

PERSPECTIVE

Heritable Human Genome Editing: The Public Engagement Imperative

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Abstract

In the view of many, heritable human genome editing (HHGE) harbors the remedial potential of ridding the world of deadly genetic diseases. A Hippocratic obligation, if there ever was one, HHGE is widely viewed as a life-sustaining proposition. The national go/no-go decision regarding the implementation of HHGE, however, must not, in the collective view of the authors, proceed absent thorough public engagement. A comparable call for an “extensive societal dialogue” was recently issued by the International Commission on the Clinical Use of Human Germline Genome Editing. In this communication, the authors lay out the foundational principles undergirding the formation, modification, and evaluation of public opinion. It is against this backdrop that the societal decision to warrant or enjoin the clinical conduct of HHGE will doubtlessly transpire.

Introduction

History is strewn thick with scientific leaps whose impact leave society reeling and searching for answers.¹ They follow a familiar pattern—there are bursts of innovation that are said to require revision of well-accepted maxims.¹ Years of contentious groping for a new world order invariably follow.¹ Fears of an “unnatural” dystopian future are rarely far behind.² Calls for a pause in the name of the precautionary principle soon bring up the rear.³ Examples of this pattern abound. Human reproductive cloning, human embryonic stem cells, and mitochondrial replacement therapy (MRT) have all marched down this road before. The application of heritable human genome editing (HHGE) to redress monogenic maladies (i.e., disease avoidance as opposed to enhancement) is but the latest case in point. It is against this backdrop that the National Academy of Medicine and the Royal Society resolved to convene the International Commis-

sion on the Clinical Use of Human Germline Genome Editing, the sweeping report of which gave rise to far-reaching recommendations.^{4,5} Relevant to this communication, the Commission called for “extensive societal dialogue ... before a country makes a decision on whether to permit clinical use of heritable human genome editing (HHGE).”^{4,5} An equally relevant call for “deliberation by a global citizens’ assembly” by an international contingent of authors followed suit.⁶

In the view of some, HHGE is best served by a moratorium until such time that a “broad societal consensus” has been attained.⁷ How such a consensus is to be reached, and how we are to know when and if it has been reached, remains unsettled. In this paper, we examine one conception of such a consensus—one that focuses on “public opinion.” To be sure it is only *one* potential way of thinking about this elusive consensus. Our aim in this paper is to show that this deceptively simple concept actually raises

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significant complexities, definitional and operational, as applied to HHGE that must be wrestled with if it is to become the touchstone for policy making.

Public Opinion

Long the subject of great interest, public opinion owes its exalted status to John Locke who ranked the “law of opinion” ahead of its divine and civil counterparts.^{8,9} Public opinion assumed added significance in the 18th century during which the American and French revolutions highlighted its significance relative to its monarchical counterparts. As seen by James Bryce, public opinion is the “aggregate of all that is thought and said on a subject” and thereby “omnipotent yet indeterminate.”¹⁰ It was not until the early 20th century, however, that the great debate between Walter Lippmann and John Dewey framed the central question as to the significance of public opinion: is the public capable of forming views of consequence to democracy, or is it incapable of rationally acquiring and processing information?^{11–14} Jurgen Habermas, for his part, characterized the public sphere as a “far-flung network of sensors” in which “streams of communication are ... filtered ... into bundles of topically specified public opinions.”¹⁵ From one-on-one conversations to email exchanges to online forums to public meetings, the citizenry is engaged astride an informal public sphere.

Still, how public opinion is in effect forged remains poorly understood. There is no sweeping unifying theory. A collective view of HHGE has yet to emerge from this complex multifactorial crucible. In the months and years to come, the public is certain to be buffeted by vigorous heuristic cues liable to contrast considerations of beneficence with value predispositions. Advocacy efforts on the part of patient groups, disease foundations, and professional associations are likely to be contravened by cultural, ethical, religious, and ideological opposition. Traditional mass and social media, not to mention interpersonal communications, are bound to play key roles as well. It is here that established science media centers and other trusted “influencers” could play a moderating role. The final synthesis of public opinion may well be left to the “rational public,” the ultimate verdict of which and the timeline thereof cannot be predicted with any degree of accuracy.¹⁶ It is against this backdrop that we now consider rival conceptions of “public opinion” and what they might mean for HHGE: the participatory public, the present public, and the future public.

