AUSTRALIAN CITIZENS' JURY ON GENOME EDITING

GENOME EDITING: FORMULATING AN AUSTRALIAN COMMUNITY RESPONSE

REPORT TO DECISION MAKERS, STAKEHOLDERS AND MEMBERS OF THE PUBLIC

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with

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EXECUTIVE SUMMARY

Genome editing is a new development in science that allows very targeted modifications to be made to DNA, the genetic material that almost all living things possess. It can potentially be used in plants and animals for such things as modifying the way they adapt to changes in the climate. It can also be used in humans to prevent or treat certain diseases and disabilities. There are many other potential uses. There are benefits and risks associated with genome editing, which raise many ethical, legal, and social concerns. One of the applications of genome editing that is seen as being particularly ethically fraught is its use to make changes to human DNA that can be inherited by future generations.

Over the past few years, a number of reports have been published on genome editing by eminent scientific and policy groups. In general, these reports reveal a cautiously optimistic outlook for the contributions that genome editing might make both to human health and welfare and to the environment. However, they recognise the need for robust regulation of genome editing applications, reflecting ethical norms and community values. They adopt a particularly cautious approach when it comes to changes to human DNA that can be inherited. The reports uniformly call for community engagement on genome editing, but provide little guidance on how this might be undertaken and to what end.

This report provides background, methods, results and policy perspectives on a community engagement project undertaken in Australia in 2020-2022, focusing exclusively on the use of genome editing techniques in humans. The project was funded by the Genomics Health Futures Mission (GHFM) of the Medical Research Future Fund (MRFF). The MRFF is a long-term investment by the Australian Federal Government supporting Australian health and medical research. The MRFF aims to transform health and medical research and innovation to improve lives, build the economy and contribute to health system sustainability. Funds from the MRFF are invested in genomics research through the GHFM, with the aim of improving testing and diagnosis for many diseases, helping personalise treatment options to better target and improve health outcomes, and reducing unnecessary interventions and health costs. The GHFM Roadmap lists 'developing a better understanding of the ethical legal and social implications (ELSI) of genomics and facilitating public trust and public engagement' as one of the priority areas for investment. This project was one of nine ELSI-related projects selected for funding in the first tranche of GHFM funding. The team undertaking this project brings expertise in respect of the ELSI of genomics and related technology (Nicol and Rudge), deliberative democracy (Niemeyer, Dryzek, Curato and Veri), science and technology studies (Paxton) and science communication (Pemberton).

The centrepiece of the project was the Australian Citizens' Jury on Human Genome Editing. Although we recognise that a discrete event such this is not a substitute for a wider process of public

engagement and debate, it can provide a valuable contribution. Deliberative events of this nature are particularly important for complex issues such as human genome editing which raise profound ELSI affecting the public interest. The citizens' jury thus has an important 'discursive' role, allowing us to learn what happens when the public interacts with the science under conditions that approach the deliberative ideal, where norms of respect, reflection, and informed reason-giving are in play. Even so, while the outcomes of these types of citizen deliberation are informative, providing important insights, they should not be seen as decisive. Forming a discursive (or considered) public view requires an extensive and ongoing approach. The outcomes of the Australian Citizens' Jury thus provide important material that can be harnessed to inform and engage the wider public.

The Australian Citizens' Jury on Human Genome Editing also has a 'decision-making' role, by identifying some of the most important policy questions that need to be addressed. These questions cannot easily be answered in this initial step, but their foregrounding as part of this project constitutes an important outcome. The citizens' jury, along with wider engagement with experts and other members of the community, has identified a range of matters that require policy consideration and further public discussion.

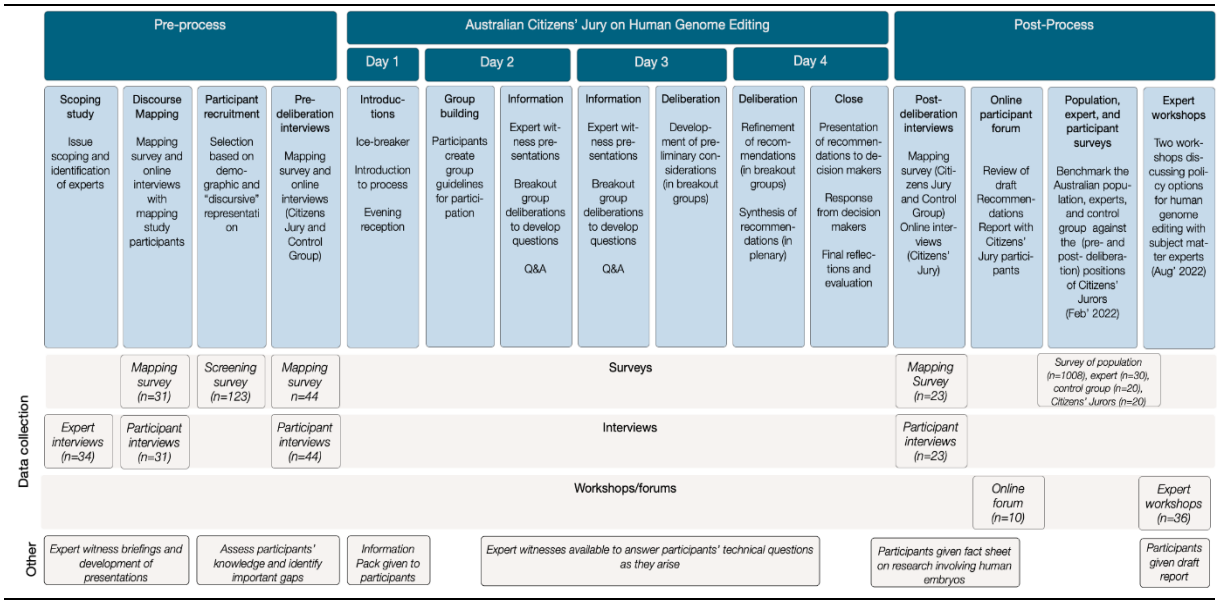
The Australian Citizens' Jury on Human Genome Editing was held at the Museum of Australian Democracy at Old Parliament House in Canberra, Australia from 17 to 21 June 2021. Participants heard from experts and engaged in a facilitated process to deliberate on the basic principles that should underpin policy responses to current and future developments in human genome editing technology. Participants were asked to deliberate on the following question: 'under what conditions (or circumstances) might the application of human genome editing technology be acceptable?'.

Alongside the citizens' jury itself, a range of associated activities involving members of the public took place, which are summarised in Figure 1. Highlights included:

- A study to examine the range of salient positions on genome editing that currently exist among the public (discourse mapping), undertaken prior to the citizens' jury.
- Recruitment of two cohorts guided by the mapping study in order to reflect both demographics and the diversity of positions on genome editing in the community (discursive representation). The first cohort comprised the 23 individuals who participated in the citizens' jury (the participant group). The second cohort comprised 21 individuals who did not participate in the citizens' jury but participated in other aspects of the project (the control group).
- Post-citizens' jury interviews with the participant group.
- A follow-up online forum with some of the members of the participant group to finalise reported recommendations.
- A survey on genome editing, the aim of which was to assess the medium-term impact of the citizens' jury on participants' positions, and to compare their responses with the control group and a broader sample of participants from the Australian population (the population group).

Figure 1 also shows the range of additional research material collected in association with the event, the preliminary analysis of which informs this report.

Figure 1: Public engagement activities conducted over the course of the project, with associated data collection methods and sample sizes.



Throughout the project, experts representing a diversity of views and disciplinary expertise (see Appendix D) in the fields of genomics, healthcare delivery, bioethics, politics, social sciences and other disciplines were also consulted. In particular, prior to the discourse mapping study, open-ended interviews with 34 experts were used to identify the relevant dimensions of the issue. These and other experts were also invited to undertake a slightly modified version of the post-citizens' jury survey on genome editing to compare the responses of experts with the participant group, the control group and the wider population. Experts were also invited to attend online workshops to canvass the policy implications of the outcomes of the citizens' jury and assist in their translation into policy recommendations. Seven experts were invited to give presentations and answer questions at the citizens' jury, to assist participants in their deliberations.

The primary outcome of the citizens' jury and the subsequent interactions with the participant group was a set of recommendations, along with supporting reasons, both of which are provided in full in Section 5 of this report. Participant discussions at the citizens' jury and in the post-jury interviews, online forum and survey revealed wide diversity in underlying discourses. This same diversity was also detected in the population, control and expert groups. Some participants in each group expressed reservations about any forms of genome editing, particularly those involving use of human embryos. Others were much more enthusiastic about the promise of genome editing, and concerned that excessive regulatory requirements could hamper progress. The citizens' jury recommendations thus reflect primarily the views of the majority of participants, which could perhaps best be described as cautiously optimistic that genome editing could provide a valuable contribution to healthcare in the future, provided that it is properly regulated, well researched and delivered equitably. To a large extent, then, these views mirror those expressed in the reports of science and policy groups mentioned above.

The recommendations include both general principles and specific points relating to non-heritable and heritable forms of genome editing. In summary, the recommendations illustrate that, in the view of the majority of participants:

- Applications of human genome editing should be restricted to the alleviation of human suffering, improvement to quality of life, and reduction of childhood mortality.

- Genome editing should be properly regulated, with regular review including stakeholder and community input.
- Genome editing should be made available equitably to those most in need, and informed consent must be assured.
- Clinical development of genome editing should be informed by adequate research to identify and assess the potential risks and benefits, both to the individual and to society.

Participants were more cautious about heritable than non-heritable forms of genome editing, emphasising that the former should only be considered at some stage in the future, after more research to assure safety and efficacy, and more community engagement for guidance on how to proceed responsibly with the technology.

Participants also considered genome editing research involving human embryos. Given that questions associated with embryo research were not fully canvassed at the citizens' jury, they were revisited in post-jury interviews and an online forum. Many participants expressed particular discomfort with the creation and use of human embryos specifically for research. For some participants, creation of human embryos for research was and would continue to be untenable. However, a majority of participants expressed in principle support, recognising the need for this form of research if heritable genome editing is to become a reality, in the absence of other suitable alternatives.

Although not discussed in detail, the majority of participants also expressed cautious support for mitochondrial donation, a technique that has since become legal in Australia, subject to stringent regulation.

From the policy perspective, five key themes have emerged from the academic and policy literature, from the citizens' jury deliberations, from the other forms of community engagement and from engagement with experts during the course of this project. Each theme is underpinned by more specific points for consideration in policy development.

1. Embedding equity and other values and principles in human genome editing policy

- As clinical applications of genome editing become available, they should be made broadly accessible to those in need, with particular focus on those applications that alleviate human suffering, improve quality of life, and reduce childhood mortality. Methods will thus need to be developed to operationalise priorities, based both on the severity of the disorder or disability and the number of people affected, taking into account considerations broader than financial burdens and benefits.
- Intellectual property should be a tool both for facilitating development of clinical applications of genome editing and for facilitating open and legitimate genome editing research. This may require the development of policies and guidelines to ensure that research remains unfettered by intellectual property constraints.
- Distributive justice demands both that genome editing applications are made broadly available, and also that research and development into new genome editing applications is targeted to those most in need in Australian society (and the broader global community). This will require further priority setting by governments.

2. Ensuring that therapy, enhancement and other applications of genome editing to humans are appropriately regulated

- Genome editing tools may be used in a range of ways, many of which may not even be in contemplation at the current time. As such, it is important to assess whether the current regulatory framework relating to therapeutic goods is adequate in assessing and monitoring the safety, efficacy and utility of the various uses to which genome editing tools might be put.
- Evidence of misuse of genome editing tools internationally indicates that the Australian federal government should consider supporting the WHO recommendation for reporting misuse of human genome editing research and other activities. The Australian federal government and other funding agencies should consider whether to require that all clinical trials involving genome editing should be included on the WHO's Global Human Genome Editing Registry. Further, Australian governments should also consider whether explicit offences should be enacted for unapproved human genome editing, whether it used for clinical or non-clinical purposes.

3. Deciding what types of human genome editing research should be allowed and supported, recognising differing views on the status of the human embryo

- Noting that various non-heritable forms of human genome editing research are already well underway in Australia, Australian governments may wish to consider funding priorities to ensure that this country remains at the forefront of this research effort. The Genomics Health Futures Mission may be an appropriate forum for this work.
- Although there appear to be no current licences for the use of human embryos for genome editing research, it would be unfortunate if no further progress is made in increasing our understanding of the legitimacy of using embryos for genome editing research until such time that the first application is made for a licence. As such, it may be appropriate for the governments of Australia to consider questions associated with the use of human embryos for these purposes in the near future.
- More particularly, the creation of human embryos for research purposes remains contested. The experience with mitochondrial donation provides a model both for how to undertake public consultations on such matters, and how a strict and tightly prescribed legislative regime might be created for this purpose, should this be deemed appropriate.

4. Preparing for a future when heritable human genome editing may be shown to be safe and effective

- We are not yet at a point in time in Australia where the application of heritable human genome editing is imminent. Indeed, it appears that we are not yet at a point in time in this country when genome editing research involving human embryos is being planned. Despite this, it is suggested that it is timely to consider the approach that might be taken in Australia, should heritable human genome editing ever be seen as a realistic option for parents desiring to have healthy, genetically related children.

5. Building meaningful public participation in governance of human genome editing into the future

- Should the Australian governments decide to explore further any of the points we have outlined above, public participation will need to be built into the process. Moreover, any new regulatory and other policy directions emerging from this exploratory process will need to be accompanied by ongoing public participation.
- Public participation planning should include culturally respectful inclusion of Aboriginal and Torres Strait Islander communities.

There were some provisos in relation to this project. The topic is both complex and anticipatory (i.e., not yet subject to substantial public debate). Funding and time limitations, together with the breadth of the inquiry, posed particular challenges. This meant that the citizens' jury had to be carefully designed, in consultation with practitioners and experts, if we were to achieve the primary goal of generating an informed and reflective account of the public view that could then be shared with the wider community as well as relevant decision makers. The resulting limitations lead to three important provisos:.

First, despite the care taken in designing the process, insufficient time was available at the citizens' jury for detailed deliberation on this complex area of scientific development and associated ELSI. The post-jury interviews and the online forum provided the opportunity for further reflection, but the shortage of time for group deliberation is duly acknowledged by the research team. Although the process succeeded in facilitating reflection across a wide range of issues (Appendix E), there were a group of concerns that were not fully worked through, and these concerns represent a particularly important perspective.

Secondly, almost half of the participants at the citizens' jury drew attention to the absence of advocates speaking in opposition to genome editing. This is despite the distribution of perspectives among the expert witnesses reflecting a diversity of views, including those reflecting the more sceptical views of participants and the community (see Appendix D, section D.3). Experts were chosen for their expertise in canvassing the wide ranging scientific, clinical, legal, social and ethical issues associated with genome editing, and for representing a wider range of views (see Section C.5). Nonetheless, many participants felt that the Australian Citizens' Jury would have benefited from inclusion of other viewpoints, in addition to expertise provided by the expert witnesses. It is noted, however, that, while this limitation, combined with limited time, impeded reflection on some potentially important issues, it did not have a regressive impact in a deliberative sense. Our analysis reveals that genuine deliberative reflection did occur, and that Australian Citizens' Jury participants did not simply adjust positions to reflect those of the participating experts (sections 6 and 7). In short, we achieved our objective of simulating a high quality deliberative public conversation, but there are important provisos, and lessons for decision making and further public engagement, including with important but potentially marginalised perspectives.

Thirdly, the absence of participants from Australia's Aboriginal and Torres Strait Islander communities represents a notable and significant gap in the perspectives canvassed at the Australian Citizens' Jury. We acknowledge that these perspectives would have been deeply valuable to the current project, as well as to future decision-making. However, we were unable to identify a model of participation that was consistent with the requirements for engagement with Aboriginal and Torres Strait Islander peoples that were articulated to us by two recognised experts in Indigenous genomics with extensive experience conducting indigenous engagement. We discuss the feedback from these experts in Section 2 and Appendix B of this report. Nor was there scope within this project to meet the definitions of inclusiveness that we surveyed from the emerging research literature on inclusive participatory democracy, and which could enable Indigenous participants to contribute in a way that shaped meaning within the broader deliberation. Given these considerations, it was determined that the detailed, respectful and sometimes sensitive task of achieving Indigenous engagement with respect to human genome editing would not be possible within the scope and remit of the Australian Citizens' Jury. On balance, then, we concluded that there were clear and compelling reasons for deferring or reserving questions relating specifically to Aboriginal and Torres Strait Islander people and genome editing to another project, where a representative and multidimensional engagement with the issues would be possible.

This project has parallels in other countries and has the potential to feed into a larger global citizens' deliberation. This report has been provided to relevant government and policy bodies and other stakeholders in Australia and internationally, and is being made publicly available. It is hoped that this report will assist relevant agencies in deciding such matters as: whether the regulation of human non-heritable genome editing is working optimally, or needs reform; and whether it would be appropriate, now or at some time in the future, to open the Australian regulatory regime for heritable human genome editing and embryo research to further scrutiny.

This report is divided into ten Sections, outlined below in the Table of Contents. Detailed material for some aspects of this report can be found in the corresponding appendices for Sections 1, 2, 3, 6 and 7.

The report also includes a detailed list of acknowledgements. In brief, we first wish to acknowledge that this project was undertaken on the lands of Aboriginal and Torres Strait Islander peoples, and we pay our respects to their elders, past, present and emerging. We gratefully acknowledge funding from the Medical Research Futures Fund Genomics Health Futures Mission. We thank the many experts globally and members of the Australian community who contributed to this project. We particularly thank the 23 exceptional Australians who participated in the Australian Citizens' Jury on Genome Editing. We thank the Museum of Australian Democracy, and particularly Daryl Karp, for hosting the citizens' jury. We also thank Genepool Productions, in association with December Media and By George Studios for filming jury deliberations, and SBS, Screen Australia and Film Victoria for providing funding for this aspect of the project. Dynata assisted with recruitment, and we would particularly like to thank Ariane Hayes. Nicole Hunter and Keith Greaves from MosaicLab facilitated our expert workshops. We thank the many members of our research, facilitation, and administrative teams who assisted us throughout the project, particularly Kath Fisher, who led the facilitation of the Australian Citizens' Jury and the table facilitators.

Our highly respected friend and colleague Professor Christine Critchley was a core member of the research team at the start of this project. Tragically Christine passed away in November 2020. We

have missed her friendship, collegiality and expertise throughout the course of this project. It would have been all the richer for her involvement.

This research was approved by the University of Tasmania Human Research Ethics Committee (project number H0021841) and the University of Canberra Human Research Ethics Committee (project number 9095).

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1
INTRODUCTION

The science of genetics has been advancing at a rapid rate for more than 50 years. In particular, techniques aimed at mapping and sequencing DNA have become faster and cheaper. It is now possible to sequence a person's entire DNA sequence (their 'genome') for under $1,000. However, the cost of interpreting this mass of information remains high. Therapies that make changes to the genome have long been touted for their potential to transform the lives of people affected by genetic disorders for the better. Yet progress has been slow, in large part due to their uncertain safety and efficacy. New techniques, allowing more precise 'editing' of the genome, have the potential to address these issues of safety and efficacy, but at the same time raise large ethical and policy questions.

In 2020, the World Health Organisation (WHO) formed an expert panel to examine global responses to the increasing availability of genome editing, culmination in three reports: a proposed governance framework, a position paper and set of recommendations (WHO, 2021a, 2021b, 2021c). Although the WHO expert panel's work was published after completion of the Australian Citizens' Jury on Human Genome Editing, the proposed governance framework is particularly useful to this project for the assistance it provides in translating the outcomes of this project into concrete policy recommendations. It is this proposed governance framework that sets this work of the WHO expert panel apart from the many other reports on genome editing that have preceded it (Cohen et al, 2022). The governance framework report emphasises why it is necessary to consider the broad ethical and social issues raised by human genome editing, and the particular issues associated with the different forms of genome editing:

> Challenges associated with somatic human genome editing include, for example, rogue clinics, medical travel, as well as the reporting of illegal, unregistered, unethical or unsafe research and other activities including the offer of unproven so-called therapeutic interventions. Heritable human genome editing also gives rise to great concerns as the edit might be passed to subsequent generations. Additional issues include enhancement to improve certain traits, the lack of diversity in collections of human samples and associated data, the need for equity of access to and benefit from human genome editing. There are important differences in the scale of the current challenges posed by somatic, germline and heritable human genome editing.

The most promising of the new genome editing techniques is known by the acronym CRISPR (standing for Clustered Regularly Interspaced Short Palindromic Repeats). It is widely seen as a transformative technology (Gaj et al, 2013; Maeder and Gerbach, 2016; Mei et al, 2016). In agriculture, for example, CRISPR and other genome editing tools are already providing more flexible, reliable and simple approaches than traditional techniques for modifying genetic traits (Gao, 2018). In humans, it is anticipated that CRISPR and other genome editing tools may be used in the future to treat a large number of diseases associated with genetic mutations. However, like more traditional forms of gene therapy, it will still be many years before these therapeutic interventions are given approval for routine clinical use (Ginn et al, 2018).

Aside from treating genetic disorders, the WHO governance framework report points out that human genome editing also has other potential uses, including in the treatment of infertility, promotion of disease resistance, enhancement of human traits, improvements to robustness or quality of life and addition of non-human traits (WHO 2021a, 6). Although speculative, this list of uses illustrates that there is a fine line between use for therapeutic purposes, use for the purpose of enhancing existing traits and use for adding new traits.

Early in the development of genome editing technology, it had been thought that CRISPR and other genome editing tools might also be employed at some stage in the future to make alterations in human gametes or embryos that could be passed to subsequent generations (that is, they would be heritable). Until recently there appeared to be international consensus that it would be inappropriate to do so until more research had been undertaken and until communities around the globe had been given the opportunity to deliberate on the appropriateness of such interventions (Baltimore et al, 2016). However, in November 2018 an announcement was made that a scientist had modified the genomes of a number of human embryos using CRISPR which resulted in three live births (Cyranoski, 2019). The response to this announcement was fierce condemnation. One consequence was the appointment of an international commission specifically to examine the use of heritable human genome editing (National Academies of Science, Engineering and Medicine, 2019).

Collectively, the WHO report and reports from other expert bodies provide strong support for ongoing research into and development of CRISPR and other genome editing technologies for non-heritable purposes, subject to appropriate regulatory oversight. The reports are more circumspect when it comes to heritable forms of human genome editing and research involving human reproductive cells and embryos (which the WHO refers to as 'not for reproduction germline genome editing', WHO, 2021a, v). Nevertheless, they do tend to provide cautious in-principle support for heritable human genome editing at some stage in the future, but only after more research and community engagement, and only in limited application. This has been described by one of us elsewhere as a cautious 'amber light' for research into heritable human genome editing to proceed (Angrist et al, 2020). If these tentative recommendations regarding heritable human genome editing were to be adopted, it would be necessary to reform the law in many countries, including Australia. What precisely should be changed, however, is not an easy question to answer.

Currently the law relating to heritable human genome editing ranges across the full gamut from outright prohibition (as in Australia - Nicol, 2020) to more permissive approaches (Boggio et al, 2020). In Australia, for example, uniform legislation was enacted in 2002 across the country, establishing both a set of criminal offences relating to the use of human embryos for reproductive purposes (e.g. the federal *Prohibition of Human Cloning for Reproduction Act 2002,* particularly section 15, which prohibits making heritable alternations to the genome) and a strict regulatory environment for the use of human embryos in research (e.g. the federal *Research involving Human Embryos Act 2002*). Non-heritable human genome editing, by contrast, is permitted provided that it complies with a range of laws, other regulations and ethical guidelines.

One consistent theme in the expert reports and other commentary is that the community should be brought into the complex and difficult conversation about the conditions and circumstances under which application of human genome editing technology might be acceptable (see, for example, Adashi et al, 2000). A broad consensus has emerged that deliberation on this important technological step should not be left only to scientists, medical practitioners, specialist government agencies or international committees. The research reported here is one of the first attempts to go beyond expert dialogue, bringing members of the public into the genome editing debate.

We already know something about public attitudes towards genome editing, both in Australia and elsewhere. A survey of the attitudes of over 1,000 Australians towards genome editing undertaken in 2018 suggests that there is a level of comfort with editing humans and animals for research and to improve human health (Critchley et al, 2019). However, the survey also revealed ongoing unease about the consequences of genome editing, both from the perspective of moral concerns with the status of the human embryo and concerns about modifying the genome of future generations. It is clear that many members of the Australian community (at least those participating in the survey) continue to recognize the special status of the human embryo. Other surveys elsewhere have shown that there are differing views on the acceptability of heritable human genome editing within populations, though there has been little or no examination as to the extent to which the special status of the human embryo influences these views (e.g. McCaughey et al, 2016; Gaskell et al, 2017; Delhove et al, 2020; Jedwab et al, 2020).

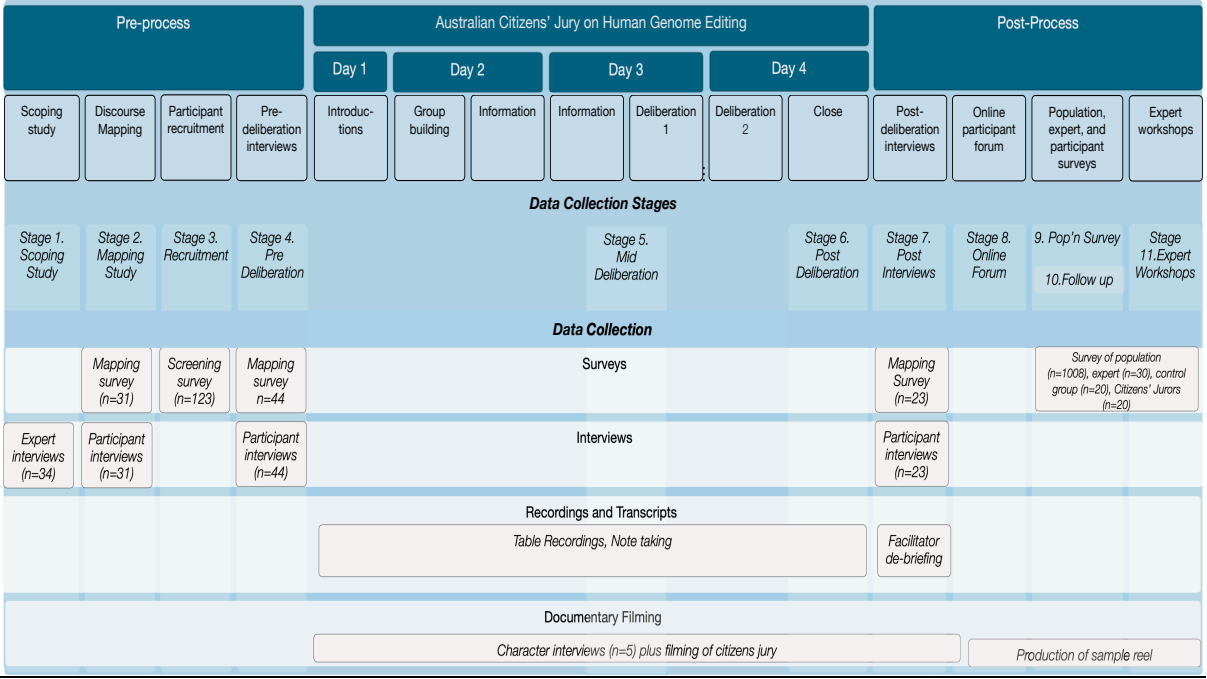
Whilst surveys of this nature provide useful summary evidence of community concerns, engaging with the public on controversial areas of science requires more, especially when it comes to emerging issues on which the attitudes of many people have yet to crystallize. It is widely acknowledged that members of the public should be actively involved in deliberating on such matters, in order to give a more nuanced picture of what reflective public opinion. This picture can assist policy makers in making policy decisions on what should/should not be permitted and how permitted practices should be regulated. Including an integrated deliberative design with lay citizens at its heart is important because, while it is broadly recognised that the public view should shape policy (particularly in respect to profound issues such as genetic technology), existing political processes do not adequately connect publics to policy for these kinds of emerging complex issues with long term consequences (Dryzek et al, 2020).

The centrepiece of this project was a citizen deliberation exercise, the Australian Citizens' Jury on Human Genome Editing, which was designed to incorporate integrated deliberative design methodology. Alongside the citizens' jury itself, a range of associated activities involving members of the public took place, which are summarised in Figure 2. Highlights included:

- A study to examine the range of salient positions on genome editing that currently exist among the public (discourse mapping), undertaken prior to the citizens' jury.
- Recruitment of two cohorts guided by the mapping study in order to reflect both demographics and the diversity of positions on genome editing in the community (discursive representation). The first cohort comprised the 23 individuals who participated in the citizens' jury (the participant group). The second cohort comprised 21 individuals who did not participate in the citizens' jury but participated in other aspects of the project (the control group).
- Post-citizens' jury interviews with the participant group.
- A follow-up online forum with some of the members of the participant group to finalise reported recommendations.
- A survey on genome editing, the aim of which was to assess the strength and prevalence of these positions in the participant group, and to compare their responses with the control group and a broader sample of participants from the Australian population (the population group).

Figure 2 also shows the range of additional research material collected in association with the event, and the stages where they were collected. The preliminary analysis of the data collected informs this report.

Figure 2: Project Stages and Data Collection



In addition to genome editing, mention should be made of another technique that has emerged in recent times aimed at ameliorating the health impact of certain genetic mutations. This technique relates specifically to the DNA found in small cellular organelles known as mitochondria (and not the DNA located in chromosomes in cell nuclei). These genetic mutations can result in mitochondrial disease, which has a range of manifestations and can be fatal. The technique, known as mitochondrial donation, replaces the mitochondria that have disease-causing mutations in eggs and embryos with mitochondria from egg donors that lack those mutations.

At the time of the citizens' jury, the Australian parliament was in the process of considering legislation aimed at amending existing laws in order to permit mitochondrial donation under a strictly regulated licensing regime. Given the currency of this issue, citizens' jury participants were asked to deliberate on mitochondrial donation as well as genome editing. The amending legislation was ultimately passed by both houses of the Australian parliament and has now entered into force. This amending legislation, and the detailed public engagement that accompanied it, may provide some guidance on how changes to Australian laws relating to heritable genome editing might be approached, should it be deemed appropriate to pursue this policy agenda by the Australian government.

Before moving on to discuss the methods, results and outcomes of this project, it should be noted that the citizens' jury that was the centrepiece of this project was deliberately framed in such a way that participants were presented with non-heritable and heritable human genome editing as two distinct applications of the technique. The rational for this was not because there are necessarily clear distinctions between these two forms of genome editing in the healthcare context, but rather because they are treated very differently at law in Australia.

To summarise, non-heritable genome editing is permitted within a well-defined regulatory environment, but heritable genome editing is prohibited and the subject of criminal offences. Research involving human embryos, which will be required to ensure that heritable human genome editing can proceed safely, is governed by a mix of prohibitions and regulations, including a licensing regime. These legal differences have a profound effect on the availability of human genome editing in each of these guises in Australia. It is thus of vital importance, at this stage of development of genome editing, to understand more about community attitudes towards these different forms of genome editing to determine whether these distinctions are still tenable.

More detailed background information on genome editing is provided in Appendix A, including a glossary of key terms.

This research was approved by the University of Tasmania Human Research Ethics Committee (project number H0021841) and the University of Canberra Human Research Ethics Committee (project number 9095).

2
IDENTIFYING GENOME EDITING ISSUES THROUGH EXPERT INTERVIEWS

The first empirical phase of this project required investigators to identify the most significant issues or controversies that should be addressed, considered and resolved through the work of the citizens' jury. To determine what these issues were, the investigators conducted a qualitative interview study with a broad range of well-regarded experts on genome editing from many jurisdictions around the world. Christopher Rudge was the primary author of this section of the report.

2.1 Qualitative interviews

A qualitative interview model was adopted on the basis that qualitative interviews have long been recognised as a valuable and valid research method for identifying, examining, testing and comparing different moral and technical views or positions in particular areas, including in health, science and technology.

The value of qualitative studies focused on the ethical implications of technologies is not generally contested. Indeed, it is widely acknowledged that qualitative studies may afford valuable insight into how participants understand and weigh different ethical problems or implications. Nevertheless, a review of bioethics research in qualitative methods revealed some critical analysis of the professed objective interpretation of interview data. In one analysis, the interview process was described as 'an emotional-intellectual activity that is not directed to lingual utterances alone.' Further review of this literature concluded that the aim of the critical studies in this area was to ensure that interviewers were cognisant of the total situational context in which participants articulated their moral or technical positions. One study recommended, for example, that interviewers should 'interpret situations [rather than simply what is said] in order to find the meanings contained in them.' Recognising these concerns, our methodology, outlined below, sought to incorporate not only linguistic data but also data related to the interview situation. To this end, video interviews were analysed in terms of the participants' broad characterisation of certain issues, having regard to their hesitation, humour, and other non-linguistic expressions.

In order to capture this data, we applied a 32-item checklist for the reporting of qualitative research known as COREQ (the Consolidated Criteria for reporting qualitative research). The original draft report contained a response for all items that appear on the COREQ checklist. The COREQ checklist is divided into three domains: namely, (1) research team and reflexivity; (2) study design; and (3) analysis and findings. Within each domain, the COREQ checklist asks such questions as: 'What did the participants know about the researcher?' (checklist item 7, domain 1); 'Was data saturation discussed' (checklist item 22, domain 2); and 'Was there consistency between the data presented and the findings?' (checklist item 30, domain 3). Each of the 32 items was addressed in the draft report, discussed below. For the purposes of this brief report, however, we shall only identify the most relevant items related to the methodology adopted.

2.1.1 The purpose of the interview phase

The purpose of this interview phase was twofold. The first purpose was to scope or map out the full range of ethical and other issues that experts identified with respect to genome editing. These issues would then be ranked and selected for inclusion as issues of importance for consideration at the citizens' jury. The second purpose of this phase was to capture new insights into the views of genome editing experts and to compare our analysis of their positions to the issues and themes already identified in the existing literature. Several published articles, reports and books were identified that had provided a typology of the ethical and technical issues raised by genome editing. It was intended that the interviews would permit these identified concerns to be clarified and provide a better-informed and more self-reflective debate on genome editing in the citizens' jury, as well as contribute to the design of the citizens' jury itself.

Participants were recruited via email invitations. Purposive or targeted sampling was used to select participants. Rather than providing a representative or statistically randomised group, the sampling method was intended to enable a greater diversity of accounts for interpretation. Experts were considered eligible for inclusion in the study if they had contributed substantially to academic literature, policy documents, or to the advancement of science in genome editing. Expertise was determined through a review of academic publications and leadership roles in the scientific community.

It was initially intended that 15-20 experts would be consulted to discuss the current state of the art of genome editing, policy developments and other relevant considerations. The number of interviewees was later adjusted to 34, in part because of the willingness of experts to engage with the project and in part to ensure that a sufficient diversity of expertise was sampled. Responses from potential interviewees were very positive, with five non-responders (11%), and five potential interviewees recommending other interviewees (11%), all of whom agreed to be interviewed. Interviewees included: bench scientists; clinicians; embryologists; religious leaders; bioethicists; policy makers; and lawyers. Fourteen interviewees were based in Australia. The other 20 interviewees were from Canada, France, Japan, New Zealand, Qatar, South Africa, Switzerland, the UK and the US. Although this project focuses primarily on gene editing in humans, the views of experts on the application of gene editing in agriculture and pest eradication were also canvassed.

2.2 Methodology

Interviews commenced on 6 August 2020, after an application for ethics approval had been approved. The last interview was conducted on 23 December 2020. All interviews were conducted in a face-to-face video conference by Nicol. For the most part, one other research team member attended.

Prior to the commencement of the interviews, an interview guide was designed around six principal questions. These questions were open-ended, broad and non-specific. They were developed based on a review of the existing literature. The questions were raised in the same order throughout each interview. However, differing degrees of detail were elicited from the participants, depending on their expressed interests and expertise. The questions asked of each participant were as follows:

- What is your background?
- What is your experience with genome editing?
- What are your views on what has been achieved so far in the field of genome editing, and what do you think is the most beneficial pathway?
- What are the ethical, legal, and social concerns relating to genome editing?
- What should be the focus of the Citizen's Jury?

In addition, where time permitted, 16 out of 34 interviewees were asked a variation of this final question:

- What might the citizens' jury achieve, or, what does success look like?

All interviewees agreed to being named. Their names are listed in the Acknowledgements section of this report. All interviews were recorded with the consent of the interviewees. Interviewees also consented to the inclusion of their responses in the data analysis. Some interviewees consented to being quoted on an anonymous basis, and some consented to being quoted on an identified basis. Others consented to being quoted on an identified basis if further specific consent was obtained in respect of the quoted materials on an approval basis. In this report, we have chosen not to identify any of the quotes we rely on.

A research assistant was employed to assist with transcribing interviews. The interviews were transcribed by the assistant with the aid of transcription software. Following the transcription process, a member of the research team then conducted an analysis of the interviews.

The interview videos and transcripts were analysed using an inductive methodology, where qualitative content analysis, discourse analysis, thematic analysis and context-dependent analysis were used to determine common themes, concerns, topics and ideas across the interviews. Given that interviews were undertaken with a diverse array of experts, from diverse fields, inevitably there was a diversity of opinions.

One of the difficulties that arose in analysing a large amount of interview data involved identifying and classifying the wide range of different genome editing applications described by the experts. Word frequency and text clustering assisted in developing insights into the different applications under discussion. However, since many of the experts used different language and descriptions to identify the same application or technique, interpretative or hermeneutical analysis was required to identify different applications described by the experts and classify them into categories. As a result of this process, six primary applications or uses were identified, as follows:

1. Heritable human genome editing.
2. Non-heritable human genome editing or 'somatic cell genome editing', including in-utero somatic cell editing or 'fetal genome editing'.
3. Genome editing research using embryos.
4. CRISPR-based genome editing for diagnostic purposes.
5. CRISPR-based genome editing for research generally.
6. Gene drives and uses of genome editing for agricultural purposes.

2.3 Overview of findings on the primary applications

Because non-human uses of genome editing were not intended to be discussed during the course of the project, gene drives and uses for agricultural purposes are not discussed further in this report. The other five applications are discussed more fully in Appendix B of this report.

Participants expressed divergent views about human genome editing. A proportion of experts identified the current science as nascent and in need of much more development. However, some common themes emerged as follows:

- It is most unlikely that heritable human genome editing will be the major application of this technology into the future.
- There is much more research work needing to be done before heritable human genome editing could be considered to be safe and effective.
- Agricultural use of genome editing is likely to be one of the most valuable interventions in terms of human health and welfare.
- Clinical trials for non-heritable human genome editing have commenced, but issues associated with distributive justice, equity and access are of significant concern.
- Community consultation is vital in helping to set the future policy agenda for genome editing.

2.4 The Australian Citizens' Jury

All experts expressed enthusiasm for the Australian Citizens' Jury on Human Genome Editing and freely offered guidance as to how it should be designed and implemented. The clearest and most common feedback focused on the following points.

The Australian Citizens' Jury should inform and educate participants in pursuance of obtaining public views

All experts were in favour of 'the public' – that is, lay citizens who are not scientists – expressing their views about where ethical and legal lines should be drawn in relation to genome editing. One expert expressed a strong view that such decisions 'should not be left to committees.'

The Australian Citizens' Jury should be diverse

Many experts focused their comments on the selection of the jurors. Most experts highlighted the need for a diverse range of jury participants. One expert indicated that 'differences between participant groups' will be important to analyse because 'studies have shown surprising results,' such as 'scepticism correlat[ing] to higher educational attainment.' Experts highlighted that the citizens' jury should include persons with disability, marginalised communities, minority groups, and non-academics.

The Australian Citizens' Jury should avoid 'sensationalism'

Many experts underlined the importance of managing the risks of discussing sensational ideas. One expert suggested that the Australian Citizens' Jury should emphasise the 'less evocative and [less] emotional' aspects of genome editing, such as 'diagnosis.' Another stated that conspiracy theories about Big Pharma and the financial stakes involved 'could be very unhelpful,' especially since private research and development was, at this point in history, needed to bring these medical technologies into the clinic. Another expert warned that the jurors should be 'steered away' from 'dystopian visions'

and 'hysteria.' Overall, experts felt that the Australian Citizens' Jury should maintain a practical and applicable approach, focused less on 'enhancement' and 'science fiction' than on more plausible and more modest medical outcomes.

The Australian Citizens' Jury should focus on the most pressing and practical issues

In a similar vein, most experts suggested that the debates be designed around what is the most likely and applicable form of genome editing. The Australian Citizens' Jury should avoid assuming that human 'genome editing is just going to happen' and instead should focus on 'whether we should ever permit it to happen [given] the real dangers and consequences.'

Given the wide variety of different views among experts on how the Australian Citizens' Jury should be designed, several key statements from different experts are set out below:

- The Australian Citizens' Jury should focus on 'producing thoughtful conversations [about] equity of access, and the fact that the West will receive the treatment first'.
- The Australian Citizens' Jury should produce a 'reasoned account' of the viewpoints 'that exist in the general public [and] tap into those voices that are completely underrepresented,' which may mean that 'these voices need to be overrepresented on any panel'.
- The Australian Citizens' Jury should have an actual impact on regulators [and this should] involve including an actual regulator in the jury. [The jurors] should come up with four or five policy recommendations and they must be relayed to the regulatory agents'.
- The Australian Citizens' Jury 'must feed the jurors knowledge about the applications of CRISPR and its uses but not about the ethical issues. [The organisers] should let the jurors determine the ethical issues themselves'.
- The Australian Citizens' Jury should 'identify the central ethical issues and come to some conclusions about whether germline [heritable] editing should be permitted and for what purpose'.

In sum, this feedback from genome editing experts validated the planning that had already been undertaken by the research team and assisted with refining the plans for the event.

2.5 Ethics and human genome editing

Questions of ethics infused what the experts had to say across the specific topics they discussed. Many experts also directly addressed the theory or philosophy of ethics as it related to human genome editing. Some expressed ethical positions that informed their understanding of the ethical issues applying in more specific scenarios. Others presented specific ethical positions in relation to different uses and ideas about human genome editing.

One expert stated their view that all of the ethical questions relating to genomes and genome editing were functionally the same as those that apply to other technologies. A small number of other experts conveyed a similar view. In this conceptualisation, the ethics of human genome editing can be addressed in a similar way to the bioethical questions and problems associated with, for instance, organ transplants, 'last-ditch' neurosurgery, or harmful pharmaceutical medications (e.g., cancer immunosuppressive drugs). The position of the patient, the extent to which they can achieve competency to consent, and the extent to which they can grant informed consent, are all existing bioethical questions that may be posed again with respect to human genome editing.

The same expert who advocated for this 'flat' approach to bioethics also noted that the only ethical position that may be necessary to ultimately be held was a position in which scientists and practitioners aim for less suffering and less disease in future generations. If one uses human genome editing to

facilitate this end, then arguably one is acting ethically. Indeed, as this expert noted, there is an ethical duty to use these tools for this purpose: 'We must use these tools to facilitate' that aim, they stated.

Some other experts did not express such a firm position but instead contended that the system for determining 'what is in the public interest or what is for the common good' must be further developed in respect of human genome editing. The question, one expert said, should be: 'What does it mean to use this technology well?' This expert emphasised priority setting and developing knowledge about what it means to use the technology of human genome editing well. This entails studying what it means to act in the public interest and for the common good, they stated. In addition, the warp-speed of science and innovation often obscures these questions, and they should arguably be considered both before, during, and in the implementation of scientific projects. A more supportive scientific culture in which scientists are free to and capable of considering such questions would be essential, this expert noted.

By contrast, another expert, considering the question of safety and the ethics of experimentation, suggested that there will never be a time at which safety can be guaranteed or epistemic certainty can be achieved. On this basis, they suggested that it might be preferable to forge ahead right away. This expert made a case for 'tinkering,' noting that we 'tinker a lot [already]' and that, in many scientific projects, the ethical lines are never clear or never perfectly drawn. As this expert suggested, it is an illusion to imagine that the ethical conditions will ever be perfect for the use of such a powerful medical technology.

In relation to the ethics of media reporting and medical technology, another expert noted that it is important to make sure that the 'hype' and promise of the technology is not broadcast without efficacy being first established. Many other experts characterised the ethical dilemmas related to human genome editing in different formulations. Some experts weighed and compared different 'unethical' and 'ethical' acts; while others described risk and harm in detail. Others noted the inevitability that genome editing will, one day in the future, be trialled. Still others described the difficulty of translating ethical positions and debates into regulatory systems and legislation, while others noted that this ethical debate is quite intractable, given that the heritability of genome editing could affect not just the patient or their immediate offspring, but many different generations of many different relatives.

A more complete analysis of the experts' comments on the ethics of human genome editing appears in Appendix B.

2.6 Engagement with Aboriginal and Torres Strait Islander Communities

In addition, attention was drawn to the particular issues facing Indigenous communities by a number of experts. Two experts, in particular, provided insights on engagement with Aboriginal and Torres Strait Islander communities in Australia. These experts both have a long history of engagement with genomics and with Aboriginal and Torres Strait Islander communities.

It was very apparent from the remarks made by these two recognised experts in Indigenous genomics that, in view of the unique and distinct genetic development of Aboriginal persons in Australia, there would be compelling reasons to distinguish questions related to Indigenous and Aboriginal genome editing from those that we intended to ask in this study, which were largely focused on the bioethical and scientific questions developed in the European and East Asian genome editing literature. Some of the comments of these experts are extracted in Appendix B.

After much consideration, we concluded that an inclusion process by which an Indigenous representative voice would be constituted by just one, or at most two, Indigenous persons within a

jury of 23 non-Indigenous persons was not consistent with any of the definitions of inclusiveness that we surveyed from the literature. According to one such definition, 'Inclusion occurs when a diversity of people… feel valued and respected, have access to opportunities and resources, and can contribute their perspectives and talents to improve their organisation.' We identified that our models of inclusion would not be sufficient to enable Indigenous participants to contribute in a way that shaped meaning within the broader deliberation context, and identified a risk that attempts to guarantee such a contribution would be unsuccessful.

We thought deeply about inclusiveness and examined the emerging research literature on inclusive practices in participatory democracy. We then weighed those findings against the comments we received from these experts. Ultimately, we were unable to identify a model of inclusion and participation that would satisfy these requirements. On balance, we concluded that there were clear and compelling reasons for deferring or reserving questions related specifically to Indigenous people and genome editing to another project, where a representative and multidimensional engagement with the issues would be possible. On the one hand, we identified a risk that the Indigenous member(s) of the deliberation process would not be included in a way that was consistent with the existing definition of inclusiveness. These included creating a conflictual environment in which Indigenous issues could not be meaningfully addressed or considered. On the other hand, we identified the risks associated with not including an Indigenous representative, which included reinforcing structural inequality and reducing accessibility to decision-making. We weighed this former risk against the latter risk. We understood the latter risk to be considerable; however, we then identified another project in which Indigenous inclusion in relation to these themes would be more appropriately and inclusively facilitated. On this basis, we then identified the former risk – of including Indigenous representative without being able to guarantee actual inclusion – as more serious than the latter risk.

Given these considerations, it was determined that the detailed, respectful and sometimes sensitive task of achieving Indigenous inclusion with respect to genomic information and genetic science would be not possible within the scope and remit of the Australian Citizens' Jury but could be more plausibly attempted in another project that was already in development.

3
DIVERSITY OF VIEWS INFORMING AUSTRALIAN CITIZENS' JURY PARTICIPANT SELECTION

The approach to the design of the Australian Citizens' Jury on Human Genome Editing, including participant selection, was informed by the overall goal of this research, namely, to understand the public mind and how values inform the development and implementation of genome editing through the lens of public deliberation under conditions that approach deliberative ideals. This is particularly important for complex issues such as genome editing, which have not been subject to much prior or widespread public discussion (MacKenzie and O'Doherty, 2011).

In terms of recruitment, the goal of the Australian Citizens' Jury was to simulate a deliberative public conversation by bringing together a diversity of views and working through the collective issues that emerged. This raises the question of how to identify what range of views exist among a public who have not yet worked through those issues. The project worked around this problem by adopting Discursive Representation to achieve of diversity of views, to "redeem the promise of deliberative democracy when the deliberative participation of all affected by a collective decision is infeasible" (Dryzek and Niemeyer, 2008). This approach understands public views on complex issues such a human genome editing that are not yet subject to wider public debate as anticipatory and pre deliberative (MacKenzie and O'Doherty, 2011). However, we have assumed it is still possible to identify contours of reasoning among in the community that eventually inform the positions that emerge during deliberation.

In short, failure to understand the pre-deliberative perspectives in the community risks failure to give them voice as part of the deliberative process. To avoid this prospect the project embarked on a dual strategy for selecting participants for the Australian Citizens' Jury, involving selection to reflect the broad demographic features of the Australian population (Descriptive Representation) as well as discursive representation. The details of how this was achieved are outlined in Appendix D. Achieving discursive representativeness involved four steps:

1. Mapping the diversity of discourses that currently exist in the Australian community (Mapping Study).
2. Establishing targets for representation of these discourses as part of the Australian Citizens' Jury and combining with targets for other (demographic) criteria for participant selection.
3. Identifying a pool of participants willing to participate in the Australian Citizens' Jury.
4. Selecting from among this participant pool using a stratification to achieve target quotas for each of the selection criteria.

From analysis of the Australian Citizens' Jury and the Population Survey (see Figure 2), it is clear that without the use of discursive representation it is highly likely that an important perspective involving concern regarding a number of the more profound legal and ethical dimensions would not have been represented among the participants (see Appendix D, D.2.2). Although the discourse map that was identified in the mapping study was not sufficiently fine grained to capture the views of the Australian Citizens' Jury participants as they evolved during deliberation (see section 6), the four discourses that the mapping study produced provided a useful benchmark for understanding and categorising the distribution of views among the Australian population.

The following section briefly describes the process of mapping the views as part of the mapping study and how this informed a wider strategy for recruiting participants for the Australian Citizens' Jury (with details found in Appendix D).

3.1 Mapping Study

An intensive mapping study was carried out early in the project (see Figure 2) to map the dispositions of the Australian public towards genome editing technology and its potential applications. The mapping study followed a discourse mapping methodology, based on Q methodology (Brown, 1980), which combines qualitative and quantitative techniques to capture and compare the subjective or first-person viewpoints of participants.

Reflecting a key feature of Q methodology, which requires the capturing of subjective positions across the range of relevant arguments, a survey instrument was assembled that can reflect the complexity of the issue. To this end, over 1,200 statements were collected from a range of sources—including the expert interviews (see Section 2), online forums, news article comments, radio segments and podcasts, responses to previous studies and public engagement, and relevant academic literature. These statements were then categorised and sampled to produce a set of that represented the relevant considerations to be weighed when deciding how human genome editing should be regulated. The result was forty-six statements that were presented to mapping study participants (see Table 1).

The representative statements were presented to mapping study participants as part of an online interview with project research staff.

The mapping study identified four main discourses on human genome editing, using a combination of survey and interview data (see Appendix C). These discourses, which are described in detail in Appendix C, include

- *Scientific Progress,* which is open-minded about new discoveries and trusting of science.
- *Principled Concern,* which raises concerns about the social and ethical implications of the technology.
- *Profound Concerns,* which reflects concern about ethical, cultural, and downstream impacts.
- *Agnostic,* which is intrigued by the possibilities of the technology but not convinced that it is necessary.

The main features of these discourses — those that are shared as well as unique to each discourse—are summarised in Figure 3.

