

Under what conditions should access to mitochondrial donation be publicly funded? An Australian public deliberation

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Recruitment Screening Survey

1. How old are you? ____
2. What is your postcode? ____
3. Are you working at the moment?
 - a. Working fulltime
 - b. Working part-time / semiretired
 - c. Retired
 - d. Unemployed
4. What did you / do you do for work? _____
5. What is your highest qualification?
 - a. School Certificate
 - b. High School
 - c. Trade Certificate
 - d. Undergraduate degree
 - e. Postgraduate degree
6. What is your country of birth?

Do you identify with a culture other than the culture of your country of birth?

7. Yes
8. no
9. Have you worked in health care in the last 5 years?
 - a. Yes
 - b. No

Has a close family member or friend of yours ever experienced mitochondrial disease?

1. Yes
2. No

IF YES – Thank you for your time and interest but we are excluding people from the research who have had a friend or close family member with mito as the discussion may be sensitive for them. Goodbye.

Are you or your partner currently pregnant?

1. Yes
2. No

IF YES – Thank you for your time and interest but we are excluding people from the research who are expecting a baby as the discussion may be sensitive for them. Goodbye.

Have you or your partner ever used IVF in the last 4 years?

1. Yes
2. No

Supplementary Table 1: The jury schedule

Day 1 – Evidence Day	
9:00-9:30am	<i>Orientation and Introductions: Jury purpose and process</i>
9:30-9:50am	<i>Health policy expert presentation (10min) and questions (10min): “How health services are funded in Australia and why this Community Jury is important.”</i>
9:50-10:10am	<i>Mitochondrial genetics expert presentation (15min) and questions (15min): “What is mito, how does MD work and what are the alternatives?”</i>
10:20-10:40am	Break
10:40-11:10am	<i>Patient perspective presentation (15min) and questions (15min): “Perspectives of people at risk of having children with mito.”</i>
11:10-11:30am	<i>Assisted reproduction expert presentation (20min) and questions (20min): “How will MD fit in with ART and what are the pathways for women to MD services.”</i>
11:50am-12:30pm	<i>Health economics expert presentation (20min) and questions (20min): “Comparing the cost of MD to the alternatives.”</i>
12:30-1:30pm	Break
1:30-2:15pm	<i>Bioethics expert presentation (20min) and questions (25min): “Ethical aspects of MD implementation in Australia.”</i>
2:15-3:25pm	<i>Facilitated discussion with jury facilitators</i>
3:25-3:30pm	Concluding remarks and depart
Day 2 – Deliberation Day	
9:30-10:30am	<i>Facilitated deliberation with jury facilitators</i> Goal: begin to address the jury question
10:30am-1:00pm	<i>Open deliberation</i> No facilitators present, free discussion between jurors
1:00-1:45pm	<i>Presentation of the jurors’ verdict on the jury question</i> Opportunity to provide additional recommendations
1:45-2:00pm	Feedback and jury conclusion

	Jury 1 (Townsville)			Jury 2 (Melbourne)			Jury 3 (Tamworth)		
	A. Wholly funded by public money	B. Funded by public with user copayment	C. Wholly funded by service user	A. Wholly funded by public money	B. Funded by public with user copayment	C. Wholly funded by service user	A. Wholly funded by public money	B. Funded by public with user copayment	C. Wholly funded by service user
#1 Saturday AM Before evidence delivered	5	7	2	2	11	1	3 [#]	8 [#]	2 [#]
#2 Saturday PM After evidence delivered	4	7	3	8	6	0	3 [*]	7 [*]	1
#3 Sunday AM After reflection overnight	3	8	3	9	5	0	5	6	2
#4 Sunday PM After deliberation	4	5	5	6	8	0	11	1	2
# 1 juror in Tamworth voted informally “Don’t know” for this round. * 2 jurors in Tamworth voted informally “either option A or B” for this round.									

Supplementary Table 2: Juror Vote tallies at different time-points during jury proceedings

Supplementary Table 3: Characteristics of community jury participants compared with Australian Bureau of Statistics Census Data (2021).

