POWERING PROGRESS

A plan to increase clinical trials for mitochondrial disease in Australia

mito FOUNDATION
Hope for mitochondrial disease

RESEARCH AUSTRALIA
Championing Australian health & medical research
Our Voice Your Innovation

A collaborative project between Mito Foundation and Research Australia

Mito Foundation is the only organisation in Australia dedicated to supporting people affected by mitochondrial disease (mito). Mito Foundation empowers people impacted by mito as they navigate their journey by providing information and support.

The foundation amplifies the voice of the mito community to influence policy and drive critical research advancements into the prevention, diagnosis, treatment, and cures of mito.

Research Australia is the national peak body for health and medical research and innovation. We use our unique convening power to position health and medical research as a driver of a healthy population and contributor to a healthy economy.

We gratefully acknowledge the insights provided by all stakeholders who have shared their experiences to inform this report. These contributions were essential to understanding the opportunities and complexities of attracting and sustaining increased clinical trial activity for mito and other rare diseases in Australia.

EXECUTIVE SUMMARY

Unprecendented progress is being made in developing new treatments for mitochondrial disease (mito). Mito is a debilitating genetic disorder that robs the body's cells of energy, causing multiple organ dysfunction or failure and potentially death. There are no cures and historically, few effective treatments. But right now, real momentum is building towards effective treatments — with over 60 treatments in development and more than 25 clinical trials already commenced.

It's a hopeful moment for the global mito community, health professionals, and researchers alike. The time is right for Australia to address the barriers that limit mito clinical trial activity, and to establish itself as an attractive site for mito trials.

There is a strong pipeline of therapeutic development and an increasing number of clinical trials for mito. Australia has had sites in some of these trials and missed out on many others. Action is needed to ensure Australia has an efficient, collaborative, and sustainable ecosystem that meets the needs of the mito community, clinicians, researchers, industry[i] and other funders. Taking action now will ensure clinical trial participation is a real option for Australians living with mito, ultimately leading to treatment options that improve their lives.

The action plan identifies 3 priority areas, each with actions for clinician researchers, industry, governments, Mito Foundation and others.

In addition to these, work in several other areas will make an important contribution to success. These areas include data infrastructure, work outside of industry-led trials, working towards registration and reimbursements and policy improvement.

Work on these actions has already begun, and many build on existing initiatives. While the plan has been developed with a 10-year timeframe in mind, ongoing monitoring, reporting, and adaptation will be required. Additional funding will be required for many actions.

Through collaboration across research, industry, and the mito community, we can build a future where clinical trials are not only possible but become a recognised tool to deliver life-changing treatments to those affected by mito. We invite our partners to join us in making this vision a reality.

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i Companies involved in the research, development, manufacturing, and commercialisation of therapeutics. This publication uses this term to be inclusive of pharmaceutical companies and biotechnology companies.

KEY FINDINGS FROM CONSULTATION AND LITERATURE:

- Australia has a strong foundation for mito clinical trials, with experienced clinician researchers particularly in Sydney, Melbourne, and Adelaide. With the appropriate resources, they are well positioned to lead future trials.
- The mito community is motivated to participate in clinical trials. Patient organisations can provide access to patient populations and insights, fund research, and support patients considering trial participation. Mito Foundation is a strong and well-resourced national patient organisation and can play a critical role in the clinical trial ecosystem.
- Collaboration, particularly between clinician researchers, patients and industry, can drive clinical trial progress. There is an opportunity to build and strengthen partnerships to ensure Australia is well-positioned for further advancements in mito research.

PRIORITY AREAS AND ACTIONS

1 Building clinical research capacity

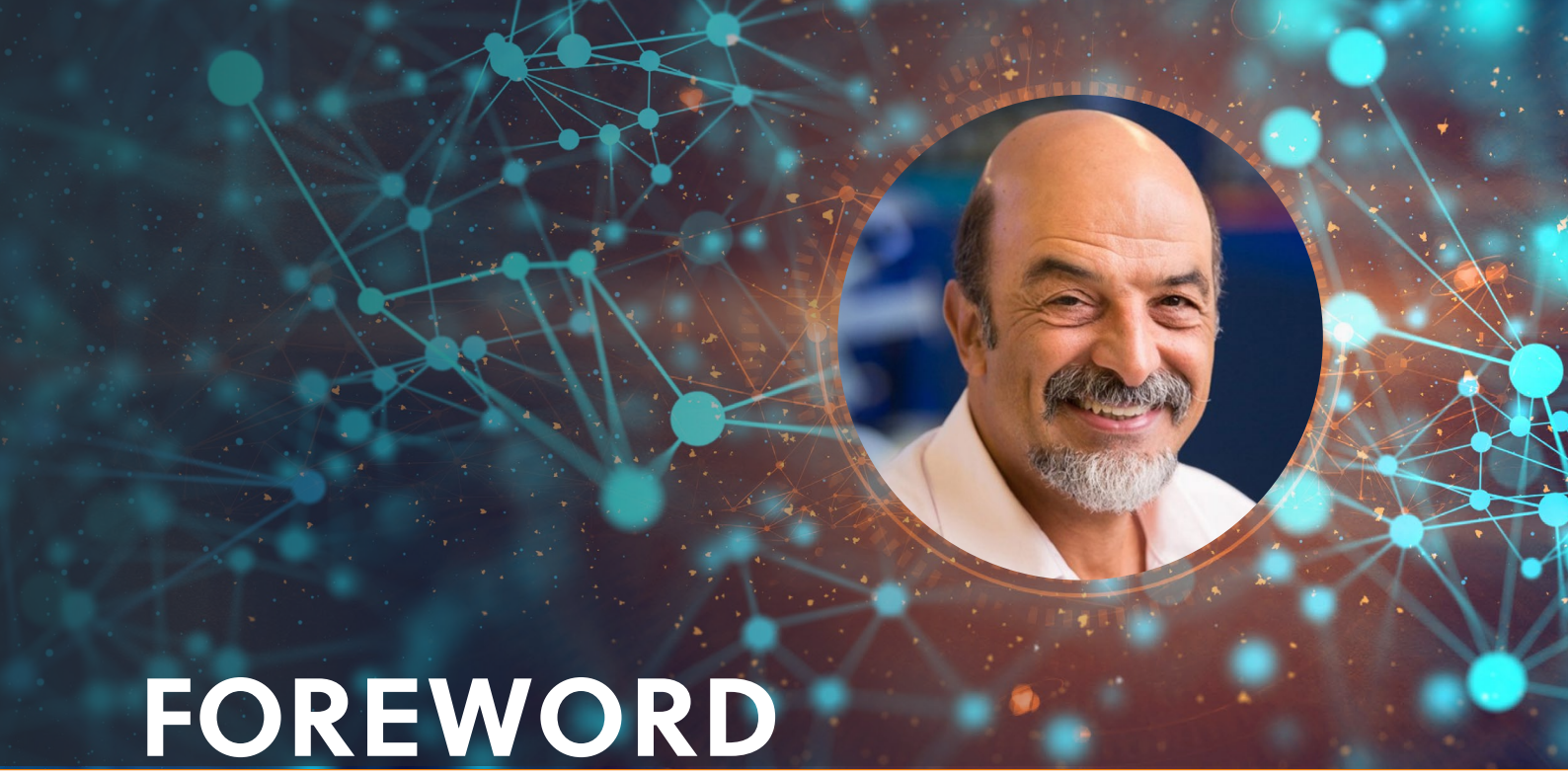
Actions to ensure that clinician researchers are engaged, empowered, and resourced to lead clinical trials

