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ARTICLE

Genetics experience impacts attitudes towards germline gene editing: a survey of over 1500 members of the public

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Abstract

CRISPR-Cas9 has revolutionised genome engineering and has the potential to radically change our approach to genetic disease. However, the potential for genetic modification of embryos has raised significant and complex ethical and social concerns. The scientific community have called for ongoing stakeholder consultation about Germline Gene Editing (GGE), in particular lay publics, to help guide policy, education, research and regulatory priorities. In response, we conducted a survey to gauge public support for GGE and describe the demographic, experiential and contextual factors that influence individual attitudes. Respondent support was measured across nine hypothetical medical and enhancement GGE applications. We received responses from 1537 participants across 67 countries. Respondents were generally supportive of GGE, particularly for medical applications. While the most opposition observed was among religious respondents, those with work experience in genetics or genomics also reported greater resistance to GGE. Personal or family-related experience with genetics or genomics, identifying as female and tertiary education were also associated with less support for GGE. Further research needs to explore a diverse range of community and group attitudes towards GGE; the reasons underlying demographic and experiential differences; and to determine where the public and genetics professionals draw the line on ethical implementation respectively.

Introduction

Medicine is on the brink of major change, with cutting-edge advances in genetic biotechnology promising new and powerful ways to understand and change our DNA. Recently discovered, the CRISPR-cas9 (clustered regularly interspaced short palindromic repeat–CRISPR-associated protein) gene editing system can cleave double-stranded DNA at a specific site and exploit DNA repair mechanisms to alter genomic sequences [1]. Compared with alternative genome-editing methods, CRISPR-Cas9 allows more precise and efficient modification of DNA, and offers higher fidelity and efficiency at lower cost [2]. As such, CRISPR-cas9 has great potential to not only treat but also to prevent disease and disability. Furthermore, by altering specific DNA sequences or repairing pathogenic variants in embryos, CRISPR-Cas9 can make heritable changes to the human germline. Combined with advances in our understanding of genotype-phenotype relationships, germline gene editing (GGE) may provide medicine with the means to reduce rates of multigenerational genetic disease and disability.

While its potential therapeutic applications are compelling, gene-editing poses unprecedented ethical and scientific challenges. Firstly, the safety of CRISPR-cas9 is uncertain, with early research that targeted disease-causing genes in human embryos resulting in undesirable and unintended off-target effects and mosaicism [3–5]. Despite this, CRISPR-Cas9 has already been used for reproductive applications in humans. In 2018, Dr He Jiankui and colleagues, announced they had overseen a project which used CRISPR to edit the CCR5 gene (involved in HIV transmission), in viable IVF embryos. This project resulted in the birth of twin girls [6]. These researchers have been widely condemned [7] for ignoring the lack of societal consensus,

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and proceeding with unregulated, unnecessary and potentially unsafe human studies [8]. Yet, with a third gene-edited baby rumoured to have been born in China and clinical applications anticipated in Russia [9], human GGE seems to be proceeding whether the international community is ready or not.

Consequently, there is mounting urgency to develop regulatory and ethical standards that ensure safe and appropriate use of GGE. Yet, the scientific community remains divided on how best to proceed. Some have argued that GGE poses an unpredictable, existential threat to future generations [10] and social harmony [11], and view the potential for irreversible and unintended consequences as unacceptable [12, 13]. Some have even proposed an indefinite moratorium until guiding principles are established and the ethical issues are resolved [10, 14]. On the other hand, some assert that once safe, it is wrong to withhold technology that holds such therapeutic and economic promise for individuals, families and society [15, 16].

Consideration of stakeholder attitudes through comprehensive community consultation about issues with such far reaching consequences is an important step in a sound pre-implementation process and the development of policy and research priorities [17]. Previous research exploring stakeholder perspectives on GGE indicates that the public generally support its use for medical purposes [18–23]. However, further exploration is required to characterise the impact of individual experiences with genetics and socio-demographic factors on attitudes. Where the public 'draw the line' on the permissibility of explicit GGE applications also remains unclear.

Alongside the mandate for public consultation, there is a need for engagement and exploration of evolving public perspectives over time [18, 19, 21]. Such considerations are especially important in the wake of Dr He Jiankui's use of CRISPR, which generated worldwide media coverage and greatly increased public awareness of GGE. It is crucial for researchers to better understand the ethical limits of the wider community to avoid violating moral boundaries and prevent rejection of gene editing altogether [24].

To address this gap in knowledge, this study used an online survey to explore public perspectives worldwide on nine specific applications (both therapeutic and enhancement in nature) of GGE, in order to clarify the limits on its ethical permissibility and examine how experiences with genetics or genomics may impact public perspectives.

