Reasons for being in favour of or against genome modification: a survey of the Dutch general public

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STUDY QUESTION: What are the general public’s reasons for being in favour of or against the use of genome modification for five potential applications?

SUMMARY ANSWER: Overall, 43 reasons for being in favour, 45 reasons for being against as well as 26 conditional reasons for the use of genome modification were identified.

WHAT IS KNOWN ALREADY: Various applications of somatic genome modification are progressing towards clinical introduction and several recent studies have reported on germline genome modification. This has incited a debate on ethical and legal implications and acceptability. There is a growing plea to involve the general public earlier on in the developmental process of science and (bio)technology including genome modification.

STUDY DESIGN, SIZE, DURATION: In April 2016, a cross-sectional survey was launched online among the Dutch general public. A documentary on genome modification on public television and calls in social media invited viewers and non-viewers, respectively, to participate.

PARTICIPANTS/MATERIALS, SETTING, METHODS: The questionnaire introduced five potential future applications of genome modification: modified wheat for individuals with gluten intolerance; somatic modification for individuals with neuromuscular diseases; germline modification to prevent passing on a neuromuscular disease; germline modification to introduce resistance to HIV; and germline modification to increase intelligence. Participants were asked to indicate whether and why they would make use of genome modification in these scenarios. The reasons mentioned were analysed through content analysis by two researchers independently. The proportion of respondents that was willing to modify was described per scenario and associations with respondent characteristics were analysed.

MAIN RESULTS AND THE ROLE OF CHANCE: The survey was completed by 1013 participants. Forty-three reasons for being in favour, 45 reasons for being against as well as 26 conditional reasons for the use of genome modification were identified. These could be categorized into 14 domains: safety of the individuals concerned; effectiveness; quality of life of the individuals concerned; existence of a clinical need or an alternative; biodiversity and ecosystems; animal homo sapiens (i.e. relating to effects on humans as a species); human life and dignity; trust in regulation; justice; costs; slippery slope; argument of nature; parental rights and duties; and (reproductive) autonomy. Participants’ willingness to use genome modification was dependent on the application: most participants would eat modified wheat if gluten intolerant (74%), would use genome modification to cure his/her own neuromuscular disease (85%) and would apply germline modification to prevent passing on this neuromuscular disease (66%). A minority would apply germline modification to introduce resistance to HIV (30%) or increase intelligence (16%). Being young (odds ratio (OR) = 0.98 per year increase), being male (OR = 2.38), and having watched the documentary (OR = 1.82) were associated with being willing to apply genome modification in more scenarios.
Introduction

The prospect of purposeful modification of DNA has been a source of both excitement and unease for decades. Although tools such as zinc finger nucleases and transcription activator-like effector nucleases for genome modification have been available for some time, the discovery of CRISPR-Cas9, given its specificity, efficiency, low-costs and ease in use, has represented a major step forward from previously available methods (Cong et al., 2013; Jinek et al., 2012).

Genome modification has various types of possible applications. It can be used in agriculture to, for example, boost yields, protect against pests or enhance nutrient content (Gil-Humanes and Voytas, 2014; Wang et al., 2014; Jones, 2015), and some clustered regularly interspaced short palindromic repeats-CRISPR-associated protein-9 nuclease (CRISPR-Cas9) generated crops have already been cleared for commercial use by the US Department of Agriculture (Waltz, 2016a,b). A large number of human clinical trials have been performed or are underway in order to treat diseases in somatic cells (i.e. all cells that will not be passed on to future progeny) (Ginn et al., 2013). In contrast, germline genome modification, involving modification of nuclear DNA in germ cells or embryos such that all cells in the resulting child and its future progeny carry the modification, has thus far never been applied clinically. Five papers have recently described successful human germline genome modification of (non-viable) human embryos using CRISPR (Liang et al., 2015; Kang et al., 2016; Fogarty et al., 2017; Ma et al., 2017; Tang et al., 2017). Although the initial experiments revealed the techniques unsafe and ineffective, the latest experiments have shown remarkable progress and scientists expect to overcome the technical hurdles in the foreseeable future (Ishii, 2015; Lunshof, 2016; Olson, 2016; Smith et al., 2012).

