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Enhanced threat or therapeutic benefit? Risk and benefit perceptions of human gene editing by purpose and heritability of edits

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ABSTRACT

Public discourse and deliberation are key to developing socially responsible and acceptable human gene editing research and applications. Researchers have raised concerns, however, that discourse about heritable gene edits, especially for non-therapeutic (or enhancement) purposes, might negatively bias public opinion of applications, including non-heritable edits to cure or prevent disease. Yet limited research exists examining how information about different gene editing applications elicits different perceptions of the technology. Using a U.S.-representative sample and survey-embedded experiment, we tested how exposure to information about different types of edits affects support and perceptions of benefits, risks, and moral acceptability of human gene editing. We randomly assigned respondents to a control or to an experimental condition in which they read information about one of four broad types of potential applications: (1) heritable edits for enhancement; (2) heritable edits for therapy; (3) non-heritable edits for enhancement; (4) non-heritable edits for therapy. Respondents then answered questions tapping multiple dimensions of support for and risk/benefit perceptions of human gene editing. Our results indicate partial evidence that exposure to information about heritable and/or enhancement edits colors perceptions of human gene editing more broadly but also that support for therapeutic edits is robust. Participants who read information about therapy edits perceived human gene editing in general more favorably in terms of benefits, risks, and moral acceptability than did participants who read about enhancements. Exposure to information about therapy versus enhancement edits, however, did not significantly influence support for therapy edits in particular. Heritability of edits had significant influence only on perceived risk, with heritable edits triggering higher risk perceptions. Interestingly, heritability seems to primarily affect views of risk of gene editing but not views of benefits, moral acceptability, or levels of support. We did not find differing effects depending on whether heritable edits were for therapy or enhancement.

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Introduction

Rapid advances in human gene editing research are outpacing the development of responsible guidelines to govern research and applications in the field (National Academy of Sciences and National Academy of Medicine 2017; Jinek et al. 2013). The field of human gene editing has moved particularly fast since the discovery of the advanced gene editing tool CRISPR-Cas9 and realization of its potential as a tool for humans in 2013 (Jinek et al. 2013; Jinek et al. 2012). Its advances have also generated considerable discussion and debate over potential risks and benefits (e.g. Jasanoff, Hurlbut, and Saha 2015; National Academy of Sciences and National Academy of Medicine 2017).

Discussions among scientists and scientific advisory institutions about how to govern new human gene editing technologies tend to make strong distinctions between different categories of applications along two dimensions: (1) edits that are non-heritable (i.e. somatic cell edits) versus heritable (i.e. germ cell edits); and (2) edits for therapy (i.e. preventing or curing disease) versus for enhancement purposes (e.g. improving memory or physical appearance) (Lanphier et al. 2015; Nature Biotechnology Editorial Board 2015; Nature Genetics Editorial Board 2017; National Academy of Sciences and National Academy of Medicine 2017). In a 2017 report on human gene editing, the National Academy of Sciences (NAS) and National Academy of Medicine (NAM) advised that all gene editing aimed at enhancements be indefinitely put on hold. With respect to therapy edits they made a distinction between non-heritable and heritable edits. They recommended that research into non-heritable edits for therapy proceed, while giving a cautious yellow light to research into heritable edits for therapy (National Academy of Sciences and National Academy of Medicine 2017). Heritable germline editing for therapy would only be considered acceptable if there were no 'reasonable alternatives' and with 'strict oversight' and 'maximum transparency' (National Academy of Sciences and National Academy of Medicine 2017, 7).

But in 2018 the scientific community was shocked when news leaked that Chinese biophysicist He Jiankui used germline editing to create the first gene-edited babies with the hope of protecting them from HIV (Regalado 2018). He's editing experiment was widely condemned as 'crazy' and 'risky and medically unnecessary' by scientists and scholars in China and abroad (Greely 2019; Ruwitch 2019; Johnson 2018, 2019). After news of the twins' birth broke, 18 scientists and ethicists representing seven countries called for a global moratorium on germline editing (Lander et al. 2019), a call supported by the U.S. National Institutes for Health (F.S. Collins 2019). Similarly, the World Health Organization (2019) called on all countries to prohibit any experiments that might result in the birth of gene-edited babies.

Taboos within the science community around enhancement and heritable edits are driven by concerns about ethical research practices and relative benefits and risks, but also by concerns that such edits could negatively impact views of, and support for, human gene editing more broadly. In a story about germline editing Jennifer Doudna, a co-discover of CRISPR, told a reporter 'one of the worst-case scenarios is having a public backlash against this powerful tool that has so much positive potential' (Mullin 2019). Many scientists worry about the potential for heritable and enhancement edits to sour public attitudes toward human gene editing generally and undermine support for other applications, including therapy applications (e.g., Baltimore et al. 2015; Lanphier et al. 2015; Otieno 2015; Mittal 2019). Such worries include concerns that media coverage of human gene editing might help stoke these negative perceptions. Even before the 'He fiasco' (Greely, 2019) media coverage often linked enhancement and heritable germline edits with negative visions of a world of 'designer babies,' a new era of eugenics, and other dystopian futures (Economist Editorial Board 2015; Kozubek 2017; Weintraub 2015).

