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

5 November 2021

Dear Committee members,

Re: MSAC application 1675 – Whole Genome Sequencing for the diagnosis of mitochondrial disease

Thank you for inviting Mito Foundation to provide input on this application. Genomic testing can be a life changing experience for people with symptoms of mitochondrial disease (mito) and Mito Foundation supports improved access to testing through Medicare listing of Whole Genome Sequencing (WGS) for the diagnosis of mito.

The aim of this submission is to provide input from the mito community into the formulation of the PICO (Population, Intervention, Comparator, Outcomes) for this submission. Mito Foundation is looking forward to providing further input at the next stage of the decision making process.

Background

The Mito Foundation 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 research projects. To prepare this submission, Mito Foundation staff also interviewed eight mito community members about their experiences with genomic testing and their hopes for the role of genomic testing in the future. This group included people with mito, parents of children with mito and other family members of people with mito. Our aim was to get a variety of perspectives. We have used their stories to illustrate the key points in this submission.

We are aware that there are two mixed methods studies in progress looking at the utility of WGS for the Australian mito community through the Murdoch Children's Research Institute. In making decisions about this application, we encourage the committee to seek out early findings of these two studies.

Current access to genomic testing

People with symptoms of mito access genomic testing through several options:

State and territory health funding: Hospital based clinical genetics services have funded genomic testing for their patients. There is significant variation in the ease of access to genetic services and to funded genomic testing for mito.

Out of pocket: Individual patients can pay directly/privately for genomic testing.

Research: Some research projects will fund (or have funded) genomic testing for people with mito. The projects run for fixed recruitment periods and criteria based on multiple factors.
Major projects include the Australian Genomics Health Alliance (NHMRC funded project), a project funded under the NSW Genomics Collaborative Grant, and more recently a new project funded by the MRFF.

Medicare: Some, but not all, children with mito can access genomic testing through MBS items 73358–73363 *Genomic testing for childhood syndromes.*

Given the variation in access to these options, particularly for those in regional, rural and remote areas, Mito Foundation supports this application to improve equity of access to genomic testing.

Outcomes

A genetic diagnosis leads to several outcomes for people with mito. We encourage these to be considered in the formulation of the PICO:

1. Reducing the duration, burden, cost and emotional strain of the diagnostic odyssey
2. Avoiding complex and risky clinical tests
3. Improving mental health from a definitive diagnosis
4. Improving access to non-health supports with a definitive diagnosis
5. Uncovering an alternate cause of mitochondrial dysfunction
6. Allowing cascade diagnosis for family members
7. Enabling reproductive confidence for families of a child with mito, and potentially their extended families
8. Supporting existing pro-active management, early intervention and targeted treatments
9. Creating foundation for more accurate information on prognosis
10. Enabling access to emerging therapies

1. Reducing the duration, emotional strain, burden and cost of the diagnostic odyssey

A diagnosis of mito in Australia can take more than 20 years. One study reported that for more than half of patients with mito, the time from first symptoms to a diagnosis was more than three years[1]. This is consistent with international studies[2]. Improving access to WGS is very likely to reduce this duration for many people with mito. For those people, the positive impact on their lives will be significant.

> I know many people who have spent more than ten years getting a diagnosis. This destroys their lives. I think particularly of one man - the testing they have put him through has risked his health. He completed an exercise stress test that caused him to collapse. This search for a diagnosis through clinical tests has caused people huge emotional and physical stress, wasted a huge amount of health resources and personal finances. If genome testing was available earlier and more easily, this could have been avoided.
>
> Mito Foundation peer support leader who is also an adult living with mito and a parent of children with mito

Mito community members tell us about the emotional impact of this process. Some describe this as negatively impacting their mental health and others describe their specific feelings.

