genome Editing in Hong Kong in November 2018, caused immediate consternation among scientists and the public, provoked numerous statements of condemnation from scientific and ethical bodies, and led to a number of academic, institutional and official investigations around the world, including a court case that ended with the conviction of Dr He and two associates in December 2019 for illegally practising medicine^{2,3}.

Of the many questions that the 'gene-edited baby case' provoked, among the most perplexing must be: given the already salient and near-universal opposition to clinical translation of human heritable genome editing (HHGE), how could those involved arrive at a point where they were prepared to carry out these unprecedented procedures? Furthermore, given that Dr He shared his intentions with many scientific peers, how were they able to go through with them despite their widely acknowledged proscription under relevant legal, professional and moral norms? The present paper offers a number of reflections that are relevant to these questions, building on presentations and discussions at the annual meeting of the Global Forum on Bioethics in Research, held in Singapore in November 2019. These reflections touch on: the significance placed on patient and research participant interests and

preferences; the perceived policy vacuum in the wake of technological developments in genome editing (in particular the rapid elaboration and diffusion of CRISPR-Cas9 techniques) and the significance of public opinion in this context; the complex motivations and incentives that bear upon ambitious biotechnology entrepreneurialism in contemporary China and elsewhere; the integrity, role and responsibilities of scientists and the international scientific community; the traction of global bioethical norms and missteps in cross-cultural understanding; and wider questions for society about the role of biomedical technologies in the collective response to societal challenges, such as the prevalence of HIV and genetic disease. In reflecting on the – so far as we know – singular case of Dr He and his collaborators our interest is not forensic but normative: our aims are to begin to understand whether this case, though singular, should truly be seen as exceptional, to what extent the conditions that appear to have been conducive to Dr He's interventions may still prevail, and what needs to change in the light of the incident if we should wish to forestall a recurrence. Due to the broad range of issues considered, this paper cannot provide the in-depth analysis these issues deserve; rather it is intended as a springboard for further analyses.

Clinical, regulatory and societal conditions

Dr He originally announced the birth of genome edited twin girls on YouTube on 25 November 2018. Subsequently, at the Second International Summit on Human Genome Editing held in Hong Kong, he revealed that another woman was in the early stages of pregnancy with a genetically modified embryo. Dr He's claims not only caused shock and controversy in the scientific community and the wider society, but also prompted urgent reflection on the application and regulation of emerging technologies in China and elsewhere⁴. The actions of Dr He and his associates posed numerous ethical challenges not just to China but also to the wider world. At the same time, this event prompted the further development of ethical norms governing genome editing and stimulated public discussion. We review this event from three aspects – clinical, regulatory and societal – before proceeding to discuss its wider implications for Chinese and international research.

Clinical Research

Three important features of ethical medical research are that researchers should (1) seek the informed consent of their patients before carrying out procedures, (2) fulfil a duty of care not to carry out procedures where the risks cannot be justified in relation to the anticipated benefits and (3) guard against conflicts of interest⁵⁻⁷.

Informed consent derives from the right of competent people to determine what happens to them (autonomy) and the need to protect from harm those who are not competent⁸. Its exercise depends on conditions of information provision, the patient or research participant's understanding of this information, and the absence of coercion⁸. However, several pieces of evidence showed that Dr He's project breached established principles of informed consent. Firstly, according to Dr He's documents, the program was registered at the Chinese Clinical Trial Registry on November 8, but the informed consent form

called the program ‘AIDS Vaccine Research,’ so it is unclear whether participants were fully aware of the potential risks and benefits of the project⁹. Seemingly, Dr He did not perform the obligation of information disclosure sufficiently, because he did not tell the participants that the transmission of HIV to a child can be effectively prevented by other safe measures, such as washing the infected father’s sperm before *in vitro* fertilization (a step Dr He’s team in fact performed)¹⁰. Secondly, Dr He said that his team recruited these particular couples, in which the father was infected with HIV and the mother was not, through an HIV/AIDS volunteer group. The problem lies in that people in such a vulnerable position are open to being induced to participate in this project by the prospect of having healthy offspring; furthermore, it is likely that the potential benefits of genome editing were exaggerated, and the risks were underestimated or concealed. Thirdly, it is understood that infected people may be subject to significant pressure and discrimination in day-to-day life, for example, they may be discriminated against in employment and denied insurance by insurance companies. Given that, they may have sought a treatment that would allow their offspring to avoid a similar predicament. These factors call into question the voluntary nature of the consent. Moreover, article 3 of the consent form mentions the risk of the editing procedure missing its target, and that there are different detection methods to minimize the possibility of causing significant harm¹¹. However, the project team did not properly take account of the risk of missing the target because neither the significance of off-target events nor their possible consequences were addressed in the consent form¹⁰. Thus the consent form failed to describe an acceptable balance of benefits against risks for the participants. To sum up, it appears that the principles of informed consent had been violated. The problem does not end there, however: participant consent is only one element, perhaps the last element, in securing ethical treatment; prior to that are questions of science and of human values, which few would allow that individual interest should override.

Dr He said that his aim of this research was to aid these vulnerable people, but the data he presented suggested that his experiments failed. Neither of the twin girls born following the first procedure to result in a live birth, possessed the 32-base pair deletion desired in the *CCR5* gene, the gene for a protein on immune cells that HIV uses to infect the cells. Furthermore, the procedure also resulted in ‘off-target’ changes elsewhere in the girls’ genomes¹². Even though the risks far outweighed the benefits, Dr He carried out the procedure anyway. Consequently, Dr He’s ‘gene surgery’ posed a number of foreseeable risks to the babies and their offspring, without providing any obvious medical benefit.

Another problem is conflicts of interest. With governmental, domestic and international investment, Dr He became the owner of six companies and a significant shareholder of seven companies, with personal wealth of several billion yuan¹³. Two of the companies in which Dr He is a shareholder are involved in genetic testing. Nevertheless, Dr He and his team declared ‘no competing financial interests’ in a paper on germline genome editing published in *The Crispr Journal* on

November 28, 2019 (since retracted)^{14,15}. Furthermore, Dr He concealed his interest in these companies when he recruited couples to participate in his program¹⁰. This tarnished the scientific integrity of his study and casts suspicion over his motivation.

Regulatory policy

The authorities in Guangdong province and Shenzhen (part of Guangdong) launched a joint investigation. As reported by Xinhua, China’s state-run press agency on January 21, 2019, they found that

‘Dr He secretly organized a project team including foreign personnel, from June 2016, deliberately evaded supervision, used techniques with unclear safety and effectiveness, and carried out genome editing in human embryos for reproductive purposes, which were banned in China. From March 2017 to November 2018, He Jiankui recruited eight couples to participate in the experiment by forging ethical review papers. Because the regulations of assisted reproduction prohibit people living with HIV to use assisted reproductive technology, Dr He’s team organized other health people to take blood tests instead of these couples, and ordered some individual practitioners to conduct genome editing on human embryos and implant them into the mother’s body.’¹⁶

This investigation was followed by formal legal proceedings which resulted in a judgment that was delivered on December 30, 2019 at the Nanshan District People’s Court in Shenzhen. Dr He, and two of his collaborators were investigated for illegally carrying out human genome editing and reproductive medical activities for the purpose of reproduction, which constituted the crime of illegal medical practice. The court held that the three defendants had not obtained the necessary medical practice qualification, and had intentionally violated the state regulations on scientific research and medical management, violated the principles of scientific research and medical ethics, and rashly applied gene editing technology to human assisted reproductive medical treatment. He Jiankui was sentenced to three years in prison and fined CNY 3 million while his collaborators received lesser sentences¹⁷.

