MSAC Secretariat
Australian Government Department of Health
MDP 960
GPO Box 9848
Canberra ACT 2601

8 June 2022

Dear Committee members,

Re: MSAC application 1637 – Expanded Reproductive Carrier Screening of couples for joint carrier status of genes associated with autosomal recessive and X-linked conditions

Thank you for the opportunity to provide input on this application. The purpose of Mito Foundations is to end the suffering from mitochondrial disease (mito). Prevention is one of our key objectives and we support equitable access to carrier screening for mito to give prospective parents options to prevent having a child with mito.

Background

The Mito Foundation[1] supports patients with mito and their families, funds essential research into the prevention, diagnosis, treatment and cures of mito, and increases awareness and education about these devastating diseases. The Mito Foundation was founded in 2009 by Doug and Margie Lingard, their friends, and experts in the field of mito. Doug and Margie have tragically lost a son and daughter to mito.

The Mito Foundation's work is informed by our Mito Community Advisory Panel, regular engagement with the wider mito community through support services and through specific projects. This submission has been informed by members of the mito community who have had children with severe and life-limiting forms of mito as well as key medical and scientific advisors to Mito Foundation.

In my role as Mito Foundation's CEO I have been a member of the Engagement Reference Group for the Makenzie's Mission project. The list of genes used in Makenzie's Mission includes 66 genes known to cause severe mito in children. I am motivated in this role, and in my other roles with Australian Genomics, by the promise of genomic medicine to transform prevention, diagnosis and management of mito. My own family has been affected by mito, so I know first-hand how devastating this disease can be. I implore the committee to recommend that expanded reproductive carrier screening is included on the Medicare Benefits Schedule.

[1] Incorporated as the Australian Mitochondrial Disease Foundation Limited ABN 841 353 243 91

Mito can have a devastating impact on children and families

While mito can affect people of any age, cause symptoms in almost any organ and have a wide range of severity, the forms of mito included in this submission are known to have childhood onset, cause multiple disabilities and lead to early death. As one example, several genes known to cause Leigh syndrome are included in the proposed gene list. Children with Leigh syndrome experience developmental delays, low muscle tone, epilepsy and problems with feeding and breathing.

Treatments for mito are limited to exercise, dietary supplements, and the treatment of symptoms. Although there are some promising treatments for some forms of mito in the research pipeline, it is not likely that these will significantly alter the prognosis of children born with severe forms of mito for many years.

> Without mito, my daughter would have been able to do what other kids her age could do: walk, talk, eat and participate in everyday life without needing additional support. Her childhood would not have been focused on trying to acquire basic skills and then to lose those as her health declined.
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> Of all the things I would have wanted to change for her, it would have been for her to be able to really communicate – to say what she wanted to say and really be heard. What she thought about things, what she wanted to wear, when she was hungry, when she was in pain.
>
> Mother to a child with mito who died before her 10th birthday

The mito community supports prospective parents being able to choose to be screened

The mito community is passionate about preventing mito, including through the use of assisted reproductive technologies. This is best illustrated by the successful community driven campaign for legalisation of mitochondrial donation, an emerging technology to enable families with a disease causing mitochondrial DNA mutation to prevent passing this on to their children.

For those parents who have had a child with a severe form of mito caused by a recessive gene mutation, almost all known to Mito Foundation either choose not to have more children or choose to use genomic technologies to reduce the risk of their subsequent children having the same form of mito. Dion's family provides one such example.

We were just like any other couple expecting their second child: excited and perhaps a little more confident than the first time round when we welcomed our little girl Erin into the world a couple of years previously. We dreamt about his first day at school, about teaching him to ride a bike and what he'd want to be when he grew up.

Dion was a perfect little package when he arrived. He was born into a doting family and had the world at his tiny feet. When Dion reached 8 months, we realised that something was wrong and after many exasperating visits to various doctors and specialists, Dion was diagnosed with Leigh syndrome, a fatal type of mitochondrial disease, for which there is no cure. At just three years old, Dion succumbed to Leigh's Disease, after a brave and inspiring fight.

We talk about Dion all the time. We'll always have that person missing at the Christmas table. We'll save a spot for him and put his star on the Christmas tree.

The loss of a child is perhaps the hardest thing anyone can experience, but we picked up the pieces of our lives and tried to move forward. I fell pregnant again but this unborn baby was also diagnosed with Leigh syndrome. We made the heart-rending decision to terminate the pregnancy. We wanted to try again for another child, but did not to risk him or her having to suffer the pain and debilitation of Leigh syndrome. So we decided try in vitro-fertilisation and pre-implantation genetic diagnosis. We identified the gene change that my husband and I carried that caused Dion's Leigh syndrome. We were able to test the embryos for a defective copy of the gene.

On the 18th November 2011, I gave birth to a beautiful, bouncing – and most importantly disease-free – little boy. Thanks to advances in science and to the big brother he'll never meet, Levi is growing into a happy, healthy little boy with his whole life ahead of him.

More recently, my eldest daughter went through genetic counselling to understand her own risk of having a child with mito. It was a relief to have this testing available to her. I look forward to having this testing available to all Australians.

Tracey, Mum to Dion, who lived with Leigh syndrome

Even for families who do not choose to use reproductive technologies to avoid having a child with mito, expanded reproductive carrier screening may allow early diagnosis of mito. This will shorten the diagnostic odyssey and create new windows for early intervention.