As, with the discovery of CRISPR-Cas9, clinical applications of germline genome modification became more feasible, the debate on the ethical and legal implications of germline genome modification and its acceptability intensified (IBC, 2015; The Academy of Medical Sciences et al., 2015; National Academies of Sciences, 2017). So far, this debate has taken place mostly at international conferences as well as in the (academic) literature (Baltimore et al., 2015; Bosley et al., 2015; Lanhier et al., 2015). There is broad consensus among experts on the need to include more stakeholders in this debate, including the general public (Holdren et al., 2011; Baltimore, 2015; Bosley et al., 2015; IBC, 2015; The Academy of Medical Sciences et al., 2015; National Academies of Sciences, 2017). The general public itself also calls for public consultation before clinical applications (Scheufele et al., 2017). Including the general public is considered appropriate as this...
may improve the quality of decisions, the potential consequences theo-
retically affect everyone, stakeholders involved so far do not neces-
sarily represent society, public involvement may help prevent abuse of
the technology due to special interests, and public involvement may
safeguard public trust in science. Despite not necessarily having com-
plete or accurate information, the general public has been shown capa-
able of holding complex social and ethical views and conducting
sophisticated discussions on genetics (Kerr et al., 1998). Perceived
risks and benefits have been repeatedly shown to affect public accept-
ability (Siegrist, 2000; Weisberg et al., 2017). As these differ, or are
weighted differently, depending on the application, the acceptability of
genome modification depends on the specific application (Frewer et al.,
1997; Trust, 2005).

This paper aims to gain insight into the reasons of the Dutch general
public for being in favour or against using genome modification for five
potential clinical applications.

Materials and Methods

The Dutch general public is an interesting population to study as familiarity
with gene therapy is the highest in the European Union (EU) (73%, as com-
pared to the EU average of 45%) (Gaskell et al., 2006) and a lack of public
education has been flagged as a major limitation of previous studies
(Blendon et al., 2016). Simultaneously, disapproval of gene therapy research
is only slightly different from the EU average (25% as compared to 29%)
(EC, 2010).

Cross-sectional surveys are in the Netherlands exempt from Institute
Review Board approval.

Questionnaire

A study-specific questionnaire was developed. It was designed to cover
applications which have previously been shown to differ in their acceptabil-
ity: curing diseases versus enhancement (Robillard et al., 2014) and curing
genetic diseases versus curing preventable diseases (Kalfoglou et al., 2005).
Furthermore, previous studies showed differences between germline or
somatic applications (Trust, 2005), and human versus plant applications
(Crne-Hladnik et al., 2009). To cover these axes, the following five scen-
arios were included: modified wheat for individuals with gluten intolerance
(Barro et al., 2016; Shewry and Tatham, 2016); somatic modification for
individuals with neuromuscular diseases (Tabebordbar et al., 2016); germ-
line modification to prevent passing a major neuromuscular disease (Long
et al., 2014; Liang et al., 2015); germline modification to introduce resis-
tance to HIV (Samson et al., 1996; Kang et al., 2016); or germline modifi-
cation to increase intelligence (intelligence is in part genetically determined
(Plomin and Spinath, 2004)). Participants were asked to consider that each
of these scenarios would be applicable to them, and to indicate whether
they would use genome modification (yes/no) and why they would or
would not (open question) (Macer et al., 1995). Of note, surveys fre-
quently operationalized genomic enhancement as improving intelligence,
and mimicking that allowed for comparison to previous studies (Congress,
1987; Macer et al., 1995; Kalfoglou et al., 2005; Meisenberg, 2009; Muller
and Shepherd, 2009; Criger and Fekken, 2013; Robillard et al., 2014; Funk
et al., 2016; Mcaughhey et al., 2016). We did inform respondents that this
application is scientifically still far-fetched.

Finally, participants were asked for their gender, age and whether they
had watched the documentary on genome modification (see below).
Information on the purpose of this study, as well as the state-of-the-art
and feasibility of the presented scenarios, was provided (see
Supplementary Data for the translated questionnaire, the announcement
of the study, and the background information provided).

The questionnaire was reviewed by an expert panel composed for this
study including a clinician (S.H.), a biologist (S.R.), two science journalists
and a senior editor of a Dutch popular science media outlet. The expert
panel focused on scientific accuracy, non-directive phrasing (Molewijk
et al., 2003), understandable use of language for the lay public, and feasibil-
ity (e.g. sufficient background information provided, acceptable administra-
tion time). Amongst others, the panel decided to refer to genome
modification as ‘genetic modification’, despite appreciating the differences
in the terms, as this is common practice in Dutch language, which has not
yet adopted the term ‘genome modification’ (e.g. not part of dictionaries,
Wikipedia, lay vocabulary). To ensure proper understanding, the docu-
mentary explained CRISPR-Cas9 as a new, highly effective technology
to cut-and-paste specific pieces of DNA.

Data collection

The survey was launched online on 30 March 2016 and was accessible for
4 weeks through the website of ‘de Kennis van Nu’, a Dutch popular sci-
ence media outlet. It was released together with a documentary (which
was available online as well as aired twice on Dutch television) providing
background information on genome modification. The documentary cov-
ered recent advancements of CRISPR-Cas9 in genome modification and
potential germline, somatic and agriculture applications. In the documen-
tary, the interviewed scientists called for the public to express their views
by filling out the survey. Additionally, calls on social media invited viewers
and non-viewers to comment on genome modification through the survey.