Figure 3: Mapping Study Discourses

3.2 Participant Selection

Participants for the mapping study, citizens jury, and control group were recruited from a research panel provided by Stable Research, a partner of Dynata. The recruitment pool comprised potential participants that were provided by Stable Research. Recruitment was conducted progressively, in a series of waves, in addition to those Mapping Study Participants who indicated a willingness to continue with the project. At the conclusion of each wave the distribution of potential participants against the core selection criteria (see Appendix D). In the case of descriptive criteria, the quotas were set to reflect the distribution of each category within the Australian population, with a different approach taken for Discursive Representation. Selection also sought to achieve distribution across several secondary categories (religion, political spectrum), as well as excluding limiting the number of participants who were either trained or worked in areas related to genomic research (Appendix D). The result of this process involved the selection of 23 citizen jurors to participate in the ACT. The 21 participants who comprised the Control group were initially selected using a similar approach.

3.2.1 Selection Using Discursive Representation

The results of the mapping study helped to ensure that the participants in the citizens' jury reflected a range of views that can be found in the wider Australian community, with the aim of achieving both discursive and descriptive representation (Dryzek and Niemeyer 2008). Prior to the citizens' jury, each of the potential participants and controls was interviewed and asked to undertake the same facilitated survey as the mapping study participants. The survey responses were used to map the positions of

respondents to the discourses identified in the mapping study. To achieve discursive representation, the mapped positions of potential participants were considered in the recruitment to the Australian Citizens' Jury and to the control group. Demographic and geographic factors, as well as availability, were also considered. The pre-deliberation positions of the citizens' jury participants and control group are further detailed in Section 1.

A more detailed account of how discursive representation was used for participant selection of the can be found in Appendix C (see esp. C.5.3) From that analysis, deploying discursive representation corrected a strong likelihood that Discourse D, or Discourse C would not have been represented among the deliberative participants for the Australian Citizens' Jury.

The prospect of Discourse C being absent would have potentially been particularly problematic, given that it most strongly expresses concern about the more profound issues that emerged during the process, but with insufficient time work through these issues. In most cases these individuals transformed their positions slightly during deliberation, ending up in the Principled Constraint discourse in the post-deliberation (six) discourse map (see Appendix C). There is also evidence that these individuals represent more than a difference in perspective. They also appear to engage in a different form of reasoning about the issue (see Appendix E, section E.2).

Moreover, when deliberative participants were surveyed in in the follow up survey (stage 10, see Figure 2), the position of the Discourse C cohort tended to have the most stable and consistent perspectives compared to the rest of the group (see Appendix E)

Overall, the deployment of discursive representation appears to have done more than help to ensure a diversity of perspectives were present for the Australian Citizens' Jury on Genome Editing. It helped to highlight the need for extended deliberation (and public engagement) regarding the core issues raised by the Discourse C cohort. Without adequate representation of this group it is conceivable that the project may have produced a much less critical account of the public view of human genome editing.

3.3 Recruitment Contingencies and COVID management

The control group also served the function of providing a reserve pool of participants for the Australian Citizens' Jury, in case of withdrawal or inability to attend due to a COVID outbreak within their residential locality. In the lead up to the Australian Citizens' Jury itself reporting on COVID cases was monitored daily and the relevant postcodes cross checked against the pool of recruited Australian Citizens' Jury participants. If an outbreak had been recorded within the previous two weeks, or a participant had withdrawn for other reasons, a substitute was sought from within the pool of selected control group participants, reflecting as far as possible the same selection categories within the selection criteria.

The combination of multiple stratification categories and need to adapt to withdrawals and ineligibility due to COVID outbreak meant that was difficult to achieve the quotas set for recruitment.

4
DEVELOPMENT OF AUSTRALIAN CITIZENS' JURY RECOMMENDATIONS

The Australian Citizens' Jury on Human Genome Editing was held on 17 to 20 June 2021. Twenty-three members of the Australian public were hosted at the Museum of Australian Democracy to hear evidence from invited expert speakers and to deliberate on the question, "*Under what conditions (or circumstances) might the application of human genome editing technology be acceptable?*".

It is important to note that participants were not asked to consider whether human genome editing should be undertaken at all. Given the rapid adoption of CRISPR and other genome editing techniques in research laboratories around the globe, it is difficult to envisage a circumstance where every use of these techniques should be brought to a halt by broad prohibitions on all uses of genome editing. Rather, in our view it was more realistic for the citizens' jury participants to consider the limits on the application of the technology and the conditions under which it should be applied. This might include that certain applications should be prohibited, or that they should be more strictly regulated than others.

Despite the ongoing COVID pandemic, it was possible to carry out the citizens' jury largely in accordance with the original project description, noting that the time frame for deliberation was extended from 2.5 to 3.5 days, given the complexity of the subject matter. The deliberation process was designed by the lead facilitator (Kath Fisher) in collaboration with the research team and with input from five table facilitators. Seven experts assisted participants with their deliberations, with expertise spanning research genomics, clinical genomics, embryology, bioethics, disability ethics and health law. Decision-makers from the National Health and Medical Research Council (both the primary funder of health and medical research in Australia and the guardian of the Australian National Statement on Ethical Conduct of Research involving Humans), the Therapeutic Goods Administration (the primary regulator of market authorisation for drugs, devices and other therapeutic products in Australia) and the Gene Technology Regulator (the primary regulator of genetic modification in Australia) attended the opening and closing events. A parliamentarian also attended the opening event.

Prior to the topic related discussions, participants discussed how they felt the 'rules' for the process should operate. Those rules agreed upon were listed as a reference for the group during the remainder of the process. This activity was part of a 'group building session' developed and led by the lead facilitator (Kath Fisher). Group building activities demonstrably improve deliberation on complex issues, such as human genome editing (Niemeyer et al. Forthcoming). Broadly, this involves establishing trust within the group, norms of behaviour that are consistent with deliberative principles, and engagement with the process.

The citizens' jury was structured as a series of expert presentations, facilitated small group deliberations, and plenary discussions, as outlined above. Initially, participants discussed the information provided by each expert and were given the opportunity to ask follow-up questions to

further inform their deliberations. At the end of the first and second day of the citizens' jury, participants identified and discussed key themes and lessons from the expert presentations and group discussions. Deliberation on the citizens' jury remit began on the second day, in facilitated group discussions. On the final day, participants were asked to formulate recommendations, associated conditions, and concerns about each of the following issue areas: non-heritable human genome editing; heritable human genome editing; the creation and use of embryos in genome editing research; and mitochondrial donation. The recommendations from each group were collated by members of the research team. In a plenary discussion, the initial set of jury recommendations were finalised, which were presented to experts and representatives from regulatory agencies.

The entire event was filmed by Genepool Productions, with assistance from December Media and By George Studios, which also selected five participants for interview on a number of occasions throughout the event. The research team and other project staff were also interviewed. Filming was funded by SBS, Screen Australia and Film Victoria. A 34-minute film is available at: https://www.youtube.com/watch?v=OskSspvORII

Participants were given the opportunity to evaluate the citizens' jury in a post-event survey. Responses to the evaluation were generally positive, and participants mostly felt that they were able to express their views and that they were heard and respected by other participants. However, half of the participants expressed the view that they felt that the information provided by the experts tended to present a favourable view of human genome editing. It is probable that the perceived favourable disposition of some experts towards genome editing, and the absence of voices in opposition to this technology, contributed to a small minority of participants feeling that the process did not provide adequate information or opportunity for them to effectively participate or express their views. This will be further discussed in section 10 of this report.

Following the completion of the face-to-face citizens' jury event, a further round of post-event discourse surveys was conducted with participants and controls, and follow-up interviews were undertaken with participants. The results of the discourse mapping study are detailed in section 6 of this report. During their post-jury interviews, participants reflected on their experiences during the citizens' jury and how their views on the topic of human genome editing had developed. Additionally, the interviews explored participants' views about creating and using human embryos for research purposes, which is an issue that was raised but not adequately discussed during the citizens' jury. The recommendation on creating and using human embryos in genome editing research was therefore informed by these interviews and a subsequent online Zoom forum, in addition to the citizens' jury deliberations.

The online Zoom forum was held on 21 August 2021. It was attended by 10 of the 23 participants, as well as members of the research team. This event provided further opportunities to develop the recommendations of the citizens' jury. The final set of recommendations, including input from the forum, were incorporated into a Participant Recommendations and Preliminary Report, which was distributed to citizens' jury participants and to relevant policy makers and regulators. It is publicly available on the project website at https://www.australiancitizensjury.org/ .

It is important to emphasise again at this point that there was diversity of views amongst citizens' jury participants, with no consensus, particularly with regard to heritable human genome editing and genome editing research involving human embryos. As such, the final recommendations, which are provided in full in the next section, are those of the majority of participants. However, minority views and more broadly held concerns or conditions are also noted.

To summarise, the recommendations are divided into a set of broadly shared principles on human genome editing and specific recommendations relating to heritable human genome editing, genome editing research involving human embryos, non-heritable human genome editing and mitochondrial donation. The broad principles emphasise the importance of ensuring applications of human genome editing are restricted to the alleviation of human suffering, improvement to quality of life, and reduction of childhood mortality. Other factors that were emphasised include recognition of the need for adequate research, equitable access, meaningful consent, proper regulation, community and stakeholder input, clear use of terms and regular revisiting of recommendations.

The specific recommendations on non-heritable human genome editing indicate that there was broad but not universal support for these types of applications amongst citizens' jury participants. In accordance with the principles outlined above, the recommendations emphasise that non-heritable human genome editing should only be used to alleviate human suffering, improve quality of life, and reduce childhood mortality; is should be properly regulated; and it should be broadly accessible to those in need. Participants emphasised that clinical applications of genome editing must be informed by adequate research to identify and assess the potential risks and benefits, both to the individual and to society and that informed consent must be assured.

Participants were far more equivocal and less unified when it came to support for heritable genome editing and genome editing research using human embryos. For some participants, the heritable alteration of the human genome could not be sanctioned in any way. Despite this, the majority of participants expressed cautious support for heritable genome editing at some point in the future, following more research and public engagement and within a strict regulatory environment. Within this majority group, there was strong support for the view that, if approved, heritable human genome editing should only be used to assist people to have healthy children, and that it should never be used for enhancement purposes.

For some participants, any intervention involving destruction of human embryos or introduction of heritable changes could not be sanctioned. This was reflected in the negative views of some participants regarding the use of human embryos in human genome editing research. In particular, some participants were vehemently opposed to the creation of human embryos for research purposes. In marked contrast, for some participants any regulatory intervention that might fetter or slow the development and uptake of genome editing technology should not be tolerated.

In summary, then, in the Australian context, the indication from the majority of participants in the Australian Citizens' Jury is that there is support for strictly regulated, equitable and fair non-heritable genome editing. There is also some support for heritable human genome editing, in some circumstances, at some future point in time, conditional upon strict regulation, more research and community and stakeholder engagement. However, this is by no means the consensus view. Despite the ostensible unanimity of the majority view, mapping of participant views pre- and post-deliberation reveal that participants brought very different perspectives to the deliberation, and although these perspectives shifted post-deliberation, they were no more uniform (see section 6).

5 AUSTRALIAN CITIZENS' JURY RECOMMENDATIONS

5.1 GUIDING PRINCIPLES

The following guiding principles were developed by participants on the final day of the Australian Citizens' Jury and clarified following the subsequent participant interviews and online forum. They reflect a widely shared, but not universal view among the group. They apply to the development and use of all the applications of human genome editing.

1. If human genome editing is permitted, its primary aim should be to alleviate human suffering, improve quality of life and reduce childhood mortality.
2. Decisions about whether to use human genome editing should be informed by adequate research to identify and assess the potential risks and benefits, both to the individual and to society.
3. Meaningful consent and equity of access should be the overarching ethical principles.
4. If human genome editing is permitted, both research into and applications of human genome editing should be subject to appropriate regulation and approval processes that include stakeholder and community education and input, as well as peer review.
5. Key terms need to be defined to lessen the possibility of miscommunication or misuse of human genome editing technologies.
6. These recommendations need to be revisited as the technology advances and we know more about the risks and benefits of human genome editing.

5.2 SPECIFIC RECOMMENDATIONS

As with the guiding principles, the following are the specific recommendations were developed by participants on the final day of the Australian Citizens' Jury and clarified following the subsequent participant interviews and online forum. It is emphasised again that these recommendations were not the consensus view of the group. In particular, a small minority of participants did not endorse the recommendations relating to heritable human genome editing and genome editing research using human embryos.

A brief commentary on each recommendation is also provided below. This commentary summarises and characterises the group discussions at the citizens' jury and online forum, and the individual participant responses to interview and survey questions. The purpose of the commentary is to clarify ambiguous terms and provide a context to help readers interpret the recommendations. Because the topics of heritable human genome editing, non-heritable human genome editing, and genome editing research using human embryos were often interconnected in the discussions, the commentary does not necessarily reflect the actual words used in the discussions. However, efforts have been made to ensure that the commentary accurately synthesises and reflects the broader scope of the relevant discussions.

5.2.1 Recommendations Regarding Heritable Human Genome Editing

Recommendation 1: Stance toward heritable human genome editing

We recommend that Australia takes a supportive stance towards potential future clinical applications of heritable human genome editing by encouraging further research to assess the potential risks and benefits; and developing appropriate guidelines and government regulation.
We recommend that heritable human genome editing be limited to circumstances where it might assist people to have healthy, genetically related children. In other circumstances, particularly the application of heritable human genome editing for human enhancement, the prohibition on heritable human genome editing should remain.
We have diverse opinions about what constitutes appropriate regulation and acceptable levels of risk. However, the majority of us recommend the use of strict guidelines and regulation for heritable human genome editing research and applications. A minority of us feel that strict regulation would hamper progress in human genome editing research and unnecessarily delay its clinical application.

Commentary on Recommendation 1

Throughout the deliberations, most citizens' jury participants tended to favour a more cautious approach to heritable human genome editing than to non-heritable human genome editing. Heritable human genome editing was viewed as a long-term project with many potential benefits and risks, which are currently largely unknown. Hence, clinical applications of heritable human genome editing might be acceptable in the long term, subject to the outcomes of further research. While also dependent on further research, clinical applications of non-heritable human genome editing were treated as a real possibility in the near term. This view provides a rationale for encouraging further research into heritable human genome editing.

Citizens' jury participants did not extensively discuss how heritable human genome editing research could or should be encouraged, or by whom. However, a reoccurring comment across several of the small group discussions was that changes to existing legislation may be needed to permit heritable human genome editing research, particularly the creation of embryos by fertilisation for research. Several participants questioned how heritable human genome editing could be improved, and remaining knowledge gaps filled, if heritable human genome editing research is not permitted. These considerations partly motivated the majority recommendation that Australia should support further research into potential future clinical applications of heritable human genome editing, possibly even going so far as to allow the creation of embryos for research.

A minority of participants preferred a less cautious approach, including removing legislative and other regulatory impediments to speedy clinical trials and clinical applications of heritable human genome editing in the near term. They argue that some consequences of heritable human genome editing can only be understood following clinical trials and clinical implementation. One participant made this rationale explicit by stating that 'treatment is research' and emphasising the ethical concerns raised by not swiftly moving towards clinical applications. According to this perspective, delaying treatments using heritable human genome editing means forgoing the potential benefits to people who currently live with, and pass on, life-threatening or debilitating diseases and disabilities.

Although the less cautious approach was only expressed by a small number of participants, others were sympathetic to the ethical dilemma that prospective parents, and society, face in deciding whether and when to go ahead with clinical trials. One participant noted that, 'it's early prevention at the cost of so many side effects that we don't even know about. But how else do we find out?'.

Ambivalence on the topic of heritable human genome editing research, and the willingness of many participants to accept such research despite reservations, is also evident in participants' positions on the use of human embryos in genome editing research (see Recommendations 8 and 9).

Both the majority and the minority positions encapsulated in Recommendation 1 are motivated by the perceived need to assess the potential risks and benefits of heritable human genome editing by supporting further research. Participants considered the benefit of heritable human genome editing to be the ability to prevent or treat diseases that are not otherwise adequately addressed by existing treatment methods. Some participants went so far as to envision a future in which some heritable diseases are eradicated using heritable human genome editing. For example, one participant was excited about the possibility that, 'Some things we could eradicate almost like a vaccine' and pictured 'a world without Alzheimer's, dementia, or Parkinson's.' and asked, 'What if we could do something about that?'.

The perceived benefit of heritable human genome editing was less straightforward for situations in which there are existing treatments. Some participants raised concerns that heritable human genome editing might compete with other treatments and thereby narrow the range of strategies and reduce available options to treat people with disease. One participant described his reticence about the hypothetical use of heritable human genome editing to eradicate relatively minor illnesses, for which there are currently alternative treatments: 'Grandma's recipe for chicken soup can get you over a cold. (...) Do we then rely on taking the chicken soup rather than say we're going to cure the common cold?' Another participant observed that people might become complacent about their lifestyle choices if they no longer need to be concerned about being genetically predisposed to various illnesses. However, other participants remarked that this is not an issue unique to genome editing and simply reflects ongoing medical progress, which inevitably will lead some prior treatments to be abandoned.

Participants recognised that reduced medical costs might be an additional benefit of heritable human genome editing, but some were uncomfortable with using this as a rationale for supporting the technology. Participants discussed the current high financial costs of ongoing medical treatments, both for individuals and publicly funded health care systems. At one of the small-group discussions, the participants shared anecdotes about the sacrifices that friends and family members have made in order to afford ongoing medical treatment, or to care for others who are living with heritable diseases or disabilities. While they were unsure whether heritable human genome editing would reduce individual medical costs, many participants anticipated that it could reduce overall healthcare costs and potentially free up resources for other types of support.

During the deliberation, however, some participants strongly objected to using such costs calculations to determine the value of treatment and felt that this dehumanises people with diseases and disabilities. One participant felt that such assessments are 'not driven by a conversation to enable the betterness of humanity'. One participant also raised a broader question of whether 'it is possible to venture into the world of human genome editing while simultaneously making a strong statement about the intrinsic value of the human being'. These questions are also relevant to discussions about private investments in genome editing, and concerning the status of the human embryo, which are further discussed in Recommendations 7 and 8 and 9, respectively.

Although the participants considered off-target effects to be a possible risk of genome editing, they largely treated this as a technical concern which could be addressed through further research. A more profound risk was thought to be that the use of heritable human genome editing might limit future expressions of human diversity: 'When you edit genomes to a standard, then that standard normalises and homogenises what the ideal human would be like.' Other risks raised by participants included unanticipated consequences, such as unintentionally triggering novel diseases, misuse of heritable

human genome editing to weaponize or control the behaviour of populations, and people becoming complacent about making healthy lifestyle choices. Additionally, participants speculated that genome editing might be rejected by society if it does not yield the anticipated benefits, relative to its costs.

The participants did not discuss how the benefits and risks of heritable human genome editing ought to be formally assessed. However, they did express concern about how such assessments might be conducted. It was considered important that members of affected communities are included in the assessment of risks and benefits. In particular, affected communities should have a say in how their quality of life is assessed and what the success or failure of heritable human genome editing would look like for them (see also Recommendation 3 on community engagement).

Although Recommendation 1 is supportive of heritable human genome editing research, it also proposes a high threshold for the acceptable use of heritable human genome editing by requiring considerably greater benefits and fewer risks than might be expected for non-heritable and non-genetic treatments.

Recommendation 2: Prioritise clinical applications

We recommend that a clear distinction is made between clinical and non-clinical applications of heritable human genome editing. Clinical applications should be prioritised. When prioritising clinical applications, both the severity of the disorder or disability (such as life-threatening conditions), and the number of people affected should be considered.
We hold differing views on the use of heritable human genome editing for non-clinical applications, including enhancement, but a majority feel that these should be prohibited.

Commentary on Recommendation 2

Most participants felt that clinical applications of heritable human genome editing should be prioritised over non-clinical applications of heritable human genome editing (see below). However, Recommendation 2 is not intended to imply that heritable human genome editing should be prioritised over alternative treatments or preventative therapies (see Recommendation 4). Similarly, Recommendation 2 should not be understood to mean that clinical applications of heritable human genome editing should be prioritised ahead of further genome editing research. A majority of participants considered further genome editing research to be a prerequisite for any potential application of heritable human genome editing, as specified in Recommendation 1.

It was not the aim of the deliberation to make recommendations about what genome editing treatments to prioritise, nor was this extensively deliberated by participants. However, the question was discussed by some participants during the citizens' jury, as well as in the individual post-deliberation interviews. Among those who discussed the topic, there was a clear preference to prioritise diseases or disabilities that cause life-threatening or severe impairments. As mentioned in the commentary on Recommendation 1, some participants also favoured prioritising treatments for which alternatives are inadequate or unavailable. One participant favoured the prioritisation of monogenic diseases. Another raised the need to prioritise treatments for disorders that place a strong intergenerational burden on families and people who were 'going through expensive treatment options'. By expensive, the participant specified 'not only in the sense of money, but also in the sense that it is emotionally draining and taxing on people who go through multigeneration (sic) disabilities or impairments that can really affect people'. Through these preferences, participants are expressing a clear principled desire to help those most in need.

In addition to these principled stances, some participants expressed practical considerations that might affect when and how treatments are made available. One participant was particularly concerned about the opportunity cost of developing and using expensive genetic treatments for a small number of patients with rare diseases: 'If you save one person's suffering, the opportunity cost for helping might be a hundred other patients'. Some participants were concerned that an early release of a controversial treatment might cause pushback that would prevent or delay the approval and use of treatments. For example, one participant argued that focusing on preventing disabilities could polarise the debate, suggesting that the use of heritable human genome editing of diseases might be less controversial (see also discussion of disability and identity in Recommendation 3).

Although Recommendation 2 calls for a clear distinction to be made between clinical and non-clinical uses of heritable human genome editing, participants struggled to draw a bright line between such applications. Participants' reflections on the distinction between clinical and non-clinical uses of human genome editing will be detailed in relation to Recommendation 5 on non-heritable human genome editing. Notwithstanding different interpretations of clinical and non-clinical uses, most participants rejected the use of human genome editing to make heritable changes that they considered to be non-clinical.

Participants who rejected non-clinical uses of heritable human genome editing did so for diverse reasons. A key concern for some participants was the inability of future participants to consent to heritable human genome editing. While most participants recognised the right of parents to consent on behalf of their unborn child, they were concerned about longer term implications for future generations. One participant pointed out that the need and preferences of future peoples might be different from our own, and so 'whether it's for the better or worse, we don't always know.' Another key concern was that non-clinical uses of heritable human genome editing might be unconstrained, and people could 'make changes on demand, for any reason', including to 'design' their ideal child. The concept of 'designer babies' was evidently a familiar touchstone for many participants, some of whom were unaware of other possible uses of human genome editing prior to the citizens' jury. One participant who objected to a blanket prohibition of non-clinical applications, felt that people were too focused on the idea of making "cosmetic" changes and not considering how certain non-clinical applications might greatly improve some people's quality of life.

In addition to the distinction between clinical and non-clinical applications of heritable human genome editing, analysis of the deliberations and interview responses suggests that another important distinction is between legitimate clinical and non-clinical uses on the one hand and misuse on the other. Misuse was a serious concern for many participants. This included abstract worries about 'mad scientists', 'weird mutants' and 'dystopian Hollywood' scenarios, but also concrete concerns, for example about interfering with people's behaviour, intentionally reducing human diversity, or potentially weaponization the technology, e.g., by creating biological weapons. There is clearly a need to address the ambiguity of the terms "non-clinical" and "enhancement", and to better understand people's opinions about the associated uses of heritable human genome editing.

For some of the citizens' jurors, participation in the deliberative process reduced their concerns about 'on-demand' and misuse of heritable human genome editing. Some participants stated that hearing from and speaking with the experts at the citizens' jury helped to allay these concerns. Two participants noted that the experts' presentations had highlighted the technical hurdles that would hinder heritable human genome editing from becoming a 'quick technological fix' for societal challenges. For example, three participants mentioned the same presentation by one of the expert speakers and noted that this presentation reassured them that spontaneous mutations in the human

genome, and genetic changes due to ageing and lifestyles, would prevent the use of heritable human genome editing to reduce human diversity.

Another participant commented that he formed a greater connection with the science and the people involved in the research, which was influential in lessening his concerns: 'Prior to that [the citizens' jury] (...) I saw it as, "those people are stuck in a lab 24/7. I don't' ever see them. They aren't part of our community.". But this event was really about, "wow they're real people. They're motivated by good things and good outcomes"'. This sentiment was echoed by several other participants, thus emphasising the importance of responsible science, including through face-to-face community engagement. Some participants also felt that they had a greater understanding of how genetic technologies are governed and were thereby reassured that there were processes in place to discourage or prevent the misuse of human genome editing. However, some participants noted that participating in the citizens' jury raised new concerns due to the process of reflecting more deeply about the implications of the technology.

The question of where to 'draw the line' between different forms and applications of human genome editing is central to the deliberations. Determining which applications of heritable human genome editing might be considered acceptable or unacceptable is a key societal and policy challenge. Recommendation 2 shows that participants consider the purpose for the application of heritable human genome editing to be a relevant consideration for determining its acceptability.

Recommendation 3: Community engagement

We recommend that any process for approving applications of heritable human genome editing must include education, engagement and other forms of capacity building to ensure that members of the public can meaningfully participate in decision making. Communities who are particularly affected, including people living with inherited disease or disability, should have input into the approval process. International peer review should also be included in the process.

Commentary on Recommendation 3

Participants strongly supported the need for community engagement on the topic of human genome editing, and mentioned activities ranging from education and perspective sharing, to participation in decision-making and oversight. However, there was little discussion about the purpose or preferred method of engagement.

The importance of increased public awareness and understanding of human genome was often treated as self-evident by participants. In part, this was informed by participants' own positive experiences of learning about the topic through expert presentations and discussions. Participants' awareness of human genome editing was generally low before the citizens' jury, and many had never heard about it prior to their initial encounter with the project. On returning from the citizens' jury, many participants found that family members, friends, and colleagues also had little or no prior awareness of the topic or familiarity with key terms such as "genes" or "heritable" / "non-heritable". One participant reflected that, 'I don't know if we've all had our head in the sand and not heard of genome editing'. Some participants also remarked that they had become more alert to discussions of human genome editing in the media following the citizens' jury.

Education and awareness raising was also viewed by many participants as a prerequisite for healthy and meaningful public debate. In fact, one participant insisted that 'if there's going to be community consultation then there needs to be education otherwise it can be quite dangerous to the process'.

Given participants' observations that the citizens' jury process reduced some of their concerns while simultaneously raising new ones, it is not surprising that participants felt that a more informed public would make better decisions about genome editing. However, in the post-deliberation interviews many participants expressed that learning more about the topic had not changed their minds on human genome editing, but rather reinforced their views and increased their confidence in speaking about the topic. This suggests that the opportunity to reflect on their own personal values and discuss their views with other participants might have been an underappreciated part of the process.

Another important function of awareness raising is to signal transparency about ongoing research. Several participants were surprised by how far the technology had progressed without their noticing. One participant commented that that genome editing research had been taking place 'under the radar' and questioned why 'we're finding out about it now (...) rather than 5 or 6 years ago when it was starting?'. The suggestion that genome editing research has been intentionally obscured from public view thereby led some participants to question the motives of people involved in genome editing research. Similarly, participants' feeling that "opposing views" were not represented at the citizens' jury, damaged their trust in the process by making it appear biased in favour of the technology. Although unintentional, this perception that information about human genome editing is being withheld from public scrutiny and debate reduces trust in the scientific, as well as the decision-making processes.

Some participants felt that the progress that has been made in human genome editing research indicates that science has 'a lot of control over our lives' without input from the public and affected people. One participant thought that 'I was initially kind of naïve to say that we should leave it to the experts. After the citizens' jury it's become more apparent that it should not just be [up to] them.' Rather than a rejection of the scientists' expertise or intentions (see also commentary on Recommendation 2), the call for greater community participation in decision-making reflected a greater appreciation for the inclusion of diverse views and experiences.

While they recognised and appreciated the achievements of science, participants also voiced the need to hear directly from the people who are affected by diseases and disabilities that might be prevented or treated using genome editing (see also commentary on Recommendation 2). In particular, one participant pointed out that people living with disabilities might question their worth, if they are not engaged and supported throughout the decision-making process. First-hand accounts were also considered important to avoid assumptions about the needs of those affected. For example, one participant reflected that, 'as able-bodied people, we want to be able to fix everybody. But not everybody needs to be fixed.' Similarly, such accounts can help distinguishing between clinical and non-clinical applications of heritable human genome editing because 'to some people it might be a disease, but to other people it's their life'. One participant summarised this view: 'We have to get more first-hand accounts of what their experiences are like and how we can listen to them to be better instead of acting on their behalf'.

Beyond decision-making about how and under what conditions human genome editing should be used, some participants also emphasised the need for members of the public and affected people to be engaged in the approval and oversight of human genome editing applications. However, the participants did not discuss how the public ought to play a role in such processes.

Recommendation 4: Availability of alternatives

We recommend that people should be informed about and have access to reproductive technologies that do not involve human genome editing, where such exist, to aid them in having healthy children.
We differ about whether parents should be permitted to refuse any treatment on behalf of their child if its application could be of significant clinical benefit (for example, preimplantation genetic diagnosis).

Commentary on Recommendation 4

It was important to most participants that the availability of human genome editing should not detract from the treatments and support that are available to those living with a disease or disability. In part, this reflected a recognition that some diseases and disabilities occur later in life, for example through injury or other circumstances, for which people will still require treatment and support. Additionally, parents may choose not to edit the genes embryos or children, for example to prevent diseases or disabilities that are detected through pre-implantation genetic diagnosis. Most participants felt that people with disabilities should not be 'punished' for the choices of their parents by having their access to treatments or support services curtailed.

Participants' concerns that clinical applications of heritable human genome editing might compete with alternative treatments was previously discussed in the commentary on Recommendation 1, and similar arguments were made about the potential loss of long-term support services for people living with disease or disability. However, one participant argued for a more punitive approach, because 'the pressure would be on society to cater and provide for such children' and refusing human genome editing should therefore be discouraged.

Relatedly, participants discussed, but did not reach agreement, about whether parents should be permitted to refuse human genome editing treatments on behalf of their children. Some participants mentioned that one expert referred to UK legislation that addresses this issue. The relevant legislative provisions are referenced in section 9 of this report. Although most participants agreed that parents should be permitted to refuse heritable- or non-heritable human genome editing if alternative treatments are available, it is not clear whether participants would accept parental refusal in situations where there are no alternative treatments. In Recommendation 4, the ambiguity is captured in the statement 'any treatment'.

For many participants, it was difficult to empathise with the decision to withhold or decline any treatment that might be of significant clinical benefit to a child. Although participants emphasised that children with diseases or disabilities 'are different but they're no less precious to their families' or that parents 'wouldn't change their child once it's born', they nevertheless asked 'but would you choose that [disease or disability]?'. One participant argued that 'It's pretty generally supported that if there is a treatment available, we try to correct it [the disease or disability]' and continued 'I think we can separate the person from the disability. I think if we removed the disability, they'd still be an amazing son or daughter.' Despite these objections, one participant pointed out that 'parents have the right to make all kinds of decisions for children' and raised the question of when parents gain this right, i.e., 'at fertilisation or birth?'. The participants evidently foresaw situations in which the rights of the parents might conflict with those of their child and had differing views about how those situations should be managed.

The question of whether parents should be permitted to refuse genome editing on behalf of their children or future children, or to choose to implant an embryo known to carry a genetic disease or

disability, sparked both strong emotions and confusion about why parents would make this choice. The deliberations might therefore have benefitted from firsthand testimony by parents who have made such decisions on behalf of their own children (albeit regarding other treatment options and not genome editing). Such firsthand testimony has been shown to increase empathy and understanding, and thereby further the deliberative process even if the participants do not change their mind on the topic (see also commentary on Recommendation 3).

Finally, some participants noted that the availability of alternatives is only meaningful if people are adequately informed about them. This raised the question of whether treatment providers should be obliged to inform parents about all available treatment options, including the respective risks and benefits. While some felt that this should be at the discretion of medical providers, others emphasised that choice of treatment is a personal as well as medical decision, which required informed consent.

5.2.2 Recommendations Regarding Non-Heritable Human Genome Editing

Recommendation 5: Support clinical applications

We recommend that Australia takes a supportive stance towards potential future clinical applications of non-heritable human genome editing to alleviate human suffering, improve quality of life, and reduce childhood mortality.
Robust processes should be established to ensure meaningful consent prior to the application of non-heritable human genome editing, with consideration for vulnerable people, including but not limited to young people.
We further recommend that non-clinical applications of non-heritable human genome editing (i.e., enhancement of appearance or athletic performance) should be prohibited for now, subject to periodic review as we learn more about the risks and benefits of human genome editing. If non-clinical applications of non-heritable human genome editing are permitted, we recommend they should receive no public funding.
We also note that greater clarity is needed to clearly distinguish between clinical and non-clinical applications.
There is a minority view that non-clinical applications of non-heritable human genome editing should be permitted with regulation, as for clinical applications.

Commentary on Recommendation 5

Recommendation 5 for non-heritable human genome editing is similar to Recommendation 1 for heritable human genome editing. However, Recommendation 5 reflects the participants' belief that non-heritable human genome editing is more likely to be applied in Australia within a shorter timeframe. Consequently, this and the subsequent recommendations on non-heritable human genome editing focus on how it should be implemented and governed, while the recommendations for heritable human genome editing focus on research. Although the need for further research is not explicitly mentioned in Recommendation 5, it is implied by the Guiding Principles.

It is evident from the citizens' jury deliberations, as well as subsequent interviews and surveys, that most participants strongly supported the eventual clinical use of non-heritable human genome editing in Australia. Most participants felt that non-heritable human genome editing could be of tremendous benefit to people living with disease or disability. No strong opposition was raised to such uses. This underscores the call for Australia to take a supportive stance towards potential future clinical applications of non-heritable human genome editing.

The meaning of "supportive stance" in Recommendation 5 is open to interpretation, which was not extensively discussed by participants. In the words of one participant, 'what does supporting look like? Does that just mean funding for research purposes? Does it mean actually conducting it [non-heritable human genome editing]?'. Fundamentally, such support would include approving clinical applications, if and when their long-term safety and efficacy has been established. Two participants specifically expressed a wish for government support to include subsidised clinical non-heritable genome editing treatment via Medicare and/or the pharmaceutical benefits scheme. This reflects a perceived need to ensure that clinical applications of non-heritable human genome editing are accessible to those who need them (see also Recommendation 7).

During table deliberations at the citizens' jury, some participants discussed challenges for how meaningful consent for non-heritable human genome editing could be achieved. For clinical applications, the aforementioned requirement is that people should be informed about alternatives treatment options, and the associated risks and benefits (see Recommendation 4). For non-therapeutic applications, some participants initially suggested a minimum age of consent of 25 years, due to a concern that younger recipients of non-clinical treatments might later regret their decision. However, other participants felt that any adult should be able to consent to such treatment, although they agreed that children could not meaningfully consent. Instead, they suggested that the question of meaningful consent is one about capacity rather than age. While they accepted that capacity to consent varies across age ranges, participants were also aware that other factors might impair a person's ability to consent. This led to a broader statement about ensuring that "vulnerable people" are able to meaningfully consent to non-clinical, non-heritable human genome editing.

Another concept which is ambiguous in Recommendation 5, is the concept of non-clinical applications. In discussions at the citizens' jury, and in the subsequent individual interviews, participants tended to treat non-clinical applications of genome editing as synonymous with enhancements, which most participants strongly opposed. It was evident from these discussions that the idea of enhancement (as well as 'designer babies', see Recommendation 2) was more familiar to participants prior to the citizens' jury, than were potential clinical applications of genome editing. For example, one participant was surprised to learn that human genome editing 'could be life changing, and not just about physical characteristics [appearance]'. The use of heritable and non-heritable human genome editing to cosmetically alter appearance was considered frivolous by most participants. Conversely, applications to improve physical or cognitive abilities beyond the current norm, or to introduce new-to-human characteristics were seen as potentially dangerous by most participants. Only one participant raised the possibility that certain applications of non-clinical human genome editing could also substantially improve some people's quality of life, for example by altering (hypothetical) genes linked to disfigurements (see also commentary on Recommendation 2).

Some participants questioned why genetic interventions should be treated differently from other types of enhancements. One participant argued persuasively that:

> We allow for enhancement in every other way. We allow for money to be inherited from families between generations which gives children a financial enhancement. We allow cosmetic surgery. We allow sporting coaches to exist to enhance sorting ability. So what's wrong with enhancing genetically?

This comment resonated with others at the deliberation and was referred to during several post-deliberation interviews as eye-opening. Although still opposed to non-clinical human genome editing, one participant noted that societal acceptance of enhancements such as dental braces or breast implants have changed rapidly and speculated that future humans would likely accept non-clinical genome editing as part of everyday life. Similarly, one participant reflected that 'if everyone enhances

themselves then it's not really enhancement'. These reflections underpin the need to periodically review the recommended prohibition on non-clinical non-heritable human genome editing.

One of the key concerns expressed by participants about non-clinical applications of non-heritable and heritable human genome editing is that this will promote profit motives that siphon resources away from clinical applications. Concerns about limiting resources for 'public good motives' also underlines many participants' strong opposition to the use of public funding to support non-clinical applications. However, some participants argued that both private and public investment in non-clinical uses could reduce the cost of clinical applications, as well as support research that improves the technology overall. Additionally, one participant argued that decisions about the provision of public funding should consider the type and purpose of non-clinical application. Although participants disagreed on specifics, the discussion of whether and how to fund non-clinical applications of non-heritable human genome editing further illustrates participants wish for human genome editing to reduce suffering and improve quality of life.

Recommendation 6: Focus on governance

We recommend that all parts of the non-heritable human genome editing process (including funding, research, applications, and reimbursements through the Pharmaceutical Benefits Scheme) be subject to regulation and oversight to ensure that risks and benefits are adequately assessed. We further recommend that national and global standards are consistently applied. Recognising that the regulation of non-heritable human genome editing involves multiple agencies, we further recommend a broad intersectoral approach. Regular reviews need to be built into the regulatory scheme to ensure it is future proofed.

Commentary on Recommendation 6

Most participants were emphatic about the need for regulation and oversight across all the processes involved in the research and application of non-heritable human genome editing. Discussions and concerns about the regulation of non-heritable human genome editing research are largely reflected in those detailed in the commentary on Recommendation 1 on heritable human genome editing. This further underscores participants' expectations about the different time scales at which the application of heritable and non-heritable human genome editing might be feasible.

Discussions about the regulation of clinical applications of non-heritable human genome editing included previously described issues, such as how to ensure meaningful consent and prevent non-clinical applications (both of which are described in the commentary on Recommendation 5), equity of access (detailed in the commentary on Recommendation 7), and misuse (see also commentary on Recommendation 2 and Recommendation 9). Regarding the misuse on non-heritable human genome editing, the main concern voiced by participants was that regulation would not prevent 'rogue actors', 'mad scientists', or individual governments from misusing the technology. The example of He Jianku was referred to as an example of an individual actor bypassing existing regulation and oversight to conduct human genome editing.

Participants also discussed who would have a role in decision making about non-heritable human genome editing. In particular, participants highlighted the risk of vested interests influencing such decision-making. This risk might have been considered greater than for heritable human genome editing due to the potential private market for personal genetic enhancements and other non-clinical applications (see also commentary on Recommendation 5 regarding profit motivations in non-heritable human genome editing). One participant noted that the risk of vested interests capturing the decision-making process would be greater if one single organisation or person has decision-

making authority. Discussions about who should participate in decision-making are also reflected in discussions on community engagement in heritable human genome editing, as detailed in the commentary for Recommendation 3.

Oversight of genome editing research and clinical applications was also considered particularly relevant to non-heritable human genome editing. According to one participant, 'oversight is just as important as research itself'. The role of oversight in genome editing research was primarily to ensure the long-term safety of non-heritable human genome editing, by understanding and comprehensively mitigating the risks prior to the approval and clinical use of the technology. As in the case of heritable human genome editing, some participants were more willing to support some early clinical uses of the technology as a step towards better understanding the associated risks (see commentary on Recommendation 1). Additionally, some participants called for regular auditing of research and treatment facilities to ensure that regulations are followed.

The question of liability was briefly discussed by some participants at the citizens' jury. One participant called for limited liability for researchers conducting clinical trials, backed by waivers. However, another participant highlighted the potential long-term moral obligation that researchers and treatment providers ought to have to monitor the health and well-being of patients and trial participants. For non-heritable human genome editing, this might imply following up on their condition throughout their lives, while for heritable human genome editing the scope of the commitment might be considerably longer.

The participants highlighted the need for collaboration and coordination at various scales in the oversight of non-heritable human genome editing. This included collaboration between multiple and diverse government agencies, as well as community representatives, to work together to ensure adequate oversight. Additionally, participants discussed the need to coordinate Australian regulation of genome editing with that of other countries. One participant hypothesised that a lack of international coordination might mean that some countries will go 'gung-ho' on the technology, and 'every other country (...) has to play catch-up or has to be the bearer of some unintended consequences of those decisions'. This concern also has implications for the sharing research results and transparency about new and ongoing research. However, arguments against greater international coordination of regulation and oversight were also raised by at least one participant. This participant argued that Australia should not turn a blind eye to uses of non-heritable human genome editing in other countries that would not be permitted in Australia. In such cases, the government 'should not be influenced to allow those things to happen if we think it's not ethical or too dangerous'. This suggests that any coordination and alignment with international standards must not compromise Australia's ethical norms and community values.

Recommendation 7: Consider accessibility

We recommend that non-heritable human genome editing be made accessible to those who need it. Consideration should be given to how best to ensure equitable access. Assessments should be people-focused and made on a case-by-case basis. Genetic counselling should be provided.

Although most of us agree that access to non-heritable human genome editing should be equitable and affordable, we hold varied views on what this means and how it might best be achieved. We are particularly concerned that vested interests and profit motivations in the private sector might distort the application of non-heritable human genome editing and limit public good. However, a minority view is that equitable and affordable access to non-heritable human genome editing may not be feasible and should not be a requirement for non-heritable human genome editing.

Commentary on Recommendation 7

Participants' insistence that people in need should have access the potential benefits of clinical non-heritable human genome editing is evidenced throughout the recommendations and associated discussions. However, Recommendation 7 explicitly points to participants' hope that special provisions will be put in place to make sure that the people with greatest need can access the most effective treatments without undue burden to their economy or wellbeing. For many participants, this also meant ensuring that those people without the greatest need are not able to access treatments with undue ease, for example due to an ability to pay higher prices for easier access. In the words of one participant, 'if you've got money, you can often get a lot further than if you're poorer or on a lower income scale. And I think for certain things, that shouldn't make a difference.' However, some participants questioned the feasibility of such case-by-case assessments of people's need. One participant asked: 'How long would that take? Who would assess? If you can't find a doctor that assesses you, would you go to another doctor?'

Participants tended to point to financial hurdles and profit seeking by the private sector as the main causes of these concerns. The potential impact of profit seeking by the private sector, particularly the potential prioritisation of non-clinical ahead of clinical applications, is described in the commentary on Recommendation 5. Other participants resisted this framing of 'equitable access' based on need, and the associated resistance to profit seeking by private research or treatment providers. These participants argued that private companies should be permitted to recoup their investments in research and technology by marketing their products and services to those who can afford to pay. One participant compared the equity argument to refusing to paying for everyday services: 'You don't get someone out to fix your house and then say (...) it's wrong for you to charge me because I needed that to be fixed'.

Unfortunately, there was not time at the citizens' jury to discuss whether a middle ground could be found between these two opposing positions.

5.2.3 Recommendations Regarding Human Genome Editing Research Using Human Embryos

For the majority of us, the considerable potential medical benefits and advancement of scientific knowledge that might result from such research outweigh the discomfort we feel about the use of human embryos in genome editing research. However, a minority of us strongly object to the creation and destruction of human embryos in genome editing research.

For the majority of us, any research using human embryos, created by whatever means, should be subject to stringent regulation and oversight, limited to maximum of 14 days after fertilisation, and subject to informed consent from all donors and their partners.

Recommendation 8: Permit the use of human embryos in heritable human genome editing research

We recommend that genome editing research using human embryos should proceed in Australia.
Where research outcomes are not compromised by using alternative embryo models (e.g., pre-embryos, embryos that are unsuitable for implantation and embryos created by means other than fertilisation), we recommend that these options are preferentially considered.
We further recommend that the creation of human embryos by fertilisation for research should be permitted in Australia subject to stringent regulation and oversight.

Commentary on Recommendation 8

The use of human embryos and their precursors in heritable human genome editing research, and in particular the creation of human embryos by fertilisation, was raised at the citizens' jury. One of the expert speakers at the citizens' jury provided background information about the legal environment for research involving human embryos, noting that there is a prohibition against the creation of human embryos specifically for research, but that some uses of human eggs and embryos are allowed under licence from the NHMRC Embryo Research Licensing Committee. Another expert speaker provided information on the nature of human embryos, human embryo development and human embryo research. Prior to the post-citizens' jury interviews, participants were sent a brief description of the following sources of embryos for human genome editing research: unfertilised human eggs and sperm or pre-embryos; human embryos that are unsuitable for use in IVF; human embryos that have been created for assisted reproduction, but that are not needed by the people who provided the egg and sperm; human embryos that have been created by a process other than fertilisation; and human embryos that are created by fertilisation specifically for research.

The creation and use of human embryos for heritable human genome editing research is a complex topic, which could not be fully deliberated within the timespan of the citizens' jury. In addition to the presentations by experts, participants debated the topic in their small group deliberations. Some participants and groups also sought further information on the topic from the expert witnesses during these discussions. Nevertheless, a number of participants remained uncertain about whether and how heritable human genome editing research relies on the use of human embryos and their precursors from various sources, and the opportunities and limitations of the different options.

At the end of the citizens' jury, some participants were surprised to learn that some types of heritable human genome editing research might not be possible without the creation of human embryos by fertilisation for research and felt that scientists should 'find a way'. Because of a lack of clarity about participants' positions on the creation and use of human embryos at the end of the citizens' jury, the topic was revisited in the individual post-citizens' jury interviews, as well as in the online participant forum. Due to time constraints, these interviews focused on the creation of human embryos by fertilisation for research, and other sources of embryos were only discussed in some of the interviews.

The individual post-deliberation interviews revealed that most participants did not have firmly held positions on the question of creating human embryos by fertilisation for use in human genome editing research. Although some participants had ethical concerns which made them uncomfortable with this use of human embryos, they also thought this use might be necessary. In the words of one participant,

'I understand that from a scientific point of view, that would be the best tool for researchers and that the current situation isn't really good enough, just using the discarded ones or the non-viable ones; In that it's limited, and they can't do everything that they want to do with them'. For these participants, their ethical qualms about the creation and use of human embryos for genome editing research were weighed against the 'greater good' that such research might produce. Some participants concluded that they could justify the use of human embryos for research targeting disease or disabilities, but not for cosmetic purposes. Even a participant who strongly objected to the creation of human embryos for research noted that her position was complicated:

> I'm not sure exactly where I fit. (...) I think I'd generally not be in support of it but I could also see myself supporting it but being uncomfortable. Allowing it but still realising that I don't really agree with it.

Another participant stated that his position on this question 'could change depending on my mood'. These results suggest that further deliberation on this topic is needed to work through some of these challenging questions.

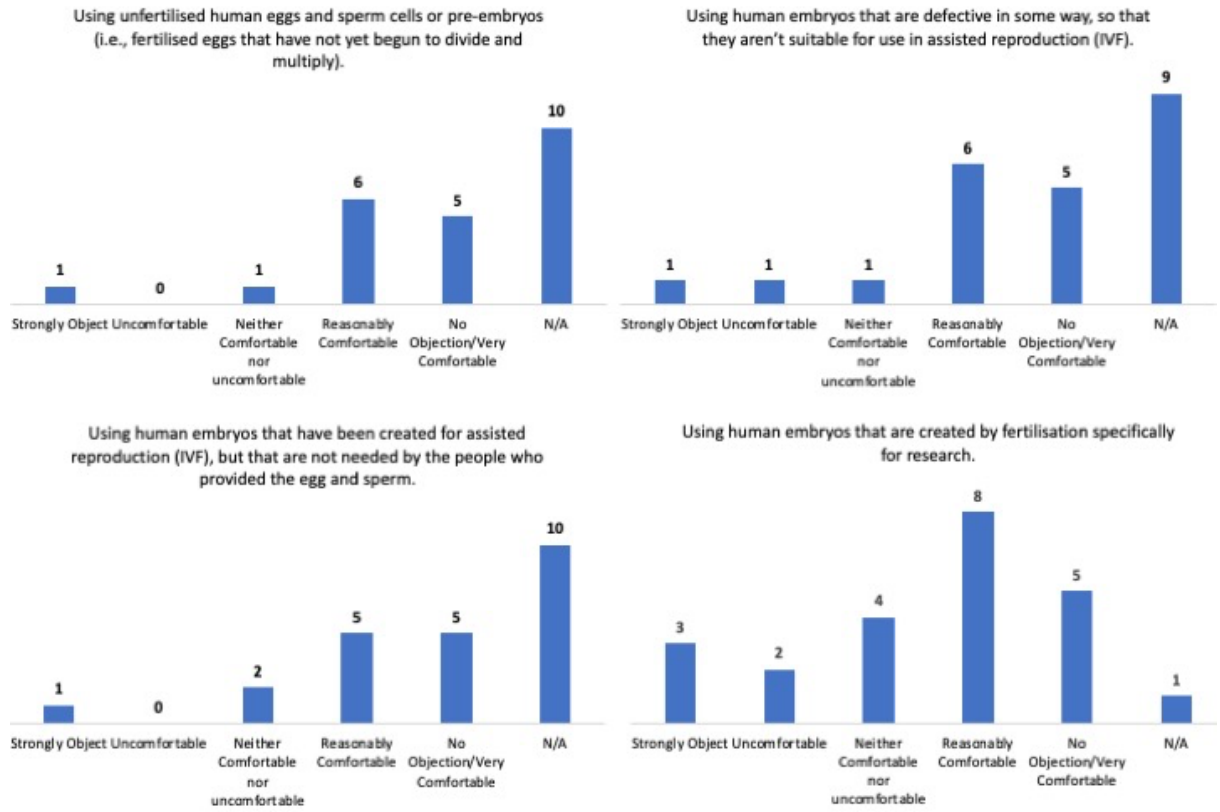
Concerns about the creation and use of human embryos for heritable human genome editing research were both principled and practical. Some 'on the fence' participants were primarily concerned that consent should be gained from sperm and egg donors, while others required that the development of the embryo should not exceed 14 days. These concerns could be at least partially addressed through appropriate regulations and monitoring, as described in the commentary on Recommendation 9. However, other concerns, such as the possible misuse, commercialisation, and mass production of human embryos might be harder to address. These issues are further discussed in section 9 of this report. For some participants, the creation of human embryos by fertilisation for research raised uncomfortable questions about the status of the human embryo and human life. One participant, who was comfortable with using human embryos that were unsuitable for IVF, was on the fence about the creation of human embryos by fertilisation for research because, 'usually when an egg is fertilised it is to bring a human life into the world, but that's not going to happen there. Don't know if fully I agree with that'. The deeply held principled concerns of those participants most strongly opposed to the creation, use, and eventual destruction of human embryos are likely to be inherent to such research. In the words of one participant, 'anything that involves killing an embryo involves killing a [human] life form (...) that shouldn't be tampered with at all'. Although this position is in the minority, it represents one end of a spectrum of concern about the status and treatment of the human embryo.

