Rathenau Instituut

The DNA-dialogue: a broad societal dialogue about Human Germline Genome Editing in the Netherlands

Authors: Sophie van Baalen[1], Jeroen Gouman[2], Diewertje Houtman[3], Boy Vijlbrief[4], Sam Riedijk[5] & Petra Verhoef [6]

Corresponding author: Jeroen Gouman[7]

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[1] Rathenau Institute, The Hague, The Netherlands. E: s.vanbaalen@rathenau.nl
[2] Rathenau Institute, The Hague, The Netherlands E: j.gouman@rathenau.nl
[3] Erasmus Medical Center, Dept. of Clinical Genetics, Rotterdam, The Netherlands. E: d.houtman@erasmusmc.nl
[4] Erasmus Medical Center, Dept. of Clinical Genetics, Rotterdam, The Netherlands. E: b.vijlbrief@erasmusmc.nl
[5] Erasmus Medical Center, Dept. of Clinical Genetics, Rotterdam, The Netherlands. E: s.riedijk@erasmusmc.nl
[6] Rathenau Institute, The Hague, The Netherlands. E: p.verhoef@rathenau.nl
[7] E: j.gouman@rathenau.nl / T:+31703421564 / A: Anna van Saksenlaan 51, 2593 HW, The Hague, The Netherlands

1.1 Abstract

For years, calls for public involvement in the debate concerning the acceptability of human germline genome editing (HGGE) have been made. A multidisciplinary consortium of eleven organizations in the Netherlands organized a broad societal dialogue to inquire the views of the Dutch society towards HGGE. The project aimed to reach a wide and diverse audience and stimulate a collective process of deliberative opinion forming and reflection. To that end, several instruments and formats were developed and employed. We present the results of 27 moderated dialogues, organized between October 2019 and October 2020. Overall, participants of the dialogues were capable of assessing and discussing the subject of HGGE in a nuanced way. Analysis of these dialogues shows that, in general, participants had no fundamental and absolute objections towards HGGE technology. However, they only deemed HGGE to be acceptable when it is used to prevent serious, heritable diseases and under strict conditions, without affecting important (societal) values. There was a small group of participants who found HGGE fundamentally unacceptable because it would cross natural, socio-ethical or religious boundaries.

1.2 Introduction

The discovery that CRISPR-Cas can be used as a gene editing technique brought the promise of precise, easy to use and cheap gene editing (Jinek et al. 2012, Cong et al. 2013 and Mali et al. 2013). It also rekindled the debate on human germline genome editing (HGGE), especially after the first experiments with human embryos were conducted (e.g. Liang et al. 2015 and Ma et al. 2017).

The current consensus within the scientific community is that existing genome editing technologies (including CRISPR-Cas) are, at least as of yet, insufficiently safe and effective for reproductive HGGE.[8] Furthermore, it is widely recognized that HGGE raises diverse ethical and societal questions beyond its clinical safety and effectiveness. However, despite calls for public involvement (e.g. Jasanoff 2015; NASEM 2017), the debate about the acceptability of HGGE has remained largely confined to the domain of experts (Jasanoff & Hurlbut 2018).

Currently, the global policy landscape restricts the clinical application of HGGE (Baylis et al. 2020). Various policy instruments like national and international legislation and human rights treaties prohibit to place a genetically altered embryo into a woman's womb to grow into a baby[9]. However, given the rapid advancement of research in this field, the safe and effective use of HGGE is increasingly conceivable, as well as the therapeutic possibilities it may provide. Within the medical field, scientists, doctors and patients hopefully anticipate the possibility of preventing the transmission of (severe) heritable diseases through HGGE (de Wert et al. 2018). Others even imagine enhancing hereditary traits of future generations, such as intelligence or strength (e.g. Savulescu & Bostrom 2009).