The Participatory Public

Scientific paternalism, the coin of the realm for much of human history, is incompatible with and suspicious of public participation. It follows that the framing of public

opinion on all matters science was heretofore bereft of scientific input. It was this state of affairs which John Dewey deemed asinine given his conviction that “lay deliberation and technical expertise can enrich each other.”¹⁷ At least three reasons undergird the import of public input on all matters science. The first is political: a hostile or distrusting public may refuse to accept the benefits that science may be in a position to offer. The second is ethical: members of the public bring important and distinctive values to bear on decisions about the development or use of science. The third is pragmatic: in a democratic society, science policy, no less than economic, social, or foreign policy, should enjoy the consent and support of the public and its representatives.

It was not until recently that the desirability of public participation in the formulation of *science policy* was articulated in the United States. Making the case to a congressional committee in 1971, Sen. Walter F. Mondale (D-MN) noted that “We need public participation if we are to develop consensus as to how society should deal with these profound problems.”¹⁸ Nobel Laureate James D. Watson, speaking in concurrence, noted that novel technologies are “...not a question for a group of scientists to decide ... It is a decision which the people as a whole must make.”¹⁹ Similar sentiments were articulated in the wake of the 1975 Asilomar Conference on recombinant DNA, the limited public engagement of which was widely noted. Leading the way was Sen. Edward M. Kennedy (D-MA) who noted that “When science develops techniques that ... fundamentally change society, society has the right to determine how the technique is to be used, whether it should be developed in the first place, and if so, under what constraints.”²⁰ Similar sentiments were enunciated by Sen. Jacob K. Javits (R-NY) at the 1976 Airlie House Conference.²¹ Several subsequent reports of the National Academies of Sciences, Engineering, and Medicine proved equally supportive.^{22–26} The above notwithstanding, stateside progress proved sparse.

Despite the importance of public engagement to the adjudication of HHGE, efforts to this end remain limited.²⁷ It was against this backdrop that Professor Sheila S. Jasanoff saw the need to emphasize that “the issue ... is no longer *whether* the public should have a say in technical decisions, but *how*...”²⁸ In this context, further research may be required if public engagement is to be equitable and inclusive—hearing from all relevant stakeholders in a way that empowers them to understand the science and articulate their views.²⁹ Drawing on the vision of the Nuffield Council on Bioethics, consideration could be given to a “commission ... independent of government ... [to] produce an understanding of public

interest(s) through promotion of public debate.”³⁰ It is in this context that the Center for Public Engagement with Science & Technology of the American Association for the Advancement of Science could take the lead.³¹

It would be easy enough to say that scientific condescendence that distances itself from and disparages the public should be avoided as at odds with the values of democracy. No one wants to be condescended to. At the same, we cannot ignore the fact that what is in the public interest is not the same thing as what the public is interested in. All cutting-edge science, gene editing no less, is fractal in its complexity. It would be too easy to suggest that we should leave the scientific questions (such as the matter of embryonic mosaicism) to the scientists while leaving values questions (such as whether it is immoral to engage in genome editing to avoid diseases that produce childhood fatalities) to the public. There are also what one might think of as truly “mixed” questions where the right approach is to equip the public better to understand and engage with the science to answer the values questions—the risks of generating embryonic mosaicism by HHGE is a good example.