Compared with the creation of human embryos by fertilisation for research, other sources of human embryos were much less controversial among participants, as illustrated in Figure 4. During the post deliberation interviews, participants were asked if they would like to comment on any of the other sources of human embryos (other than their creation by fertilisation for research). Among those participants who discussed other embryo sources during their interviews, most were reasonably or very comfortable with the surveyed options. Insufficient responses were collected about human embryos that have been created by a process other than fertilisation to display quantitative results. However, this option was also one of the most difficult for participants to understand and tended to raise technical questions rather than considered assessments of its acceptability. One participant strongly objected to all the surveyed sources of human embryos due to the eventual destruction of the embryos used for research.

Questions about the status of the human embryo were also raised by a small number of other participants as reflected in comments such as, 'It comes down to the opinion of when an embryo

becomes a human' and 'At what point do we put value on life?'. The point of fertilisation was a significant moment that sparked discomfort for some participants, since this represented the point at which the potential for human life began.

Figure 4: Participant Attitudes to Human Embryo Use in Research



Most participants preferred eggs, sperm and embryos to be used in genome editing research, rather than discarded if they are unsuitable for, or surplus to the requirements of, assisted reproduction. A frequent comment about the use of non-viable or surplus embryos was that 'it seems like a bit of a waste'. In the words of one participant, 'I'd probably feel more uncomfortable if it was just destroyed (..) and opportunities denied where there could be enormous potential for research purposes'. Conversely, two participants argued that it was wasteful and 'silly' to use non-viable embryos or embryolike structures for genome editing research, if these are not going to adequately answer researchers' questions. Both participants thought that 'You might as well do it right [I.e., with the most suitable embryos] from the start'. However, this was a niche position, and most participants were more comfortable with other sources of embryos than they were with creating human embryos by fertilisation for research.

Post-deliberation interviews with participants revealed that they held diverse and nuanced views about the use of human embryos in genome editing research. This diversity was not as apparent in the citizens' jury deliberations, in which some participants felt that there was a consensus view that was opposed to the creation of human embryos by fertilisation. In the words of one participant, 'nobody wanted life created in the lab for research purposes'. This may reflect the discomfort that was broadly felt about the creation of human embryos. When weighed against other considerations, such as the potential 'greater good' of genome editing research, many participants supported the creation and use of human embryos, including by fertilisation, for research. Nevertheless, only a small number of participants held strong positions for or against the creation of embryos by fertilisation for research. A larger number were ambivalent and uncertain about their position. This suggests that the topic has

not yet been fully deliberated and that questions remain about how to appropriately value and respect the status of the embryo in human genome editing research.

> ***Recommendation 9: Non-commercialisation of embryo production***
>
> *We recommend that the creation of human embryos for research by fertilisation be strictly regulated and monitored to prevent mass production and commercialisation, and to limit opportunities for misuse.*

Commentary on Recommendation 9

Recommendation 9 addresses the question of how the use of human embryos created for research by fertilisation should be regulated, if approved. Participants' views on the creation of human embryos by fertilisation for research are detailed in the commentary on Recommendation 8.

Discussions about the regulation of human embryo research centred on the 14-day post-fertilisation time limit on the use of human embryos. The long-standing 14-day limit on the use of human embryos for research was contested by some participants. Further information on the 14-day rule is provided in section 9 of this report. A minority of participants expressed that they would accept fewer limitations on the creation and use of human embryos than are expressed by the majority position. This was particularly the case if such restrictions limited the ability to answer key medical questions. In the words of one participant, 'You're destroying them [embryos] anyway. I wouldn't have a problem with them being used for a tad longer [beyond 14 days]. If it's for advancement of technology or research. (...) It's for medical advancement. Think of the lives that are being saved and changed.' Another respondent echoed this sentiment: 'I'm not worried about that [14-day limit], as long as the parents have consented to the research. You'd hate to think that they were so close to a breakthrough and because of the 14-day time limit they missed out'.

More broadly, there was confusion about why the 14-day limit exists and might be applied to embryos created by fertilisation for research in the future. For example, one participant questioned why a 14-day limit is needed in situations where the embryos are considered non-viable. Others stressed that it is the ability of the embryo to experience pain, rather than a certain number of days, that is key to determining acceptable length of use prior to destruction: 'The 14-day [limit] was important to me because they stressed that that's when they [embryos] started getting a brain and nervous system'; 'At what point does that embryo feel and experience pain? (...) you can't ask a human embryo at that age "are you experiencing pain?". I can only take science for what it is (...) I put trust in their opinion about that'. The latter example also highlights that the acceptance of such a limit is contingent on participants trusting the information they receive from scientists.

The possibility of commercialisation of embryos was raised by one participant as a potential practical consequence permitting the production of human embryos specifically for research. The participant flagged their ethical concerns about the possible mass production of human embryos with the group, but this was not discussed extensively at the citizens' jury. Other participants emphasised the need for labs conducting human embryo research to be licensed. Some participants suggested that avenues for reporting misconduct in such labs should be put in place, including protections for 'whistle-blowers'. Although the topic of commercialisation and mass production of human embryos for research was not widely discussed among participants, these comments suggest that participants' general discomfort about the status of the human embryo and its creation for research (see commentary on Recommendation 8) is likely to be sharpened, if mass production were considered.

In addition to the ethical and practical concerns, ambiguous terminology and lack of clarity about the process of creating and using human embryos in genome editing research also increased uncertainty and discomfort about creating and using human embryos in genome editing research. The meaning of the term 'viability' was queried by two participants during the post-citizens' jury interviews, particularly in relation to the use of embryos that are unsuitable for assisted reproduction: 'Suitable involves a judgement based on a preference whereas viable (...) does not have the potential to develop. (...) They're not the same'. Similarly, the use of viability as a standard for determining the acceptability of genome editing applications was also questioned during the citizens' jury: 'how do we value life biologically - is it just viability? by what standards?' These questions suggest that some interpretations of viability might not be acceptable when determining if an embryo is suitable for use in genome editing research, as well as in assisted reproduction.

Discussions about the misuse of human genome editing research and application was previously detailed in the commentary on Recommendation 2. Broadly, the term 'misuse' appeared to indicate the intentional use of genome editing or genome editing research to do harm and produce social ills. However, one participant noted the ambiguity of the term and recommended that parameters for the use of human genome editing be codified in order to prevent slippage in the future. The participant pointed out that future governments might wish to use the technology for ill and asked, 'are we going to let them decide what misuse means?'.

5.2.4 Recommendations Regarding Mitochondrial Donation

Recommendation 10: Permit mitochondrial donation

We recommend that mitochondrial donation be permitted in Australia for the purpose of preventing mitochondrial disease, but only with appropriate regulation.

Recommendation 11: Non-commercialisation of mitochondrial donation

We recommend that mitochondrial donation should not be offered for profit and no financial transactions should take place between donor and recipient. We further recommend that restrictions are considered regarding the number of eggs donated by any one person.

Recommendation 12: Consider accessibility

We recommend that mitochondrial donation be made accessible to those who need it, and consideration should be given to how best to ensure equitable access. We further recommend that the use of mitochondrial donation to prevent mitochondrial disease should be the individual choice of parents.

Commentary on Recommendations 10-12

There was not sufficient time for mitochondrial donation to be discussed in detail at the citizens' jury. Where there was discussion, it followed similar lines to the discussions regarding heritable human genome editing and genome editing research involving embryos. In other words, although people

understood that this was not a genome editing technique, they did not see this as being fundamentally different in the issues that it raised for them.

Nevertheless, in the post-deliberation survey, most participants agreed that mitochondrial donation is more like an organ transplant than genome editing. For several participants, this represented a considerable change in their views on mitochondrial donation from their pre-citizens' jury positions. Participants tended to explain this shift in position as the result of being more informed about the topic following the citizens' jury.

6
TRACKING CHANGES RESULTING FROM THE AUSTRALIAN CITIZENS' JURY

By conducting pre-and post-deliberation interviews with the Australian Citizens' Jury participants and the control group, we were able to track any changes in attitudes towards human genome editing which might have resulted from participation in the citizens' jury.

Analyses were conducted of the data collected before, during and after the citizens' jury to identify pre-and post-deliberation positions on human genome editing in Australia. We have also conducted a complementary analysis of deliberative reason (using the Deliberative Reason Index, DRI; see Niemeyer et al forthcoming), which uses the same survey items as for the discourse analysis, in conjunction with the policy options presented to participants before and after deliberation.

In summary, the analyses performed involve analysis of :

- Analysis of transformation (in perspectives, using discourses)
- Deliberative reason (measuring collective reflection across the complex array of issues associated with the issue.

This section begins with analysis of transformation in the positions and perspectives of the participants in the Australian Citizens' Jury on Genome Editing. It then provides a synopsis of how the reasoning of the group transformed, before drawing the main conclusions that follow from the analysis.

6.1 Transformation of Perspectives—Using Discourses

The approach to analysis of transformation in perspectives that occurred during deliberation uses a discursive approach, rather than tracking changes to individual survey items, which provides a better fit for understanding the deliberative implications (see Dryzek 2005). A discursive approach provides a window into the public views on a complex issue, one that is anticipatory (MacKenzie and O'Doherty, 2011)—where there is little actual current public discussion on an issue. It addresses limitations with commonly used methods, such as opinion surveys, which pick up non-attitudes, or unreflective responses that are overly sensitive to cues in the questions asked (Dryzek, 1990). Deliberative processes also provide a better context for reasoning through ethical trade-offs and dilemmas than opinion surveys. Deliberative processes involving lay citizens are well-established globally (Grönlund et al, 2014; OECD, 2010) and have been carried out on a wide range of issues involving complex science and public value interactions (MacKenzie and O'Doherty, 2011; Secko et al., 2009).

According to Dryzek (2005), a discourse is:

> 'a shared way of apprehending the world. Embedded in language, it enables those who subscribe to it to interpret bits of information and put them together into coherent stories or accounts.

> Discourses construct meanings and relationships, helping to define common sense and legitimate knowledge.'

Although opinions and attitudes towards an issue or topic might align with discourses due to the presence of a similar underlying reasoning, they are not necessarily associated. Similarly, certain discourses might be prevalent within particular groups because members of these groups have shared experiences. However, discourses also cut across ascriptive groups and individuals belonging to such groups encompass multiple discourses.

Finally, discourses incorporate aspects of underlying reasoning, which lend them to measurement, comparison, and representation. In the following, the method used to identify, characterise, and compare discourses as part of an intensive discourse mapping study of Australian discourses on human genome editing is outlined.

To achieve a discursive outcome, it is important to ensure that the full range of pre-deliberative views are included in the process, where important questions are raised, and where different perspectives interact in a manner that maximises potential for integrating into a coherent whole and resolve tensions. Where differences remain (for good reason) there is also a need to understand why, and the associated implications for further public engagement and decision making.

Transformation in a discursive sense can take two forms:

1. *Positional Transformation*: Transformation of position within a discourse map (measured at the individual level)
2. *Discursive Transformation*: Transformation of the discourse map, representing a change in collective understanding of the issue.

Positional transformation is by far the most common of the two types, where individuals adjust their perspectives, usually in response to changes in understanding regarding specifics about the issue.

Discursive transformation is far less common, usually only occurring where an issue is complex, emerging, or where public debate has been disrupted or distorted though disinformation or other forms of political information (climate change being the most common example where this kind of transformation takes place; see Hobson and Niemeyer 2011, Schlosberg et al 2017). This kind of transformation reflects changes to the understanding regarding the issue—reflecting a process of meaning making—rather than adjustments within an existing understanding.

The following describes the discourse maps used to follow the positional transformations experienced by deliberative participants. This is followed by a brief examination of possible discursive transformation, before concluding and drawing together the main findings and implications.

6.1.1 Discourse Maps

Appendix C provides an account of the method used to identify the two sets of discourses reported here:

- Mapping Study Discourses—Four discourses identified during the mapping study (stage 2, see Figure2)
- Post-Deliberation Discourses—Six discourses identified among deliberative participants at the conclusion of the citizens' jury.

Here the focus will be on the second set of discourses, particularly for analysis of positional transformation. This is mainly because the map provides the necessary detail to adequately capture the relevant positions of participants, particularly following deliberation where the emerging views exhibit greater levels of sophistication and nuance.

6.1.2 Post-Deliberation (Six) Discourse Map

Figure 5 provides an overview of the main features of the six discourses identified following deliberation, similar to that provided for the four Mapping Study discourses provided above in Figure 3.

The six positions identified post-deliberation include:

- *A) Beneficial Scientific Progress* – enthusiasm about the potential medical benefits from the science of human genome editing, and relative unconcern about the potential negative social and ethical implications of human genome editing, including enhancement.
- *B) Social Benefits/Precautionary Risks* - strong concerns for the potential social benefits and risks of human genome editing, especially if it is not motivated by the pursuit of the public good.
- *C) Principled Constraints* – explicit normative or cultural opposition to human genome editing and its intended applications.
- *D) Revolutionary Medicine* – a focus on the positive potential of human genome editing as a medical technology, but concern about possible non-medical applications.
- *E) Profound Social Risks* – strong concerns that genome editing will change society for the worse and that the pursuit of perfect people and societies will lead to a dystopian future.
- *F) Libertarian Revolutionary Medicine* – relatively high-risk tolerance for genome editing research and clinical applications, and support for individuals' and parents' right to choose genome editing treatments.

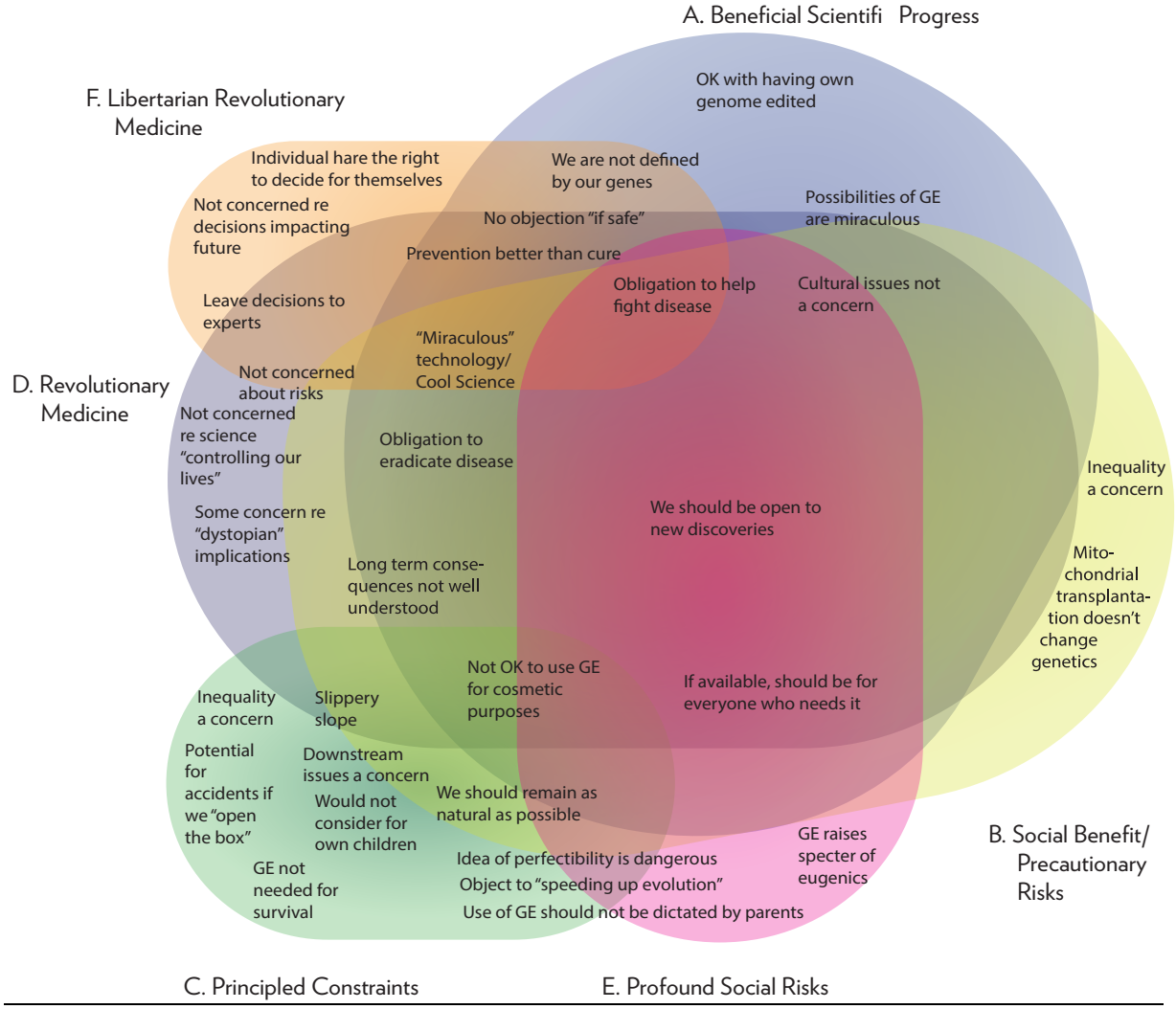
A detailed account of the discourses, map, and comparisons with its mapping study counterpart are provided in Appendix C. A few points are worth noting in relation to the differences, and similarities:

- There is less overlap in positions compared to the mapping study, reflecting in part greater specificity in the positions.
- There are strong overlaps with two of the Mapping Study discourses. The nature of the overlaps is discussed in the next section.

One shared feature across the discourses is an openness to new discoveries and scientific progress, with variation in positions mainly expressed in terms of management of risks, or differences in emphasis on potential benefits. Discourses A and F are the most supportive of human genome editing. Discourse B is precautionary. As will be seen Discourse C reflects its near namesake from the Mapping Study (B: Principled Concern). Discourse D supports the science but shows concern regarding long consequences and potential for dystopia. Discourse E reflects a more profound concern, sharing features of the principled concern of C, but with emphasis on more evocative issues.

Of the six discourses, only one (E) appears to express strong reservations regarding human genome editing. Discourse C reflects a number of strong concerns, but not outright objection to the technology. Others appear to conditionally support the technology, or at least certain applications.

Figure 5: Post-Deliberation (Six) Discourse Map—Summary



The most important finding in relation to the post-deliberation map is the diversity of views on a controversial topic such as genome editing within the Australian population. Analysis of the pre- and post-CJ discourses revealed that participants brought very different perspectives to the deliberation, and although these perspectives shifted post-deliberation, they were no more uniform.

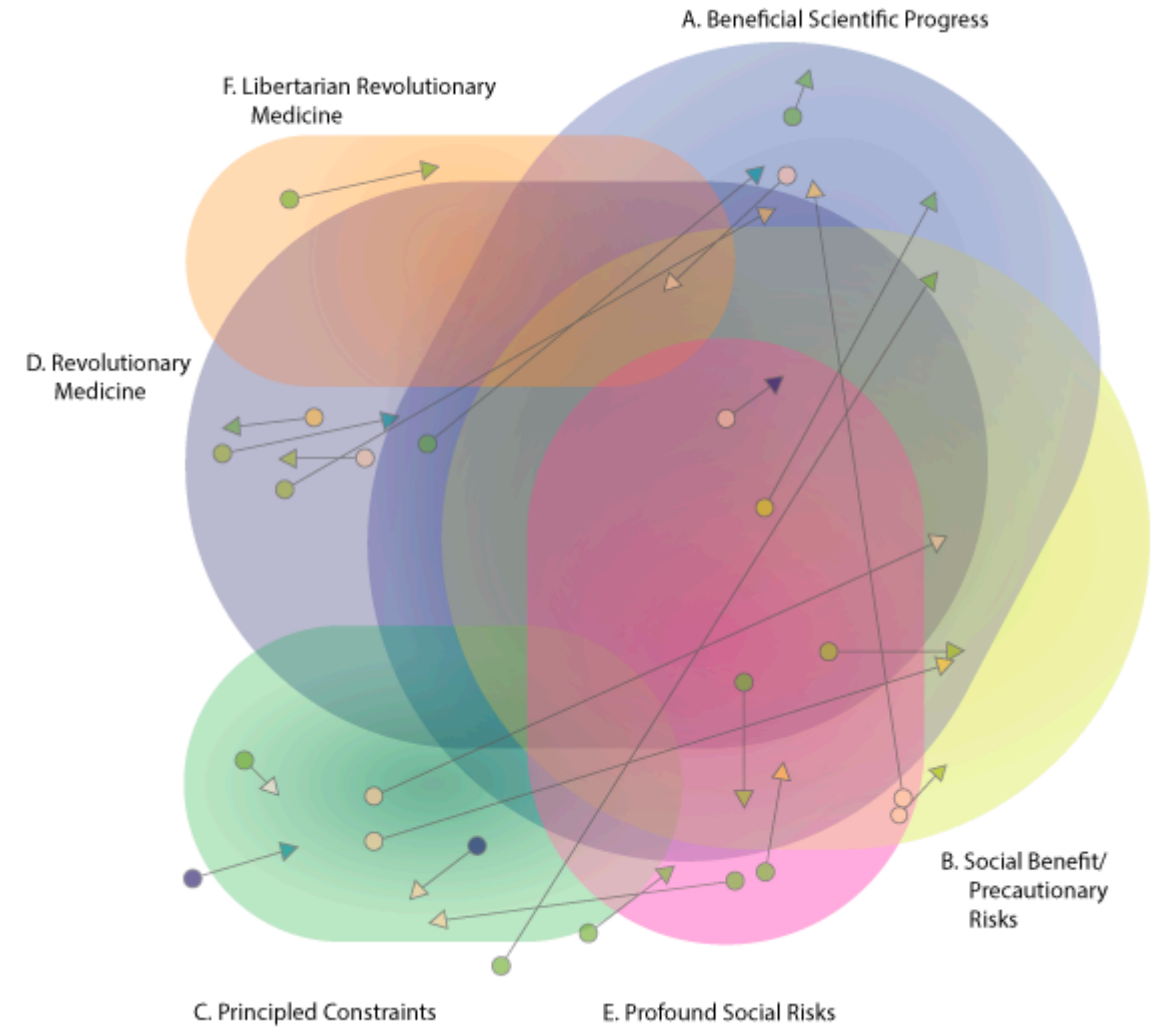
The fact that six distinct positions could be identified from a group of 23 participants illustrates the divergent attitudes towards heritable genome editing and genome editing research involving human embryos that are likely to exist within the Australian population. Despite this, the group was able to come together and reach broad majority views on both non-heritable and heritable human genome editing.

6.2 Positional Transformation

6.2.1 Deliberative Transformation

The positions of participants before and immediately after the deliberation are mapped in Figure 6. Participants' location on the map broadly represents their disposition at that stage of the process. Six types of position were identified following deliberation. The preferred policy option of participants before and after deliberation is also represented in the figure, using colour coding (as indicated by the Legend below the figure).

Figure 6: Deliberative Participant Transformations—Six Discourse Map



Legend (Transformations)

Deliberative Stage Pre	Post	Most Preferred Policy Option
		Permit all applications
		Permit all (Public use only)
		Permit all (Community oversight)
		Permit Non-Heritable and Mitochondrial (Clinical)
		Permit Non-Heritable (Clinical)
		Permit Non-Heritable (Clinical, Public use only)
		Prohibit all (Except for research)
		Prohibit all applications

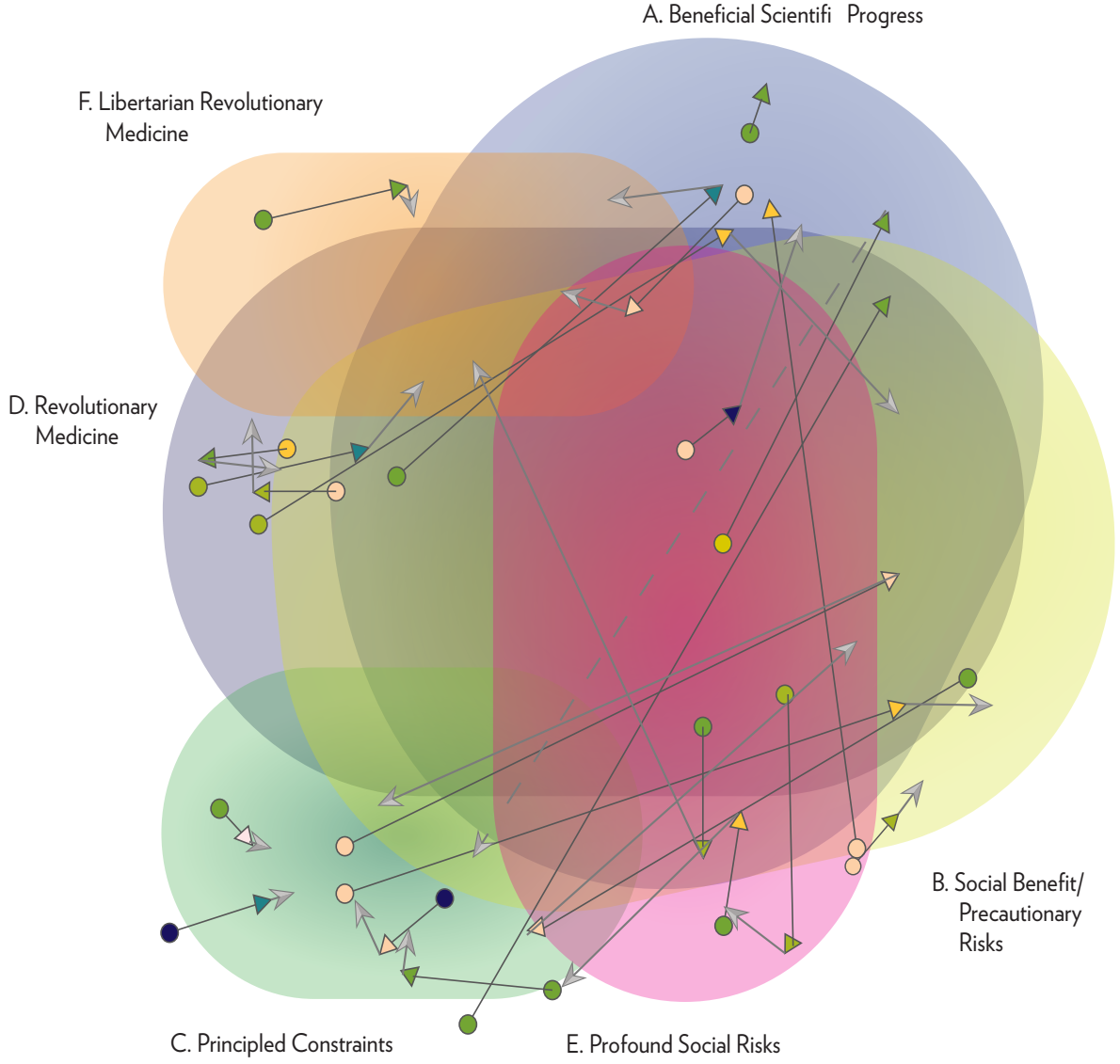
Although the movements across the discourse map in Figure 6 are far from uniform, a number of patterns can be identified. First is the movement toward the top right of the map, particularly Discourse A (Beneficial Scientific Progress), with others moving more toward Discourse B (Social Benefit/Precautionary Risks). These movements are consistent with the overall findings, that there was generally a strong interest in the possibilities involved with the technology, tempered by concern about potential negative impacts, and equity implications in particular.

As discussed earlier, Discourses C and E represent positions that are much more cautionary in nature. Although there is no particularly strong movement toward these positions following deliberation, they remained important, with a significant number of participants remaining in that part of the map.

6.2.2! Transformations Following the Citizens' Jury

Importantly, the resilience of discourses C and (to a lesser. Extent E) can be observed in relation to their persistence in the follow up survey. Figure 7 shows the positional transformations experienced between post-deliberation and the follow-up (stage 6 and stage 10, see Figure 2) by twenty participants who responded to the post-deliberation follow-up survey.

Figure 7. Deliberative Participant Follow up (stage 10) Transformations—Six Discourse Map



Most participants exhibited relative stability in their positions after deliberation, although there are notable exceptions. One of the participants who migrate from C toward B returned to a position very close to their pre-deliberation location in C. That the remainder of the C cohort tended to be particularly stable in their views makes this retreat particularly interesting. It reinforces the observation that the position represented by this discourse is potentially the most trenchant, as well as representing the more important threads that we not thoroughly addressed by the deliberative process.

6.3 Discursive Transformation

The transformation in positions across the six-discourse map only tells part of the transformational story. More detailed analysis is needed, but there is enough evidence to support the conjecture that not only did the deliberative participants change their views, but they also transformed in terms of their collective understanding of the issues associated with human genome editing.

The process of identifying the relevant discourses pre- and post-deliberation indicated that the strongest candidate for the pre-deliberative discourse map is (unsurprisingly) similar to the four-discourse map identified as part of the Mapping study. The differences and overlaps between these discourses are discussed in some detail in Appendix C (section C.5.1). In short, that there are six viable discourses following deliberation, compared to four pre-deliberation indicates greater differentiation and, potentially, sophistication of views among participants. This finding is further supported by analysis of deliberative reason.

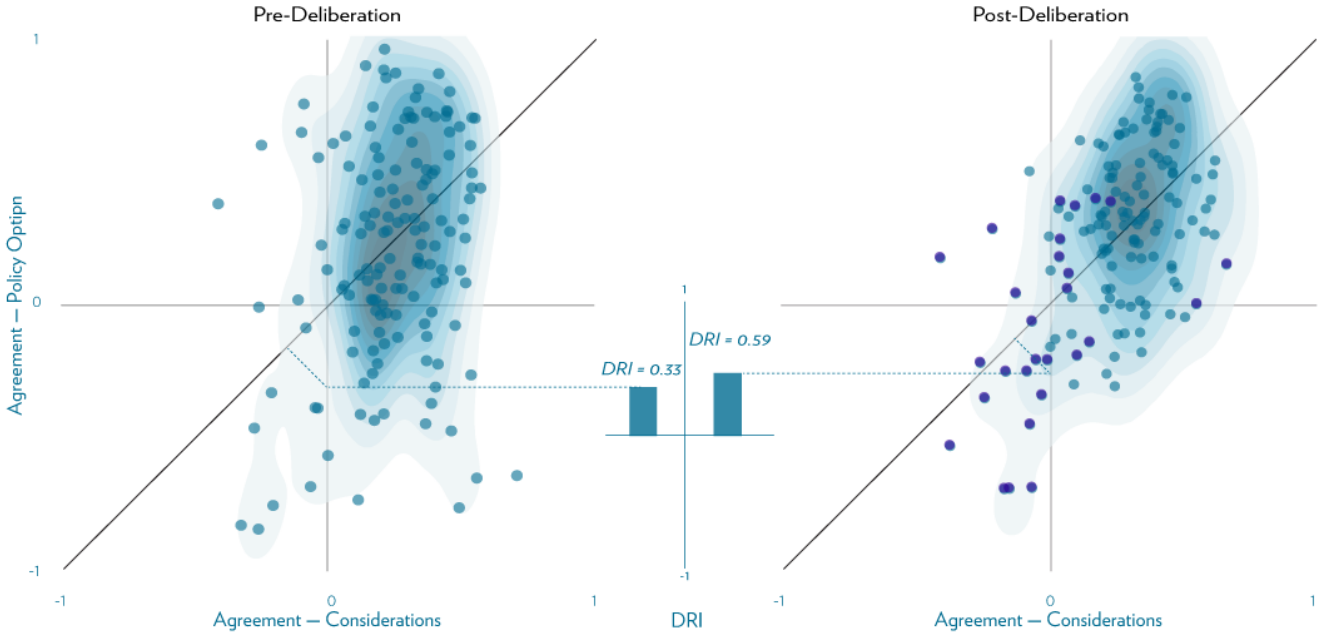
6.4 Analysis of Deliberative Reason

Analysis of deliberative reasoning has been performed using the Deliberative Reasoning Index (DRI) (Niemeyer and Veri, 2022). DRI is a measure of the extent to which the participants are "reasoning together" as a group and are on the same page in terms of how they understand the issues. Importantly, the method does not measure agreement. It does not assess the capability to reason for any given individual. Nor does it involve forming judgements about the "right" outcome. What the method does capture is the extent to which members of a deliberating group consider the same kinds of issues to be relevant to the discussion and whether they share a similar pattern of reasoning. These qualities act as proxies for deliberative ideals, where participants take seriously the concerns that are raised within the group and integrate these concerns into their reasoning (Niemeyer et al., 2021).

To the extent that these internalising processes have been achieved, a consistency of reasoning forms reasoning, where a given pair of participants' positions regarding considerations such as equity, ethics, cost etc is consistent with their policy preferences.

A more detailed account for the deliberative reason analysis is provided in Appendix E (sections E.2) In short, Figure 8 plots consistency across all pairs of participants in the Australian Citizens' Jury before and after deliberation. It shows improving DRI from 0.33 to 0.59.

Figure 8: DRI Plots and Graph



The level of improvement in DRI experienced during the Australian Citizens' Jury is comparatively small compared with other cases (Niemeyer et. al. forthcoming). This is likely partly a result of the high complexity involved in the issue, which requires more time in which to learn, discuss and process. The finding is consistent with the feedback from participants that there was not enough "deliberative time" to work through everything that they felt they needed to discuss.

A related point follows observation in Figure 8, which distinguishes the group of participants who were most strongly associated with Position C after deliberation, reflecting much more restrictive view on human genome editing. This lower level of policy consensus of this group compared to the remainder in terms of both their discursive positions (x-axis) and policy positions (y-axis) can also be observed.

The results suggests that in addition to higher levels of disagreement with the rest of the group, those with position C also understand the issues somewhat differently. One explanation for this follows the argument that the Australian Citizens' Jury did not provide the opportunity – in terms of both time and content – to work through of issues that are important to this group. This is consistent with other observations made in this report.

More research is needed to properly understand the implications. Although it is not clear whether simply allocated more time for deliberation during the Citizens' Jury would have remediated the situation, engagement with the specific concerns expressed by Discourse C is important, if challenging. In short, a failure to adequately listen to, and engage with the concerns of associated with Discourse C risks contributing to polarisation.

7
COMPARING THE VIEWS AND POSITIONS OF GENOME EDITING EXPERTS, AUSTRALIAN CITIZENS' JURY PARTICIPANTS AND CONTROLS WITH THE BROADER POPULATION

Following the deliberation, a set of surveys were conducted with Australian Citizens' Jury and control group participants, experts in genome editing and related fields, and members the Australian public. The purpose of the surveys was to gauge the extent to which the citizens' jury and its recommendations reflect sentiments within the broader Australian population and align with the views of subject matter experts on the topic of human genome editing. Additionally, the follow-up surveys of citizens' jury and control group participants aimed to capture any medium-term changes in participants' positions, and to assess whether participation in the deliberation resulted in stable views.

Members of the citizens' jury and control group were surveyed in May-June 2022. Twenty of twenty-three members of the citizens' jury and 14 of 21 control group participants completed the follow-up survey (stage 10). In parallel, the views of experts in the fields of genomics, healthcare delivery, bioethics, politics, citizen deliberation, and related disciplines were surveyed. (Stage 9) In total, 27 experts completed the survey. The population survey was conducted in March-April 2022 and received 1008 responses from Australians who are representative of the wider population in terms of gender, age, education level, religion, and state of residence, resulting in 845 viable responses used for the analysis here. The sample included participants from regional and metropolitan areas.

All the survey cohorts were asked to rate their level of agreement or disagreement with a subset of the statements used to estimate their positions relative to those identified in the mapping study. Additionally, all survey respondents were asked to rate their level of (dis)agreement with editing the genes of embryos/children or adults to prevent/cure life threatening/debilitating diseases; editing the genes of embryos to alter physical/cognitive abilities; editing the genes of embryos for research purposes; and editing the genes of plants or animals used in food production. Respondents were asked to indicate whether there are other uses of genome editing which they would or would not agree with, and to describe these uses. Finally, all survey respondents were asked to rate and comment on the recommendations from the citizens' jury, and to indicate the extent to which they trust citizens' juries to formulate good policies on genome editing. Expert, citizens' jury, and control group respondents were also asked to rank their preferences for a set of hypothetical policy options.

7.1 Overview of Results

Preliminary analyses of the data collected from these surveys suggest that all cohorts share similar attitudes towards the surveyed uses of genome editing. Editing the genes of embryos, children and adults to prevent or cure debilitating or life-threatening diseases were supported by a majority of

respondents in all cohorts. Notably, the expert respondents were the least supportive of editing the DNA of embryos to prevent both debilitating and life-threatening diseases. Conversely, experts were the only cohort with majority approval for editing the DNA of embryos in genome editing research. Editing the DNA of embryos to alter cognitive or physical abilities received the lowest level of support for uses of genome editing across all the cohorts.

Respondents' overall willingness to accept the recommendations from the citizens' jury was also relatively high across the survey cohorts. Members of the citizens' jury were most willing to accept the recommendations, while national survey respondents were the least willing to accept the recommendations. Nevertheless, nearly half of the national survey respondents were more willing than unwilling to accept the recommendations, and a quarter were neutrally disposed to the recommendations. Support for the individual majority recommendations was also high across the survey cohorts.

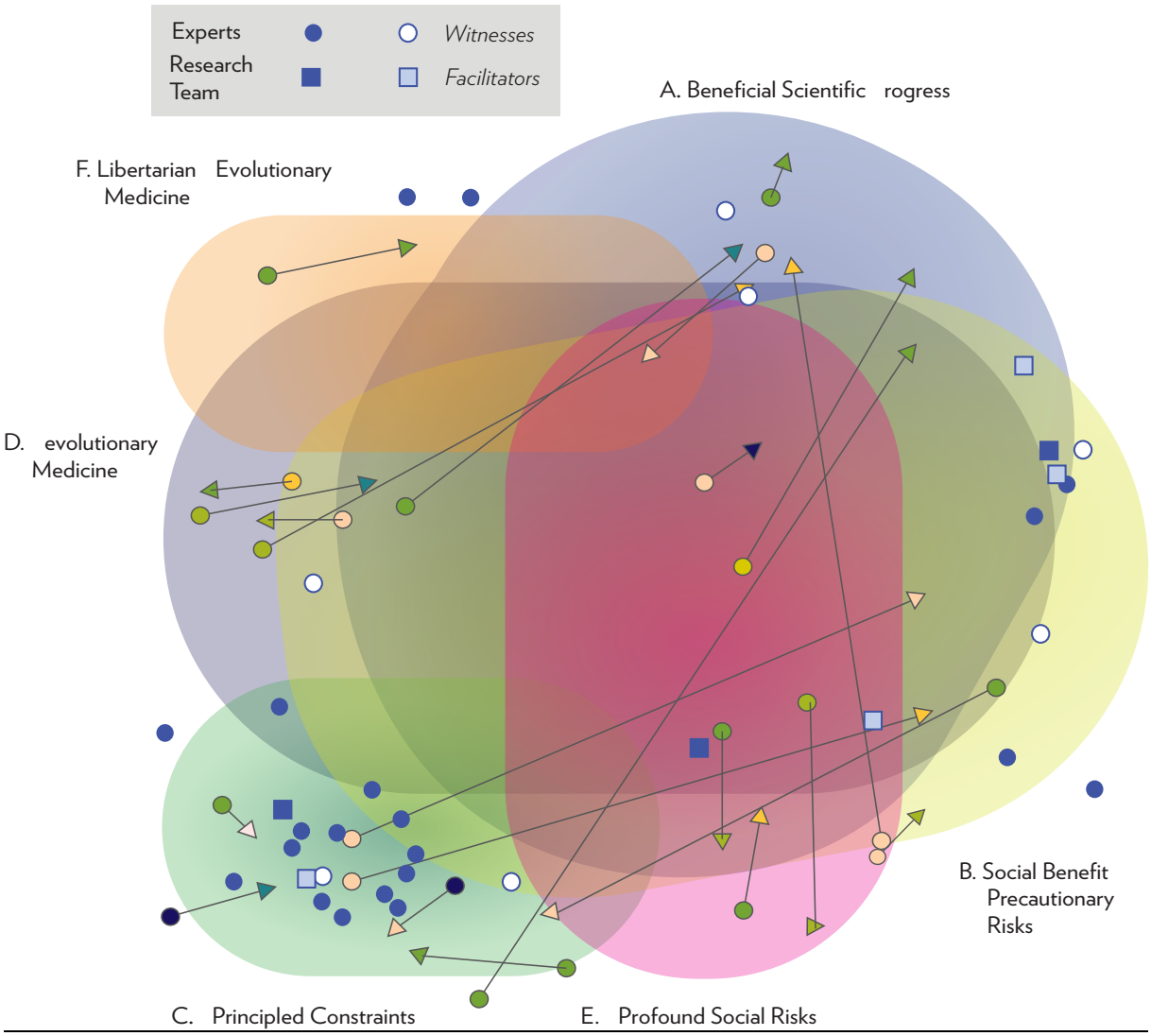
7.2 Comparison of Experts/Witnesses to Participants

Appendix F (section F.1) uses the Mapping Study four discourse map to compare the discursive positions of experts (and witnesses who presented at the Citizens' Jury) compared to the participants. In short, although there is greater diversity among participants, there is also a much higher level of diversity among experts, and witnesses than might be expected—given the concerns about potential framing and stacking of witnesses expressed in this report (in the Executive Summary, and below in section 10).

Figure 9 shows the Post Deliberative (six) discourse map, with expert, witness and research team positions superimposed over the positional transformations of deliberative participants (from Figure 6). Overall, the distribution of witnesses compared to the pattern of participant migrations to address any lingering concerns about any undue (non-deliberative) influence or blandishment via witness testimony.

Notably, the concentration of both expertise and witnesses in Discourse C combined with the earlier observation of migration by some participants out of C toward A or B is inconsistent with concerns about undue influence. The overall finding is supported by detailed analysis of participant positions compared to those of experts on individual survey items, provided in draft form in Appendix F (section F.2.1).

Figure 9: Positions on Six Discourse Map—Experts, Research Team and Participants

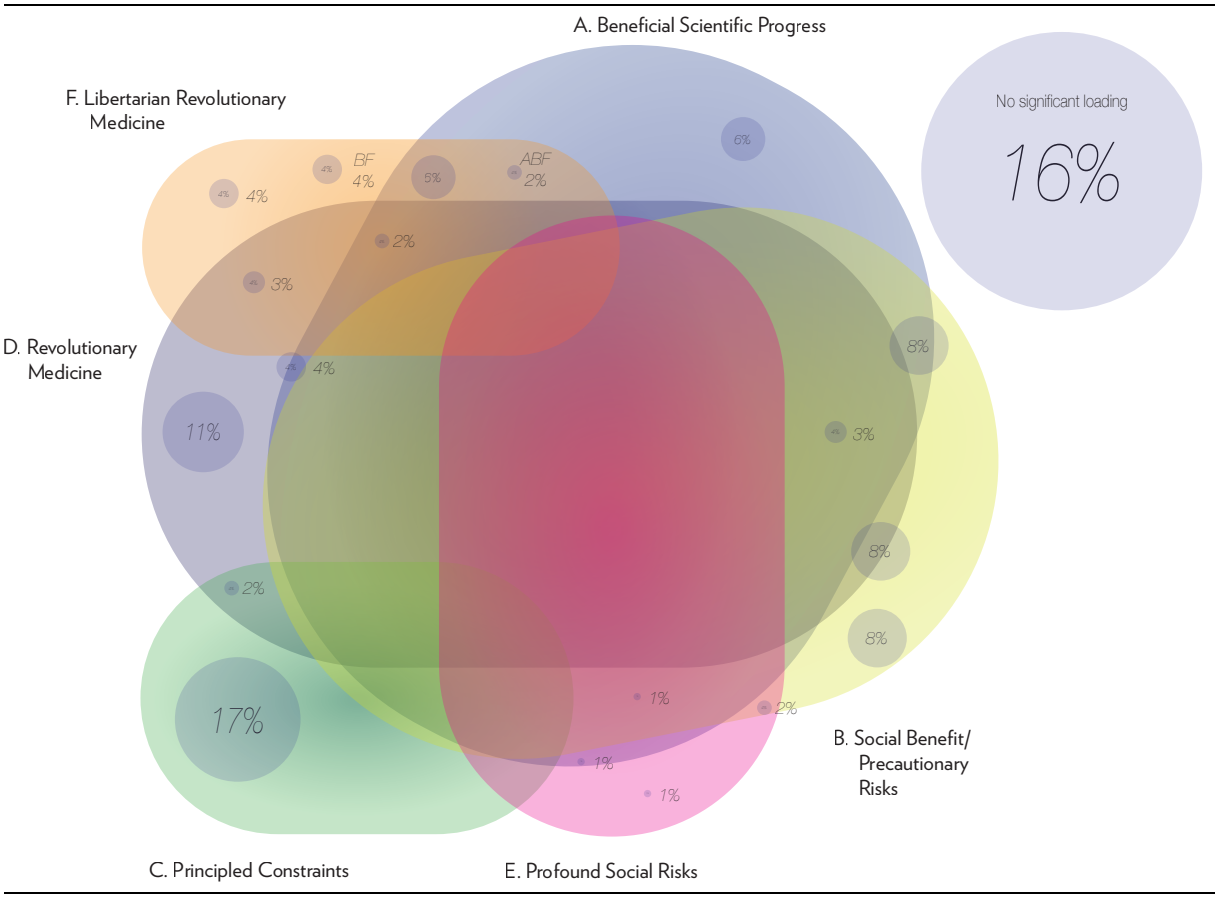


7.3! Positions of Participants, Experts and the Australian Community

Analysis is ongoing to compare the positions of the citizens' jury participants with control group, expert, and population positions, and to estimate the prevalence of these positions within the Australian community. Nevertheless, a number of preliminary findings can be reported, including the relative distribution of perspectives among the Australians using the discourse maps.

A provisional analysis of the distribution of the Australian Community using the six Post-Deliberative Discourses is summarised in Figure 10.

Figure 10: Distribution of Australian Public Positions—Six Discourse Map



Although the results are yet to be verified, it can be seen in Figure 10 that a substantial proportion of the community appears to identify with Discourse C. If confirmed, the finding is potentially important in terms of understanding how community views concerning human genome editing might evolve over the medium term. It is conceivable that, despite an apparent abundance of community interest in the technology, there may be a significant reservoir for whom the relevant concerns regarding principles, including some of the deeper, more fundamental issues, are strongly felt.

Concerns regarding the inability of the Australian Citizens' Jury to adequately engage with these concerns thus appears to have macro as well as micro-level implications. Discourse C reflects a particularly trenchant, and stable view, at least within the parameters of deliberation afforded by this research. While part of this deficit may be due to limitations with design, the complexities raised by these issues—and difficulty in providing adequate information, time, and deliberative resources to working through them as part of a dedicated, multi-day deliberative process—suggest that more work needs to be done to listen, understand, work through them with members of the community. Any such extended work would also benefit from further engagement with important perspectives among the Aboriginal and Torres Straight community (see section 2.6), in addition to other targeted and marginalised groups.

7.4 Conclusion

The transformations observed as part of the Australian Citizens' Jury on Genome Editing, combined with analysis of relative distribution of positions of participants, surveyed experts and the wider Australian community support the view that research achieved a result that approached a strongly deliberative result, if not quite achieving the highest ideals.

Concerns regarding any non-deliberative influence due to poor design tend not to be supported by the analyses in the previous two sections. Nonetheless, there were gaps in the process. it is less clear exactly where those gaps are — it in the form of witness testimony, information, absence of community advocate, or lack of time — or whether they could be adequately remedied, given resource and time constraints.

Although some of the findings reported here are provisional, a number of clear themes do emerge. The Australian Citizens' Jury has provided an important window into the issues that are relevant to the community, the broad contours of how their views develop during deliberation. The transformations and positions observed cannot (and should) be interpreted as constituting a definitive, and final decision on the matter (see Lafont 2019), but they can and should provide important inputs into decision making.

Perhaps most importantly, the findings here suggest that, although there is clearly widespread interest in the technology among the community, a deeper, more systematic assessment using a discursive approach, combined with deliberation, highlights a need to stimulate a wider engagement with the community, and to engage particularly with minority or marginalised views using an approach capable at once of deep listening, engagement across perspectives, and informative.

8
DEVELOPING POLICY THEMES WITH ASSISTANCE FROM EXPERTS

The aim of this phase of the project was to begin to develop policy themes on human genome editing based on citizens' jury recommendations and other outputs from the project. Some of the leading experts in the fields of genome editing, deliberative democracy, bioethics, social sciences, and other disciplines have provided valuable assistance to us in developing this policy advice.

Following completion of the citizens' jury, experts were first invited to complete a slightly modified version of the survey presented to the citizens' jury participant group and the control group, as discussed above in Section 7 of this report. Invitations to participate in the survey were sent to 85 experts, comprising four cohorts: experts who were interviewed in the first phase of the project; expert witnesses at the citizens' jury; experts involved in other citizens' deliberation projects (particularly the Global Citizens' Assembly on Genome Editing: https://www.globalca.org/); and other experts who provided advice during the course of the project.

The survey included the opportunity to provide open-ended responses to our requests for feedback on the citizens' jury recommendations. These responses have provided us with some initial guidance in shaping policy advice. In particular, the responses highlighted that there is scope for misinterpretation of the recommendations in the absence of further contextual guidance. More specifically, the recommendation that non-medical forms of genome editing should be banned was not supported by a number of experts. Some experts also expressed surprise about recommendations calling for strict regulation of research using human embryos and preventing mass production of human embryos. For example, one expert noted that 'I am more concerned about the potential exploitation of women as providers of eggs/embryos, than the status of the embryos themselves'. This feedback was of assistance by providing guidance on the types of contextual information that should be provided alongside the citizens' jury recommendations.

The same experts were invited to participate in online interactive workshops via Zoom. They were advised that they would be asked for their opinions on how we might provide meaningful advice to policy makers and other stakeholders on human genome editing, based on the outcomes of the project, and whether there were any other lessons that could be drawn from the project.

Nicole Hunter and Keith Greaves from MosaicLab, a team of professional facilitators and community engagement practitioners, were engaged to assist with the running of the workshop. They used a variety of tools and methods (see https://www.mosaiclab.com.au/workshop-design-facilitation). Each workshop was of two and a half hours duration. To accommodate the time differences in the participants' locations, the workshops were held at different times on two separate days:

- Tuesday 30 August 2022 at 9am to 11.30 am (AEST) (16 participants).
- Wednesday 31 August 2022 at 6pm to 8.30 pm (AEST) (20 participants).

In addition to the two scheduled expert workshops, a pilot workshop was held on Wednesday 24 August at 2pm to 4.30pm (AEST) to provide the opportunity to test the format and timing for the workshops. Four team members and four of the experts who participated as witnesses at the Australian Citizens' Jury participated in this pilot.

In developing the themes for the policy discussions at the workshops, the research team first identified ten areas for potential policy consideration based on: a review of the Australian Citizens' Jury recommendations; observations of deliberations at the Australian Citizens' Jury; a review of post-jury interviews and online forum discussions; and our knowledge of the existing academic and policy literature and debates on genome editing.

Prior to the pilot workshop, the areas for discussion were reduced to six key themes, focusing on: embedding values and principles in the governance of human genome editing, with particular focus on how equity of access might be achieved; addressing concerns about the impact of commercial involvement on public good; regulatory distinctions between therapeutic and non-therapeutic uses; reconciling different views on the status of the human embryo; preparing for possible future heritable applications of human genome editing; and building meaningful public participation into future human genome editing governance.

These policy themes were further developed following feedback from the pilot workshop and a set of brief notes was developed to help guide the discussions at the expert workshops. Several weeks prior to the workshops, the experts who were invited by us to participate were provided with links to the preliminary report of the Australian Citizens' Jury together with the film of the event produced by Genepool Productions. In the week immediately before the workshops, they received copies of the Australian Citizens' Jury Recommendations, together with the notes on the six policy themes emerging for recommendations and an early draft of this report.

The workshops commenced with a brief overview on project progress. Workshop participants were then asked to reacquaint themselves with the citizens' jury recommendations. Participants were again reminded that recommendations of the citizens' jury were not reached by consensus. They were then placed in breakout groups of 3-4 participants to discuss and report on their views on the recommendations.