In the aftermath of He Jiankui's announcement of the birth of two genetically modified baby's on YouTube[10] in November 2018 (Regalado 2018) and the resulting global outrage and condemnation, several international bodies were tasked with assessing whether the introduction of HGGE in clinical (reproductive) practice can be safe, effective and ethical[11], or whether and how global standards for governance and oversight of human genome editing can be developed.[12] However, extensive societal dialogue on the desirability of HGGE remains limited and is now considered to be even more important to inform (inter)national decision-making processes on the steps

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[8] See, for example, the statements from the 2015 and 2018 international summits on human genome editing (https://www.nationalacademies.org/news/2015/12/on-human-gene-editing-international-summit-statement and https://www.nap.edu/read/25343/chapter/1#7)

[9] Examples are the Universal Declaration on the Human Genome and Human Rights (1997) by Unesco, which states that the human genome underlies "the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity" and therefore advocates a provisional ban on interventions in the human germline (a claim that was repeated in 2015), and called for 'reflection on all possible consequences for human rights and fundamental freedoms and the future of humanity itself' (IBC, 2015). According to Article 13 of the Council of Europe's Convention on Human Rights and Biomedicine, an intervention to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes and only if its aim is not to introduce any modification in the genome of any descendants (Council of Europe, 1997).

[10] https://www.youtube.com/watch?v=th0vnOmFltc

[11] The International Commission on the Clinical Use of Human Germline Genome Editing (https://www.nationalacademies.org/our-work/international-commission-on-the-clinical-use-of-human-germline-genome editing).

[12] WHO expert advisory committee on governance and oversight of human genome editing (https://www.who.int/ethics/topics/human-genome-editing/en/).

towards its potential clinical application (Hurlbut 2019; Vijlbrief et al. 2020; Adashi et al. 2020).

In the Netherlands, at the end of 2018, a multidisciplinary consortium of eleven organizations joined forces to organize a broad societal dialogue to ascertain the views of Dutch society towards the clinical application of HGGE. The consortium included patient's representative groups, academic departments in clinical genetics and reproductive medicine, professional associations, a technology assessment institute, the National Institute for Public Health and the Environment, and science communication organizations[13]. The Ministry of Health, Welfare and Sport welcomed the initiative of this consortium and has, therefore, financed the project titled 'A public dialogue on germline genome editing'. The consortium operated independently from the ministry in the design and organization of the project as well as the collection, analysis and reporting of the results. The aim of the project was to reach and include a wide and diverse audience, inform them about the opportunities and uncertainties (e.g. on efficacy or safety) of HGGE and the societal and ethical issues that surround it, and invite people to discuss their hopes, questions, wishes and concerns on the clinical application of HGGE. With this approach we aimed to stimulate a collective process of opinion forming and reflection in the Netherlands: a nation-wide dialogue. The rich diversity of perspectives and considerations that were gathered within this project will inform political decision-making and bring further societal reflection on HGGE. In this paper we present the methods of the Dutch "DNA-dialogue" and the results of a thematic analysis of what participants discussed during dialogue sessions.

1.3 Methods and Materials

Transdisciplinary communication

At the onset of the project, the consortium worked on documenting what terminology to use and avoid, and how to explain the biology and technology involved in HGGE to participants in a sound and understandable way. This ensured consistent use of language that was intelligible to a broad public. For example, in project publications, during events or contact with the press, the phrase "modifying DNA of embryo's" was used instead of "germline genome editing".

1.3.1 Lessons for the dialogue

To identify the societal and ethical issues that are relevant to HGGE, and to assess to what extent, and by whom these had been discussed in the Dutch public debate so far, a study of the relevant ethical literature, expert interviews and an analysis of articles about HGGE in the biggest Dutch newspapers were conducted between January and June 2019. The results thereof have been published in a comprehensive report, that

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[13] Erfocentrum, NEMO kennislink, Erasmus MC, Rathenau Instituut, NPV- Zorg voor het leven, Centrum Media & Gezondheid (CMG), Rijksinstituut voor Volksgezondheid en Milieu (RIVM), Amsterdam UMC, Nederlandse Associatie voor Cummunity Genetics en Public Health Genomics (NACGG), Vereniging Samenwerkende Ouder- en Patiëntenorganisaties (VSOP) and Vereniging Klinische Genetica Nederland (VKGN)

concluded with ten lessons relevant to the design and contents of a societal dialogue on the clinical use of HGGE (Van Baalen, Gouman & Verhoef 2019).

1.3.2 Techno-moral scenarios

In addition, the report by Van Baalen et al. describes four techno-moral scenarios (Boenink et al. 2010) or foresight studies, that are based on the social and ethical issues that were identified in the interviews and desk research (see 'Lessons for the dialogue' above) and a workshop in which experts refined and supplemented drafts of scenarios written by the researchers (SB, JG, PV). These scenarios each sketched a different society based on four different application strategies for HGGE in the Netherlands, but potentially anywhere else in the world. These scenarios imagine the year 2039, in order to specify and elucidate the possible consequences and the underlying moral dilemmas for individuals and society as a whole. The scenarios aimed to provide guidance for reflection on, and discussion of, both short- and long-term consequences during the public dialogues (Van Baalen, Gouman & Verhoef 2019).