2 Supporting the mito community to participate in clinical trials

Actions to create a clinical trial-ready mito community, and to ensure participants are well supported during and after trials.

3 Strengthening collaboration

Actions to enhance connections and partnerships, including between the mito community, health professionals, and industry.



FOREWORD

Professor John Christodoulou

MB BS PhD FRACP FRCPA FAHMS
Chair of Genomic Medicine, Department of Paediatrics, University of Melbourne
Co-Leader of the Brain and Mitochondrial Research Group and Director of the Genetics Research Theme, Murdoch Children's Research Institute
Founding member of Mito Foundation's Board of Directors and Scientific and Medical Advisory Panel

As a paediatrician since the 1980s, I have provided care for many children impacted by mito. Almost universally, when a diagnosis of mito is made, families will ask their health care teams, "So, what are we going to do about it?" For mito, we really don't have any suitable answers to this question.

In the last 5 years, we have seen a dramatic increase in investment, particularly by the pharmaceutical industry, in the development of targeted therapies for rare diseases generally, and mito specifically. We must take advantage of this exciting time. This plan sets out a compelling vision and a comprehensive set of actions that will play a key role in making Australia an attractive location for mito clinical trials.

While our small population may make us seem less appealing to the pharmaceutical industry, our highly committed clinical community offers an opportunity to establish a collaborative clinical trial network dedicated to delivering mito trials. Relying on results from international trials can delay the approval of new therapies in Australia. Conducting trials locally not only accelerates this process, but also helps our local clinicians to gain experience with these therapies and be able to influence decision-making of Australian regulators.

Success will require partnership of health services and governments. All the healthcare providers caring for the mito community are already working at maximum capacity. Investments in the additional resources will not only enable Australians to access therapies through clinical trials, but also beyond.

This is a bold 10-year plan. I look forward to a time where we can, first, accurately diagnose individuals with mito before symptoms appear or early on in their disease course, and second, provide targeted therapies that we know will significantly improve their health. During my career, I have seen amazing progress in many rare diseases. I believe that together we can ensure we have a better answer to the question "So, what are we going to do about it?"

FOREWORD

Mia Bell and Kim Harrison

Co-chairs, Mito Community Advisory Panel
Both Kim and Mia are personally impacted by mito.

The Australian mito community is excited about clinical trials because they offer tangible evidence that there is hope. Trials are the most effective way for our community to support innovation that can lead to better health. Of course, we're hopeful for better health for ourselves, but we are also hopeful for better health for others in the mito community, including those that will join our community in the future and those that are affected by similar conditions.

Our mito community is ready to have more trials in Australia. When we speak to others in our community, we hear of so many that are actively looking for research they can participate in. Too often they find clinical trials that are not available in Australia. Living with mito forces us to be pretty tough, but even the most resilient of us feel despondent about missing out.

Increasing the number of trials available in Australia is important so that more of the mito community will have an option to participate. It is also important that we have trials that involve people with different types of mito, people of different ages and living in different parts of Australia. This plan aims to achieve this and that's exciting.

We're also excited about the possibility that having more clinical trials will lead to better health care. The timely care received by Australians who have participated in mito clinical trials shows what we can achieve. By supporting our over-stretched mito clinicians through the actions in this plan, we hope we can improve monitoring of mito symptoms and strengthen connections between specialists, primary care, and allied health.

It feels wildly ambitious that clinical trials will deliver life-changing treatments for mito. This plan itself is a 10-year "to-do" list! But less than 10 years ago, work to allow Australian families to access mitochondrial donation began. And here we are, on the precipice of the rollout of the pilot project. And just like the campaign for mitochondrial donation, we know this next challenge will require strong collaborations. We invite you to work with us on achieving the vision in this plan so that we can offer the hope of clinical trials to as many Australians impacted by mito as possible.

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WHY ACTION IS NEEDED NOW

The time is right for Australia to address the barriers that limit mito clinical trial activity, and to establish itself as a attractive site for mito trials.

Clinical trials are crucial to address the unmet needs of people living with mito

Mitochondrial disease (mito) is a group of genetic disorders that impair mitochondria, which are essential for producing energy in cells. This energy production failure can lead to cell malfunction and cause organ failure. There are over 350 identified types of mito, affecting one in 4,300 people, with a further one in 200 Australians having genetic changes that put them at risk of developing mito.[1]

Mito is a progressive condition that affects both children and adults, leading to significant disability and, all too often, premature death. It can impact multiple organ systems, causing symptoms such as seizures, strokes, severe developmental delays, dementia (including childhood dementia), inability t o walk, talk, see, or digest food. In addition, seemingly benign symptoms such as muscle weakness and fatigue often limit a person's ability to work or perform daily activities.