In summary, while some experts pointed to the nuanced, well considered, and sensible nature of the recommendations, others expressed concern that they were largely in line with the recommendations form expert reports, suggesting that 'framing' is a concern that needs to be considered. These issues associated with framing are discussed further in section 10 of this report. As with the survey responses, experts pointed to ambiguity or confusion in some of the language used in the recommendations. They emphasised that it was critically important to hear and understand more about disagreements and minority views. Experts also noted the challenges involved in translating some of these general principles into more concrete policy recommendations.

It should be noted that both expert survey participants and expert workshop participants were only provided with the citizens' jury recommendations, without any associated commentary. In response to feedback from experts about potential misunderstandings in the wording of the recommendations, both in their survey responses and in the expert workshops, commentary has been now provided for each of the recommendations (see section 5 of this report). This commentary provides information on the context within which the recommendations were developed, to explain their intended purpose and to resolve any ambiguities. This commentary also provides some detail to explain the differing views of participants, particularly where there were strong views opposing the majority recommendations.

Expert workshop participants were subsequently asked to consider the key policy development themes identified by the research team. Participants were placed in breakout groups of three to four participants and were allocated two of the six themes for discussion. Following these discussions, they were placed in different breakout groups and asked to summarise their discussions relating to their two allocated themes with the other participants in the new groups (who had all considered other themes). Participants were also asked to identify and discuss what they saw as the most important policy deliverable from the citizens' jury recommendations. All breakout group sessions were of 15 minutes duration. The outcomes of these discussions are summarised below.

8.1 Equity of access

Many experts reminded us that the question of equitable access is not a new one, or one that is unique to genome editing. Some questioned whether there was any good rationale for expecting access to genome editing therapies to be equitable, but not to have the same expectations for other treatments. It could be argued, however, that it is the promise of genome editing in offering treatment options for such a broad range of genetic disorders that makes it unique. As some experts reminded us, the potential breadth of available treatments using genome editing inevitably raises questions about the extent to which it could exacerbate existing disparities in access to new health technologies.

One expert suggested that an early priority should be single locus mutations relating to serious diseases. This certainly seems to fit with citizens' jury recommendations that the primary aim of genome editing should be to alleviate human suffering, improve quality of life, and reduce childhood mortality and that, when prioritising treatment options, both the severity of the disorder or disability (such as life-threatening conditions), and the number of people affected should be considered.

The challenging is in operationalising these priorities. One expert noted that often all that is provided in regulatory instruments or guidelines or policy documents relating to health care more generally is a list of diseases, but these tend to be subjective, with no objective criteria for inclusion of exclusion. This expert recommended that it is necessary to 'develop and vet some conceptual guidance towards what things like "severe" and "therapeutic" actually mean (or are based on) so that they can be used in policy development and application'.

Experts also reminded us that equity involves much more than affordable pricing of individual treatments. One group pointed out that genome editing treatments themselves should not be considered in isolation from other technological and social solutions. Others questioned whether public funding should go to genome editing if another cheaper but somewhat inferior treatment option is available. Yet another group queried whether the recommendations of the citizens' jury on equitable access were about access to genome editing or access to the outcome of the intervention.

Some experts noted that, when weighing up the costs and benefits of particular treatment options in public funding decision-making, benefits tend to be viewed too narrowly, focusing on the specific treatment and its outcomes. Rather, as pointed out by a number of experts, benefits and costs should be viewed across the whole of a person's lifecycle. For example, the large up-front costs involved in one-off genome editing applications may result in lower costs later in life.

It was also recognised in the expert workshops that while access is one aspect of equity, the issues are much broader. One group drew particular attention to the importance of equity in decision making. As they put it, equity is required not just in the allocation of the intervention, but also about 'the allocation of the voices that make decisions'. This illustrates the critical importance of understanding what is important to members of the public. One expert expanded on this point in a follow up email, noting the tension that can arise when 'we base policy that affects people on technical/philosophical points they really don't care about'.

8.2 Commercial involvement

Experts tended to be somewhat unfamiliar with public concerns around commercialisation, aside from recognising that commercial involvement in healthcare raises concerns for many members of the public. However, many recognised and drew attention to the challenge of developing new health technologies without involvement from the commercial sector. As one group noted, this is 'an issue but not a new one - every new expensive therapy goes along this journey'. Another group reminded us that 'there are unanswered questions about commercialisation and how this interacts with public good(s) - care [should be taken] with assuming commercialisation is just "a given"'. It was further recognised that while commercialisation can speed up the availability of new gene therapy treatments, it may do nothing to facilitate equitable access.

One expert recommended greater support for public sector-led innovation. They suggested that there needs to be a 'regulatory review to ensure hospital led innovation is possible for non-commercial gene editing [... where there are low patient numbers (e.g. rare diseases)]. But they emphasised that there needs to be a 'clear and robust review structure to avoid situation like stem cell tourism'. Others also emphasised the need to ensure that commercial imperatives do not overtly drive policy positions. Some experts focused on the need for public funding to support the translation of genome editing into the clinic, which one described as a 'moonshot for commercialisation'.

One important aspect of genome editing was emphasised by one expert – that it is a broadly applicable technology that serves as a platform that can be used for a diverse array of purposes.

> Think of gene editing as a platform technology that is applied in agriculture, conservation, military, environment etc. which may drive innovation that human gene editing can benefit from down the road. There may not be a market for genome editing if we just look at healthcare right now, but we will then miss opportunities that may come about in the future because of breakthroughs in other areas.

Presumably, this expert is suggesting that undue burdens should not be placed on commercialisation of genome editing, because to do so might discourage innovative uses of genome editing tools in fields other than healthcare (agriculture and others). If innovation is deterred or delayed in those fields, this might ultimately be detrimental to the future development of genome editing in those fields and in healthcare. The challenge here is similar to the challenges that have been faced in other areas of rapidly developing technology: how to ensure that commercialisation and patenting are used in ways that encourage rather than stifle innovation.

8.3 Regulatory distinctions between therapeutic and non-therapeutic uses

For many experts, therapeutic uses of genome editing are no different from therapeutic uses of other technologies in the regulatory context and therefore do not need new regulatory interventions. One expert suggested that it should be referred to as genetic surgery rather than genome editing. In direct contrast, another expert recommended the institution of 'a new and specific regulatory process to approve new therapies for gene/genome editing.' Clearly there are mixed views on the extent to which genome editing presents novel regulatory challenges.

Many experts did note that relative ease of use of genome editing techniques could open the door to other uses that may lack the same level of regulatory oversight that we see for therapeutic interventions. For this reason, adequacy in the regulation of all potential uses of genome editing does need to be considered.

All experts appeared to reject any suggestion that there is a bright line between therapeutic and non-therapeutic interventions. Be that the case, one expert emphasised that 'it is important to draw the line even if not a bright line. This is where the public is most concerned, so we need to address that'. This expert recommended that there should be a conversation with the public about this, because 'it is very contested. Certainly, in Australia, given the egalitarian focus, this will be a big debate'.

Others downplayed the importance of the distinction, with one group noting that:

> There is a suggestion that whilst the distinction between therapeutic and non-therapeutic forms of genome editing excite many scholars, in practice governments and medical insurance companies etc make these kinds of distinctions routinely - for instance, in deciding whether aesthetic surgery is for medical purposes or for aesthetic purposes, and therefore whether it will be paid for by the healthcare sector or by the patient.

Some experts raised further questions relating to the rationale included in the citizens' jury recommendations for prohibiting non-therapeutic uses, such as: 'What are we trying to avoid? A market for private enhancement for those who can pay'.

One breakout group emphasised in their comments that therapeutic/non-therapeutic distinction has much broader implications,

> The distinction is doing work related to responsibility and not merely the distinction between disease and non-disease. When the distinction is made, look for the work that it is doing for conceptions of public responsibility, individual entitlements, and systems of distribution and power (science, market, health care).

This is an important point that has resonance in other areas that sit on the boundaries of traditional healthcare delivery. For example, in Australia the cosmetic surgery sector has largely been allowed to develop without the regulatory safeguards present in other areas of healthcare, perhaps because it is seen as a matter of personal choice. There is a recently completed independent review of the regulation of medical practitioners who perform cosmetic surgery (https://www.ahpra.gov.au/resources/cosmetic-surgery-hub/cosmetic-surgery-review.aspx). The summary of the review lists a number of key findings, including 'that when it comes to cosmetic surgery, universal minimum standards for education, training and qualifications are non-existent in Australia' and 'that the cosmetic surgery sector has become somewhat of a market disrupter as it sits outside existing traditional health system frameworks that tend to ensure that patients access appropriately qualified medical practitioners'. It would clearly be unfortunate for Australian society if this type of anomalous situation were allowed to develop for so called 'non-therapeutic' applications of genome editing.

8.4 Reconciling different views on the status of the human embryo

As noted above, in survey responses some experts expressed surprise about the call for strict regulation in relation to research involving human embryos, and the views of some citizens' jury participants that any research involving human embryos is inappropriate. Those same sentiments were shared by some of the workshop experts. Indeed, two experts independently recommended the need for a clear legal pathway and legal standards for human embryo research. Yet there was recognition of the need to acknowledge differences in views and explain how decisions are made.

Importantly, one breakout group reminded us that

> the question of the status of the human embryo is not just a problem' that needs to be solved for genome editing purposes, but a question that needs to be discussed more broadly, including to understand people's narratives.

Some of the expert comments relating to public participation (discussed below) are highly relevant here, particularly those relating to 'majoritarian hazards'.

8.5 Preparing for possible future heritable applications of human genome editing

Experts emphasised the challenge of driving legislative change in advance of technological development and societal debate. As one breakout group said,

> Policy makers, in UK at least, can only focus on these questions when a decision is imminent. And it isn't yet, so developing a wide societal debate is difficult. But decisions are coming down the line and there's a risk that the debate happens very quickly when battlelines may already have been drawn. How do we get policy attention and focus on developing the debate when it's not in their interest to do it until they need to?

Others added that 'law is not what dictates change but attitudes in society' and that it is 'not clear how much law can "lead" change - social situation/perception[s] lead change more.' These comments tend to affirm that, from the perspective of many of our experts, societal debate must occur before policy debates about law reform.

For many experts, if heritable genome editing is to be allowed to proceed, this will need to be done slowly and progressively. As one expert put it, 'a stepwise translational pathway to reproductive gene editing [would start] with catastrophic early onset conditions, to lethal childhood conditions, to adult-onset conditions to ultimately enhancement when shown to be safe'. This expert went on to say that this stepwise progress would not 'necessarily [be] heading to enhancement - direction and limits will evolve over time.'

Other experts also suggested that what is needed as a starting point is 'a preliminary list of [the types of] conditions suitable for the very first reproductive applications heritable genome editing'.

8.6 Building meaningful public participation into future human genome editing governance

Many of our expert cohort had either already engaged in public participation projects on genome editing, or were planning for them. As such, they were firmly committed to the concept of public participation. However, there was broad recognition that meaningful participation is difficult - 'how can we get that right (and what is "right" here?)?'

One expert emphasised that public participation should be undertaken in a way to avoid the 'majoritarian hazard of deliberation by identifying persistent disagreements that require sustained public dialogue'. They cautioned that it is critical 'to avoid framing the issue, deliberation and policy as a problem to be solved, instead of an ongoing social issue'. For them, 'the authoritarian overriding of persistent social disagreements [risks] further marginalizing people, and concealing social unrest'. Others also warned against hiding conflict, because 'sometimes the goal of participation is to shed light on controversial topics'.

A number of experts pointed to the risk of overpromising on the influence of public engagement in policy development, and the importance of recognising that it is 'one of many factors in decision-making'. Questions around whose voices are heard, who funds public engagement, and how engagement feeds into policy development were all recognised as relevant considerations.

Other experts spoke of their concerns when a series of carefully considered recommendations are reached but government dismisses them out of hand or never enacts them'. For them, it is important to ensure that 'government cannot nefariously interfere with policy processes, when careful consensus is reached'.

Many experts recognising that to be meaningful, public participation needs to be ongoing. What is needed, in the words one expert, is the creation of a 'clearly defined process for ongoing public review of policy and implementation, with clear expectations of what it is intended to achieve and what its limits are'. This may need to be lighter touch than a citizens' jury, but needs to be a continuing process that reflects the diversity of views presented in the jury is necessary to ensure ongoing public legitimacy and relevance.

Another expert also emphasised that 'one citizens' jury can't answer all the questions:' and that it would be appropriate to 'develop a programme of systematic engagement on the topic focusing on supporting civil society to engage in the issues to build capacity'.

8.7 Summing up

In summary, the expert workshops provided us with valuable insights from experts across a wide range of disciplines. Feedback broadly validated the range of policy matters that we had previously identified as being worthy of further consideration. It also helped us to identify the particular points that needed to be considered under each heading. The workshops also illustrated that there is no single 'expert view' on human genome editing. Rather, the view of experts appear to be as diverse as those of other members of the community. Further, viewpoints on genome editing are not clearly aligned with disciplinary background.

9 THEMES FOR CONSIDERATION IN THE DEVELOPMENT OF GENOME EDITING POLICY

The first step in this part of the project involved bringing together and synthesising the findings from the Australian Citizens' Jury on Genome Editing together with the various other forms of citizen and expert engagement undertaken during the course of this project. This synthesis, together with key findings from the existing literature, was then used to draw out themes for potential consideration in policy development relating to genome editing. A total of five themes were identified, based largely on the six themes already identified by the research team prior to the expert workshops. The expert workshops helped us to refine and expand on each of these themes. Specifically,

- The *Equity of access and Commercial involvement* themes have been combined and expanded into a single theme: *Embedding values and principles in genome editing – a case for ensuring equity*. This is in recognition of the fact that many of the issues relating to equity of access and commercial involvement intertwine, and that issues of equity go beyond access.
- The *Regulatory distinctions between therapeutic and non-therapeutic uses* theme has been expanded and clarified to emphasise the difficulty in drawing bright lines between the different uses of genome editing in humans, and the need for appropriate regulation across all applications. The title for this theme is now: *Ensuring that therapy, enhancement, and other applications of genome editing to humans are appropriately regulated.*
- The theme *Reconciling different views on the status of the human embryo* has been reframed into the theme: *Deciding what types of genome editing research should be allowed and supported, recognising differing views on the status of the human embryo*.
- The title of the theme *Preparing for possible future heritable applications of human genome editing* has been recast to: *Preparing for a future when heritable human genome editing may be shown to be safe and effective* to clarify the focus of this theme.
- Finally, the theme *Building meaningful public participation into future human genome editing governance* remains unchanged.

A short outline of each of the themes is presented below. Each theme then ends with a set of dot points summarising the key points for policy consideration.

9.1 Embedding values and principles in human genome editing governance – a case for ensuring equity

One of the key findings from the Australian Citizens' Jury on Genome Editing was that the majority of participants appear to support strictly regulated, equitable and fair human genome editing. This is clear from the guiding principles and recommendations 1 and 5. Participants appear to favour these

requirements for both non-heritable and heritable forms of human genome editing, but have greater reservations in in respect of the latter, as well as genome editing research involving human embryos. These reservations and their potential policy consequences are explored further later in this section of the report. Notably, there was a minority view that equitable and affordable access may not be feasible and should not be a requirement in order for genome editing to become a form of mainstream clinical treatment.

The six broadly shared Guiding Principles articulated by the majority of citizens' jury participants reflect many of the ethical norms that are commonly required to be considered in any research involving humans and in clinical practice more broadly. They also largely reflect the values and principles listed by the WHO in its governance framework report on genome editing (WHO 2021a, 13-14). The WHO report emphasises that these values and principles are intended to be used to describe both how governance and oversight measures should be reviewed and strengthened and what needs to be considered when they are. In informing how decisions are made, the report emphasises the importance of openness, transparency, honesty and accountability and the need for responsible stewardship in the context of regulation, science, and research resources. These points are reflected in citizens' jury recommendations on the need for adequate research and regulation, the need to define key terms and the need to revisit the recommendations as the technology advances (Guiding Principles 2, 4, 5 and 6).

A broader collection of values and principles are listed in the WHO governance framework in respect of what decisions are made. Many of these are reflected in some of the other Australian Citizens' Jury Guiding Principles. In particular, limiting human genome editing to the alleviation of human suffering, improving quality of life, and reducing childhood mortality (Guiding Principle 1) reflects such values and principles as caution, fairness and solidarity. Furthermore, the overarching requirements for consent and equitable access (Guiding Principle 3) recognise the importance of inclusiveness, fairness, social justice non-discrimination, equal moral worth and respect for the person.

Australia, like most other countries, has a comprehensive regulatory regime covering research involving humans, clinical trials and market approval of new therapeutic goods. Consent, efficacy, safety and clinical utility are all firmly embedded as core requirements. Although some tinkering might be required, international expert reports on genome editing suggest that these existing regulatory requirements are appropriate, at least in the context of non-heritable genome editing. Australia also has well developed protections against unlawful discrimination, and misuse of private information. Indeed, health technologies sit in a veritable 'soup' of regulatory requirements (Nicol et al, 2016a). Despite this, concerns have been raised in the literature that genome editing will pose particular challenges for existing regulation, leading for calls to examine its adequacy (Nicol et al, 2017). There was a divergence of views in our expert workshops as to whether there is anything so unique about genome editing that it requires special consideration, beyond this existing regulatory soup.

9.1.1 Equity of access

There does seem to be some consensus in the views of experts and many other citizens that the issues associated with equity of access to new healthcare are likely to be heightened in the context of genome editing if it enters into clinical practice. This is, of course, the case whenever innovative healthcare technologies first become available. We have seen this writ large during the course of the

COVID pandemic, with the massive disparity in access to vaccines and treatments between the global north and global south, and between disadvantaged and advantaged communities within countries. Many experts and members of the Australian community understandably share deep concerns that genome editing could be yet another a tool to improve the lot of the wealthy, at least in the short term.

Perhaps the most obvious issue when it comes to equity of access is the cost of treatment, exacerbated by the need for biopharmaceutical companies to recover their huge investment in research and development and the role that intellectual property plays in allowing them to do so, together with the rarity of diseases for which genome editing clinical trials are underway (Muigai, 2022). This situation may change once more genome editing therapies become available, but this is a long way off.

Although there are no approved treatments using genome editing at the current time, we have seen that the first gene therapy treatments have been staggeringly expensive. Zolgensma, a gene therapy for the treatment of spinal muscular ataxia, cost US$2.1 million for a one-off treatment when it first became available, making it the most expensive therapy on the market at the time. The tragedy for individuals with some of the most pernicious diseases is that long-awaited therapeutic advances are likely to be priced well beyond their reach, making them inaccessible without government or philanthropic support or insurance cover (Nicol, 2021). One question, then, is whether Australian governments should fund future genome editing treatments and if so, how might it be encouraged and assisted to do so.

Inevitably, if Australian governments chooses to support genome editing treatments, the trade-off is that funds have to be diverted from other healthcare imperatives. While citizens' jury participants understood this dilemma, many were persuaded that the promise of genome editing in alleviating suffering justifies government support. They also recognised that although a one-off treatment might be extraordinarily expensive, this is still worthwhile when compared with the human, social and economic costs of lifelong treatment for debilitating illnesses. Similar cost-benefit discussions have occurred in citizens' juries on human genome editing in other jurisdictions. In South Africa, for example, participants felt the genome editing for serious health conditions might have short term costs, but entail long-term cost savings from a public health care perspective (Thaldar et al, 2022).

We have seen from our citizens' jury deliberations that bringing these financial cost-benefit calculations into decision-making about access to medicines, though seemingly inevitable, can be deeply distressing. Indeed, some of our participants described this as dehumanising and not driven by a conversation about the betterment of society. Nevertheless, they did recognise that decisions will need to be made on what genome editing treatments to prioritise. The challenge of developing suitable 'quality of life' measures that take into account the whole range of relevant factors has long been discussed by scholars and policy makers for healthcare more broadly (for example, Brock, 1993) and remains fraught (in the context of public health, for example, see Kaplan and Hays, 2022).

9.1.2 Commercialisation and intellectual property

Issues associated with commercialisation and intellectual property were raised by many participants during the course of the citizens' jury. This was the case for both non-heritable and heritable forms of human genome editing. It has already been noted that, in the context of non-heritable forms of genome editing, the majority of participants agreed that access should be equitable and affordable (despite varied views on what this means and how it might best be achieved). Participants expressed particular concern that vested interests and profit motivations in the private sector might distort the

applications of genome editing and limit public good.
Recommendation 9 suggests that the majority of citizens' jury participants accepted the reservations voiced by one participant, in particular, about commercialisation of the use of human embryos. This participant expressed particular concern about the possibility that human embryos could be mass produced for commercial research purposes.

These concerns about commercialisation are not unfamiliar, both in the Australian context and elsewhere. Previous research undertaken by members of the research team provides clear evidence that involvement of for-profit entities in genomic and stem cell research, in particular, has the propensity to undermine public trust and deter participation (Critchley and Nicol, 2017; Nicol et al, 2016b; Critchley and Nicol, 2011). Our research has shown that people do understand that the for-profit sector can have a vital role to play in the translation of research into clinical products, particularly given the prolonged, costly and risky nature of clinical trials, and that there are currently no real alternatives. However, they do have expectations that the for-profit sector should not be given an entirely free rein: they should not be involved in governance and should be required to engage in benefit sharing in one form or another.

In the field of genome editing, we are already seeing a rush to patent and commercialize foundational elements of the technology, and a fierce legal battle about who owns the intellectual property rights associated with the core technology (Egelie et al, 2016). The ethical, legal and social issues raised by this rush to patent foundational genome editing tools have also been examined (Sherkow, 2017; Feeney et al, 2018). We are also seeing the emergence more cooperative strategies, including open licensing of intellectual property and sharing of resources for genome editing research (Nielsen et al, 2018; Nicol and Nielsen, 2021). Even more interestingly, some patent holders are using intellectual property licences as a tool to foster ethical conduct (Guerrini et al, 2017). As such, there is some indication of an appetite for self-regulation to ensure that the promise of genome editing is broadly shared. This has been referred to as "ethical governance by patent" Sherkow et al, 2021). Notably, however, some commentators have expressed unease about leaving such decisions to patent holders rather than to democratically elected governments (de Graff et al, 2018).

Members of the team have in the past made calls for governments to explore optimal ways to support, guide and regulate public research organisations and private companies in their use of the patent system (Nicol and Nielsen, 2021). Some guidance already exists in this regard. In 2007 the Organisation for Economic Co-operation and Development (OECD, 2007) called for member nations to adopt patent licensing practices that foster innovation in the development of new genetic inventions related to human healthcare and to ensure that therapeutics, diagnostics and other products and services employing genetic inventions are made readily available on a reasonable basis. Australia has not yet developed policies that reflect this OECD recommendation. Independently, the US-based National Institutes of Health (National Institutes of Health, 1999; 2005) and Association of University Technology Managers (2007) have developed their own licensing guidelines. One question for consideration in the policy context is whether Australia should be adopting commercialisation and intellectual property policies for genome editing (and beyond that, for other innovative technologies more broadly) that reflect these guidelines.

9.1.3 Distributive justice

Although financial cost is one aspect of equity of access, Australian Citizens' Jury participants also understood the importance of distributive justice, by which we mean the fair allocation of resources among diverse members of a community. If human research and clinical trial recruitment favour socially advantaged groups, there is a risk that results are skewed, potentially leading to uneven

distribution of improvements in diagnosis and treatment. These and other concerns about the 'pernicious and pervasive effects of inequality' were recently addressed in an issue of the prestigious science magazine *Nature* dedicated to the topic (Anon, 2022). Citizens' jury participants likewise recognised the failures of distributive justice for disadvantaged groups and people with disability. The question of how distributive justice can be appropriately recognized and addressed is a complex and pressing issue.

As Nicol has discussed elsewhere (Nicol 2021, references omitted),

> Distributive justice is failing to find traction when it comes to genome editing research and clinical trials, even in regions like Europe and North America. Individuals of European ancestry are often favoured in clinical trial recruitment, risking skewing results and potentially leading to uneven distribution of improvements in diagnosis and treatment. Ethnically and socially disadvantaged groups, scarred by past experiences, are reluctant to participate in research and clinical trials. Discussions relating to disabled people tend to focus on their medical conditions rather than their social situations. The benefits arising from these research efforts are even less likely to be available to the vast majority of the global population in the developing world, as observed from the broader experience with access to medicines.

These points have clear resonance with the points raised in discussions in the citizens' jury and expert workshops. Though finding solutions to the problems associated with lack of distributive justice will be challenging, it is becoming even more important that they are addressed. Otherwise, genome editing and other innovative health technologies are only likely to widen the justice gap.

Points for consideration in embedding equity and other values and principles in human genome editing policy

1. As clinical applications of human genome editing become available, they should be made broadly accessible to those in need, with particular focus on those applications that alleviate human suffering, improve quality of life, and reduce childhood mortality. Methods will thus need to be developed to operationalise priorities, based both on the severity of the disorder or disability and the number of people affected, taking into account considerations broader than financial burdens and benefits;
2. Intellectual property should be a tool both for facilitating development of clinical applications of genome editing and for facilitating open and legitimate genome editing research. This may require the development of policies and guidelines to ensure that research remains unfettered by intellectual property constraints;
3. Distributive justice demands both that human genome editing applications are made broadly available, and also that research and development into new genome editing applications is targeted to those most in need in Australian society (and the broader global community). This will require further priority setting by governments.

9.2 Ensuring that therapy, enhancement and other applications of genome editing to humans are appropriately regulated

As noted on various occasions in this report, the vast majority of citizens' jury participants strongly supported the view that the primary aim of human genome editing should be to alleviate human suffering, improve quality of life and reduce childhood mortality (see particularly Guiding Principle 1, Recommendations 2 and 5). In Recommendation 5, in particular, participants expressed concern that about the risk that genome editing could be used for non-clinical purposes, for example the enhancement of appearance or athletic performance. On this basis, the majority recommended that non-clinical applications of non-heritable human genome editing should be prohibited until the benefits of genome editing are better known. They further suggested that if non-clinical applications

are permitted, they should receive no public funding. They also noted that greater clarity is needed to distinguish between clinical and non-clinical applications.

Many participants were particularly concerned about non-clinical applications of human genome editing in the heritable context. In Recommendation 2, the majority called for the prohibition on heritable human genome editing to be maintained for non-clinical applications. A fear about designer babies was obviously one of the drivers for this concern in this heritable context. However, as noted in the reasons for citizens' jury recommendations, this concern was possibly more to do with the risk that this technology could be misused than a simple distinction between clinical and non-clinical uses. Participants drew attention to concerns about behavioural modifications, loss of human diversity, and weaponisation.

The WHO governance framework report illustrates that there is considerable nuance to the ways in which genome editing can be utilised beyond the simple distinction between clinical and non-clinical uses. As noted in the introduction to this report, applications range from treatment of infertility, promotion of disease resistance and enhancement of human traits, through to improvements to robustness or quality of life and addition of non-human traits (WHO, 2021a, 6). This illustrates that there is no single 'bright line' between therapy and non-therapy, or between therapy and enhancement. Expert workshop participants agreed that there is a continuum rather than a bright line. Citizens' jury participants likewise recognised the difficulty in drawing lines between clinical and non-clinical applications.

One of the regulatory dilemmas in this area is that there is a robust regulatory regime for clinical applications of genome editing and other therapeutic goods, but this regulatory regime does not apply if uses are non-clinical (or non-therapeutic, using the language in the legislation). The *Therapeutic Goods Act 1989 (Cth)* defines therapeutic uses in section 3 as, use in or in connection with:

- Preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury.
- Influencing inhibiting or modifying a physiological process.
- Testing the susceptibility of persons to a disease or ailment.
- Influencing, controlling or preventing conception.
- Testing for pregnancy.
- Replacement or modification of parts of the anatomy.

There are clear options for legal redress, even in the non-clinical context, when there is actual bodily harm, for example through criminal law and tort law. Australia also has nationally consistent laws regulating health practitioners through the *Health Practitioner Regulation National Law Act 2009* (Qld). There has been a successful prosecution under this legislation for the use of 'innovative' practices which were later found to have been scientifically unsupported, dangerous to patients and grounds for cancelling the health practitioner's registration (Stewart et al, 2020). Otherwise, the act of performing non-clinic genome editing may be regulation-free, particularly if it is performed outside of traditional models for the development and use of healthcare innovations and not by registered health practitioners. Although regulators like the US-based Food and Drugs Administration appear have regulatory authority over use of CRISPR kits, for example, even for self-administration (Zettler et al, 2019) the situation is less clear in other jurisdictions, including Australia. This is particularly so if the kits are used for purposes such as 'amusement or entertainment', which are listed as possible uses in the WHO governance framework report (WHO, 2021a, 6).

Most innovative health technologies are complex to perform, requiring specialist knowledge, equipment and reagents, and therefore they tend to be exclusively undertaken in specialist laboratories which are well versed in complying with best practice standards and regulatory requirements. Genome editing, particularly CRISPR technology is often said to be 'democratising', in the sense that it is relatively simple to use and low cost, especially now that the US-based non-profit company Addgene makes essential CRISPR components available at minimal cost (Montenegro de Witt, 2020). Significant obstacles remain on the path to democratisation, with intellectual property and institutional barriers continuing as prominent concerns (Montenegro de Witt, 2020).

While there is much to be said for this process of democratisation, it is likely to be accompanied by increased risk of misuse, particularly if there is an absence of accountability and appropriate regulation. Concerns have already been raised regarding the potential outcomes of unregulated uses of genome editing, ranging from the fear of transhumanism, designer babies, bioterrorism and eugenics. These concerns are not without foundation. As noted in the WHO governance framework report (WHO, 2021a, 2),

> The Committee saw and heard evidence of challenges associated with rogue clinics, medical travel, as well as the reporting of illegal, unregistered, unethical or unsafe research and other activities including the offer of unproven so-called therapeutic interventions.

These concerns caused the WHO expert panel to recommend the development of 'an accessible mechanism for confidential reporting of concerns about possibly illegal, unregistered, unethical and unsafe human genome editing research and other activities' (WHO, 2021b, Recommendation 5).

Beyond this reporting mechanism, a number of jurisdictions are implementing laws to deter biohacking. For example, in 2019, the State of California enacted a law to ban the sale of CRISPR kits without a sign 'not use on one's self' and there has been at least one prosecution for sale of improperly labelled kits. (Mehlman and Conlon 2021). The European Union and the UN and the WHO are also taking steps to address the risk of biohacking in the context of genetic modification. In Australia, to the best of our knowledge the only recorded legal action to date was the prosecution of a biohacker for implantation of a travel card chip, on the basis that he breached the terms and conditions of the travel card. However, his conviction for the offence was subsequently overturned (see https://www.theguardian.com/australia-news/2018/jun/18/man-who-implanted-opal-travel-card-chip-has-conviction-overturned).

It should also be noted that in 2019 the WHO approved the creation of a global human genome editing registry, the goal of which is to make information on clinical trials involving human genome editing publicly accessible (WHO, 2021b, 8). Further information about the registry is available here: https://www.who.int/groups/human-genome-editing-registry. According to the WHO recommendations report, the registry was still in its pilot phase when that report was completed in mid-2021 (WHO, 2021b, 8).

Points for consideration in ensuring that therapy, enhancement and other applications of genome editing to humans are appropriately regulated

- Genome editing tools may be used in a range of ways, many of which may not even be in contemplation at the current time. As such, it is important to assess whether the current regulatory framework relating to therapeutic goods is adequate in assessing and monitoring the safety, efficacy and utility of the various uses to which genome editing tools might be put.
- Evidence of misuse of genome editing tools internationally indicates that the Australian federal government should consider supporting the WHO recommendation for reporting misuse of human genome editing research and other activities. The Australian federal government and other funding agencies should also consider whether to require that all clinical trials involving genome editing should be included on the WHO's Global Human Genome Editing Registry. Further, Australian governments should consider whether explicit offences should be enacted for unapproved human genome editing, whether for clinical or non-clinical purposes.

9.3 Deciding what types of genome editing research should be allowed and supported, recognising differing views on the status of the human embryo

As noted earlier, one of the greatest points of divergence in the views of citizens' jury participants relates to the status of the human embryo and the extent to which the human embryo can be used in research aimed at assessing the viability of heritable forms of human genome editing. Because questions associated with research involving human embryos were not fully resolved during the citizens' jury itself, participants were asked to provide more details as to their own personal views in follow up interviews, and the issue was further discussed in a later zoom meeting, as mentioned earlier in this report.

In part, the reason why the issues associated with research involving human embryos were not fully resolved at the citizens' jury is because the topic is quite complex, with different layers of research, regulation, ethics and community sentiment. Genome editing research generally starts in animal models, to test whether a particular genome editing tool is effective and produces the right kind of changes. This method sometimes also involves using cells from living humans who have consented to their cells being used for research. Once this pre-clinical research has passed certain thresholds, it might be possible to commence clinical trials for non-heritable forms of genome editing. This research is overseen by Animal Ethics Committees and Human Research Ethics Committees.

However, if the goal is to investigate the safety, efficacy and utility of heritable forms of human genome editing, there are some research questions that cannot be answered using these methods because human embryos develop differently from animals, and because experiments on individual cells in petri dishes cannot provide sufficient understanding of how an embryo as a whole might develop. Indeed, it would be unthinkable to apply the genome editing technique to an embryo for the very first time in an embryo that is intended for implantation and live birth, without any pre-clinical research or clinical research and training. This is why some genome editing research studies that are currently underway in the UK, US and China, are using human reproductive cells and embryos. To date, the outcomes of these research efforts indicate that there continue to be such significant safety and efficacy concerns that heritable human genome editing continues to be far from safe to use (Ledford, 2020).

Five different types of genome editing research involving human reproductive cells and embryos were presented to citizens' jury participants:

- Using unfertilised human eggs and sperm cells or pre-embryos (prior to the first mitotic division).
- Using human embryos that are defective in some way, so that they aren't suitable for use in assisted reproduction.
- Using human embryos that have been created for assisted reproduction, but that are no longer needed by the people who provided the egg and sperm.
- Using embryo-like structures (sometimes called embryoids) that have been created by a process other than fertilisation (e.g., using stem cells modified to act like embryos).
- Using human embryos that are created by fertilisation specifically for research.

Citizens' jury participants broadly recognised the value of genome editing research (Guiding Principle 2) because of the potential medical benefits and advancement of scientific knowledge that might result from it. The majority of participants supported research involving human embryos, on the basis that the potential benefits outweighed the discomfort they felt about using human embryos in this way. Indeed, when it comes to embryos already in existence and in frozen storage, if the alternatives were either destruction of embryos or use of embryos for research, many participants were more comfortable with the latter.

The majority of citizens' jury participants also seemed to accept that the creation of human embryos by fertilisation specifically for research might be the best option for furthering research into heritable human genome editing. However, as noted earlier in this report, it was clear in these discussions that some felt deep discomfort with the creation and use of human embryos for this purpose. The special status of the human embryo was broadly recognised by citizens' jury participants. The opening statement to the recommendations regarding human genome editing research using human embryos shows that those participants who supported creation of embryos for research were nevertheless of the view that it should be stringently regulated, that the 14-day rule should be complied with and that informed consent from all relevant parties must be assured. A small number of participants, however, appeared to be less concerned with rigid application of the 14-day rule.

Fourteen days post-fertilisation has been widely accepted globally for many years as an appropriate time limit on research involving human embryos as this marks the start of the development of the primitive streak, the precursor to the nervous system. However, more recently the rationale for the 14-day limit has been questioned. One significant example can be found in the 2021 review, Guidelines for Stem Cell Research and Clinical Translation produced by the International Society for Stem Cell Research. The review called for national academies of science, academic societies, funders, and regulators to lead public conversations touching on the scientific significance as well as the societal and ethical issues raised by allowing research beyond 14 days post-fertilisation (recommendation 2.2.2.1 https://www.isscr.org/guidelines). At the time of writing, there has been no obvious public discussion about relaxation of the 14-day rule in Australia.

As noted previously, these divergent views on the status of the human embryo have long been reflected in community engagement in Australia (Nicol et al, 2022). They are also reflected in parliamentary debates. For instance, 29 members of parliament voted against the recently passed mitochondrial donation legislation, largely based on their concerns about the status of the human embryo (Nicol et al, 2022). This was the case even though this issue had been extensively canvassed in public forums prior to the introduction of the legislation in the Australian parliament (Nicol et al,

2022). In contrast, the special status of the human embryo appears not to have featured in citizen deliberations on heritable human genome editing in other jurisdictions (for example, in South Africa: Thaldar et al, 2022).

If legislation were ever be introduced into the Australian parliament to allow the creation of human embryos for genome editing research, it seems inevitable that similar concerns will be raised. It is clear from expert input during the course of this project and from the academic literature that Australian researchers are embracing genome editing research, particularly CRISPR. Moreover, a number of clinical trials are already under way in Australia (Eckstein and Nicol, 2020). However, there are no reports of any licences being issued for use of embryos in genome editing research on the NHMRC Embryo Research website (https://www.nhmrc.gov.au/research-policy/embryo-research-licensing/database-licences-issued). This suggests that there may be no particular interest in investigating the viability of heritable human genome editing in Australia at the present time.

A licence would be required for use of embryos in any of the embryo research activities listed above, save for the last activity, which is currently prohibited. As such, it may be premature to open debate on these issues. However, questions have also been raised in some commentary about the legality of any form of genome editing research involving human embryos, even when there is reliance on the use of embryos that are excess to artificial reproductive technology needs (Taylor-Sands and Gyngell, 2018). There admittedly is some ambiguity in the wording of relevant provisions in the legislation (Taylor-Sands and Gyngell, 2018; Nicol, 2020), suggesting that it would be timely to seek greater clarity at this stage in the development of CRISPR research in laboratories in Australia.

One pertinent question is whether research of this nature actually needs to be undertaken in Australia. As noted above, genome editing research involving human embryos is currently being undertaken in other jurisdictions. Should there be a groundswell of support for heritable human genome editing in the future (discussed under the next theme) but continued discomfort with using, and particularly creating human embryos for research, it may be necessary to consider whether it would be appropriate to allow clinical trials in the absence of Australia-specific pre-clinical research.

From the ethical perspective, this begs the question of whether it is appropriate to rely on findings from research undertaken in other jurisdictions that would be illegal if undertaken in Australia. Irrespective of the answer to this question, should heritable human genome editing ever be permitted, it would be vital for the embryologists performing this technique to have suitable training to ensure they were competent to perform the task. The amendments to the Australian legislation allowing mitochondrial donation deal with these issues by providing for licences for pre-clinical research, clinical research and training and clinical trials. This approach may provide a useful model, should this pathway towards heritable human genome editing ever be opened in Australia.

Points to consider in deciding what types of human genome editing research should be allowed and supported, recognising differing views on the status of the human embryo

- Noting that various non-heritable forms of human genome editing research are already well underway in Australia, Australian governments may wish to consider funding priorities to ensure that this country remains at the forefront of this research effort. The Genomics Health Futures Mission may be an appropriate forum for this work.
- Although there appear to be no current licences for the use of human embryos for genome editing research, it would be unfortunate if no further progress is made in increasing our understanding of the legitimacy of using embryos for genome editing for research until such time that the first application is made for a licence. As such, it may be appropriate for the governments of Australia to consider questions associated with the use of embryos for these purposes in the near future.
- More particularly, the creation of human embryos for research purposes remains contested. The experience with mitochondrial donation provides a model both for how to undertake public consultations on such matters, and how a strict and tightly prescribed legislative regime might be created for this purpose, should this be deemed appropriate.

9.4 Preparing for a future when heritable human genome editing may be shown to be safe and effective

Despite the unverified claim by He Jianku that he has already undertaken heritable human genome editing on a number of embryos and that this has led to live births, there is a very strong view amongst some within the scientific community that this form of genome editing is very far from being safe and effective enough to use in practice. As a consequence, calls have been made for a global moratorium on all heritable human genome editing for the time being (Lander et al, 2019). Recent research involving human embryos has revealed disquieting results, perhaps lending support to the view that there should be a moratorium (Ledford, 2021). However, the call for a global moratorium has not been accepted by all scientists using this technology (Adashi and Cohen, 2019; Yua et al, 2021). Rather, they call for more inclusive global governance including through journal editors and conference organisers, international professional organisations and public and private funders.

Although these above listed 'soft' tools are no doubt important components of the toolbag that could be used to achieve globally consistent governance, it is most unlikely that governments that have enacted stringent prohibitory legislation (like Australia) would cede their authority to regulate in such contentious areas to bodies such as those described above, since they can only use enforcement measures such as peer opprobium, publishing embargos and withdrawal of funding. In a controversial and ethically fraught area such as this, it would seem to be far more appropriate to employ the full governance toolbox listed in the WHO governance framework report including: declarations, treaties, conventions, legislation and regulations; judicial rulings; and ministerial decrees to the mix. Regulating in the genome editing space is clearly not a trivial exercise.

Whilst the scientific community and policy makers wrestle with these issues, research and clinical trials for non-heritable human genome editing continue and, where permissible, research involving human embryos is being undertaken. This means that it would be unwise to defer all discussion about how we as a society might deal with heritable human genome editing, should it be deemed safe and effective, to some time in the future. We have the present opportunity to future proof for that eventuality and this opportunity should be embraced.

In the context of this study, citizens' jury participants were far more equivocal and less unified when it came to support for heritable genome editing than for non-heritable human genome editing. We

have seen that, for some participants, the creation of embryos for research purposes and the heritable alteration of the human genome could not be sanctioned in any way. However, the majority of participants expressed cautious support for heritable genome editing at some point in the future, provided that it followed on from more research and public engagement and was undertaken within a strict regulatory environment, as illustrated in Recommendations 1 to 4. Much of the discussion associated with the development of the Guiding Principles was also undertaken within the specific context of heritable human genome editing. As such, issues of equity and distributive justice particularly come to the fore in this context.

Within this majority group, there was strong support for the view that, if approved, heritable human genome editing should only be used to assist people to have healthy children, and that it should never be used for enhancement purposes. This majority group was of the view that, where possible, other techniques, such as prenatal genetic testing, should be given preference. A small number of participants were much less cautious, suggesting that any delay in making heritable genome editing available is inappropriate because of the risks associated with passing on life threatening or debilitating diseases or disabilities.

The views expressed by the majority of citizens' jury participants are very much in step with international expert reports, which are leaning towards the possibility of opening the door to certain forms of heritable human genome editing, but at some time in the future and subject to stringent safeguards. Indeed, the closeness of the recommendations to those provided in the expert reports triggered the concerns raised by some experts attending the workshops about framing, discussed earlier in this report. Although we accept the legitimacy of this critique, we note that similar community attitudes regarding heritable human genome editing have been reported in other studies (see particularly Critchley et al, 2018), suggesting these findings are not out of step with community values more broadly. In any case, this project was never intended to be a source of definitive policy advice to the governments of Australia. Rather it is hoped that this study might provide some guidance on the direction for future inquiry.

As such, irrespective of framing issues, we suggest that it is legitimate, at this point in time, to explore how Australia should prepare for a future where heritable human genome editing may be shown to be safe and effective. The three-pronged question that needs to be asked is whether Australia should make legislative changes to allow for heritable human genome editing once there is evidence of safety and efficacy, or whether we should continue to take a cautious approach until more evidence of safety and efficacy emerges, or whether we should reject this option absolutely.

Significant reform of Australian law would be required should heritable human genome editing become a reality in the future. There are two key pieces of legislation that would need to be amended Amongst a raft of criminal offences, the *Prohibition of Human Cloning for Reproduction Act 2002 currently* prohibits reproductive technologies that make hereditary changes to the human genome or result in the creation of a human embryo by fertilisation with genetic material from more than two people. The *Research involving Human Embryos Act 2002* permits use of human embryos for research purposes only in strictly limited and regulated circumstances. The Embryo Research Licensing Committee of the National Health and Medical Research Council was created to administer the licensing regime. The creation of embryos for research purposes is prohibited when it involves fertilisation of a human egg by a human sperm.

Australia is not alone in imposing a restrictive regulatory framework on heritable human genome editing and human embryo research. Germany and Canada, to name but two countries, have similarly strict regimes. Other countries have a somewhat more open research environment, most have either legislation or another form of regulation that prohibits/deters/discourages heritable human genome

editing and provides oversight of human embryo research. These differing legislative approaches to the regulation of human heritable genome editing have recently been extensively reviewed by two sets of authors (Boggio et al, 2000; Baylis et al, 2020). As such, the debate about the permissibility of heritable human genome editing is a complex global one.

Legislation allowing mitochondrial donation in Australia may provide a model for how a heritable human genome future might look (should there be societal, scientific and policy support for such an eventuality). The legislation specifically provides that only limited mitochondrial donation techniques can be used, and that licences must be obtained for pre-clinical research and training, clinical research and training, clinical trials and, eventually, clinical practice. This legislation was being debated at the time of the Australian Citizens' Jury and was used as a case study during the Citizens' Jury. As such, participants were provided with some insight on a potential model for how a heritable human genome editing future might look.

One specific matter that was canvassed at the citizens' jury was whether parents should be permitted to refuse human genome editing on behalf of their children (by refusing foetal or early childhood genome editing) or future children (by refusing reproductive cell or embryo genome editing). The tragic current case of the trial for murder for failure to provide necessary insulin to Elizabeth Struhs, an eight year old diabetic, reminds us of the duty not to withhold medical treatment.

The situation is more complicated when it comes to children not yet in existence as it raises issues associated with the so-called 'non-identity problem'. According to Doolabh et al (2019), this problem 'has been vexing philosophers for decades. It concerns a moral question about potential people who do not yet exist, but could exist in the future'. Although there is no existing regulation specifically on point in Australia in relation to future children, an important context for these discussions is Section 13(9) of the Human Fertilisation and Embryology Act 1990 (UK), as amended by Section 14(4) of the Human Fertilisation and Embryology Act 200 (UK), which prevents the preferential selection for implantation of embryos that are known to have a gene, chromosome or mitochondrion abnormality involving a significant risk that a person with the abnormality will have or develop (a) a serious physical or mental disability, (b) a serious illness, or c) any other serious medical condition'.

The Act was mentioned by an expert witness at the citizens' jury and was referred to by several participants. In the small group discussions, participants reflected on the implications that similar legislation might have, if applied to heritable human genome editing in Australia. In discussing this topic, participants tended not to distinguish between parents' right to decline genome editing of embryos and preferentially selecting an embryo known to be at significant risk of serious physical or mental disability, illness or medical condition as described in the Act.

Points to consider in preparing for a future when heritable human genome editing may be shown to be safe and effective

- We are not yet at a point in time in Australia where the application of heritable human genome editing is imminent. Indeed, it appears that we are not yet at a point in time when such genome editing research involving human embryos is being planned. Despite this, it is suggested that it is timely to consider the approach that might be taken in Australia, should heritable human genome editing ever be seen as a realistic option for parents desiring to have healthy, genetically related children.

9.5 Building meaningful public participation in governance of human genome editing into the future

In their recommendations, citizens' jury participants clearly recognised the importance of stakeholder and community education and input. They emphasised that meaningful participation requires

education, engagement and other forms of capacity building and that specific input should be sought from communities who are particularly affected, including people living with inherited disease or disability. This recognises that there should be public input at all stages of the regulatory and approval processes for genome editing.

As a starting point, the involvement of members of the public in setting a reform agenda for genome editing is widely supported internationally, both in policy reports and academic commentary. It is further recognised that this agenda-setting should not be left only to scientists, medical practitioners, specialist government agencies or international committees. We hope that our Australian Citizens' Jury plays a small role in responding to this call. Although citizens' juries are a demanding form of citizen engagement compared with opinion polls, focus groups and other forms of public engagement, they are well recognised for delivering outcomes that can inform policy and practice.

If the Australian government is to engage in regulatory reform it will be crucial to engage fully with stakeholders and the public alike to facilitate inclusive and rigorous debate about the risks and benefits of this complex and ethically fraught, but potentially transformative, scientific tool. Recent regulatory reform in Australia allowing mitochondrial donation within a strictly regulated environment was accompanied by an extensive public engagement exercise, featuring a citizens' jury, calls for public submissions, webinars, roundtables, surveys and other forms of engagement. This multimodal approach could provide a model for how public participation may be embedded in other regulatory reform proposals.

As noted above, citizens' jury participants recognised that public participation must go beyond the reform process into governance itself. Government agencies, too, are recognising that public participation, alongside transparency and accountability, is a pillar of good governance. These pillars become particularly important for innovative, personalised health technologies, because they raise distinct scientific, ethical, legal and social issues. Although clinical trials for genome edited products are only just underway, lessons can be drawn from the marketing approvals pathways for gene therapy products. The US Food and Drugs Administration, the European Medicines Authority, and the Australian Therapeutic Goods Administration are all attempting to include public participation processes and transparency and accountability of review pathways are incorporated into marketing approval policy and practice. To date, however, such steps have been piecemeal and, in some cases, controversial (Nielsen et al, 2001).

There are increasing calls for these agencies to be more democratic in their decision-making generally, and to move away from an exclusive focus on the technical benefit-risk calculation towards a more participatory, public model. The question is how to put public participation into effect. On the one hand, slavish adoption could reduce the weight given to scientific evidence. On the other hand, formalisation could result in public participation requirements being applied in a tokenistic fashion. New models are urgently needed, particularly given the speed with which genome editing is being adopted in the laboratory and promising new genome editing product leads are emerging.

In planning for future public participation in developing governance strategies for genome editing, Australian governments should be mindful of the need to include all sectors of society. It was decided early in this project that specific attention could not be given to the perspectives of Aboriginal and Torres Strait Islander communities, given the lack of expertise within the research team together with funding and time constraints. We urge Australian governments to commit to consultation by and with these important groups in Australian society.

Points to consider in building meaningful public participation in governance of human genome editing into the future

- Should Australian governments decide to explore further any of the points we have outlined above, public participation will need to be built into the process. Moreover, any new regulatory and other policy directions emerging from this exploratory process will need to be accompanied by ongoing public participation.
- Public participation planning should include culturally respectful inclusion of Aboriginal and Torres Strait Islander communities.

10
ASSESSMENT AND LIMITATIONS

The design of the Australian Citizens' Jury on Genome Editing was challenging. It not only involved complex scientific and ethical issues, it was also anticipatory, to the extent that there was relatively little existing public debate to guide the formulation of the content (MacKenzie and O'Doherty, 2011) — which also demonstrated why this engagement and associated research was necessary. The design drew on previous experience (O'Doherty and Hawkins, 2010; Burgess, O'Doherty, and Secko, 2008), within the constraint of the available funding, and the need to bring together participants safely to deliberate together in Canberra during the ongoing COVID-19 pandemic.

10.1 What Did the Process Achieve

Human genome editing is a challenging topic to address in a four-day deliberative process. The complexity of the topic and the breadth of the remit (or question) that was addressed by participants in the Australian Citizens' Jury on Genome Editing posed several serious challenges (AusCJ, 2021). H

Our own research suggests that complexity poses a particular barrier to high quality deliberation (as measured using the criterion of deliberative reason; see Niemeyer et. al. forthcoming) and that compared to comparable cases, the Australian Citizens' Jury on Genome Editing represented a particularly high level of complexity. The same analysis applied to the citizens' jury suggests that the process in large part achieved the aim of participants working through the relevant issues and integrating them into reasoning, the process, the previously mentioned limitations regarding working through some of the more profound issues notwithstanding (see Appendix E, section E.2).