Materials and methods

A cross-sectional 38-item online survey was designed to explore public attitudes on the acceptability of potential applications of GGE. A short educational video, embedded at the beginning of the survey, was used to illustrate how the CRISPR-Cas9 gene editing system works (See Supplementary Report). To minimise dropout rates, the survey was designed to take no longer than 10–15 min to complete. Survey design and refinement involved seven iterations by the study's researchers followed by a pilot study with 21 voluntary participants. Questionnaire wording and branching logic were modified in response to feedback prior to study recruitment.

Demographic data collected included gender, religiosity, ethnicity, highest level of education, country of residence and parental status. We also asked whether participants had either personal/familial, or work-related experience with genetics or genomics.

Questionnaire items were grouped under two broad categories: therapeutic applications (items 1–5) and enhancement applications (items 6–9) (See Supplementary Report). For example: 'To what extent do you agree with using germline gene editing to prevent the development of untreatable diseases that begin in early childhood and that lead to death before they reach adulthood?'

Participants were asked to answer the questions on the basis that GGE was safe, accurate, and effective. For each item, participants were asked the degree to which they agreed with the proposed application of GGE using a five-point Likert scale—1: 'strongly disagree' to 5: 'strongly agree'. The middle option, 'unsure', was used to encourage continued responses from those who did not wish to reveal, or were uncertain of, their attitudes. Questionnaire items followed with a free-text space to invite participants to explain their answers.

The web-based questionnaire was available to individuals with internet access. Individuals were invited to participate in the study by social media, including via twitter and Facebook posts promoted by the University of Melbourne and the Murdoch Children's Research Institute. Physical fliers were also posted throughout universities and hospitals in the local area. Only those over the age of 18 with English comprehension were encouraged to complete the questionnaire.

Participants implied consent if they agreed to the consent statement prior to commencing the survey. Responses to the survey were anonymous and could not be withdrawn. This study was approved by The Royal Children's Hospital Human Research Ethics Committee, Melbourne.

Data analysis

Statistical analysis was conducted using STATA 16. Survey responses were included if the first section of the questionnaire was attempted. All responses to survey questions, including demographic and experiential variables, were summarised.

Country of residence data was grouped by frequency into the following geographical categories: 'United States of America', 'Australia and New Zealand', 'Canada', 'United Kingdom', 'Europe' and 'Other'.

A Pearson's correlation was used to test for correlations between participant characteristics, and Q–Q plots to confirm non-normal distribution of Likert data for non-parametric tests. Demographic groups were modified for summary and non-parametric analysis. Age was collapsed into two groups: 'under 44 years of age' and 'over 45 years of age' for Mann–Whitney *U* (MWU) testing to determine direction of mean rank shift; and three groups for summary statistics. Highest Level of Education was collapsed into two groups: 'Tertiary' and 'Non-Tertiary'. 'Personal or Family Experience with Genetics or Genomics' and 'Work Experience with Genetics or Genomics' were each collapsed into two groups: 'Yes' and 'No/Unsure'

For summary analyses, responses were averaged over items 1–5 to describe attitudes towards 'therapeutic applications', and over items 6–9 to describe attitudes towards 'enhancement applications' of GGE.

MWU and Kruskal–Wallis H (KWH) tests were used to determine differences between independent participant groups where the dependent variable was the ordinal Likert data per questionnaire item.

To run the MWU test, nominal categorical variables (demographic variables with no intrinsic rank or order) were transformed into a dichotomous variable by division into two mutually exclusive, independent groups (n_1 and n_2). The test was undertaken to determine whether one group (n_1) showed more or less support for the proposed GGE application than the alternate group (n_2) by calculating and comparing the mean Likert ranks of each group.

Similarly, a KW test was performed to compare the mean ranks of multiple independent variable groups (i.e. age groups, gender and country of residence).

Results

Participants

Data was collected between June 2019 and August 2019. 2101 individuals consented to participate by progressing to the first section of the survey. Participants who did not attempt the first section of the questionnaire were considered missing data ($n = 554$, 26.4%).

Participants were from 67 countries with the majority of respondents from the United States of America ($n = 567$, 36.63%); Australia ($n = 494$, 31.91%); Canada ($n = 103$, 6.65%) and the United Kingdom ($n = 100$, 6.46) (See Table 1). Respondents largely identified as white ($n = 1346$, 86.95%).

Table 1 Participant demographics and experiences

Variable	Frequency	Percent
Gender ($n = 1549$)		
Male	625	40.35
Female	882	56.94
Prefer not to disclose	38	2.45
Other	4	0.26
Country of residence ($n = 1549$)		
United States of America	567	36.63
Australia	494	31.91
Canada	103	6.65
Countries in the United Kingdom	100	6.46
Other	285	18.35
Age group ($n = 1548$)		
18–24 years old	272	17.46
25–34 years old	548	35.17
35–44 years old	396	24.42
45–54 years old	204	13.09
55–64 years old	100	6.42
65–74 years old	36	2.31
75 years or older	2	0.13
Highest level of education ($n = 1548$)		
Tertiary	1,359	87.23
Secondary	195	12.52
Primary	3	0.19
Other	1	0.06
Children ($n = 1537$)		
Yes	592	38.27
No	945	60.65
Prefer not to disclose	10	0.64
Religiosity ($n = 1537$)		
A religious person	230	14.87
Not a religious person	1317	85.13
Personal or family experience with genetics or genomics ($n = 1537$)		
Yes	470	30.38
No	920	59.47
Unsure	157	10.15
Work experience with genetics or genomics ($n = 1537$)		
Yes	379	24.50
No	1143	73.88
Unsure	25	1.62

Demographic and experiential impacts on attitudes

No evidence of a difference in attitudes by geographical location was found ($p > 0.05$) (see Table 2).