The Present Public

Nearly a decade since its discovery as a gene-editing tool, CRISPR has proven omnipresent in both scientific and lay outlets. Touted as the leading breakthrough of the century and as a major driver of the fourth industrial revolution, CRISPR is widely acknowledged for its therapeutic promise. Through it all, matters of safety and efficacy as well as an assortment of ethical, legal, and sectarian qualms were extensively aired. The subject of international summits, international commissions, committee reports, and position statements, HHGE is never far from the daily news feed. This bounty notwithstanding, the U.S. public, heretofore limited to heuristic shortcuts rather than to reliable scientific input, remains ill-prepared to formulate its views. The public’s opinion formation in this area has been compromised by the failure of the scientific community to convene or actively engage the present public in robust deliberation. What precious little is known of the views of the present public on HHGE draws on recent opinion polls such as the one by the Pew Research Center.³² Deliberative efforts or Big Data approaches have yet to be applied to this end. As a result, little is known at this time as to the shape of a potential consensus and its policy implications.

The Future Public

With a few exceptions, history bears out the notion that the arc of public opinion is rarely stationary. Rather, it is in a constant state of evolution toward a new steady

state. In some instances, past societal schisms eased toward mutual accommodation, if not conciliatory resolution. Other equally contentious discords persist in resisting closure. It is here that the generational churn assumes an all-important role. As baby boomers give way to generations X, Y, Z, and their successors, attitudes and outlooks evolve. Emerging libertarian and secular leanings often lead the way. In the process, once seemingly irreconcilable notions may, against all odds, go mainstream. The timeline of such self-sorting if enigmatic transformations is subject matter specific and, as such, unascertainable. In all matters reproduction, not least the new reproductive technologies, progression toward public acceptance has proven especially challenging. The contentious transition of *in vitro* fertilization (IVF) from pariah to standard of care comes to mind. Whether HHGE will follow a similar evolutionary path remains to be seen. The latest Pew Research Center poll suggests that accelerated secularization and growing scientific literacy are likely to favor public acceptance of HHGE.³² Yet another future public is the one whose views are unknowable, since it has yet to be born. Important as this challenge might be, it is hardly reproduction specific. Climate change poses similar dilemmas. Grossly imperfect redress of this conundrum may well require that the present public engage in difficult questions—well beyond the purview of science—as to what their future descendants might need, want, or indeed be owed.

The Affective Public

While much of the discussion thus far has pertained to intellectual engagement of the public, affective responses are also important. For those who have tried to sway the public in the past on new reproductive technologies, combining the powers of pathbreaking innovation has been a winning (though opponents might criticize “unfair”) strategy. The promise of reducing if not eliminating the scourge of unintended pregnancies blazed the trail for female contraception. Aided and abetted by women’s suffrage and the rising tide of feminism, the Pill affirmed the power of empathetic utilitarianism. Vanquishing the bane of barrenness won the day for IVF. Sectarian concerns notwithstanding, IVF came to be seen for what it is: a family-building pro-life medical technology. With new reproductive technologies, the connection to beneficence is more complicated and in particular the distinction between producing new children versus helping existing ones. Here, the intersection between the technical details of the ways in which gene editing or MRT are carried out, philosophical debates about the continuity of identity, and religious or folk conceptions of ensoulment may prove particularly difficult to reconcile for the public.

The Polled Public

Non-deliberative opinion polls are by far the most common method to gauge and capture the views of the public. Pioneered in the first part of the 20th century by George H. Gallup, polls typically involve the administration of a survey to a representative sample of the public. As such, polls are widely used by journalists, marketers, and social scientists to name a few. The resultant “crowd wisdom” and the actionable insights so derived frequently end up guiding public policy. Expressed as opinion ratios within confidence intervals, the aggregative data of public polls also dominate the forecasting of public preferences such as election outcomes. No longer limited to the erstwhile obligatory person-to-person contact, opinion polls presently resort to multiple modes of telecommunication. Increasing reliance on Internet-based polling is particularly noteworthy. Plagued by sampling limitations, framing flaws, ignorance, disinterest, and inattention, opinion polls must be interpreted with care. One important criticism of opinion polls is that respondents often offer “non-attitudes” to pollsters because their underlying views are unstable.³³ Furthermore, when it comes to complex topics or those that have escaped sustained public attention, individual responses are unlikely to have benefitted from information, reflection, and judgment.³⁴ The aforementioned imperfections notwithstanding, the bent of public opinion polls must not be dismissed or ignored as a potential driver of public action. A similar admonition applies to recent public polls on the matter of HHGE. The latest Pew Research Center poll reveals that the majority of adults in the United States support the “changing of a baby’s genes to treat a serious congenital disease.”³² A comparable majority, however, hold the view that the “testing of human embryos” in the course of relevant research would “take the technology too far.”³²