Pre-test and post-test genetic counselling is essential

Mito Foundation recognises that genomic medicine is leading to increased demand for genetic counselling services. Medicare funding for expanded reproductive carrier screening will further increase demand. We believe this will be a challenge for implementation but should not be a barrier to making this technology available.

Mito Foundation supports two different approaches to the two stages of pre-conception carrier screening. We have some concerns about the readiness of the health workforce, which are outlined below:

Stage	Health professionals involved	Key issues
Pre-test counselling for all couples	General practitioners, obstetricians, midwives, nurses, fertility specialists, and genetics health professionals.	It is vital that health professionals who order the test are able to explain what is included in the test, what is not included in the test, and to help couple choose between laboratory providers. If a couple has carrier screening and subsequently has a child diagnosed with a genetic condition, being confused about the testing they have had can cause unnecessary additional grief and anxiety. Mito provides a relevant example as there are so many genes that can lead to childhood forms of mito that there will continue to be couples who show no elevated risk results from carrier screening but who will still have a child subsequently diagnosed with this devastating disease. Mito Foundation supports a wide range of providers being able to order the test, and that online consent is available, to improve access to testing particularly in regional, rural and remote areas. Telehealth services can be a useful tool to ensure equitable access to skilled health professionals. We also believe that ongoing investments in training and resources are key to ensure that health professionals have the knowledge and skills needed to support couples to make an informed choice. T
Post-test counselling for those with elevated risk results	Specialist genetic counsellors and clinical geneticist This is complex and beyond the reasonable skills/knowledge of a GP, nurse or midwife.	This is a complex genetic counselling process that often requires medical input to help couples understand meaning of test results, the uncertainty of phenotype/genotype correlations, understanding lived experiences of the condition and guide couple through decision making process. Mito Foundation supports ongoing work to increase the size of the genetic counselling and clinical genetics workforces. We are also concerned about how already overburdened specialist services cope with these additional referrals. Although we understand this is beyond the scope of MSAC's decision making on this application, we encourage the Department of Health to ensure that the implementation of this new item number does not extend existing waiting times for clinical genetics services.

We support a flexible approach

Mito Foundation supports the application's approach to drafting the proposed MBS item to not be specific to testing technologies or a fixed gene list. This will allow the program to respond to changing testing technology and improving knowledge of disease causing gene variants. We encourage MSAC to make recommendations to the Department of Health for establishing a robust process that will ensure that the list of genes included in funded testing can be refined as new disease causing variants are discovered and knowledge of other genes improves. The process for changing the gene list needs to be flexible and responsive.

This is important to mitochondrial disease because:

- there are a large number of different autosomal recessive genes that can lead to mito
- there are new gene variants being discovered frequently
- our knowledge, particularly about genotype-phenotype correlation, is improving.

Ongoing consumer and community input is vital

Mito Foundation believes that improved community and consumer engagement in future review of genes being considered for screening is important. We do not suggest that the current gene list is incorrect or inappropriate, as it has focussed on some of the most severe paediatric onset, life limiting conditions with relatively consistent phenotypes. However, future decisions may be less clear and a robust process should be established as a part of implementing these new MBS items.

Mito Foundation was involved in the citizen's panel[2] and citizen's jury[3] convened as a part of the process to legalise mitochondrial donation research. These models may be useful in determining which conditions a 'reasonable' couple would take steps to avoid having a child with, one of the criteria suggested in the application.

Our experience was that this process allowed complex scientific information, varied community perspectives and the lived experiences of the mito community to be considered in the decision making process. We also found that the process of a full citizen's jury was resource intensive and took considerable time, so we suggest that a nimbler process informed by a citizen's jury approach may be more appropriate.

A similar process could improve on the review process used for Mackenzie's Mission by including more input from people with lived experience of rare disease. While both medical knowledge of conditions and relevant published research are vital to these decisions, we implore MSAC to consider the lack of published research into the lived experience of families with children with these conditions, particularly non-medical

[2] The report from this panel is available at Mitochondrial Donation Community Consultation Citizens' Panel Position Statement

[3] A J Newson, S de Lacey, D K Dowling, S Murray, C M Sue, D R Thorburn, L Gillam, C Degeling, Public attitudes towards novel reproductive technologies: a citizens' jury on mitochondrial donation, Human Reproduction, Volume 34, Issue 4, April 2019, Pages 751–757, https://doi.org/10.1093/humrep/dez021

perspectives. Mito Foundation understands that this process needs to be able to make decisions on uncertain information. For example, with many forms of mito the age of onset of symptoms varies significantly between individuals.

We support this application rather than a less comprehensive approach

MSAC Application *1671 Targeted carrier testing for severe monogenic conditions* proposes testing for a much smaller list of conditions that does not include any forms of mito. Mito Foundation understand that less than 1% of Australia's population has the potential to benefit from this testing approach. We support a more comprehensive approach to providing important information about genetic risk to all couples who make an informed choice to be tested for this risk.

Further information

Clare Stuart, Mito Foundation's Policy and Advocacy Manager, is available for further discussion regarding this submission: clare.stuart@mito.org.au or 0410 685 181.

Yours faithfully,

Sean Murray
Chief Executive Officer