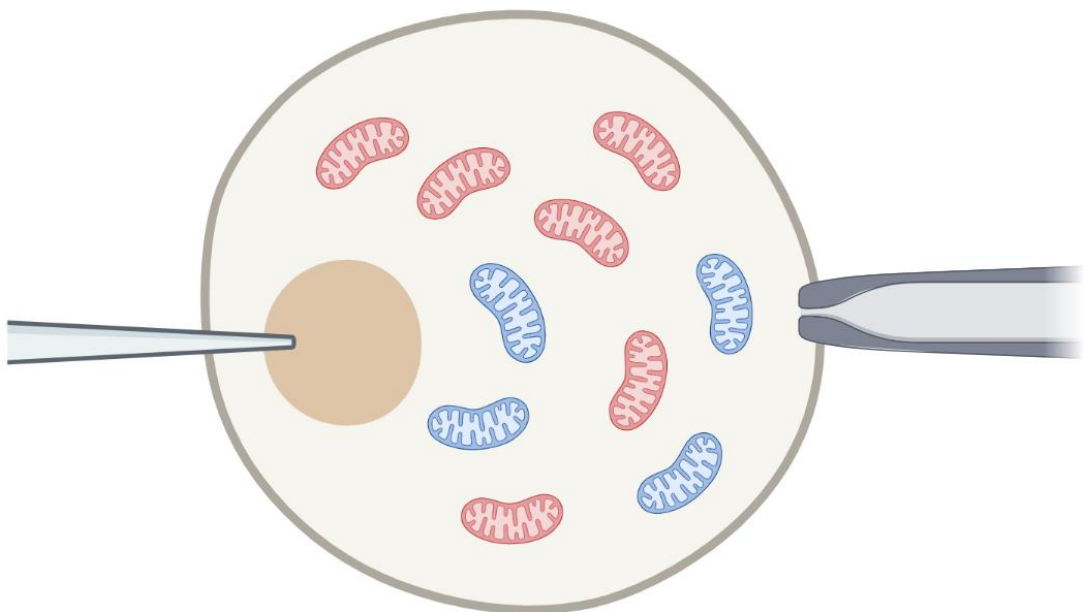
	Jury 1 Townsville (n=14)	Jury 2 Melbourne (n=14)	Jury 3 Tamworth (n=14)	Proportion (as %) of participants in the three community juries (n=42)	Proportion (as %) of people in Australia over 18 years of age*
Age (years)					
18-39	4	4	5	14/42 = 33%	41%
40-60	8	5	5	18/42 = 42%	36%
> 60	2	5	4	11/42 = 26%	23%
Gender					
Man	7	7	7	21/42 = 50%	49.3%
Woman	7	7	7	21/42 = 50%	50.7%
Highest Educational Attainment					
High School	4	5	4	13/42 = 30%	24%
Trade / Diploma	5	3	5	13/42 = 30%	29%
Undergraduate Degree	3	3	3	9/42 = 21%	32%
Postgraduate Degree	2	3	2	7/42 = 16 %	15%
Had Children (biological / adopted or step)					
No	8	5	7	20/42 = 47%	40%
Yes	6	9	7	22/42 = 53%	60%
Current Employment Status					
Working full time	2	3	4	9/42 = 21%	40% [#]
Working part time or casually	2	4	2	8/42 = 19%	24% [#]
Self employed	2	1	2	5/42 = 11%	13% [#]
Carer duties	1	0	1	2/42 = 5%	12% [#]
Unemployed	3	1	2	6/42 = 14%	4% [#]
Studying	2	3	1	6/42 = 14%	11% [#]
Retired	2	2	2	6/42 = 14%	37% [#]
Speaks Language Other than English at Home					
Punjabi	1			8/42 = 19% of community jury participants speak a language other than English at home	22.3% of the population in Australia speaks a language other than English at home
Hindi	1				
Italian		1			
Greek		1			
Croatian		1			
Tamil		1	1		
Vietnamese		1	1		
Tagalog			1		

* This information was discerned from publicly available Australian Census data from the most recent census (2021) through the use of the AI overview function in Google Chrome, powered by Google Gemini.