The Networking Public

In a departure from past practices, present day “sentiment analysis” is making increasing use of social media. Useful as this approach may well be, its utility must be moderated by the reality that the views of active social media users may differ from those of the public at large. Represented by vast archives (e.g., Twitter feeds), crowdsourced Big Data is being subjected to analysis by novel paradigms reliant on computational linguistics. Deep machine learning, natural language processing, and text classification methods constitute leading examples of this new wave. Deployed over a finite time span, this approach can give rise to a sequential high-resolution imprint of the public opinion under study. Similar approaches are bound to be applied to platforms

such as Reddit, the focus of which is on social news aggregation, web content rating, and web-based discussions. Here too, great care is required in the interpretation of the results due to the concurrence of unvetted, indeed false informational input. A recent example of this novel paradigm imputed the public views of CRISPR using tweets only in the English language generated over the period 2013–2019.³⁵ The results suggest significant fluctuations in the public sentiment index in response to widely publicized CRISPR-related developments.³⁵ One such shift was evident in reactions to news accounts of the birth of twins whose genomes were said to have been edited in China.³⁵ This shift in public sentiment illustrates a thread common to all of the conceptions of public opinion, that is, it is not just the *how* but the *when* that drives the collective communal verdict. It follows that any serious attempt to gauge the views of the public on matters such as HHGE must be the subject of multiple iterations to capture different slices of the “when” and the “who.”

The Deliberative Public

Deliberative democracy, a leading example of government by the people, has risen to assume a weighty role in the valuation of public opinion.^{36–38} Building on the principles of discourse and collective reasoning, this leading school of democratic theory rests on the epistemic and reflective virtues of expert-mediated face-to-face deliberation. It is in this public space that long-held views of a pluralistic society may be revised through contestatory civic engagement. A newly forged enhanced state of mutual understanding often emerges as it might in the course of jury deliberations. Meant to inform policy makers, this enriched communal “discursive turn” relies on reflective “considered judgments” as envisaged by John Rawls.³⁹ Commonly deployed “mini-publics” include deliberative polling, consensus conferences, citizens’ juries, or citizen panels to name a few. These and other deliberative democracy constructs are increasingly ensconced in the process of governing. The Canadian biobanking research initiatives comprise one such successful example.⁴⁰ In some locales, deliberative democracy constructs have been effectively codified into law. The Irish Citizens’ Assembly constitutes one such shining national example of deliberative constitutional reform.⁴¹ The Oregon Citizens’ Initiative Review, for its part, enables state-level deliberation.⁴² The United States has yet to apply the principles of deliberative democracy to the question of HHGE. The United Kingdom, in contrast, has concluded one such “deliberative public dialogue” on behalf of the Royal Society.⁴³

Concluding Thoughts

Now limited to preclinical research by a prohibitive federal statute, the conduct of HHGE in the United States may well be at the mercy of the mutable arc of public opinion, the trajectory of which is unknowable.⁴⁴ Eventual public acceptance of HHGE may well follow if it can be shown to have a unique and favorable impact on the global burden of incurable genetic disease. Such a trajectory would be further buttressed by the plight of parents and their children, which is universally resonant and hard to ignore. Medical science has, after all, been down this road before. Standing in opposition to the prospect of HHGE are deep-rooted misgivings over runaway technological progress that is liable to shatter millennia-old societal norms. Additional concerns draw on the prospect of liberal eugenics, access inequities, imponderable impairment, and progeny-related harm. Reconciling the conflicting views of the current steady state will require time, perhaps generational time, before the dust settles. In the interim, it is nothing short of imperative that HHGE be subjected to the rigors of public deliberation along the lines applied to MRT and related reproductive technologies.⁴⁵ What is called for is informed public judgment that has accounted for both the relevant concerns and the potential to advance human welfare.

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