At the time the treatments were carried out, China had not established explicit and legally binding rules or standards for interventions in the human genome. While technical guidelines and standards were in place, either these documents lacked legally binding force, or the guidelines lacked ethical components. Relevant provisions are found in the ‘Key Points for Quality Control of Clinical Research on Human Cell Therapy and Gene Therapy’ published by the Former Ministry of Health in 1993, the ‘Interim Measures for Human Genetic Resources Management’ published by the State Council in 1998 and the Measures for the Administration of Human Assisted Reproductive Technology of 2001. However, the (non-binding) 2003 ‘Ethical Guiding Principles for the Research of Embryonic Stem Cell’ issued by China’s Ministry of Science and Technology and the Former Ministry of Health (now National Health Commission) unequivocally rule out any research beyond 14 days after the creation of an embryo as well as any implantation of a genetically modified embryo into

the human reproductive system¹⁸. The activities of Dr He's team, which led to the birth of two baby girls and a further pregnancy, breached these principles. In addition, it was found that ethical review materials had been forged by Dr He's team to evade supervision, the existence of informed consent was questionable, and the project violated the Biomedical Research Ethics Review Method Involving People published by the National Health Commission¹⁹.

Societal consideration

Public opinion on this event is mixed. In 2019, the Key Laboratory of Public Opinion in Big Data Analysis and Simulation of Guangdong Province at Sun Yat-Sen University released the first research report on the public's understanding and attitude towards gene editing technology in China²⁰. They report the results of a survey of the attitudes of the public and people living with HIV towards genome editing techniques. The report shows that more than 60% of the Chinese public supported therapeutic use of genome editing in adults and children, while nearly 70% of people did not support the use of genome editing for non-medical purposes, such as to enhance IQ or athletic abilities. Over 60% of people believed that the Government should provide funding for genome editing²¹. Such a supportive attitude favors the promotion of research in genetics and also demands rigorous ethical governance and oversight of emerging technologies. Ensuring the healthy, ethically warranted, sustainable development of science is always of paramount importance for the well-being of humankind.

The support for genome editing and willingness to adopt genome editing approaches that is found among the Chinese public may also contribute to the development of policy, which could, in turn, provide a framework to support technological development. In reality, however, the relationship between scientific advancement and the development of public policies presents challenges because the development of policies often fails to keep pace with developments in technology²². Public involvement in science policy development is often limited, but events such as the 'gene-edited baby' perhaps highlight the role publics ought to play in all jurisdictions given the global reach of such technologies. Indeed, the importance of attending to public opinion on genome editing has been asserted with varying degrees of vigor, and for a variety of reasons^{23–27}. These reasons include that public participation can offer new perspectives on the issues and, more importantly, the public have a presumptive right to know about new developments and take part in the governance of scientific research because they will be affected by its consequences. Besides, the impact of emerging technologies is so widespread, there are issues with new technologies that cannot be left to researchers and participants but which are properly in the domain of public policy, and, arguably, international ethical debate^{24,28}.

Political, cultural and economic conditions

Then, why China? From a broad political, sociological and historical perspective, Dr He's genetic transgression is not an isolated case. Set within the context of China's approach

to biomedicine and bioethics and its global ambitions, Dr He's experiments fit into a radical and dangerous climate. It is true that his action was condemned by the genome editing community in China and other committees and government agencies, such as the Genetics Society of China, the Chinese Society for Stem Cell Research²⁹, and the National Health Commission in China³⁰ rightly pointed out that Dr He seriously violated ethics, scientific research integrity and relevant state regulations, causing adverse effects at home and abroad. However, as Nie rightly pointed out, to blame Dr He alone disregards the wider responsibilities of his university and other authorities³¹. In the past several decades, a permissive regulatory climate and a pragmatic approach have fostered unprecedented growth of the biomedical revolution in China. This climate has created a fertile environment for Chinese researchers to pursue daring but unethical 'world firsts'. Furthermore, as there are also structural, systemic and institutional flaws behind this experiment, it is important to examine 'what created him, what incentivized him and what failed to stop him'³².

Development of biomedicine in China: strategic national goal

The Chinese government recognized that bioscience could play a major role in its global competitiveness and determined to be a key player and leader. Biomedicine, synthetic biology, brain research and regenerative medical techniques are listed as strategic fields and industries in China's '13th Five-Year Plan' National Strategic Emerging Industry Development Plan and Healthy China 2030 strategy³³. Life science and health-related projects account for 17 out of 60 targeted areas with high investment priority. In the '13th Five Year Plan', 'The Program of Six New Free Trade Pilot Zones' and other programmatic documents related to economic and social development all have incentive policies for industrial development in the field of gene therapy. In terms of technology and industry promotion, gene therapy has wide ranging prospects both as a new medical technology and as a biomedical industry. As China's healthcare industry grows and diversifies, so do the opportunities – its healthcare market is expected to reach CNY 198 billion (USD 28.59 billion) in 2026, increasing tenfold from 2016³⁴. China has also become the top destination for research involving primates, which are invaluable models for studying human disease, especially in the brain³⁵. Other countries do not breed primates in such large numbers or to the standard produced in China. In research that is controversial internationally but which drew little attention domestically, researchers from the Chinese Academy of Sciences have genetically modified monkeys so they show autistic behaviors with the aim of increasing understanding of brain disorders³⁶. Another controversial case was that scientists from Shanghai have created the first primates cloned with a technique similar to the one used to clone Dolly the sheep. Researchers hope to develop populations of genetically identical primates to provide improved animal models of human disorders, such as cancer and Parkinson's disease³⁷.

In the Nature Index, China is the second leading contributor to biomedical engineering articles after the United States,

measured by its contribution to the authorship of papers in 82 high-quality research journals in 2015–17³⁸. With respect to CRISPR, in a recent analysis of more than 2,000 patent applications for distinct inventions that involved CRISPR, the United States barely edged out China: publicly available CRISPR patent applications as of December 2018 show that the United States has 872, China 858 and Europe 186. Applications from China have climbed rapidly in recent years, and the country dominates in the agricultural and industrial realms.

World's first: Catching up with – and surpassing – the West with translation

The genome editing experiment was not the first time He Jiankui had gained publicity and attention in China. Earlier in 2017, Chinese state broadcaster CCTV showed a series promoting China's achievements in science and technology³². One episode profiled a Chinese scientist who claimed to have invented a gene-sequencing machine that outperformed those in the 'West'. 'Somebody said we shocked the world with our machine', Dr He said in front of the camera with a proud smile³². Another interesting phenomenon was that when Dr He's research was first reported, in November 2018, the *People's Daily Online*, one of the most influential official media outlets, promoted and celebrated it as 'the world's first gene-edited babies genetically resistant to AIDS were born in China', and 'a historical breakthrough in the application of gene editing technology for disease prevention'³⁹. However, as more detailed information about his work was released and also the worldwide outcry and condemnation was reported by media, the *People's Daily* quickly deleted that news item.