The clarity and applicability of the lessons and the scenarios were tested in two focus groups consisting of ten and eight Dutch citizens, respectively.[14]

1.3.3 Dialogues: format and target audiences

The project aimed to give a voice to diverse groups of people, in order to include a wide variety of perspectives. In addition to a broad, general audience, some dialogues specifically targeted medical professionals (such as midwifes, embryologists, fertility doctors, human geneticists and clinical geneticists), school children, (child) patients, youth, elderly, people with a migrant background or with lower literacy. To reach all these audiences, a so-called 'impact plan' was developed, outlining which media outlets were to be used to recruit for or report on dialogue events. Each dialogue was tailored to the target audience, for example by using simpler language or start the dialogue from the experience of the specific group.

To instruct moderators and experts invited to introduce certain aspects of HGGE a manual was developed, describing their role in the dialogue. Experts were expected to not only inform and explain, but to also take part in the dialogue and to be responsive to the questions and arguments raised by the public. Moderators were asked to stimulate participants to formulate their perspective on HGGE and to give arguments to underpin it. Participants were also invited to respond to each other and to reflect on their own perspectives and arguments and those of others. This contributed to making explicit the underlying values and considerations and to formulate specific (societal) conditions for the application of HGGE.

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[14] https://www.rivm.nl/bibliotheek/rapporten/2019-0181.pdf (in Dutch)

1.3.4 Questionnaire

Parallel to the organizations of the dialogues, a questionnaire on various aspects concerning HGGE was developed and distributed among two independent samples of the Dutch population, each consisting of around 1200 citizens. This public opinion polling took place at two moments: August 2019 (right before the start of the broad societal dialogue) and April 2020 (in the middle of the series of societal dialogues). The aim of this questionnaire was to stimulate reflection on HGGE among a large group of citizens and learn about their perspectives in a quantitative manner. These questionnaires were also sent to participants of the public dialogue events, before and after the event, in order to study whether taking part in a dialogue would change a person's attitude towards HGGE . The results of the studies will be published elsewhere by Houtman et al.

1.3.5 Dialogue instruments

Several instruments were developed to engage the public with the topic and to stimulate participants to share their perspectives, arguments, questions, hopes, wishes and concerns.[15]

Techno-moral vignettes
From the future scenarios described above, three techno-moral vignettes were devised: brief, thought-provoking animated four-minute films that are set in the future societies described in the scenarios. Each animation focused on a couple with a desire to have children in the year 2039. The animations differed in the strategy on clinical application and governance of HGGE and hence addressed various ethical and societal aspects. The vignettes (animated films) were used to initiate discussion and stimulate deliberative opinion forming at the moderated events. Shorter versions were available for public engagement through social media. The animations helped the audience to imagine different futures and possibilities, and to empathize with the people who will live in these future societies[16]. See figure 1 for screenshots from the techno-moral vignettes.

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[15] Not all instruments that were developed in the context of this project are discussed here. A complete overview can be found in the Report and accompanying attachments (in Dutch): https://dnadialoog.nl/

[16] "Caring for babies starts before conception", "Equality begins in the genes", "The Netherlands says no to genetic modification"

Figure 1: Stills from the techno-moral vignettes. Illustrations by Zaou Vaughan.

Expression cards

Color neutral cards (i.e. avoiding red and green) with different emoji's representing emotions such as happy, sad / angry, shocked / amazed and thoughtful were handed out to all participants in different dialogues. Participants could use the cards to respond to animations or questions. They served as a quick means to gauge the mood in the room. The moderator could also use the raised cards to invite people from the audience to share their thoughts and perspectives.

Other ways of engaging the public

To engage the public in diverse dialogue settings, several other instruments and formats were developed.

- CityLab – An interactive concept to engage the public and investigate the public perspective concerning societal questions regarding science and technology. [17] Combining theater, co-creation, design and information, a set of on-site activities regarding HGGE were developed to be employed at festivals and other large public events.
- "Sketching the future" – Whilst a small group of participants discussed the potential consequences of HGGE, an artist made a comprehensive drawing of the topics that were discussed.
- "Flaw-fixers" – A package of "flaw-recoveroid", a mock-up drug (i.e. peppermints) to repair genetic flaws, was distributed to participants of dialogue events. The package contained more information about DNA, HGGE and the DNA-dialogue. It was also used as a vehicle to conduct one-on-one conversations on HGGE with visitors of festivals.