Clinical trials are crucial for advancing treatment of mito. Currently, there is no cure for mito, and available treatments focus only on symptom management rather than addressing the underlying disease.[2] Clinical trials provide essential insights and novel therapies that can form part of patient care, benefitting both individuals and the global mito community. Increasing mito clinical trials in Australia can also hasten the approval and funding of new treatments in Australia.

Mito clinical trial activity is growing, but Australians have had limited opportunities to participate

There is unprecedented research activity and industry investment. Several decades of advances in the understanding of mitochondrial biology have laid the foundation for the current surge in therapeutic research.[3] Therapeutic development for mito primarily focuses on gene therapies and small molecule therapies. Due to complex regulatory frameworks in Australia and globally.

Globally, there is a growing number of clinical trials for mito with 37 recent phase II, III, or IV clinical trials for 20 individual therapeutics.

27 clinical trials for mito were sponsored by industry and 10 were investigator-led.

Across phase II clinical trials for all disease types, Australia ranks 4th internationally.[4]

For mito, Australia only ranks 10th, for combined industry-led phase II, III, and IV trials.

Only 3 mito clinical trials had local access in Australia.

Mito trials were limited to 3 capital cities, likely affecting equitable access to these trials.

Based on Mito Foundation Horizon Scan (unpublished), completed in March 2024.

Australian access to mito clinical trials is limited compared to the rest of the world. Despite relatively high clinical trial activity for mito globally, Australians have limited access to these trials. Mito Foundation identified over 60 mito treatments currently in development, with 25 therapies in phase II or III trials. However, Australians only have local access to clinical trials for 3 of these emerging therapies. Limited and inequitable access to clinical trials means that Australians with mito are not being offered the chance to access treatments that may improve health outcomes.

Australia is ready to lead in mito clinical trials

Australia is globally competitive as a preferred location for clinical trials due to its excellent research community, sophisticated healthcare system and diverse population.[5] Australia continues to perform well as a clinical trial site across both investigator and industry-led trials in more common domains such as oncology, mental health and cardiovascular disease. Despite this, there are specific challenges and barriers for rare disease clinical trials, including for mito.

The Australian mito community is eager to participate.
Many Australians impacted by mito, along with their family and carers, are highly engaged and motivated to participate in clinical trials, driven in part by Mito Foundation's efforts to mobilise and activate the community.[6] The strong engagement seen in natural history, diagnosis, and quality-of-life studies highlights the community's readiness for expanded clinical trial access.

Australia's strength in mito diagnosis and rare disease trials provides a strong foundation. Australia excels in mito diagnosis, particularly through recent publicly funded access to genetic testing. This means those with mito can get earlier access to care and may have lower barriers to obtaining a genetic diagnosis, frequently an inclusion criterion for clinical trials.[7] The networks built through key diagnostic projects are a valuable foundation for future interventional studies.[8–10]

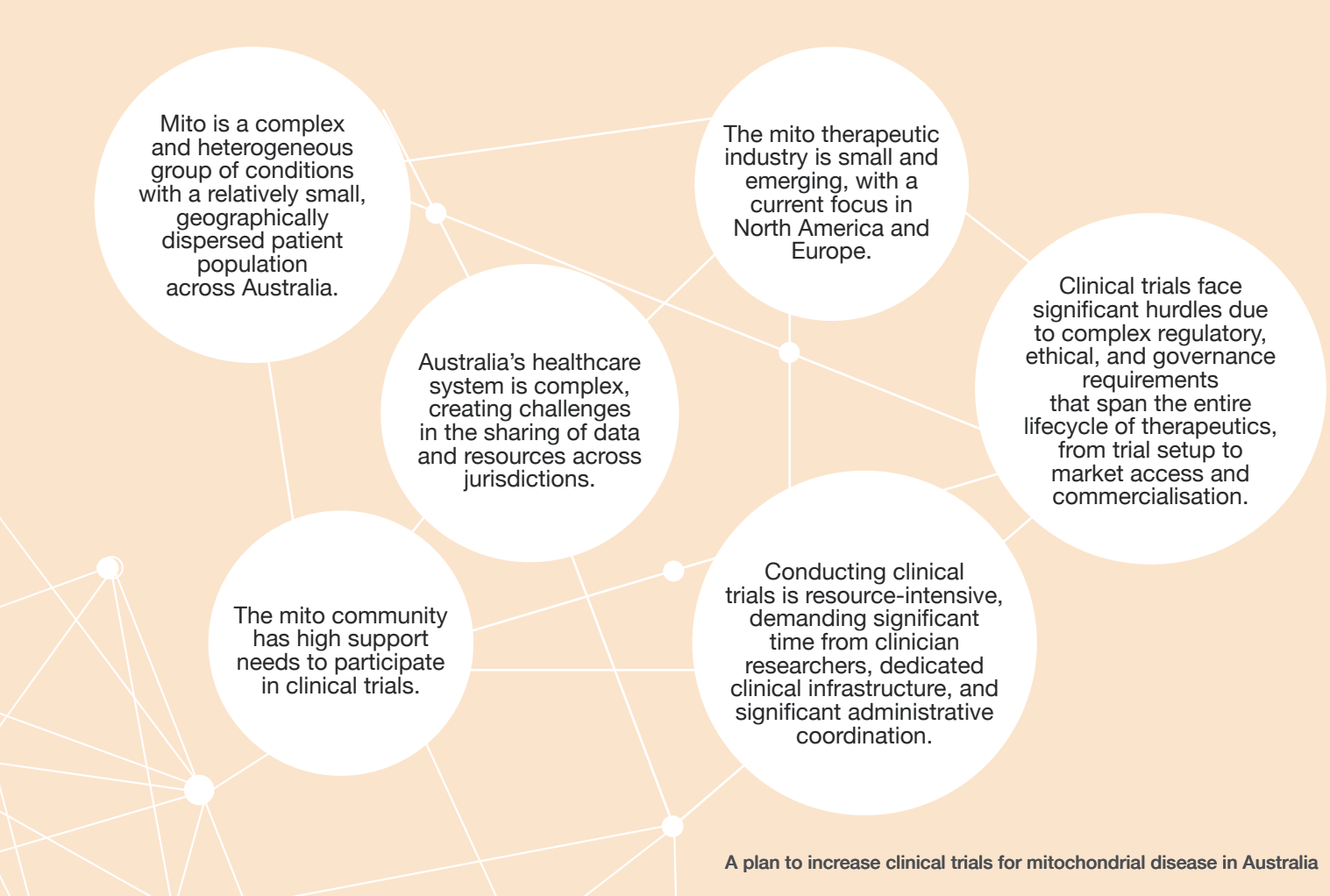
Building on the success in driving clinical trial activity for other rare diseases, such as Duchenne muscular dystrophy, spinal muscular atrophy, and inherited retinal diseases, will help to ensure Australians with mito can access the very latest treatments locally as part of their care.