> There is a huge mental health impact of all the testing. It affects not just the person with mito but their family and friends too. I've lived through that – feeling like you're on the edge. Dreading the next test result in the never-ending process of elimination.
>
> Parent of a child who had mito

> It was just hard. I found supportive colleagues and friends really reassuring, particularly those that also worked in healthcare. I often thought about all the possible outcomes and how I might cope with each of them. I had one specialists informally provide a diagnosis and I got really excited by that, but then this was also ruled out, which was another challenge. This was all on top of being in huge amounts of nerve pain and had severe cramps, so I wasn't sleeping. We were just trying to manage symptoms and get through each day and night.
>
> Adult living with mito

As the above quote highlights, people navigating this odyssey are also managing often debilitating symptoms, particularly fatigue.

> It all took so much time and energy. Because of the time taken to organise and attend all of the tests and appointments I had to stop my part time study – I just couldn't fit it all in. If I had been working full time I expect I would have had to change to part time.
>
> Adult living with mito

Genomic testing may also reduce the out of pocket costs household face through the diagnostic odyssey.

> The tests and appointments were mostly done through the private health system, with only some Medicare funding. It was expensive, but we were fortunate that we could afford it. Let's just say that we hit the safety net quite quickly!
>
> Adult living with mito

2. Avoiding complex and risky clinical tests

This application proposes genomic testing replaces tissue analysis for some people. While there is a potential cost saving to this change, there is also the opportunity to avoid the risks and pain of these tests on the patient and their family.

> The muscle biopsy and MRIs were complicated because of risks of anaesthetics and the use of contrasts that were mito toxins. It took a lot of self-advocacy to organise these tests to minimise the damage they did to me– but I just didn't want to get any worse.
>
> Adult living with mito

> My daughter had a profound hearing loss and then a massive seizure. The doctor suspected mito, but she told us that sadly, we had to go through the whole process of multiple tests to eliminate everything else first.
>
> For our little girl this meant four lumbar punctures, which triggered her to have more seizures. Lumbar punctures also were a source of potential infection and were really distressing for all of us. Our daughter had two muscle biopsies as the first one failed. That meant a second anaesthetic which impacted her physically. This was in addition to other tests - the moment we took her into the pathology room I knew she knew: 'I am going to get poked!' I remember every part of her body having band-aids on it because she was prodded so many times.
>
> Earlier access to whole genome sequencing would have meant less hospital stays, less infections, less anaesthetics. Every admission shortened her lifespan.
>
> Parent of a child who had mito

3. Improved mental health from a definitive diagnosis

It is common for many people in the mito community to live with a provisional diagnosis of mito when clinical tests are inconclusive. Improved access to genomic testing will reduce this number by providing a definitive diagnosis for more people with mito.

> Not knowing was the hardest thing. My mind was always wandering: Is it MS? Is it some other weird disease? Is my wife going to be here in three years' time?
>
> Spouse of an adult with mito

> It was an amazing relief to get the diagnosis. Even though this was followed by confusion and lots of questions for my doctors.

Adult with clinical diagnosis of mito

> I always believed that my symptoms were personal character failings: I thought I was lazy, depressed and just not very good at things. Finding out I had a genetic disease helped me understand a whole set of symptoms under that diagnosis. Getting a formal diagnosis also allowed me to educate myself on how to manage my mito symptoms, which has improved my health and enabled me to keep working. Overall, this improved my quality of life, my access to support and understanding from my employer. It led to a huge improvement in my mental health.

Adult with mito

Mito community members without a genomic diagnosis tell us they have to convince health professionals of their clinical diagnosis and that this not only prevents them from accessing the health care they need, but takes an emotional toll.

> Not having a confirmed diagnosis of mito is extremely frustrating and debilitating. I live with a constant doubt about the underlying cause of my symptoms. When I see doctors I always have to say "I think…" or "I believe…" about my mito. Often they don't believe me, they think I have been on Dr Google and am making it up. On top of my mental fatigue, this is just exhausting.

Adult with undiagnosed mito

For mito community members with a definite clinical diagnosis, the promise of genomic testing is valued to remove the remaining uncertainty

> There are some symptoms that don't quite match the (clinical) diagnosis. A genetic diagnosis will give us more certainty and peace of mind, to really know that the diagnosis is correct.

