

Reproductive genome editing and the U.S. National Academies Report: knocking on a closed door or throwing it wide open?

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In the United States, the recently reignited debate about inheritable genetic modification has been strongly shaped by the National Academy of Sciences (NAS) and the National Academy of Medicine (NAM), non-governmental organizations whose funding comes mostly from the federal government. In February 2017, a committee formed by NAS and NAM released a much-anticipated report, *Human Genome Editing: Science, Ethics, and Governance* [1]. The 310-page document, which made headlines in daily newspapers as well as scientific publications, recommended limitations on using gene editing for human reproduction, yet also concluded – in a striking departure from current widespread policy agreement, including legal prohibitions in dozens of countries as well as the Council of Europe’s Oviedo Convention – that “clinical trials using heritable germline genome editing should be permitted”.

The leaders of the committee that authored the report took pains to present it as a cautious and limited step. As MIT biologist Richard Hynes put it, “We say proceed with all due caution, but we don’t prohibit germline” [2]. Alta Charo, a bioethicist at University of Wisconsin-Madison, commented that reproductive genome editing “is not ready now, but ... if certain conditions are met, it might be permissible to try” [3].

Supporters of the long-standing view that inheritable genetic modification should remain off-limits evaluated the report differently. They emphasized both that the report represents a radical rupture with existing policy and public opinion, and that the stated intent to limit use of germline gene editing is unlikely to hold up. For example, the Center for Genetics and Society (CGS), a California-based public interest organization with which the authors of this viewpoint are affiliated, responded by stating, “Permitting human germline editing for any reason would likely lead to its escape from regulatory limits, to its adoption for enhancement purposes, and to the emergence of a market-based eugenics that would exacerbate already existing discrimination, inequality, and conflict” [4].

Most media coverage of the report included both points of view, though with far more attention to the NAS/NAM committee than to the scientists, bioethicists, and public interest advocates who criticized it. Also striking was the amount of confusion and uncertainty about

what the report actually says and means. For example, while *Science* titled its story “US Panel Gives Yellow Light to Human Embryo Editing” [5], *Ars Technica* chose “Genome-edited humans get green light from expert panel” [6]. Similarly, while *Science* quoted committee member Jeffrey Kahn, a bioethicist at Johns Hopkins University, as saying, “It’s frankly more of a knock on the door” [7], the *Wall Street Journal* titled its article, “Door Opens to Gene Editing in Embryos” [8]. Part of a larger trend, these examples reflect one of the major problems of the report: its ambiguity and vagueness.

In this commentary, we briefly outline some of the main problems of the NAS/NAM report, and argue that it throws the door wide open for reproductive human gene editing, with serious implications.

Not as cautious as it claims

Just how cautious is the NAS/NAM report? What real-world checks would its proposed restrictions provide? Let’s look at the very first item in the list of “criteria and structures” that the report recommends putting in place before clinical trials using heritable germline editing are permitted: an “absence of reasonable alternatives” [1, p. 7].

Most readers will assume this means that germline editing would be limited to cases in which all possible medical options for avoiding transmission of an unwanted genetic condition to a future child had been exhausted. To those familiar with the germline modification debate, this refers to the availability and relative safety of the embryo screening technique known as pre-implantation diagnosis (PGD). Though PGD, like germline editing, raises concerns about which genes and traits will be socially valued or devalued, it permits nearly all prospective parents who carry unwanted genetic disease variants to have children who are unaffected and genetically related to them, without the additional physical and societal risks of manipulating genes in gametes or early embryos [9].

Since the report gives no definition of the criterion “absence of reasonable alternatives”, one of us (Lowthorp) submitted a question to the panel of authors at the report’s official release event, asking whether it would be

satisfied by a person with moral objections to PGD. Committee member Robin Lovell-Badge of the Francis Crick Institute replied affirmatively that it would [10]. This is perhaps unsurprising, since other advocates of reproductive germline modification have ventured similar opinions, though none have addressed the questionable assumption that PGD would destroy more embryos than would gene editing. Lovell-Badge's reply illustrates that, at a minimum, the notion that the report's recommendations would limit germline modifications to a narrow range of cases is open to question. If an individual's moral belief can override any limitations included in guidelines, the report is far less cautious than its authors claim.