The Australian government has demonstrated commitment to clinical trials. Recent announcements towards a national clinical trial "one-stop-shop" provide an opportunity for advancing equity in rare disease clinical trial access, and in positioning Australia as a global preferred site for rare disease trials.[11] It is important that mito is prioritised within this to align with the global uptake in mito treatment development.

Increasing clinical trial activity is a complex, interconnected challenge

The current level of clinical trial activity for mito in Australia is the result of multiple, longstanding, and interdependent factors. While some challenges are systemic — affecting rare diseases both nationally and globally — others are more specific to mito. Patient organisations — including Mito Foundation — and the mito clinical community have been working to address these for many years. Further progress will require coordinated efforts across several fronts. Challenges can be broadly categorised into the below areas, with detailed insights and potential solutions outlined in the action plan.

This plan responds to insights gathered on barriers, enablers, and opportunities to increase clinical trial activity for mito in Australia. It sets out a range of key actions for Mito Foundation and others to progress.



> Australia has a wonderful patient advocacy group that understands the challenges and has access to patients… Regulatory and IRB [Institutional Review Board] interactions have been very positive.
>
> — Industry representative

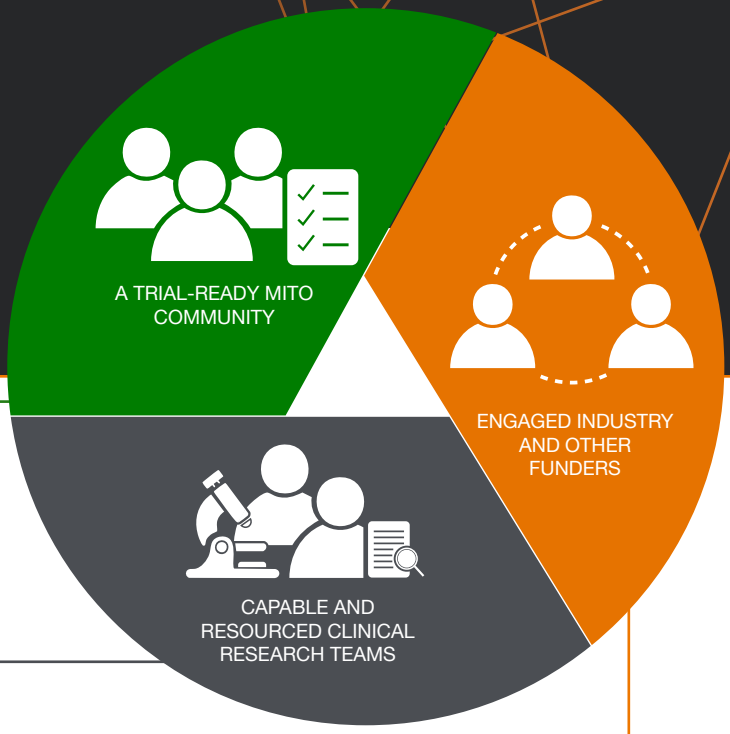
Opportunity across the wider region

Australia is a leader in clinical trials within the Asia Pacific region and commonly considered alongside New Zealand as a potential site for international clinical trials. Initially, this project set out to be inclusive of New Zealand. Due to limited engagement from New Zealand stakeholders, including clinician researchers and mito community members, the scope was revised to focus on Australia.

Many of the actions in this plan are relevant to the wider region, including New Zealand. Mito Foundation is committed to improving outcomes for the global mito community and will consider partnerships beyond Australia in the implementation of this plan.

THE ACTION PLAN
VISION

Australia is a global leader in clinical trials for mito, with an efficient, collaborative, and sustainable ecosystem that meets the needs of the mito community, clinicians, researchers, industry and other funders.



A trial-ready mito community

Accessible participation:
Individuals with mito have equitable access to clinical trials through effective recruitment, transparent communication, as well as practical and psychosocial support. Clinical trials are considered part of a range of management options for mito.

Empowered involvement:
Mito community members are knowledgeable about clinical trials. The design, implementation, and evaluation of clinical trials involves the mito community. Because of this involvement, there is low attrition of patients in Australian clinical trials.

Improved outcomes:
Clinical trials address real-world patient needs, leading to therapies that improve quality of life and long-term care.

Capable and resourced clinical research teams

Infrastructure and support:
Clinician researchers have access to administrative support, clinical infrastructure, and can access pooled resources to enable them to take part in and lead clinical trials.

Collaborative networks:
Robust mito clinical trial networks to share expertise, referrals, resources, and innovative methodologies.

Research capacity:
Positions that include dedicated time for clinical research and career development opportunities for clinician researchers to ensure long-term sustainability.

Engaged industry and other funders

Streamlined processes:
Simplified and harmonised regulatory and ethical requirements to accelerate trial setup and safe implementation.

Strategic partnerships:
Strong collaborations with patient organisations and local institutions to enhance recruitment and trial success.

Sustainable investment:
A commercially favourable environment with robust infrastructure, comprehensive data, and a highly skilled workforce to attract and retain industry sponsors. Growing investments by philanthropic and Government funders to complement research by industry.

THE PLAN

PRIORITY AREAS AND ACTIONS

1 Building clinical research capacity

Actions to ensure that clinician researchers are motivated, empowered and resourced to lead clinical trials

2 Supporting the mito community to participate in clinical trials

Actions to create a clinical trial-ready mito community and to ensure participants are well supported during and after trials.

3 Strengthening collaboration

Actions to enhance connections and partnerships, including between the mito community, health professionals and industry.

CONTRIBUTING WORK

Enhancing data infrastructure, including patient registries to support participant recruitment.

Preparing for the future through proactive work towards registration and reimbursement in Australia.