10.2 Limitations

Nevertheless, there are important lessons to be learnt regarding challenges faced in design and implementation. Three of those challenges and associated lessons are highlighted here:

- Framing
- Provision of information
- Distribution of time allocated to deliberation

These assessments and limitations are detailed in the following, drawing on feedback from participants, facilitators at the citizens' jury, and reflections made be members of the research team

10.3 Framing of the Australian Citizens' Jury on Genome Editing

In many respects, the citizens' jury recommendations align with the recommendations in the various expert reports mentioned in the introductory and background section to this report. It is possible that the framing of the citizens' jury deliberation, and especially the prominent role of the expert speakers in the process, contributed to this alignment of the citizens' jury recommendations with other expert

reports. We are grateful to Michael Burgess, Mahmud Farooque, Ben Hurlbut, and others for pointing out that the prioritisation of academic and scientific evidence might have limited other types of reasoning and expressions of alternative narratives. The facilitators at the citizens' jury, who moderated the table discussions, also highlighted that the experts were academics with specialisations in technical fields or bioethics, and that 'perspective from outside the academy', and particularly from political economy, were absent from the process.

Assessing the selection of witnesses against a priority of achieving a diversity of views (Roberts et al., 2020) provides a mixed, if generally positive result. Our analysis suggests that witnesses who presented represent a diverse if specialist voice (see Appendix C, C.5.4), but there is scope for improvement.

We have also conducted analysis of transformation during the Australian Citizens' Jury to examine whether participants tended to migrate toward the perspectives of the expert witnesses. Overall, while participants did tend to migrate on average toward positional modalities held by presented in some areas, in others the opposite is the case. Moreover, our own analysis also shows that, where framing effects may serve to reduce authentic reasoning by participants, the level of deliberative reason improved considerably during the process, which is difficult to achieve for complex issues such as human genome editing (see Niemeyer et al forthcoming).

Support for this critique can also be found in statements made by some participants in the follow-up interviews. Several participants felt that their reasoning was more 'scientific' following the citizens' jury. According to one participant: 'The more we learned about it [human genome editing] the more it gave me a "scientist soul". This particularly affected the participant's reasoning about the use of human embryos for research: 'I felt a sensitive, emotional connection with my imagination [of human embryos]. After coming back [from the citizens' jury] (...) I found myself not looking at it as a little baby. I started seeing it as a substance that is going to help me build up the future in a better way. I think I lost that emotional connection with that embryo.'

Another participant described self-censoring their emotions 'to be a little more reasonable'. In a post-deliberation interview, one participant lamented that jury members had not shared more emotional content, and thought that hearing about people's personal experiences related to the topic might have made the discussions more impactful for him. However, another participant felt that the sharing of personal stories by other participants made it harder to share opposing views because, 'it feels like you're arguing against that person's whole existence (...) you feel like you just have to support them'. These and similar statements from some participants suggest that the framing of human genome editing as a scientific and medical issue might have prevented other perspectives, such as emotional, ethical, and religious discourses, from being expressed and fully deliberated.

10.4 Provision of Information

The combination of the complexity and breadth of applications the jury members were asked to consider created challenges regarding the ability to provide and digest all the relevant information necessary to form judgements over the course of a four-day event. The principle guiding the provision of information to participants is to create a broad and accessible foundation for deliberation, so that there is common ground and sufficient background to enable reasoned discussion.

An information packet (here) was prepared by the research team and provided to participants prior to the event. It contained a glossary of key terms and concepts; a brief explanation of the different applications; FAQs on genome editing; QR codes to access learning videos and a short background on what to expect in a citizens' jury.

The expert witnesses included research scientists, clinicians, a lawyer, an embryologist and three bioethicists (listed here). They presented information concerning the science of human genome editing, development of the technology, issues associated with its application, social and ethical considerations, and the nature of the existing regulatory framework. While the provision of expert witness presentations was an important feature of the process, some participants would have liked to hear from speakers who had views opposed to the technology. In their feedback about the deliberative process, the facilitators pointed out that a narrower remit might have allowed experts' 'presentations to be more tailored'.

While, overall, most participants agreed that there was enough information provided during the Australian Citizens' Jury, about half felt that there was a lack of balance between different viewpoints. Many participants found the absence of direct advocacy, particularly from positions that are against the application of human genome editing, to be a gap in the program.

In post-citizens jury interviews, some participants also stressed that they would have preferred access to the information packet earlier.

10.5 Distribution of Time Allocated to Deliberation

Another challenge for the process design involved the deliberation among participants when developing the recommendations for decision makers. The approach of the Australian Citizens' Jury involved participants developing recommendations from scratch. This entailed plenary sessions and small group deliberations, supported by trained facilitators, that allowed participants to shape the reasons in support of their conclusions.

This was done in preference to a simpler approach where participants discuss and vote on a set of pre-established options, because there was no established set of relevant options capable of covering the scope of the remit and because evidence supports the idea that a reason-focused approach to constructing recommendations helps to deal with complex issues and improve knowledge (Niemeyer et al. Forthcoming; Setälä, Grönlund, and Herne 2010).

A set of recommendations from the citizens jury were compiled on the afternoon of the 3rd day and the morning of the final day. Members of the citizens' jury presented these recommendations to decision makers and expert witnesses in the House of Representatives on the final day of the process.

Despite careful design, participants expressed concern about the lack of time to deliberate and reflect on their conclusions. The research team and facilitators shared this concern. The facilitators particularly emphasised that at least an additional half a day would have been needed to adequately address the complexity of the topic. Additionally, the facilitators echoed comments by participants that a final plenary session was needed on the last day to deliberate the recommendations produced by each small group discussion, noting that 'There was insufficient time allotted to bringing the whole group to agreement on the recommendations'. There remained several incompletely processed issues — an observation that is supported by preliminary analysis of 'deliberative reasoning' (See Appendix D).

To support participants in working through these loose threads, the protocol for the post-event interviews focused on the most salient areas where clarity could be improved in the original recommendations (particularly regarding the use of embryos for human genome editing research). Input from the post-event interviews was used to update the outcomes report with additional reflections from participants, which was then subject to further group deliberation as part of the follow-up forum conducted via a Zoom session on 21 August, attended by ten of the original 23 participants and members of the research team. The event was facilitated by the lead facilitator from

the citizens' jury, to ensure that the process was as deliberative as possible. Nevertheless, we agree that the post-deliberation activities were not a direct substitute for additional time allocated to deliberation at the citizens' jury. This event provided further opportunities for recommendation development, which have been incorporated into the recommendations provided in Section 6 of this report. .

11
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Attendees/speakers at the introduction and concluding ceremony

Dr Nitin Bagul, Therapeutic Goods Administration

Dr Raj Bhula, Gene Technology Regulator

Daryl Karp, Director, Museum of Australian Democracy

Professor Anne Kelso, National Health and Medical Research Council

Hon Dr Andrew Leigh MP, Federal Member for Fenner

Professor Paddy Nixon, Vice Chancellor, University of Canberra

Dr Monique Stone, Therapeutic Goods Administration

Video recording

Sonya Pemberton's team at Genepool Productions

Tony Wright at December Media

Georgina Jenkins and her team at By George Studios

Video credits

Australian Citizens' Jury on Genome Editing video available at: https://www.youtube.com/watch?v=OskSspvORII

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DISCLOSURES

Dianne Nicol is chair of the Embryo Research Licensing Committee of the National Health and Medical Research Council. Her role on this project is entirely independent of this role and should not in any way be seen as representing the National Health and Medical Research Council or the Australian federal government.

APPENDIX A.
BACKGROUND

A.1. KEY BASIC TERMS

As with most areas of science, the genome editing field is littered with complex jargon. The aim of here is to provide a basic account of some of the key terms and techniques used in this field to assist those unfamiliar with this technology to navigate through the rest of this report.

Cells: The bodies of all living things are made up of building blocks called cells. In humans for example, there are a number of different types of cells – muscle, nerve, skin, kidney, liver and so on. One of the main ways of dividing up the types of cells is to separate out the cells that get passed on to future generations (germline cells) from all of the other cells (somatic cells).

Germline cells: These are the cells in a living thing (whether a human, a plant or an animal) that get passed on to future generations (which means that they and their contents are heritable). Sperm cells and egg cells are examples of germline cells. When they fuse during the process of fertilisation they form an embryo.

Somatic cells: These are the cells in a living thing (whether a human, a plant or an animal) that do not get passed on to future generations (which means that they and their contents are not heritable). Liver cells, nerve cells, muscle cells and skin cells are all types of somatic cells.

Embryos: An embryo is the first step in creating a new living thing, whether a human, a plant or an animal. An embryo is created when an egg cell is fertilised by a sperm cell. Over time, the embryo goes through a series of cell divisions. The cells start to develop their own distinct functions (e.g. muscle, nerve, etc.). One of the things that happens early in the development of the embryo is that the germline cells separate off from the somatic cells.

Genetic information: In all living things, almost all cells carry the same set of genetic information. This information provides the necessary instructions to tell the cell what to do. These instructions are often referred to as the genetic code.

DNA: DNA is a long chain-like chemical molecule that carries the genetic code. One of the key features of DNA is that it generally exists as two closely intertwined mirror image strands. These two strands twist around one another to form the so-called 'double helix'. The DNA molecule is made up of many thousands of components, called nucleotides. There are four different types of nucleotides, identified by the letters A, C, G and T. The precise sequence of these nucleotides within a cell is its genetic code.

Chromosomes: Almost all of the DNA in cells is organised into separate units, called chromosomes. In human somatic cells there are 46 chromosomes, organised in pairs (23 x 2). The egg and sperm cells only have one member of each pair (that is, they have 23 chromosomes). When they fuse, the number of chromosomes goes up to 46 again (23 from the egg and 23 from the sperm).

Nucleus and mitochondria: Cells are made up of various small specialised microscopic structures, including two called the nucleus and the mitochondria. Cells generally have a single nucleus but many mitochondria. These two parts of the cell are particularly important because each carries DNA. The chromosomes are located in the nucleus, but the mitochondria have their own set of DNA. Mitochondria are important because they produce the cell's energy. Errors in either nuclear or mitochondrial DNA can lead to mitochondrial disease, which can be fatal.

Genome: The genome is the sum total of all the DNA in a cell, including both nuclear and mitochondrial DNA. Whole genome sequencing is a technique that can be used to identify the entire genetic code.

Genes: The genome within each cell is divided up into various sub-components, some of which are called genes. Genes provide individual packets of information that instruct the cell what to do to carry out its particular functions. There are two copies of most genes in human cells. The only exception is that males have two different sex chromosomes (X and Y) with different genes. In contrast, females have XX chromosomes.

Mutations: Errors in the genetic information carried in a cell are called mutations. These may be small, for example a missing letter in the genetic code, or a misplaced letter (for example, an A instead of a C), or they may be quite large. Depending on where the mutation is located, it may have a very large effect on the function of the cell, or no effect at all. For diseases like cystic fibrosis, for example, a number of known mutations within a single gene can cause the disease. Although each mutation is small, the effect on the health of the person with the disease is profound. Whole genome sequencing can be used to identify these mutations, by comparing the sequenced genome with a reference genome.

A.2. Techniques For Modifying the Genome

Genetic modification: Techniques have existed for almost fifty years that allow the introduction of foreign DNA into cells that can change the way that the cells function. In plants and animals, for example, genetically modified organisms have been created with different characteristics from those existing in nature. These characteristics in plants and animals are capable of being inherited (that is, they are heritable). Genetic modification in plants and animals may be used both to repair defects caused by mutations and to introduce new (enhanced) traits.

Gene therapy: In humans, the term 'gene therapy' is generally used instead of 'genetic modification'. Current medical uses of gene therapy focus on genetic diseases that are very serious and often otherwise deadly. Gene therapy involves the delivery of DNA into cells in much the same way as genetic modification in plants and animals. However, the genetic changes caused by these treatments are not allowed to be passed on, which means they are not heritable. Heritable gene therapy is not currently regarded as safe or ethically acceptable in humans. Non-therapeutic (enhancement) gene therapy, even if non-heritable is also not currently regarded as safe or ethically acceptable in humans. To date, three gene therapies have been approved for non-heritable use in Australia. These are Kymriah, for treatment of a type of leukemia, Luxturna, for treatment of retinal dystrophy and Zolgensma, for treatment of spinal muscular atrophy.

Genome editing: Recently, various new techniques have emerged with names like CRISPR, TALENS, Zinc Fingers, Prime and Base Editing (it is not necessary for the purpose of this Occasional Paper to understand the specific details of each new technology). These new technologies offer significant advances over earlier gene therapy techniques. The technique known as CRISPR is particularly notable. It involved making very precise cuts in both strands of DNA, which are then either allowed to heal naturally (*unguided*) or are *guided* in the healing process. Where the DNA heals naturally, some of the code will be lost, which may result in a defective gene losing its function (often called being 'silenced'). Where the healing is guided, defects may be corrected or new functions introduced.

Non-heritable (somatic) human genome editing in humans: There is much discussion about the promise of genome editing to treat diseases that are not currently treatable. To date, however, no non-heritable human genome editing has been approved for use in medical care in Australia, or globally for that matter. This is because genome editing is still very new.

Heritable (germline) human genome editing: Genome editing is said to be 'heritable' if the edit is present in the germline cells that will be used to create the next generation (that is, the offspring of the offspring, or the grandchildren). The way this would normally arise is when the genome editing is done very early in embryo development, usually in the egg or sperm or in the newly formed embryo, before it divides. The result is that every cell in the offspring carries the edit, that is, all the somatic cells and all the germline cells of the offspring and future generations.

Mitochondrial donation: Mitochondrial donation is a process where the mitochondria in one living thing are replaced with the mitochondria from another living thing. For example, the mitochondria in the egg of a woman who has mitochondria disease could be replaced with the mitochondria from the egg of a woman who does not carry the disease. As the process involves replacing all the mitochondria carrying a DNA mutation with healthy mitochondria, this technique involves genetic modification, but does not involve genome editing in the form that we have described above. Instead, some people compare it to an organ transplant, in which a healthy biological component replaces the faulty component.

Alternatives to modifying the human genome: Most people are familiar with in vitro fertilisation (IVF), which has been an accepted part of birthing since 1978 when the first IVF baby was born. Scientists have developed various artificial reproductive technologies since that first birth. One of these is preimplantation genetic diagnosis, which involves taking one or more sample cells from an embryo and analysing those cells for the presence of a known mutation that causes a single severe genetic condition in a family. Because pre-implantation genetic diagnosis allows healthy embryos to be selected and embryos that carry mutations are not implanted, it is a diagnostic rather than a therapeutic, in the sense that it identifies but does not treat genetic conditions. In contrast, genome editing involves changing the genome, and hence could be said to be a therapeutic rather than a diagnostic.

A.3. Genome Editing Research

All of the various techniques discussed in the above section have been the subject of many years of painstaking research. Generally speaking, research into new techniques for modifying the genome starts in the laboratory using single cells in petri dishes. Once the research shows some promise, it may then progress to application in whole living plants and animals. It is only much later, when there is some confidence as to the safety, efficacy and utility of a technique, that clinical trials may be undertaken in living human beings.

If heritable human genome editing is ever to be undertaken, it will not only require research showing that the technique is safe, effective and useful in living humans, but also some indication that it will be as safe, effective and useful as possible for their offspring and for future generations of humans. Research examining these questions both during the course of embryonic development and in successive generations of living animals is likely to provide important findings on these questions of safety, effectiveness and utility. However, because humans develop differently from animals, these research findings are likely to be of limited value.

Research involving human reproductive cells and embryos is likely to provide a greater level of confidence about safety, efficacy and utility for offspring and future generations. Five different types of genome editing research involving human reproductive cells and embryos are outlined below.

- Using unfertilised human eggs and sperm cells or pre-embryos (i.e., fertilised eggs that have not yet begun to divide and multiply). This helps in understanding how genome editing affects the process of fertilisation but does not answer questions about subsequent stages of embryo development, after the first cell division.
- Using human embryos that are defective in some way, so that they aren't suitable for use in artificial reproductive technologies. Research using these types of embryos helps in understanding how genome editing affects the early development of the human embryo, but because these embryos are defective it is difficult to know for sure what is causing any effects that are observed.
- Using human embryos that have been created for artificial reproductive technology, but that are not needed by the people who provided the egg and sperm. Research using these types of embryos can help answer some questions about the development of human embryos following genome editing, but because these artificial reproductive technology embryos will have undergone a number of cell divisions and been frozen, their usefulness for research is limited.
- Using embryo-like structures (sometimes called embryoids) that have been created by a process other than fertilisation (e.g., using stem cells modified to act like embryos), and exposed to genome editing during very early embryonic development. Whilst this technique might be useful for observing embryo development, it is technically complex to perform and there isn't much research on how well embryoids mimic normal embryo development.
- Using human embryos that are created by fertilisation specifically for research. This option allows researchers to answer the broadest range of research questions about how genome editing affects the development of human embryos, but it is the most challenging option ethically and legally.

A.4. Ethical, Legal and Social Implications of Genome Editing

There is much discussion internationally about what types of human genome editing should be undertake and supported by governments and international agencies, and what should be the underlying rationales supporting these decisions. This section outlines some of the 'big questions' and the regulatory responses, with particular focus on the situation in Australia.

A.4.1. Non-Heritable Human Genome Editing

In the context of non-heritable human genome editing, these are some of the types of questions that might be raised:

- How can people receiving genome editing be protected from harm?
- Should genome editing only be used for disease, or can it be used to change characteristics like sporting ability and physical appearance?
- How will genome editing affect our views on disability?

- Can the benefits of genome editing be shared equitably?

Although not universally accepted, a set of four ethical principles have been widely adopted in countries like Australia to aid decision making in biomedicine. These four principles were first articulated in 1979 by two American philosophers, Thomas Beauchamp and James Childress. In summary, the first principle of autonomy recognises free will, and the right of a person to make uncoerced decisions relating to their personhood. The requirement for informed consent to medical treatment and participation in research stems from this principle of autonomy. The principle of nonmaleficence focuses on the avoidance or minimisation of harm, physically, psychologically, financially, or in other ways. This principle requires that all new innovations in healthcare are assessed for safety, efficacy and utility before they become routinely available. The principle of beneficence involves acting kindly and charitably and with mercy, recognising that a person is much more than their disease or disability.

Finally, the principle of justice raises wider ranging concerns regarding such matters as equitable access to treatment, non-discrimination, freedom from exploitation and profiteering, and the right to health care. A number of questions can be posed under the principle of justice. For example, in the development of clinical applications of genome editing, is it better to focus on diseases that have catastrophic consequences for small numbers of individuals, or diseases that are less catastrophic but affect larger numbers of individuals? Is it problematic from the justice perspective that genome editing research tends to focus on diseases that affect individuals of northern European origin? Diseases that are more common in other parts of the world (particularly Africa and South America) tend to be much less well studied. One notable exception is sickle cell disease, which has been the subject of extensive genome editing research and is currently in clinical trials. This disease tends to be most prevalent amongst people of African descent.

The legal landscape for biomedicine is highly complex. Included in the body of laws and other regulatory instruments applicable to biomedicine are generalist consumer protection, privacy, anti-discrimination and tort laws; specific health- and technology-related laws (such as prohibitions on heritable human genome editing in some countries, including Australia); regulatory approvals laws for drugs and diagnostics and for genetic modifications; intellectual property laws; internationally recognized good practice standards; professional and research guidelines; and more.

The safety of genome editing is currently assessed through clinical trials. We have by now all seen that in some circumstances the safety of a particular treatment can be assessed quite quickly (the prime example being the speed with which COVID vaccines were assessed and approved). Usually, however, the process is far more slow, and can take many years. The average time for assessment of a new drug, for example, is usually around 10 to 12 years.

In Australia, any goods that are being used for therapeutic purposes have to be listed on the Australian Register for Therapeutic Goods, unless they are explicitly exempted from this requirement. The Therapeutic Goods Administration administers this system of regulation, through the *Therapeutic Goods Act 1989* (Cth). Before any product can successfully be listed on the Register, the sponsors of the product need to show that it is clinically safe, effective and useful. They do this through a series of clinical trials:

- Pre clinical trials are carried out in animals or cell cultures to test if the product holds any therapeutic benefit.
- Phase 1 trials involve a small number of participants to test for safety, pharmacological activity and side effects
- Phase 2 trials involve a small group of participants (100-200 with the disorder to be treated to assess efficacy and safety and establish appropriate dosing regime.
- Phase 3 trials are extended, often multi-centre trials to assess comparative efficacy, clinical benefit and whether the risk of adverse effects is at an acceptable level.

Clinical trials are expensive, and many products do not make it through all phases. Phase 3 trials are particularly expensive, given that they require many participants. Generally, only large pharmaceutical firms have the financial resources to invest in Phase 3 trials, and they tend to make sure their investment is protected by patents. Currently, there are around 35 or so clinical trials for gene editing products relating to blood-borne diseases (including sickle cell disease, mentioned above), neurological diseases, cancers and other conditions.

The cost of taking each genome edited product through these research and clinical trials phases is considerable, many millions of dollars, and this cost needs to be recovered in the price of the clinical product. As a result, unless there is government support the price of the clinical product makes it out of reach for most people. Issues of justice, equity and access become profound in such circumstances.

The Australian government provides support for access to healthcare through the Pharmaceutical Benefits Scheme and the Medicare Benefits Scheme. However, the public purse is not big enough to support all innovative treatment options. As a consequence, it may take many years before they are included on the PBS (if at all). Governments around the world are recognising the need to include principles of public participation, accountability and transparency in their healthcare decision-making, to ensure there is public trust in the whole process. However, calls are being made for even greater emphasis on new forms of democratic decision-making, with particular focus on public participation. Given the benefits and risks of genome editing, consideration of new models of regulation seems particularly apt in this context.

A.4.2. Heritable Human Genome Editing

At the very least, the regulatory regime outlined above for non-heritable human genome editing would also apply in the context of heritable human genome editing. However, heritable human genome editing raises different types of questions and is governed by additional laws which are more prohibitory in nature. These questions are not so much about how genome editing should be undertaken, but whether it should be undertaken at all. The prospect of eliminating some of the most pernicious genetic diseases through heritable human genome editing has much appeal. Indeed, an argument could be made that there is an ethical duty to pursue heritable human genome editing to alleviate human suffering. However, apart from current concerns about the safety of heritable human genome editing for offspring and future generations, there are significant ethical concerns that weigh against its adoption.

Without attempting to be comprehensive, some of the most commonly raised ethical concerns associated with heritable human genome editing (and research involving human embryos) include: the impossibility of securing consent from those most affected by the intervention (offspring and future generations); the notion that these human-made interventions are akin to 'playing God'; interventions undertaken for therapeutic purposes will open the door to 'designer babies'; and any interventions involving human embryos fails to recognise their moral status as human beings. The moral status of the embryo is the dominant concern for people of certain religious affiliations. However, ethical opposition to heritable human genome editing is of both religious and secular foundation. If heritable human genome editing is ever to become a reality, it will be necessary to find some middle ground between these conflicting ethical considerations.

At this point in time, no country in the world has laws or other regulations that clearly allow heritable human genome editing. There are some countries that do not have any relevant laws or other regulations, but as a general rule these countries do not have the technical capacity to perform heritable human genome editing. Still, there is always a risk that it could be performed in places in the world where it is not clearly prohibited. In 2018, it was announced that a Chinese scientist had performed heritable human genome editing on a small number of human embryos using CRISPR. From media reports, it appears that three children may have been born as a result. It sparked worldwide controversy and, according to media reports, led to the imprisonment of the scientist, on the basis of medical malpractice.

Many countries, including China, have laws or other forms of regulation that prohibits or deters the practice of heritable human genome editing. Australia has one of the most robust forms of regulation; heritable human genome editing is clearly prohibited by section 15 of the *Prohibition of Human Cloning for Reproduction Act 2002*, which states it is a criminal offence to make heritable changes to the human genome. The penalty for committing the offence is 15 years imprisonment. If heritable human genome editing were ever to be considered ethically and socially acceptable in Australia, this law would need to be reformed. This legislation came about in 2002 because of increasing concerns that it might be possible at some stage in the future to clone a human being, following the birth of Dolly, the world's first cloned sheep. This legislation prohibits the use of cloning for reproductive purposes, but also prohibits a number of other interventions in human reproduction.

A.4.3. Genome Editing Research Involving Human Embryos

As mentioned earlier in this report, if heritable human genome editing is ever to become a reality, a great deal more research will need to be undertaken, including research involving human embryos. Recognising that any research involving human participants raises issues associated with autonomy, beneficence, nonmaleficence and justice, most countries have a system for ethical review and monitoring that research. In Australia, for example, the National Health and Medical Research Council (NHMRC) is responsible for administering the ethics review system for research involving humans. The National Statement on Ethical Conduct in Human Research (the National Statement) provides guidance that all researchers are required to follow.

Every institution where human research is conducted must have a Human Research Ethics Committee (HREC), whose task it is to review and approve applications for research involving humans and monitor progress of the research, guided by the National Statement. Each institution, hospital or company in which human research is conducted must have access to a HREC that is properly constituted under the National Statement. Before any research involving humans is undertaken, the HREC must approve the research. The National Statement also provides guidance on the conduct of clinical trials.

Research involving human embryos involves an additional layer of regulation under the *Research involving Human Embryos Act 2002*. This Act was enacted in parallel with the *Prohibition of Human Cloning for Reproduction Act 2002*. At around the same time that Dolly the sheep was being created, other researchers were undertaking research to explore the extent to which human embryonic stem cells might be used to treat disease. This research was starting to show real promise, but because the creation of human embryonic stem cell lines involved the use of human embryos, it was also ethically controversial. The aim of the Research involving Human Embryos Act 2002 was to strike a balance, allowing limited research using human embryos in a strictly regulated and monitored environment. The Act prohibits any use of human embryos in research unless they are:

- Unsuitable for implantation in a woman; or
- Excess to the artificial reproductive technology needs of the man and woman who created them; or
- Created using a process other than fertilization.

A licence from the NHMRC's Embryo Research Licensing Committee is required for use of any of these types of embryos for research and training purposes. The research itself is overseen by HRECs under the National Statement.

Attention must also be drawn to section 12 of the *Prohibition of Human Cloning for Reproduction Act 2002*, which makes it an offence to create embryos by fertilisation for purposes other than to achieve a pregnancy, with a penalty of up to 15 years in prison. This means that embryos cannot be created specifically for the purpose of genome editing research in Australia.

Although it may be possible for a licence to be issued for use of any of the three types of embryos listed above for research, this would not allow the type of genome editing research that would be particularly useful in advancing the field, that is, research that involves genome editing in a germline cell (gametes or zygotes) and development of the embryo. Whatever the circumstances in which a licence for research is issued, there is an absolute prohibition on extending research beyond 14 days post-fertilisation, after which research must cease because it marks the time when the embryo starts to develop the nervous system, heart and other organs.

Like Australia, many countries other in the world do not allow embryos to be created for research purposes. The UK is one country that takes a more liberal attitude, but even there, creation of embryos for research is very strictly controlled and licences are only provided to a small number of laboratories doing world class research. In 2016, the UK Human Fertilisation and Embryology Authority granted the first authorisation for CRISPR-based genome editing on human embryos to Kathy Niakan at the Francis Crick Institute in London, provided that the embryos were destroyed 7

days after the experiments and not implanted in humans. Important findings are already emerging from this research. For example, it has been shown that in some instances the changes resulting from application of the CRISPR technique are not always as precise as intended. These findings illustrate why it is important to be able to undertake research if the long-term goal is to allow some form of HHGE.

A.4.4. Other Forms Of Artificial Reproductive Technology

There is a variety of types of legislation relating to artificial reproductive technology in Australia, because this area of regulation is a matter for the states and territories. The state of Victoria was the first place globally to enact specific artificial reproductive technology legislation, in the form of the *Infertility (Medical Procedures) Act 1984*. This Act imposed a strict system of regulation based on criminal penalties. South Australia, Western Australia, and New South Wales also have their own legislation. The Northern Territory requires clinics to comply with South Australian legislation.

In addition, the NHMRC has ethical guidelines on the use of artificial reproductive technology in clinical practice and research. There is also a self-regulatory process of accreditation of artificial reproductive technology clinics through the Code of Conduct of the Fertility Society of Australia's Reproductive Technology Accreditation Council. In addition to other matters, accreditation requires is dependent on compliance with the NHMRC ethical guidelines.

As mentioned earlier in this report, mitochondrial donation offers the possibility for a woman afflicted by mitochondrial disease to give birth to a child without the disease, because the mother's mitochondria are replaced with the mitochondria from an egg of another woman. This raises what are now familiar ethical issues associated with the rights of the child and future generations and the status of the human embryo; as well as issues associated with the interests of the donor and community considerations, amongst others. It should be noted that the law in Australia currently prohibits mitochondrial donation, as it involves making heritable changes to the human genome which is a criminal offence.

In 2019 the Australian government asked the NHMRC to undertake a public engagement process to better understand community concerns about mitochondrial donation. The community engagement process was undertaken in 2019 and 2020, and included a citizens' panel, webinars, a call for written submissions, public forums and a targeted roundtable event with invited stakeholder groups. Equity of access and consequences for the child born following mitochondrial donation appeared to be particularly prominent concerns. Although there was no clear direction from the community engagement process endorsing changes to the law, the severity of the disease and the promise that mitochondrial donation could alleviate suffering caused by the disease were widely acknowledged.

Following the community engagement, the Australian government introduced legislation into Parliament seeking to create a regulatory framework allowing mitochondrial donation to proceed, but only with strict oversight. The *Mitochondrial Donation Law Reform (Maeve's Law) Act 2022* was passed by both Houses of Parliament in early 2022. One of the key amendments is a limited exception to the criminal offence of making heritable changes to the human genome in section 15 of the *Prohibition of Human Cloning for Reproduction Act 2002* in the specific circumstance where authorisation is given by the NHMRC's Embryo Research Licensing Committee through a mitochondrial donation licence. There is also a limited exception to the criminal offence in section 12 of the Act, allowing the creation of human embryos specifically for mitochondrial donation research

purposes. Maeve's law also amends the *Research involving Human Embryos Act 2002* allowing certain mitochondrial donation techniques to be carried out in Australia under licence issued by the Embryo Research Licensing Committee. As a consequence, i is now possible to obtain a licence to undertake mitochondrial donation in Australia, only the second country in the world (after the UK) where such laws exist.

A.4.5. Future Development of Human Genome Editing — Expert Reports

In response to ongoing developments in genome editing, several national and international expert bodies have held meetings and produced reports addressing the many ethical, technical and legal questions posed by this new capability to make precise, targeted and predictable alterations to the human genome for therapeutic and other purposes.

The United States National Academies of Science, Engineering and Medicine produced one of the earliest reports considering the multifaceted ethical, legal and scientific issues raised by genome editing in 2017. The report followed an International Summit on Genome Editing held in Washington, DC in 2015. The Summit was organised jointly by the National Academies, the Chinese Academy of Sciences, and the Royal Society of the United Kingdom. The report made several detailed recommendations on genome editing. It recommended that basic laboratory research on genome editing should follow the existing regulatory pathways established with respect to other research on human cells and tissues.

For non-heritable human genome editing, the report recommended that existing ethical norms and regulatory infrastructure should be used to investigate and evaluate proposed interventions, that clinical trials be conducted strictly for the treatment or prevention of disease and disability and that regulators should carefully evaluate the risks and benefits for each intervention. The report also recommended that heritable human genome editing be permitted under 'only the most compelling circumstances' (such as where couples who want to have genetically related children cannot do so by any other means) and only with ongoing, rigorous oversight and after robust public discussion. The report also recommended against authorising clinical trials of non-heritable human genome editing or heritable human genome editing for purposes other than to treat or prevent disease or disability, indicating the need for more policy debate before enhancement-oriented applications might be permissible.

Following the 2015 International Summit on Genome Editing and the 2017 National Academies report, a Second International Summit on Human Genome Editing was held in Hong Kong in November 2018. The Organizing Committee of the Summit released a statement shortly after the close of the Summit and the revelation just prior to the start of the Summit that He Jiankui had ostensibly edited human embryos and implanted them into women, leading to live births. Perhaps surprisingly, the Committee appeared to adopt a less strict approach than the National Academies in 2017, proposing that, despite wide variability in its potential risks, HHGE 'could become acceptable in the future if these risks are addressed and if a number of additional criteria are met'. The Committee listed these criteria as 'strict independent oversight, a compelling medical need, an absence of reasonable alternatives, a plan for long-term follow-up, and attention to societal effects'. While not

making specific reference to community engagement, the Committee acknowledged that 'public acceptability will likely vary among jurisdictions, leading to differing policy responses'.

In 2020, the United States National Academies published a report on heritable human genome editing written by the International Commission on the Clinical Use of Human Germline Genome Editing, appointed following the He Jianku announcement. No doubt in part due to the widespread and ongoing shock of the scandal, the language used in report was much more circumspect than both the first report of the National Academies and the statement released by the Organising Committee of the Second Summit. The report set out strict criteria to be satisfied in advance of any initial uses of heritable human genome editing, and recommended extensive societal dialogue, noting that it is not possible to define any one responsible translational pathway due to the wide and variable possible applications of heritable genome editing.

Similar caution has been expressed in the European context. In March 2021, the European Commission and Directorate-General for Research and Innovation, through its European Group on Ethics in Science and New Technologies, published a report titled *EGE Opinion on Ethics of Genome Editing*. It acknowledged that there is '(almost) unanimous consensus' that heritable human genome editing is not safe enough for application. It made several recommendations, including the establishment of global governance initiatives, a registry for research, and the creation of a platform for information sharing.

In July 2021, the World Health Organization's Expert Advisory Committee on Developing Global Standards for Governance and Oversight on Genome Editing published a framework for governance and a set of recommendations on human genome editing. The governance framework identified a raft of ethical concerns, including principles relating to access, responsiveness, caution, broad-based participation and inclusion, fairness, social justice, non-discrimination, solidarity and global health equity. Regarding heritable human genome editing, the governance report posed questions relating to criminal and civil penalties and violations, interjurisdictional permissions, multigenerational follow-up, and so on. In general, the kinds of questions posed were rather more detailed and practical than those contemplated in previous international reports. The Committee also made a series of recommendations on the governance of human genome editing across several topics, including leadership, collaboration, research and medical travel, illegal, unethical and unsafe research, education and ethical principles.

Read together, the reports and statements of these national and international agencies lead to the conclusion that there is cautious in-principle support for heritable human genome editing, albeit only at some stage in the future, and only in limited application. In essence, then, international science policy is leaning towards future approval of heritable human genome editing in strictly limited circumstances and subject to stringent oversight. If the recommendations included in these reports are to be adopted, it will be necessary to reform the law in many jurisdictions, including Australia. What precisely should be changed, however, is not an easy question to answer. One consistent theme in all the international reports and research is that the community should be brought into this complex and difficult conversation. A broad consensus has emerged that deliberation on this important technological step should not be left only to scientists, medical practitioners, specialist government agencies or international committees. The research reported here is one of the first attempts to address the significant challenge of bringing members of the public into the genome editing debate.

Readers are directed to the World Health Organisation's governance framework report for a comprehensive list of these and other expert reports:

World Health Organization, Human Genome Editing: A Framework for Governance (2021) <https://apps.who.int/iris/handle/10665/342484>

A.5. Further literature on genome editing

There is a vast and ever-growing body of literature on genome editing. It is not possible to do justice to this literature here. As a starting point, further information on Australian regulation of genome editing and associated technologies and some of the challenges in regulating this technology is provided in following publications by Nicol and her colleagues:

Lisa Eckstein and Dianne Nicol, Gene Editing Clinical Trials Could Slip Through Australian Regulatory Cracks' (2020) 27 Journal of Law and Medicine 274-283

Dianne Nicol, Christopher Rudge, Rebecca Paxton and Simon Niemeyer,' 'How Should We Regulate Heritable Human Genome Editing in Australia?' (2022) 29 Journal of Law and Medicine 322-336

Dianne Nicol, 'CRISPR – A Challenge for National and International Regulation' in Margherita Brusa and Michael Barilan (eds) Can Precision Medicine be Personal; Can Personalized Medicine be Precise? (Oxford University Press; 2021),

Dianne Nicol, 'The Regulation of Human Germline Genome Modification in Australia. in: Andrea Boggio, Caesare Romano, and Jessica Almqvist, Human Germline Modification and the Right to Science: A Comparative Study of National Laws and Policies (Cambridge University Press; 2020), 543-576.

Dianne Nicol, et al 'Key Challenges in Bringing CRISPR-Mediated Somatic Cell Therapy into the Clinic' (2017) 9 Genome Medicine 85-88, doi.org/10.1186/s13073-017-0475-4

Jane Nielsen, Lisa Eckstein, Dianne Nicol and Cameron Stewart, 'Integrating Public Participation, Transparency and Accountability into Governance of Marketing Authorisation for Genome Editing Products' (2021) 3 Frontiers of Political Science Article 747838 doi: 10.3389/fpos.2021.747838

Tess Whitton, Dianne Nicol and Don Chalmers, 'Human Embryos, Genome Editing and Future Directions' In Ian Freckelton and Kerry Petersen (Eds), Tensions and Traumas in Health Law (Sydney: The Federation Press; 2017) Chapter 21, pp384-400

APPENDIX B.
IDENTIFYING GENOME EDITING ISSUES THROUGH EXPERT INTERVIEWS

As indicated in Section 2 of this report, a broad range of issues were identified from expert interviews. In this Appendix, each of these issues is canvassed more fully. Christopher Rudge was the primary author of this appendix.

B.1. Heritable human genome editing

B.1.1. It is unlikely that heritable human genome editing will be the major application of genome editing technology into the future

Some experts noted that heritable human genome editing is the least likely of all genome editing technologies to be used. One noted that there is a 'perfect inverse of panic and actual [prospective] use,' and highlighted the paradox that, although it is unlikely to ever be used at all, it has 'got more people upset about interfering with the evolution of the human species' than any other modern medical intervention. Similarly, another expert noted that HE is technically not possible, and that to debate the merits or demerits of the science is folly and the discussion should be 'closed' until that changes.

B.1.2. There is much more research work needing to be done before heritable human genome editing could be considered to be safe and effective

Many experts noted that the science is in a very early stage of development and that more research will be necessary if and before heritable human genome editing will be deployed in a therapeutic setting. One expert noted that heritable human genome editing, if it is possible at all, is extremely primitive, and that much more research would be needed before it was administrable in the clinic. Similarly, again, a different expert noted that heritable human genome editing would never be 'easy' to administer in any medical setting. This expert compared the human body to a city and referred to human genome editing as a process of 'fixing potholes,' illustrating the very limited and small-scale ways in which it might be used therapeutically.

Similarly, some experts, in contemplating the question of what to focus on in the citizens' jury, noted that heritable human genome editing should not be the focus. This was because the complex questions of 'heritability' and 'germline editing' were too remote from reality at the moment (that is, they were too unlikely to be realised in the foreseeable future). One expert felt that these issues could therefore take up an outsized or disproportionate amount of attention in discussions and detract from more pressing concerns. Even those experts who identified the rapid improvements in base editing (the introduction of single nucleotide variants without inducing double-strand breaks) or PRIME editing ('search-and-replace' editing) conceded that heritable human genome editing is not yet well-enough established to be understood as a plausible, or lawfully permissible, therapeutic technique.

By contrast, one expert suggested that heritable human genome editing was not as novel as made out. For instance, one expert noted that heritable human genome editing is actually only a 'minor adaption' of other technologies in the field of genetic modification and that the events that occurred in China (involving the experimental and unlawful intervention administered by He Jiankui) were not surprising in the context of the emergent development of gene editing capabilities.

Finally, one expert noted that there was currently very little clinical need for heritable human genome editing. However, this expert noted that there were rare circumstances that may call for heritable human genome editing. For example, where two patients with sickle-cell disorder sought to reproduce and wished to

B.1.3. The distinction between heritable human genome editing and non-heritable human genome editing may be less clear-cut than previously thought

A small number of experts questioned the clear-cut distinction between heritable human genome editing and non-heritable human genome editing. One expert noted that non-heritable human genome editing will be far more complicated than simply 'taking medicine' and will, like heritable human genome editing, involve complicated intervention. Another expert suggested that the distinction often drawn between heritable human genome editing and non-heritable human genome editing could have been a 'strategic move' on the part of those seeking to associate non-heritable human genome editing with safety and reliability and heritable human genome editing with danger (to make the latter seem 'really, really dodgy'). Another similarly noted that the effect of the distinction might be to draw focus away from the dangers and risks of non-heritable human genome editing, as well as to indicate that they are 'ethically unproblematic.'

B.1.4. Questions remain about the legal status of some forms of heritable human genome editing, and more questions may yet emerge

One expert noted the philosophical and legal ambiguity related to 'heritability.' As the expert asked, if there is no intention that a modification of the human genome will be inherited because it is intended to be made only to an embryo that is used for research purposes only and then discarded, would this constitute a 'heritable' change? This expert compared the situation in the United Kingdom to that in Australia. In doing so, they asked the following:

> Could we do what [they are] doing in England in Australia? There are two ways to interpret the legislation: one in which it is still clearly you cannot do it in Australia because when you're making a germline edit to an embryo you are potentially intending to make a heritable change to that embryo, because all [the] changes are heritable... The second interpretation... would say [that] research involving an embryo destined for disposal is not intended to result in any descendants ... and therefore I am not intending to make any heritable changes because I'm not intending [for there] to be anyone [for those changes] to be inherited by.

Despite the Australian legal question raised by this one expert, many other experts commented more generally on the legal issues that emerged from the controversial case of Dr He Jiankui, who announced that he had altered the CCR5 gene in twin girls in November 2018, was imprisoned in December 2019, but was reportedly released from custody in April 2022.

Various experts noted that the case of Jiankui has been 'unhelpful' because it suggested he was a 'bad apple' and allowed the scientific community to distinguish its own actions from that of this single individual. Another expert noted that the Jiankui case was characterised by 'reactionism' and there had not been enough reflection on whether 'we should regulate or respond differently.'

B.1.5. the future of heritable human genome editing is super-personalised medicine

One expert proposed that, ultimately, and perhaps in a distant future, heritable human genome editing would constitute a super-personalised form of medicine that would involve multiple edits and modifications depending on the risks and mutations discovered in a pre-implantation genetic test. As the expert stated, any person wishing to conceive could undergo a genetic screening test to determine the kinds of genome modifications that might be appropriate in the circumstances:

> They [the potential parents] have the lymphocytes, their blood taken, they have a relative's DNA taken. They have an entire case work which is made up around just those two and their offspring. Their potential for that mutation in their embryos, then each of their embryos are dealt with. So for their particular mutation, the primers are designed and that is one case, [then] on a case by case basis, you could have success very easily. Just to be able to target and adapt and create by design tools a molecular workup for them. I think that is where I think it needs to start: on individual cases.

In describing this potential future of personalised medicine, the expert highlighted the conditional legalisation of mitochondrial replacement techniques in the UK (and, as of March 2022, Australia). They suggested that, as the effect of legalising mitochondrial donation was to effectively allow one form of genome modification, then the argument for correcting the mutation is stronger. As they stated,

> After all, in the UK we have allowed transgenerational genetic alteration, per se, with mitochondrial replacement therapies (MRT) and that, to me, looks like an example of a technology, which after all that debate and deliberation [allows us to say] we should just mutate them or correct the mutation in the mitochondrial genome. Maybe we don't need to swap around nuclei. Maybe we don't need a donor egg, after all.

B.1.6. Reproductive rights should remain the same, and depend on the development of the law

All experts bar one expressed a view that using genome editing to create pregnancies or to reproduce should and would be prohibited until the law was changed and the global moratorium, which is only normative and has really only been advocated, is normatively relaxed. One expert, however, advocated for the rights of the individual to choose what they do with their body, including to make changes capable of being inherited by their offspring. As this expert asserted,

> ... it's not my business if someone wants to do something that does not affect me. I can't comment on that. It might be passive smoking someone nearby or it might be, it might be polluting a river or the atmosphere, climate, but if someone just wants in their own reproductive life to do something, I sort of feel that's not [okay]. We have a society, there are parts of society that believe in interfering in other people's reproductive rights, and I can understand why they have that view; there's a particular time in history. But I don't really have that view.

B.2. Somatic cell genome editing (non-heritable human genome editing)

B.2.1. Somatic cell genome editing (administered to humans post-natal) is a promising and practical intervention

Respondents were generally supportive of non- heritable human genome editing, which was described in the interviews as somatic cell genome editing, with many encouraging its use and expressing excitement about human clinical trials involving the administration of CRISPR constructs to patients (through hematopoietic stem progenitor cells). One expert noted that the results of these trials "are pretty amazing" even where "only a half dozen people around the world [in] total had been clinically trialled. One responded expressed excitement: 'taking someone's cells, editing them and putting them back [is] miraculous... [and] these people with sickle cell are getting cured... I just want to jump up and, like, it's incredible; that is incredible.'

Many experts emphasised the fact that somatic cell genome editing applications were being developed at this very moment and showed great clinical promise. As one expert pointed out, 'Studies

in humans are taking place right now in the clinic. [They are] actively injecting patients with CRISPR constructs and [while] the cohort is extraordinarily small (we're talking like a half dozen people around the world total) … the results of these "n of 6… are pretty amazing." It is happening just as quickly as people have hoped and imagined.'

Some respondents stated that the regulatory frameworks operative in the US and EU for somatic cell genome editing were already sufficient, especially given that the ethical questions and controversies for somatic cell genome editing were far fewer and less substantive than those related to heritable human genome editing.

B.2.2. Somatic cell genome editing might pose different ethical issues when administered to children

Several experts discussed the ethical issues raised by the application of somatic cell genome editing to children. One expert noted that medical practitioners, for existing cancer treatments, do not like to perform myeloablation treatments on of children and prefer to perform them on adults. However, as this expert noted, adults have "accumulated a lot of damage by that time and, accordingly, 'there's an argument that you should do it as early as possible.' As this expert noted, however, one of the problems with performing any intense treatment on children is that the practitioner will ordinarily need to 'obtain parental consent and [be] very cautious about doing anything on infants.'

Another expert offered similar comments. They spoke of the problem of determining consent to the treatment in cases where it was administered to children. This was made more problematic, they noted, where serious interventions involving immune system suppression (through cell ablation drugs) might be dangerous and may turn out to be unnecessary in some less severe forms of disease. As this expert stated:

> I think from an ethical perspective, I think it comes down again to what are the risks of what you're doing, how sure you are, and what is the risk of the overarching disorder, [and] what are we trying to correct? And, again, my fear is that you don't really know the risks… and you have parents who are very concerned about something that would obviously have some negative impact on their child but may not have the same kind of outcome [as they predict].

By contrast, another expert noted that the consent issues for somatic cell genome editing in adults were more straightforward because the adult has legal capacity and can make a reasoned decision about the medical procedure being proposed. However, as this expert also noted, there may be difficulties obtaining informed consent in circumstances where the information held about the treatment is either partial or incomplete, or unknown to be partial or incomplete. As this expert stated:

> [B]ecause you have an adult who is aware of their condition and is aware of the effect of their condition on their body and their ability to function, … I think the biggest legal issues there are: 'Do we have enough information to give them adequate informed consent?' Do we even know? I mean, this has been a particular issue.

Many experts underlined the efficacy and safety of somatic cell genome editing for specific diseases. Most such experts expressed excitement for the use of somatic cell genome editing for hemoglobinopathies such as beta thalassemia and sickle cell anaemia. In expressing their views about the likelihood that this treatment would turn out to prove safe and efficacious, they emphasised the reliability and epistemic certainty of the scientific evidence of somatic cell genome editing, primarily for hemoglobinopathies. As one expert noted, the treatment targets an 'erythroid-specific enhancer for [the] BC11A [gene], which is the repressor [for foetal haemoglobin].' As they continued, 'We know there are variants of that type in humans [and] we know that CRISPR is making those types of variants.

And it happens just as we would expect it to.' The same expert explained this position in very affirmative language: 'Every data point confirms the efficacy and safety of somatic cell genome editing; the science is very clear and the mechanisms are very clear.'

B.2.3. Whether somatic cell genome editing is harmful or sufficiently safe is uncertain

There were differing views among experts about the safety of somatic cell genome editing. Some respondents cautioned against the use of somatic cell genome editing as a health intervention except where it constituted a 'complete' cure. As one expert warned: 'If we keep people alive who have these genetic disorders, and then they become reliant on these [genome] therapies... this population ... becomes increasingly reliant on technologies, which might be a bad thing.'

A different expert identified the possibility that multiple somatic cell genome editing interventions might cause harm due to the need for patients to undergo immune suppression therapy (myeloablation) in order to receive new and edited blood cells via a bone marrow transplant. As they stated,

> the risks of somatic gene therapy are high. A bone marrow transplant is not a trivial medical procedure, and if you had to do that, generation after generation after generation, the risk and the harm you could cause would be arguably more than doing it once.

By contrast, another expert expressed a view that any potential DNA damage – a ***different kind of harm*** to that described above relating to bone marrow transplants – could be eliminated. As this expert noted, if the method involved 'base editing,' which involves the introduction of point mutations without the need to generate double strand breaks, then the treatment would not any damage. In these comments, the expert cited the view of George Church, who is often quotes as having described genome editing as 'genetic vandalism.' As the expert said: 'somatic cell genome editing is actually damageless when you swap out the base pairs; it is not, as George Church says, 'genome vandalism,' because actual base editing is where the phosphate backbone of the DNA molecule is broken down, and individual nucleotides are swapped.' This process, the expert emphasised, did not involve any damage to the DNA and was therefore harmless.

A different expert advanced a view that any decision to administer somatic cell genome editing should depend on the nature of the disease and whether the phenotype, or pathological symptoms of the genetic disease, is sever enough to justify the intervention. As they noted, one could imagine a 'sliding scale' that ranged from 'the disastrous (terminal cancers and the devastating childhood onset incurable rare diseases, where you know the cost benefit ratio is a lot clearer) through to modifying traits.' Ultimately, this expert suggested that somatic cell genome editing should be used only for 'very severe phenotypes.'

B.2.4. Rare diseases and very severe diseases could make the risk/benefit calculus for somatic cell genome editing acceptable

A small but resolute group of experts acknowledged that, while somatic cell genome editing might pose a risk, the potential benefits outweighed the risks where the target disease was very serious or rare, and where few other treatments were available. One expert noted that 'if you have a child with Tay Sachs or cystic fibrosis... people would give a lot to be able to make that edit.'

In a similar manner, another expert noted that where the probability of mortality was high, then the treatment would be justified, even if the treatment created 'off-target' effects: that is, unwanted

events, such as large deletions, rearrangements, or translocations of genes. While off-target effects would certainly be damaging and could result in genotoxicity and other adverse responses, one expert noted that, in 'life-or-death' situations, such negative outcomes might be preferable to a loss of life. As this expert stated:

> So even if you have some additional mutations and even if, in some cases it could raise a new tumour as you treat a life-threatening disease, what you want to do is to save the patient first and then you will cope with what happened [later]. Because if the patient dies, you have no more to do. So, it's clear that the balance benefit risk ... is better than nothing. And if you are not trying this, the patient is going to die.

However, this same expert characterised the treatment as a 'black box,' highlighting the epistemic uncertainty associated with the treatment at the present time. As they stated:

> ... We need to remind [ourselves] always that when we are making genome editing, it is an incredible black box. We are able to very precisely make the cut ... but we are absolutely ignorant of what is happening then with the DNA repair machinery. And a lot of effort are [being made] to control the targeting and the way the repair machinery works but, at the same time, it remains a black box.

Another expert view of CRISPR-Cas9-facilitated genome treatments was directed towards identifying the different risks that might arise with administering the treatment to different parts of the body. As this expert noted, using CRISPR-based therapies "on the back of the eye, [where there is a] very small number of cells on the retina [is a good option] because you can get to them, and that's okay.' Similarly, as this expert noted, some neurological disorders where the cells 'are baked into the brain' so that they are hermetically encased or quarantined from the surrounding organs may ultimately prove effective. Having said that, this same expert ultimately concluded that it would remain likely that these treatments would be used mostly for genetic disorders of the blood and immune system: 'blood and immune system will be disproportionately prominent in the CRISPR world,' they stated.