To date, there is little empirical evidence to validate or refute concerns about particular types of edits or information about those edits negatively biasing public opinion, and very little research that explicitly examines public perceptions of heritable edits at all. Further, although public attitudes toward human gene editing are likely to be defined by a complex range of

perceptions about risks, benefits, and ethical concerns, researchers have focused primarily on the acceptability of, or support for, edits depending the purpose of the application, rather than capturing a range of relevant risk and benefit perceptions. This study, therefore, was designed in response to the limited body of research examining risk and benefit perceptions related to particular types of human gene editing, as well as to the scientific community's concern that perceptions about one use of the technology could color perceptions of other uses.

In this study, we use an experiment embedded in a representative survey of the U.S. residents to test whether exposure to information about different types of gene editing applications results in more or less favorable attitudes toward human gene editing more broadly. In particular, we test for distinctions that emerge in perceptions depending on whether that application is for therapeutic or enhancement purposes and whether it is heritable or not. We are interested in whether and how exposure in information about these different potential edits triggers particular attitudes and risk and benefit perceptions concerning human gene editing.

Risk perceptions of human gene editing

Although the body of research on public views of human gene editing in particular is small, especially in the years since the advent of CRISPR (Delhove et al. 2020; Howell et al. 2020), previous studies of genetic engineering more broadly indicate that public perceptions of the risks of genetic engineering do vary by application. For example, people tend to perceive medical applications as less risky than food applications (Savadori et al. 2004; Frewer, Howard, and Shepherd 1997; Frewer and Shepherd 1995). Frewer and Shepherd (1995) suggest people may perceive medical applications as less risky because the risks of using those applications are evaluated relative to the alternative risk of not receiving treatment. In contrast, food-related applications may seem riskier because edits to food are not seen as addressing a particularly salient hazard. A similar logic might shape people's views of enhancement versus therapy applications of human gene editing. Enhancement could be seen as creating a potential unnecessary health risk in an otherwise healthy individual. On the other hand, people may view human gene editing applications for therapy as less risky compared to the alternative of not receiving treatment.

How people evaluate risks can also be influenced by a hazard's 'personality' profile. Decades of psychometric research has identified key hazard characteristics important in shaping perceived risk (Slovic 1987; Sparks and Shepherd 1994; Finucane and Holup 2005). In particular, two main dimensions can drive risk perceptions: the extent to which a hazard is (1) unknown and (2) dreaded. The unknown risk dimension (known vs. unknown) reflects the extent to which a hazard is unobservable, unfamiliar, and has delayed consequences. The dread risk dimension (not dreaded vs. dreaded) reflects the extent to which the hazard is viewed as uncontrollable, fatal, inequitable, putting future generations at risk, being not easily reduced, involuntary, and being potentially catastrophic (Finucane and Holup 2005).

Given this previous research, it seems likely that heritability concerns could play an important role in how people evaluate the risks of human gene editing. Human gene editing already exhibits characteristics consistent with the unknown and dread dimensions. As a relatively new science—and one now developing at a faster rate than ever before due to the discovery of CRISPR—the risks involved in human gene editing are poorly understood compared to many other medical procedures. Furthermore, any inadvertent harmful changes made to a person's DNA may not be immediately obvious, resulting in delayed consequences. People may also tend to perceive human gene editing as risky along the dread dimension given that the consequences could be fatal.

Applications of human gene editing that are heritable (germline editing) seem likely to amplify risk perceptions along both dimensions. Along the unknown dimension, unforeseeable consequences include both risks to the individual as well as risks involved in reshaping human

evolution. Further, any possible negative consequences would not be limited by an individual's lifetime but might not manifest for a generation or more—resulting in more extreme delay in possible consequences. Along the dread dimension, heritable edits put future generations at risk, and impose risk on individuals involuntarily. Furthermore, the heritability of edits reduces controllability, as harmful consequences would no longer be limited to a single individual and could also, therefore, seem more potentially catastrophic.

Benefit perceptions of human gene editing

As with perceptions of risk, perceptions of the benefits of emerging technologies also vary by application. Benefit perceptions of emerging technology applications, for example, tend to be higher for medical applications than for food applications (Frewer, Howard, and Shepherd 1997; Frewer and Shepherd 1995; Savadori et al. 2004). This and other examples from past research suggest modifications or interventions that are perceived of as more necessary or as having a direct benefit for consumers tend to be perceived as more beneficial overall. For example, researchers have found higher perceived benefits for artificial sweeteners than for artificial colors in food (Bearth, Cousin, and Siegrist 2014) and higher perceived benefits for modifications in staple foods than in 'fun foods' (Dean et al. 2007). Given this past research, it seems likely that perceived benefits will be greater for therapeutic than enhancement edits.

It is less clear how heritability might influence benefit perceptions. On the one hand, individuals might perceive the benefits of gene editing as greater if those benefits can be passed on to future generations, rather than limited to an individual. On the other hand, if heritability increases perceptions of risk, as the literature cited earlier suggests it well could, that may cause people to discount any perceived benefits. Individuals' perceptions of risk tend to negatively correlate with their perceptions of benefit (Alhakami and Slovic 1994; Frewer, Howard, and Shepherd 1998). Furthermore, heritability may undermine factors associated with higher benefit perceptions, such as familiarity (Fischer and Frewer 2009) and perceived control (Siegrist et al. 2008).