Overall, younger participants were more supportive of the proposed GGE applications. There was a significant difference in attitudes ($p < 0.05$) between participant age groups in five of the nine questionnaire responses.

Table 2 Kruskal–Wallis *H* test to determine influence of demographic and experiential factors on participant attitudes

Domain and Questionnaire Item	Gender			Age			Country of residence		
	χ^2	df	*p*	χ^2	df	*p*	χ^2	df	*p*
Therapeutic applications of germline gene editing									
To what extent do you agree with using germline gene editing…									
… to prevent the development of untreatable diseases that begin in early childhood and that lead to death before they reach adulthood?	52.839	3	0.0001[a]	27.239	6	0.0001[a]	74.377	66	0.2243
… to prevent the development of treatable diseases that begin in childhood, generally do not lead to death before 40–50 years of age, but require lifelong, invasive treatment?	79.138	3	0.0001[a]	20.694	6	0.0021[a]	78.582	66	0.1379
… to prevent the development of untreatable and fatal diseases that begin in adulthood and lead to a slow decline in the ability to think and function normally?	65.666	3	0.0001[a]	19.326	6	0.0036[a]	77.834	66	0.1512
… to prevent the development of treatable and non-fatal conditions that begin in adulthood that involve changes to mood and behaviour that can affect day-to-day life (such as depression or schizophrenia)?	48.411	3	0.0001[a]	16.583	6	0.0109[a]	68.596	66	0.3894
… to prevent a child being born with a disability, such as blindness or deafness?	102.823	3	0.0001[a]	11.795	6	0.0667	74.106	66	0.2308
Enhancement applications of germline gene editing									
To what extent do you agree with using germline gene editing…									
… to enhance resistance to infectious diseases (such as HIV or malaria)?	70.940	3	0.0001[a]	33.133	6	0.0001[a]	64.166	63	0.4354
… to enhance physical traits (such as improving vision or sports performance)?	188.890	3	0.0001[a]	10.939	6	0.0903	74.517	63	0.1520
… to enhance mental/psychological traits (such as increased intelligence)?	199.041	3	0.0001[a]	12.491	6	0.0681	78.545	63	0.0896
… to alter an individuals' traits such as empathy, tolerance or self-discipline?	81.314	3	0.0001[a]	7.543	6	0.3178	62.445	63	0.4960

χ^2 value with ties reported; a χ^2 distribution greater than the critical value of χ^2 when $p < 0.05$ indicates rejection of H_0: There is no difference in mean rank of Likert scores between groups (i.e. age groups) for each questionnaire item

df (degrees of freedom) $= k - 1$, where $k =$ number of groups within the demographic variable

[a]Indicates statistical significance ($p < 0.05$) and rejection of H_0

Outcomes of a MWU test showed that mean Likert ranks for participants ≤44 years old were higher than those aged ≥45 years old (see Table 3), indicating that a younger participant (≤44 years old) is more likely to demonstrate support for GGE than an older one (≥45 years old).

A KWH test showed evidence of a difference in attitudes between gender groups for all questionnaire items (see Table 2). Male-identifying participants demonstrated more support for GGE overall. It was not possible to describe non-binary attitudes due to small subsample size ($n = 4$).

Tertiary educated participants were less supportive of all applications of GGE and mean ranks of attitudes in this group were lower ($p < 0.05$) for eight of the nine questionnaire items (see Table 3).

Mean ranks of religious participant attitudes ($p < 0.001$) and parents ($p < 0.05$), were lower for all questionnaire items (see Table 3), demonstrating that religious participants and parents were less supportive of all uses of GGE.

Personal or family-related experience with genetics or genomics was also associated with reduced support for GGE ($p < 0.05$) (see Table 3).

Similarly, the attitudinal mean ranks of (see Table 3) participants with work-related experience with genomics showed significantly less support for GGE across all questionnaire items ($p < 0.001$) (see Figs. 1 and 2).

Discussion

This study provides evidence of the growing acceptance of GGE as a medical technology by the public, mediated by intended application and demographic factors. It also highlights an emerging divide between the attitudes of the general public and those with experience in genetics and/or genomics.