He Jiankui used rhetoric such as 'world's first' and 'surpassing the West', which are sensational, nationalistic, and stimulating. This rhetoric also resonates with the grander Chinese dream, chased by the government and society, of catching up and surpassing the West⁴⁰. Dr He received extremely generous support from central and local governments and scientific organizations. More importantly, he was selected for the Central Government's top science program, the 'Thousand Talents Plan'. With governmental and domestic investment, he has become the owner or significant shareholder of at least seven genetic biotechnology companies³¹. Perhaps, when he announced the 'world's first' genome edited babies, he was expecting the congratulations and acclaim that he had always been accustomed to in China. To some extent, Dr He's human experimentation constitutes one of the fruits of his personal ambition 'nourished and supported by China's drive for superpower status in science, technology, and medicine.'³¹

In recent decades, the Chinese government has strongly promoted the transformation of scientific discoveries and technological inventions into clinical practice, products and economic growth. In 2016, the Communist Party of China Central Committee and the State Council issued a policy document on 'strategy for innovation-driven development'⁴¹. In August 2016, the Ministry of Science and Technology and the Ministry of Education issued 'Opinions on Strengthening the Role of Higher Education Institutions in Transfer and

Transformation of Scientific and Technological Achievements.'⁴² University researchers, including students, are encouraged to transform their scientific investigations and technological inventions into economic development. This also became one of the evaluation standards for universities, which are now required to submit their performance on translating scientific research into economic growth and production annually. These policies aim to promote scientific research and innovation. At the same time, China still lacks rigorous ethics governance and oversight, especially on conflict of interest. As Nie has rightly pointed out:

'as manifested in the rising cases breaching scientific integrity and especially He Jiankui's human experiments, China's science schemes have much to do with the developing mentality that ethics is merely secondary and instrumental for cutting-edge scientific investigation and technological invention. Ethical considerations and the ultimate moral goals of science and medicine can be compromised or alienated by the unchecked pursuit of personal ambition, financial interests, interests of the party-governments and institutions, economic growth, or national glory.'⁴³

A similar example is the growing business of stem cell tourism in China: although many concerns have been raised regarding fraudsters that operate unsafe stem cell therapies, the local officialdom 'turns a blind eye to the questionable technology.'⁴⁴ Increasing government funding of scientific research has promoted rapid developments in stem-cell research in China. The number of translation studies, including basic and preclinical investigations, has also increased. Around 100 stem-cell banks have been established in China, 10 stem-cell drugs are currently in the approval process, and more than 400 stem cell-based clinical trials are currently registered in China⁴⁵. The Chinese regulatory approach to biomedical research is based on Guidelines and Administrative Measures, rather than legislation. Therefore, the force of governance measures is very limited, and certain institutions such as military hospitals are not subject to even this level of control. In 2016, Wei Zexi, a 21-year-old student died after receiving an experimental immunotherapy cancer treatment at the No 2 Hospital of the Beijing Armed Police Corps⁴⁶. Wei underwent the procedure, which cost his family more than CNY 200,000 (USD 29,130), after using the online search engine Baidu to research treatments. The hospital's details topped the list returned by Baidu, but it failed to save Wei.

After the 'Wei Zexi incident' involving biological immunotherapy in 2016, the National Health and Family Planning Commission immediately suspended all unapproved clinical applications of the third class of medical technology (those designated by the Ministry of Health as having significant ethical issues and higher risks, whose safety and effectiveness are yet to be proved), and the regulatory policies on gene therapy were revised³⁹. Under the new policies, the admission and management of the second- and third-class technologies was moved from health administration departments to the medical institutions providing the treatment to ensure that process

could be more easily tracked⁴⁷. This approach has already been adopted by many developed countries such as France, Britain, and Canada⁴⁸.

Lack of compelling ethical oversight and regulation, difficult implementation

Although many hospitals and universities in China have established institutional review boards (IRBs) and bioethics centers in accordance with internationally recognized principles, they are not home-grown institutions⁴⁹. For many researchers, they are treated as imported Western bureaucratic instruments not rooted in Chinese culture. In the West, the medical experiments in Nazi Germany, the Tuskegee syphilis experiment in the US and other scandals led to the establishing of IRBs, which approve and oversee medical experiments involving human subjects. In China, there is also a history of notorious human experiment including the Japanese army unit 731 that conducted experiments on Chinese citizens during World War II, but it did not give rise to the development of practices and institutions of research ethics as in the West⁴⁹. Some studies have revealed IRBs are not properly established and consistent in practice, mainly owing to their limited experience in handling relevant ethical questions, or coming under pressure from the authorities, or sometimes existing merely for the sake of formality^{50,51}.

Despite ethical guiding principles and management measures applied to research involving human embryonic stem cell and human assisted reproductive technology, up till now China has not formed a comprehensive and systematic, legally underpinned regulatory system for human genetic technology issues, including genome editing and gene therapy. The current oversight norms are mainly technical management methods and ethics principles at a low-level, with no directly applicable legislative provisions. In contrast to US and European regulations, they are not enforceable by law. In response to the ‘gene-edited baby’ case, the Chinese government brought forward legislation in areas such as biosecurity, genetic technology, and biomedicine. In early 2019 the National Health Commission issued draft regulations on the clinical applications of the new biomedical technologies, focusing on so-called ‘high-risk’ biomedical technologies like human germline genome editing, which need to be reviewed at national level⁵². In July 2019, China approved a plan to establish a national commission for ethics in science and technology. The National Science and Technology Ethics Committee was charged with promoting the development of ‘a more comprehensive, ordered and coordinated governance system’ in 2020⁵³; meanwhile, the ‘Biosafety Law’ made its way through the legislative process⁵⁴.

Silence and complicity

Beyond the Chinese context, there was a substantial number of individuals around the world whom He Jiankui had informed about his experiment prior to its public release. These individuals have been referred to as part of Dr He’s ‘circle of trust’⁵⁵. The extent to which they were aware of the trials varied, as well as their reactions to the information. None, though,

decided to release the information of the first reproductive use of gene editing to the broader scientific community or public at large.

There is reason to believe that releasing information earlier could have prevented the experiment from proceeding with the pregnancy that resulted in the first live births of twin girls, or if made after the first live births, that it could have prevented the pregnancy that resulted in the third live birth that was recently confirmed by a Chinese court⁵⁶.

‘Whistleblowing’?

The whistleblowing literature distinguishes between ‘internal whistleblowing’ – involving organizational structures and processes- and ‘external whistleblowing’ – involving external bodies such as ‘agencies, professional bodies, regulators and the media’⁵⁷. In almost all cases of whistleblowing, concerns are raised internally on more than one occasion before the whistleblower turns to external bodies⁵⁷. The case of He Jiankui is complicated by the fact that the ‘circle of trust’ comprised individuals external to Dr He’s organization, who were mostly based abroad and may have been unfamiliar with China’s regulatory regime. Given this, releasing information about Dr He’s experiment would not strictly have been a standard case of whistleblowing. However, theoretical and terminological issues aside, the central question that remains is: What should we make of the failure to release information by those who were in a position to do so, ethically speaking?

Silence

Clearly, it was a case which should have raised ethical concerns for the ‘circle of trust’ as evidenced by the world’s reaction to it. Dr He’s experiment was widely derided as premature due to scientific and safety concerns. Those in the ‘circle of trust’ must have known that this was an ethically dubious experiment that required public deliberation considering the numerous statements on this issue. For example, a widely-publicized and discussed statement from the organizing committee of the 2015 International Summit on Human Gene Editing stated that

‘It would be irresponsible to proceed with any clinical use of germline editing unless and until

- (i) the relevant safety and efficacy issues have been resolved, based on appropriate understanding and balancing of risks, potential benefits, and alternatives, and
- (ii) there is broad societal consensus about the appropriateness of the proposed application.’⁵⁸

Indeed, Dr He himself wrote that proceeding with germline editing would be ‘extremely irresponsible’ without resolving safety issues – just weeks before commencing his experiment⁵⁵.

Given the substantial potential harm that can be avoided if the experiment is stopped at an early stage, one might be led to believe that there was a duty to release such information. Initial support in favor of sounding the alarm about the

experiments might come from the general ‘duty of easy rescue’, a plausible moral principle stating that if one could bring about a substantial benefit or prevent substantial harms to others at little cost to oneself, one should do so. However, this principle does not apply in the current case because the potential reputational cost of releasing such information could be substantial. Individuals who release the information would likely have suffered reputational harm, as others may have deemed them as ‘uncooperative troublemakers’ and become unwilling to engage in scientific collaborations or communication with them. Furthermore, scientific correspondence such as that sent out by He Jiankui is typically made under a presumption of confidence. Reporting such correspondence may have been seen as a breach of trust.