Spouse of an adult with mito

Mito community members who have a genomic diagnosis describe how valuable this was:

> Having a definite diagnosis, even if it's not what you want to hear, is way more beneficial to the person with mito, because the uncertainty is far worse.

Parent of a child who had mito

One family shared with us that the emotional challenges extended to their children:

> Our children have been through trauma linked to my wife's symptoms and mito. During that period of time when my wife was not able to move it really impacted them and we weren't able to offer much re-assurance as we didn't know what was going to happen. Now that we know it is mito we can answer their questions and get help from Mito Foundation. One example of this was when they each took the Mito Foundation picture book to school to explain why their Mum wasn't able to come to birthday parties or other events.

Spouse of an adult with mito

4. Improving access to non-health supports with a definitive diagnosis

Mito community members who have received a genomic diagnosis of mito tell us that the definitive nature of the diagnosis is helpful in accessing health, disability, workplace and education supports.

> Once my kids had a formal diagnosis of mito, we were able to access a whole range of supports that we couldn't get previously. During the time that their records said 'suspected mitochondrial disease' we couldn't get allied health services at the hospital, we couldn't get disability supports and we couldn't get help at school for them. That piece of paper with the gene test result was the deciding factor to get support and get support for them at school.
>
> Without a diagnosis we are just two annoying parents with a child with a range of non-specific issues. With a diagnosis we can ask them to provide the supports they need and to follow the best medical advice.

Parent of children with mito

Recent Australian research reports on the significant burden mito community members face in negotiating for access to health and social care[3]. A genomic diagnosis of mito can make this a little easier.

5. **Uncovering an alternate cause of mitochondrial dysfunction**

Mito Foundation understands that genomic testing is a useful tool for identifying patients who may have been given a clinical diagnosis of mito, but actually have another underlying condition causing their mitochondrial dysfunction. Some of these conditions have treatments and/or management approaches that can drastically improve health and quality of life.

We encourage the committee to consider the improvements in quality of life for these individuals.

6. **Allowing cascade diagnosis for family members**

The discovery of the gene change causing mitochondrial disease allows other members of the same family to be more easily tested, even if they are not showing enough symptoms.

> Genetic testing for myself and my two children was very straightforward. But this was only because members of my family went through a tortuous process to confirm the diagnosis and find the gene change in our family. Particularly one of my aunts, who spent ten weeks in hospital seeking a diagnosis. This included a muscle biopsy under general anaesthetic which was a life-threatening procedure for her.
>
> Adult with mito who is also a parent of children with mito

> Trying to get my clinical symptoms of mito understood has been incredibly difficult. My sister was diagnosed in 2004, and following discussions with her she suggested that my symptoms were also indicative of mito. Genetic testing could be a way for me to get a faster diagnosis and stop me having to push each doctor to take me seriously.
>
> Adult with possible mito

7. Enabling reproductive confidence for families of a child with mito

A genomic diagnosis of a child with mito can allow their parents to plan further pregnancies. Depending on the nature of the gene change causing their child's disease, parents can use assisted reproductive technologies or prenatal testing to ensure future children will not be born with mito. When mito is caused by a change in mitochondrial DNA, access to mitochondrial donation may be possible in the future.

> Without a formal diagnosis, how on earth are you supposed to make reproductive choices for your future children? The genetic diagnosis was key for us

Adult with mito who is also a parent of children with mito

> Our daughter was diagnosed with mito when she was 18 months old. It took a lot of fighting to have her various symptoms recognised but eventually an MRI revealed changes in her brain typical of Leigh syndrome. This was great to help us understand her health condition, but it didn't give us answers for the rest of our family.
>
> As we learnt more about mito we understood that it can be passed through a family in many different ways. We were really concerned for our two other children as we knew they could also have mito and just not be showing any signs or symptoms yet. Or maybe they were carriers and their children, our future grandchildren, would have mito. One of our siblings put her plans to start a family on hold because she was unsure if she should be having a child. It was haunting to hear the stories of other families where mito is inherited. We were frequently overwhelmed by concern for our other children.
>
> We were really fortunate to have our daughter's gene change found as part of a research project. We got the results only recently, which was 4 years after she was diagnosed with mito. They found that our daughter was a de novo mutation, which meant there was minimal risk of any of our other family members having mito.
>
> This gave us clarity and has helped us get on with living our best lives with all of our children. We are fortunate and grateful.