Public attitudes toward human gene editing

There is a growing body of research on public attitudes toward human gene editing (for a review see: (Delhove et al. 2020), especially across therapeutic versus enhancement edits. This body of research has found less favorable attitudes toward human gene editing applications used for enhancement purposes than for those used for therapy purposes (Scheufele et al. 2017; STAT and Harvard T. H. Chan School of Public Health 2016; Funk, Kennedy, and Sciupac 2016; Gaskell et al. 2017; AP-NORC 2018; Funk and Hefferon 2018). In particular, many studies focus on levels of support and find lower acceptance and support for enhancement compared with therapeutic applications (Scheufele et al. 2017; AP-NORC 2018; Funk and Hefferon 2018; Critchley et al. 2018) In a Pew Research Center survey, for example, 72% and 60% of Americans viewed human gene editing as acceptable when used for treating or preventing disease, but only 19% viewed human gene editing to enhance intelligence as acceptable (Funk and Hefferon 2018). Research reveals a similar pattern in moral evaluations of therapeutic and enhancement edits (AP-NORC 2018; Gaskell et al. 2017). In a survey of the U.S. and European residents, for example, respondents viewed altering genes for enhancement purposes as less morally acceptable compared with altering genes for therapeutic purposes (Gaskell et al. 2017).

Relative to research comparing attitudes toward therapeutic versus enhancement edits, research comparing attitudes toward non-heritable versus heritable edits are in its infancy (Howell et al. 2020). Several types of cells can be edited in a way that would alter characteristics in a child and their descendants. Heritable edits can take place in the cells of an early-stage

embryo, or further upstream in eggs, sperm, or the cells that give rise to eggs and sperm (National Academy of Sciences and National Academy of Medicine 2017). Previous studies examining how attitudes differ depending on cell type include studies comparing attitudes toward somatic versus embryonic cell edits (e.g., Gaskell et al. 2017; McCaughey et al. 2016; Critchley et al. 2018; Hendriks et al. 2018). Unfortunately, many of these studies rely on convenience samples and therefore cannot be generalized to broader populations (e.g., McCaughey et al. 2019; McCaughey et al. 2016; Hendriks et al. 2018).

Those studies that do rely on representative samples suggest people in the Western nations hold less favorable views of edits in embryos or 'unborn children' compared with somatic cell edits. Gaskell et al. (2017) found that the U.S. and European residents viewed altering genes in an unborn child less morally acceptable than altering genes in an adult, although the study did not explicitly clarify for participants whether edits to either would be heritable or not. A survey in Australia found similar attitudinal differences: respondents indicated greater support on average for somatic cell versus embryonic cell edits across a range of applications (Critchley et al. 2018).

Although edits in early stage-embryos can result in heritable edits, studies that ask respondents about embryonic cells are somewhat limited in what they can tell us about how heritability concerns might influence attitudes toward human gene editing. As Critchley et al. (2018) point out, by focusing on questions involving the editing of embryonic cells, research results may confound concerns about heritability with other factors. In particular, there are religious and moral values attached to embryos (Allum et al. 2017) that may be shaping perceptions of edits in embryos or in 'unborn children' beyond opinions about the heritability of those edits.

Very little research asks about heritable edits without priming respondents to think about embryos or unborn children. However, studies conducted thus far suggest that people might not necessarily give a lot of weight to heritability concerns in their evaluations of human gene editing when they are not asked about embryonic editing in particular. Scheufele et al. (2017), for example, found similar levels of support for non-heritable and heritable edits among Americans when asking about edits to a hypothetical child. The Critchley et al. (2018) study surveyed Australians about their support for somatic, embryonic, and germ cell editing across a range of applications—including edits for therapeutic, enhancement, and research purposes. The distinction between germ and embryonic cell edits had a stronger influence on support overall (more support for germ cell edits), than the distinction between germ and somatic cell edits (more support for somatic edits), suggesting that the moral associations with the word or ideas of 'embryo' and edits to embryo were a larger factor in shaping people's views of edits than are concerns about heritability per se.

Evidence from the Critchley et al. (2019) and Scheufele et al. (2017) studies provides better footing for beginning to understand how concerns about heritability—separate from concerns related to embryos—may influence attitudes toward human gene editing. However, their analyses are limited to examining how heritability influences support. An examination of how heritability influences other attitudinal dimensions, including perceptions of the risks, benefits, and the moral acceptability of human gene editing would provide a more nuanced understanding of heritability concerns. This more nuanced understanding could in turn, help researchers better anticipate how attitudes may shift in response to new developments in research, policy, or news coverage of human gene editing.

Current study

As we discuss in the introduction, many researchers are concerned that enhancement edits—and particularly heritable enhancement edits—could result in less favorable perceptions of human gene editing in general and set back public support for research on non-heritable, therapeutic

applications (Lanphier et al. 2015; Nature Biotechnology Editorial Board 2015; Mittal 2019). To our knowledge, however, research has not yet tested whether exposing individuals to information about one particular type of edit (e.g. enhancement edits) might shape subsequent evaluations about other types of edits (e.g. therapy), or evaluations of human gene editing more generally.