As has been argued elsewhere⁵⁹, a more promising way of grounding the duty to release information may be found in a scientist’s professional responsibilities as they are articulated in recognized professional codes of conduct. According to these codes, scientists have a responsibility to report suspicions of wrongdoing and research misconduct, on the grounds that such instances ‘undermine the trustworthiness of research’⁶⁰. Unlike the ‘duty of easy rescue’, the professional responsibility to report instances of research misconduct, including ethical failures, would hold even if there are substantial reputational costs involved for individuals who release the information.

Complicity in the experiment

A further point worth exploring is the idea that the members of Dr He’s ‘circle of trust’ were, to an extent, complicit in the unethical experiment due to their silence. This can be best understood by applying Chiara Lepore and Robert Goodin’s account of ‘complicity’, which holds that performing an action (or, in some cases, an inaction, as described below) ‘that contributes to the wrongdoing of another and knowing that it does so (but without necessarily sharing the other’s wrongful purpose), [...] are minimally required for one to be complicit with the wrongdoing of another.’⁵⁷ For someone to be complicit in wrongdoing means that that a person shares at least some of the blame for the wrongdoing. If those in the ‘circle of trust’ were complicit, they would not only be criticizable for failing to discharge a duty to report wrongdoing, but could furthermore be deemed partly responsible for the wrongdoing itself. This raises the moral stakes, so to speak, of failing to report, and in turn provides additional motivation to support reforms that ensure scientists report future wrongdoing.

As described above, there were numerous aspects of wrongdoing in He Jiankui’s experiment. While some details, including inadequate consent, improper medical procedures, and alleged unverified approvals, would not have been accessible to members of the ‘circle of trust’, they were reportedly informed about the more basic facts of the case: that He Jiankui was editing the DNA of embryos to prevent HIV transmission, and implanting those embryos⁵⁵. They also would have or should have known that such a procedure was premature due to concerns about efficacy and safety of the intervention as well as a lack of social license. Pronouncements of well-established national and international bodies over several years had been

unanimous on that front⁶¹. The basic facts on their own would be sufficient to merit condemnation of the study and necessitate its closure.

Notably, most members of the ‘circle of trust’ were not actively involved with any study procedures – they were just kept informed. Because complicity with wrongdoing implies a degree of blameworthiness, and blame is only appropriate when there is some sort of causal contribution, complicity in turn requires some sort of causal contribution. One might argue that omissions cannot be causes, and so in this case members of the ‘circle of trust’ were not complicit. We, however, find that Lepore and Goodin’s rejoinder relating to omission is helpful: ‘What is crucial in making something a causal contribution is the fact that had you done something else, the wrongdoing would not have occurred.’⁶² This counterfactual is almost certainly fulfilled in the present case, as the eventual public release of information did lead to the experiment’s immediate closure.

The case for scientists’ inaction being a causal contributor is bolstered by their duty to release information about deeply unethical research. For such cases, Lepore and Goodin tell us that ‘[w]here there is a duty to do something and you do nothing, your ‘doing nothing’ counts as a cause.’⁵⁷ Thus a life guard who does not take any action to save a child from drowning in a swimming pool would be deemed responsible for contributing casually to the child’s death precisely because the life guard was under a duty to watch over the children⁵⁷. Scientists may not be in exactly the same role as a lifeguard, but, as argued above, scientists may nevertheless have professional responsibilities in relation to wrongdoing of their peers.

Still, we should not overstate this claim. Complicity comes in degrees, attenuated by the centrality of causal contribution. Moreover, the extent to which complicit individuals are blameworthy depends on the ‘extent of contribution, and extent of shared purpose with [a] principal wrongdoer.’⁶³ In this case, most members of the circle of trust were not integrally involved in the study design and conduct, so could hardly be considered central players. As for endorsement, some apparently responded positively to Dr He when informed of the experiment, others negatively⁵⁵. A charitable interpretation, based on subsequent statements, is that generally members of the ‘circle of trust’ did not strongly endorse the study’s aims and therefore did not share Dr He’s purpose.

Beyond the individuals involved, a question can be raised about the role of the broader scientific community. A culture in which those who inform on colleagues’ unethical behavior are ostracized and disregarded, and conversely, risk-takers are rewarded for even questionable experiments as long as the outcomes are successful, foreseeably contributes overarchingly to wrongdoings of the kind that He Jiankui committed⁶³.

Because the scientific community was not generally informed of He Jiankui’s experiment, this community cannot strictly be said to be complicit in the wrongdoing. Nevertheless, we should

keep squarely in view the effects of pervasive scientific culture. This culture might enable or tacitly encourage not only He Jiankui's experiment itself but also the decision by those in the 'circle of trust' not to inform the scientific community, or society more broadly. Preventing future wrongdoing will require critically reflecting on the factors, including scientific culture, that possibly contributed to the 'circle of trust' becoming complicit.

Taking responsibility

We have, then, a degree of complicity in He Jiankui's experiment by members of the 'circle of trust', and the contributory role of the international scientific community towards that complicity. This highlights the extent to which individuals and groups need to acknowledge a level of responsibility for their actions – and inactions – in order to improve practice going forward. In particular, work is needed to remove the barriers that prevent reporting of instances of wrongdoing and thereby facilitate complicity.

Elsewhere, it has been argued that one concrete step to improve the likelihood of scientists coming forward would be to create an international reporting mechanism. This would at least partially address the practical problem of there being no obvious body to report to when gene editing research occurs abroad⁵⁹. Perhaps the absence of such a mechanism signals erroneously to the broader research community a general reluctance towards disrupting the scientific status quo and perhaps even tolerating certain conduct. If certain behaviors are truly intolerable, a response to counter such behaviors and to signal their unacceptability should be mounted.

Another complementary approach is to push back against the norm of silence. In this case, there may have been a presumption of confidentiality on the part of He Jiankui, that those to whom he sent communications would not leak or otherwise disclose the contents. In general, such a presumption may be well-justified. Beyond general privacy concerns, making private scientific communications public might have a chilling effect on scientific discourse, discouraging honest discussion that might be misinterpreted if released without appropriate context⁶⁴. It could also discourage innovation by allowing third parties to 'scoop' certain novel approaches before they are ready to be implemented. However, it would be inappropriate to infer from this an absolute right of confidence. In the area of moral rights, the right of confidence is merely *prima facie*: a relevant moral consideration that can be overridden by competing considerations. As for legal rights, there is no general legal right to confidentiality in scientific communications analogous, for instance, to physician-patient or reporter-informant confidentiality⁶⁵.

The *prima facie* right to confidence would presumably not preclude the release of information that is unambiguous evidence of research fraud, even if this information emerged from personal correspondence. Likewise, clinical research involving human heritable genome editing in the present state of scientific research and public discourse would be just the sort

of consideration weighty enough to outweigh any such *prima facie* right.

It is a much more complex and difficult task to identify and evaluate practical actions that would be effective at reforming those norms of silence – too ambitious for the scope of the present discussion. We will simply note, though, that the scientific community should take active steps to work towards such reforms, not just in the area of germline gene editing, but for the wider array of scientific conduct. The silence and complicity in the case of the first gene-edited babies is not an isolated incident, but part of a broader pattern of scientific behavior around the world that calls out for reform.

Thus far we have discussed areas of responsibility and measures that could be taken to avert such condemnable scientific conduct in the future from the perspective of the established scientist and the scientific community to which s/he belongs. It is perhaps instructive also to consider the broader context within which scientists are educated and trained. For many decades unethical academic practices that undermine research integrity have plagued academic institutions and research facilities⁶⁶. Here we highlight two areas from a vast area of enquiry: scientists in training and organizational responses to alleged academic misconduct.