Parents of a child with mito

8. Supporting existing pro-active management, early intervention and targeted treatments

While there are no cures and very limited pharmacological interventions for mitochondrial diseases, non-pharmacological interventions can play critical roles in helping to reduce symptoms or slow disease progression and decline in health. Because of this, the earlier an accurate diagnosis can be made the better the prognosis and health outcomes for patients.

> For the whole time that we were investigating the cause of my symptoms I was advised to rest as much as possible. This was to keep my lactate levels from going any higher, so I understand why this was important. By the time I was diagnosed and could start rehab, my husband had to carry me upstairs and help me get ready for bed – I just couldn't manage stairs anymore.
>
> I do sometimes wonder what it would be like if that rest was for just one month. So only one month of lost muscle tone. I don't think the rehab would have been as complex as it has been. I now receive supports under the NDIS to help get the kids to school when my husband is working, maybe some of those supports could be reduced or avoided.
>
> Adult with mito

Some examples of these interventions are:

- exercise and endurance training
- heightened attention to nutrition
- mitigation of symptoms in times of physiological stress
- oral arginine supplementation for patients with MELAS (Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes)
- Avoidance of particular toxins, such as smoking in LHON (Leber's Hereditary Optic Neuropathy)
- co-factor treatment in some other forms of mito.

Management can be better informed by knowing the risk of acute symptoms of mito, such as stroke-like episodes.

> My diagnosis did mean that my other specialists find it easier to know their role in my care and acknowledge that I know more about my condition than they do. The diagnosis has meant that I can see a specialist clinic that sees multiple patients with the same form of mito. The management approaches still involve some trial and error but I know I am seeing the doctors with the most experience possible.
>
> Adult with mito

> If I could get an accurate genetic diagnosis of mito it would really clear things up in my head. I could move forward with my life. I also know that it would help me get appropriate treatments and avoid things that could make my symptoms worse.
>
> Adult with undiagnosed mito

> If we had a diagnosis sooner, we could have been proactive with supplements and other active management. I think this could have given my daughter more years of life with better quality and less suffering. I would have done anything for another two years with my daughter.
>
> Parent of a child who had mito

An accurate diagnosis can also ensure that known mito toxins are avoided. For example:

- a common anti-epilepsy medication, sodium valproate, which is toxic to patients with some forms of mito.
- streptomycin and certain related antibiotics that can cause deafness in patients with one of the most common mitochondrial DNA mutations.

> My wife was prescribed an antibiotic to treat a gastrointestinal problem. Unfortunately, this brought on a metabolic crisis. This caused worsening physical symptoms – every step she took was like walking through concrete. The silver lining was that this is what led to her eventual diagnosis, but it would have been so much better to avoid this toxic medication.
>
> Spouse of an adult with mito

9. Creating foundation for more accurate information on prognosis

Mito community members tell us that one of the hardest parts of living with mito is the uncertain future. More research is needed to build the natural history data for different types of mitochondrial disease. More people with mito having a genomic diagnosis will play a key role in building this knowledge.

One family told us how important prognosis was for them:

> After we understood the type of mito my daughter had I was desperate for information about other children with the same condition. I managed to find five other children around the world with a mutation on the same gene as my daughter. That was informative.
>
> One of the worst parts was that doctors had to give us their best guess on what the future would hold. They told us she had probably ten years, but we only got two. I feel robbed. I wish they could have been more precise.
>
> I would love to be able to have my daughter's story inform a future child's experience with mito. If research could help us understand her particular type of mito that would be a meaningful legacy for her to leave behind.
>
> Parent of a child who had mito

10. Enabling access to emerging therapies

There has been an exponential expansion in the development of new pharmacological and non-pharmacological treatments for mito, including an unprecedented period of gene therapy development[4,5]. More than 130 clinical trials involving pharmacological intervention in the treatment of mito have been registered publicly on Clinicaltrials.gov.