[#] In census data, employment status categories do not add up to 100% as there are many overlapping categories (with more than one option able to be selected), whereas participants in the three juries chose the most suitable category.

Should mitochondrial donation be funded by Medicare?

Information for Participants



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Glossary

DNA: DNA (deoxyribonucleic acid) carries the information and templates for making and maintaining all living things, including people. DNA contains long chains of chemicals called bases. These chains coil into 46 chromosomes, 23 inherited from each parent.

Gene: a segment of DNA that forms the basic unit of inheritance.

Genome: the complete set of genetic material in a human, made up of DNA and genes.

In-vitro fertilization (IVF): a medical procedure whereby an egg is fertilised by sperm in a laboratory. The fertilised egg is then grown in the laboratory for several days and then placed in a uterus.

Maeve's Law: changes to several Australian laws around reproductive technologies and genetic modification to enable mitochondrial donation.

Mitochondria: small structures found in every cell in the body except red blood cells. Mitochondria are responsible for the generation of energy in our cells to sustain life and support growth.

Mitochondrial disease (also called mito): a group of genetic conditions that stop mitochondria working properly and starve the body's cells of energy, causing multiple organ dysfunction or failure and potentially death.

Mitochondrial Donation (MD): an IVF-based technique which creates an embryo containing:

- the DNA from both parents (the prospective parents) and
- the mitochondria in an egg donated by another person (the mitochondrial donor).

Mitochondrial DNA: DNA found in the mitochondria.

Mutation: a detrimental change in our DNA. A mutation is also called a 'gene change' or 'variant'.

Frequently Asked Questions

What would mitochondrial donation (MD) cost the public health system?

We don't yet know how much MD will cost the public health system. However, we do know that the cost is substantially lower than the lifetime cost of caring for a person with mito.

Are Australian private health insurance companies likely to cover MD?

Gold tier private health insurance does cover some costs related to an IVF cycle, including day admission and anaesthetist fees. Because MD involves some of the same steps involved in IVF, patients undergoing MD who have private health insurance would be able to have these costs covered. However, we don't yet know whether the costs of the MD technique itself will be covered.

How many people might be likely to use MD?

It is anticipated that ten or fewer people will likely use MD per year.

Why is there a clinical trial in Australia if the procedure has been made legal elsewhere?

Although this technology has been approved for use in the UK, there are no published results yet showing that mitochondrial donation is safe and effective in humans in the way we expect it will be. Offering it as a clinical trial also has some advantages. Australian clinicians need to build their expertise and skills with this highly specialised technique and a clinical trial holds them accountable whilst monitoring outcomes.

Who is eligible for MD?

Only people who are at very high risk of passing a serious mitochondrial disease onto their children are eligible to undergo MD .

What is mitochondrial disease?

Mitochondrial disease, or mito, is a group of chronic, genetic conditions. The disease may present at birth but can also present at any age. Adult onset mito, for example, is becoming more commonly recognised as health professional awareness improves. Because of its genetic basis mito often affects multiple family members.

How are patients impacted by mito?

Depending on which parts of their bodies are affected and to what degree, people with mito can:

- Lose their sight or hearing
- Suffer muscle weakness and pain
- Be unable to walk, eat, swallow, or talk normally
- Have strokes or seizures
- Develop liver disease or diabetes
- Suffer heart, respiratory or digestive problems
- Experience developmental delays or intellectual disability.

Needing to regularly rest and recharge is a common outward symptom of mitochondrial disease. Mito may cause any symptom in any organ at any age however, nearly half of all mito patients develop symptoms in childhood. Research has found that the average age of survival in affected children can be under 12 years of age, but some research shows an average age of survival of less than 3 years.