Where biomedical doctoral students are concerned, for example, there is some evidence of a correlation between their attitudes towards misconduct and whistleblowing, and their own self-reported involvement in questionable research practices⁶⁷. The same research also found a positive correlation between involvement in undergraduate ethics education and conduct in accordance with expected norms⁶⁷.

A recent analysis has highlighted the manner with which organizational responses perpetuate ineffective responses to alleged academic misconduct via three processes: the inexperience of committees set up to investigate alleged misconduct can, on occasion, lead to misunderstanding of standards, concepts, and acceptable practices; the disconnect between stated action and implementation of such action; and efforts to contain reputational damage and organizational assertions that specific cases are the exception to organizational behavior⁶⁸.

Conclusion

It would be convenient to cast He Jiankui as rogue or maverick, the bearer of sole responsibility, working independently of the wider research community, institutions and systems. Whatever the details of the case itself, however, this cause célèbre has drawn attention to a number of contributory conditions, the persistence of which cannot and should not be ignored. These include the way in which biomedical innovations are implicated in multiple systems of practice (those of research, medicine, business, techno-nationalism and responses to broader societal challenges) and rely on the support or complicity of others (of colleagues, research participants, patients, mentors, institutions and officials).

On the question of how this project could come about in the first place, given the ostensibly overwhelming opposition to clinical translation of HHGE, we risk ignoring powerful contributory conditions if we treat biomedical technologies as simply the outworking of scientific research. As we have shown in this paper, the ‘gene-edited baby’ case reveals the extent to which the traction of other interests, such as those of personal ambition, national prestige and economic reward can intervene in biomedicine. But no more can biomedical technologies be thought of as simply a response to clinical need. Though *CCR5* had been an early target for proof-of-concept research, few could have expected the first efforts to edit the human genome to have the aim of conferring resistance to an easily avoidable disease. To make such assumptions is, however, to ignore the local conditions of access to assisted conception treatment for those with HIV, the societal challenge it represents and the waiting market for expanded reproductive choice. When the object was to pioneer a new service, the choice of target that might have seemed achievable and publicly popular, rather than one that was clinically desirable (such as obligatorily heritable disease), could have appeared perfectly reasonable: cracking *CCR5* would demonstrate a translational pathway for other indications to follow⁶⁹. This becomes more plausible if HHGE is understood not as a therapeutic intervention but as a technology for expanding reproductive options⁷⁰. But this dichotomy, too, is merely complacent – it suggests that evaluation can be laid out on a simple scale, though in reality it is much more complicated.

On the question of why a vaulting ambition like that of He Jiankui could not be reined in, despite the fact that it was shared with many eminent and influential scientists, once again, it is easy to defer to failures of formal oversight or the absence of clear and effective sanctions. But while relevant instruments and procedures existed to an extent, the

prevailing culture flowed around them and built networks of circumvention. As we have shown in this paper, a culture of responsible research cannot rely on individual actors calculating what is in their own best interests. The confusion of entrepreneurialism with science only makes the gaming of responsibility more likely. The response of those who knew of Dr He’s intentions was an example of a phenomenon that explains failures of collective action in fields from the prevention of anthropogenic climate change to financial crises, that of ‘organized irresponsibility’, where responsibility is diffused and passed around a system rather than vested in any identifiable actor⁷¹. Failures by omission can be seen as non-culpable because it can be assumed that either someone else will see to it or, if not, all will be equally culpable (and therefore none will be).

We cannot say that the ‘gene-edited baby’ case has been salutary, so long as many of the conditions that nourished it remain. The prevention of future events of this kind must begin with an understanding of these conditions rather than the search for causes and the assigning of liabilities.

Data availability

Underlying data

No data are associated with this article.

Acknowledgments

The authors wish to express their thanks to the organisers of the 2019 Global Forum on Bioethics in Research. Contributions to this work by ML, GOS, and VX were supported by the Singapore Ministry of Health’s National Medical Research Council under its NMRC Funding Initiative grant (NMRC/CBME/2016).

References

1. Cyranoski D, Ledford H: **Genome-edited baby claim provokes international outcry.** *Nature.* 2018; **563**(7733): 607–608. [PubMed Abstract](#) | [Publisher Full Text](#)
2. Normile D: **Chinese scientist who produced genetically altered babies sentenced to 3 years in jail.** *Science.* 2019. [Publisher Full Text](#)
3. Cyranoski D: **What CRISPR-baby prison sentences mean for research.** *Nature.* 2020; **577**(7789): 154–155. [PubMed Abstract](#) | [Publisher Full Text](#)
4. Lei R, Zhai X, Zhu W, et al.: **Reboot ethics governance in China.** *Nature.* 2019; **569**(7755): 184–186. [PubMed Abstract](#) | [Publisher Full Text](#)
5. World Medical Association Declaration of Helsinki: **Ethical Principles for Medical Research Involving Human Subjects.** World Medical Association, 1964. [Reference Source](#)
6. UNESCO Universal Declaration on Bioethics and Human Rights. 2005. [Reference Source](#)
7. CIOMS&WHO: **International ethical guidelines for health-related research involving humans.** 2016. [Reference Source](#)
8. 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.: The Commission, 1978. [Reference Source](#)
9. Beijing Daily News: **He Jiankui jiang xian shen guo ji ren lei ji yin zu bian ji feng hui fa yan ceng dui 7 dui fu fu 16 ge pei tai ji yin bian ji [He Jiankui will speak at the International Human Genome Editing Summit, He has conducted gene editing of 16 embryos from 7 couples].** 2018.
10. Pengpai News: **Ji yin bian ji ying er zhi qing tong yi shu bao guang: jing fei lai zi nan ke da [Informed Consent for Gene-Edited Babies: funding from South University of Science and Technology].** 2018.
11. Shaw D: **The Consent Form in the Chinese CRISPR Study: In Search of Ethical Gene Editing.** *J Bioeth Inq.* 2020; **17**(1): 5–10. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
12. Cohen J: **Did CRISPR help—or harm—the first-ever gene-edited babies?** *Science.* 2019. [Publisher Full Text](#)
13. Xinjing News: **He Jiankui qi xia gong si qu nian gu zhi 15 yi shang shi gong si jian jie chi gu [He Jiankui’s company was valued at 1.5 billion yuan last year, with the listed company holding indirect shares].** 2018.