Data analysis

The proportion of respondents being willing to use modification was
described per scenario and an ordinal regression analysis assessed whether
respondent characteristics affected the number of scenarios in which parti-
cipants were willing to apply genome modification. Data were analysed
with the Statistical Package for the Social Sciences (SPSS 22.0) (IBM,
Chicago, IL, USA).

The responses to the open questions were analysed using phenomen-
ology methodology involving multiple readings to understand the context;
highlighting meaningful units of text that were relevant to the research
question; clustering meaningful units of text into distinct reasons and over-
arching domains; contextualizing the identified domains (i.e. checking for
consistency with the full response to maintain the context) (Hycner, 1985;
Graneheim and Lundman, 2004). The identified reasons were organised
into reasons for being in favour of using genome modification, reasons for
being against using genome modification, and conditional reasons for using
genome modification. Reasons representing flip sides of the same coin
were highlighted, for example: ‘genome modification would not impose a
high treatment burden’ and ‘genome modification would impose a high
treatment burden’. For data presentation, examples of patient quotations
were selected and translated.

Finally, the reasons for and against germline genome modification identi-
fied by the general public were compared to reasons identified by experts
as reported in a recent systematic literature review, and novel considera-
tions were flagged (van Dijke et al., 2017).

Results

Respondents

A total of 1013 participants filled out the questionnaire (Table 1). About
half (54%) of the respondents were male. The respondents’ age ranged
from 11 to 90 years, with a mean of 44 years. Most respond-
dents (69%) had watched the documentary on genome modification.
Willingness to use genome modification

The differences in respondents’ willingness to alter the human germ-line for different purposes or use genome modification for non-germline purposes is reported in Fig. 1. A majority of participants (66%) was willing to use germline modification to prevent passing on a neuromuscular disease. Participants were least willing to use germline modification to increase intelligence of their embryo (16%). However, the scenarios that did not involve human germline modification were considered acceptable by more participants. About 1 in 10 participants (OR = 1.82) were associated with being willing to use genome modification in more scenarios (Table I).

Being young (odds ratio (OR) = 0.98 per year increase), being male (OR = 2.38), and having watched the documentary on this topic (OR = 1.82) were associated with being willing to use genome modification in more scenarios (Table II).

Table I Characteristics of respondents in the survey on views of the Dutch general public on the use of genome modification.

| Respondent characteristics | Proportion % (n) |
|----------------------------|------------------|
| Gender                     | Proportion %     |
| Male                       | 54% (n = 542/1013) |
| Female                     | 46% (n = 471/1013) |
| Age (mean ± SD in years)   | 44 ± 19          |
| Watched television documentary on GM | Proportion % (n) |
| Yes                        | 69% (n = 704/1013) |
| No                         | 31% (n = 309/1013) |

GM: genome modification.

Reasons for being in favour or against using genome modification

A total of 6333 meaningful units (i.e. text describing a motivation in favour or against genome modification) were identified. Between zero

Table II Reasons for being in favour or against using genome modification.

| Application                             | Proportion % (n) |
|-----------------------------------------|------------------|
| Wheat (gluten)                          | 73.5%            |
| Somatic cells (neuromuscular disease)   | 85.2%            |
| Embryo (neuromuscular disease)          | 65.9%            |
| Embryo (HIV resistance)                 | 30.2%            |
| Embryo (increased intelligence)         | 16.1%            |
| Embryo (normal copy replacing defective gene) | Yes No |
|                                        | 26.5%            |
|                                        | 14.8%            |
|                                        | 34.1%            |
|                                        | 69.8%            |
|                                        | 83.9%            |

Figure 1 The willingness of participants in survey to use genome modification in different scenarios. Reporting the results of a sample of 1013 participants that is not representative of the overall Dutch general public.

Discussion

Studying the general publics’ perspectives on germline genome modification has been frequently called for [Baltimore, 2015; Bosley et al., 2015; IBC, 2015; The Academy of Medical Sciences et al., 2015; National Academies of Sciences, 2017]. Such a study is timely considering that CRISPR/Cas9 brings clinical applications of germline genome
modifications closer, which means both international and national governance should be installed now (Baltimore, 2015; Bosley et al., 2015; IBC, 2015; National Academies of Sciences, 2017; The Academy of Medical Sciences et al., 2015).