To address this gap in the research, we designed an experiment in which we assigned participants to either a control group that received no additional information on human gene editing or to an experimental group, in which participants read one of four vignettes manipulated to highlight therapy or enhancement edits and non-heritable or heritable edits. We then tested the influence of exposure to the different edits in the vignettes on a wide range of attitudinal measures. These outcome variables include measures of support and perceived moral acceptability, as well as multiple measures of perceived risk and benefit at societal and individual levels.

Based on our review of the risk and benefit literature and human gene editing public opinion literature, we pose the following two broad hypotheses. First, we expect that study participants exposed to information about therapeutic edits would indicate more positive views about and more support for human gene editing than will participants exposed to information about enhancement edits (Hypothesis (1). Second, we expect that participants exposed to information about heritable edits will indicate more negative views about and less support for human gene editing than will participants exposed to information about non-heritable edits (Hypothesis 2). Finally, we also explore whether any influence of exposure to information about heritable or non-heritable edits will differ depending on whether those edits are for enhancement or therapeutic purposes, testing whether there is an interaction between heritability and purpose of edits (Research Question 1).

Methods

Participants

The data used for this study are from an experiment embedded in an online survey of 1,600 U.S. adults conducted by YouGov in December 2016 and January 2017 (completion rate (AAPOR RR6): 41.7%; (Callegaro and Disogra 2008)). To ensure representativeness across sociodemographic characteristics, YouGov matched respondents to a sampling frame based on gender, age, race, education, political ideology, party identification, and political interest. The sampling frame was constructed using stratified sampling from the Census Bureau's 2010 American Community Survey. Matched cases were weighted to the sampling frame based on propensity scores. Before the survey was distributed, study approval was obtained from the researchers' home institution's Institutional Review Board. Descriptives comparing survey respondents with the U.S. Census demographic data are in Table1.

Study design

We tested our hypotheses and research question with a 2 (therapeutic vs. enhancement) x 2 (heritable vs. non-heritable) between-subjects factorial design. At the beginning of the survey, all respondents received a brief definition of human gene editing and CRISPR-Cas9 in general (see Supplementary material). We randomly assigned respondents to one of our four experimental conditions and a control group. In the experimental groups, respondents were assigned one of four vignettes about possible types of human gene editing. The vignettes ranged from 135-164 words in length and each described one of four possible human gene editing applications representing our experimental conditions: (1) heritable edits for enhancement; (2) heritable edits for therapy; (3) non-heritable edits for enhancement, and; 4) non-heritable edits for therapy (see Supplementary Table 1).

Prior to receiving the vignette, participants in the experimental conditions read the following transition: 'So far we have been talking about gene editing more broadly. Please carefully read the following statement about a specific example of one of the leading possibilities of gene editing technology use.' After reading the vignette, participants first answered question items included to measure support for human gene editing for therapeutic purposes and for enhancement purposes. Participants then answered question items designed to measure perceptions about the moral acceptability, risks, and benefits of human gene editing.

Measures

Measures of perceived risk

We included three measures related to risk perceptions, including perceived: (1) societal risk; (2) personal risk; and (3) likelihood of negative outcomes. We measured societal and personal risk separately because information intake can have distinct effects on perceptions of societal risk compared to perceptions of personal risk (Coleman 1993; Tyler and Cook 1984). We measured perceived societal risk with a single item asking participants how risky they thought human gene editing would be for 'society as a whole' ($M = 3.4$; $SD = 1.09$). Similarly, we measured perceived personal risk by asking participants how risky they thought human gene editing would be for 'you personally' ($M = 2.6$; $SD = 1.39$). Responses to both of these questions were measured using a five-point scale ranging from 1 = 'not at all risky' to 5 = 'very risky.' We measured the perceived likelihood of risky outcomes due to human gene editing as the averaged response to three question items, asking participants how likely they thought it would be that human gene editing will: (1) lead to unintended health problems; (2) lead to discrimination against those who are or are not genetically edited; and (3) give some people too much power to change the course of human development. These items were developed based on possible risks of human gene editing identified in the scientific and scholarly literature (e.g., Nature Biotechnology Editorial Board 2015; Jasanoff, Hurlbut, and Saha 2015; Klein 2018). Responses were measured on a seven-point scale ranging from 1 = 'not at all likely' to 7 = 'certain'. There was good inter-item reliability ($\alpha = .80$; $M = 4.5$; $SD = 0.27$).

Measures of perceived benefit

Mirroring the risk perception variables, we included three measures of perceived benefit that captured perceived: (1) societal benefit; (2) personal benefit; and (3) likelihood of beneficial outcomes. We measured perceived societal benefit with a single item asking participants how beneficial they thought human gene editing would be for 'society as a whole' ($M = 2.9$; $SD = 1.13$). Similarly, we measured perceived personal benefit by asking participants how beneficial they thought human gene editing would be for 'you personally' ($M = 2.2$; $SD = 1.17$). Responses to both of these questions were measured using a five-point scale 1 = 'not at all beneficial' to 5 = 'very beneficial.' We measured the perceived likelihood of beneficial outcomes due to human gene editing as the averaged response to three items. We asked participants how likely they thought human gene editing will: (1) help fix human health problems and diseases; (2) remove stigmas around birth defects and genetic diseases; and (3) improve the economy through medical and research advances. As with the specific risk items, these were developed based on possible risks of human gene editing identified in the scientific and scholarly literature (e.g., Achenbach 2016; Doudna and Sternberg 2017; National Academy of Sciences and National Academy of Medicine 2017). Responses were measured on a seven-point scale ranging from 1 = 'not at all likely' to 7 = 'certain' ($\alpha = .81$; $M = 4.0$; $SD = 0.57$).