14. Greely HT: **CRISPR'd babies: human germline genome editing in the 'He Jiankui affair'**. *J Law Biosci.* 2019; **6**(1): 111–183. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
15. LeMieux J: **He Jiankui's Germline Editing Ethics Article Retracted by The CRISPR Journal**. *GEN*, 2019. [Reference Source](#)
16. Xinhua News Agency: **Guang dong chu bu cha ming ji yin bian ji ying er shi jian**[Preliminary investigation of genome edited babies in Guangdong]. 2019. [Reference Source](#)
17. Xinhua News Agency: **Ji yin bain ji ying er an yi shen xuan pan he jian kui deng san bei gao ren bei zhui jiu xing shi ze ren** [He Jiankui and other defendants were sentenced to criminal liability in the first trial of the gene editing baby case]. 2019. [Reference Source](#)
18. Chinas Ministry of Science and Technology: **ren pei tai gan xi bao yan jiu lun li zhi dao yuan ze** [Ethical Guiding Principles for the Research of Embryonic Stem Cell]. 2003. [Reference Source](#)
19. National Health and Family Planning Commission: **She ji ren de sheng wu yi xue yan jiu lun li shen cha ban fa** [Ethical review of biomedical research involving humans]. 2016.
20. Li W: **Majority supports gene editing for treatment, prevention**. *China Daily*. 2018. [Reference Source](#)
21. Chen L, Zhang Z: **Chinese Public Attitudes on Gene Editing**. *Global Times*. 2018. [Reference Source](#)
22. Nuffield Council on Bioethics: **Genome editing: an ethical review**. London: Nuffield Council on Bioethics. 2016. [Reference Source](#)
23. Organizing Committee for the International Summit on Human Gene Editing: **On Human Gene Editing: International Summit Statement**. 2015. [Reference Source](#)
24. Nuffield Council on Bioethics: **Genome editing and human reproduction**. London. 2018. [Reference Source](#)
25. Hurlbut JB, Jasanoff S, Saha K, et al.: **Building Capacity for a Global Genome Editing Observatory: Conceptual Challenges**. *Trends Biotechnol.* 2018; **36**(7): 639–641. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
26. Baylis F: **Human Genome Editing: Our Future Belongs to All of Us**. *Issues in Science and Technology*. 2019; **35**(3): 42–44. [Reference Source](#)
27. Lander ES, Baylis F, Zhang F, et al.: **Adopt a moratorium on heritable genome editing**. *Nature*. 2019; **567**(7747): 165–168. [PubMed Abstract](#) | [Publisher Full Text](#)
28. Committee on Science, Technology, and Law; Policy and Global Affairs; National Academies of Sciences, Engineering, and Medicine; Olson S, editor: **International Summit on Human Gene Editing: A Global Discussion**. Washington (DC): National Academies Press (US); International Summit on Human Gene Editing: A Global Discussion: MEETING IN BRIEF, 2016. [Reference Source](#)
29. Stem Cell Branch of Chinese Society for Cell Biology (news release): **Two professional societies speak out on the "gene-edited baby incident"**. 2018. [Reference Source](#)
30. Chinanews: **National Health Commission, Ministry of Science and Technology, and China Association for Science and Technology respond to gene editing baby incident**. 2018. [Reference Source](#)
31. Nie JB, Xie G, Chen H, et al.: **Conflict of Interest in Scientific Research in China: A Socio-ethical Analysis of He Jiankui's Human Genome-editing Experiment**. *J Bioeth Inq.* 2020; **17**(2): 191–201. [PubMed Abstract](#) | [Publisher Full Text](#)
32. National Public Radio (US) online: **Gene-Editing Scientist's "Actions Are A Product Of Modern China"**. 2019. [Reference Source](#)
33. Xinhua News Agency: **Outline of the 13th Five-Year Plan for National Economic and Social Development of the People's Republic of China**. 2016. [Reference Source](#)
34. Frost & Sullivan: **Global Healthcare Market Outlook, 2019**. 2018. [Reference Source](#)
35. Vogel G: **Monkey facility in China lures neuroscientist**. *Science*. 2020; **367**(6477): 496–497. [PubMed Abstract](#) | [Publisher Full Text](#)
36. Liu Z, Li X, Zhang JT, et al.: **Autism-like behaviours and germline transmission in transgenic monkeys overexpressing MeCP2**. *Nature*. 2016; **530**(7588): 98–102. [PubMed Abstract](#) | [Publisher Full Text](#)
37. Liu Z, Cai Y, Wang Y, et al.: **Cloning of Macaque Monkeys by Somatic Cell Nuclear Transfer**. *Cell*. 2018; **172**(4): 881–887.e887. [PubMed Abstract](#) | [Publisher Full Text](#)
38. Mallapaty S: **Engineering a biomedical revolution**. *Nature*. 2018; **564**(7735): S66–S68. [PubMed Abstract](#) | [Publisher Full Text](#)
39. Peoples Daily: **The world's first gene editing baby immunized with AIDS was born in China**. 2018. [Reference Source](#)
40. Mohanty M: **Xi Jinping and the 'Chinese Dream'**. *Economic and Political Weekly*. 2013; **48**(38): 34–40. [Reference Source](#)
41. Communist Party of China Central Committee and the State Council: **zhong gong zhong yang guo wu yuan yin fa guo jia chuang xin qu dong fa zhan zhan lue gang yao** [The CPC Central Committee and the State Council Issued the Outline of the National Strategy for Innovation-Driven Development]. 2016.
42. Ministry of Education and Technology: **Several Opinions of the Ministry of Education and the Ministry of Science and Technology on Strengthening the Transfer and Transformation of Scientific and Technological Achievements in Colleges and Universities**. 2016. [Reference Source](#)
43. Nie JB: **He Jiankui's Genetic Misadventure, Part 1: Why Him? Why China?** Hastings Bioethics Forum (The Blog of The Hastings Center Report). 2018. [Reference Source](#)
44. Jiang L, Dong BH: **Fraudsters operate and officialdom turns a blind eye: a proposal for controlling stem cell therapy in China**. *Med Health Care Philos.* 2016; **19**(3): 403–410. [PubMed Abstract](#) | [Publisher Full Text](#)
45. Hu L, Zhao B, Wang S: **Stem-Cell Therapy Advances in China**. *Hum Gene Ther.* 2018; **29**(2): 188–196. [PubMed Abstract](#) | [Publisher Full Text](#)
46. The Guardian: **China investigates Baidu after death of student who sought cancer cure on internet**. 2016. [Reference Source](#)
47. Wu SW, Chen T, Wu M, et al.: **Management of Medical Technology under the New Medical Policy Background in China**. *Chin Med J (Engl)*. 2016; **129**(22): 2745–2748. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
48. Hanna E, Rémuat C, Auquier P, et al.: **Gene therapies development: slow progress and promising prospect**. *J Mark Access Health Policy*. 2017; **5**(1): 1265293. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
49. Stevens H: **China's win-at-all-costs approach suggests it will follow its own dangerous path in biomedicine**. *The Conversation*. 2018. [Reference Source](#)
50. Sisi X, Yang Y, et al.: **Research on the construction status and governance mechanism of medical ethics committee in China**. *Chinese Medical Ethics Journal*. 2016; (1): 17–19 (in Chinese).
51. Lina A: **Research on the changes, current situation and supervision of China's ethics committee**. *Chinese Journal of Shandong University of Science and Technology*. (Social Science edition). 2019; **3**: 26–32 (in Chinese).
52. Division of Medical Administration and Management: **Announcement for public consultation on Regulations on the management of clinical application of new biomedical technologies**. 2019. [Reference Source](#)
53. CRIonline: **Form the National Science and Technology Ethics Committee! Xi Jinping points out the direction for regulating the development of frontier science and technology**. 2019. [Reference Source](#)
54. China National People's Congress Magazine: **The Standing Committee of the National People's Congress deliberates the draft biosafety law in groups**. 2019. [Reference Source](#)
55. Cohen J: **The Untold Story of the 'Circle of Trust' behind the World's First Gene-Edited Babies**. *Science*. 2019. [Publisher Full Text](#)
56. Houser K: **China Quietly Confirms Birth of Third Gene-Edited Baby**. *Futurism*. 2019. [Reference Source](#)
57. Vandekerckhove W, Phillips A: **Whistleblowing as a Protracted Process: A Study of UK Whistleblower Journeys**. *J Bus Ethics*. 2019; **159**(1): 201–19. [Publisher Full Text](#)
58. Organizing Committee for the International Summit on Human Gene Editing: **On Human Gene Editing: International Summit Statement**. Office of News and Public Information, National Academies of Sciences, Engineering and Medicine. 2015. [Reference Source](#)
59. Schaefer GO, Xafis V, Labude M, et al.: (under review) **International Reporting**