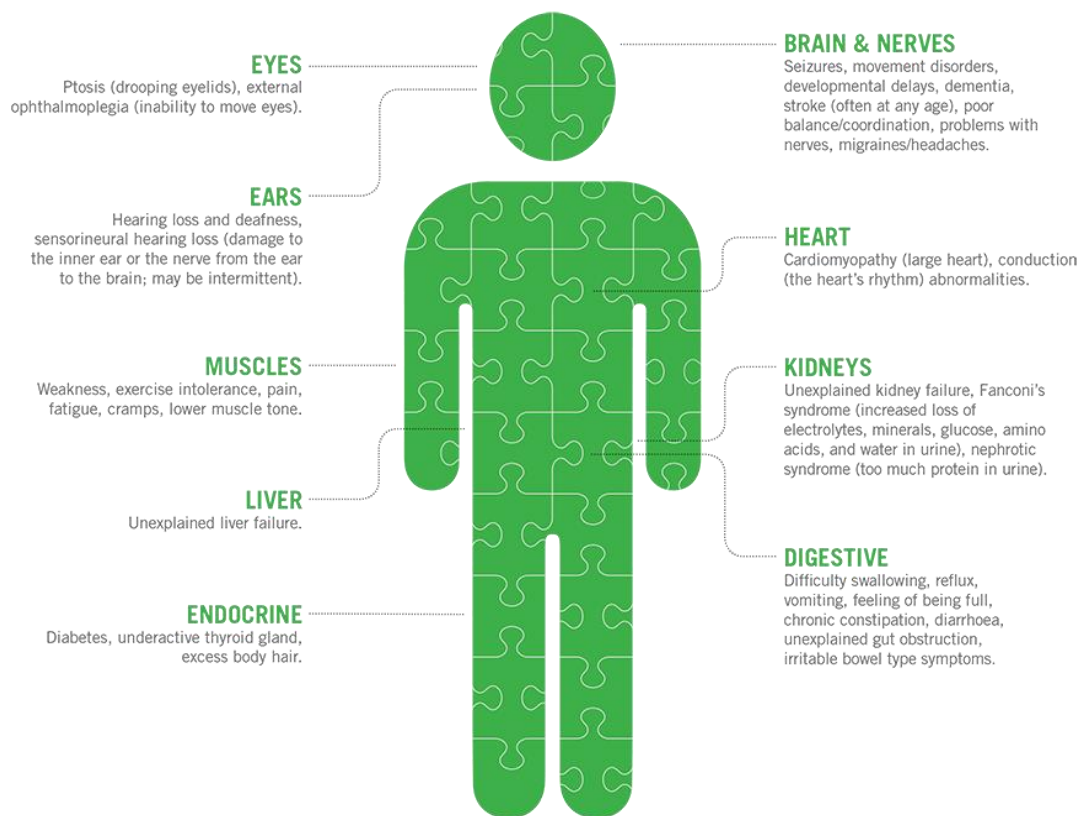


Diagram of the wide range of symptoms that can be caused by mito (image from www.mito.org.au).

Is there a cure?

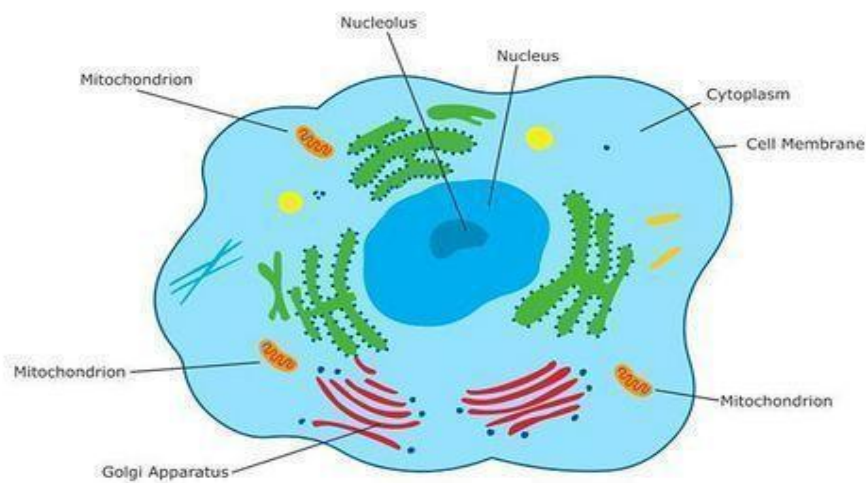
There is currently no cure for mito and very few effective treatments. It impacts every patient differently, so doctors can't easily predict the progression of the disease or symptoms, or the likely outcome for each patient.