Continuing work beyond industry-led trials, such as investigator-led trials, outcome measures, and translational research.

Advocating for long-term improvements through policy change.

PRIORITY AREA 1
Building clinical research capacity

ACTIONS

Actions to ensure that clinician researchers are engaged, empowered, and resourced to lead clinical trials:

Actions	Involved stakeholders
Define and expand clinical trial sites for mito Build on the work of this project to define requirements for a new mito clinical trial site. These requirements could include the health disciplines required, recruitment processes, patient support, and remote participation. Establish a structured process for regularly reviewing mito clinical trial sites against these requirements. Use these reviews as the focus of practice sharing between sites and to identify system gaps, inform future investment priorities, and enhance national clinical trial capability.	Mito Foundation Clinician researchers
Fund practical support for clinician researchers Create a targeted call for projects that increase clinical trial capacity in Australia. Projects funded could include salary support for trial coordination, provided there is a plan for sustainable outcomes beyond the project.	Mito Foundation Clinician researchers Government
Expand the national coordinator model* Evaluate the use of a single coordinator to support multiple Australian sites in the Leigh Syndrome Natural History Study.[12] Based on these results, consider the role of this model for clinical trials for mito in Australia.	Mito Foundation Clinician researchers
Fund trial setup and salary costs Ensure funding agreements for clinical trial sites support team salaries and cover trial establishment costs, rather than relying on conventional fee-per-enrolment funding arrangements.	Industry
Include research in clinical roles Provide clinician researchers with resources to support reduced clinical loads through dedicated paid research hours, administrative staffing support, dedicated trial coordinators, and access to capacity-building programs to enable active participation in trials.	Health services Government
Include clinical trial experience in training pathways Invest in training for health professionals, especially early and mid-career clinician researchers, to build skills to lead and participate in trials. Consider initiatives that involve junior clinicians in trials through mentorship and shadowing.	Health services Government
Fund mito clinical fellowships* Support clinical research involvement of mito clinicians by continuing to offer annual clinical fellowships. These should focus on clinical research experiences and capacity building and be targeted to specialties and/or geographies to address known gaps. Explore co-funding or part-funding opportunities to increase the number of fellowships available in the future.	Mito Foundation Clinician researchers Health services
Strengthen centres of expertise Strengthen centres of expertise for mito by diversifying expertise, fostering cross-jurisdictional collaboration, and integrating multidisciplinary care. These centres are ideal candidates for becoming clinical trial sites. Sustainable funding models are required to support these centres.	Health services Government Clinician researchers
Develop a National Health and Medical Research Workforce Plan[13] The Australian Government, in collaboration with the states and territories, should aim to boost the clinical research workforce, such as through the integration of clinical practice and research training and implementing the recommendations in the National Strategy for Australia's Rare Metabolic Disease Workforce.[14]	Government

*Actions are already underway.

Building clinical research capacity

SUCCESS INDICATORS

An increasing number of engaged mito clinician researchers Our goal is to have at least one engaged clinician researcher in each major state (VIC, NSW, QLD, SA, WA) in each priority specialty for mito trials (neurology, metabolics, and ophthalmology) with demonstrated capacity to conduct trials as a part of their workload.

Early and mid-career clinicians working in mito are regularly involved in clinical research Our goal is that each mito clinician has opportunities to participate in both clinical trials and other types of clinical research, creating a pipeline of future clinician researchers.

Building clinical research capacity

KEY FINDINGS

Key findings from consultation and a literature review that have informed the development of these actions:

Clinical research capacity is required in a diverse range of medical specialties to meet predicted demands for future clinical trials for mito.
Recent clinical trials for mito have been led by neurologists and ophthalmologists and it is likely that future trials may also be led by metabolic specialists. This action plan focuses on these high-priority specialties.

Local site investigators are essential for industry-led trials.
Having qualified investigators in Australia, ideally already connected to mito community members who may be eligible for participation, is a key factor when industry considers global sites for clinical trials. Local investigators also play a gatekeeper role, assessing preclinical data for therapeutic options as a part of their decision to take part.

There is an opportunity to build on Australia's strong mito clinical research foundation by supporting clinician researchers.
Australia has a solid base of clinicians engaged in clinical research, with varying levels of involvement in mito research. Several factors influence clinicians' decisions to be involved in clinical trials, including limited financial and institutional support for studying rare diseases. Similarly, clinical decisions to recommend clinical trials are influenced by time constraints for supporting families and limited awareness of existing trials.

Work in other rare diseases suggests that stronger incentives are required to support and retain clinician researchers, including increased funding, improved job security, and better integration of research into clinical practice. Jointly funded clinician researcher positions with dedicated research time, clearer career pathways for clinical trial staff, and recognition of research within hospital performance metrics could help build a more sustainable clinical trial workforce.

Current funding models make it challenging to have capacity available when it is needed.
Mito specialists often work in public hospital services with heavy clinical workloads. Many have limited or no time dedicated to research, and limited funding and other resources to support their involvement in clinical trials. Industry-led trials are often funded on a per-patient-enrolled basis, meaning no initial funding is available for feasibility, site setup and pre-screening activities.

Limited government funding, minimal financial incentives, and regulatory hurdles deter industry from investing in trials for less prevalent diseases. Interventions, such as strategic funding for international trials, programs to support clinician researchers, and mutually beneficial partnerships, could improve funding availability.

Building clinical research capacity

Improving health care and increasing clinical research are interdependent.
Patient-centred trials for mito will be enabled through the leadership of teams already providing care for mito community members. These teams bring a deep understanding of mito and trusted relationships with mito community members. This approach may also support better integration of clinical trial participation with other health care interactions. Efforts to improve health care are likely to improve clinical research capability. Clinical trial activity in these teams will strengthen health care for mito beyond the care provided to clinical trial participants.

Workforce education and training are essential to build teams and trial staff with global standing.
The lack of standardised training opportunities for clinical trial oversight may contribute to variation in skill sets, while the shortage of trained clinician researchers limits the feasibility of clinical trials, particularly investigator-led trials.