Typically, to be eligible for a clinical trial, patients need to have a confirmed genetic diagnosis of mito and present early in their disease progression. Early genetic diagnosis is key to ensuring Australian patients have equitable opportunities to access emerging therapies through clinical trial participation. Increased numbers of genetically diagnosed patients make Australia more attractive for site selection in international clinical trials.

The Australian Government invests significantly in clinical trials through the Medical Research Future Fund (MRFF) and through National Health and Medical Research Council (NHMRC) funding. This includes $614.2 million MRFF funding over 10 years to increase clinical trial activity in Australia, with a focus on rare cancers, rare diseases and unmet needs[6]. The NHMRC provided $74.2 million funding towards clinical trials in 2020-21 financial year[7] The economic benefits of clinical trials have been widely reported[8,9].

There have been over 182 interventional clinical trials for mito[4]. Less than 10 of these trials have Australian sites. Only one industry sponsored trial has established sites in Australia. This means Australian patients are effectively unable to access these medicines and there is no Australian data for any future regulatory approvals or reimbursement.

Being able to participate in clinical trials is important to the mito community:

> We have found one study that we're not eligible for. We might be eligible if we had a genetic diagnosis. That's pretty disappointing and frustrating.

Adult with mito

> If I am properly diagnosed, I know I will be on the books. If there are research trials in the future, I might be able to be part of that research or be able to access those treatments.

Adult with possible mito

Population

In developing the PICO, we would like the PASC to consider a flexible definition of the population eligible for genomic testing. The mito community tells us it is important to them that:

- The number of painful and risky clinical tests are minimised, such as muscle biopsies, CSF tests (spinal taps / lumbar puncture) and imaging under sedation.
- Tests can be ordered by a set of specialists that are accessible, rather than needing long waiting times for access to super-specialised clinics.

Mito Foundation asks the committee to ensure that a variety of clinical experts are involved in refining the draft listings, particularly the clinical features indicative of mitochondrial disease. It is important that both adult and paediatric mito experts are consulted to ensure the listing will deliver benefits to patients while ensuring the test is targeted to the intended population.

Restriction of the providers able to order the test will play a role in defining the population. Allowing a wide range of clinicians to order genomic testing for mito will enable testing to occur while patients are awaiting their first appointment with a mito specialist centre. We hear from people seeking a diagnosis when they have symptoms of mito that General Practitioners and General Physicians can play a significant role in their diagnostic odyssey. They also tell us they have trouble accessing specialist clinical services, including metabolic clinics and genetics services.

> I have struggled for years to get a referral to genetic services or to the specialist mito clinic. If my GP could at least order the test to look for the gene change that we know my sister has, this would help to give me answers while I wait to access a specialist.
>
> Adult with possible mito

Mito Foundation supports a relatively low threshold of suspicion of mito for genomic testing as continuing reductions in costs of genomic testing will only strengthen the economic case for a genomics-first approach to diagnosing mito. Needing to wait for a subsequent application to MSAC to alter the listing will unnecessarily delay access to this important health service for people with symptoms of mito.

Intervention

Mito Foundation asks that the committee ensures that whole genome sequencing (WGS) for the diagnosis of mito is made accessible through this Medicare listing. One of the key benefits of testing for mito community members is obtaining a definitive diagnosis in as many cases as possible in as short a timeframe as possible. The separate submission on this application from an individual with LHON illustrates one example of the difference WGS can make over exome sequencing for a person with mito.

Mitochondrial DNA mutations are not well detected by whole exome sequencing but are thought to underline about two thirds of adult-onset disease and one third of childhood-onset disease. WGS is able to identify complex rearrangements and gene changes outside of exomes[10]. An alternative approach may involve less expensive initial testing, however a follow up WGS will delay definitive diagnosis, undermining potential benefits of early intervention and prolonging the diagnostic odyssey.