Attitudes influenced by application

Supporting prior research, attitudes towards GGE depend on the intended use [20, 21]. Support for GGE is higher when used to improve health and prevent disease, and opposition to GGE is highest when used for enhancement and cosmetic purposes in otherwise healthy individuals

Table 3 Mann–Whitney *U* Tests to determine influence of demographic and experiential factors on participant attitudes

Domain and Questionnaire Item	Highest level of education n_1: tertiary n_2: non-tertiary			Religiosity n_1: a religious person n_2: not a religious person		
Therapeutic applications of germline gene editing	*n*	*p*	$P\ (n_1 > n_2)$	*n*	*p*	$P\ (n_1 > n_2)$
To what extent do you agree with using germline gene editing…						
… to prevent the development of untreatable diseases that begin in early childhood and that lead to death before they reach adulthood?	n_1: 1216 n_2: 176	0.0305[b]	0.460	n_1: 204 n_2: 1188	0.0000[b]	0.377
… to prevent the development of treatable diseases that begin in childhood, generally do not lead to death before 40–50 years of age, but require lifelong, invasive treatment?	n_1: 1215 n_2: 176	0.0025[b]	0.439	n_1: 204 n_2: 1187	0.0000[b]	0.341
… to prevent the development of untreatable and fatal diseases that begin in adulthood and lead to a slow decline in the ability to think and function normally?	n_1: 1215 n_2: 176	0.0386[b]	0.460	n_1: 204 n_2: 1187	0.0000[b]	0.364
… to prevent the development of treatable and non-fatal conditions that begin in adulthood that involve changes to mood and behaviour that can affect day-to-day life (such as depression or schizophrenia)?	n_1: 1214 n_2: 176	0.0549	0.458	n_1: 204 n_2: 1186	0.0000[b]	0.335
… to prevent a child being born with a disability, such as blindness or deafness?	n_1: 1213 n_2: 176	0.0086[b]	0.445	n_1: 204 n_2: 1185	0.0000[b]	0.348
Enhancement applications of germline gene editing						
To what extent do you agree with using germline gene editing…						
… to enhance resistance to infectious diseases (such as HIV or malaria)?	n_1: 1178 n_2: 173	0.0047[b]	0.438	n_1: 199 n_2: 1152	0.0000[b]	0.339
… to enhance physical traits (such as improving vision or sports performance)?	n_1: 1178 n_2: 173	0.0002[b]	0.415	n_1: 199 n_2: 1152	0.0000[b]	0.332
… to enhance mental/psychological traits (such as increased intelligence)?	n_1: 1178 n_2: 173	0.0000[b]	0.391	n_1: 199 n_2: 1152	0.0000[b]	0.329
… to alter an individuals' traits such as empathy, tolerance or self-discipline?	n_1: 1177 n_2: 173	0.0005[b]	0.421	n_1: 199 n_2: 1151	0.0000[b]	0.338

Domain and Questionnaire Item	Personal or family experience with genetics or genomics n_1: yes n_2: no/unsure			Work experience with genetics or genomics n_1: yes n_2: no/unsure		
Therapeutic applications of germline gene editing	*n*	*p*	$P\ (n_1 > n_2)$	*n*	*p*	$P\ (n_1 > n_2)$
To what extent do you agree with using germline gene editing…						
… to prevent the development of untreatable diseases that begin in early childhood and that lead to death before they reach adulthood?	n_1: 430 n_2: 962	0.0191[b]	0.469	n_1: 342 n_2: 1050	0.0000[b]	0.434
… to prevent the development of treatable diseases that begin in childhood, generally do not lead to death before 40–50 years of age, but require lifelong, invasive treatment?	n_1: 429 n_2: 962	0.0024[b]	0.456	n_1: 341 n_2: 1050	0.0000[b]	0.429
… to prevent the development of untreatable and fatal diseases that begin in adulthood and lead to a slow decline in the ability to think and function normally?	n_1: 429 n_2: 962	0.0278[b]	0.469	n_1: 341 n_2: 1050	0.0000[b]	0.431
… to prevent the development of treatable and non-fatal conditions that begin in adulthood that involve changes to mood and behaviour that can affect day-to-day life (such as depression or schizophrenia)?	n_1: 428 n_2: 962	0.0174[b]	0.463	n_1: 340 n_2: 1050	0.0000[b]	0.405
… to prevent a child being born with a disability, such as blindness or deafness?	n_1: 428 n_2: 961	0.0000[b]	0.435	n_1: 399 n_2: 1050	0.0000[b]	0.410
Enhancement applications of germline gene editing						
To what extent do you agree with using germline gene editing…						
… to enhance resistance to infectious diseases (such as HIV or malaria)?	n_1: 418 n_2: 933	0.0005[b]	0.445	n_1: 330 n_2: 1021	0.0000[b]	0.398
… to enhance physical traits (such as improving vision or sports performance)?	n_1: 418 n_2: 933	0.0006[b]	0.444	n_1: 330 n_2: 1021	0.0000[b]	0.401