The study has several limitations. First, research comparing open questionnaire questions to individual/group interviews is limited and conflicting (Bowling et al., 1993; Bowling, 1996; Dolan et al., 1999; Hanratty and Lawlor, 1999; Shiel et al., 2000; Contandriopoulos, 2004; Delli-Carpini et al., 2004). For example, questionnaires allow for a larger sample size and intuitive responses, but allow for less in-depth understanding of participants’ perspectives than interviews. Second, we could not confirm understanding of the provided information and scenarios. Although it is still unclear whether and how knowledge of genome modification effects its acceptability (Trust, 2005; Muller and Shepherd, 2009; Scheufele et al., 2017), proper understanding is important for the validity of responses (Bradburn et al., 1982). Therefore, we attempted to facilitate understanding through providing balanced information and a documentary. Third, we questioned specific applications (e.g. HIV resistance) instead of broad categories (e.g. preventable disease), to ensure respondents considered comparable scenarios. However, the specific diseases may not represent the entire category as, for example, the severity of the disease determines acceptability (Evans et al., 2005; Trust, 2005; Xiang et al., 2015). Fourth, as the survey was disseminated through social media, our respondents were not representative and likely interested in the topic (Eysenbach and Wyatt, 2002). Fifth, despite using two independent reviewers, content analysis of the responses involves interpretation and the potential for misinterpretation. Sixth, for accurate representation, we report all reasons provided by the participants even though some may be fallacious (e.g. genome modification would not cure the cause of the problem but merely its expression). Furthermore, we report on their frequency of being spontaneously mentioned, which portrays attention, rather than importance. For example, a respondent mentioning safety concerns in only the first three scenarios does not necessarily imply that safety was no longer important in the final two scenarios.

Our identification and structured analysis of the reasons mentioned by members of the general public added to the existing literature. Many previous studies quantified the importance of only a preselected, limited number of attitudes/reasons to the general public (Singer et al., 1998; Siegrist, 2000; Trust, 2005; Meisenberg, 2009; Muller and Shepherd, 2009; Criger and Felken, 2013; Robillard et al., 2014; Xiang et al., 2015; Funk et al., 2016; Weisberg et al., 2017). A number of previous studies from different countries did qualitatively inquire for reasons (Congress, 1987; Macer, 1992; Macer et al., 1995; Frewer et al., 1997; Lewis et al., 1997; Iredale et al., 2003, 2006; Kalfoglou et al., 2005; Massarani and de Castro Moreira, 2005; Crne-Hladnik et al., 2009; Funk et al., 2016; McCAughhey et al., 2016). However, most of them lack the precision that scientists might prefer (Blendon et al., 2016) and/or had substantial methodological limitations, such as not reporting on a structured qualitative analysis (Frewer et al., 1997; Iredale et al., 2003; Massarani and de Castro Moreira, 2005; McCAughhey et al., 2016); only reporting on a selection of the obtained domains (Funk et al., 2016); only inquiring for reasons against genome modification (Congress, 1987); not differentiating between germline modification and other reproductive genetic technologies (Kalfoglou et al., 2005); and only including high school students (average age 17 years) (Lewis et al., 1997; Iredale et al., 2006; Crne-Hladnik et al., 2009). The fact that the general public identified 20 arguments that were not mentioned by experts as reported in a systematic overview of the literature (van Dijke et al., 2017) supports the added value of public consultations.

Referring to the content of the reasons that were identified in this survey, the advantage of improving the quality of life of those directly affected, and the disadvantage of potential health risks were frequently and consistently mentioned for the different scenarios. This is similar to the reasons brought forward by professionals (van Dijke et al., 2017). Interestingly, the ‘yuck-factor’, or the explicit lack thereof, was in the top five of reasons for and against all applications. It would be interesting to qualitatively explore the roots of these gut feelings, which by themselves may not form a moral argument but with time may be articulated, weighed, and either endorsed or dismissed (Midgley, 2000).

Although specific arguments were used for specific scenarios and various arguments have only been mentioned in the scenario’s that reflect altering the germline, there were no structural differences in the top five listed arguments of germline and non-germline applications. The following section discusses differences in the top five most frequently reported reasons of the five applications. Interestingly, participants often argued for modifying wheats by stating this would not pose health risks and that modified wheats would not be commercially available if they would not be safe. This may be related to the explanation in the documentary about regulatory approval of modified foods, and/or knowledge otherwise obtained regarding regulations (safety assessment by the European Food Safety Authority) and the reassuring safety data of currently available genetically engineered crops (NASEM, 2016). Specific disadvantages that were frequently addressed in relation to modified wheats included the potential harm to ecosystems and not curing the cause of the problem (i.e. individuals would still be intolerant to gluten). Indeed, these reasons seem less applicable to the other modifications, which are in human. Of note, there is no conclusive evidence on cause-and-effect relationships relating to genetically engineered crops and environmental problems (NASEM, 2016).