Table 1. Demographic characteristics of survey sample (2016–2017) compared to national U.S. population (2016–2018).

Characteristics	U.S. population[†]	Survey sample
Gender	50.8	52.5
% female		
Race	60.7	68.2
% white		
Education	87.3	95.4
% High school & above	30.9	26.5
%Bachelor's & above		
Income	$57,652	$40-49,000
Median; household		

[†]From U.S. Census Bureau (United States Census Bureau 2019). Education percent include only persons 25 years old or more. Age not included because available census data does not include separate information on central tendencies for only adults.

Moral acceptability and measures of support

Moral acceptability of human gene editing was measured using a single item asking respondents how much they agree that, 'Human gene editing is morally acceptable.' Responses measured on a seven-point scale ranging from 1 = 'strongly disagree' to 7 = 'strongly agree' ($M = 4.1$; $SD = 1.63$). Our study includes two single-item measures of support for human gene editing, support for gene editing for enhancement and support for gene editing for therapy. We measured support for therapy by asking respondents how much they agreed that 'Overall, I support the use of human gene editing to treat human medical conditions or restore health' ($M = 4.8$; $SD = 1.63$). We measured support for enhancements by asking respondents how much they agreed that 'Overall, I support the use of human gene editing to enhance or improve human abilities' ($M = 3.8$; $SD = 1.74$). Responses measured on a seven-point scale ranging from 1 = 'strongly disagree' to 7 = 'strongly agree.'

Experimental condition effects were captured with two dummy variables, one representing our therapy versus enhancement manipulation and the other representing our non-heritable versus heritable manipulation. For the first dummy variable, vignettes highlighting *therapy* edits were coded as '1' and those highlighting *enhancement* edits as '0.' For the second dummy variable, vignettes highlighting *non-heritable* edits were coded as '1' and those highlighting *heritable* edits as '0.'

Data analysis

To test our hypotheses, we ran a two-way ANOVA predicting each outcome variable. In each two-way ANOVA, we tested the main effects of each factor: (1) therapy or enhancement genetic editing; (2) non-heritable or heritable genetic editing; and (3) the interaction effect of the two factors. Partial effect sizes η^2 were reported for the significant effects. Due to our larger sample size, we evaluated our results using a more conservative significance level, interpreting only those results with an alpha equal to or less than 0.01. Analyses were conducted with the software SPSS Version 25 by IBM.

Prior to analyses, we removed respondents in experiment groups who spent less than 1.5 seconds on the vignette – the time it would take to quickly skim the main, bolded points of the vignette and click to the next page. We also removed cases that spent extremely long amounts of time on the vignettes to help ensure that respondents had not left the stimulus to do something else before completing the survey, which could weaken or skew the responses. We used Tukey's method for addressing outliers to set bounds, cutting times that were than 1.5 times IQR (Inter-Quartile Range) above the upper quartile, which resulted in removing respondents who spent longer than 34 minutes on the vignette (Tukey 1977). The final sample included in analyses was N = 1484.

Table 2. Risk variables by gene edit purpose (therapy v. enhancement) and heritability (non-heritable v. heritable).

	F	*Df*	*P*	η^2
Perceived societal risk				
Therapy	8.986	1	0.003	0.008
Non-heritable	9.422	1	0.002	0.008
Therapy × non-heritable	0.990	1	0.320	0.001
Perceived personal risk				
Therapy	5.244	1	0.022	0.005
Non-heritable	9.569	1	0.002	0.008
Therapy × non-heritable	1.028	1	0.311	0.001
Perceived likelihood of risky outcomes				
Therapy	1.792	1	0.181	0.002
Non-heritable	17.204	1	0.000	0.015
Therapy × non-heritable	2.849	1	0.092	0.003

Note: Results are considered statistically significant at a p-value of .01 or less.

Results

Overall, the results provide support for Hypothesis 1, partial support for Hypothesis 2, and no evidence of interaction effects between purpose and heritability of edits (RQ1). For clarity, we divide the results into the differences in (1) risk perceptions (Table 2), (2) benefit perceptions (Table 3), and (3) moral acceptability and support (Table 4). We also include a table with average responses across each condition, including the control, to illustrate whether receiving a particular vignette increased or decreased perceptions relative to not receiving any additional information on human gene editing (Table 5).

Risk perceptions

The ANOVA results indicated a significant main effect of the therapy versus enhancement manipulation on one of the three risk outcome variables, providing some support for Hypothesis 1. The perceived societal risk of human gene editing was lower among participants assigned to read a vignette highlighting therapy edits compared with participants who read a vignette highlighting enhancement edits (Table 2). Results showed a main effect of the heritable versus non-heritable edits manipulation on all three risk outcome variables, supporting Hypothesis 2. Perceived personal and societal risks of human gene editing was lower among participants assigned to read a vignette highlighting non-heritable edits compared with participants who read a vignette highlighting heritable edits. Participants in the non-heritable edits condition also perceived human gene editing as less likely to result in negative outcomes. None of the interactions significantly influenced any risk perception measures, indicating there were not distinct effects of therapy- versus enhancement-focused information depending on the heritability of the edits described (RQ1).