WGS was also shown to be useful to provide a definitive diagnosis for people who have symptoms that overlap mitochondrial disease but who actually are found to have a non-mito diagnosis. We understand that during the Australian Genomics Mitochondrial Flagship project several children were provided with a diagnosis of a different genetic condition that had targeted treatment available[11]. Potential delays to accessing WGS while pursuing an alternative testing type could be a tragedy for those children and their families.

We also ask the committee to consider the importance of speed in genomic testing. As more clinical trials for mito come to Australia and a precision medicines advances, confirming a genomic diagnosis of mito quickly will be important for access to treatment.

Comparator

Mito Foundation's work with the mito community tells us that people currently take a variety of paths from first symptoms to diagnosis. It is important for the committee to consider that there are almost always multiple health professionals and multiple clinical tests before the person with symptoms of mito reaches a mito specialist service.

Pathways vary greatly between states, by age of presentation, by symptoms and by family history. We encourage the committee to actively seek a variety of clinical experts to ensure that this diversity is considered.

Further information

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

Yours faithfully,

Sean Murray
Chief Executive Officer

References

1. International Centre for Community-Driven Research. Mitochondrial Disease Australian Study [Internet]. Report No.: Volume 1 Issue 6. Available from: https://www.cc-dr.org/au/peek/complete/2018aumit/

2. Grier J, Hirano M, Karaa A, Shepard E, Thompson JLP. Diagnostic odyssey of patients with mitochondrial disease: Results of a survey. Neurol Genet. 2018 Apr;4(2):e230.

3. Long JC, Best S, Hatem S, Theodorou T, Catton T, Murray S, et al. The long and winding road: perspectives of people and parents of children with mitochondrial conditions negotiating management after diagnosis. Orphanet J Rare Dis. 2021 Dec;16(1):310.

4. Tinker RJ, Lim AZ, Stefanetti RJ, McFarland R. Current and Emerging Clinical Treatment in Mitochondrial Disease. Mol Diagn Ther. 2021 Mar;25(2):181–206.

5. Ng YS, Bindoff LA, Gorman GS, Klopstock T, Kornblum C, Mancuso M, et al. Mitochondrial disease in adults: recent advances and future promise. Lancet Neurol. 2021 Jul;20(7):573–84.

6. Australian Government Department of Health. Medical Research Future Fund 10-year plan [Internet]. 2019. Available from: https://www.health.gov.au/resources/publications/medical-research-future-fund-mrff-10-year-investment-plan

7. National Health and Medical Research Council. National Health and Medical Research Council Annual Report 2020–21 [Internet]. 2021. Available from: https://www.nhmrc.gov.au/about-us/publications/annual-report-2020-21

8. The joint ACTA/ACSQHC Working Group. The value proposition of investigator-initiated clinical trials conducted by networks. Med J Aust. 2021 Mar;214(4):159.

9. MTPConnect. Australia's Clinical Trials Sector. [Internet]. 2021. Available from: mtpconnect.org.au

10. Frazier AE, Compton AG, Kishita Y, Hock DH, Welch AE, Amarasekera SSC, et al. Fatal Perinatal Mitochondrial Cardiac Failure Caused by Recurrent De Novo Duplications in the ATAD3 Locus. Med. 2021 Jan;2(1):49-73.e10.

11. Thorburn D, Christodoulou J. The Australian Genomics Mitochondrial Flagship: Summary and progress to date [Internet]. 2020. Available from: https://vimeo.com/user100181140

Appendix: Kathy's Story

Kathy asked us to share her story to explain what life with mito is like and what genomic testing means to her.

I have suspected Mitochondrial Disease and first developed symptoms as a young child and am now 55. My journey has been long, frustrating and at times cruel, and impacted every area of my life.

On living with mito

Every day I live with significant fatigue, muscle weakness, stiffness and pain. I find it difficult to accomplish even small tasks.