Potential solutions include embedding research into clinical roles, establishing joint clinician researcher positions, and fostering partnerships between health services and research institutes and/or universities to build workforce capability. Providing mentorship, ongoing site training, and integrating clinical research into hospital accreditation and performance indicators can further strengthen trial leadership and participation. Expanding training to include research nurses and multidisciplinary team members can enhance overall trial readiness. A nationally coordinated Clinician Researcher Workforce Strategy was suggested as a mechanism to provide the necessary framework to support these efforts.

> “There is funding for industry-sponsored trials but the first payment is often provided once you have received ethics approval. This can take a number of months of planning to get to that stage. Payments are made to the site on a per participant per visit basis, which does not adequately cover the time required for planning and scheduling assessments in between the visits and is challenging to manage in terms of staffing.”
>
> — Member of a clinical trial team

PRIORITY AREA 2
Supporting the mito community to participate in clinical trials

ACTIONS

Actions to enhance connections and partnerships between the mito community, professional organisations, industry, and regulators.

Actions	Involved stakeholders
Increase clinical trial readiness in the mito community Mito Foundation will create a new clinical trial education initiative to encourage mito community members to prepare for clinical trial participation. This may include having a conversation about trials with their mito specialist, obtaining a genetic diagnosis, and joining Mito Foundation's Mito Registry. This work should build on work done by others and on the findings of the consultation done as part of this project. This initiative will aim to reach community members who are not in regular contact with Mito Foundation, including by working with mito clinicians.	Mito Foundation Clinician researchers
Encourage people with a diagnosis to connect to Mito Foundation and mito specialist centres Health professionals should encourage people with a diagnosis of mito to connect to Mito Foundation to learn about clinical trials and consider joining the Mito Registry. Health professionals providing care outside of mito specialist centres should ensure their patients are connected to a mito specialist centre to facilitate future clinical trial participation.	Clinician researchers Health services
Grow and strengthen the Mito Registry Mito Foundation will improve how genetic diagnosis information is managed in the current Mito Registry. Mito Foundation will partner with key mito health services to increase the number of participants in the registry.	Mito Foundation Clinician researchers
Ensure current support services are clinical trial-ready Mito Foundation will strengthen its existing support services by providing targeted training to equip the team with the skills and knowledge needed to assist mito community members participating in and considering clinical trials.	Mito Foundation
Develop a dedicated clinical trials-focused support service Mito Foundation will explore funding a dedicated role with appropriate clinical expertise to provide formal psychosocial and referral support, enhancing the resources available to Australians involved in clinical trials. This could be a service delivered in collaboration with clinical trial sponsors.	Mito Foundation Industry
Ensure sufficient funding and practical support for trial participants Ensure that sufficient funding and practical support are provided to trial participants to support participation from a wide geographic area.	Industry Clinician researchers
Integrate mental health and psychosocial support into trial protocols Integrate mental health and psychosocial support into trial protocols to help patients and families navigate risks and burdens.	Industry Clinician researchers
Consider how mito clinical trial protocols can support teletrials Consider how mito clinical trial protocols can support teletrials, home visits and other measures to reduce the burden of participation. Seek to collaborate with and learn from established programs such as the Australian Teletrial Program.	Industry Clinician researchers
Ensure new therapies are not a barrier to receiving disability supports Mito Foundation will work with the National Disability Insurance Agency to ensure that emerging therapies for mito and/or clinical trial participation do not become a barrier to accessing disability related supports.	Government Mito Foundation

Supporting the mito community to participate in clinical trials

SUCCESS INDICATORS

Improvements in key mito community measurements
Our goals

- Increasing engagement with Mito Foundation resources and education materials regarding clinical trials
- Increasing knowledge and confidence regarding clinical trials
- An uptake in community members receiving information from their health care teams on trials and trial opportunities
- Positive experiences reported by community members who have participated in trials

Improvements in Mito Foundation's Mito Registry
Our goal is an expanded Mito Registry that improves recruitment success and trial relevance.

Our goals

- Increasing the number of participants enrolled in the registry, from 500 to 1000, by 2030
- Increasing proportion of registry participants with a genetic diagnosis
- High data accuracy and consistency
- High community confidence in the usefulness of the Mito Registry

Integrated psychosocial support included in trials
Our goal is an increasing proportion of Australian industry and investigator-led clinical trials include dedicated psychosocial supports.

High retention rates for Australian mito clinical trials
Our goal is that a lack of practical, psychosocial, or other supports is not a reason for Australian participants to leave a mito clinical trial. We will measure this through qualitative data collection from the mito community and through working with clinician researchers to understand factors influencing retention.

Supporting the mito community to participate in clinical trials

KEY FINDINGS

Key findings from consultation and literature review that have informed the development of these actions:

Awareness of clinical trials for mito and related conditions varies
Patient organisations, including Mito Foundation, and health care teams are key sources of information for the mito community. This information could include details about clinical trials and patient registries. Lack of referrals to clinical trials by health care teams is a significant barrier to recruitment. Potential solutions include establishing robust referral networks at site, clinician and institution levels, which could be supported by third-party recruitment tools such as referral apps, patient registries and service providers.

There is a strong interest amongst the Australian mito community in participating in clinical trials
This is consistent despite varied awareness and previous involvement. The most common motivators were improving the quality of life for the broader mito community, gaining knowledge about mito, and accessing better treatments.

Attendees of the 2024 Mito Community Summit also demonstrated significant interest in collaborating with Mito Foundation, industry, and researchers to make clinical trials successful in Australia.

Australia's strength in mito diagnosis, particularly genetic testing, offers an opportunity to improve the mito community's trial readiness
Australia is a leader in the diagnosis of mito, particularly in the access to genetic testing. As genetic diagnosis is a key eligibility criterion for clinical trials, encouraging greater uptake of testing would help the mito community become more trial-ready.

Mito specialists are confident in their ability to recruit patients to relevant trials, but geographic barriers remain
Current literature suggests that the relationship between a patient and their clinician is the strongest determinant of clinical trial participation. Patient engagement is also closely linked to clinician expertise. Insights from the community workshop reinforced this finding, with many attendees preferring to receive trial information from their health care teams.

Our consultation found that mito specialists are generally confident in recruiting patients from their existing cohorts. However, geographic distribution remains a significant barrier in recruitment. Access to trials often depends on location, with rural and remote mito community members facing substantial financial and logistical challenges. Even in urban areas, recruitment can be hindered by factors such as population diversity, high mobility, and long travel or wait times.