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[17] https://www.nemokennislink.nl/pagina/city-lab/

- Teaching materials – Two e-learning packages were developed for children between 10 and 13 years and 16 and 18 years, to be used for teaching and dialogue in an educational setting.
- Online quizzes - A Facebook quiz to stimulate the dialogue and an informative quiz about DNA and HGGE.
- Online videos: A film in which patients with a hereditary disease give their perspectives on HGGE and a film in which passers-by are asked about their opinion on HGGE.

1.3.6 Analysis of the moderated dialogues

To qualitatively analyze the conversation of each dialogue, reports were made of the moderated dialogues using a semi-structured report form. Because of logistical issues, no (appropriate) report was made of three moderated dialogues, resulting in 24 reports for analysis.

A random selection of three reports out of 24 reports was used to cluster and categorize the results of the dialogues. This resulted in the identification of six recurring themes that were formulated as six key questions that were central to the conversations.[18] Next, two researchers (SvB and JG) coded all reports, by providing each text fragment with one or multiple color codes, corresponding with the relevant theme(s). Each dialogue report was firstly coded by one of the researchers, and subsequently the coding was checked by the other. In case of disagreement, the researchers discussed until consensus was reached.

After coding, all text fragments were compiled for each theme to identify and summarize the central lines of conversation using pre-defined questions for analysis:

- What concerns, hopes and expectations do participants express?;
- Which issues are addressed within this theme?;
- (How) do participants' perspectives on these issues differ?;
- Which dilemmas do participants see and which considerations do they make?;
- About which issues do participant largely agree, and which issues give rise to disagreement?

Answers to these analysis questions were formulated in terms of the *values, concerns, hopes, and expectations* underlying the perspectives and dilemma's and the *conditions* that participants formulate to be able to accept the clinical use of HGGE in the future.

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[18] Do we want to use HGGE and if so, for which purposes? (1), How should we shape the clinical practice in which HGGE is embedded? (2), What risks are connected to HGGE and how should we deal with them? (3) What organizational and ethical issues are connected to basic and clinical research of HGGE? (4), What societal implications could application of HGGE have? (5), What notions of the good life, reproduction and parenthood exist in relation to HGGE? (6)

1.3.7 Ethical approval

This study did not require review by an Ethical Review Board because it falls outside the scope of the Dutch laws that regulate medical research with humans.

1.4 Results

Twenty-seven moderated dialogues were organized between October 2019 and October 2020. The dialogues took place in various settings and had different forms. They ranged from intimate conversations with a small group of people to dialogues with tens to hundreds of people at large events like festivals. They were mostly organized ‘offline’ (live events) but also online or a combination of the two (‘hybrid’ event). They were held across the country; with specific audiences or mixed audiences. An overview of all dialogue sessions, numbers of participants and target audiences can be found in Table 1. Figure 2 illustrates the diversity and spread of the dialogue events across the country by pinpointing a variety of the events on a map of the Netherlands.

Table 1: Details of the 27 dialogue events

Dialogue event title	**# of Participants**
General public (mixed audience)	
DNA-dialogue Kick-off Event	142
InScience Film Festival – the Opinion Factory	50
InScience Film Festival - Sketching the Future	30
InScience Film Festival – Talkshow ‘Baby Building Site’	45
DNA-dialogues at the Nine Months (pregnancy) Fair and the Housekeeping Fair	20 (+ 30 individual conversations)
Veritas Forum: Human on Demand	75
DNA-Festival at Science Museum NEMO	45 (+ 90 online)
DNA-dialogue “Discuss your malleable future” at science museum Boerhaave	15 (+24 online)
Is DNA holy? A dialogue from ideological perspectives	A panel of 4 religious leaders and a small, diverse audience (+ 71 online)
DNA-dialogues at the Radboud University Discovery Days for patients and family	8 (online)
DNA-Dialogue at the Bethlehem Church,	20