Benefit perceptions

In our second set of analyses, we tested the effect of the experimental conditions on the variables measuring benefit perceptions (Table 3). The results support Hypothesis 1. The perceived personal and societal benefits of human gene editing were higher among participants assigned to read a vignette highlighting therapy edits compared with participants who read a vignette highlighting enhancement edits. Participants in the therapy edits condition also perceived human gene editing as more likely to result in beneficial outcomes. The results do not support Hypothesis 2, as we did not find any main effect of heritability on benefit perceptions. We also did not find any significant interaction effects between purpose of edits and heritability on benefit perceptions (RQ1).

Table 3. Benefit variables by gene edit purpose (therapy v. enhancement) and heritability (non-heritable v. heritable).

	F	*Df*	*P*	η^2
Perceived societal benefit				
Therapy	9.599	1	0.002	0.009
Non-heritable	2.269	1	0.132	0.002
Therapy × non-heritable	2.854	1	0.091	0.003
Perceived personal benefit				
Therapy	23.485	1	0.000	0.015
Non-heritable	4.347	1	0.074	0.003
Therapy × non-heritable	2.028	1	0.222	0.001
Perceived likelihood of beneficial outcomes				
Therapy	18.265	1	0.000	0.016
Non-heritable	0.004	1	0.951	0.000
Therapy × non-heritable	0.393	1	0.531	0.000

Note: Results are considered statistically significant at a p-value of .01 or less.

Table 4. Moral acceptability and support variables by gene edit purpose (therapy v. enhancement) and heritability (non-heritable v. heritable).

	F	*Df*	*p*	η^2
Moral acceptability				
Therapy	30.1	1	0.001	0.010
Non-heritable	11.3	1	0.039	0.004
Therapy x non-heritable	0.1	1	0.839	0.000
Support gene editing for therapy				
Therapy	2.0	1	0.160	0.002
Non-heritable	0.1	1	0.921	0.000
Therapy x non-heritable	1.1	1	0.305	0.001
Support gene editing for enhancement				
Therapy	30.5	1	0.000	0.026
Non-heritable	1.1	1	0.296	0.001
Therapy x non-heritable	0.1	1	0.702	0.000

Note: Results are considered statistically significant at a p-value of .01 or less

Moral acceptability and support

In our third and final set of analyses, we tested the effect of our manipulations on moral acceptability, support for enhancement gene editing, and support for therapeutic gene editing. The results for moral acceptability only support Hypothesis 1 (Table 4). The perceived moral acceptability of human gene editing was higher among participants who had been assigned to read a vignette highlighting therapy edits, compared with those assigned to read a vignette highlighting enhancement edits.

As for support for enhancement and therapeutic gene editing, the results revealed a main effect of the therapy versus enhancement manipulation on support for enhancement but not on support for therapy, providing partial support for Hypothesis 1 (Table 4). Individuals indicated more support for enhancement edits when exposed to a vignette highlighting therapeutic gene edits than if they were exposed to a vignette highlighting enhancement gene edits. Support for therapeutic edits, however, was high regardless of what information respondents received, compared to the control that did not receive any additional information on gene editing (see Table V for mean responses across each condition). Those higher levels of support for therapeutic edits did not significantly differ across the experimental conditions.

The results did not reveal a significant effect of the heritable versus non-heritable manipulation on either support for therapy or support for enhancements (H2). The results also did not reveal any significant interactive effects between purpose and heritability of edits on responses to the support variables (RQ1).

Table 5. Mean response levels on each outcome variable by experimental condition.

Condition ***Outcome variable***		Therapy non-heritable	Enhancement non-heritable	Therapy heritable	Enhancement heritable	Control
Support & Acceptability	***Support treatment*** Mean (*s.d.*) *7-point scale* *1 = strongly disagree; 7 = strongly agree*	4.95 (*1.66*)	4.74 (*1.61*)	4.84 (*1.59*)	4.78 (*1.69*)	4.53 (*1.56*)
	Support enhancement Mean (*s.d.*) *7-point scale* *1 = strongly disagree; 7 = strongly agree*	4.09 (*1.78*)	3.61 (*1.71*)	4.08 (*1.73*)	3.41 (*1.81*)	3.67 (*1.58*)
	Moral acceptability Mean (*s.d.*) *7-point scale* *1 = strongly disagree; 7 = strongly agree*	4.39 (*1.61*)	4.11 (*1.61*)	4.18 (*1.58*)	3.86 (*1.78*)	3.95 (*1.52*)
Risk	***Societal risk*** Mean (*s.d.*) *5-point scale* *1 = not at all risky; 5 = very risky*	3.22 (*1.02*)	3.33 (*1.10*)	3.32 (*1.13*)	3.59 (*1.10*)	3.38 (*1.08*)
	Personal risk Mean (*s.d.*) *5-point scale* *1 = not at all risky; 5 = very risky*	2.47 (*1.28*)	2.55 (*1.35*)	2.64 (*1.43*)	2.89 (*1.52*)	2.66 (*1.35*)
	Likelihood of specific risk outcomes Mean (*s.d.*) *7-point scale* *1 = not at all likely; 7 = certain*	4.37 (*1.16*)	4.35 (*1.44*)	4.53 (*1.32*)	4.81 (*1.31*)	4.54 (*1.25*)
Benefit	***Societal benefit*** Mean (*s.d.*) *5-point scale* *1 = not at all beneficial; 5 = very beneficial*	3.18 (*1.09*)	2.85 (*1.18*)	2.97 (*1.17*)	2.85 (*1.07*)	2.84 (*1.10*)
	Personal benefit Mean (*s.d.*) *5-point scale* *1 = not at all beneficial; 5 = very beneficial*	2.42 (*1.17*)	2.07 (*1.12*)	2.22 (*1.23*)	2.02 (*1.16*)	2.18 (*1.12*)
	Likelihood of specific benefit outcomes Mean (*s.d.*) *7-point scale* *1 = not at all likely; 7 = certain*	4.15 (*1.15*)	3.92 (*1.31*)	4.22 (*1.30*)	3.86 (*1.16*)	3.81 (*1.27*)