Potential solutions include financial reimbursement, transport support, and improved access through teletrials to enable participation. Additionally, attendees of the 2024 Mito Community Summit suggested minimising travel burden by reducing the number of visits required for a trial wherever possible.

Supporting the mito community to participate in clinical trials

Improved education and support can improve trial participation and retention
Our consultation highlighted the main education and support barriers to clinical trial participation, including a lack of easy-to-understand information, concerns about potential risks and side effects, and trust issues with industry. Community members suggested that more accessible and proactive communication is needed to help mito community members learn about trials. They also emphasised the need for support particularly when making a decision on whether to participate in a trial and throughout the trial. Consultation with another rare disease community highlighted the valuable role that patient organisations can play in supporting members of the community as they decide whether to participate in a specific trial, adapt when clinical trials fail, and manage gaps in access to effective therapies after a clinical trial finishes.

Outward communications need to be proactive yet proportional
There is a risk that actions to educate the mito community about clinical trials could inadvertently create false hope. For example, hope that a specific person with mito will be eligible for a specific trial, or that a specific therapy will be effective. Communication and education initiatives need to be designed with this risk in mind.

Work with other rare disease organisations also highlighted a risk that increasing access to therapies for mito through clinical trials may inadvertently create a new barrier to mito community members receiving disability supports. If a decision maker within the National Disability Insurance Scheme (NDIS) believes that there are treatment options that a mito community member has not yet accessed, this may delay or stop that person from accessing support through the NDIS.

> “In my experience, patient engagement has been extremely high even for very intensive and invasive clinical trials as there is no other option for families. They are usually aware of a trial before the clinician through patient support groups or industry websites. Mito Foundation could keep patients engaged by having a list of active clinical trials in Australia on their website and contact details of the team.”
>
> — Member of a clinical trial team

PRIORITY AREA 3
Strengthening collaboration

ACTIONS

Actions to enhance connections and partnerships between the mito community, professional organisations, industry, and regulators.

Actions	Involved stakeholders
Create a mito clinical trials taskforce This small group will guide the implementation of this plan and foster collaboration between industry, clinician researchers, and the mito community.	Mito Foundation Clinician researchers Industry
Be the Australian 'front door' for mito clinical trials* Building on its current role, Mito Foundation will maintain a directory of trial sites across all states, improving visibility and access for both prospective sponsors and patients. Mito Foundation will also build on existing efforts to engage the Australian mito community in influencing the design of clinical trials, including through facilitating direct involvement with industry earlier in the clinical trial planning process.	Mito Foundation
Actively encourage global industry organisations to consider Australia as a mito clinical trial location* Mito Foundation will continue its horizon scanning to identify emerging therapeutics and build connections with industry organisations planning mito clinical trials. This work will include attending key mitochondrial medicine conferences and maintaining key information about clinical trials for mito in Australia. This will support Mito Foundation's role as the Australian 'front door' for mito clinical trials.	Mito Foundation
Promote mito research knowledge and activities Promote collaboration through research dissemination and promotion of mito as a disease area of heightened clinical trial activity and research opportunity. Strengthen networks between mito clinician researchers through conference activities, supporting mentor-mentee relationships, and other networking and collaboration opportunities. Work with existing professional societies for priority mito specialties. Stronger connections among researchers will enhance coordination, knowledge sharing, and clinical trial capacity.	Clinician researchers Mito Foundation Other
Collaborate through a formal clinical trial network Formalise a clinical trial network (CTN) of clinician researchers. This network should foster partnerships between patient organisations, peak bodies, professional organisations, and industry to align priorities and resources.	Mito Foundation Clinician researchers Industry
Offer one-off collaboration and career development funding Mito Foundation will establish a travel scholarship program supporting clinician researchers to grow their connections and learn new clinical skills through attending international mito conferences, visiting clinical sites and other activities. Scholarships should be available to nursing and allied health professionals who have less access to funding. This aims to strengthen Australia's profile in mito research, promote collaboration, and help to disseminate mito research in Australia.	Mito Foundation

Strengthening collaboration

SUCCESS INDICATORS

Increasing collaboration involving clinicians researchers
All clinician researchers engaged in mito clinical trials are connected formally to a CTN with regular opportunities to engage and collaborate with other mito clinician researchers.

An increasing number of mito clinician researchers work in partnership with a unit or team with experience in running clinical trials.

Increasing collaboration involving industry
Increase in the proportion of industry-led clinical trials that actively consider Australia as a site.

Engagement with industry organisations working on mito therapeutics shows favourable attitudes towards Australia as a trial location.

Strengthening collaboration

KEY FINDINGS

Key findings from consultation and literature review that have informed the development of these actions:

