

MITOCHONDRIAL DONATION

Q&A Webinar Summary

Now that Maeve's Law has passed, what are the immediate next steps and how long will they take?

Maeve's Law involved a series of changes to several laws around reproductive technologies and genetic modifications. The bill that was passed removes the legal barriers to using the reproductive techniques for mitochondrial donation as well as setting out the pathways for implementation.

Initially mitochondrial donation will be available through a pilot stage, expected to last for 10-14 years. The pilot stage will begin with a training, and research phase before progressing to a clinical trial. As part of a clinical trial, mitochondrial donation will be rolled out carefully in a highly regulated manner, with monitoring of health, outcomes of pregnancies and births.

The positive news is the Federal government has already put out the funding for the pilot stage (AU\$15 million) and is seeking applications for a grant that will be awarded to a single consortium. The National Health and Medical Research Council (NHMRC) Embryo Research Licensing Committee will manage the licensing framework.

We might expect to see the stakeholders apply for research and training licenses, some time from around six months from the passing of Maeve's Law in March 2022. The exact timing is a little unknown but the fact the funding has already been allocated and the call for applications is now open is a positive sign that we will see action according to proposed timelines. Our job at Mito Foundation is to keep the pressure on various parties to ensure action continues.

CLINICAL TRIALS

Why is there a clinical trial if the procedure has been approved elsewhere?

There are several reasons for this:

- To build a knowledge base – although this technology has been approved for use in the UK, some privacy concerns have meant there are no published results yet showing that mitochondrial donation is safe and effective in humans in the way we expect it will be. This lack of evidence was a concern voiced by some politicians and a clinical trial will allow for rigorous scrutiny, monitoring and reporting of outcomes to grow evidence of the safety and effectiveness of mitochondrial donation in Australia.
- Offering it as a clinical trial 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.
- Centres and families engage in follow-up to ensure both good health outcomes and data are collected to ensure everything is working as expected.
- Clinical trial data enable health economic studies to justify future funding for the roll-out.
- Perhaps most importantly, in addition to the federal legislation there are also different laws in each state relating to reproductive technologies or access to these. Individual state regulations would impact on delivering mitochondrial donation in each state and require further state-based legislative changes. Running this as a clinical trial for now means these state laws don't have to be addressed until we shift into seeing this used in clinical practice.

Overall, the people involved in campaigning for this legislation realised along the journey that implementing mitochondrial donation initially under a regulated and carefully monitored clinical trial would be the best option.

When will the clinical trial start? Can mito community members register their interest to participate in the clinical trial?

It's hard to say for certain, but the law was written in a way that the successful group/consortium would be selected in about six months' time from when Maeve's Law was passed. We would anticipate the clinical trial will commence in 2023 but it will take time to obtain licenses and train staff.

For now, speak with your mito specialist about your desire to have children. Until clinical trial investigators have been appointed, your own medical team members are the best people to speak to. If you don't have a mito specialist or are still on a pathway to diagnosis, you can contact the [Mito Foundation Helpline](#) on 1300 977 180 for help finding a specialist or navigating your next steps.

Once the clinical trial has started, will people go directly to IVF clinics? How or where can they access mitochondrial donation – will this be limited to Sydney?

Access to mitochondrial donation will all come down to how the selected consortium design the clinical trial, which IVF clinics are involved and where they are located. It's important that there is a partnership between mito specialists, IVF clinics, researchers, ethicists and other important parties for this clinical trial. Mito Foundation has advocated for access to be equitable across Australia and not only offered by one clinical service. However, there is also the need for highly trained embryologists, technicians, clinicians, counsellors and more to effectively perform this technique so initially mitochondrial donation will not be available at every IVF clinic. Part of advocating for the patient and accessing this technology is the attempt to reduce the burden of travelling interstate. There are many possibilities being explored, including freezing eggs and embryos and moving these around, or having specialists travel. Telehealth is also an option for reducing travel requirements before procedures.

For now, it's difficult to fully answer this question as the request for applications for the clinical trial licensed investigators have only just come out and a decision is not due until October/November 2022. As these important conversations will continue, we acknowledge the need for balance and equitable access and will continue to advocate for the mito community to be able to access mitochondrial donation at multiple sites across Australia.

HEALTH CONSIDERATIONS

Who is eligible for mitochondrial donation? Are there tests required before the procedure?

Eligibility is defined by Maeve's Law and requires that the NHMRC Embryo Research Licensing Committee who issue the licenses for mitochondrial donation need to be satisfied that the female applicant is at increased risk of having a child severely affected by mitochondrial disease and that other reproductive techniques are unsuitable to reduce this risk. Another consideration is the woman's own health status and how a pregnancy may impact her mito symptoms or increase risk.

Genetic testing in mothers is required to further understand the medical picture and determine the risk of passing on to any future children. This technology is only suitable where a woman has changes in her mitochondrial DNA, confirmed by genetic testing and known to potentially cause severe mito. An expert clinician will assess each individual situation. Counselling is also required to discuss all reproductive options. For anyone affected by mito with an unknown genetic cause or caused by changes in nuclear DNA, this technology is not applicable. Egg donors will also require genetic testing to ensure there is no chance they will pass on a mitochondrial DNA mutation.