Understanding Mitochondrial Donation (MD)

Mitochondrial Donation (often referred to as MD) is a significant technological development that allows some women with mito to have biologically related children with a much-reduced chance of passing on the condition. Recently the law has been changed so that MD is now legal and will soon be trialled in Australia. To understand how MD works and who MD is suitable for, we must first understand the science of the disease.

What is DNA?

DNA contains all the genetic information needed for animals and plants to develop, grow, reproduce, and function. Around 99% of our DNA is contained in a part of our cells which is called the “nucleus” (see diagram below). This DNA is called “nuclear DNA” and it is inherited from both parents. The last one percent of our DNA is contained within a different part of our cells which is called the “mitochondria” (singular = mitochondrion). This is called “mitochondrial DNA” and is inherited almost exclusively from the mother.



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Diagram of a human cell containing mitochondria (image from www.sciencelearn.org.nz).

What are Mitochondria?

Mitochondria generate energy for our cells to use. They convert the energy in foods we eat into packages that can be used as energy by that cell. When mitochondria do not function properly, this can cause mitochondrial disease. The more cells in the body that have mitochondria that don't work well, the more quickly the disease will develop and the more severe symptoms will be.

The DNA that looks after how our mitochondria functions is contained within the nucleus and the mitochondria. Some types of mito are caused by detrimental gene changes (mutations) in the nuclear DNA - we are going to put these to one side, as this type of mito is not the type that MD is used to prevent. Other types of mito are caused by mutations in the mitochondrial DNA. Because mitochondrial DNA is largely inherited from our mothers, we in turn only inherit so-called 'mitochondrially encoded' mito from our mothers too. That is to say, MD is designed to help women (and their partners, if they have one) who have mito because of mutations in their mitochondrial DNA, not their nuclear DNA.

There are approximately 30 children born per year (or one a fortnight) in Australia that will develop a severe form of mitochondrially encoded mito during their lifetime.

How does Mitochondrial Donation (MD) work?

MD will take place in a laboratory that has the necessary equipment and staff to perform this specialist technique, for example an approved fertility clinic. As to the technique itself, MD involves removing the nucleus from an egg obtained from the intending mother, leaving the dysfunctional mitochondria and the rest of the egg behind. This nucleus is then inserted into a healthy egg from a donor, which has had its own nucleus DNA removed (see diagram below).

The use of the nucleus (which contains our DNA) maintains a genetic link between the mito patient and their baby. At the same time, leaving behind the mutated mitochondria greatly reduces the chance that the resulting child will go on to develop mito.