My weeks are filled with numerous appointments such as physio, exercise programmes, speech therapy and visits to specialists.

I have a severe breakdown of my core muscles making it difficult to stay upright for long. My diaphragm muscle is very stiff and tight making breathing difficult. My back is extremely stiff and tight making sitting uncomfortable, and even when lying down, my back is unable to relax into a mattress.

I'm often nauseous and vomiting is very unpleasant due to the tightness of my diaphragm muscle, and usually involves fainting and choking.

My mobility and balance are also affected and I have a fluctuating cognitive decline. As well as this I live with visual disturbances and some hearing loss. Also episodes where the right side of my body becomes weak and occasionally I find myself drifting in and out of consciousness.

The psychological impact of living with this is huge and not having a confirmed genetic diagnosis and therefore a specific treatment plan adds to this load. I have felt alone on this journey and as the years go by it is harder to keep going.

The consequences of uncertainty

Living with such significant symptoms without a clear genetic diagnosis has been very challenging for me and my medical treatment has often been compromised as a result. I have often been placed in the too hard basket, had my emotional stability questioned, had to live with a trial and error approach to treatment, and had to pay a high cost for inappropriate physio programmes over many years.

One example of this is when I was given a diagnosis of chronic fatigue. I was prescribed anti-depressants to treat this condition that I didn't have. My throat swelled due to these medications. An earlier diagnosis could have avoided this.

Recently I was at the emergency department as I was unsure if I was having a stroke like episode related to my mito. My neurologist and my GP had both told me the call an ambulance when I had these symptoms. The doctor that was on call repeatedly finished his discussions with me by adding "… and that's if you do have mito". This happened around six times. It made me feel hopeless. It told me that there was no point being there, that no one was going to listen to me. I wasn't going to be given appropriate consideration, let along appropriate treatment. It also brought up traumatic experiences from before I even had the provisional diagnosis of mito- when people would not take me seriously and questioned my mental health.

As a result of an abnormal brain scan I was given IV steroid treatment, as my neurologist at the time believed I may have systemic lupus erythematosus. My body struggled to deal with this treatment, and is a good example of the trial and error approach often used.

The highest cost to me over the longest period of time has been inappropriate physio treatment and exercise programmes. Although my limbs have been significantly affected by this condition, it is my trunk that has been impacted to a greater degree. It was common for health professionals to tell me that they knew of no condition that could affect me in this way, and would consequently brush me aside. I have a diagnosed severe breakdown of my core muscles which is a lot like being a house with a crumbling foundation. I struggle to stay upright for long, my diaphragm muscle is very tight and I experience painful diaphragmatic muscle spasms and difficulty breathing. I need my diaphragm muscle, intercostal muscles and thoracic spine released weekly by my physio to assist with breathing and to make me more comfortable. This has been a positive physio experience for me.

A lot of what I live with daily could have been avoided by a genetic diagnosis, which would have led to more timely and appropriate treatment and understanding. Instead, physio treatment exacerbated the symptoms. The physios had no idea. They pushed me beyond the exercise limitations that a person with mito should stay within– I just crashed and got worse.

Having a genetic diagnosis wakes people up to the fact that there is an underlying cause and they will take you seriously. I believe I would have found physiotherapists that either knew about mito or were willing to learn. I could have learnt more myself and passed that information onto physios. I could have gotten the treatment I needed at least 20 years earlier.

What a genetic diagnosis would mean to me

Peace of mind after years of uncertainty and a huge weight off my shoulders. Even though I have numerous medical reports and test results to confirm my symptoms, I feel it would validate what I have suffered.

Having knowledge of the specific genes affected would lead to clarity and direction in my care and would assist my neurologist, endocrinologist and others in the team that care for me to form an appropriate treatment plan. It would be useful in planning treatment for the future. At present if I end up in an emergency situation it is unlikely I will receive appropriate help, but with a genetic diagnosis, it will be easier to pinpoint and treat problems.