*DIY Dialogue**	
Children and Youth	
Youth Think Tank (University students)	5
NEMO Science Night (high school teachers)	41
DNA-dialogue at the Erasmus Medical Centre- Sophia Children's hospital (ages 8-12 years)	12
DNA-dialogue at the Emmauscollege (high school students)	19
DNA-dialogue at the Science Café Deventer (ages 7-10 years)	22
Klokhuis Meetup (ages 10-12 years) *DIY Dialogue*[a]	9 primary school classes + live stream
Special target audiences	
Low Literacy Think Tank	3
Low Literacy Think Tank	3
DNA-dialogue at the Karma Care Cooking Club (senior citizens)	14
DNA-dialogue at the Community center Hof 't Spoor (women with a migration background)	12
DNA-dialogue at Karma Zorg Utrecht Overvecht (senior citizens with a Surinamese background)	19
Medical professionals	
DNA-dialogue at Scientific Conference of the Dutch Organization for Clinical Embryology	100
DNA-dialogue with midwives	17
DNA-dialogue with medical students	20
DNA-dialogue with fertility doctors and students	21
DNA-dialogue at the annual congress of the Dutch Society for Human Genetics (NVHG)	210
[a]DIY Dialogue: organized by others in consultation with DNA-Dialogue	

Figure 2: Map of the Netherlands with a selection of dialogue events.[19] Illustration by Laura Marienus.

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[19] For a complete overview of dialogue events, see table 1. Due to the corona measures, planned dialogues in other provinces have been canceled. As a result, the physical gatherings were less spread across the country than intended.

1.4.1 Do we want to use HGGE and if so, for which purposes?

Participants considered the ability to prevent suffering to be an important value. The possibility of HGGE to contribute to that value by preventing a severe heritable disease to be passed on to one's offspring was considered to be an important reason to find clinical application of HGGE an acceptable medical option in the future. How to judge whether the severity of a heritable disease warrants preventing it through HGGE was a question participants found particularly important and complex. Many of them discussed this in terms of the impact that the disease could have on the quality of life of the child. Others also took into account whether the prospective parents were psychologically or financially capable of caring for a child with special needs.

Furthermore, participants who were familiar with the field of artificial reproductive technologies often questioned whether a significant unmet medical need exists for HGGE, since the vast majority of prospective parents at risk of passing a severe heritable disease to their offspring could prevent this through preimplantation genetic diagnostics (in vitro fertilization in combination with the genetic testing and selection of embryos).

1.4.2 What risks are connected to HGGE and how should we deal with them?

Generally, participants considered HGGE to be more risky than existing reproductive technologies. A large concern they had with HGGE is the risk of unintentional, harmful modifications of the genome that would not only affect the person whose genome was edited, but would also be passed on to his or her offspring. Many participants therefore found clinical use of HGGE only acceptable if strict precautionary measures can be taken to ensure its safety and only if there is proper oversight.

1.4.3 What organizational and ethical issues are connected to basic and clinical research of HGGE?

Related to the former, participants recognized the importance of pre-clinical research into the safety and efficacy of HGGE before its potential implementation in clinical practice. However, perspectives differed on whether such research could be done using human embryos. A significant group of participants (mostly with a Christian background) was opposed to this. Many others agreed that whilst human embryos deserve some degree of respect and protection, their use in research into HGGE is justified by its potential medical benefits.

Participants found it important that the children who are born as a result of clinical research or application of HGGE are closely monitored to check for unintended, harmful effects. For some participants, preventing harm to (future) edited children warrants frequent, potentially, life-long monitoring. Others were more hesitant because they imagined that such intense monitoring might overly infringe on their lives.

1.4.4 How should we shape the clinical practice in which HGGE is embedded?

Many participants noted, or had experienced firsthand, that pregnancy and reproduction are increasingly surrounded by technology, such as preconception and prenatal genetic tests. Some participants welcomed these development and new technologies such as HGGE, for giving prospective parents valuable reproductive choices. Other participants feared that, as a result of these technological possibilities, prospective parents are confronted with, and sometimes overwhelmed by, (increasingly) complex decisions that are often morally and emotionally charged and often accompanied by (perceived) societal pressure. They suspected that this will further increase if parents would have the possibility to alter their children's genome.

Related to this, participants often stressed the great importance of future parents being able to make a free, well-considered choice whether or not to use HGGE, without any social or societal pressure. Participants expected that extensive and objective counseling by medical professionals could contribute to this. However, some participants noted that such counseling could also undermine autonomous choice, if medical professionals advise pro HGGE rather than inform. Others recognized that for prospective parents' decisions to be truly free, they should be able to trust that proper care and facilities will remain accessible for future people born with diseases that could have been prevented by HGGE (i.e. in a society where HGGE would be commonly used), thus ensuring that it remains a realistic option not to use HGGE. This relates to the value of solidarity.