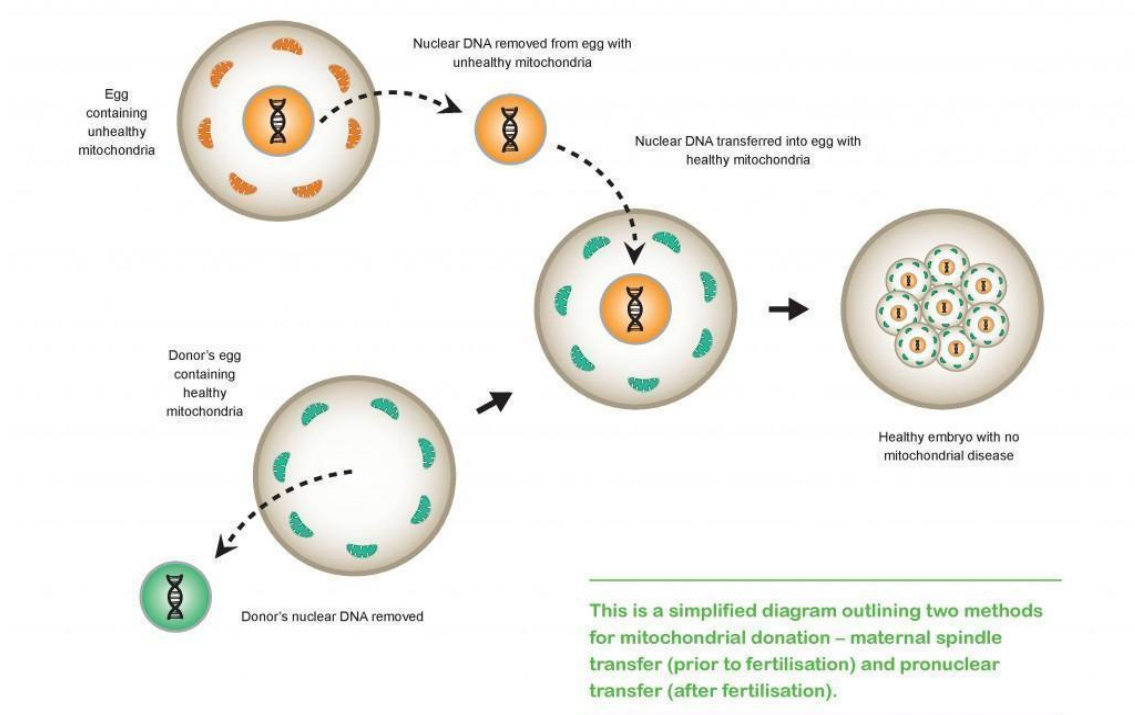


Diagram of MD (image from www.mito.org.au)

Is MD available in Australia?

No, but it will become available soon. This practice was previously illegal in Australia because of laws which prevent the creation of embryos that contain the genetic material from more than two people. MD creates an embryo with the nuclear DNA from both prospective parents and the mitochondrial DNA from the donor i.e. three people.

Recently however, the Mitochondrial Donation Law Reform ACT 2022, otherwise known as Maeve's Law, was passed in Australia. Maeve's Law' allows the introduction of MD in a staged process, beginning with clinical trials. If the trial is successful, then a second stage will involve introducing MD into clinical practice more broadly. Under Maeve's Law, only those with an increased risk of having children severely affected by mito will be eligible.

For this jury, we are asking you to think about MD as if the trial has been successful and the wider availability of this intervention (as part of the health care system) is being considered. We don't yet know the details of what this will look like, and your input here will help inform policy-makers about what the future clinical use of MD might look like. The cost of this procedure may prevent access for many people. This is why discussions on funding are essential to the best implementation of MD in Australia.

What are the alternatives to MD?

There are two other technologies which can prevent the transmission of mito while still enabling the mito patient to have a genetic connection to their child. Prenatal diagnostic testing can be performed on a foetus before birth to determine the risk of transmission. The mito patient can then choose to continue or terminate the pregnancy. Alternatively, preimplantation genetic testing can be performed on embryos in a fertility lab to select the embryo with the lowest risk of transmission.

However, these techniques do not always give an accurate indication of the risk of developing mito and they are not appropriate for patients with a high risk of transmission. For patients with a high risk of transmission, MD is the only method that allows the possibility of having a child who is genetically related to both parents but without the risk of passing on the disease.

Being genetically related to one's child can be of vital importance to potential parents. In fact, the possibility of having a genetically related child may be a primary consideration for some people in deciding whether and how to have children, along with the importance of having a physically healthy child, free of preventable diseases which may affect the child's quality of life.

For mito patients who are open to not being genetically related to their child, there are alternative options. These include adoption, fostering, and regular egg donation.

What do Australians think about MD?

There are a few sources that can provide some information about the attitudes Australians have towards mitochondrial donation. Possibly the most informative of these is the National Health and Medical Research Council Community Consultation Report. This report is based on written submissions from the Australian public and demonstrates a wide variety of views on this new technology. Identifiable themes included the value of mitochondrial donation for the prevention of disability and disease, the importance of parents being able to have children who are genetically related to them, and the importance of protecting the rights of the child resulting from MD.

A previous citizens' jury carried out in 2017 asked whether to legalise MD in Australia. Out of 14 jurors, 11 answered the question: 'Should Australia allow children to be born following mitochondrial donation?' favourably. Out of those 11 jurors, 4 answered favourably unconditionally, 7 responded 'yes, with conditions'. These conditions overlapped significantly with some of the themes raised in the Community Consultation Report mentioned above in the sense that a majority were concerned about unknown factors within the technology, future effects on the child, the parental status of the egg donor, etc.