- Mechanism for Unethical Germline Gene Editing Experiments Needed.**
60. Resnik DB, Shamoo AE: **The Singapore Statement on Research Integrity.** *Account Res.* 2011; **18** (2): 71–75.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 61. Brokowski C: **Do CRISPR Germline Ethics Statements Cut It?** *CRISPR J.* 2018; **1**(2): 115–25.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 62. Lepora C, Goodin RE: **On Complicity and Compromise.** (Oxford: Oxford University Press). 2013.
[Publisher Full Text](#)
 63. Hurlbut JB, Jasanoff S, Saha K: **The Chinese Gene-Editing Experiment Was an Outrage. The Scientific Community Shares Blame.** *Washington Post.* 2018.
[Reference Source](#)
 64. Lewandowsky S, Bishop D: **Research Integrity: Don't Let Transparency Damage Science.** *Nature.* 2016; **529**(7587): 459–61.
[PubMed Abstract](#) | [Publisher Full Text](#)
 65. Robinson E: **No Confidence: Confidentiality, Ethics and the Law of Academic Privilege.** *Communication Law and Policy.* 2016; **21**(3): 323–81.
[Publisher Full Text](#)
 66. Gross C: **Scientific Misconduct.** *Annu Rev Psychol.* 2016; **67**(1): 693–711.
[PubMed Abstract](#) | [Publisher Full Text](#)
 67. Holm S, Hofmann B: **Associations between attitudes towards scientific misconduct and self-reported behavior.** *Account Res.* 2018; **25**(5): 290–300.
[PubMed Abstract](#) | [Publisher Full Text](#)
 68. Horbach SPJM, Breit E, Mamelund SE: **Organisational responses to alleged scientific misconduct: Sensemaking, sensegiving, and sensehiding.** *Science & public policy.* 2019; **46**(3): 415–429.
[Publisher Full Text](#)
 69. Mills PFR: **Preimplantation genome editing: CCR5 in China.** *Emerg Top Life Sci.* 2019; **3**(6): 695–700.
[PubMed Abstract](#) | [Publisher Full Text](#)
 70. Mills PFR: **Genome editing and human reproduction: the therapeutic fallacy and the 'most unusual case'.** *Perspect Biol Med.* 2020; **63**(1): 126–40.
[PubMed Abstract](#) | [Publisher Full Text](#)
 71. Beck U: **Ecological Politics in an Age of Risk.** tr.Amos Weisz. (Cambridge: Polity Press). 1995.
[Reference Source](#)

Open Peer Review

Current Peer Review Status:  

Version 2

Reviewer Report 04 August 2021

<https://doi.org/10.21956/wellcomeopenres.18740.r44615>

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Giulia Cavaliere 

Dickson Poon School of Law, King's College London, London, UK

Thank you for taking the time to read our reports and engage with our comments. The revised version is excellent, and I take your point about breadth. There's certainly a value in that, especially when the paper is the product of a number of authors with such a heterogeneous expertise.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Applied Ethics, Political Philosophy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 15 July 2021

<https://doi.org/10.21956/wellcomeopenres.18740.r44616>

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Yann Joly 

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I agree with the changes and justification provided by the authors. I only have one minor point of contention left.

Regarding the statement of the author that:

"The paper tries to show how the political and scientific climate and pragmatic approach have fostered unprecedented growth of the biomedical revolution in China. This climate has created a fertile environment for Chinese researchers to pursue 'world firsts'. Some Chinese media and press industry are ignorant of bioethical principles and values (both Chinese and other values), but that does not mean Chinese academic community (both scientific and bioethics) and medical authorities are indifferent or ignorant of the medical ethics principles. On the contrary, many Chinese academic bodies issued statements condemning the experiment quickly. Also, from personal communication with many scholars, they feel ashamed that Chinese media did not respond to this event appropriately."

I agree with the authors that many Chinese scholars in this field, including He Jiankui, are well aware of the core bioethics principles. However, knowledge of the norms might be in itself insufficient. Researchers need to have integrated their content in their practice to a point where they've become part of the scientific & social norms of the field. In China, the interest in bioethics and adoption of such norms are a recent event. Furthermore, there remains important uncertainties regarding how several of these norms should be applied to concrete cases. Together this context explains why some Chinese scientists, while well aware of the law & policies, still decide to attempt "world firsts" that are unethical.

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 09 February 2021

<https://doi.org/10.21956/wellcomeopenres.17906.r42270>

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Song Lingqiao

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Yann Joly

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This very well written, ambitious, manuscript seeks to provide an account of the circumstances that led to He Jiankui's controversial germline gene editing experiment that resulted in the birth of genetically edited twins. While it does a good job as an open letter, the broad scope of factors (political, legal, cultural and economic) considered, prevents a deep treatment of each of these circumstances. The result is an interesting attempt to explain the circumstances of the gene editing incident and to identify changes needed to prevent similar ones to happen again in the

future. However, given the summary treatment given to different factors identified, this account should be accepted with some reserve. Claims will need to be carefully assessed and validated through additional in-depth research.

In the section of 'political, cultural and economic conditions', the authors could write more about the Chinese cultural differences with Western countries. For instance, Confucianism influenced the Chinese public perception of human life through its various stages of development and of the concept of humanness. This deeply rooted tradition likely contributed to a full account of He Jiankui's incident.

On page 4, the authors claim that "China had not established explicit and legally binding rules or standards for interventions in the human genome" needs additional nuances. Technical guiding standards published by the Ministry of Health were in place, but the issue is these documents have low binding power.

In addition, on page 4, one important document was missing for the section, which is Article 22 of the Management Statement on the Human Assisted Reproductive Technology (人类辅助生殖技术管理办法). For a complete list of related laws and regulations on gene editing, [you can refer to this book chapter](#).

On page 5, the authors mentioned at the very beginning, that He Jiankui was praised by the Chinese media. This fact also reveals a lack of familiarity with western bioethics principles and values within the Chinese press industry and other professional groups, as well as, the general public. This is also an important reason why He Jiankui's case occurred in China.

On page 7, the authors mentioned several regulatory reforms on gene editing. But this enumeration is incomplete. More relevant regulations have been released in response to He Jiankui's incident. I suggest updating the regulatory paragraph accordingly.

Additional references are needed in some places to support the claims of the authors: For instance, on page 3, 'They include reflections on: the significance placed on...genetic diseases' 'Three important features of good medical practices...' Also, on the same page, 'Informed consent derives from ...of coercion.' On page 6, 'This approach has already ...' On page 5, 'some people assert ...ethical debate.'

Is the rationale for the Open Letter provided in sufficient detail?

Yes

Does the article adequately reference differing views and opinions?

Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Yes

Is the Open Letter written in accessible language?

Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?

Yes

Competing Interests: No competing interests were disclosed.**Reviewer Expertise:** East-Asian Bioethics & Policy Studies, Genetic Tests, Identity and Equity, Health Law, Intellectual Property Law, International Human Rights Law, Social Sciences Research Methods**We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.**

Author Response 08 Jun 2021

Peter Mills, Nuffield Council on Bioethics, London, UK

We are grateful to both reviewers for the trouble they have taken to offer their thoughtful and helpful comments.

Both reviews note the difficulty with the ambition to cover such a range and variety of issues. This arises from three considerations. The first is its genesis in presentations at the Global Forum on Bioethics and Research in 2019, the virtue of which was to bring together complementary perspectives that could be mutually illuminating and together foster a more complete understanding of the subject. The second is, as both reviewers note, that there is an extent to which there must be a trade-off between the virtues of breadth and depth, and the aim in the present paper was to take advantage of the multiple authors' perspectives to pursue the first virtue while in no way foreclosing the second. The third is the selection of the Open Letter format, as an appropriate vehicle for this, in that it offers scope to identify and juxtapose many of the key points of interest, which, as the second reviewer implies, in effect defines a programme of further research, contextualises it and signposts how it may be pursued. We are, nevertheless, conscious that some of the signposts might be missing and others could be clearer, which we have endeavoured to address through additional referencing and clarifications in the text.