B.2.5. In utero somatic cell editing is problematic, dangerous

A small range of experts commented on the possibility of editing somatic cells in utero, which is sometimes known a foetal genome editing. While this treatment option is hypothetical and speculative only, it raises the possibility of treating genetic disorders or diseases after conception and fertilisation but before birth.

All of these experts expressed a view that in utero somatic cell genome editing was unlikely to become a viable treatment in the short or medium term. One expert commented on the political and bioethical questions that could be raised in circumstances where a termination of the pregnancy might depend on the success or failure of the intervention. As this expert noted,

> In utero is going to be very interesting, but it has a host of problems because by the time you diagnose a problem and then construct the intervention, we're well into the second trimester. And so now the politics of the legality issues around abortion are going to be front and centre... the uncertainties around the foetus are still vast and if something goes wrong, then you're looking at having a very late termination as an option, which again is going to raise all kinds of questions.

A different expert described the specific biological risks and genetic dangers associated with administering a genome editing intervention to a developing organism in utero. As they noted,

> Regarding foetal editing [and gene editing in early infants], the degree of uncertainty is just magnified because you're talking about a time period where there are so many developmental

> events going on. There are so many alterations in gene expression profiles that are just dynamically occurring and so an, off target effects in an set of mature cells may be very different to an off target in a setting of a rapidly evolving developmental process.... But I just think the technicalities around that [create] several orders of magnitude of [more] uncertainty.

In a different vein in relation to in utero somatic cell genome editing, another expert noted that where an intervention was proposed to a foetus, then the pregnant person's health could also be at risk. For this reason, they suggest that any attempt to edit the genome of a new organism should occur outside the body: that is, where assisted reproductive technology is used and the egg and sperm are fertilised in vitro. As the expert noted:

> If you're performing the edits while the embryo is in her body, [you] have to perform the fetal manipulation in her uterus. So this increases the risk profile and the likelihood of complications. It would be preferable... to do [the treatment] in the in vitro stage, rather than in [that] future [ie, later] stage.

B.2.6. Economic inequality will pose a significant problem for genome editing treatments

Almost all experts agreed that economic inequality will have a major impact on the way in which genome editing technologies are made accessible and by whom they are used. One expert asked a rhetorical question:

> how do we deal with the problem of the exacerbation of inequities if you're developing a technology that's going to be widespread but still limited to one class? Or one part of the planet that has these kinds of [health and laboratory] facilities?

Other commented on the cost of gene therapies, noting that one current therapy, Zolegensma, costs some 2 million US dollars (and, as at the time of writing this report, a new gene therapy called Hemgenix, has been brought to market by CSL Behring at 3.5 million US dollars]. In this context, several experts posed questions about the cost of genome editing. As on expert noted,

> So then the issues become: Who can access this [and] how much does it cost? If you can get around that. I mean, it seems like the consent issues are pretty straightforward in the adult case. But then you want to look at if you're doing this on a societal level; Who's paying for this?

A different expert suggested that the prohibitive cost of some treatments may prevent genome editing treatments from becoming a standard or normative treatment, which may also slow down research and development. They also alluded to the prospect of harmonised price regulation across different jurisdictions (which could be achieved, theoretically, through an international trade agreement):

> I think the cost of it will push it from becoming a norm and I think that's great and fine. I think having regulations within countries and having – if you're not going to have global agreements, which would be great, but – having many countries coming together – groups and collectives of countries coming together – I think is also very positive.

Other experts understood the nature of these treatments, which are highly personalised, as contributing to their expensiveness. They are 'going to be expensive,' they noted, because 'individualized medicine – cancer therapies, modified cells... CAR-T – are higher than other medicines'

Another aspect raised in relation to the health economics of genome editing was based on resources. As one expert noted, 'the science is everywhere but resources are not.' In other words, there is knowledge about what is possible, and what has been discovered; however, there is not enough

money or material resources to enable that knowledge to be translated into practice in most parts of the world. Speaking of the city in which they reside, the expert continued that,

> In [my city], we're not curing malaria, because it's just not really an issue... But there was an issue or concern about Eastern equine encephalitis; there's some occasional cases [of that disease] and so we're spraying for mosquitoes... [But] there are so many places in the world where [malaria] is such a huge problem... and those people have to have access to the same tools as we do in [my city].

Many experts described the risk that the countries or populations who might most need access to genome editing therapies would be precisely those who were the last or least likely to have such access. Several experts referenced the importance of developing somatic cell genome editing interventions, such as CTX001 (manufactured by Vertex Pharmaceutical and currently in clinical trial) for sickle-cell disease, for patient populations in sub-Saharan Africa, where sickle-cell disorder is extremely prevalent. In this regard, one expert said 'If the interventions work, and perhaps it's a pipe dream. But if they work, are they made affordable in the US, and would they be made affordable in Africa?' The same expert noted that some charitable organisations, such as the Bill and Melinda Gates Foundation, have 'announced a funding drive... targeted at genome editing, somatic genome editing and HIV and SCD [sickle cell disease] for 100 million dollars for a couple of years, both for intervention and delivery.' As this expert noted, there

> is a concern that these interventions, [if] this research will take place in Africa (because this is where the burden of disease is largely), but that these innovations will be owned by [and] controlled by institutions in the Global North... that have no incentive in making these things available in a way that is cost effective or affordable.

Only one expert of the entire participant group expressed a different view in relation to the economic equality and access question. That expert refuted the argument that genome editing interventions will only be for the wealthy, describing it as 'not a strong argument.' They asserted that if this were the case, then 'this would apply to all medical technologies when, instead, economies of scale take over and things are improved [over time.]'

In contrast, another expert noted (not strictly in relation to economic equity), that it could be difficult to 'scale-up' somatic cell genome editing, however, because they depended on the patients' own cells being edited. Thus 'super-personalised,' genome editing using the patients' own cells might remain expensive by virtue of the fact that, unlike a pharmaceutical drug, there is an inability to reproduce the medical intervention.

B.2.7. Jurisdiction shopping, 'genome editing tourism' and 'ethics dumping' are all likely to occur

Several experts predicted that differences in the way genome editing is and will be regulated will contribute to the likelihood that several ethical problems arising, including: jurisdiction shopping or genome editing tourism, where patients travel to more permissive counties to seek treatment; and ethics dumping, where developed or privileged countries (that are usually highly regulated) 'export' unethical experiments or clinical trials to less developed counties where ethical standards are lower and less oversight prevails.

As one expert noted,

> [There] are some countries that have strong regulatory regimes that prevent certain kinds of interventions from being tested, [and] researchers will go and find researchers or companies [in] other countries where [genome editing interventions] are not regulated and use those gaps to do research [or] to offer treatments that wouldn't be ethical or permissible in other countries.

As this same expert continued,

> We know that some ethics committees in Panama, for instance, have been asked to approve gene therapies or gene therapy research that wouldn't be allowed in the United States or in Europe. [So there are] concerns... around gene drive work that is happening Burkina Faso as well. Why Burkina? You know if the South African government didn't want this and South Africa has a strong... regulatory [system]—we have a lot of faults but we're not Burkina Faso [where] there's very little in terms of regulatory development. [And so a] second concern is how do we equip countries... to have sufficient regulation so that they don't become an easy target for research that is considered unethical elsewhere.'

While this expert's advertences to 'gene drives' are beyond the scope of this study, their concerns regarding the risks of genome editing tourism and ethics dumping apply with equal force to genome editing generally. By way of background, gene drives are a way to reduce or eliminate insect-borne diseases by propagating (or 'driving') a particular gene or set of genes throughout an insect population.

B.3. The complexities of research involving human embryos

Only five experts commented on the practice in which the use of (potentially heritable) genome editing could be administered to embryos that were created 'surplus' to assistive reproductive technology strictly for research purposes on the condition that the embryo was strictly disposed of within 14 days of its creation and not implanted for reproduction. Among those five experts, there was broad agreement that such research-directed editing was, it strictly controlled and regulated, acceptable and permissible.

As one noted,

> Using CRISPR for research on human embryos is acceptable and we should do what is done in Belgium, where they create embryos specifically for research purposes and where they are attributed the status of "artifacts." They must use them only for research and must stop after 14 days, as in the UK... There's discussion of extending that period in the UK.

Another expert expressed similar sentiments; however, they noted that using CRISPR for research on human embryos (that is, excess embryos created for artificial reproductive purposes) should be carefully managed. It should be 'carefully designed [and] the embryos should be minimalised [and] the aim should never be to transfer or implant them in [human] bodies.' Another expert noted that Japan was taking steps to reform its regulations relating to research-based embryo genome editing and suggested a similarly permissive approach could be adopted in other countries, including Australia.

However, in contrast to the above, three of these experts spoke more generally about the potential to apply genome editing in the embryo stage. One expert noted that too little is known about embryo implantation to justify it as this time. Regarding embryo implantation, they said the following:

> So I think there's two big parts to that, you know, there's the embryo research that's not specifically to implant an embryo and, you know, to some degree personally I don't have a massive issue with it. To implant an embryo at the stage where we have such limited knowledge, even in an ex-vivo sitting, I think it's real tiger country. So, not a fan. The risk benefit is just... it's not there [yet].

Another similarly identified the risks of attempting to edit the genome of an embryo, noting that, while there is not a lot of promise, 'the "specificity" is not there, with off target effects... so there is more momentum around base editors at the moment.' A third highlighted the ethical threats: 'the ethics are concerning because the risks of harm [are] too high.'

B.4. Genome editing for diagnostic purposes

A number of experts identified the specific potential for CRISPR-based endonucleases to be used for diagnostic purposes. Given that the interviews occurred during COVID-19, many of the experts were familiar with a protocol that had been developed (or proposed) to enable CRISPR endonucleases to diagnose SARS-CoV-2.

For diagnosing SARS-CoV-2, the CRISPR endonuclease is guided by a special guide or template RNA (just as in genome editing generally); however, rather than repair a double strand break in DNA, the RNA is designed as a complementary match to the target RNA sequence that it wants to identify (eg, 20 RNA base pairs long). When the RNA template binds to the RNA target, the CRISPR-Cas13 endonuclease then uses the cas13 scissors to cut the nearby single-stranded RNA. The cuts then release a fluorescent particle that has been inserted into the test solution, and when that sample is put under laser light, the fluroscent chemical illuminates, which indicates the presence of the virus. However, these tests also required RNA amplification, and this adds considerable cost and complexity, including through the use of added chemicals.

In relation to such diagnostic method of using CRISPR in human patients, several experts commented. One expert noted that this editing machinery has had 'a massive impact in the diagnostic space.' This was, they suggested, because other uses of CRISPR editing tools were not possible due to regulatory and cost burdens. As they noted,

> I think it's coming in; you see things sort of trickling out, and we've been through this before with TALENS. I mean: this is better, this is less off-target... We didn't see a massive explosion of ... (well, we did sort of see a massive explosion of research), but in terms of products and access to those products, not so much. Again, it comes down to its regulation: it's pricing, it's all those sorts of things.

Another expert who compared therapeutic and diagnostic uses of CRISPR highlighted that the latter was having the 'greater impact' of the two. As they noted, this has been useful for for 'proving or disproving variance and then using that to inform potential therapies.' They noted that a diagnostic use of CRISPR was a 'very safe non-controversial use of the technology [and so] the biggest impact will be that; and scaling it and [making] it cheaper to scale up and use it.'

Many of the experts referred to the precise, quick and inexpensive way in which CRISPR diagnostics could work and spoke effusively about the way in which it had the potential to easily 'slot into' existing diagnostic programs and 'change the way we operate and screen for disease.'

B.5. CRISPR-based genome editing for research generally

Several experts expressed concerns about unlicensed or unapproved research outside the clinical trial setting. For instance, several experts identified biohacking as a concern, especially where materials purchased online were not being registered or recorded through a repository but were instead sourced through private channels. As one expert noted, the 'sequences of the plasmids may be unavailable [and] the quality control may be non-existent.'

Other experts were effusive about CRISPR's general research potential. Another noted that CRISPR was faster and cheaper than non-CRISPR technologies in many applications, including for studying brain organoids to do functional mapping. As the expert noted, 'while researchers may ask "Which gene pathways contribute to a specific form of neuronal development?" CRISPR has [meant] that this gets answered in a year instead of in decades.'

Another expert spoke of the potential for CRISPR to aid in disease modelling, including animal modelling of human diseases, as well as drug discovery (and specifically vaccine discovery).

B.6. The Australian Citizens' Jury

B.6.1. The Australian Citizens' Jury should inform and educate participants in pursuance of obtaining clear-minded public views

Many experts expressed enthusiasm for the citizens' jury and freely offered guidance as to how it should be designed and implemented.

All experts were in favour of 'the public' – that is, lay citizens who are not scientists – expressing their views about where ethical and legal lines should be drawn in relation to genome editing. One expert expressed a strong view that such decisions 'should not be left to committees.'

Others emphasised the methodological and design aspects of the citizens' jury. One noted that 'the focus should be on establishing different, useful ways of presenting the information so you can tease out the philosophical dilemmas.' Another expert suggested that the citizen's jury should 'explain through illustration and [show] the deliberative choices people are making through a compare-and-contrast model.'

B.6.2. The Australian Citizens' Jury should be diverse

Other experts focused their comments on the selection of the jurors. Most experts highlighted the need for a diverse range of jury participants. One expert indicated that 'differences between participant groups' will be important to analyse because 'studies have shown surprising results,' such as 'scepticism correlat[ing] to higher educational attainment.' Another expert emphasised that diversity in the jurors should be achieved 'not just around disability but around marginalised communities.' Another focused more closely on why diversity was important for experimenting with the process of coming to an outcome or a consensus. They noted that the organisers should 'try to map or show how a diverse group of stakeholders comes to a consensus and where that consensus is.' Another expert suggested that the citizen's jury should include participants from both non-academic and minority groups.

B.6.3. The Australian Citizens' Jury should avoid 'sensationalism'

Many experts underlined the importance of managing the risks of discussing sensational ideas. One expert suggested that the citizen's jury should emphasise the 'less evocative and [less] emotional' aspects of genome editing, such as 'diagnosis.' While these topics might be very dull, they said, they 'are still very important and may in fact be the most transformative.' Another expert stated that conspiracy theories about Big Pharma and the financial scales involved 'could be very unhelpful [because] if someone in pharma is not making money [then] none of these cures are going to get developed.' They further noted that 'the miracle [of] modern medicine does cost money, so that might need to be acknowledged.'

Another expert expressed a similar sentiment; they noted that the jurors should be 'steered away' from 'dystopian visions' and 'hysteria.' As they continued, 'far too often the debate immediately [descends [into a vision of the future that is terrible [when the focus] should be on the here and now.' The citizen's jury should try and maintain a practical and applicable approach, this expert argued, 'if for no other reason than the scientists deserve acknowledgement of what is real and the patients deserve acknowledgement of what is necessary and relevant.' In particular, discussion of 'enhancement' was not desirable, the expert said. The debate, they suggested, should be redirected to the 'relevant possibilities... every time the enhancement argument comes up.'

B.6.4. The Australian Citizens' Jury should focus on the most pressing and practical issues

In a similar vein, other experts suggests that the debates be designed around what is the most likely and applicable form of genome editing. One expert suggested that the CH should focus on 'the scenarios that we [or the law] will allow.' For instance, 'Because PDD [pre-implantation genetic diagnosis] has been around for thirty years, nobody's rushing to [implement heritable human genome editing]. We could use PGD for this purpose so it's important to keep it within the here and now and the ***possible*** potential.' Another expert echoed these sentiments closely. They said the citizen's jury should avoid assuming that 'genome editing is just going to happen' and instead should focus on 'whether we should ever permit it to happen [given] the real dangers and consequences.'

Given the wide variety of different views among experts on how the citizens' jury should be designed, several key statements from different experts are set out below to illustrate the diversity of opinion. Various experts expressed a view that the citizens' jury:

- should focus on 'producing thoughtful conversations [about] equity of access, and the fact that the West will receive the treatment first'.
- should produce a 'reasoned account' of the viewpoints 'that exist in the general public [and] tap into those voices that are completely underrepresented,' which may mean that 'these voices need to be overrepresented on any panel'.
- should 'have an actual impact on regulators [and this should] involve including an actual regulator in the jury. [The jurors] should come up with four or five policy recommendation and they must be relayed to the regulatory agents'.
- 'must feed the jurors knowledge about the applications of CRISPR and its uses but not about the ethical issues. [The organisers] should let the jurors determine the ethical issues themselves'.
- should 'identify the central ethical issues and come to some conclusions about whether germline [heritable] germline editing should be permitted and for what purpose'.
- should go about 'framing gene editing in a considered way [so that] the deliberation process is a process of considering whether to use gene editing [rather] than when or how we should proceed. I think the way it is currently framed on the website is really problematic because there's already an assumption that [the] technology is going ahead... The citizen's jury therefore risks just talking about producing a series of principles to guide it, which... straight away closes off other potential technological futures.

B.7. Ethics and human genome editing

While questions of ethics infused much of what the experts had to say in all the topics they discussed, many experts addressed the theory or philosophy of ethics directly. Others expressed paradigmatic ethical positions that tended to inform the way they under understood the ethical issues applying in more specific scenarios.

B.7.1. Ethics and human genome editing generally

One expert stated their view that all ethical questions relating to genomes and genome editing were functionally the same as those that apply to other technologies, and we have good tools to address them. This same expert noted that the only ethical position to hold was that less suffering and less

disease should be felt by the future generation; and so the ethical answer in relation to health technology is that 'we must use these tools to facilitate' that aim.

Another expert did not express such a firm position but instead contended that system for determining 'what is in the public interest or what is for the common good' must be established. The question, they said should be: 'What does it mean to use this technology well?' As this expert stated:

> We need to have a clear conversation about priority setting and, given all the problems we have in the world, how can we use this technology well? And then we have to have a question: What does it mean to use the technology well? We have different understandings of what's in the public interest and, in my own work, I actually draw distinctions between the public interest and the common good and for me, one of the things that's really important as the common good is us all.

As the expert elaborated, ethical questions are sometimes rendered impossible by the 'warp-speed' culture of science and innovation. Accordingly, it is important to make time for reflection and contemplation:

> ... we just embrace something, it gets normalized, and we keep on going. So I'm thinking that it becomes really important to find space to talk, to think, to reflect, to share ideas and yet we're... asking scientists to do this in a context where the environment doesn't support any of that.

By contrast, another expert, considering the question of safety and the ethics of experimentation, suggested that there will never be a time at which safety can be guaranteed or epistemic certainty can be achieved. On this basis, they suggested that it might be preferable to forge ahead:

> I think, safety is important. Do I think that these are lines that we should never cross? I don't. I think that in some ways we've been crossing all kinds of lines like these, right? We've been and we're inching towards them in all kinds of different ways. And so I think to say: You can test an embryo for a specific condition and discard it, but you can't change this one – [unless we] knew that it was safe and fine and whatever. To me, I think it's not aligned that we have to say you should never tinker. I think we tinker a lot [already], and I don't see a clear ethical line there.
>
> I do think that where the challenge comes is in all the things we are bound not to know. That we will rush into this, no matter how thoughtful we want to be, no matter how much we think we understand. I think that even the best people will not have the clearest picture on what's happening, and people will [make decisions] (we already know that people don't make great decisions and have full understanding of complex issues). And so I think that asking people [is tantamount to] assuming people really understand and they know what the risks are and they're willing to accept them and the science and the scientists know exactly what they're doing. And I think all of those are quite false assumptions.

In relation to the ethics of media reporting and medical technology, another expert noted that it is important to make sure that the 'hype' and promise of the technology is not broadcast without efficacy being first established. As they stated,

> I think the efficacy is important because it ties in with the hype that it's been getting, and the ethical responsibility to be absolutely sure it's doing what it's supposed to be doing [and] what people are saying it will be doing. And that message about its limitations and its possibilities [must also be] clearly communicated to the public.

Many other experts characterised the ethical dilemmas related to genome editing in many ways and formulations. Some experts weighed and compared different 'unethical' and 'ethical' acts; some described risk and harm in detail; while others noted the inevitability that genome editing will, one day in the future, be trialled. Still others described the difficulty of translating ethical positions and debates into regulatory systems and legislation, while others noted that this ethical debate is quite intractable,

given that the heritability of genome editing could affect not just the patient or their immediate offspring, but many different generations of many different relatives.

B.7.2. Genome editing and its relationship with race and identity politics

Many experts identified the Western-centric or Eurocentric way in which ethical debates about genome editing had been framed. As one expert noted, Western individualism and utilitarianism dominates the ethical debate; and very few non-Western voices are engaged in these issues in, for instance, East Africa. On this basis, one of the experts stated that there was a need to engage with voices from these communities in much great depth. This same expert noted that there WHO framework, similarly, depends on and showcases almost exclusively Western perspectives; they claimed that there should be more African and Aboriginal worldviews considered. Moreover, this expert also stated that much of the 'outrage' directed towards heritable human genome editing mandates from Western perspectives. As the expert noted:

> My sense is that not everybody across the world shares that [view] and that communities that that are more kind of solidarity-based possibly, do not actually share the outrage and are more permissible [and inclined] to allow certain kinds of enhancements, or certain kinds of editing.

B.7.3. Genome editing poses difficulties for evolution, eugenics (and dysgenics), and disability

In relation to evolution and eugenics (programs focused on 'good genes') and dysgenics (programs focused on 'bad genes'), one expert raised the point that to identify specific genes and genetic disorders as 'good' or 'bad' or 'healthy' or 'pathological' is to identify and reify a normative view of what health looks like. In addition, this expert made the point that this was not merely a principled objection. There was, the expert noted, also a hubristic risk of identifying the nature of 'health' too narrowly. To illustrate, the expert pointed to the example of the passenger pigeon, whose genes were so radically optimised (in other words, genetic diversity was low within the species), that they ultimately rendered extinct, despite being the most abundant bird in North America in the nineteenth century.

A related analysis of disability was adumbrated by one expert. As the expert noted, the 'disability question overlaps with the enhancement question. If you can "edit out" disability, are you not just treating the same question from a medical approach? Since every society is "disablist," there is an underlying assumption that disability is a regrettable thing and that preventing it, editing it out… trumps practically everything.' The expert was not being sincere in this remark, but was illustrating the way in which a prejudicial or ableist rationalisation of 'preventing' or 'correcting' a person's disability may pose problematic ethical and social questions about what is and is not characterised as a disability and, similarly, what is or is not treatable as such.

By contrast, another expert noted the 'far-fetched' notion that genome editing could be used as a means by which to achieve genetic narrowness and control genetic diversity (in a (eugenics-style program) because, as they stated,

> the mathematics, the numbers, do not work out. It's not inconceivable that eugenic crimes could be committed by using CRISPR. But it wouldn't be the same as what happened in the Second World War.

Similarly, a different expert denied that a eugenics program could be implemented through the administration of genome editing. As they noted,

> I don't feel it's the form of eugenics that we're all horrified about [but] it's more like ***eugenic counselling***... So, if two people are carriers for a really horrendous disease [then], to me, correcting the disease [through genome editing] is the same as what already occurs in genetic counselling.

B.7.4. Religious ethics may mean that genome editing is problematic for some faith traditions

One expert shared their view in relation to certain faith traditions. As they noted, for some of Islamic faith, medical treatment is acceptable, but enhancement is not. This is based on a conception of the body as perfect, and the idea that intervening in the process of perfecting the body, which is God's role or job, is unethical. As this expert noted, since it is believed that humans have perfect potential, humans may ethically intervene to achieve that potential.

> Our role as humans is to discover this potential and to realize it and concretise it in our life, and science is one of the tools to improve that. They said we are not born perfect, cognitively speaking. We're not born as mathematicians or as scientists. We have to get education, good school[ing]. And this is all enhancement; if you don't do it, you will not get better.

As this expert continued, one of the reasons some religious scholars see enhancement as morally unjustifiable is that it seems to assume that humans have a capacity to intervene that is equal to that of God.

So, one group thought God created us in the perfect state and you have references in the Quran that can be interpreted to mean this. We have been created in the best moulds, or the best form... So whatever we have, we should accept it... If this nature was an impairment by some accidents [or] by disease, [then] yes, we are permitted to interfere to bring back to the perfect original state' but that's it. This is all that we may do.

However, as the expert was keen to underline, not all persons in this faith tradition hold the same view. For some others of Islamic faith, the expert noted, enhancement is morally justified.

B.7.5. **Genome editing should not be misused through enhancement or for military purposes**

One expert was relatively confident that, in the long run, genome editing would be used to enhance human for the purposes of military operations. As this expert noted,

> I think the second area of real application (after agricultural gene drives) is unfortunately, I think, going to be in the area of defence... But I don't know how to speculate exactly how extensive it will be because a lot of it's going to be classified.

As this expert emphasised, it was a concern that such uses of the science could be imagined; however, it was also concerning that it was possible such concerns would be difficult to confirm or deny, as such operation might occur without disclosure to the general public.

By contrast, most other experts denied that enhancement was a plausible concern. For instance, one expert parsed their doubt in the following terms:

> I think it's pie in the sky stuff because technically I just think it's a fantasy. And I think at a community level, the communities won't embrace that. And then at the legislative level, there's just too many hurdles. Of course, there'll be mavericks. And of course, there will be people that try; and of course, people will go outside processes to do it. But I think most people are pretty reasonable people and I don't get concerned about that.

Nevertheless, this same expert noted that the risk of enhancements or treatments being adopted for those with mental health issues or identity issues – where, in their view, the borderline between pathology and enhancement may be less clear – was high. This expert expressed concerns that some identities, personalities, character traits, or disabilities could be subject to coercive alteration.

> If they find genes associated with certain behaviours – with things that we categorize as mental illness, things categorized as learning disabilities, things categorized as homosexuality – people may want to alter [those attributes or traits] in their children [and] I think could be incredibly detrimental to diversity in society.

Another expert contended that the 'enhancement debate' was a 'red herring' because the distinction between treatment and enhancement is too blurred to be meaningful. As this expert stated,

> My argument back a couple of decades ago... was that, in order to say that something is an enhancement, you have to define what a norm is. And if you are trying to define what the norm is for human beings, in law or in governance, you're going to enter some ethically difficult territory very quickly. So the quasi case-by-case basis of trying to evaluate: it's not about deciding 'Is this an enhancement or a therapy? What class of activity is it? [Instead, the better question is]: What does it mean for the well-being of the individual concerned and the social impact on society?

Another expert maintained that the risk of frivolous uses of genome editing leading to enhancement was very low, especially since the technology, now, is so inefficacious. Comparing the human body to a city, the expert noted that 'genome editing is like bridge building or fixing potholes.' As they continued, 'If someone wants to repair a bridge or pothole in a city, then that is possible. However, you cannot perfect a city or create a wonderfully designed city simply by fixing bridges or potholes.' And so, as they concluded, 'There is no risk... of genetic modifications gone mad in some ***Gattaca*** world; that is like saying that in the future all cities will be like Milton Keynes [a City in England]; they won't, it's not going to happen, and so there is no problem.'

B.7.6. Genome editing should not be mandatory or compulsory

Several experts expressed the view that genome editing should never be compulsory. However, some experts considered the effects that social pressure and community values may distort this debate and render a person virtually powerless to resist some genome alterations, especially if not editing the gene would pose a threat to the community. As this expert remarked,

> What had been an individual issue [may] suddenly become more of a community issue [if there is a risk to the community]. And then you have to deal with a political philosophy in different countries about at what point a community effect triggers a legitimate role for government to somehow circumscribe individual choices. And that's a matter of political culture, but it doesn't arise until you've actually got something big enough that it's going to affect society.

Just as some other health conditions are required to be treated by various social and legal controls (such as vaccination in some countries), so it could be with genome editing for some conditions. Similarly, one expert posited to the unthinkably (but illustrative) example in which a limit or 'cap' could be placed on human height and size by virtue of a specific genome alteration being administered. In a world of scarce resources and energy and waste limitation, such an in-built 'cap' on human growth could redound to the benefit of the environment and would likely be considered by many communitarians as sensible.

B.7.7. The opportunity cost algorithm must be justifiable for genome editing to be justified

Two experts raised the issue of opportunity costs quite adamantly. Both experts argued that the size of the fiscal investment that is directed towards genome editing may be, or may become, disproportionate to the investment directed at preventative health and preventative medicine. One expert compared this situation to the prospect of investing heavily in cancer treatments and in research for a cure, when the causes of cancer were relatively well-established in many cases, such as in the case of smoking or in the case of carcinogens used in many foods.

B.7.8. Genome regulation through the legal frameworks

Finally, in terms of regulation and legal frameworks, several experts had substantial things to say. There were varied responses and models proposed; however, it may be helpful to summarise a range of experts' points in a list, for brevity's sake. Among the experts many suggestions, the following were clearly expressed:

- A tiered approach to genome editing is needed, where different priorities and risks are ranked.
- There is a risk that the West will dominate the regulation debate and conversation; historical discussion, however, should not be made with only one side of the world leading the discussion.
- A lack of funding for research on embryos in the US means that there is not possibility that a public institution may engage in this research; however, 'the private sector can go ahead and do it... Although there are many FDA and NIH guidelines – actually regulations -- on what to do, how long to do it for private companies (so there's a set of rules for these companies) ... no federal money can come from or have anything to do with doing research on embryos, no matter what kind, be it CRISPR or what have you.'
- Academics cannot regulate this form of health technology itself; 'governments may [and should] wish to discuss it, rather than relying on academic communities.'
- The law should adopt a 'welfarist approach to regulation [so that] genome editing should be used wherever a benefit may be obtained. So you [may use] it for serious disorders like [spinal muscular atrophy], but also for less serious disorders like asthma, autism and dyslexia.'
- There are two periods of regulation: before Jiankui and after Jiankui. As they explained, 'Before Jiankui, regulation was sound. Everyone was developing the tools, sharing information, cautiously exploring – and it was also giving time for things like the base editors to be invented.' After Jiankui, that changed, [as he] prematurely went for a big splash. I was interested in the criticism that he got; I mean people criticised everything he did. They said it was a bad experiment, the wrong target; it was a stupid idea. I actually think it wasn't. I don't want to endorse him in any way, but I don't think every criticism that was made was right. I think that people threw the kitchen sink at him, where[as] the only criticism was he shouldn't have done it in humans at that stage. But everything else, I think, was [unnecessary]. He did do some preliminary stuff, he just shouldn't have done it in humans.
- It is not acceptable that licenses to conduct gene editing for research in Australia are unavailable, because there is wonderful work taking place at the Crick Institute [and elsewhere].

B.7.9. Engagement with Aboriginal and Torres Strait Islander communities

Attention was drawn to the particular issues facing Indigenous communities by a number of experts. Two experts, in particular, provided insights on engagement with Aboriginal and Torres Strait Islander

communities in Australia. These experts both had a long history of engagement with genomics and with Aboriginal and Torres Strait Islander communities.

It was very apparent from the remarks made by these experts that, in view of the unique and distinct genetic development of Aboriginal persons in Australia, there would be compelling reasons to distinguish questions related to Indigenous and Aboriginal genome editing from those that we intended to ask in this study, which were largely focused on European and East Asian genome editing.

One of these two experts identified that there were 'up to 800,000 variants that are unique to the Aboriginal person' and that knowledge about these genetic variants was so sparse, that it would not be productive or consistent with principles of dignity and respect to treat Indigenous persons in the same way as other participants in the study. The experts identified some intrinsic limitations in our current ability to study Indigenous genetics. For instance, one expert said the following:

> It's going to be hard to get really deep in-depth, detailed conversations from Aboriginal perspectives around genome editing. That's the truth of it. There's a bunch of principles that you can probably cover off on and you'll get a good sense of it because most of the activity of this moment is sort of setting the ground rules that we see as important from an Aboriginal and Torres Strait Islander perspective. But we don't have Aboriginal geneticists and it's a huge mess and gap in terms of our current architecture that we need to work towards overcoming. As a consequence, we've got people who are speaking on behalf of us. Some or all of which is probably well-intentioned, but we know that the road to health is paved with good intentions. It's so true in the space. We're now being sold these sort of hope-and-hype narratives. Which is we'll reconnect the stolen generation with genomic science, which we won't.

In addition to this statement, there were other strong and compelling comments from these experts that identified, with respect to approaching debates and questions of the ethics of genome editing and Aboriginal people in particular, that it was not possible – without a much more detailed and involved level of engagement with Indigenous people, both in the preliminary stage and throughout the project – to respectfully and appropriately approach these issues. The comments of one expert are illustrative in this regard:

> I would sample widely and I would pick conversations that you have with people specifically around the indigenous issues and then make a sort of a collaborative decision about what the next step needs to be with those people and others... That should be informed by your preliminary conversations and then decide on where to from here. But it may be that we just can't service it. But what will happen... is there'll be an assumed level of concordance [even if] we couldn't go down that path. That means that the broader ethical framework conversations that were had are probably good enough to progress a conversation about the Aboriginal space, which is not the case. It may be that everything lines up but [it] will not actually be participatory. Yeah, empirically we should see if that's in fact the case, because my view is when you're dealing with really disadvantaged and marginalized communities, the way you do business should be absolutely top shelf, gold standard.

Further comments from this expert suggested that not 'cutting corners' was paramount. Relations with Indigenous people and communities should not, they said, be an 'add-on' or a 'bonus' but should be central to the way the project proceeds. In relation to genome editing and the ancestral history of Indigenous peoples, the expert said the following:

> ... if we're deeply think[ing] in a cultural context about how slicing and dicing and sequencing of someone's historical and ancestral narrative, [more engagement] is required. If we we're to think deeply about what it means to change that story, a story handed down from generation to generation.... (Just water or 'choplepa' right, that's what we call in in the dessert, that's the law, it doesn't change, it's passed down from generation to generation for ever.) If you're playing with that narrative, the narrative handed and embodied within your DNA, what are the ramifications of that? Do people truly understand that? I would say no.

> Have we had those conversations with the communities and I say we absolutely haven't. What does it mean from a cultural context about, even if it's, you know, DNA derived from a saliva sample from someone if we're going to do things to it, do we have license to do that? I would say no.
>
> Do communities trust the scientific endeavour? I don't think they do. They trust the agents that perpetuate or produce the narrative of engagement, people like me, okay, so they do, trust me, but is that well founded? I would say sometimes yes and I would like to think always yes, but I'm not sure that that's true.
>
> I think there's presumed trust, there's a level of protection that I offer and my narrative around the importance of maintaining the integrity of the gift that I have given me in the research relationship, which I'm very proud to care for. But can I truly in a in a completely cultural context, say that everything that I will do will preserve the integrity of your view of the importance of unbroken lineage and narrative. I don't know that I can say yes when it comes to genome editing.

The aggregate of comments thus suggested to the project team that it was neither feasible nor appropriate to include Indigenous people in the Australian Citizens' Jury because it would not be possible to do so in a way that adequately inclusive.

After much consideration, we concluded that a process by which an Indigenous voice would be constituted by just one, or at most two, Indigenous persons within a jury of 23 non-Indigenous persons was not consistent with the criteria they articulated, nor with definitions of inclusiveness in the literature. According to one such definition, 'Inclusion occurs when a diversity of people... feel valued and respected, have access to opportunities and resources, and can contribute their perspectives and talents to improve their organisation.'

Based on the guidance from experts, and preliminary surveys with potential participants, we found that we were unable to develop a model of inclusion that satisfied the above criteria. We thought deeply about inclusiveness and examined the emerging research literature on inclusive practices in participatory democracy. We then weighed those findings against the comments we received from these experts. Ultimately, we were unable to identify a model of inclusion and participation that would satisfy these requirements.

On balance, we concluded that there were clear and compelling reasons for deferring or reserving questions related specifically to Indigenous people and genome editing to another project, where a representative and multidimensional engagement with the issues would be possible. Given these considerations, it was determined that the detailed, respectful and sometimes sensitive task of achieving Indigenous inclusion with respect to genomic information and genetic science would be not possible within the scope and remit of the Australian Citizens' Jury.

APPENDIX C.
ENGAGING A DIVERSITY OF VIEWS: DISCOURSE MAPPING AND AUSTRALIAN CITIZENS' JURY PARTICIPANT SELECTION

C.1. Introduction

To achieve these outcomes, careful attention must be paid to the conditions of deliberation, including participant recruitment. A discursive approach transforms the question of representativeness as traditionally understood, from wider representation across populations to a deeper approach that captures various types public values relevant to the issue, that tend to coalesce into patterns of reasoning we refer to as discourses (Dryzek and Niemeyer, 2008). Consequently, the emphasis of participant recruitment for deliberative processes is on discursive, as well as descriptive representation. Discursive representation means making sure that the range of discourses relevant to the issue at hand are both understood and represented.

In terms of understanding the issue discursively, an intensive discourse Mapping Study, which identified and described four key discourses on human genome editing within the Australian community. These mapping study discourses were then used to ensure representation in the deliberative process. In the following, we briefly introduce discourses and the key significance of discursive representation to the design of deliberative processes. This is followed by a detailed overview of the methods used in the discourse mapping study and a description of the resulting discourses. Finally, we explain how these discourses were used to ensure discursive representation at the Australian Citizens' Jury on human genome editing through their use to inform the recruitment of 23 participants in the citizens' jury and 21 participants to an associated control group.

C.2. Discourses and Discursive Representation

The aim of discursive representation is to include all relevant discourses within a target population. Dryzek and Niemeyer (2008) have argued for discursive representation on rational, ontological, and ethical grounds. In brief, the rationality justification refers to the likelihood that policy proposals that are subjected to critique from a greater number of perspectives will lead to more robust policy outcomes. The ontological justification derives from an understanding of subjectivity as multifaceted, meaning that individuals encompass many discourses and the representation of individuals themselves is therefore a practical impossibility. The ethical justification goes on to argue that once we accept that individuals engage multiple discourses, it is important that all these discourses are represented. Discursive representation also addresses the problem of scale confronting deliberative democracy. That is, that normative legitimacy requires all those affected to have a say, and yet effective face-to-face deliberation is limited to small groups of people.

According to Dryzek (2005), a discourse is:

> 'a shared way of apprehending the world. Embedded in language, it enables those who subscribe to it to interpret bits of information and put them together into coherent stories or accounts. Discourses construct meanings and relationships, helping to define common sense and legitimate knowledge.'

Discourses are distinct from opinions, beliefs, and attitudes, and do not necessarily correspond with ascriptive characteristics, such as age, gender, or education level, which are often used to achieve descriptive representation in social science studies (Dryzek and Niemeyer 2008). Although opinions and attitudes towards an issue or topic might align with discourses due to the presence of a similar underlying reasoning, they need not be associated. Similarly, certain discourses might be prevalent within particular ascriptive groups because members of these groups have shared experiences. However, discourses also cut across ascriptive groups and individuals belonging to such groups

encompass multiple discourses. The representation of discourses should therefore be considered separately from descriptive representation and issue positions (e.g., for or against genome editing) in the design of deliberative processes.

Finally, discourses incorporate aspects of underlying reasoning, which lend them to measurement, comparison, and representation. In the following, the method used to identify, characterise, and compare discourses as part of an intensive discourse mapping study of Australian discourses on human genome editing is outlined. The four discourses that were identified through this mapping study are described. The use of these four discourses to recruit a discursively representative sample of participants to the Australian Citizens' Jury on human genome editing is detailed in section C.5.3.

C.3. Discourse Mapping— Mapping Study and Post-Deliberation Discourses

Discourse mapping to identify the prevailing perspectives among the Australian community was informed by Q-methodology, which combines qualitative and quantitative techniques to capture and compare the subjective or first-person viewpoints of study participants (Brown, 1980). The aim of the method is to enable each participant to fully express their subjective views by ranking a set of pre-selected statements according to their level of agreement or disagreement with the sentiment expressed by each statement (Paige and Morin, 2016).

Two separate discourse maps were produced for the AusCJ study.

1. Mapping Study Discourse Map—Four discourse
2. Post-Deliberation Discourse Map—Six discourses

The first (Mapping Study) map was produced during the mapping study phase of the project (Stage 2; see Figure 2; see also section C.3.2). It used primarily to establish a baseline for the variety of views that can be found in the Australian community and to ensure that a diversity of views were recruited to be present at the AusCJ (See Discursive Representation; Appendix D).

The second discourse map—

C.3.1. Statement Instrument Development: Sampling Public Discourse

The statements used in Q-methodology are representative of the existing discourses within the target population. To this end, the statements that were used to map discourses on human genome editing were drawn from online forums, news article comments, radio and podcasts, responses to previous studies and public engagement, and relevant academic literature, as well as from the expert interviews described in Section 2 of the main report. A search across these sources yielded a complete set of over 1,200 statements, which were separately thematically coded by two members of the research team and ultimately grouped into emic themes. Representative statements were selected for each theme. If no single representative statement captured the theme, statements were selected for each sub-theme, or a composite statement was created. When necessary, grammatical errors were corrected to improve the clarity of the statements. The final set of forty-six statements that were ranked by participants in the mapping study are listed in Table 1.

Table 1: List of the statements that were ranked by participants in the mapping study

No.	Statement
1	It's a slippery slope from genome editing for medical reasons to using it for other reasons.
2	Parents and guardians have a right to edit the genes of their children before they are born.
3	Parents want 'designer babies' with certain traits out of vanity.
4	If you can have strong genes, you will have wellbeing.
5	I'm concerned that genome editing will lead to a reduction in genetic diversity.
6	I think it would be amazing to have a choice in the way someone behaves.
7	The idea that gene editing can make perfect people and societies is extremely dangerous.
8	I think it's okay to use genome editing to change someone's appearance.
9	I'm concerned that gene editing will be used as a quick techno-fix without actually dealing with real problems.
10	My concern is that as we start to tinker with the genome, we're going to accidentally introduce a whole host of other problems.
11	If this technology is available then it should be available to everyone who needs it, not just those who can afford it.
12	I'm worried that genetic technology will widen the gap between those who can afford it and those who can't
13	If we open the box of genome editing we will not know where to draw the line.
14	I am concerned that the use of gene editing will advantage one group over another.
15	Decisions about the use of genome editing are best left to the experts.
16	If genome editing works, the future will be like a dystopian movie.
17	Genome editing is really cool science.
18	The real aim of genome editing will be enhancement for wealthy people.
19	I have a very different feeling about gene editing in humans than I do for animals or plants
20	Editing genes that will be inherited is problematic because it means making decisions for future people who don't exist yet.
21	My cultural beliefs make me cautious about genome editing.
22	When you change someone's genes you are fundamentally changing who they are.
23	Genome editing in agriculture will have the biggest impact on people's health.
24	Anything that's been artificially created in a lab gives me Frankenstein vibes.
25	Mitochondrial donation doesn't fundamentally change our genetics should be viewed like any other organ transplant.
26	I worry that something will go terribly wrong with this technology.
27	It's better to prevent a disease from happening rather than it happening and then having to treat it.
28	The idea that people with genetic conditions might get cured in my lifetime is miraculous and incredible!
29	Genome editing technologies gives us power over human life itself.
30	It makes me sick to hear that genome editing will 'cure' disability.
31	I would be OK with using genome editing to speed up evolution.
32	As a society, we have an obligation to help strengthen coming generations by eradicating diseases.
33	We find strength when we face illness and adversity. It makes us who we are.
34	If genome editing is proven to be safe, then I see no reason to oppose it.
35	It is better to accept our genes the way they are than to tamper with things we don't understand.
36	I would strongly consider using genome editing for my children if it could safely give them an advantage in life.
37	I don't think we know enough about genetic diseases or the long term consequences of genome editing
38	I think we should keep an open mind about new discoveries.
39	I would be OK with having my own genome edited.
40	Each individual has a right to decide for themselves whether to undergo gene editing.
41	Interfering in people's genes is intervening a bit too far in human creation.
42	I admit that the idea of editing the human genome is a bit scary.
43	The use of gene editing for non-medical reasons reminds me of the Nazis during the Second World War.

No.	Statement
44	Science and technology are controlling our lives.
45	I believe that future humans will need genome editing to survive.
46*	I believe we should remain as natural as possible but we should not shy away from furthering medicine and the chance to save lives.

Note. *Statement 46 was dropped following the Mapping Study and not used in subsequent surveys

C.3.2. Data Collection

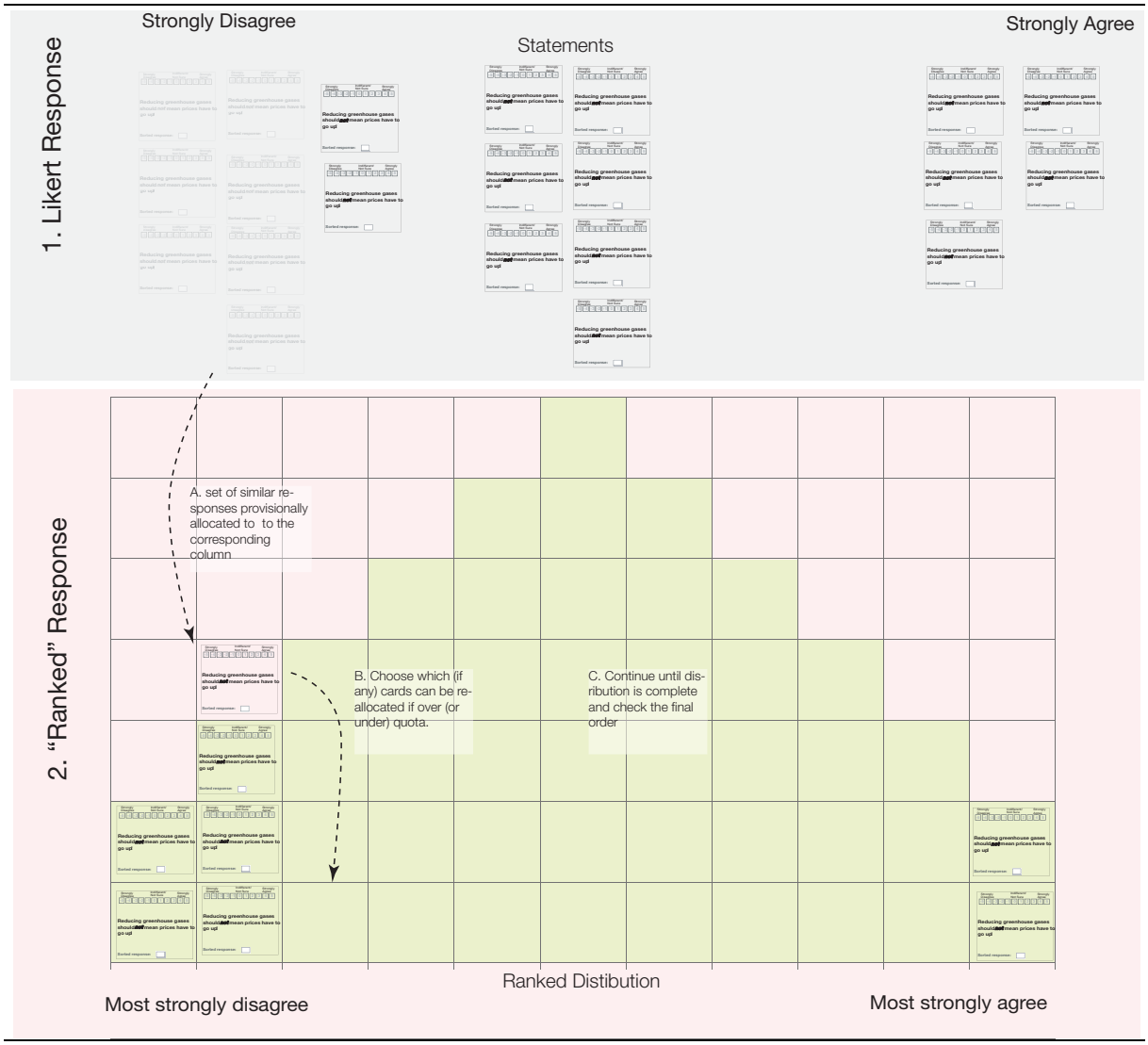
Obtaining a standard Likert scale ratings for each statement along a disagree to agree scale.

Sorting the statements into a quasi-ranked order, with those that they most disagreed falling into the same column at one end, and those that they most agree with in a column the other within a pre-determined distribution.

Within the Q-sort each statement is ranked relative to all the other statements used in the study. This is accomplished by constraining the ranking space to a quasi-normal distribution of ranks, known as a Q-sort. Once completed, the Q-sort provides a snapshot of the respondent's subjective view on a topic. The process of sorting statements was facilitated using an algorithm that drew on the Likert responses to allocate statements to a column and, where the number of statements exceeded the quota asked them to select which among them involved less/more agreement and could be sorted into the next column-with provision for participants to go over the quote if they wished. The process, and the resulting distribution is summarised in Figure 5.

It is not essential to obtain a quasi-ranked distribution, but there are advantages for the next stage of analysis, extracting the factors (or here, discourses) that emerge from the accumulated data for participants.

Figure 11: Q Sorting



C.3.3. Mapping Study Interviews

The approach to identifying the main public discourses is analogous to the process of conducting an ecological survey to discover the array of endemic species. This requires an intensive approach using a smaller sample size than a study that seeks to determine the extent of the population. A small and purposive participant sample is therefore appropriate for this methodology (Stenner and Marshall, 1995).

Thirty-one mapping study participants were recruited for the Mapping Study, focussing on achieving a diversity of 'interesting and relevant viewpoint(s)' (Watts and Stenner 2012, p. 71) on the topic of gene editing. A strategic sampling approach was used ensure demographic and geographic diversity. Because discourse mapping examines individual subjectivity, the mapping study participants need not be representative of the population at large (Brown, 1996). Participants were recruited from a panel provided by the recruitment company Dynata Pty Ltd—an ISO certified global provider of market research panels. A screener was used to recruit participants to the mapping study. The screener included questions based on age, gender, highest level of education, residence state and

location, religious beliefs and practices, experiences with genetic conditions, awareness of genome editing, and open-ended and scalar responses to a sample of the surveyed statements.

The data used to identify the mapping discourses were obtained during a one-hour online interview, with the survey process using a variation of the standard "Q-sorting" format using a specifically designed web survey. The process involved participants reading through each of the statements under a condition of instrument where they were encouraged to imagine that they were encountering the claims that they embody under everyday conditions (e.g., hearing them as part of a media broadcast). They were encouraged to discuss the statements and their understanding of it with the interviewer— and the recorded transcript then used to assist with interpretation of the results. The process of obtaining the data itself involved two steps:

C.3.4. Analysis: Identifying Discourses

The two sets of discourses were obtained using the standard approach in Q-Methodology, which deployed inverted factor analysis (Principle Components) to identify commonalities in perspectives among groups of participants based on correlations between their viewpoints (Stephenson, 1935). Although it is possible to engage in an extensive process of "judgemental" factor rotation, depending on any theoretical perspective the researcher might wish to explore, in this case a simple varimax rotation was performed on the four largest factors extracted using Principal Components.

For the Mapping Study Discourses this involves a lower level of resolution than the Post-Deliberation (six) discourses reported in conjunction with the deliberative process where the focus is on a finer grained assessment of positions and deliberative transformation.

The discourses that resulted are interpreted based on the factor scores — or "typical" responses to each of the statements for a given discourses. For both sets of discourses, interpretation was facilitated by drawing on the interview transcripts to elaborate underlying reasoning and aided, in addition to facilitator notes and follow up interviews with participants for interpreting the post-deliberative discourses..

C.4. Mapping Study (Four) Discourses

The array of 'factor scores' (z-scores that indicate the extent of agreement or disagreement for each statement that is typical for each discourse) is provided in Table 2 for the four mapping study

discourses. The discourses are also depicted stylistically in Figure 6, which shows a summary of the main propositions that are uniquely associated with a discourse, or shared between two or more.