Reasonably, the consequences being limited to the individual was used to advocate for somatic modification. Without necessarily being specific to somatic modification, the benefits outweighing the risks and diseases having a purpose in life were only among the top five reasons this application. This may partially be an artefact of structuring in groups of top five responses (e.g. diseases having a purpose in life was more frequently raised against introducing HIV resistance but did not make it in that top five). Alternatively, respondents may feel more comfortable making these types of analyses for themselves than for others.

| Table II | Respondents’ characteristics determining the number of applications in which participants are willing to use GM. |
|----------|----------------------------------------------------------------------------------------------------------|
| Respondent characteristic | Adjusted odds ratio | 95% CI | P-value |
| Being male | 2.38 | 1.90–2.98 | <0.001 |
| Age (per year increase) | 0.98 | 0.98–0.99 | <0.001 |
| Having watched documentary | 1.82 | 1.42–2.31 | <0.001 |

...
### Table III The five most frequently mentioned reasons per application.

| Application            | Order | Reasons provided \((n = x)\)^* | In favour                                                                 | Conditions                                                                 | Against                                                                 |
|------------------------|-------|----------------------------------|---------------------------------------------------------------------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Wheat (gluten)         | 1     | GM would improve my/my child’s  | I would only use GM if it would not pose unacceptable health risks \((n = 78)\) | GM would not be acceptable as there are alternatives available to obtain the same result \((n = 82)\) |                                                                            |
|                        | 2     | GM incites the ‘wow factor’ and/or does not incite the ‘yuck-factor’ \((n = 102)\) | I would only use GM if it would not do ecological harm \((n = 15)\) | GM would pose unacceptable health risks \((n = 53)\) |                                                                            |
|                        | 3     | GM would merely raise the speed and efficiency of a naturally occurring process \((n = 77)\) | I would only use GM if there are no alternatives available to obtain the same result \((n = 8)\)/I would only use GM if the extent of the manipulation is limited \((n = 8)\) | GM would have negative long-term consequences for society \((n = 43)\)/GM would be too unnatural \((n = 43)\) |                                                                            |
|                        | 4     | GM would not pose health risks \((n = 63)\) | I would only use GM if it would not affect biodiversity \((n = 7)\) | GM would cause harm to ecosystems \((n = 18)\) |                                                                            |
|                        | 5     | GM would not be inherently different than currently accepted vaccines and medications \((n = 29)\) | I would only find genetic modification acceptable if it would be applied for disease rather than enhancement \((n = 6)\) | GM incites the ‘yuck-factor’ (i.e. a feeling of horror, revulsion or disgust)/GM would not cure the cause of the problem but merely its expression \((n = 17)\) |                                                                            |
| Somatic (neuromuscular disease) | 1     | GM would improve my/my child’s quality of life \((n = 578)\) | I would only use GM if it would not pose unacceptable health risks \((n = 82)\) | GM incites the ‘yuck-factor’ (i.e. a feeling of horror, revulsion or disgust) |                                                                            |
|                        | 2     | GM would pose limited health risks but those are acceptable considering the benefits \((n = 59)\) | I would only use GM if it would improve my/my child’s quality of life \((n = 41)\) | GM would pose unacceptable health risks \((n = 32)\) |                                                                            |
|                        | 3     | GM incites the ‘wow factor’ and/or does not incite the ‘yuck-factor’ \((n = 47)\) | I would only use GM if potential consequences are limited to myself \((n = 22)\) | GM would be unacceptable because disease has a purpose in life \((n = 19)\) |                                                                            |
| Germline (neuromuscular disease) | 1     | GM would improve my/my child’s quality of life \((n = 366)\) | I would only find GM acceptable if it would be applied for disease rather than enhancement \((n = 16)\) | GM would be too unnatural/GM would have negative long-term consequences for society \((n = 14)\) |                                                                            |
|                        | 2     | GM is a moral obligation as I do not have the right to withhold my child from the possibilities created by germline modification \((n = 54)\) | I would only use GM if it would improve my/my child’s quality of life \((n = 27)\) | GM would not be acceptable as there are alternatives available to obtain the same result \((n = 188)\) |                                                                            |
|                        | 3     | GM is better than, or an acceptable alternative to, current options \((n = 37)\) | I would only find GM acceptable if it would be applied for disease rather than enhancement \((n = 24)\) | GM incites the ‘yuck-factor’ (i.e. a feeling of horror, revulsion, or disgust) \((n = 57)\) |                                                                            |
|                        | 4     | GM incites the ‘wow factor’ and/or does not incite the ‘yuck-factor’ \((n = 29)\) | I would only use GM if there are no alternatives available to obtain the same result \((n = 14)\) | GM is unacceptable as I do not have the right to decide on modifying genes on behalf of my unborn child \((n = 31)\) |                                                                            |
|                        | 5     | GM would improve the quality of life of the family and friends of the cured individual \((n = 25)\) | I would only use GM if the risk of acquiring the disease is high \((n = 10)\) | GM prevents the disease, and this is not preferable over curing the disease if it manifests/GM would have negative long-term consequences for society/GM would be too unnatural \((n = 18)\) |                                                                            |
| Germline (HIV resistance) | 1     | GM would improve my/my child’s quality of life \((n = 145)\) | I would only use GM if it would not pose unacceptable health risks \((n = 26)\) | GM would not be acceptable as there are alternatives available to obtain the same result \((n = 292)\) |                                                                            |
|                        | 2     | GM would reduce the frequency of or eradicate diseases \((n = 34)\) | I would only find GM acceptable if it would be applied for disease rather than enhancement \((n = 17)\) | GM would not be necessary as the risk of acquiring the disease is low \((n = 100)\) |                                                                            |