Table 3 (continued)

Domain and Questionnaire Item	Personal or family experience with genetics or genomics n_1: yes n_2: no/unsure			Work experience with genetics or genomics n_1: yes n_2: no/unsure		
Therapeutic applications of germline gene editing	n	p	$P\ (n_1 > n_2)$	n	p	$P\ (n_1 > n_2)$
… to enhance mental/psychological traits (such as increased intelligence)?	n_1: 418 n_2: 933	0.0007[b]	0.444	n_1: 330 n_2: 1021	0.0000[b]	0.391
… to alter an individuals' traits such as empathy, tolerance or self-discipline?	n_1: 418 n_2: 932	0.1061[b]	0.473	n_1: 330 n_2: 1020	0.0000[b]	0.427
Domain and Questionnaire Item	Parental status n_1: Children n_2: No children			Age n_1: ≤44 years old n_2: ≥45 years old		
Therapeutic applications of germline gene editing	n	p	$P\ (n_1 > n_2)$	n	p	$P\ (n_1 > n_2)$
To what extent do you agree with using germline gene editing…						
… to prevent the development of untreatable diseases that begin in early childhood and that lead to death before they reach adulthood?	n_1: 546 n_2: 846	0.0000[b]	0.442	n_1: 1069 n_2: 323	0.0005[b]	0.550
… to prevent the development of treatable diseases that begin in childhood, generally do not lead to death before 40–50 years of age, but require lifelong, invasive treatment?	$n1$: 546 n_2: 845	0.0009[b]	0.455	$n1$: 1068 $n2$: 323	0.0616	0.529
… to prevent the development of untreatable and fatal diseases that begin in adulthood and lead to a slow decline in the ability to think and function normally?	n_1: 546 n_2: 845	0.0005[b]	0.454	n_1: 1068 n_2: 323	0.0207[b]	0.535
… to prevent the development of treatable and non-fatal conditions that begin in adulthood that involve changes to mood and behaviour that can affect day-to-day life (such as depression or schizophrenia)?	$n1$: 545 $n2$: 845	0.2629[a]	0.483	$n1$: 1067 $n2$: 323	0.1578	0.524
… to prevent a child being born with a disability, such as blindness or deafness?	n_1: 545 n_2: 844	0.0014[b]	0.454	n_1: 1066 n_2: 323	0.2405	0.519
Enhancement applications of germline gene editing						
To what extent do you agree with using germline gene editing…						
… to enhance resistance to infectious diseases (such as HIV or malaria)?	n_1: 530 n_2: 821	0.0000[b]	0.431	n_1: 1036 n_2: 315	0.0000[b]	0.578
… to enhance physical traits (such as improving vision or sports performance)?	n_1: 530 n_2: 821	0.0001[b]	0.437	n_1: 1036 n_2: 315	0.0185[b]	0.542
… to enhance mental/psychological traits (such as increased intelligence)?	n_1: 530 n_2: 821	0.0000[b]	0.433	n_1: 1036 n_2: 315	0.0159[b]	0.543
… to alter an individuals' traits such as empathy, tolerance or self-discipline?	n_1: 529 n_2: 821	0.0074[b]	0.458	n_1: 1035 n_2: 315	0.1325	0.527

U the smaller rank sum value of the two groups (n_1 or n_2), $P\ (n_1 > n_2)$ the probability that a random sample from n_1 will be greater than a random sample from n_2

[a]Indicates statistical significance ($z < 1.96$) when compared with normal quantiles and rejection of H_0: The two populations represented by the two demographic/experiential groups have the same distribution of Likert scores for each questionnaire item

[b]Indicates statistical significance ($p < 0.05$) using normal approximation and rejection of H_0

[18–23, 25]. Contrary to the findings of a previous large-scale study [26], only half of respondents in our study disapproved, or strongly disapproved of the use of GGE for enhancement purposes (see Fig. 3). This may reflect increasing public acceptance of GGE. However, the relatively large proportion of participants who responded with 'unsure' to enhancement applications in our study underscores the complexity of the ethical issues raised.

Support for therapeutic GGE was lowest for applications in adult mental illness and to impart infectious disease resistance, although in both cases over 65% of respondents supported such applications. Resonating previous findings [27], respondents curb their approval for gene editing technology as disease severity decreases. This trend may be underpinned by a preference to use GGE as a last resort where medical intervention is not an option.