Table 2: Discourse Mapping Discourses—Factor Array

No.	Item	Factor Scores A	B	C	D
1	Mitochondrial donation doesn't fundamentally change our genetics should be viewed like any other organ transplant.	0.62	-0.61	1.35	-0.31
2	It's a slippery slope from genome editing for medical reasons to using it for other reasons.	-0.05	0.86	1.35	-1.26
3	Parents and guardians have a right to edit the genes of their children before they are born.	0.36	-1.84	-0.80	-0.88
4	Parents want 'designer babies' with certain traits out of vanity.	-0.09	-0.14	-1.16	1.20
5	I'm concerned that genome editing will lead to a reduction in genetic diversity.	-0.74	0.89	0.63	-1.17
6	I think it would be amazing to have a choice in the way someone behaves.	-0.70	-1.51	-1.16	-0.31
7	The idea that gene editing can make perfect people and societies is extremely dangerous.	0.25	1.24	-0.09	-1.36
8	I think it's okay to use genome editing to change someone's appearance.	-0.66	-1.91	-1.52	0.35
9	I'm concerned that gene editing will be used as a quick techno-fix without actually dealing with real problems.	-0.70	0.57	0.63	-0.13
10	My concern is that as we start to tinker with the genome, we're going to accidentally introduce a whole host of other problems.	0.28	1.47	0.27	1.29
11	If this technology is available then it should be available to everyone who needs it, not just those who can afford it.	1.77	1.39	0.27	-0.60
12	I'm worried that genetic technology will widen the gap between those who can afford it and those who can't	0.30	1.27	0.63	-0.13
13	If we open the box of genome editing we will not know where to draw the line.	-0.57	0.81	-0.45	0.54
14	I am concerned that the use of genome editing will advantage one group over another.	0.05	1.25	0.99	-0.13
15	Decisions about the use of genome editing are best left to the experts.	1.23	0.39	-1.52	0.63
16	If genome editing works, the future will be like a dystopian movie.	-1.47	-0.19	-0.45	-0.69
17	Genome editing is really cool science.	0.80	0.12	1.35	1.29
18	The real aim of genome editing will be enhancement for wealthy people.	-1.26	-0.12	-1.52	-1.26
19	I have a very different feeling about gene editing in humans than I do for animals or plants	-0.28	-0.32	-0.45	0.25
20	Editing genes that will be inherited is problematic because it means making decisions for future people who don't exist yet.	-0.60	0.77	-0.45	-0.60
21	My cultural beliefs make me cautious about genome editing.	-1.81	-1.50	1.35	0.16
22	When you change someone's genes you are fundamentally changing who they are.	-1.17	0.87	0.63	0.54
23	Genome editing in agriculture will have the biggest impact on people's health.	0.37	-0.33	-0.45	0.73
24	Anything that's been artificially created in a lab gives me Frankenstein vibes.	-1.78	-0.92	-0.80	-0.79
25	I worry that something will go terribly wrong with this technology.	-0.80	1.32	0.99	-1.36
26	It's better to prevent a disease from happening rather than it happening and then having to treat it.	1.85	0.93	1.71	1.48
27	The idea that people with genetic conditions might get cured in my lifetime is miraculous and incredible!	1.66	1.27	0.63	0.63
28	Genome editing technologies gives us power over human life itself.	-0.56	-0.04	0.27	-1.17
29	It makes me sick to hear that genome editing will 'cure' disability.	-1.27	-1.08	-1.88	-0.79
30	I would be OK with using genome editing to speed up evolution.	-0.27	-2.01	-0.80	-2.02
31	As a society, we have an obligation to help strengthen coming generations by eradicating diseases.	1.42	-0.84	-0.09	0.44
32	We find strength when we face illness and adversity. It makes us who we are.	-0.24	-0.28	-0.09	1.77
33	If genome editing is proven to be safe, then I see no reason to oppose it.	1.70	-0.58	-0.80	-0.69
34	It is better to accept our genes the way they are than to tamper with things we don't understand.	-1.06	-0.13	-1.16	0.35
35	I would strongly consider using genome editing for my children if it could safely give them an advantage in life.	0.87	-0.64	-1.16	-0.79

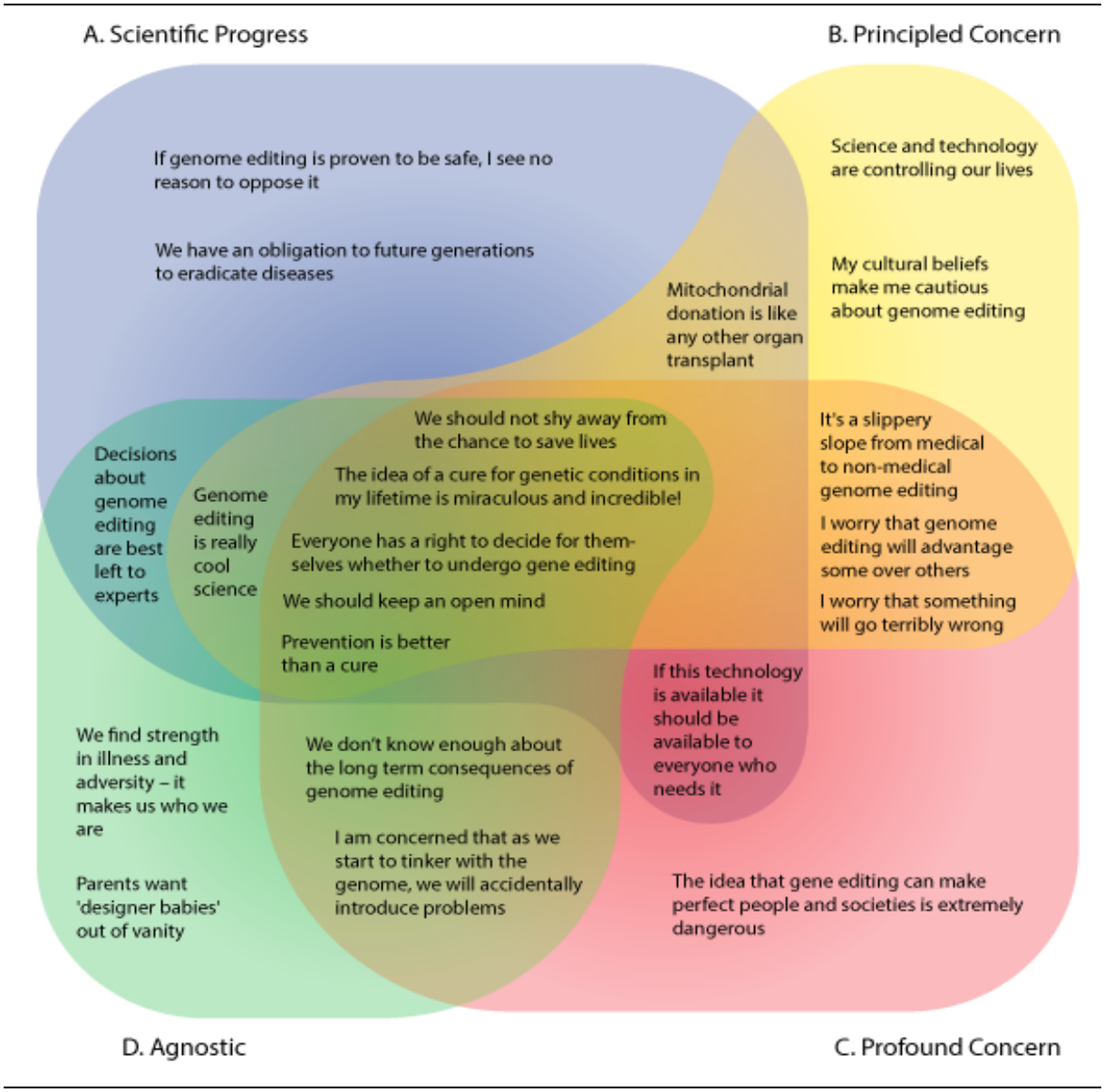
No.	Item	Factor Scores			
		A	B	C	D
36	I don't think we know enough about genetic diseases or the long-term consequences of genome editing	0.46	1.17	-0.09	1.29
37	I think we should keep an open mind about new discoveries.	1.82	0.76	1.35	1.86
38	I would be OK with having my own genome edited.	0.88	-0.64	0.27	0.63
39	Each individual has a right to decide for themselves whether to undergo gene editing.	1.38	0.94	0.99	1.58
40	Interfering in people's genes is intervening a bit too far in human creation.	-1.41	-0.56	0.99	0.06
41	I admit that the idea of editing the human genome is a bit scary.	-0.01	0.52	0.27	-0.60
42	The use of gene editing for non-medical reasons reminds me of the Nazis during the Second World War.	-0.99	-0.92	-0.09	-0.03
43	Science and technology are controlling our lives.	-0.49	-0.55	1.71	0.44
44	I believe that future humans will need genome editing to survive.	0.03	-1.31	-1.88	-2.21
45	I believe we should remain as natural as possible but we should not shy away from furthering medicine and the chance to save lives.	0.57	1.18	0.99	1.20
46	If you can have strong genes, you will have wellbeing.	0.33	-1.05	-0.80	0.54

Table 3 shows the correlations between the discourse based on the array of factor scores in Table 2. It shows at least some degree of overlap among the discourses. That discourses A and C exhibit the least similarity is unsurprising, with each representing the extremes in terms of overall enthusiasm regarding human genome editing.

Table 3: Correlations—Mapping Study Discourses

	A	B	C	D
A		0.32	0.22	0.36
B	0.32		0.48	0.28
C	0.22	0.48		0.34
D	0.36	0.28	0.34	

Figure 12: Mapping Study Discourses



A series of descriptive narratives has been developed for each of the discourses, drawing on a combination of the factor scores and interview transcripts. These descriptions are provided below:

Discourse A: Scientific Progress

Participants loading on this discourse tended to be open-minded about new discoveries. If genome editing is proven to be safe, they see no reason to oppose it. They trust in science and medical professionals and tend to agree that decisions about genome editing should be left to the experts.

This trust is also reflected in disagreement with statements expressing doubts about the motivations and possible consequences of genome editing. They disagree with statements that suggest that the real aim of human genome editing will be enhancement for the wealthy and that gene editing for non-medical reasons will have negative social consequences.

Scientific optimists do not feel discomfort about anything that's been created in a lab and nor do they feel like genome editing is interfering too far in human creation. Importantly, they feel strongly that their cultural beliefs do not make them cautious about genome editing.

People subscribing to scientific optimism are more likely than other discourses to be OK with having their own genes edited, or using it for their children to give them an advantage in life. They emphasise the potential benefits of genome editing for medical treatment and feel excited that people with genetic conditions could be cured in our lifetime, agreeing that it's better to prevent a disease happening than having to treat it later, and that we have an obligation to strengthen future generations by eradicating disease.

Discourse B: Principled Concern

Participants loading on this discourse are not opposed to genome editing per se but are concerned about the social and ethical implications of the technology. They worry that as we start to tinker with the genome, something could go wrong. They tend to feel strongly that genome editing should not be used for non-medical purposes and are concerned about issues of equity and access.

This discourse emphasises the potential social consequences of human genome editing. Participants associated with this discourse are concerned about equity and access, and feel strongly that the technology, if available, should be available to everybody. Concomitantly, they are worried that genome editing will advantage some groups over others and widen the gap between those who can afford to use the technology and those who cannot. Nevertheless, they find that the possibility of curing genetic conditions is incredible.

People associated with this discourse feel strongly that genome editing should not be used for non-medical purposes, such as changing someone's appearance or behaviour. They do not believe that parents should not have the right to edit their children's genes before they are born. They are also concerned about possible futures of genome editing such as reducing genetic diversity, making decisions for future generations, and gene editing being used as quick fix, although they don't feel as strongly about these as they do about inequality.

When it comes to the relationship between our genes and identity, this discourse takes an interesting perspective. Whilst they do feel that when you change someone's genes you change you who they are, they don't think that having strong genes is the key to wellbeing.

Discourse C: Profound Concern

Participants loading on this discourse are cautious about genome editing. They tend to feel that science and technology are controlling our lives, but while they think we should remain as natural as possible, they do not think we should shy away from the chance to save lives. Like Scientific Optimists, they tend to be open-minded about new discoveries, but they disagree that decisions about genome editing should be left to the experts.

They feel that their cultural beliefs make them cautious about gene editing. They view gene editing as interfering a bit too far in human creation. At the same time, the culturally cautious do think we should keep an open mind about new discoveries. Out of all four discourses, this is the only one disagreeing that decisions about gene editing are best left to the experts.

The culturally cautious viewpoint thinks we should remain as natural possible, without shying away from furthering medicine that saves lives. Along the same lines, the culturally cautious do agree it's

better to prevent a disease from happening rather than treating it later, and strongly agree that mitochondrial donation is just like any other organ transplant. It definitely does not sicken them to hear that genome editing will 'cure' disability and they don't necessarily think it's better to accept things the way they are. Yet this viewpoint does not believe humans will need gene editing to survive. They are also concerned about the slippery slope from medical to nonmedical uses and do not think it's okay to use gene editing to change someone's appearance.

The results of the mapping study helped to ensure diversity in the selection of Australian Citizens' Jury participants, as described in the next section.

Discourse D: Agnosticism

Participants loading on this discourse are relatively unconcerned by the risks of genome editing when compared to other discourses. They are intrigued by the possibilities of the technology but are not convinced that it is necessary — it could be better to accept things the way they are.

The third discourse accounts for just 5% of the study variance, but this doesn't mean it should be dismissed. It still means that this viewpoint exists in the wider community and we can't say anything about its wider prevalence it is at this stage. The overall perspective from the intrigued agnostic seems to be relatively unconcern about genome editing compared to other viewpoints - unconvinced it will become a necessity, aware that there are unanswered questions and less worried than other discourses about the medical benefits or ethical implications. At the same time, they are intrigued by the possibilities of genome editing.

Intrigued agnostics keep an open mind about new discoveries, and for them genome editing is really cool science. At the same time, they seem to doubt the necessity of gene editing for humans, disagreeing that we will need it to survive or that it would be OK to use it to speed up evolution.

Although intrigued agnostics agree that we don't know enough about the long-term consequences of gene editing and we could accidentally introduce other problems, they are not worried about something going terribly wrong. Intrigued agnostics also appear relatively unconcerned about possible non-medical uses such as enhancement for wealthy people and they're not worried about the idea that gene editing can make perfect people, reflected in their cautious agreement with using the technology to change peoples' appearance. Intrigued agnostics do think that parents want to create designer babies out of vanity but from their response to other statements, it's possible they don't think this is necessarily a bad thing. They do have some doubts about genome editing and think it could be better to accept things as they are, whilst at the time would consider having their own genes edited, since everyone has a right to decide that for themselves.

The intrigued agnostic strongly believes that we find strength when we face illness and adversity, and that if you have strong genes, you will have wellbeing although it is difficult to make a direct connection between this and their position on gene editing. Intrigued agnostics share similarities with scientific optimism when they agree that it's better to prevent a disease than treat it later, but they don't place the same emphasis that scientific optimists do on the medical implications and benefits of genome editing. They also seem relatively unconcerned with the ethical and social implications that worry ethical sociologists.

C.5. Post Deliberation (six) Discourse Map

A similar method was used to identify the main positions among participants, using the responses to the mapping survey performed by AusCJ participants following deliberation to that used for the mapping study (see Appendix C.3). Where the mapping study resulted in four discourses being identified, in this case the analysis resulted in six positions being identified using the post-deliberation surveys.

The increase in number of discourses from four to six is due primarily to deliberation resulting in more nuanced reasoning by participants, thus requiring a finer grained map to understand the different positions.

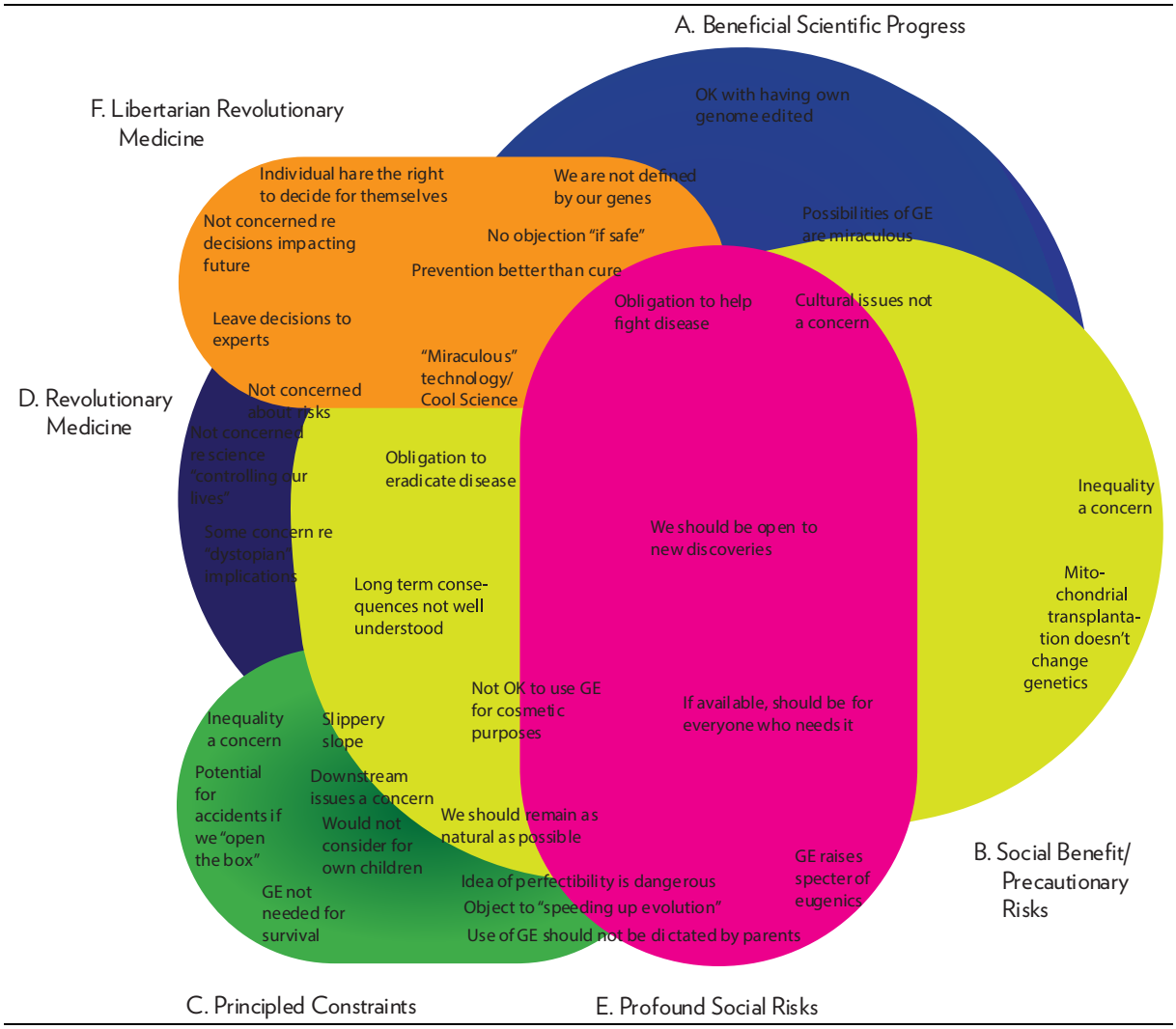
Figure 13 provides an overview of the main features of the six discourses identified following deliberation, similar to Figure 12for the four Mapping Study discourses.

There are a few notable overall features of this more detailed map:

- There is less overlap in positions compared to the mapping study, reflecting in part greater specificity in the positions.
- There are strong overlaps with two of the Mapping Study discourses. The nature of the overlaps are discussed in the next section.

One shared feature across the discourses is an openness to new discoveries and scientific progress, with variation in positions mainly expressed in terms of management of risks, or differences in emphasis on potential benefits. Discourses A and F are the most supportive of human genome editing. Discourse B is precautionary. As will be seen Discourse C reflects its near namesake from the Mapping Study (B: Principled Concern). Discourse D supports the science but shows concern regarding long consequences and potential for dystopia. Discourse E reflects a more profound concern, sharing features of the principled concern of C, but with emphasis on more evocative issues.

Figure 13: Post-Deliberation (Six) Discourse Map—Summary



C.5.1. Comparison of Discourse Maps

Before elaborating the six post-deliberative discourses it is worth pausing to first consider the relationships with the original set of four discourses identified in the Mapping study.

Table 4 shows that two of the discourses overlap strongly between the two maps. Discourse A from the 6-Discourse Map is closely related to Discourse A from the mapping study. The most notable overlap pertains to Mapping Study Discourse A (MS-A) and the strong overlap with five of six Post-Deliberation discourses— and the Post-Deliberative Discourse A (PD-A) in particular. While this reflects at least some level of consensus among most of the PD discourses and MS-A—reflecting a strong interest in the technology—there are important differences that can be identified within this view.

Table 4: Correlations — Mapping Study (Fours) vs Post-Delib (Six) Discourse Map

		Mapping Study (Four Discourses)			
		A	*B*	*C*	*D*
Post-Deliberation (Six Discourses)	*A*	0.77	0.11	0.12	0.39
	B	0.58	0.50	0.40	0.16
	C	-0.13	0.73	0.42	0.22
	D	0.57	0.50	0.25	0.26
	E	0.57	0.47	0.48	0.34
	F	0.59	0.24	0.10	0.23

That PD-C stands apart from the other PD discourses is also notable. Not surprisingly, as can be seen from Table 4, it is the most distinguishable of the PD discourses, with the remainder exhibiting at least a moderate level of overlap. As noted above, PD-C is most similar to MS-B.

Table 5 shows the correlations among the Post Deliberative discourses. Discourse A and B are most similar, with C being the most distinguished.

Table 5: Correlations—Post-Deliberation (Six) Discourses

	A	B	C	D	E	F
A		0.56	-0.10	0.44	0.35	0.48
B	0.56		0.35	0.53	0.53	0.45
C	-0.10	0.35		0.30	0.27	-0.04
D	0.44	0.53	0.30		0.47	0.45
E	0.35	0.53	0.27	0.47		0.21
F	0.48	0.45	-0.04	0.45	0.21	

Curiously, PD Discourse E overlaps strongly with B, D and E, and less with C even though both reflect a high level of concern about human genome editing.

Table 6 shows 'factor arrays' for the two discourse maps, with the level of agreement with each of the surveyed statements indicated as z-scores and are colour coded accordingly. The areas of agreement between MS-A and PD-A, and MS-B/PD-C can be readily seen.

Discourse C from the Mapping Study does not find a close correlate with the new 6-discourse post-deliberative map. However, some of its more important elements can be post deliberation Discourse E. And it is also Discourse E where many of the participants who were associated with Mapping Discourse C before deliberation ended up. The changes between these discourses could thus be said to at least partially reflect the transformation of that perspective during deliberation.

Some of the concerns raised in Mapping Study Discourse C remain after deliberation for these individuals. For example, statement 39 (Each individual has a right to decide for themselves whether to undergo gene editing, as long as the changes cannot be passed on to future generations) tended to produce a positive response for all four Mapping Study discourses, but was most strongly expressed in C. Among the post-deliberative discourse, it is only E and (to a lesser extent, F) that exhibit strong agreement. Objection to Statement 30 (There is nothing wrong with using genome

editing to speed up evolution and help living things (including humans) adapt to challenges), in MS-C is much stronger in PD-E.

Other elements of that perspective have not been carried across. For example, PD-E expresses a much stronger stance on matters of equity of access (e.g. Statement 11), is less concerned with accidental impacts (Statement 10).

Another interesting difference between the discourses is that Statement 21 (My cultural beliefs make me cautious about genome editing), which is one of the defining features of MS-D, no longer finds expression in any of the post deliberative discourses.

Table 6: Factor Scores—6-Discourse vs Mapping Study

	6-Discourse Map						Mapping Study			
Statement #	*A*	*B*	*C*	*D*	*E*	*F*	*A*	*B*	*C*	*D*
1	0.4	1.8	-0.9	-0.8	0.7	0.4	0.6	-0.6	-0.3	1.4
2	-0.8	1.5	1.3	0.7	-0.1	1.1	0.0	0.9	-1.3	1.4
3	0.8	-0.5	-1.5	0.7	-1.0	1.5	0.4	-1.8	-0.9	-0.8
4	0.1	0.0	0.6	0.9	-1.2	0.4	-0.1	-0.1	1.2	-1.2
5	-0.6	-1.3	0.6	-0.6	-0.5	-0.8	-0.7	0.9	-1.2	0.6
6	0.0	-1.7	-1.3	-2.1	-1.8	0.0	-0.7	-1.5	-0.3	-1.2
7	-0.4	0.9	1.4	0.9	1.4	0.0	0.3	1.2	-1.4	-0.1
8	0.3	-1.6	-2.0	-0.8	-1.9	0.0	-0.7	-1.9	0.3	-1.5
9	-0.7	-0.9	0.7	-0.3	0.5	0.8	-0.7	0.6	-0.1	0.6
10	0.4	1.1	1.3	0.6	-0.3	1.1	0.3	1.5	1.3	0.3
11	1.2	1.7	0.0	1.4	2.2	-0.4	1.8	1.4	-0.6	0.3
12	0.3	1.7	0.7	0.3	0.7	-0.8	0.3	1.3	-0.1	0.6
13	-0.4	-0.2	1.3	-0.1	-0.6	0.8	-0.6	0.8	0.5	-0.4
14	0.2	1.0	1.6	0.0	-0.1	0.8	0.1	1.2	-0.1	1.0
15	-0.4	-0.6	-0.9	1.3	0.4	1.9	1.2	0.4	0.6	-1.5
16	-2.0	-0.6	0.2	1.0	0.6	-0.4	-1.5	-0.2	-0.7	-0.4
17	1.5	1.7	0.0	0.9	1.0	1.5	0.8	0.1	1.3	1.4
18	-0.3	0.1	0.6	-0.5	-0.9	0.8	-1.3	-0.1	-1.3	-1.5
19	0.1	-1.1	-1.2	-0.2	-0.4	0.0	-0.3	-0.3	0.3	-0.4
20	-0.2	-0.6	0.7	-0.7	-0.3	-1.1	-0.6	0.8	-0.6	-0.4
21	-1.1	-1.1	0.1	-0.3	-1.4	-1.9	-1.8	-1.5	0.2	1.4
22	-1.3	-0.8	0.4	-0.2	-0.9	-1.5	-1.2	0.9	0.5	0.6
23	-0.2	-1.2	0.1	-0.9	-0.4	-1.1	0.4	-0.3	0.7	-0.4
24	-1.6	-1.2	-0.3	-0.8	-1.1	-1.9	-1.8	-0.9	-0.8	-0.8
25	-0.2	0.6	1.2	0.2	-0.2	0.0	-0.8	1.3	-1.4	1.0
26	1.4	0.8	-0.5	1.8	1.2	1.5	1.8	0.9	1.5	1.7
27	1.9	1.3	0.3	1.7	0.6	1.9	1.7	1.3	0.6	0.6
28	-0.8	0.0	0.4	-0.2	-1.4	0.0	-0.6	0.0	-1.2	0.3
29	0.2	0.0	-0.2	-0.5	-1.2	-1.1	-1.3	-1.1	-0.8	-1.9
30	0.9	-0.3	-1.4	-0.4	-1.1	-0.8	-0.3	-2.0	-2.0	-0.8
31	1.7	0.6	-0.1	1.2	1.3	1.1	1.4	-0.8	0.4	-0.1
32	1.0	1.1	1.4	-1.2	1.5	-0.4	-0.2	-0.3	1.8	-0.1
33	1.4	0.1	-1.0	1.2	0.9	-1.1	1.7	-0.6	-0.7	-0.8
34	-0.5	-1.3	0.4	-1.5	-0.5	-1.5	-1.1	-0.1	0.3	-1.2
35	-0.3	0.3	-1.7	-1.2	-1.1	0.4	0.9	-0.6	-0.8	-1.2
36	0.5	1.1	0.5	1.4	-0.2	0.0	0.5	1.2	1.3	-0.1
37	1.7	1.4	0.7	1.1	0.7	0.8	1.8	0.8	1.9	1.4
38	1.4	0.1	-1.8	-1.0	0.6	0.4	0.9	-0.6	0.6	0.3
39	0.4	-0.4	-0.2	-0.2	1.4	1.1	1.4	0.9	1.6	1.0
40	-1.9	-1.3	0.2	-1.3	0.3	-1.5	-1.4	-0.6	0.1	1.0
41	-1.4	-0.3	0.3	-0.3	-0.1	-0.4	0.0	0.5	-0.6	0.3
42	-1.5	-0.5	-0.4	-0.3	1.2	-0.4	-1.0	-0.9	0.0	-0.1
43	-0.8	-0.7	-0.5	-1.5	0.4	-0.8	-0.5	-0.5	0.4	1.7
44	-1.0	-0.5	-2.3	-1.2	-0.6	0.4	0.0	-1.3	-2.2	-1.9
45	0.4	-0.1	1.3	1.7	1.7	-0.8	0.6	1.2	1.2	1.0

Note. The statements can be found in Table 1.
Descriptions for the Mapping Study Discourses can be found in Appendix C.

C.5.2. Discourse Narratives—Six Discourse Map

Position A: Beneficial Scientific Progress

The first position is most strongly characterised by its enthusiasm about the potential medical benefits that might be reaped via the science of human genome editing. Although all the positions favour continued research, this one particularly endorses the science and "keeping an open mind" about new discoveries. People holding this position are more likely than those holding other positions to accept having their own genes edited. Their enthusiasm for scientific progress is driven by the desire to reduce the burden of human disease and suffering.

Despite enthusiasm for genome editing science, the *Beneficial Scientific Progress* position agrees with other positions that more science is needed before genome editing can be clinically applied. However, Position A is relatively unconcerned about the potential negative social and ethical implications associated with human genome editing, including enhancement.

Participants who are strongly associated with the *Beneficial Scientific Progress* position tend to prefer policies that permit both non-heritable and heritable genome editing with strict oversight. These participants are unanimous in their rejection of a blanket prohibition of human genome editing technologies.

Position B: Social Benefits/Precautionary Risks

This position is distinguished by a strong concern for the potential social benefits and risks of human genome editing. Although equal access to genome editing is a common concern across positions, Position B is particularly worried that unequal access will advantage some groups over others and result in a society of haves and have-nots. People associated with the *Social Benefits/Precautionary Risks* position are particularly worried that private investment will direct genome editing research towards non-medical interventions (i.e., enhancements) and away from pursuit of the public good.

Nevertheless, the *Social Benefits/Precautionary Risks* position is strongly supportive of genome editing and mitochondrial donation that will benefit human health and increase wellbeing. As with Position A, people associated with this position would like to see further research take place regarding potential risks before genome editing is applied. However, in contrast with Position A, Position B does not consider safety of the technology to be a sufficient requirement for approval of genome editing.

Of the surveyed policy options, participants associated with Position B tended to rate the option that prohibits clinical applications but permits genome editing research as most preferable. Permitting non-heritable and heritable genome editing with oversight tended to be rated second highest. Their least preferred policy options is to permit all uses of human genome editing.

Position C: Principled Constraints

Of the positions identified in this research, only Position C is explicitly opposed to human genome editing. People associated with this position emphasise the potential of unintended risks of genome editing and object to its intended applications. This objection extends to clinical and non-clinical applications. They would not be okay with having their own genome edited nor consider using genome editing for their children.

While the safety of genome editing is a concern for Position C, the social and ethical implications of the technology are central. Unlike Position B, however, equal access to the technology is not a major concern. Compared with the other positions, people associated with Position C are more likely to cite

cultural beliefs as reasons to oppose genome editing. This includes a belief that facing illness and adversity gives us strength and that changing someone's genes means fundamentally changing who they are.

People associated with Position C have a less unified set of policy preferences than do those who align with Position A or Position B. Nevertheless, the participants associated with this position tend to favour policies that prohibit the use of human genome editing, except in research. Among the policy options that permit clinical applications, participants associated with this position favour permitting non-heritable and prohibiting heritable human genome editing.

Position D: Revolutionary Medicine

Position D is characterised by its singular focus on the positive potential of human genome editing to prevent genetic diseases or improve the lives of those living with such diseases. Unlike Position C, the *Revolutionary Medicine* position does not see any value in facing illness and adversity. Instead, people associated with this position feel that we have an obligation to strengthen coming generations by eradicating disease.

Although strongly supportive of medical applications of human genome editing, this position is concerned about the use of the technology for enhancements and worry about the long-term consequences of genome editing. Nevertheless, this position trusts science and feels that decisions about genome editing should be left to the experts.

Participants aligned with Position D prefer policy options that permit human genome editing with certain conditions. They appear to be less concerned about the type of genome editing (heritable versus non-heritable) than on the conditions by which it is governed, such as strict oversight and not for profit. Their least favoured policies are those that provide a blanket permission or prohibition of human genome editing.

Position E: Profound Social Risks

Position E represents the view of genome editing as presenting profound social risks. This position is distinguished by a strong concern that genome editing will change society for the worse. People associated with this position find the idea that genome editing can make perfect people and societies extremely dangerous and fear it will lead to a dystopian future.

Nevertheless, people associated with this position are not opposed to genome editing *per se*. If the changes cannot be passed on to future generations, they agree that everyone has a right to decide for themselves whether to undergo genome editing.

Participants aligned with Position E have diverse policy preferences, but mostly agree that a blanket prohibition or permission would be among their least favoured policy options. Their strongest agreement in favour of a policy is for the approval of non-heritable human genome editing and mitochondrial donation, if these are provided not for profit.

Position F: Libertarian Revolutionary Medicine

Position F is distinguished by a relatively high-risk tolerance when it comes to genome editing research and clinical applications. Compared with the other positions, the *Libertarian Revolutionary Medicine* position is less concerned about potential social and ethical issues that might result from the use of human genome editing. In particular, this position is not worried that the cost of the technology will limit access to genome editing to the wealthy.

This position strongly supports the rights of parents and guardians to edit the genes of their children before they are born. They disagree that editing genes that will be inherited is problematic because it means making decisions for future people who don't exist yet.

Only one Australian Citizens' Jury participant was strongly associated with this position. They prefer the policy outcome that permits all application of genome editing, with oversight.

APPENDIX D.
ENSURING REPRESENTATIVENESS AND DIVERSITY IN PARTICIPANT SELECTION AND AMONG EXPERT WITNESSES

D.1. Introduction

This appendix details the recruitment and selection process used to constitute the Australian Citizens' Jury. A unique feature of the approach involved the use of discursive representation, which drew on methods to identify, characterise and map the prevailing Australian discourses on the subject of human genome editing in order to represent a variety of views as part of deliberation.

Achieving a representation of the Australian community for a small forum like the Australian Citizens' Jury involves a different approach to, for example, conducting a population survey. The focus here is on achieving a distribution of characteristics within the Australian Citizens' Jury that reflects the broader public. Most commonly this involves focussing on mirroring broad demographic characteristics (Descriptive Representation). However, there are arguments for broadening the selection categories to reflect the range of positions in the community. For this study we used the approach of Discursive Representation to achieve this goal. This is particularly important because a primary goal for the Australian Citizens' Jury is to generate a conversation across a range of (pre-deliberative) views.

Why the focus on diversity of views through a discursive approach? The discursive component of this research seeks to provide a window into the public views on a complex issue, one that is anticipatory (MacKenzie and O'Doherty, 2011)—where there is little actual current public discussion on an issue. A deliberative approach addresses limitations with commonly used methods, such as opinion surveys, which pick up non-attitudes, or unreflective responses that are overly sensitive to cues in the questions asked (Dryzek, 1990). Deliberative processes also provide a better context for reasoning through ethical trade-offs and dilemmas than opinion surveys. Deliberative processes involving lay citizens are well-established globally (Grönlund et al, 2014; OECD, 2010) and have been carried out on a wide range of issues involving complex science and public value interactions (MacKenzie and O'Doherty, 2011; Secko et al., 2009). To achieve a discursive outcome, it is important to ensure that the full range of pre-deliberative views are included in the process, where important questions are raised, and where different perspectives interact in a manner that maximises potential for integrating into a coherent whole, and resolve tensions. Where differences remain (for good reason) there is also a need to understand why, and the associated implications for further public engagement and decision making.

The following discussion outlines the overall approach used for selecting participants for the Citizens' Jury, including the implications for using a discursive representative approach. The distribution of witnesses who provided evidence to the process is also assessed.

D.2. Participant Selection

Participants for the mapping study, citizens jury, and control group were recruited from a research panel provided by Stable Research. The recruitment pool comprised potential participants who were provided by Stable Research. Recruitment was conducted progressively, in a series of waves, in addition to the Mapping Study Participants who indicated a willingness to continue with the project. At the conclusion of each wave the distribution of potential participants was checked against the core selection criteria (see Table 7 and Table 8). Together, the five primary descriptive and discursive criteria comprise 38 categories, each involving a target quota. In the case of descriptive criteria the quotas were set to reflect the distribution of each category within the Australian population, with a different approach taken for Discursive representation. Where possible, there was an attempt to

achieve a distribution of participants across a secondary set of criteria that, listed in , but without the use of target quotas.

Selection also sought to achieve distribution across several secondary categories (religion, political spectrum), as well as excluding limiting the number of participants who were either trained or worked in areas related to genomic research (see section D.2.2).

The result of this process involved the selection of 23 citizen jurors to participate in the ACT. The 21 participants who comprised the Control group were initially selected using a similar approach.

The following describes in greater detail how participants were selected.

D.2.1. Sampling for Descriptive Representation

The aim of descriptive representation is to include all relevant groups, often defined by ascriptive characteristics such as gender, race and class. In this case, descriptive representation was sought by stratified sampling of survey respondents according to location, gender, age, and education. Table 7 shows the distribution of CJ participants across descriptive sample characteristics.

Table 7: Selection Stratification: Descriptive Criteria

	Category	Code	Australia‡	Recruitment Sample		Sampling Quotas			Australian Citizens' Jury
			%	n	%	Min	Target	Max	
Gender	Female	1	48%	71	50%	10	12	12	11
	Male	2	52%	124	50%	10	12	15	12
State	New South Wales	1	32%	29	33%	4	8	8	8
	Victoria	2	26%	14	25%	0	6	5	2
	Queensland	3	20%	40	21%	2	5	4	4
	South Australia	4	7%	10	8%	1	2	3	2
	Western Australia	5	10%	46	8%	1	2	3	2
	Tasmania	6	2%	1	0%	1	0	3	0
	Northern Territory	7	1%	1	0%	0	0	1	1
	ACT	8	2%	54	0%	2	0	6	4
Remoteness	Major Cities of Australia	1	72%	151	71%	12	17	17	19
	Inner Regional Australia	2	18%	32	17%	4	4	5	3
	Outer Regional Australia	3	8%	10	13%	2	3	4	0
	Remote Australia	4	1%	2	0%	0	0	1	1
	Very Remote Australia	5	1%	0	0%	0	0	1	0
Age Category	18-24	1	13%	7	17%	2	4	6	4
	25-34	2	19%	30	17%	2	4	6	5
	35-44	3	17%	59	17%	2	4	6	4
	45-54	4	16%	40	17%	2	4	6	4
	55-64	5	15%	33	17%	2	4	6	1
	65+	6	20%	26	17%	2	4	6	5
Educatio n Level	Junior Secondary Education	1	26%	7	25%	4	6	8	2
	Senior Secondary Education	2	18%	20	17%	2	4	6	3

TAFE/CIT Certificate	3	17%	48	17%	2	4	6	4
Diploma or Advanced Diploma	4	10%	36	8%	0	2	4	3
Bachelor's degree	5	19%	68	21%	3	5	7	9
Graduate Diploma or Certificate	6	3%	23	4%	0	1	2	1
Postgraduate Study	7	8%	33	8%	1	2	3	1

Notes: Total number of recruited participants in the recruitment pool = 195. Number of valid population survey responses = 845
‡ Australian population percentages are based on ABC census figures except for Discursive Representation, which draws on the population survey data.

D.2.2. Discursive Representation

Discursive representation was sought by stratified sampling of survey respondents according to their position across the four main discourses identified in the mapping study.

Association with Discourses: Factor Loadings and Indexing

The extent to which participants were associated with a discourse was assessed using factor loadings. Briefly, factor loadings are calculated by correlating the responses to the factor scores for the discourse statements (Table 6).. For some states of the project, including recruitment in (Stage 3 of the project, see Figure 2) a smaller sample of statements was used in the survey than the complete set of statements (Table 1).

Sampling of these items was informed by an approach developed by Niemeyer (2010), which is done to maximise the correlation between the indexed loadings and the factor loadings that are obtained when using the full statement set. For the Mapping Study Discourses the sampling of statements was tested by comparing the loadings obtained from participants using the full statement set, against the indexed loadings obtained using the sub-sample. In most cases the correlation is greater than 0.9.

The criteria for discursive sampling is provided in Table 8. Respondents were coded depending on whether they achieved a significant loading for a discourse, with a high loading also being coded—with a significant loading level set at 0.5 and high loading at 0.7.

Table 8: Discursive Representation Coding

Code	Criteria
0	No sig' loading
1	Confounded Loading
2	A Moderate Loading (>0.5)
3	B Moderate Loading (>0.5)
4	C Moderate Loading (>0.5)
5	D Moderate Loading (>0.5)
6	A High Loading (>0.7)

7	B High Loading (>0.7)
8	C High Loading (>0.7)
9	D High Loading (>0.7)

Table 9 shows the distribution of the recruitment of individuals among the discourse categories in the Australian population, obtained retrospectively as part of the population survey (project Stage 9, Figure 2), distribution among the pool of recruited participants, and final distribution of citizens' jury participants across the four mapping study discourses.

In contrast to descriptive stratification outlined in Table 7, discursive stratification did not seek to mirror the distribution of discourses among the Australian community. The priority for discursive representation is to ensure a distribution of participants across the relevant discourses. The quotas were allocated accordingly, to ensure that there were individuals who were uniquely associated with each of the discourses. Allocations were also provided for individuals who were not associated with any of the mapping discourses, as well as those who were associated with more than one discourse.

Table 9: Selection Stratification: Discursive Criteria

Category	Code†	Australia‡	Recruitment Sample		Sampling Quotas			Australian Citizens' Jury
		%	n	%	Min	Target	Max	
No sig' loading	0	53%	63	28%	4	4	8	5
Confounded Loading	1	12%	27	12%	0	4	6	3
A Moderate Loading (>0.5)	2	11%	32	14%	2	2	6	3
B Moderate Loading (>0.5)	3	12%	22	10%	2	2	6	1
C Moderate Loading (>0.5)	4	6%	9	4%	2	2	6	3
D Moderate Loading (>0.5)	5	0%	1	>1%	2	2	6	0
A High Loading (>0.7)	6	4%	47	21%	1	2	4	2
B High Loading (>0.7)	7	2%	21	9%	1	2	4	3
C High Loading (>0.7)	8	1%	4	2%	1	2	3	2
D High Loading (>0.7)	9	0%	2	1%	1	2	3	1

Notes: † The coding for discursive representation can be found in Table 4.
‡ Australian population percentages were obtained from the population survey in stage 9 of the project, after recruitment.

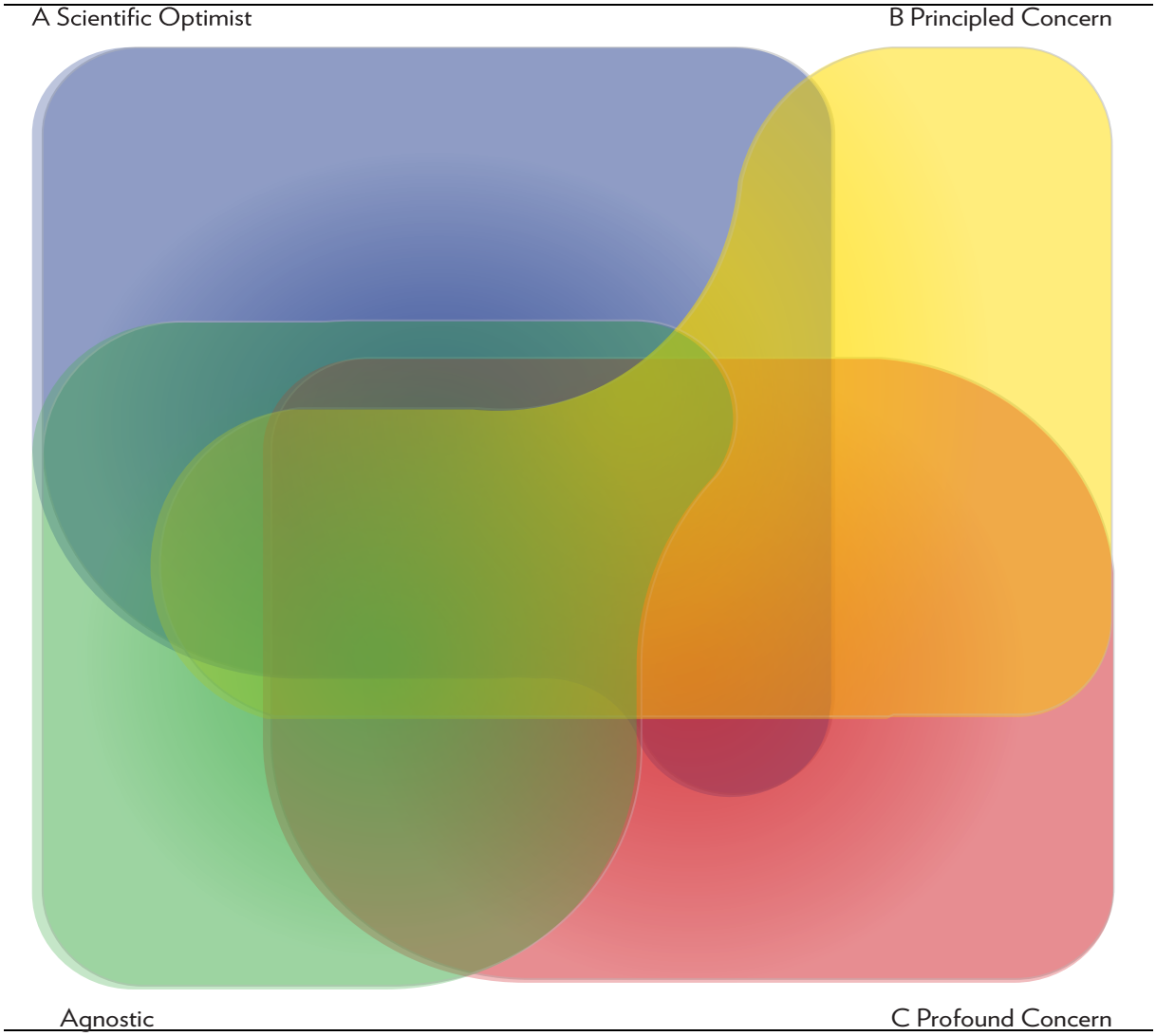
Table 9 shows the numbers of Australian Citizens' Jury participants in each of the discursive categories. And Figure 6 shows the distribution of Australian Citizens' Jury participants on the Mapping Study discourse map. In two cases the quota for a category was not met (code 3, moderate loading on discourse B; and code D, moderate loading on discourse D). It can be seen from the table that the available pool of recruits associated with discourse D was exceedingly small. All three individuals were selected, but two withdrew. It can also be seen that the extent of this perspective in the wider population appears to be exceedingly small. While it is possible that this view is important in the wider discussion about human genome editing, it is also one that reflects a degree of ambivalence toward the technology. The position itself appears to have dissipated altogether during

deliberation, and we do not have any evidence to suggest that the themes raised by the discourse factored significantly in deliberation, or that its absence constituted an issue for deliberation.

By contrast, discourse C, which also features in the community in relatively small measure, turned out to be particularly relevant during deliberation. It is this discourse that is focussed on the more profound issues raised by human genome editing, the same issues that participants flagged as being important, but did not have time to work through sufficiently during the Australian Citizens' Jury. Based on our recruitment pool of 195 with a 6% prevalence of Discourse C and a deliberative process of 24 participants, the probability of recruiting any given individual from the pool is 0.12. The probability that an individual who shares the perspective of Discourse C being recruited (by accident) is 0.007, or less than 1%.

In other words, without including a discursive representative strategy as part of recruitment it is very unlikely that perspective would have been given voice as part of the deliberative process. This is particularly critical given the emphasis on the more profound issues raised during the process. Clearly there was insufficient time to work through the issues raised, but they did get a heard, which we attribute in at least some measure to our recruitment strategy.

Figure 14: Discourse Positions of Recruited Australian Citizens' Jury Participants



D.2.3. Secondary Selection Criteria

Diversity of participation was also sought for religion and location on the L-R political spectrum. (Table 10) Religion was included, given the likelihood that at least some of the participant positions would be informed by their religious background. Political spectrum was also included for similar reasons, in conjunction with longstanding experience suggesting some measure of skewness in self-selection along political lines (e.g. Jennstål, 2018), as well as greater rates of withdrawal among individuals who self-identify as toward the right of the political spectrum which the overall selection strategy sought to mitigate.

Similar experience suggested that issues involving a strong technical dimension also appear to disproportionately attract members of the public who are technically trained and/or employed as a professional in a related industry. To address this possibility, a screening question was added to the recruitment survey asking if potential recruits were trained or employed in relevant areas (see Table 10).

Table 10: Selection Stratification: Secondary Criteria

		Code	Recruitment Sample		Australian Citizens' Jury
			n	%	
Religion	Christianity	1	93	48%	13
	Islam	2	5	3%	2
	Buddhism	1	6	3%	2
	Hinduism	2	4	2%	0
	Judaism	3	1	1%	0
	Other	4	3	2%	0
	None of the above	5	80	41%	6
	Prefer Not to say	6	3	2%	0
Political Spectrum	Strongly Left	1	2	1%	0
	Left	2	14	7%	2
	Moderately Left	3	35	18%	4
	Slightly Left	4	33	17%	2
	Neutral (left)	5	65	33%	10
	Neutral (right)	6	16	8%	3
	Slightly Right	7	9	5%	0
	Moderately Right	8	14	7%	1
	Right	9	3	2%	1
	Strongly Right	10	4	2%	0
Professional Interest	No Professional Interest	1			
	Medicine/Medical Studies	2	2	0	0
	Public Health	3	10	1	1
	Biochemistry and cell biology	4			0
	Genetics	5	1	1	1
	Microbiology	6			
	Biological Sciences	7	4	0	0

D.2.4. Recruitment Contingencies Management

The ongoing COVID-19 pandemic posed several challenges which affected participant recruitment for the citizens' jury and control group cohorts. While travel between all states was possible at the time of recruitment, the imminent possibility of travel restrictions, meant that recruitment from Covid-19 affected areas was limited. A large Covid-19 outbreak in Melbourne prior to the citizens' jury, prevented the recruitment of participants from large areas of Victoria. Several panel members also chose not to participate in the citizens' jury due to concerns about potential exposure to Covid-19 due to interstate travel and face-to-face deliberation. Consequently, a higher-than-expected number of participants were recruited locally from within the Australian Capital Territory and the neighbouring state of New South Wales.

Trade-offs between descriptive and discursive representation of Australian Citizens' Jury and control group participants were necessary as a further consequence of the restricted recruitment pool. This was particularly the case when seeking to recruit participants who held less common positions.

A contingency was built into the recruitment design where the control group also served the function of providing a reserve pool of participants for the Australian Citizens' Jury, in case of withdrawal or inability to attend due to a COVID outbreak within their residential locality. In the lead up to the Australian Citizens' Jury reporting on COVID cases was monitored daily and the relevant postcodes cross checked against the pool of recruited Australian Citizens' Jury participants. If an outbreak had been recorded within the previous two weeks, or a participant had withdrawn for other reasons, a substitute was sought from within the pool of selected control group participants reflecting as far as possible the same selection categories within the selection criteria.