*continued*
Germline modification to prevent a neuromuscular disease raised two arguments that were not in the other top fives: parents having the duty not to withhold their child from this possibility and it improving the quality of life of the family of the affected individual. Arguably, these arguments are indeed more relevant here, due to the combination of the severity and unavoidability of the disease, and the notion that parenthood entails special obligations towards one’s offspring. Of note, although we can speculate about the strong moral claim that genome modification is a moral duty (which participants only state in relation to germline modification), it would be interesting to study why this duty is perceived and what the extents of this duty are. Additionally, genome modification being a better or acceptable alternative to current options is especially relevant here as alternatives (PGD or terminating the pregnancy) are also ethically contested (Porteus and Dann, 2015). The view that preventing a disease is not preferable over curing a manifested disease should theoretically also apply for the HIV scenario, where it was indeed mentioned more frequently although not as frequent as to come out in the top five. Finally, parents not having the right to decide on behalf of their child is not necessarily linked to this specific germline application, and it only being in this top five may be an artefact of there being less arguments against curing severe genetic diseases (National Academies of Sciences, 2017).

Unsurprisingly, specifically germline genome modification to introduce HIV resistance, our operationalization of curing preventable diseases, was considered less necessary because of the low risk of acquiring the disease. Interestingly, introducing HIV resistance, and not the germline genome modification scenario that was questioned first (neuromuscular disease), most incited the slippery slope argument. In contrast, professionals use this argument against any germline application (Lanphier et al., 2015). It is unclear why introducing HIV resistance specifically was applauded for reducing the prevalence of diseases and for its effectiveness, as genome modification could do the same for genetic diseases. Perhaps respondents associate infectious diseases with eradication more easily.

Using germline genome modification for enhancement, operationalised as increasing intelligence, incited more considerations about our species and the society than the other applications. More specifically, the top five included concerns about losing valuable human diversity, concerns about falling behind if others use it, the consideration that shifting the normal curve would not have much effect, and the advantage that it could allow users to contribute more to society. Similar types of considerations are voiced by the general public about pharmacological cognitive enhancement (Schelle et al., 2014).

Previous scholars have suggested that the arguments brought forward in the debate on human germline modification are not new, but are in fact similar to arguments used in relation to other novel technologies, such as PGD (Harris, 2016; Tonkens, 2011). However, even when the arguments are not new, this does not diminish the need to reflect on human germline modification, as sometimes a difference in degree can amount to a difference in kind.