After MD was legalised, the Mito Foundation performed sixteen interviews among members of the mito community, in order to determine their wishes and needs for the clinical trial. This community includes patients but also family and carers; anyone whose life is directly impacted by mito in some way. Key findings were that these members of the community had strong and clear expectations for the clinical trial, including the expectation for equal and widespread access to MD, access to emotional support in conjunction with medical support during this pilot stage, and access to clear and consistent information throughout the process. Additionally, questions were raised about who would be eligible for the trial, and what would count as a 'successful trial'.

Finally, a survey was conducted among 1,000 Australians concerning their understanding of and attitudes towards MD. While some ethical concerns were

raised (half of respondents agreed that creating embryos using the genetic material from three people is problematic), it was found that Australians believe the technology is ultimately beneficial as it allows people with mito to have genetically related children without the risk of passing on their disease. 9 out of 10 respondents were in support of MD becoming available in Australia following clinical trial results.

What is Medicare?

Medicare is a national insurance scheme that provides free or subsidised healthcare in Australia. Medicare funding is available for Australians visiting general practitioners (GPs), medical specialists and public hospitals.

How does Medicare fund other fertility treatments?

Many fertility treatments receive some level of Medicare rebates. For example the fertility clinic 'Melbourne IVF' estimates that an IVF treatment cycle costs \$9,950.00, with out-of-pocket costs only at \$5,090.70. People are eligible for Medicare rebates as long as they have a medical need for IVF i.e. cannot have a baby without it.

Will Medicare fund MD?

MD involves many of the same steps that IVF uses, such as egg collection and the transfer of the embryo to the prospective mother. Mito patients undergoing MD will receive Medicare rebates for these steps. However, we don't yet know whether Medicare will fund the MD technique itself. This is what we are asking you, the jury, to deliberate on. Medicare does fund other technologies which can also be used to reduce the risk of mito transmission - preimplantation genetic testing and prenatal diagnosis.

What does MD cost?

We don't yet know how much MD will cost because an Australian estimate has never been calculated. Nine years ago, the UK estimated the cost of MD at \$23,800 AUD (Table 1). This cost includes three rounds of IVF (the same process used by those seeking fertility treatment), the MD technique itself, and the equipment costs. However, because this estimate was from some time ago and from a different health care system, we don't know if it could apply to Australia.

Table 1. Approximate cost of MD compared to alternative options

Reproductive method	Cost
Mitochondrial Donation	Approx. \$23,800 AUD
Reproduce without MD (assuming no prenatal testing feasible)	Approx. \$5,000,000 AUD (lifetime cost to healthcare system of caring for a person with mito)
Adoption	Approx. \$12,000 AUD
Child Fostering	No cost, possible remuneration
Involuntary Childlessness	Difficult to quantify – likely to be psychological and emotional impacts for those wishing to become parents

While reproducing without using MD is the only other way of being genetically related to one's children, it also carries the risk of passing on mito. The table contains the estimated lifetime cost to the healthcare system if the child does inherit mito.

It's important to note that in addition to the considerable cost of adoption, in practice it is also very difficult to successfully achieve. Complicating factors in finalising the adoption process include things such as document preparation, travel, organising visas, etc. Beyond the cost considerations, wait times of several years are not at all uncommon.

Ethical aspects of MD implementation in Australia

MD has given rise to a range of ethical questions about the risks, costs, and permissible uses of the technology. Some of the issues raised have been resolved in Australia, at least in the scientific and legal sense. For example:

Safety

All new medical technologies contain an element of risk when first used in humans and there are different views about the level of certainty and risk that is acceptable for MD to be “safe enough” for introduction into clinical practice. In general, Australian experts have agreed that while there are potential risks, these are worth taking if it means that a child will not be born with a condition that gives rise to a high chance of morbidity and/or mortality.

Changing the genome?

Some people are concerned that if we allow MD, this will lead to acceptance of other changes to the genome (genetic modifications) more generally, including the possibility of allowing ‘designer babies’. Australian law reflects the position that MD is ethically distinct from other more worrying kinds of genetic modification and that accepting MD will not lead to more widespread acceptance of genetic modification and designer babies.