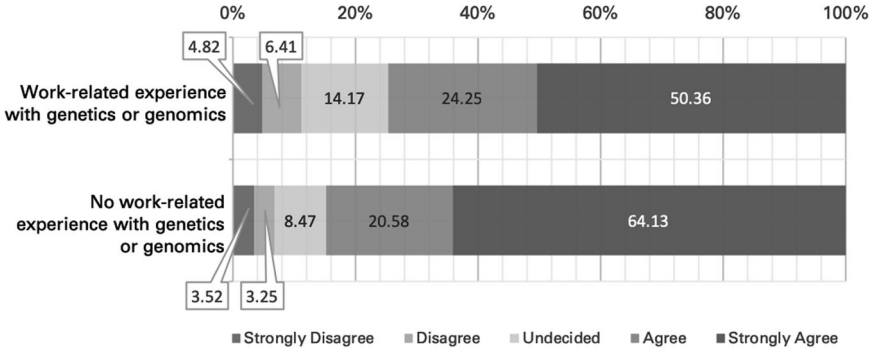

Fig. 1 Mean frequency (%) of participant responses to questionnaire items about therapeutic applications of GGE by work experience with genetics or genomics. Each section of the bar graph represents the mean frequency of Likert scale responses to the five therapeutic themed questions (items **a**–**e**) of participants with ($n = 342$, MED response: Strongly Agree) and without work-related experience with genetics or genomics ($n = 1039$, MED response: Strongly Agree)

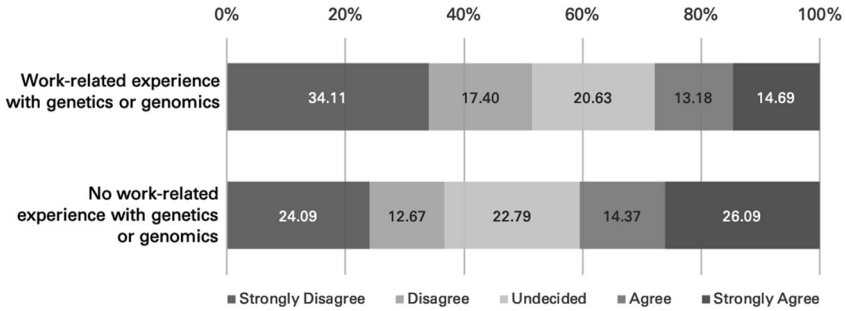

Fig. 2 Mean frequency (%) of participant responses to questionnaire items about enhancement applications of GGE by work experience with genetics or genomics. Each section of the bar graph represents the mean frequency of Likert scale responses to the four enhancement themed questions (items **f**–**i**), among participants with ($n = 332$, MED response: Disagree) and without work-related experience with genetics or genomics ($n = 1011$, MED response: Undecided)

Ultimately, it appears that rather than simply being 'for or against' the technology, the apparent severity, treatability and impact of the disease being edited appear to shape more nuanced public and professional attitudes [20]. This indicates that ethical discussions about GGE ought to take a targeted approach, where the context of its use can determine support or rejection of the technology.

Exposure to genetics and genomics divides opinions

We observed greater support for GGE from participants without professional exposure to genetics, bolstering evidence of an emerging disconnect between clinical and community perspectives about the appropriate place of genetics in healthcare [28]. Clear reservations towards GGE have been observed in a study of geneticists and genetic counsellors in Japan, with under a third supporting its use to prevent serious, untreatable disease [29]. Such opposition has been ascribed to concerns relating to misuse, improper regulation and insufficient clinical evidence. Armsby et al. [27] also reported less definitive attitudes held by surveyed members of genetics societies. Though, similar to our findings, less than half of their participants deemed current use of GGE morally acceptable and 78% (389/500) supported future uses of GGE.

The reasons behind the diverging attitudes between the potential gatekeepers and beneficiaries of GGE have not been explored. We postulate it might be due to an increased appreciation of the complexity of genomics (and therefore the ethical complexities associated with GGE) by those with experience in the field. This would suggest a need for more targeted and deliberative research, which helps educate the public before we can truly gauge public attitudes toward GGE.

A novel finding in our study was that those with personal or family experience with genetics or genomics were less supportive of GGE. This challenges a similar investigation by Weisberg et al. [18], who reported personal or family experience with a genetic condition did not affect attitudes towards gene editing research. It is probable, however, that the differences in domains studied—gene editing research [18] and germline gene editing applications—explain the disparity between results. Notably, our study presented participants with a number of real-world applications of