Is there really a definition of what “severely affected” means for mito?

An interesting question that is not easy to answer at this stage. Effectively this is what the embryo research and licensing committee, managed by NHMRC, will be judging. It is difficult to know how it will be assessed in Australia but we can learn from the UK. The comparable committee in the UK has, over time, received applications for a broad range of mitochondrial diseases. Patient impact statements offer the opportunity to share an applicant’s personal experience of the impact of mito in their family, alongside considerations of age of onset, affected organs, risk of more severe presentations or other potential variations.

How does egg donation work? Is the age of the mother and/or the egg donor important?

Collecting eggs from donors for mitochondrial donation will involve similar techniques to that are used when women donate eggs to help infertile couples achieve a pregnancy using IVF. Most fertility clinics in Australia have experience in counselling, ovarian stimulation, collection and selection of eggs from donors. Drugs are required to stimulate the donor’s ovaries, then approximately two weeks later the eggs are harvested by a transvaginal needle. The embryologist in the lab isolates the eggs from the fluid and these are placed in an incubator in readiness for later use.

While it can sometimes be challenging to know how a donor will respond to hyperstimulation drugs, an important consideration will be the reproductive age of the donor. Traditionally fertility clinics do restrict age of egg donors, this may vary between clinics but usually donors will need to be under 40 or even younger. There are considerations other than age about who can donate eggs. In the case of mito, maternal relatives may also carry mitochondrial DNA mutations. We want to ensure the donor’s health is cared for, both physical and emotional, as IVF comes with challenges.

The age of the mother, and her health, will also be a consideration as she will also need to undergo ovarian stimulation in order to collect her eggs.

People considering mitochondrial donation need to understand that like all reproductive technologies, it may require multiple cycles to produce enough embryos to achieve a pregnancy using this new technique. IVF is a numbers game and may not work the first time.

Have we thought through where the donor eggs can come from? What options are there?

Egg donation is already possible in Australia for other reproductive purposes. Donors may either be known or anonymous. In Australia egg donation is altruistic and no payment to donors is allowed under our law. Given that egg donation requires invasive medical procedures and medications that do come with risks, medical assessment is required along with counselling and psychological assessment for any donor. Consent and understanding are key features of this pathway. We will also use our close relationship to learn from the UK group how they recruit their egg donors and manage their care.

Maeve’s Law also outlines that a mitochondrial donor registry will be established, and any children born will be able to access information about their egg donor once they reach 18 years of age.

What are the other reproductive options that might be relevant for someone with mito?

Mitochondrial donation is just one option that prospective parents could explore. The Mito Foundation encourages anyone in the mito community to really know their diagnosis, including their genetic test results. The reproductive options available for any individual depend on what genetic change has been found, which type of mito amongst other factors. Options will also vary depending on if changes are in the nuclear or mitochondrial DNA.

A couple could proceed with a natural pregnancy and then use prenatal diagnostic tests such as CVS or amniocentesis to test a foetus for some types of mito. Another option is IVF with preimplantation genetic testing to check embryos for the genetic change identified in their parent, then selecting only those embryos with low or no risk of developing mito to be implanted. There are also options for not having children, adopting or using donor eggs, sperm or embryos.

The UK experience has shown that not everyone who explores mitochondrial donation will go down that path. Seeking expert advice from your mito specialist or genetic service specific to your circumstances is really important. The Mito Foundation supports the right for any family impacted by mito to explore all available reproductive options and make an informed choice about what option is best suited to their individual circumstances and personal values.

REFERRAL PATHWAYS

How can medical professionals refer their patients?

If you're still seeking a mito diagnosis, speak with your GP about referring you to a specialist mito clinic or a diagnostician (that's a doctor who specialises in making diagnoses). The [Mito Foundation Helpline](#) manages a Mito Professionals Directory if you need help finding a specialist.

If you have not had genetic testing, speak with your medical team about whether this is available to you based on your medical history or request a referral to your state's Genetic Service. For information about eligibility for referral or waiting periods, you may ring your local Genetic Service and ask to speak to the genetic counsellor on duty. You can locate your nearest genetic clinic within each state and territory here.

In closing, the Mito Foundation will continue to advocate on behalf of the mito community and working with our partnerships to ensure progression to the next stage swiftly and in a complete and equitable manner. We are ensuring that the appropriate expertise on mitochondrial disease clinical management and genetics are involved in the decision-making process. The achievement of passing this legislation is a result of many people coming together and we are grateful to every individual who was involved on this journey.

RECOMMENDED RESOURCES

- [Mito Foundation's Mitochondrial Donation resources](#)
- ["The facts about mitochondrial donation supported by scientific and medical evidence"](#)
- ["A brief explanation of mitochondrial disease and the mitochondrial donation process"](#)
- ["A quick and printable guide to mitochondrial donation"](#)
- ["Mitochondrial Disease and Donation – Q&A"](#)
- ["Preventing Mitochondrial Disease: Reproductive choices for families"](#)