1.4.5 What societal implications could application of HGGE have?

A recurring concern was that existing and future people who have a heritable disorder will experience negative consequences if their disorder could have been prevented by HGGE, such as stigmatization, or the diminishing quality and accessibility of the care they need. Participants who were themselves affected by hereditary disease sometimes expressed the fear of not being accepted for who they are. Most participants expected that the potential societal consequences of HGGE will be much more severe if its application was not limited to preventing severe hereditary disorders, but would also include improving certain characteristics of future children. The vast majority of participants opposed such applications and expressed concerns that this could lead to the emergence of a "class society", the increase of existing socio-economic inequality, loss of diversity, or (mis)use by powerful parties or countries to "create" people with certain characteristics. Apart from these societal consequences, many participants found that 'improving' or 'choosing' traits of future children, would hamper their ability to shape their own lives. Some participants did not oppose all 'improvements'. They had no objection to altering traits such as eye color, since they deemed them trivial and not to be a meaningful part of one's identity.

1.4.6 What notions of the good life, reproduction and parenthood exist in relation to HGGE?

Participants had different views of what a good life entails, about reproduction, or of what constitutes ‘good’ parenthood. These notions permeated the conversations, whilst often remaining implicit. For example, some participants were hesitant towards HGGE because they found it important that parents accept their future children, despite potential diseases or imperfections. They stressed that parents should experience their children as being given to them, and not as something to be chosen or designed. Whilst others embraced HGGE because in their view it helped (prospective) parents to fulfil their responsibility to prevent harm to their future children.

We summarize the discussion during the dialogue events, structured by the six recurring themes we identified. Table 2 illustrates the discussion within each theme with several quotes from different dialogues.

Table 2: Recurring themes with quotes from dialogue events

Theme	Quotes
1) Do we want to use HGGE and if so, for which purposes?	“It’s fine if parents make changes in the DNA of their child if this prevents disease. But they should not interfere with other things” “Within the Jewish Faith, a long and healthy life is of great importance. HGGE may contribute to that.” “With some diseases, such as autism, it is much less clear whether these are severe enough to prevent through HGGE. It also depends on how well parents can deal with it.” “Every prospective parent should be able to choose whether they want to use HGGE. If you can safely switch off a defective gene early on, that's great.”
2) How should we shape the clinical practice in which HGGE is embedded?	“It's up to the patients. They have the experience of what it is like to live with a genetic disease.”

	“Future parents are getting more and more choices. Can they handle them? Or does it only cause stress?” “It would be undesirable if the decision of prospective parents whether to make use of HGGE is influenced by financial considerations”
3) What risks are connected to HGGE and how should we deal with them?	“You might edit genes that then turn out to have been beneficial. For example if they protect against certain diseases” “I wouldn’t trust that this technique is entirely safe.”
4) What organizational and ethical issues are connected to basic and clinical research of HGGE?	“Nobody wants to be the first to have a genetically modified child without knowing the consequences.” “Will it be necessary to monitor a genetically altered child its entire life? Or can you just check at once whether everything went okay?” “Scientists say that the development of the technique requires the cultivation of embryos. I find that ethically unacceptable.”
5) What societal implications could application of HGGE have?	“In my opinion, what’s scary are not the technical options that couples (will) have, but the pressure from government or society to use them” “I don't see my language skills as something that needs to be edited. Poor language skills are a handicap, but one that is mainly caused by society. Society should change.” “If we can edit out every disease, won’t that lead to overpopulation?”

	"Differences make society better." "This technique could be used to create an army of genetically modified soldiers." "Will all of society have access to this technology, or only the privileged few?" Imperfections do not equate an unhappy or less valuable life."
6) What notions of the good life, reproduction and parenthood exist in relation to HGGE?	"Our generation didn't even know whether they were getting a boy or girl. You just hoped that your baby would be born healthy. I don't know whether I would have wanted to know beforehand. It's very difficult." "With DNA-modification, I might not have been who I am now." "In the future, children might blame their parents for not intervening genetically when it was possible." "The carefree experience of pregnancy is already affected by current technologies for screening the unborn child." "Won't we just get used to HGGE? We used to think a test tube baby was very strange."