In line with previous studies, a significant proportion of responders (40–90%) indicated being willing to use genome modification (Congress,
| Table IV | Domains of the reasons provided in favour and against using GM. |
|---------|---------------------------------------------------------------|
| **Reason** | **Favour** | **Against** |
| **Human life and health** | I would only use GM if it would improve the quality of life. | Reason Citation |
| **Quality of life of the individuals concerned** | "We know what you have, but not what you need or alternative is considered." | "It won’t overrun species of wheat with unacceptable health risks." |
| **Safety of the individuals concerned** | "Only for serious diseases that would cause the problem to be an effective treatment based on modified genes are acceptable health risks." | "The child would be partly sterile; it could be done to get rid of it. (1985, E_NMD)"
| **Effectiveness** | "This way you tackle the root of the cause of the problem." | "It would be 10% safe, I wouldn’t throw it away, but I would use it. (1991, E_NMD)"
| **Safety of the alternative** | "I would certainly take the risk." | "It would pose unacceptable health risks that could be worse." |
| **Biodiversity and ecosystems** | "GM would not reduce human diversity; it would only use the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Animal homo sapiens** | "Modifying human embryo’s give me the chills (1999, E_NMD)." | "It’s wrong to use GM to improve the quality of life." |
| **Genetic diversity** | "Without there being any movement which might allow a human embryo..." | "We know what you have, but not what you need or alternative is considered." |
| **Regulation** | "If it is allowed, it’s safe (1998, W_GLU)." | "There is no other option for the cure for our species (1999, E_HIV)."
| **Human dignity** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Ethical considerations** | "Human embryos can’t be long-term consequences for human dignity..." | "It would not be acceptable for the purpose of research." |
| **Quality of life** | "My kid should just learn to use a condom." | "It would not be acceptable for the purpose of research." |
| **The environment** | "It’s clear that I wouldn’t use it, but we’re not doing so far." | "It would not be acceptable for the purpose of research." |
| **Nature** | "It would not be acceptable for the purpose of research." | "It would not be acceptable for the purpose of research." |
| **Human reproductive system** | "It would not be acceptable for the purpose of research." | "It would not be acceptable for the purpose of research." |
| **Trust in regulation** | "If it’s allowed, it’s safe (1998, W_GLU)." | "It would not be acceptable for the purpose of research." |
| **Genetics** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Human rights** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Animal welfare** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Animal rights** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Animal experimentation** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Animal research** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| **Animal testing** | "We would have the ethical questions..." | "It would not be acceptable for the purpose of research." |
| Justice | GM would improve equality as everyone would have access to beneficial genetic traits | ‘Because the sick want healthy children just like anyone else’ (#414, E_NMD) | I would only use GM if not using it would make me fall behind | ‘If the rest of the world is doing “it”, you have no other choice’ (#587, E_INT) | GM would increase segregation | ‘Being strong and smart are important conditions for a good and successful life. I wonder what happens if you can buy those things. I imagine it will cause segregation. A gab between those who can afford it, and those who can’t’ (#608, E_INT) |
| Costs | GM would lower healthcare costs | ‘Such a disease entails substantial societal costs. If this leads to a more productive life and less (medical) expenses, this is a win-win situation’ (#241, S_NMD) | I would only use GM if costs of GM are not high for the individual | ‘Depending on how much it would cost…’ (#34, E_HIV) | GM would increase healthcare costs | It would make healthcare, which is already too expensive, entirely unaffordable (#842, S_NMD) |
| Slippery slope | GM would strictly be applied to those purposes considered acceptable | ‘A list of which diseases are and are not allowed will have to be created. No matter how bad some cases may be, you don’t want to just do everything’ (#429, E_NMD) | I would only use GM if it would not change societal norms and induce a slippery slope effect | ‘As long as modification doesn’t become the norm’ (#438, E_NMD) | GM would start a slippery slope towards morally unacceptable applications | ‘If you allow this, where will it end?’ (#587, E_INT) |
| Argument of nature | GM would merely raise the speed and efficiency of a naturally occurring process | ‘Mankind will always be evolving whether we speed this up with GM or not, we’ll become smarter anyways’ (#883, E_INT) | I would only use GM if the extent of the manipulation is limited | ‘I also want them to have their own characteristics so I wouldn’t do too much with it’ (#776, E_INT) | GM would be too unnatural | ‘It’s important to, however hard it is, respect nature’s boundaries and not to bend them for your own benefit’ (#975, S_NMD) |
| Parental rights and duties | GM is a moral obligation as I do not have the right to withhold my child from the possibilities created by germline modification | ‘Allowing your child to be born with an abnormality if you could have done something should be a crime. They should put these people in prison and make them pay for the health expenses for life’ (#631, E_NMD) | N/A | N/A | GM is unacceptable as I do not have the right to decide on modifying genes on behalf of my unborn child | ‘You shouldn’t be allowed to decide that for your unborn child’ (#359, E_HIV) |
| (Reproductive) autonomy | GM would fall under my right for autonomy and thus should not be prohibited | ‘My body, my life, my decision’ (#755, S_NMD) | I would only use GM if it remains a free choice to do so | ‘I should never be required to do it. It will become problematic once e.g. health insurance starts demanding it and there will be social pressure’ (#755, E_NMD) | GM would create choices and thereby responsibilities that people are not able to carry out | ‘Once you will have these choices, you may experience guilt complexes for things you attributed to if they go wrong. That’s why you shouldn’t be asked in the first place’ (#245, E_NMD) |

*See Supplementary Table SI for all reasons provided.

W_GLU: Response to the scenario ‘I would eat modified wheat if I would be gluten intolerant’.

S_NMD: Response to the scenario ‘I would cure own neuromuscular disease to prevent ending up in a wheelchair’.

E_NMD: Response to the scenario ‘I would modify my embryo to prevent passing on a severe neuromuscular disease’.

E_HIV: Response to the scenario ‘I would introduce resistance to HIV in my embryo’.