The combination of multiple stratification categories and need to adapt to withdrawals and ineligibility due to COVID outbreak meant that is was difficult to achieve the quotas set for recruitment. However, despite these challenges selection within the target range was achieved for 31 of the 38 target categories (see Table 7 and Table 8).

D.3. Diversity of Perspectives Among, Witnesses, Experts and Research Team

D.3.1. Diversity of Perspectives Among Expert Witnesses

Roberts et al. (2020) argue in favour of achieving diversity among witnesses in deliberative mini publics, although they do not distinguish between technical expert witnesses and advocates. Feedback from participants, facilitators and experts participating in the workshops assessing the Australian Citizens' Jury and its outcomes also raised the absence of witnesses from advocacy groups who could speak to the more profound questions, those that are associated with Discourse C.

If the main criteria is diversity among witnesses, the Australian Citizens' Jury is a qualified success. The relative positions of witnesses, experts and recruited participants is analysed below in section F.1 It can be seen from right hand side of Figure 17 below that there is a strong degree of diversity among the expert witnesses. Some do not fit onto the same discourse map—which at least partly reflects a different structure of reasoning compared to the non-specialist community. Only one of the witnesses appears to be associated with Discourse C, and non with Discourse D. The latter observation is unsurprising — experts are unlikely to be ambivalent about the technology, which would also be expected for advocates. The lack of voice among experts associated with Discourse C, however, might be considered as reflecting a deficiency in the distribution of perspectives among the pool of witnesses.

APPENDIX E. TRACKING CHANGES RESULTING FROM THE AUSTRALIAN CITIZENS' JURY

This section provides preliminary analysis of transformation during deliberation (from pre- to post-deliberation) of participant. The analysis serves two main purposes,:

1. To demonstrate the diversity of positions among participants before and after deliberation and provide context for understanding the level of agreement with the various recommendations reported above;
2. To understand the nature of changes that occurred during deliberation, interpretation of which can be used to better understand how the wider public view may evolve as they are engaged with the issue of human genome editing
3. To facilitate a preliminary interpretation of these positions considering the potential for improvement of the deliberative process, and the possibility/likelihood of further development of these positions.

The analysis below draws on the six-discourse map to track the changing positions of deliberative participants. A description of these discourses can be found in Appendix C (section C.4).

Interpretation of post-CJ positions

Figure 9 plots the pre- and post-deliberation of AusCJ participants. There is no overwhelmingly strong trend in terms of the observed transformations, although there is a stronger movement toward the upper right-hand side of Figure 1 toward positions that reflect a more positive disposition toward human genome editing.

However, it is important to note that even those most enthusiastic about the technology maintain some level of concern and maintain contingencies regarding their acceptance of any application (especially heritable applications). Even the most supportive position (F) involves a desire to maintain community oversight of the development and application of human genome editing.

Although there are significant shifts in position among individuals, and a slight trend in favour of (at least exploring) the technology, there is no strong overall movement of policy preferences in favour of greater application of the technology. This is consistent with participants' recommendations, to the extent that there is interest in the possibilities for reducing the burden of disease, but in most cases, (except for F) approval is heavily conditional upon demonstrating minimal risk (via research) and addressing concerns regarding access and equity.

Importantly, there is a group of participants associated with position C who (in most cases) hold a much more restrictive view of the technology. There is greater tendency to prefer a ban on any application, but this varies among members of this group. What is widely shared by this group is an identification with principled objections to the technology, based on deeply held principles, or concern about the fundamental implications that its application raises.

The implications of this view and its extent need to be examined further, considering the forthcoming population survey. In their feedback on the Australian Citizens' Jury many participants felt that a more critical perspective including the concerns of position C was missing. It is possible that this gap, along with time pressures meant that these concerns were not adequately discussed, resulting in an incomplete picture of a considered community position regarding the technology.

These results suggest that failure to properly engage with the concerns of position C risks increasing polarisation among the wider community.

Despite the limitations discussed above, the Australian Citizens' Jury did succeed in creating conditions for high quality deliberation about human genome editing, resulting in well-developed positions. There is majority acceptance that the technology is worth exploring through further

research, even excitement regarding its possibilities to prevent human suffering. However, for many participants acceptance is contingent. There is a need for careful examination of risks, and ongoing community oversight to ensure equitable access and prevent misuse. There is also concern regarding the deeper implications associated with the technology, represented most strongly by positions C and E. These concerns are directly mainly at HHGE, but there is also potential for these concerns to spill over and impact the acceptance of the technology more broadly.

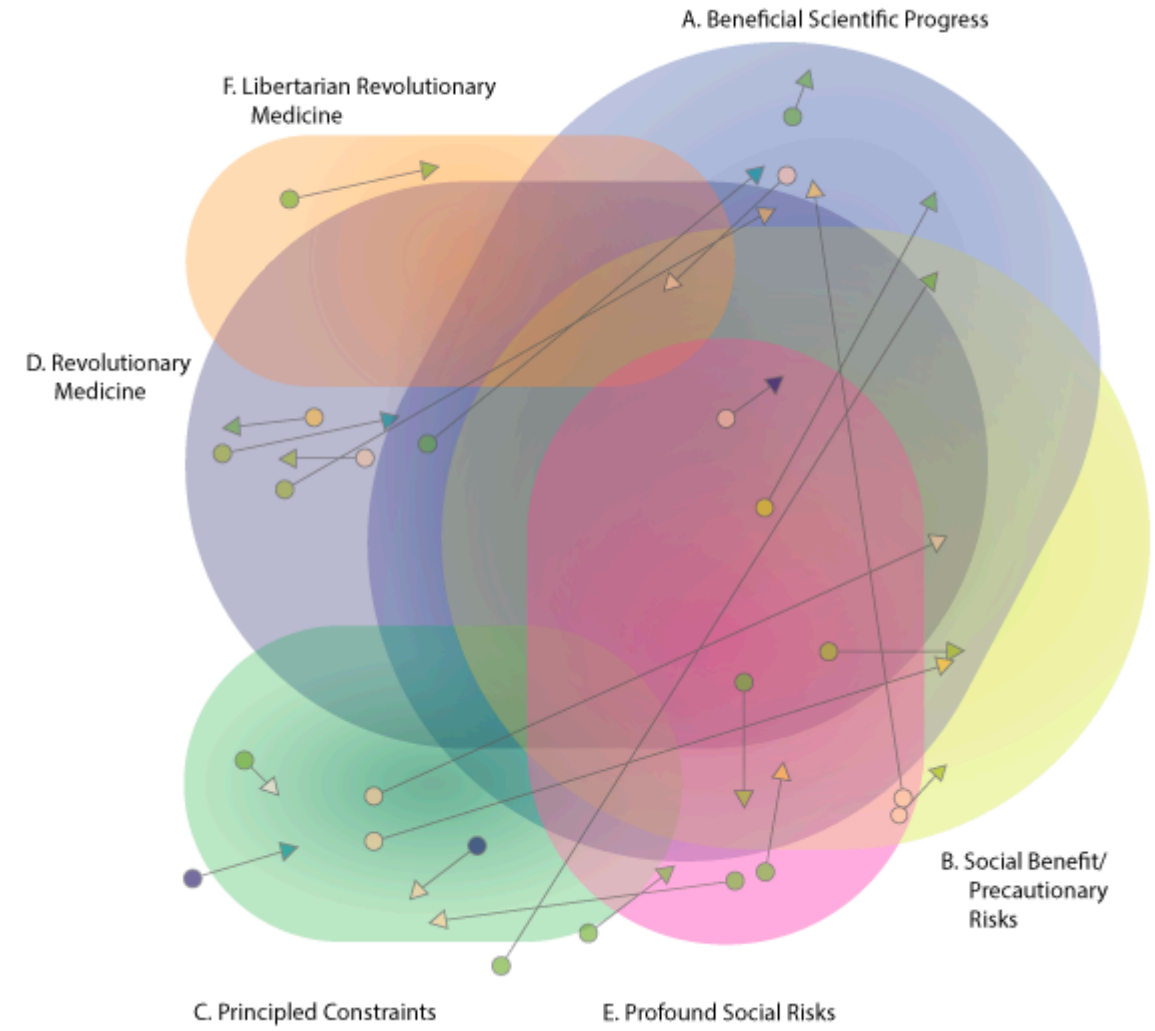
It is important that these concerns are engaged. The alternative is to risk growing community polarisation and distrust, impacting on any potential benefit. The observations from the Australian Citizens' Jury, and the research that is to follow will help to inform how that engagement can best proceed.

E.1. Post Deliberation Positions and policy preferences

The positions of participants before and immediately after the deliberation are mapped in Figure 15. Participants' location on the map broadly represents their disposition at that stage of the process. Six types of position were identified following deliberation.

The preferred policy option of participants before and after deliberation is also represented in Figure 15 using colour coding (as indicated by the Legend below the figure).

Figure 15 Deliberative Participant Transformations—Six Discourse Map



Legend (Transformations)

Deliberative Stage Pre	Post	Most Preferred Policy Option
		Permit all applications
		Permit all (Public use only)
		Permit all (Community oversight)
		Permit Non-Heritable and Mitochondrial (Clinical)
		Permit Non-Heritable (Clinical)
		Permit Non-Heritable (Clinical, Public use only)
		Prohibit all (Except for research)
		Prohibit all applications

E.2. Analysis of Deliberative Reason

Analysis of deliberative reasoning has been performed using the Deliberative Reasoning Index (DRI) (Niemeyer and Veri, 2022). DRI is a measure of the extent to which the participants are "reasoning together" as a group and are on the same page in terms of how they understand the issues.

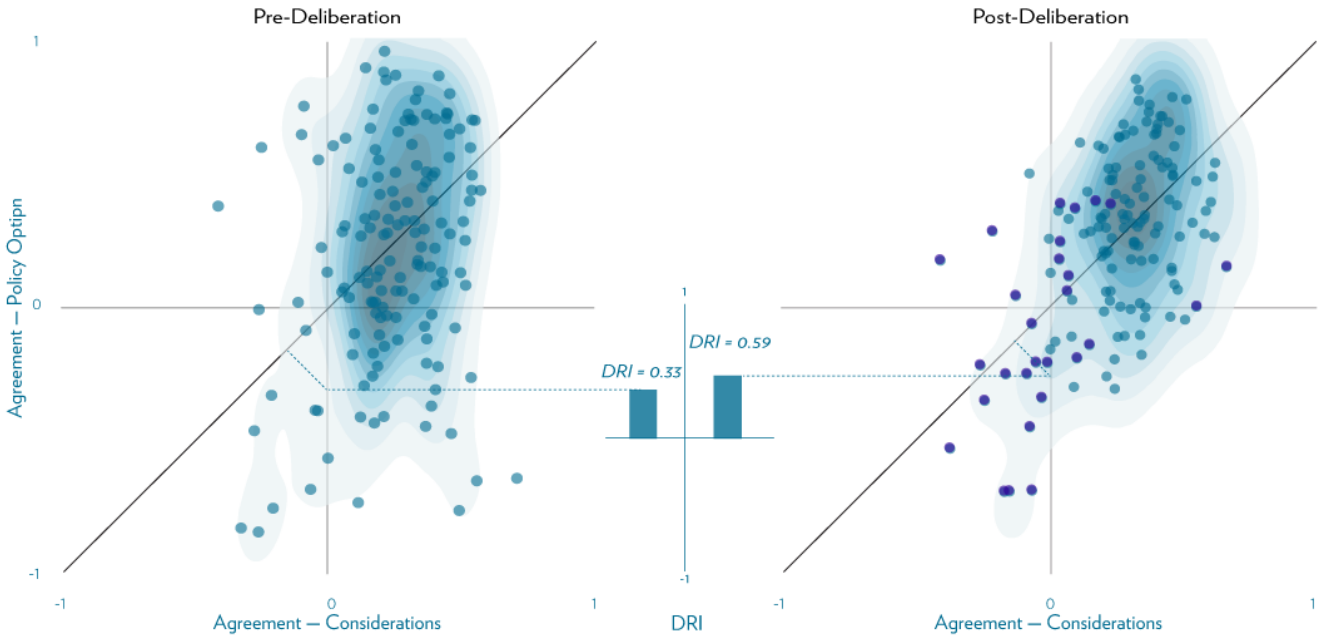
Importantly, the method does not measure agreement. It does not assess the capability to reason for any given individual. Nor does it involve forming judgements about the "right" outcome.

What the method does capture is the extent to which members of a deliberating group consider the same kinds of issues to be relevant to the discussion and whether they share a similar pattern of reasoning. These qualities act as proxies for deliberative ideals, where participants take seriously the concerns that are raised within the group, and integrate these concerns into their reasoning (Niemeyer et al., 2021).

To the extent that these internalising processes have been achieved, a consistency of reasoning forms reasoning, where a given pair of participants' positions regarding considerations such as equity, ethics, cost etc is consistent with their policy preferences.

Figure 16 below plots consistency across all pairs of participants in the Australian Citizens' Jury before and after deliberation. DRI measures the extent that the points (representing pairs of participants) fall toward the diagonal line in the graphs. It can be seen from the figure that there is a tendency for consistency to improve as a result of the Australian Citizens' Jury, where DRI improves from 0.33 to 0.59 (on a -1 to 1 scale), where 1 represents "perfectly consistent reasoning" that would only likely be approached under very high quality deliberative situations, involving sufficient time to work through the issues and develop a shared understanding of how opinions inform the conclusions that participant's draw about their preferred policy outcome.

Figure 16: DRI Plots and Graph



The level of improvement in DRI experienced during the Australian Citizens' Jury is comparatively small compared with other cases {Niemeyer, Forthcoming #7328}. This is likely to be, at least in part, a result of the high complexity involved in the issue, which requires more time in which to learn, discuss and process. The finding is consistent with the feedback from participants that there was not enough "deliberative time" to work through everything that they felt they needed to discuss.

The post-event graph in Figure 8 also distinguishes the group of participants who were most strongly associated with Position C after deliberation, where pairs involving these participants are highlighted using the darker dots. This group expressed a much more restrictive view on human genome editing than their peers. This lower level of policy consensus is reflected in the distribution of these points toward the lower end of the figure. They also tend to be in less agreement regarding the set of consideration that were collected as part of the mapping survey.

The results in Figure 10 suggests that the disagreement associated with Position C is consistent with the reasoning of the rest of the group — in other words, although they disagree, they still understand the issues in the same way. However, although shared reasoning has improved during deliberation, those with position C do not appear to reason in quite the same way as the rest of group — where the point in the post deliberation graph falls further away from the diagonal line than the average.

One possibility is that the Australian Citizens' Jury did not provide the opportunity – in terms of both time and content – to work through the kinds of issues that are important to this group. And this limitation served to either amplify their concerns, or at least fail to attenuate them, creating salience effects where they were focused specifically on these issues. This effect would have resulted in higher levels of polarisation than might have been the case with greater levels of deliberation.

Addressing the limitations of the Australian Citizens' Jury poses a counterfactual. More research is needed to properly understand the implications. However, it is conceivable that, by providing more time for deliberation, and witnesses speaking more critically regarding genome editing technology and more specifically to concerns about the ethical, cultural, or religious considerations may have impacted the outcome, at least to some extent. Greater engagement with the specific concerns that were felt by group C might have resulted in greater integration of those concerns into the overall outcome. This might have resulted in a more cautious approach to human genome editing (particularly regarding heritable applications and a more ambivalent view regarding research). Or it might have resulted in greater detail in the recommendations addressing these concerns as they pertain to specific forms of research and application, for example, concerning the use of human embryos for HHGE research.

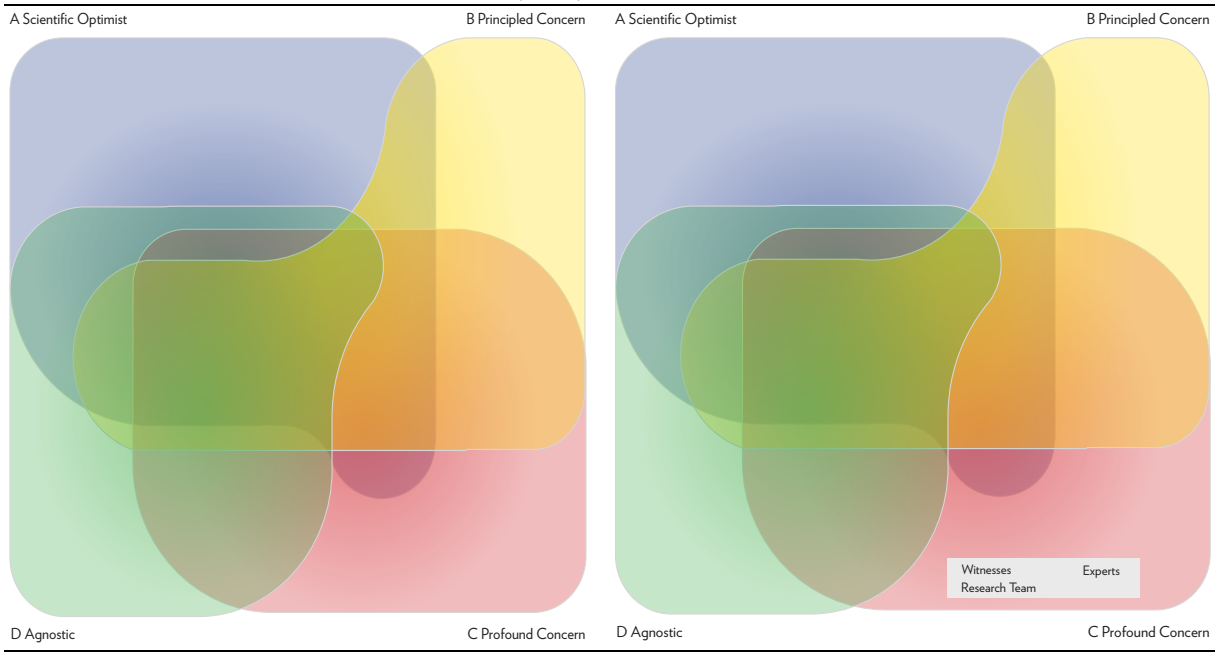
This scenario requires confirmation and will be the subject of further investigation. Nevertheless, the results as understood so far are instructive. A failure to adequately engage with the concerns of group C risks contributing to polarisation among the public.

APPENDIX F.
COMPARING THE VIEWS AND POSITIONS OF GENOME EDITING EXPERTS, PARTICIPANTS AND CONTROLS WITH THE BROADER POPULATION

F.1. Comparison of Experts/Witnesses to Participants

Figure 18 below shows the approximate locations of experts and the project research team using the Mapping Study Discourse Map. The figure shows a reasonable distribution of both experts and witnesses across these discourses, except for MS-D (Agnostic), and only one witness being associated with MS-C, in addition to one of the experts who provided a survey in Stage 11 of the project (see Figure 2). Two of the experts witnesses (and one research team member) are not associated with any of the four Mapping Study discourses, in which case they are placed closest to the discourse that they are most strongly loaded on.

Figure 17: Positions of Australian Citizens' Jury Participants compared to Experts—Mapping Study (four) Discourse Map

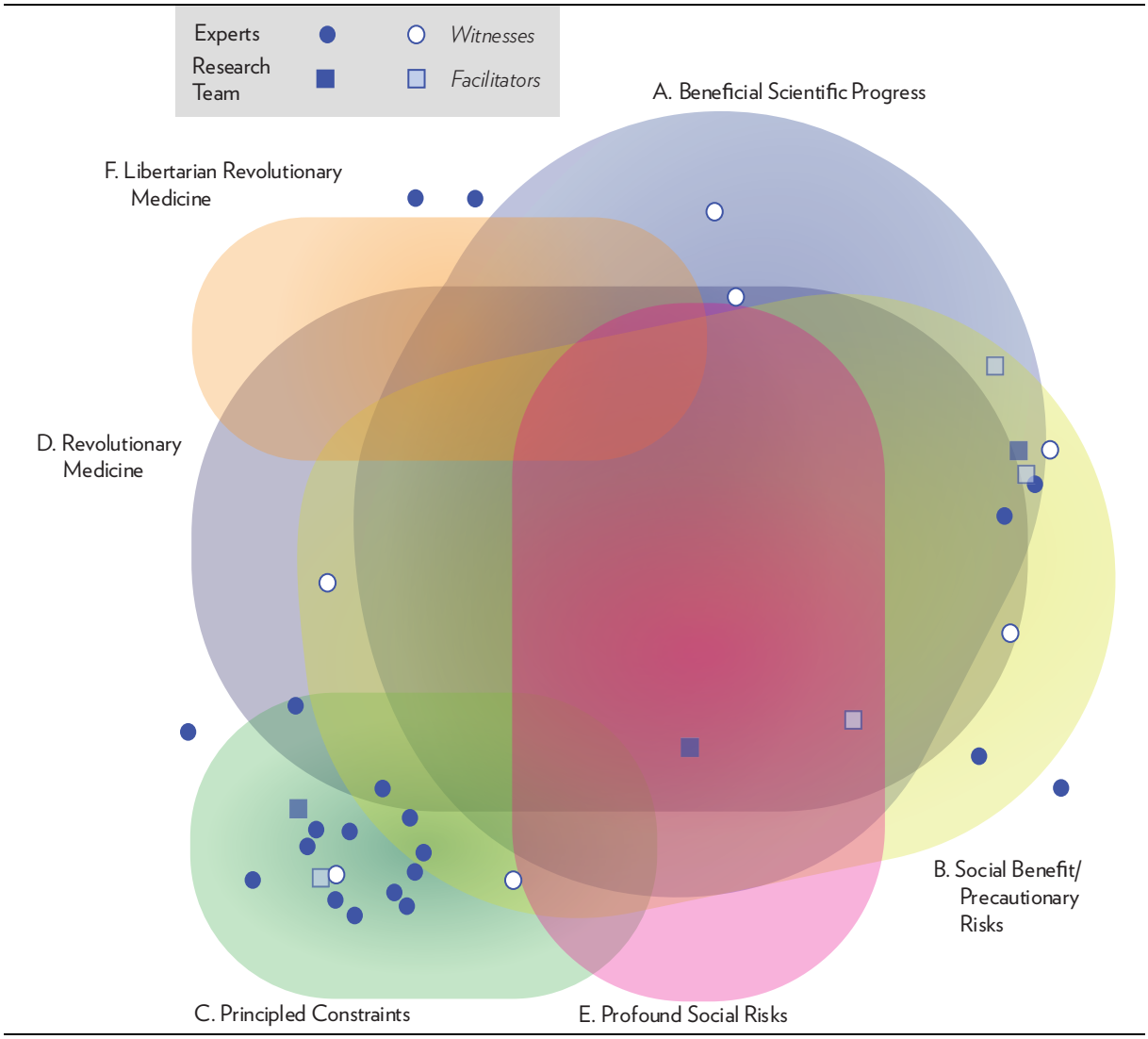


It is not surprising that there are no experts associated with MS-D—experts are unlikely to be agnostic about the very technology that is the subject of their research—the paucity of representation on MS-C warrants further consideration. Nor is it surprising that three experts/research team members are not associated strongly with any discourse. As outlined in Appendix C, these discourses involve a fairly coarse level of resolution capturing the pre-deliberation perspectives among the Australian community.

A better way to represent the relative positions of experts and the research team compared to participants utilised the more detailed post-deliberation (six) discourse map (PD-A,B,C,D,E), as shown in Figure 18. The figure overlays the positions of experts and research team over the migrations of deliberative participants (which have been faded to improve clarity, the original version is provided above in Figure 14).

Figure 18 shows a similar form of distribution to that shown in Figure 17, with all witness now able to be located on the Post Deliberative (six) discourse map, except for one witness that falls just short of a significant association with PD-B and PD-A. It is notable that there are now two witnesses associated with PD-C (with one also overlapping PD-B), where individuals who were associated pre-deliberation with MS-C tended to end up following deliberation (see section E.1).

Figure 18: Positions on Six Discourse Map—Experts, Research Team and Participants



F.1.1. Witness Positions compared to Deliberative Participant Transformation

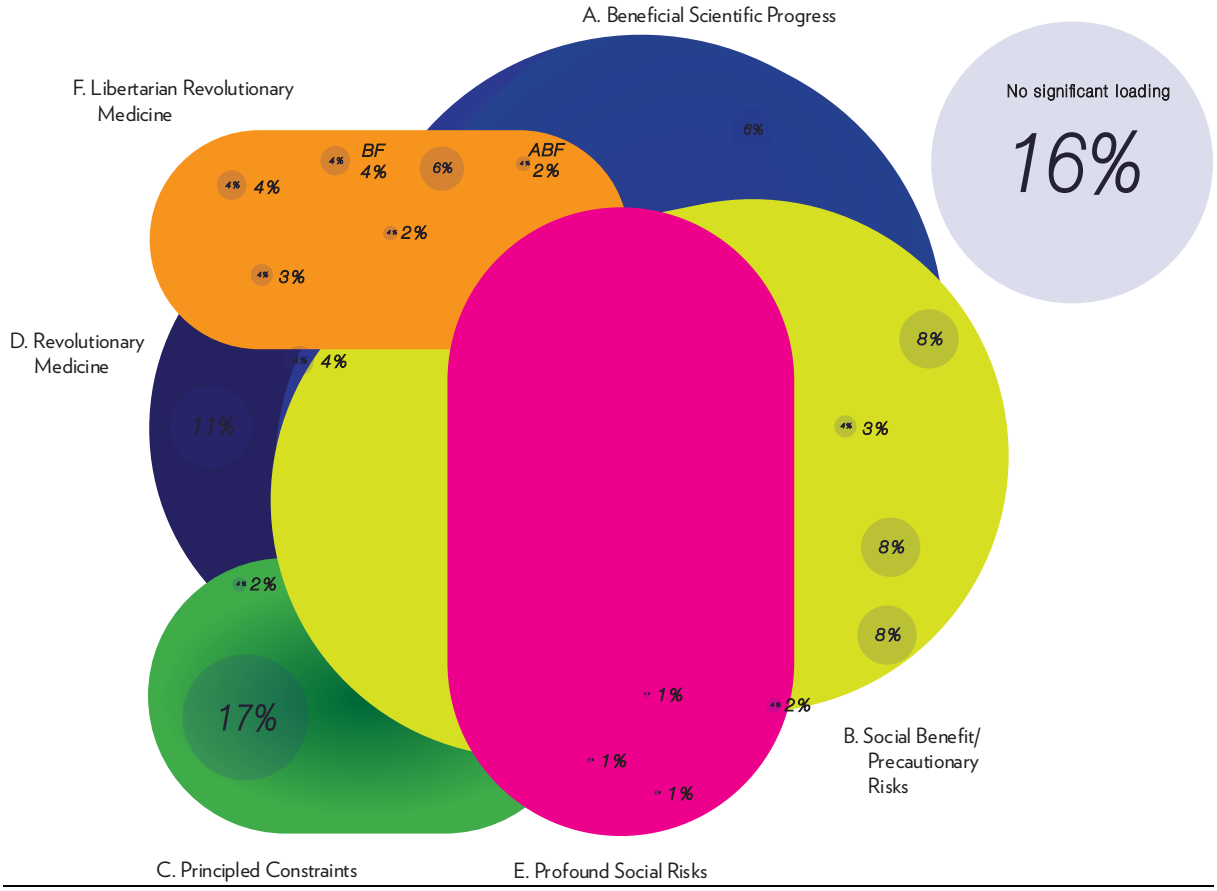
The diversity of views among witnesses already obviates at least to some extent any concern that there might be any distortion among the transformations experienced by participants during the process, which is also supported by analysis of deliberative reason in section E.2.

The pattern of migrations that can be seen in Figure 18 also serve to address one lingering concern. It is possible to argue that those participants who migrated toward PD-C, and who do not appear to share the same pattern of reason compared to the rest of the deliberative group, might have been subject to blandishment by those experts located in that discourse. However, this is very unlikely. It can be seen from Figure 18 that the two individuals most strongly associated with PD-C before deliberation migrated away from the position, toward PD-B.

F.2. Positions of Post-Deliberative Participants, Experts and the Australian Community

Figure 19 shows the distribution of the Australian Community using the Post-Deliberative Discourses. That a large proportion of the population is associated with PD-C is notable. Recall that the (post-deliberative) advocates of this position tended to be the most trenchant, and stable in their views, it is plausible that a similar dynamic may be observed among a significant proposition of the wider population. While it is important to note that, those deliberative participants associated with PD-C before deliberation tended to migrate toward B, it is worth paying attention to the concentration of the wider public in this corner of the map, and considering the implications for wider public engagement and communication.

Figure 19: Distribution of Australian Public Positions—Six Discourse Map



F.2.1. Testing Specific Differences in Positions

The cross examination between the group of experts, the population survey and the group of participants is undertaken considering the following three steps:

- First we analyse the differences in responses between group of experts, population and participant group in the Pre deliberative survey;

- Second we analyse the differences in responses between group of experts, population and participants group in the Post deliberative survey;
- Third, we compare the trends between the subgroup of experts that have been witnesses at the deliberative process with the responses between pre and post deliberative stages.

The test undertaken for the first two analytical steps are the Dunn test, while in the third step we use difference in median value responses and Mann-Witney U unpaired test, given the small sample of expert witnesses that might be source of strong results bias.

Pre deliberative phase: In general, during the pre-deliberative survey, the group of participants tends not to align with population believes in most of the considerations' responses.

In contrast it is observable a general pre-deliberative discourse alignments with the group of expert's positions in Q1, Q2, Q6, Q8, Q10, Q11, Q14 and Q16. This alignment reflects a median more cautious view on genome editing within expert and participants, while in the population such views are generally more liberal.

Indeed, in both the expert and participant group, while human genome editing is not considered as particularly scary (Q14), there are some evident doubts on using genome editing on themselves (Q12) or on their own children (Q11) even if it is proof to be safe (Q10).

Table 11: Dunn test – Participants before deliberation, Experts and Population

Question	Group 1	Group 2	p. value	Median value
Q1	Participants PRE	Expert	0.108	3.5
	Participants PRE	Population	<0.001***	5
	Expert	Population	0.798	6
Q2	Participants PRE	Expert	0.731	5
	Participants PRE	Population	<0.001***	6
	Expert	Population	0.0017**	7
Q3	Participants PRE	Expert	<0.001***	4.5
	Participants PRE	Population	<0.001***	7
	Expert	Population	1	7
Q4	Participants PRE	Expert	<0.001***	4
	Participants PRE	Population	<0.001***	7.5
	Expert	Population	1	7
Q5	Participants PRE	Expert	1	3
	Participants PRE	Population	0.519	5
	Expert	Population	1	6
Q6	Participants PRE	Expert	1	5.5
	Participants PRE	Population	0.003**	5
	Expert	Population	<0.001***	7
Q7	Participants PRE	Expert	0.018*	4.5
	Participants PRE	Population	<0.001***	8
	Expert	Population	0.264	7.5
Q8	Participants PRE	Expert	1	5.5
	Participants PRE	Population	<0.001***	5
	Expert	Population	<0.001***	7
Q9	Participants PRE	Expert	0.915	6
	Participants PRE	Population	<0.001***	6
	Expert	Population	1	7
Q10	Participants PRE	Expert	0.201	5.5
	Participants PRE	Population	<0.001***	6.5
	Expert	Population	0.171	7
Q11	Participants PRE	Expert	0.915	4
	Participants PRE	Population	<0.001***	4
	Expert	Population	0.014**	6
Q12	Participants PRE	Expert	0.611	4
	Participants PRE	Population	<0.005**	4.5
	Expert	Population	0.190	6
Q13	Participants PRE	Expert	<0.001***	4.5
	Participants PRE	Population	<0.001***	7.5
	Expert	Population	0.609	8
Q14	Participants PRE	Expert	1	5
	Participants PRE	Population	<0.001***	6
	Expert	Population	0.0016**	8
Q15	Participants PRE	Expert	0.02**	3.5
	Participants PRE	Population	<0.001***	6
	Expert	Population	0.532	6
Q16	Participants PRE	Expert	1	3
	Participants PRE	Population	<0.001***	3
	Expert	Population	<0.001***	6

Note: Dunn Test, p.adj Bonferroni

The group maintain strong differences with the population sample with the majority of questions that are significantly different from the median value of the population. In contrast the similarities with the expert group are maintained even if we observe changes in the median values towards more liberal understanding of the issues at stake. In this respect we can for example point out an higher median value on the possibility of using such technology on our own gene (Q12) or the gene of our children (Q11), but more awareness on the potential social impact of such technology as techno-fix solution (Q3).

Table 12: Dunn test – Participants after deliberation, Experts and Population

Question	Group	Group	p. value	Median value
Q1	Participants PRE	Expert	0.97	5
	Participants PRE	Population	0.09	5
	Expert	Population	0.796	6
Q2	Participants PRE	Expert	0.088	4.5
	Participants PRE	Population	<0.001***	6
	Expert	Population	0.017**	7
Q3	Participants PRE	Expert	<0.001***	5
	Participants PRE	Population	<0.001***	7
	Expert	Population	1	7
Q4	Participants PRE	Expert	<0.001***	4
	Participants PRE	Population	<0.001***	7.5
	Expert	Population	1	7
Q5	Participants PRE	Expert	0.355	2.5
	Participants PRE	Population	0.056	5
	Expert	Population	1	6
Q6	Participants POST	Expert	0.685	4.5
	Participants POST	Population	<0.001***	4.5
	Expert	Population	<0.001***	7
Q7	Participants PRE	Expert	0.007**	5
	Participants PRE	Population	<0.001***	7.5
	Expert	Population	0.263	8
Q8	Participants PRE	Expert	1	5
	Participants PRE	Population	<0.001***	5
	Expert	Population	<0.001***	7
Q9	Participants PRE	Expert	0.141	5.5
	Participants PRE	Population	<0.001***	6.5
	Expert	Population	0.171	7
Q10	Participants PRE	Expert	1	5
	Participants PRE	Population	0.005**	5
	Expert	Population	<0.001***	6
Q11	Participants PRE	Expert	1	5
	Participants PRE	Population	0.003**	4
	Expert	Population	0.014*	6
Q12	Participants PRE	Expert	1	4.5
	Participants PRE	Population	0.072	4.5
	Expert	Population	0.189	6
Q13	Participants PRE	Expert	0.005**	5
	Participants PRE	Population	<0.001***	7.5
	Expert	Population	0.61	8
Q14	Participants PRE	Expert	0.171	5
	Participants PRE	Population	<0.001***	7
	Expert	Population	0.017**	8
Q15	Participants PRE	Expert	0.0125*	3.5
	Participants PRE	Population	<0.001***	6
	Expert	Population	0.533	6
Q16	Participants PRE	Expert	0.693	2
	Participants PRE	Population	<0.001***	3
	Expert	Population	<0.001***	6

Note: Dunn Test, p.adj Bonferroni

However, by taking an overall approach we can observe that the trend towards the expert mainly coincide on the question in which experts result to be more liberal than the group of participants. The groups trend toward liberal views is also observable in other question in which experts tend to be more cautious as in Q11 and Q12.

Participants' opinions seem to go in the same direction of the expert when we only account for the expert-witnesses. In this respect the overall gap between expert and the participants view is reduced in most questions (Q1, Q3, Q5, Q6, Q8, Q12, Q13), and raised in only four questions (Q7, Q9, Q10, Q11) with an overall average gap that pass from 1.72 before deliberation to 1.56 after deliberation (Table 13).

Table 13: Differences in median values between Experts witnesses – Participants pre and post deliberation

	witnesses	Participants PRE	Participants POST	Δ witnesses / PRE	P-value pre	Δ witnesses / POST	p-value post
Q1	7	3.5	5	3.5	0.025*	2	0.131
Q2	3.5	5	4.5	1.5	0.335	1	1
Q3	7.5	4.5	5	3	0.024*	2.5	0.015*
Q4	5.5	4	4	1.5	0.083	1.5	0.038*
Q5	2.5	3	2.5	0.5	0.642	0	0.901
Q6	4	5.5	4.5	1.5	0.011**	0.5	0.687
Q7	7.5	6	5	1.5	0.106	2.5	0.103
Q8	3	5.5	5	2.5	0.354	2	0.456
Q9	6	6	5.5	0	0.875	0.5	0.803
Q10	6.5	5.5	5	1	0.558	1.5	0.556
Q11	3	4	5	1	0.458	2	0.454
Q12	6.5	4	4.5	2.5	0.103	2	0.196
Q13	7.5	4.5	5	3	0.026*	2.5	0.052
Q14	3.5	5	5	1.5	0.069	1.5	0.208
Q15	5.5	3.5	3.5	2	0.148	2	0.108
Q16	3	3	2	1	0.755	1	0.592

Notes: Average gap: Δ witnesses / PRE : 1.72. Average gap: Δ witnesses / POST: 1.56

The Mann-U-Whitney statistic highlights that the convergence is statistically significant for Q1. Q6 and Q13 which highlight more social awareness over human genome editing (Q13) but more individual responsibilities on the decisions (Q13).

The questions that go in the opposite direction to the expert-witnesses are usually taking a more liberal perspective than the experts. In this respect after the deliberation the group of participants perceived the human genome editing as overall less scary (Q7) that what it is perceived by the experts, and are more open to the idea of applying human genome editing to their children if there is a concrete advantage to them (Q12)

F.3. Specific Comparisons

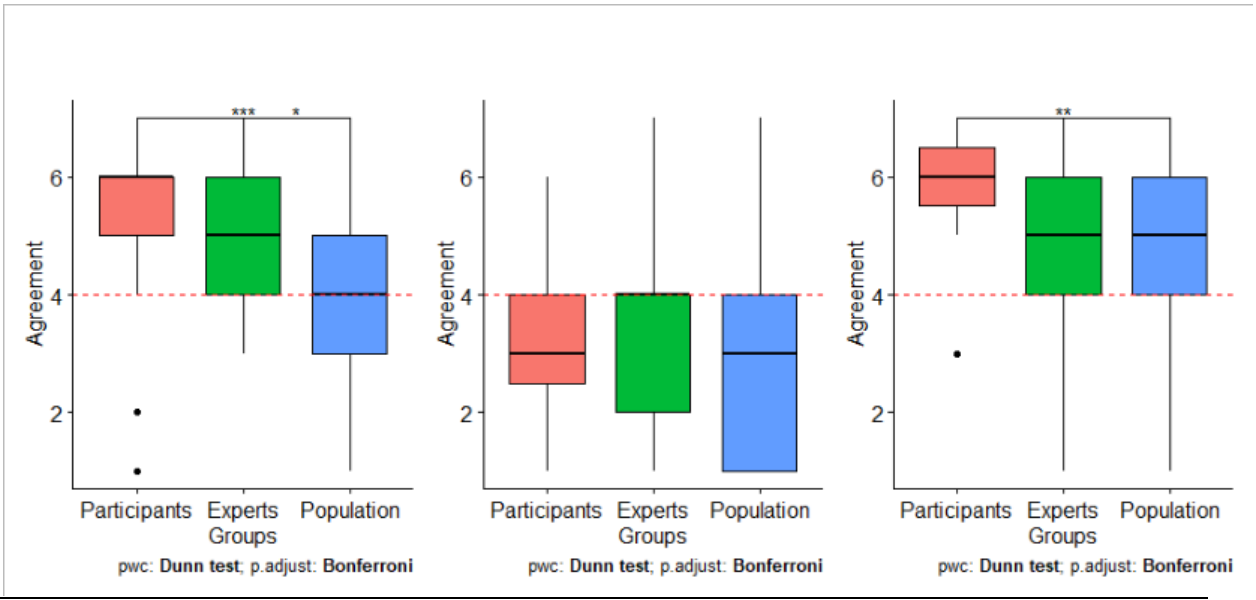
F.3.1. Good policy on Genome Editing: who do we trust?

Cohorts were requested to respond to three questions on who they trust to formulate good policies on gene editing considering three options: 1) a jury made up of ordinary citizens such as the ACJ; 2) the Australian Parliament or, 3) a body of experts.

By and large, all cohorts trust the most bodies of experts, with a relatively high trust towards the Citizens' Juries and low trust towards the Australian Parliament.

A more detailed analysis displayed in figure 3 highlights that the overall trust for bodies of experts for Citizens' Juries is different across cohorts.

Figure 20: Dunn test – Trust in citizens juries, trust in parliament, trust in bodies of experts



In this respect, while the deliberative group tend to have higher levels of trust in both citizens juries and body of experts than other cohorts, such trust only significantly differs with the population.

Table 14: Trust in citizens' juries, parliaments and bodies of experts

Group 1	Group 2	Trust in Citizens Juries	Trust in Government	Trust in Experts
Participants	Experts	0.91	0.98	0.097*
Participants	Population	0.001***	0.75	0.002***
Experts	Population	0.012*	0.74	1

Note: Dunn test, Bonferroni adjustment

F.3.2. ACJ policy recommendations

In general, we observe a very high level of support for the ACJ's recommendations on gene editing with very compact support from the participants and the control group side. Despite the expert agreement on ACJ's recommendations is less strong than the cohort participants, it still aligned with the deliberative and the control group in supporting the recommendations formulated by the ACJ. Table 15 displays the main differences across the four analysed groups.

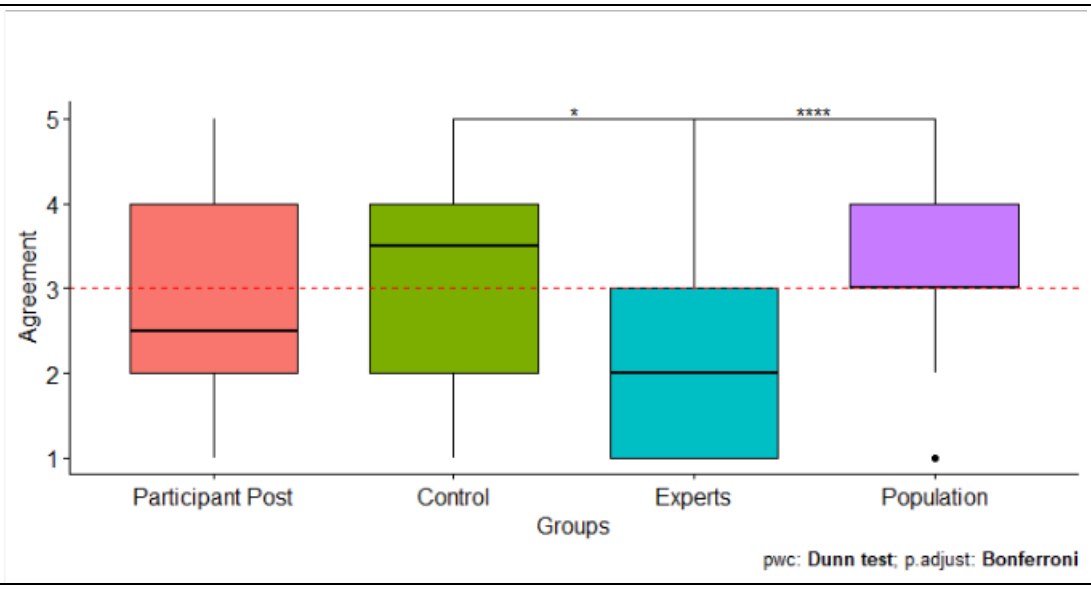
Table 15: Dunn Test ACJ recommendations

	Recommendation	Cont' Vs Part'	Cont' vs Expert	Cont' vs Popn	Parti' vs Expert	Part' vs Popn	Expert vs Popn
1	Research on heritable human genome editing should be supported.	0.593	1	1	1	1	1
2	Medical applications of heritable human genome editing should be prioritised and non-medical applications, including enhancement, should be banned.	1	0.896	0.157	1	0.283	1
3	Any process for approving applications of heritable human genome editing must ensure meaningful participation by members of the public.	1	1	0.060^	1	0.076^	0.011**
4	People should be informed about and have access to reproductive technologies that do not involve human genome editing, where such technologies exist.	0.510	0.932	1	1	0.002**	0.003**
5	Medical applications of non-heritable human genome editing should be supported to alleviate human suffering if meaningful consent can be ensured. Non-medical applications should be banned for now.	1	1	1	0.599	0.0167*	1
6	All parts of the non-heritable human genome editing process should be subject to intersectoral regulation and oversight to ensure that risks and benefits are adequately assessed.	1	1	0.140	1	0.0253*	0.0204*
7	Non-heritable human genome editing should be made accessible to those who need it. Decisions about equitable access should be motivated by concern for the public good.	0.734	0.384	1	1	0.00372**	<0.001***
8	Genome editing research using human embryos, including human embryos created for research through fertilisation, should proceed subject to stringent regulation and oversight.	1	1	0.989	1	1	1
9	Strict monitoring and regulation should be used to prevent mass production and commercialisation of human embryos for research through fertilisation.	1	1	0.563	1	1	1
10	Regulation should not hamper progress in human genome editing research or unnecessarily delay its medical application.	1	1	1	1	1	1
11	Equitable and affordable access to non-heritable human genome editing should not be a requirement.	1	0.03*	1	0.480	0.458	<0.001***

In general participants and experts tend to agree more than the population on the request of participation from the public in the process to approve the application of heritable human genome editing (Q3); the accessibility to reproductive technologies not linked to human genome editing (Q4); to ban the non-medical application of non-hereditable genome editing technologies (Q5); and the request of submitting to intersectoral regulation the non-heritable human genome editing process (Q6) and the request to make accessible non-hereditable human genome editing if motivated by concern for public good (Q7)..

Finally, as also displayed in figure 4, the recommendation to not require equitable and affordable access to non-hereditable human genome editing (Q11) receives higher support from the population than the other cohorts, with stronger opposition from the expert side.

Figure 21: Dunn test

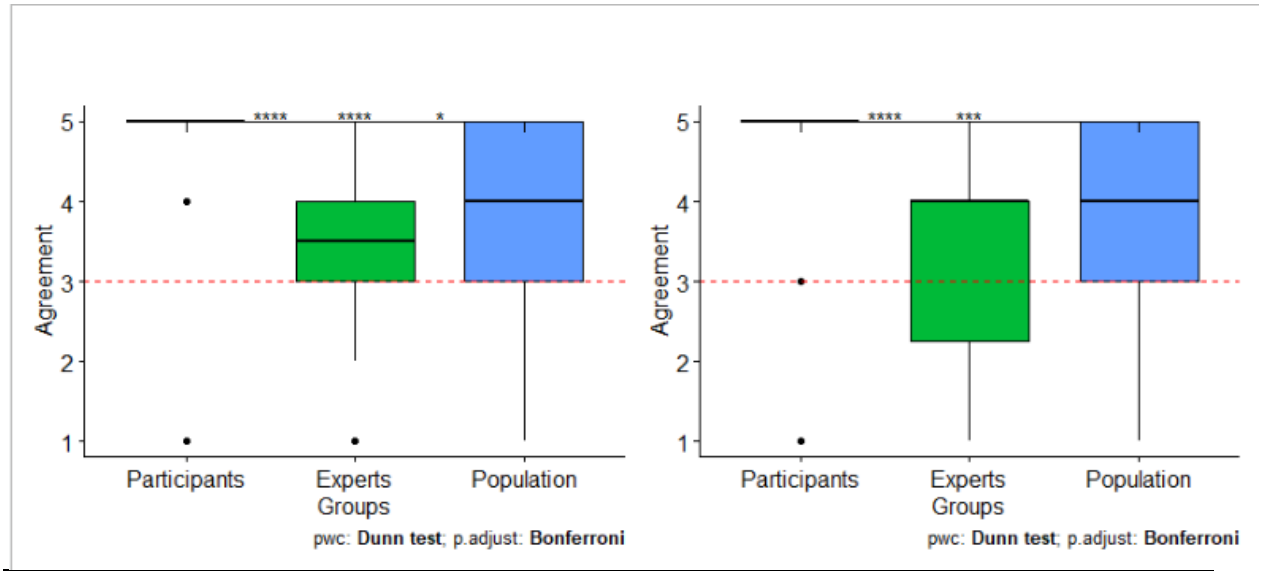


F.3.3. The potential uses of genome editing

Questions related to the potential uses of genome editing point to the possibility of editing DNA on children, human embryos and plants or animals as technology to cure or prevent existing diseases or enhance human physical or mental abilities.

While, in general, all groups support the idea of editing the DNA of children or adults to cure life-threatening or debilitating diseases, it is possible to observe substantial differences between the group of experts, the population and other groups. As displayed by figure 5, the group of experts is significantly more reluctant than the deliberative group in editing the DNA of embryos to prevent life-threatening (Q3) and debilitating (Q4) diseases.

Figure 22:Editing DNA of human embryos – Q3 and Q4



APPENDIX G.
EVALUATION OF THE AUSTRALIAN CITIZENS' JURY ON GENOME EDITING

G.1. Participant Evaluations

Table 16: Australian Citizens' Jury Evaluation Results

		Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree	Don't know/ unsure
1	I have learned a lot about genome editing during the citizens' jury					100%	
2	I have had enough information to participate effectively		14%	9%	59%	18%	
3	The information I have received has been fair and balanced between different viewpoints	5%	45%	23%	18%	9%	
4	I understood almost everything that the other members of my small group said during our discussions		9%	9%	41%	41%	
5	I understood almost everything that was presented by the speakers		9%	9%	59%	23%	
6	I had ample opportunity to express my views in the small group discussions		14%	14%	36%	36%	
7	My fellow participants respected what I had to say, even when they didn't agree with me			9%	5%	82%	5%
8	One or more people in my small group tended to dominate the discussions so that others found it difficult to contribute	23%	32%	5%	23%	18%	
9	My views about genome editing have changed as a result of the citizens' jury process	5%		14%	41%	41%	
10	The citizens' jury has helped me clarify my views about genome editing				36%	64%	
11	Citizens' juries like this should be used more often to inform government and parliamentary decision making			9%	5%	86%	
12	The presence of filmmakers and media added value to the deliberative process in reaching out to wider audiences around the world	5%	5%	18%	23%	45%	5%

		Very poor	Poor	Okay	Good	Very Good	Excellent
1	Overall organisation of the event			10%	14%	52%	24%
2	The lead facilitation			5%	5%	36%	55%
3	The table facilitation			9%	23%	36%	32%
4	The invited experts				14%	27%	59%

How would you talk about your experience in the citizens' jury to your family and friends?

Absolutely, to pass on to my grandchildren and to all involved

Probably a more balanced section of speakers of academics that [illegible] the issue to provide a mere balanced argument to the table

Positively :-)

I'll tell them what I did, what I learnt and to get their thoughts as well

The ciitizens' jury is an eye opening educational experience. Each day was both a frightening but wonderful experience that left my mind spinning with new exciting thought processes. A citizens' jury process is democracy in action.

I won't talk, I will do a powerpoint presentation. Thanks a lot :-)

It was extremely informative. And could change the world. At first I thought the bias was toward positivity but the outcome surprised me compared to all I had heard from my fellow jurors

I would talk to my family and friends in a very positive way. Many of them I think won't know about the topic or won't have heard of it before.

I would very much recommend my family and friends to participate when given the opportunity. My experience was excellent and look forward to seeing the outcome of our efforts

Very empowering. A wonderful experience.

In glowing terms - as much for the process (CJ) as about exploration of the topic. I will seek to commence discussions on both the topic and the process.

Explain what I Have been informed and let them discuss their opinion.

The cutting edge of genetic technology

Absolutely fantastic

It was very eye opening. I enjoyed it. I am very grateful that I get to be part of something so important!

Well done!

A great opportunity to unpack some really complex sociological ideas which potentially affect our generation and future generations.

It was a great chance to have our voices heard and to participate in deliberative democracy!

I would encourage my family and friends to get involved in something like this! It was very eye opening and made me think

It was interesting to observe how a worldview can shape so many facets of topics such as genome editing.