1.5 Conclusion

In the DNA-dialogue, a wide and diverse audience, has discussed their hopes, questions, wishes and concerns on the clinical application of HGGE. Overall, participants of the dialogues were capable of assessing and discussing the subject of HGGE in a nuanced way. Their perspectives were the result of weighing different arguments and considerations. In doing so, they took into account both the (medical) benefits and risks as well as the potential broad societal consequences of HGGE. From these discussions, a set of values was derived, that need to be protected in decision-making about further research and the possible introduction of the technology into clinical practice. These values fall into three groups 1) important for deciding whether or not the clinical use of HGGE is acceptable; 2) important values that need to be protected in the practice surrounding the clinical application of HGGE; and 3) values in society that need to be protect when the clinical application of HGGE is introduced. An overview of these values can be found in Table 3.

Table 3 : Participants' values regarding HGGE

Important for acceptance:	**Important to protect in society:**
Safety / precaution	Diversity
Prevention of suffering / illness	Acceptance (of differences) / inclusivity
Protection of early human life	Non-discrimination and non-stigmatization Equality
Respect for the autonomy of the future child	Solidarity
Important to protect in practical application:	
Freedom / self-determination / autonomy	
Accessibility	
Oversight regarding accessibility and use	

Synthesizing the perspectives, arguments and concerns expressed in the dialogues, participants in general had no fundamental or unchangeable objections to HGGE technology. However, this does not mean they automatically favored its clinical application. They only deemed HGGE to be acceptable when it is used for a very specific purpose: to prevent serious, heritable diseases, and under strict conditions, without impairing important (societal) values. The diversity of questions and concerns participants voiced shows many deem HGGE a controversial topic. Participants noted that it is difficult to make a sharp distinction between the prevention of diseases and enhancement, and between diseases that are severe or not severe enough. There was a small group of participants that found HGGE fundamentally unacceptable because in their eyes it would cross important natural, socio-ethical or religious boundaries.

1.6 Discussion

Recent questionnaire studies investigating the public opinions corroborate our findings. A vignette study among the Dutch general public, for example, found that participants were not categorically opposed to HGGE, but strongly opposed using HGGE for enhancement, and that safety is an important factor for the acceptability (Van Dijke et al., 2020). An international survey among Canada, the U.S., Brazil, Germany, Sweden, the Netherlands, the UK, France, Spain, Italy, Poland, Czech Republic, Russia, South Korea, Japan, Taiwan, India, Singapore, Malaysia and Australia shows that, although the public is cautious towards scientific research on gene editing, most publics support therapeutic use and oppose use to improve characteristics such as intelligence (Pew Research, 2020). The results from the DNA-dialogue enrich these quantitative studies by providing insight into the, sometimes competing, values that underlie the public's opinion, and the multitude of perspectives that exist among the public.

The DNA-dialogue has successfully engaged a wide and diverse audience from the Dutch public to be informed on and to exchange their perspectives, arguments, questions, hopes, wishes and concerns about clinical use of HGGE. Together, the perspectives, conditions and values that were collected in the DNA-dialogue can guide policy-makers, scientist, experts and the Dutch society as a whole to shape future research, legislation and potential future clinical application of HGGE.

The DNA-dialogue can be used as a model for societal dialogue in other countries. However, governance and policy-making regarding HGGE does not take place in a national vacuum: the global discussion has intensified over the past years and steps have been taken to strengthen governance and regulations internationally. As an issue that concerns scientists, clinicians, patients, citizens and societies around the world, governance of HGGE requires international alignment. The insights of the DNA-dialogue can be used to stimulate and enrich the international discussion.

1.7 Acknowledgments

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1.8 Author Contribution Statement

All authors contributed to, reviewed, revised and approved this manuscript. Sam Riedijk and Petra Verhoef were involved with the design of the project (the Dutch DNA-Dialogue), Sophie van Baalen, Jeroen Gouman, Diewertje Houtman and Boy Vijlbrief were responsible for the data-collection (reporting what was said during each dialogue). Analysis of the dialogue reports was performed by Sophie van Baalen and Jeroen Gouman and the first draft of this manuscript was written by Sophie van Baalen, Jeroen Gouman and Petra Verhoef.

1.9 Author Disclosure Statement

None of the authors have any conflicting interests to declare (personal, financial, or otherwise).

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