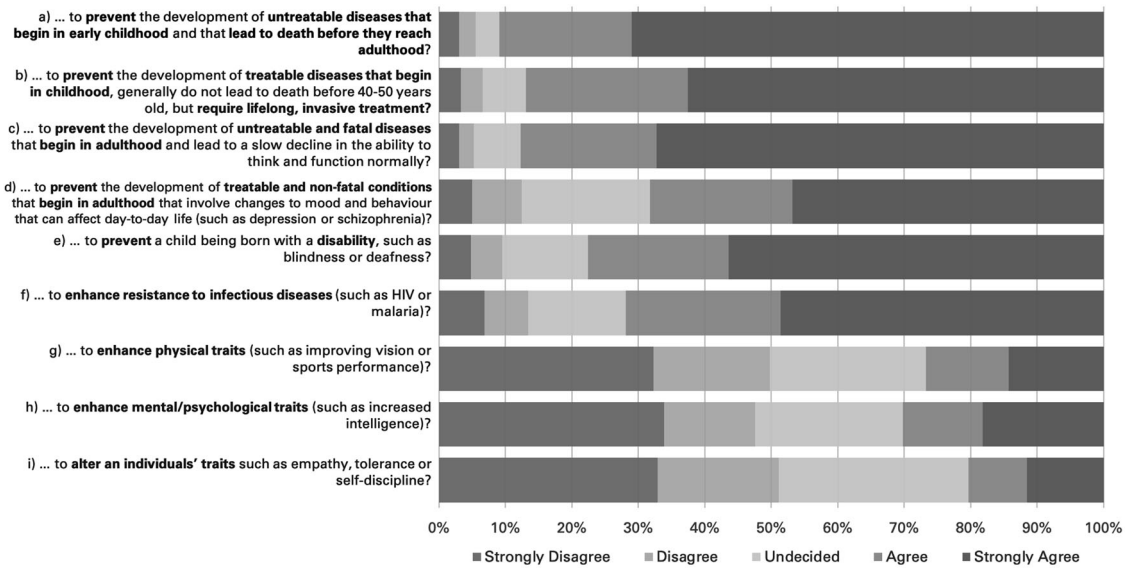

Fig. 3 Overall frequency (%) of participant responses to nine questionnaire items about applications of GGE. Survey responses were categorised using a Likert scale and summarised by mean frequency in the bar graph. Questionnaire items were preceded by 'To what extent do you agree with using germline gene editing…' in the online questionnaire and response options were 'Strongly Disagree', 'Disagree', 'Undecided', 'Agree' and 'Strongly Agree'. The majority of participants chose 'Strongly Agree' and 'Agree' to therapeutic items **a**–**e** and enhancement item **f**, and conversely chose 'Strongly Disagree', 'Disagree' and 'Undecided' more often to enhancement items **g**–**i** Summary results: **a** $n = 1{,}402$, MED response: Strongly Agree **b** $n = 1401$, MED response: Strongly Agree **c** $n = 1401$, MED response: Strongly Agree **d** $n = 1400$, MED response: Agree **e** $n = 1399$, MED response: Strongly Agree **f** $n = 1361$, MED response: Agree **g** $n = 1361$, MED response: Undecided, **h** $n = 1361$, MED response: Undecided, **i** $n = 1360$, MED response: Disagree

germline gene editing. It would be reasonable to surmise that these hypotheticals may elicit a stronger and, in this study, more negative response from participants overall. Future investigations, however, should be geared towards what it is about personal and family experience with genetics that drives relative resistance to GGE. Such views are likely to be informed by the relative nature and value of individual experience [30] and warrant further attention and exploration.

Demographic impacts on attitudes

We found tertiary education to be a negative predictor for attitudes towards GGE. This contradicts existing data, where some researchers report a positive association between higher education and GGE approval [21] and others report no association whatsoever [31]. Uchiyama *et al*. [19] reported that those with no prior knowledge were much more likely to perceive genome editing as inappropriate in all circumstances. Given our survey was conducted after the birth of the first ever gene edited children, and associated widespread media coverage of GGE, it could be that increasing familiarity with the technology is driving growing acceptance in those without a tertiary education.

Our findings stack more evidence against the deficit model, which implies that scientific acceptance is achieved through scientific knowledge [32]. Others have argued that differing levels of scepticism towards controversial science, as observed in our cohort, is not caused by differences in knowledge [32] but rather by divergent value systems. In our cohort, those without a tertiary education might attach more value to the potential benefits of GGE and less to the potential risks. This again necessitates prioritisation of research that involves promotion of public understanding of GGE as a precursor to canvassing public perspectives.

Gender was a strong attitudinal modifier in our data. Supporting earlier findings [18, 20, 21], women were more resistant to GGE than men. Women are typically better informed about biology and health [33], more resistant to genetic biotechnology [22, 33], and have more concerns about its use [34]. This supports trends in our dataset suggesting that having more knowledge in this area is related to scepticism towards GGE. It may be that women better appreciate the potential medical risks and uncertainty presented by GGE. Additionally, women may consider themselves obligate participants in the implantation of edited embryos, and in the context of unequal gender roles, are likely to carry the burden of associated reproductive decision-making, risks and outcomes [35].

Strikingly, over half our male cohort support all uses of GGE and were twice as likely as women to endorse enhancement applications. This may be because men tend to be more supportive of biotechnology as a vehicle for both scientific [36] and social progress [31, 34]. Though there are clear attitude differences between genders, the reasons for this disparity remain largely speculative and likely deeply

complex [22]. Unfortunately, perspectives of individuals who identify as non-binary remain largely unexplored, and as stakeholders in this debate, require consideration in future investigations. Future research ought to address the underlying beliefs, perspectives and values of both women and men to understand the factors driving gender differences in support for GGE. Such research will be vital in order to inform targeted public engagement and education activities.