Erasing a bright line

The NAS/NAM report is characterized by another problematic rhetorical strategy: it repeatedly acknowledges, and then dismisses or undercuts, a range of concerns about germline modification that have been central to the long-standing discussion of it. This is most evident and consequential in the report's erasure of the bright line between somatic interventions that would affect existing patients, which are widely supported, and germline alterations that would be passed on to future generations, which are widely opposed.

One example of this acknowledge-and-dismiss strategy is the report's mention of, but scant attention to, the Oviedo Convention. Signed by thirty-five countries, the Convention establishes a clear distinction between somatic and germline interventions, prohibiting the latter. Despite the committee's charge to "identify principles that many countries might be able to use to govern human genome editing", its report refers to this key international treaty just twice in eight chapters – once in order to explain why it should not be considered influential [1, p. 132].

Another example can be found in a box titled "Making Distinctions" [1, p. 146]. Sketching a history of the classic schematic counterposing somatic vs germline interventions and therapeutic vs enhancement applications, the narrative briefly mentions the former while foregrounding the latter. In stating that, "[b]y the mid-1980s, scientists and bioethicists had begun to call for the morally relevant line to be between disease and enhancement rather than somatic and germline", the report fails to acknowledge that this call represented a decidedly minority viewpoint worldwide, both then and now.

The report's conclusion that germline editing should be permitted for therapeutic purposes replaces a bright line with one that most observers believe is conceptually murky and impossible to regulate: therapy vs enhancement [11]. The report itself references the "blurry boundaries of enhancement," and concedes that this distinction is "not rigid or easily discernible in

all cases" [1, p. 191, 192]. Similarly, it grants that "even the definition of what is considered a 'disease' can be open to debate" [1, p. 191] – though it nonetheless pairs "disease and disability" without caveat some two dozen times.

Denying democratic deliberation

The NAS/NAM report problematically departs not only from the laws of dozens of other nations, but also from a commitment recently made by the National Academies themselves. In December 2015, NAS and NAM collaborated with the Chinese Academy of Sciences and the UK Royal Society to organize the "International Summit on Human Gene Editing". At the end of the three-day event, the Summit organizing committee issued a statement stipulating that it would be irresponsible to proceed with germline editing for reproduction unless and until a "broad societal consensus" had been reached [12]. The statement called for "an ongoing international forum ... (that) should be inclusive among nations and engage a wide range of perspectives and expertise – including from biomedical scientists, social scientists, ethicists, health care providers, patients and their families, people with disabilities, policymakers, regulators, research funders, faith leaders, public interest advocates, industry representatives, and members of the general public".

While the meaning of these provisions can and certainly should be debated, the 2017 report dispenses with the idea of broad societal consensus altogether. Summit organizing committee member Françoise Baylis, Dalhousie University Professor and Canada Research Chair in Bioethics and Philosophy, observed that "with nary a word, the second element of the 2015 proposed ethics framework – broad societal consensus – has been jettisoned" [13]. In its place, the 2017 report substitutes its own judgment that germline gene editing should go forward, and limits public participation to questions such as which genetic modifications should or should not count as enhancements. In so doing, it effectively eviscerates democratic deliberation about whether human germline modification is acceptable in the first place.

Conclusion

In the instances sketched here and numerous others, the NAS/NAM report presents itself as cautious and incremental even while it radically shifts long-standing, internationally accepted policy conclusions and process commitments regarding human inheritable genetic modification. It repeatedly raises but then dismisses serious concerns – about the dubious nature of medical claims for germline gene editing's utility; the inadequacy of a biomedical ethics framework for con-

sidering a technology that could have significant social, cultural, and economic consequences; the unacceptable societal risk of creating a world of genetic “haves” and “have-nots”; and the implausibility of a policy regime built on a blurry and subjective distinction between “therapy” and “enhancement”. The report mentions a robust range of evidence and argument, but without explanation gives dramatically less weight to anything that might disrupt its support for pushing ahead toward human germline modification.

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10. See Lovell-Badge's comment at 1:28:25 of the release event video here: www.nationalacademies.org/gene-editing/consensus-study/index.htm (accessed 5/9/2017).
11. See Baylis F. Human germline genome editing and broad societal consensus. *Nature Human Behavior*. 2017; May 8;1:1.
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