Who is a parent of a child born from MD?

Because MD involves a genetic contribution from three different people, questions have also been raised about whether a child born following MD can be said to have 3 parents. Australia has determined that an egg donor for MD will not be a legal parent to the child born (just as a donor of gametes for other assisted reproduction will not be a legal parent). However, children born from MD will be able to request certain information about their donor once they become adults.

Should Medicare fund MD?

One ethical issue that is yet to be resolved is access to the technology. The benefit of MD, in that it reduces the risk of mito transmission while enabling a genetic connection between parents and children, can only be achieved if the technology is affordable to those who wish to use it. The high costs of fertility treatments are well known to prevent some people from accessing them. Providing Medicare funding for MD may reduce these financial barriers, but on the other hand, the cost may be better spent elsewhere. Societies generally see the immediate needs of those who are sick or at risk of death as most important and funding for this is often prioritised over preventative measures. This is called the “rule of rescue”: the strong human impulse to rescue people facing avoidable death, regardless of cost. If the Australian health system had endless funds, this would not be a problem, but unfortunately this is not the case. This is why we are asking you, our jurors, to address this question - should MD be funded by Medicare?

Legal aspects of MD in Australia

Maeve’s Law does several things to make MD available in Australia:

- it made some changes to the strict national laws around what can be done with human embryos,
- it sets up the regulatory structure for the staged rollout of MD beginning with the clinical trial, and
- it lays the ground work for MD regulation in clinical IVF .

Australia is the second country to legalise MD, after the UK’s legalisation in 2015. This means that Australia, like the UK, has created a regulatory framework specifically for MD. MD is also available in other countries but without specific laws around it. The Australian MD laws have many similarities to those in the UK, but there are important differences. Some of these differences are because as a federation, Australian law is made up of both national and state laws. Maeve’s Law has changed national laws, but clinical use of MD in a particular state or territory will also need changes to the laws of that state or territory. But we can still make informed assumptions about what will be done. There are also details around protocols and processes that need to be worked out.

Australian law also has greater restrictions around the use of human embryos than laws in the UK. In 2002, two national Acts (*Prohibition of Human Cloning for Reproduction Act 2002* and *Research Involving Human Embryos Act 2002*) created a complex regulatory framework for embryo research. Maeve's Law creates exemptions to prohibitions in those Acts, if particular conditions are satisfied. Importantly, these conditions control *who* will be able to offer MD and *when* MD can be used.

Who will be able to offer MD in Australia?

Any clinic wanting to provide MD must be licensed to do so. It is not known if that licensing will be done by the same expert body controlling the MD clinical trial or by the professional body that already licenses fertility clinics in Australia is not known. In either case, clinics will need to comply with relevant state and territory laws and guidelines of the national medical research regulator, the National Health and Medical Research Council (NHMRC). Only permitted forms of MD can be licensed and before they are licensed, clinics must demonstrate expertise and have required processes in place.

When can MD be used?

Use of MD is also strictly controlled. Maeve's Law requires that any person seeking to use MD must first be approved by an expert body. Approval will be given only if there is a 'particular risk' of inheritance and a 'significant risk' that the mito that would develop in those offspring would lead to serious illness or another serious medical condition. Finally, it must be shown that other available techniques that could be used to minimise risks (such as prenatal diagnosis or preimplantation genetic diagnosis) are inappropriate or unlikely to succeed. The information needed to decide these issues is still to be developed but will be available before wider clinical use occurs. Prospective parents also must attend pre-treatment counselling to consider alternatives and potential risks.

What are the responsibilities of donors towards children born of MD?

Children born of MD will be entitled to know the identity of the donor of the egg used in the MD but the donor will not have any legal responsibilities to the child. Maeve's Law requires clinics keep a record of donors' identities which will be added to a specific national register. Just as for children born from other forms of reproductive donation, children born of MD will be able to access identifying information about donors when they reach an appropriate age. Donors are counselled about this during the donation process and will be able to check whether a child has been born from their donation. Donors will not be paid for their eggs, but as for donation for other IVF donors' costs such as healthcare and travel are reimbursable under state and territory law.