E_INT: Response to the scenario ‘I would increase the intelligence of my embryo’.
Our finding that willingness to use genome modification depends on the scenario in which it is used corresponds to previous findings. More specifically, curing diseases is considered more acceptable than enhancement (Congress, 1987; Macer et al., 1995; Lewis et al., 1997; Singer et al., 1998; Iredale et al., 2003; Evans et al., 2005; Kalfoglou et al., 2005; Massarani and de Castro Moreira, 2005; Meisenberg, 2009; Muller and Shepherd, 2009; Criger and Fekken, 2013; Robillard et al., 2014; Xiang et al., 2015; Blendon et al., 2016; Funk et al., 2016; McCaughey et al., 2016; Scheufele et al., 2017). Curing genetic diseases is considered more acceptable than curing diseases that may be prevented (Singer et al., 1998; Kalfoglou et al., 2005). Somatic modification is considered more acceptable than germ line modification (Lewis et al., 1997; Commission, 2000; Iredale et al., 2003; Trust, 2005; Crne-Hladnik et al., 2009; Blendon et al., 2016; Funk et al., 2016) although some studies highlight the difference as small (Macer et al., 1995; Meisenberg, 2009) and two studies found no distinction at all (Congress, 1987; Scheufele et al., 2017). Even though modifying plants was seen as more acceptable than somatic human modification in some older studies (Congress, 1987; Frewer et al., 1997), this was not the case in our, and other more recent studies, which may be related to the lower clinical need (alternative to a gluten-free wheat versus a neuromuscular disease leading to needing a wheelchair) (Crne-Hladnik et al., 2009; Gaskell et al., 2006).

That men are more likely to support the technology is consistent with previous studies in various other countries (Evans et al., 2005; Meisenberg, 2009; Criger and Fekken, 2013; Xiang et al., 2015; McCaughey et al., 2016). This may be related to women having less trust in the institutions involved (Siegrist, 2000) or women perceiving the applications for genome modification as less valuable (Siegrist, 2000; Crne-Hladnik et al., 2009) or the risks as higher (Xiang et al., 2015). In addition, two previous studies also report that being young (in various countries) is associated with more favourable attitudes towards certain applications of human genome modification (McCaughey et al., 2016; Weisberg et al., 2017). Age was not significant in another US study, however, in this study the age-range may have been limited as all participants were students (Meisenberg, 2009).

In our study, there was a positive association between watching the documentary and acceptability of genome modification. Several explanations may apply. First, it is possible that watching the documentary increased knowledge on genome modification and more knowledge increases acceptability. However, a previous UK study found that increased knowledge from watching a documentary had little effect on attitudes towards gene therapy (Trust, 2005). At this point, the evidence for a positive association between knowledge and acceptability is insufficient (Trust, 2005; Muller and Shepherd, 2009; Scheufele et al., 2017). Second, although the documentary aimed to avoid this, it could have framed genome modification positively. However, a former study showed that framing did not affect participants’ attitudes towards genome modification (Weisberg et al., 2017). Third, people with a priori more positive attitudes towards genome modification may have been more likely to electively watch the documentary.

This study revealed a large number of reasons for the general public to use, or refrain from using, genome modification. Qualitative interviews with individuals or focus groups may provide more in-depth understanding into these reasons. Future quantitative studies may provide insight into which reasons carry the largest weight in the deliberations of representative samples of the general public in various countries. Furthermore, respondents phrasing acceptability as conditional to certain aspects incites interest in determining more exact levels of acceptability (e.g. what risk of off-target effects that would be considered acceptable for which indication?). In addition, studying the impact of more respondent characteristics, genetic literacy, preparatory study information and of recent media attention on perspectives may be relevant.

Moreover, it seems invaluable to incorporate empirical data in an ethical analysis when one wants to make well-informed and pro-active normative claims about a certain practice (Dunn et al., 2012). Therefore, the data provided here and elsewhere may provide a valuable input for further ethical analysis.

Finally, we should evaluate the efficacy of various approaches of public engagement and how these can and should be incorporated into policy-making (National Academies of Sciences, 2017).

Implications for future practice

Further public consultation and a more in-depth ethical and societal debate on principles and conditions for responsible use of germline genome modification is required to develop balanced oversight prior to future clinical introduction. Our study, and another non-representative international survey (McCaughey et al., 2016), provide some preliminary evidence that moral intuitions of the general public support professional statements, which state that the acceptability of germline genome editing should be considered per application rather than banned altogether (Chan et al., 2015; National Academies of Sciences, 2017). Experts in the field and policy-makers should consider the reasons provided by the general public for or against germline genome modification in their deliberations on acceptability and appropriate and balanced oversight (Holdren et al., 2011).

As for communication with the general public, it seems unfeasible to discuss all potential reasons for or against germline genome modification (as there are over a hundred (van Dijke et al., 2017)). Unfortunately, this implies the need to make a selection when providing information, which introduces the potential for biasing the public’s views that experts need to be cognizant of. The results of our study can provide some assistance, as one may wish to address frequently considered and/or fallacious reasons, as well as reasons considered important by professionals but uncommonly reflected on by the public. Although finding a neutral balance between information overload and information deficit may be challenging, maintaining a public dialogue is crucial.

Supplementary data

Supplementary data are available at Human Reproduction Open online.

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Authors’ roles

S.H. contributed to all aspects of the study. N.A.A.G. contributed to the data analysis and critical discussion. A.L.B. contributed to the critical discussion. S.R. contributed to the study design and critical discussion.

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Conflict of interest

None.

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