Mean responses to each dependent variables within each condition are listed in Table V, to illustrate the direction of the differences in average responses to each risk, benefit, and support variables across the experimental conditions, as well as how they compared to the control condition (in which participants did not read any of the vignettes).

Discussion

This experimental study was motivated in part by concerns among scientists that human gene editing applications developed for enhancement purposes – and especially heritable enhancement edits – could undermine support for somatic cell therapeutic edits and result in less favorable attitudes toward human gene editing generally (e.g., Baltimore et al. 2015; Lanphier et al. 2015; Otieno 2015; Mittal 2019). Our study provides partial support for this concern but also revealed robust support for therapy edits among participants regardless of what information they received about a particular edit. Participants who began our experiment by reading a vignette highlighting enhancement and/or heritable edits indicated less favorable views of the risks, benefits, and moral acceptability of human gene editing, compared with participants reading a vignette highlighting therapy and/or non-heritable edits. But when asked specifically about support for therapeutic edits, participants remained supportive, regardless of which human gene editing vignette they were exposed to. Further, support for therapeutic edits was higher across all experimental conditions compared to the control, suggesting that even information about enhancement edits can increase support for therapeutic edits, perhaps by making therapeutic edits look even better in comparison.

This study also contributes to the limited empirical data available on how public attitudes are influenced by heritability concerns when no reference is made to fetuses or unborn children. Our results show that whether a vignette highlighted non-heritable or heritable edits influenced three measures of risk perception, but not perceived benefits, moral acceptability, or support. Interestingly, we found little overlap in the attitudinal measures influenced by the non-heritable/heritable distinction and the therapy/enhancement distinction.

Before we explain our findings in greater detail and discuss implications, several limitations should be considered in interpreting our findings. First, our results yielded small effect sizes. This is not surprising, given that we only exposed people to a single instance of information about human gene editing. A longitudinal study involving repeated message exposure would likely better capture real-world conditions and result in larger effect sizes but would require larger investment in resources.

We should also note that we cannot with full confidence clearly identify the causal mechanism explaining our results. One possible explanation for why our experimental conditions influenced subsequent measures is priming. Priming occurs when exposure to a word, idea, or other stimulus sets the stage for how we evaluate subsequent stimuli. Different vignettes may have primed different negative and/or positive associations in the minds of participants. These associations could then set the stage for subsequent evaluations of therapy and enhancement edits and of human gene editing more generally (A.M. Collins and Loftus 1975). Because human gene editing is an emerging issue that few members of the U.S. public are likely to be highly familiar with, attitudes about human gene editing could be especially susceptible to such priming effects (Cacciatore, Scheufele, and Corley 2011; Zaller and Feldman 1992).

Alternatively, it is possible that participants may have interpreted some questions—questions about the risks, benefits, and moral acceptability of human gene editing—as referring to the particular type of edit highlighted in the vignette that they read. Following the vignette, all participants first answered questions asking about their support for enhancement and support for therapy. Subsequent questions about risks, benefits, and moral acceptability asked respondents about 'human gene editing' more broadly, without any mention of the edits being enhancement, therapy, or heritable. Although we designed these questions to measure participants evaluations of human gene editing *in general*, we cannot dismiss the possibility that participants interpreted them as referring to the edit highlighted in the vignette that they read. Future research could try to make the general nature of these questions more explicit or instead ask about risks, benefits, and moral acceptability in relation to specific edits.

Finally, this study was conducted before news leaked about He's experiment creating the world's first gene edited babies in China—a pivotal event in the field of human gene editing, generating widespread news coverage (Belluck 2018; Qiu 2019; Stein 2018; Regalado 2018). Public opinions may have shifted in response to this announcement and other developments that have occurred since we collected our data. Similarly, the COVID-19 pandemic could influence views of edits if the idea of developing new therapies and disease resistance is more salient. Even as major events have reshaped the public discourse around human gene editing, our results, first, provide useful baseline data that researchers can compare with similar future studies to help gauge how Americans' attitudes change over time, and before and after the birth of He's gene edited babies. Second, our experimental results highlight relationships between information exposure and attitudinal measures that can help researchers understand and anticipate how the American public may respond to pivotal events in the field such as the 'He fiasco' depending on, for example, whether such events make moral, benefit, or risk dimensions more salient. Finally, it also does so by helping fill the gap in our understanding of how heritability in particular can affect views of human gene editing.