In response to specific comments:

Regarding the section on 'political, cultural and economic conditions', we acknowledge that Confucianism is an influential ethical theory in China and presents a distinctive understanding of human life, dignity, humanness, etc. Confucian understanding of human life and dignity would contribute a valuable perspective to the question of whether the application of gene editing technology related to human birth violate human dignity and humanness. However, the discussion of this issue would be beyond the scope and focus of this paper, despite it is worthwhile to explore in another attempt.

Regarding the nuance with regard to rules and standards in place relevant to He Jiankui's

experiment, the reviewer is right: technical guidelines and standards were in place, but the problem is either these documents have low legal binding power, or the guidelines have no ethical components. For example, the Chinese Government's 2003 legislation (the one explicitly prohibits genetic manipulation of human gametes, zygotes, and embryos for reproductive purposes) belongs to Departmental rule, which generally cannot be used for conviction by judges (so could not be used in the He Jiankui case). We have amended the text for clarity.

We are grateful to the reviewers for their advice regarding effective legal documents and have added a reference to the Measures for the Administration of Human Assisted Reproductive Technology of 2001.

Regarding He Jiankui's initial lauding by the Chinese media, the reviewer notes that this suggests a lack of familiarity with international bioethical principles and values. The paper tries to show how the political and scientific climate and pragmatic approach have fostered unprecedented growth of the biomedical revolution in China. This climate has created a fertile environment for Chinese researchers to pursue 'world firsts'. Some Chinese media and press industry are ignorant of bioethical principles and values (both Chinese and other values), but that does not mean Chinese academic community (both scientific and bioethics) and medical authorities are indifferent or ignorant of the medical ethics principles. On the contrary, many Chinese academic bodies issued statements condemning the experiment quickly. Also, from personal communication with many scholars, they feel ashamed that Chinese media did not respond to this event appropriately.

We have generally updated the legal references to be correct at the time of submission. Additional references have been supplied throughout.

We remain grateful for the attention and advice of the reviewers and hope that the revisions have addressed their concerns satisfactorily.

Competing Interests: N/A

Reviewer Report 25 September 2020

<https://doi.org/10.21956/wellcomeopenres.17906.r40531>

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Giulia Cavaliere

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Thank you for the opportunity to review the manuscript titled: Making sense of it all: Ethical reflections on the conditions surrounding the first genome-edited babies.

It is an interesting article that sets out to trace and discuss key ethical, political and legal aspects of the first "gene-edited baby" case". It is generally well written and it provides an interesting analysis of some of the key ethical issues surrounding the clinical use of CRISPR-Cas9 by He Jiankui. It lacks some depth of analysis due to the variety of issues that it discusses, but it is overall an important contribution to the literature on the ethics and governance of emerging technologies (genetic and non). In my view, the article would benefit from being revised according to some of the comments that I have outlined below.

- One of the strengths of this paper is the breadth of the analysis that it carries out. It touches upon many significant issues, from informed consent and complicity to broader considerations concerning science culture of silence and societal views on emerging technologies. Such breadth however also represents one of the weaknesses of the paper, in that some reflections are significantly underdeveloped and do not engage with the existing literature on the ethics and governance of gene editing. Some examples:
 - The section titled 'Societal Considerations' is vague and underdeveloped. It starts with reporting the results of a survey, then it moves to a brief mention of 'ethical governance' and it incorporates some sweeping claims such as 'science will always endeavor to make breakthroughs, while policy makers strive to secure that the use of the technology benefits people safely". While this is broadly correct, it represents a crude generalization of the pursuit of scientific inquiry and efforts aimed at governing it. Moreover, there has been a substantial debate on these issues - none of which is referred to in this paper.
 - The second paragraph on p. 3 is symptomatic of one of the general problems of the paper, namely to try to achieve too much. As a result, some sections read a bit list-like and are just mentioned and subsequently dropped (see for instance the list that follows "they include reflections on:" in said paragraph).
 - The section on Taking Responsibility is also significantly underdeveloped and it seems to reduce questions of responsibility to confidentiality and breaches thereof. These are just some examples.
- Another worry I had whilst reading this paper concerns the value system that it implicitly refers to. One thing is saying that China falls short on having regulatory systems and governance of science in place, but it is quite another thing to say that "China lacks rigorous ethical governance and oversight". From my reading of the paper (but I might be wrong), the value-system used to appraise what HJ did (and what China did not?) is 1) western 2) universalised and 3) realist (from a meta-ethical point of view). That is: what HJ did is ethically problematic if one looks at it, as the authors do, from ethical frameworks and values that are widely shared in the West. But what is the value of carrying out such a reflection? In particular, the sections under the heading "Political, cultural and economic conditions" are quite problematic in that the authors carry out an analysis of what went wrong in China without considering the specificity of local ethical framework and governance, giving the impression of treating China as the "far east" so to speak.
- Relatedly, and as the authors mention later on in the paper, most of the people who did not speak out against HJ were Western scientists. So why then insisting that the problem is necessarily "local", i.e. the product of a lax approach to ethics and governance?

- Lastly, it might be that it is appropriate for this specific format (open letter) not to reference other works on the issues discussed in the paper, but given the wealth of scholarship produced in the last two years, it is puzzling to see so few references in this paper.

Is the rationale for the Open Letter provided in sufficient detail?

Yes

Does the article adequately reference differing views and opinions?

Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Partly

Is the Open Letter written in accessible language?

Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Applied Ethics, Political Philosophy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 08 Jun 2021

Peter Mills, Nuffield Council on Bioethics, London, UK

We are grateful to both reviewers for the trouble they have taken to offer their thoughtful and helpful comments.

Both reviewers note the difficulty with the ambition to cover such a range and variety of issues. This arises from three considerations. The first is its genesis in presentations at the Global Forum on Bioethics and Research in 2019, the virtue of which was to bring together complementary perspectives that could be mutually illuminating and together foster a more complete understanding of the subject. The second is, as both reviewers note, that there is an extent to which there must be a trade-off between the virtues of breadth and depth, and the aim in the present paper was to take advantage of the multiple authors' perspectives to pursue the first virtue while in no way foreclosing the second. The third is the selection of the Open Letter format, as an appropriate vehicle for this, in that it offers scope to identify and juxtapose many of the key points of interest, which, as the second reviewer implies, in effect defines a programme of further research, contextualises it and

signposts how it may be pursued. We are, nevertheless, conscious that some of the signposts might be missing and others could be clearer, which we have endeavoured to address through additional referencing and clarifications in the text.

In response to specific comments:

In the section entitled 'Societal Considerations' we have revised the text to make it more precise and added supporting references to address the reviewer's concern about the vagueness of the claims.

In the section on 'Taking Responsibility' we have now added content to highlight the rich array of interactions that underlie behaviours not acceptable to the scientific community and areas to focus on when attempting to minimise such behaviours.

The review questions the value system that the paper implicitly references. The value system used in China to appraise what He Jiankui did is a standard that is also widely accepted by Western countries, although this is not meant to imply that it is a "Western standard". We have identified political, cultural and economic aspects that make the implementation of such standards difficult, but we did not imply that China is "alien" or "wide east" to an international value-system.

In relation to those who failed to speak out against He Jiankui, the paper points out that mechanisms are lacking on several sides: local oversight is lax or lacking; and, there is no global mechanism that could help rectify lax or lacking local oversight. He Jiankui's experiment could happen because of deficiencies on all sides.

We remain grateful for the attention and advice of the reviewers and hope that the revisions have addressed their concerns satisfactorily.

Competing Interests: N/A