We identified a strong association between religiosity and resistance to GGE. These findings reinforce observations that religiosity has a negative modulating impact on attitudes towards GGE [22, 25, 31]. This might be explained by findings from Funk et al. [31], who found most religious participants deemed GGE amoral and 'meddling with nature'. Use of this technology appears to violate some religious principles and is thus less acceptable for some religious respondents. It is clear that a religious worldview can dampen support for GGE, and the challenge for future research will be how to reconcile these perspectives with the scientific worldview, and how to best integrate religious belief into the process of community reflection.

Our study also showed parents were less supportive of GGE than respondents without children, with the exception of preventing adult psychiatric illness. Our data echo the findings of Funk et al. [31], who found that parents of younger children were less supportive, and often considered GGE unnatural and 'morally unacceptable'. This conflicts with social media poll and discourse analyses, showing parents are 14% more likely to approve of genetic engineering to prevent serious disease [37]. Highlighting this conflict, however, a study of patients with heritable retinal disease found some participants perceived GGE as an acceptable part of parental decision-making, and others were concerned about taking choice away from a future child [30]. Such disparate parental priorities may explain the conflicting data on their attitudes. Moreover, some have argued that GGE may mean people will see embryos as systems to edit [38], and children as a sum of their traits [39]. This could be argued as being in conflict with the nature of parenting, described as an emotional, familial, and communicative relationship to one's child as a whole human being [38]. Parents may object to how children are impassively framed by GGE, and thus consider it less acceptable overall.

Our findings indicate that age impacts attitudes towards GGE, consistent with younger respondents demonstrating more general support for the technology [18, 21]. Similarly, previous findings suggest younger people are more open to pharmacologic enhancement and are less concerned about its risks [40], perhaps explaining their comparative enthusiasm for GGE. With the exception of enhancing personality traits, older age groups were less likely to strongly agree or strongly disagree with the use of GGE in any circumstance when compared with their younger counterparts. This trend has not been previously reported. The reasons for these more conservative attitudes to GGE are unclear, however insights into why older generations are hesitant to support medical enhancement include concerns about distributive justice and social access [40].

Perspectives of the international cohort were not influenced by their geographical location. This is important, as consistent attitudes across jurisdictions may mean recent efforts to develop international guidelines for GGE are more likely to succeed. Though data regarding Australian attitudes is limited, our findings add to, and support, the representative findings of Critchley et al. [22] whose data showed approval for medical and disapproval for non-medical uses of GGE by Australians.

Despite the usefulness of a web-based recruitment, our study design compromised generalisability for scale. Convenience sampling via social media resulted in a high representation of young, tertiary-educated, white participants from western countries, many of whom reported professional exposure to genetics/genomics. Furthermore, our findings rely on self-reported data which may be inaccurate and are impossible to verify.

As our questionnaire instrument is not validated; both design and variations in comprehension may have affected results. We advised respondents to assume GGE is safe and effective, where other studies have shown explicit mention of real risks weakens support for GGE [18]. Our findings may show strong support due to lack of real-world context yet may demonstrate public sentiment if safety issues are resolved.

Our analyses approach assumed the following about the survey data: dependent variables (Likert data) were ordinal; variable groups were independent and categorical; and each observation corresponded to different participants. It is impossible to identify duplicate attempts due to participant anonymity.

Given gene-edited children have already been born, it is easy to view the clinical adoption of GGE as a forgone conclusion. The speed of technological advancement can make it seem that careful deliberation, discussion and attempts at regulation are futile. It would be remiss, however, to consider indiscriminate use of GGE as inevitable and the ethical debate redundant. Instead, the sheer pace at which GGE has been used reproductively, and the lack of transparency in the process reinforce the urgency to elicit stakeholder perspectives, both public and professional, in order to inform a robust and socially acceptable regulatory framework.

This survey adds to our understanding of the attitudinal dimensions towards GGE's future place in healthcare.

Importantly, we add weight to findings that the public and genetics community have disparate views about the future of GGE. Considering these attitudes, exploring beliefs and addressing concerns are vital research priorities to ensure science proceeds with GGE in an ethically and socially acceptable way. As with other technologies, the application of GGE is a strong determinant of individual attitudes. Thus, governing bodies ought to focus on applications rather than the technology itself to properly accommodate stakeholder perspectives. Although further research is necessary to validate the findings, this study indicates the community do support GGE to promote human health and thus may consider current bans too restrictive.

Finally, we found that the public are not a uniform group with like perspectives. Ongoing consultation should address attitudes through the lens of diversity and individual experience to gather rich and meaningful data. Only then can the community truly inform our endeavour to develop an ethically and principled framework for introducing human GGE, a simple but powerful tool that may change the future of humankind.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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