He created gene edited babies with edits in early-stage embryos. Results from previous public opinion studies suggest that there is less support for and greater moral concern regarding gene edits in embryonic cells than somatic cell edits (Gaskell et al. 2017; Critchley et al. 2018). But what if He had created gene edited babies with germ cell edits in eggs or sperm rather than fetuses? In a survey of Australians, Critchley et al. (2018) found that heritable embryonic cell edits reduced support for gene editing applications more than did heritable germ cell edits that did not involve embryos. Meanwhile, the distinction between (non-embryonic) heritable germ cell and somatic cell edits played a much smaller but still significant role in influencing support.

Our study builds on this previous research by examining the links between heritable edits and a wide range of attitudinal measures—particularly with a focus on several measures of the perceived risks and benefits of human gene editing and on perceived moral acceptability. Results show that the distinction between non-heritable and heritable edits in our experimental vignettes influenced only perceptions of the risks. Compared with vignettes highlighting non-heritable edits, vignettes highlighting heritable edits appear to have made risk concerns more salient in the minds of study participants. Participants exposed to a vignette highlighting heritable edits evaluated human gene editing as riskier for society and themselves and as more likely to result in negative outcomes.

Heritability did not significantly influence other attitudinal measures. Average benefit perceptions and moral acceptability were somewhat higher among participants exposed to a vignette highlighting non-heritable edits, compared with those exposed to a vignette highlighting heritable edits (Table 5), but these differences were non-significant (Tables 2 and 3). Previous survey research has found lower moral acceptability for edits in unborn children than somatic cell edits (Gaskell et al. 2017). However, our study asked participants about heritable edits without priming them with questions about fetuses or unborn children, a difference that might help separate views of germline editing from views of research involving embryos (Critchley et al. 2018).

Our second experimental condition, which manipulated whether a vignette highlighted therapy or enhancement edits, influenced a wider range of attitudinal measures. Vignettes about therapy edits resulted in more favorable views of human gene editing across three measures of benefit perceptions, one out of three measures of risk perceptions, and perceived moral acceptability. The fact that the therapy/enhancement distinction influenced a wide range of attitudinal measures—and especially perceptions of the benefits of human gene editing—is consistent with the large body of research that consistently show higher levels of support for therapy edits, compared with enhancement edits (e.g., Scheufele et al. 2017; AP-NORC 2018; Funk and Hefferon 2018; Critchley et al. 2018). The consistent findings regarding increased perceptions of the benefits of gene editing among respondents exposed to information on therapeutic edits is striking, however, as previous research suggests that benefit perceptions can, in some respects, be more

important than risk perceptions in influencing support for controversial science and technologies, such as genetically modified crops (Gaskell et al. 2004).

Overall, our findings suggest that researcher concerns that germline enhancement edits might negatively bias public opinion toward human gene editing are partially supported but could be somewhat overstated. In particular, we found support for therapy was robust among participants. Regardless of which vignette participants read, support for therapy wavered little across the experimental conditions and even increased relative to support among those who did not receive any additional information in the control condition. On the other hand, we found support for enhancements exhibited more variability in response to the vignettes. Participants who read a vignette on therapy were significantly more supportive of enhancement edits than participants who read a vignette about enhancement edits (Table 4). Average mean support among the four experimental groups and control group (Table 5) suggest the therapy vignettes boosted support for enhancements more than the enhancement vignettes decreased support relative to the control group.

Our results therefore did not provide evidence supporting the idea that heritable or enhancement edits might decrease support for somatic cell therapies, but instead suggest therapy edits could soften opposition to possible enhancement applications. This finding would seem to provide at least some evidence in support of concerns raised by critics that the adoption of therapy edits could create a 'slippery slope.' According to the slippery slope argument, the adoption of therapy applications could create a social climate of acceptance for the wider adoption of gene editing for other purposes including edits aimed at enhancements (Walton 2017; Evans 2018). The line between therapy and enhancement edits is already notoriously blurry. Commentators often point to preventative health edits, such as reducing vulnerabilities to alcoholism or the consequences of a poor diet, as ambiguous examples (Baylis 20192018). Some commentators have also suggested the type of edits carried out in He's experiment might be considered enhancement (So et al. 2017; Regalado 2018). He's edits were aimed at conferring resistance to HIV—a trait not typical in the general human population—rather than treating a disease. Our findings suggesting that the adoption of therapy edits may soften opposition to less widely accepted edits have important implications for the policy and lawmakers who have to decide where to draw the line on what gets publicly defined as 'therapy' and 'enhancement.'

We need much more research into how differences in the public information landscape might influence perceptions of and support for human gene editing. The results of this study contribute important early insights to this area by helping researchers better understand how different dimensions of human gene editing could shape individual considerations of the technology, particularly through risk and benefit perceptions concerning the future that human gene editing could create. We need additional research, and particularly representative correlational studies and experimental studies and studies from beyond the U.S. These will be necessary to continue filling in a more complete picture of views of particular edits, how information on particular edits shapes perceptions, and how these effects vary across different individual value orientations and experiences. Such insights in these areas of public views of gene editing across heritability and purposes of edits also need to keep pace with advances and events in the human gene editing field could rapidly shift public discourse on the issue. This understanding of the dimensions of public discourse and the public attitude landscape concerning human gene editing will be key to ensuring that research and applications correspond to public values and preferences.

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