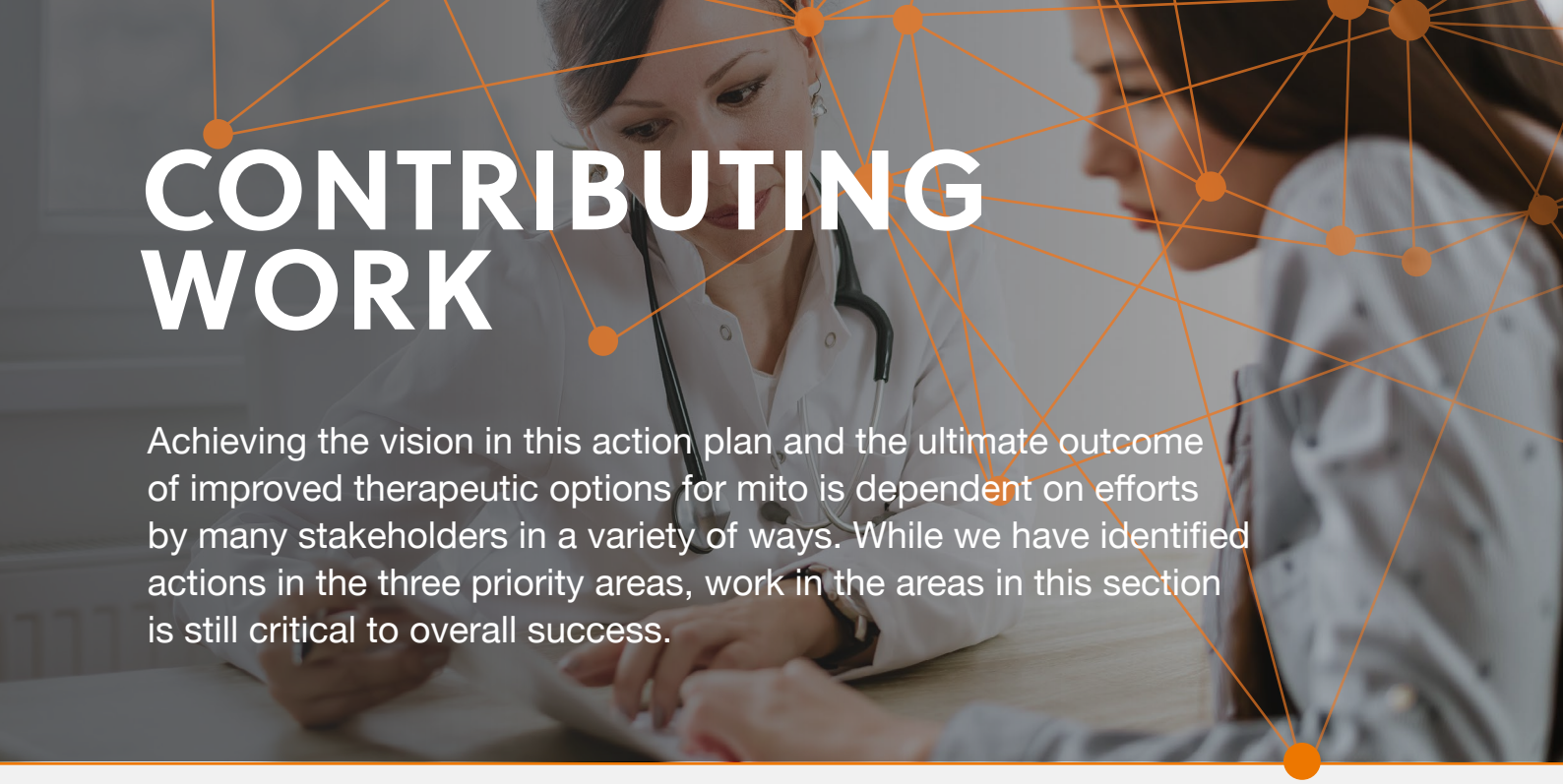
There is interest in increasing collaborations to support clinical trials for mito.
Our consultation suggests that there is interest from all stakeholder groups, particularly clinician researchers, in more collaboration. This includes stronger connections between clinician researchers, patient organisations, and industry.

Informal networks of Australian mito clinician researchers have developed through clinical research projects.
Previous clinical studies have strengthened connections between clinician researchers with an interest in mito. The pilot program for mitochondrial donation and the Leigh Syndrome Natural History Study are further expanding and strengthening these networks. While some of these projects have specifically aimed to establish a sustainable CTN, a single CTN that is inclusive of all Australian mito clinician researchers does not currently exist.

CTNs and other collaborations are a recognised enabler of clinical trials.
Our literature review identified that CTNs have been used to improve trial design and quality, enhance recruitment, facilitate multi-centre trials, foster knowledge sharing, and develop reusable infrastructure. National networks of centres of clinical expertise are recognised to have benefits beyond clinical trials, such as influencing broader medical research, professional development and routine health care and care coordination. The review also highlighted the role of partnerships between health services and Australian universities to improve education and training pathways for clinician researchers.

Sites in industry-led trials are influenced by both relationships and the prominence of key investigators.
In the process of considering locations for clinical trials, industry organisations start with their existing networks. This includes mito clinician researchers already known in the field and those connected to the clinicians already involved in developing therapies. We specifically heard that in-person attendance at key mito research meetings is a common enabler of these relationships. Mito Foundation is frequently contacted by industry for assistance in identifying possible clinical trial sites in Australia.

Partnerships between mito clinician researchers and experienced clinical trial units (CTUs) can help to overcome barriers to clinician participation in clinical trials.
Mito clinicians noted that working with CTUs, which handle trial operations, can allow them to focus solely on patient care. Our literature review highlighted that Australia's global competitiveness in phase I trials has been driven by specialised (phase I) CTUs with dedicated staffing, robust quality management, advanced IT systems, and streamlined regulatory processes. Leveraging these strengths for later-phase trials could enhance mito trial capacity while reducing the operational burden on researchers.



CONTRIBUTING WORK

Achieving the vision in this action plan and the ultimate outcome of improved therapeutic options for mito is dependent on efforts by many stakeholders in a variety of ways. While we have identified actions in the three priority areas, work in the areas in this section is still critical to overall success.

Enhancing data infrastructure, including patient registries, to support participant recruitment

KEY INSIGHTS

While patient registries are transformative enablers, there are significant challenges in realising their benefits.
Our literature review describes the potential for patient registries to support clinical trials and other types of research, such as improving knowledge about the natural history of a disease, and monitoring treatment use and outcomes. The review also collates many of the challenges, including sustainable funding, low patient numbers, and standards to enable data sharing.

It is likely that there will always be multiple patient registries for mito.
Currently, there are multiple international mito patient registries (such as the North American Mitochondrial Disease Consortium, GENOMIT, and mitoSHARE). Our stakeholder consultation suggested that few Australians are aware of these. There are also registries established for specific types of mito (such as the USA-based registry for PDCD[i] and Australian clinical registries for LHON[ii] and MELAS[iii]). It seems likely that, for the foreseeable future, multiple registries will operate for mito.

Data sharing and standardisation offer significant opportunities.
Our literature review highlights that efficient data linkages can boost clinical trial activity by improving accessibility and coordination. Key recommendations include establishing a national framework for trial documentation, mandating Australian New Zealand Clinical Trial Registry (ANZCTR) reporting, strengthening data integrity through good clinical practice, implementing internet-based registry designs, and leveraging high-quality databases like Orphanet. Integrating health data from My Health Record and Medicare could enhance trial feasibility and participant identification. Other findings suggest that patient organisation-led registries, which often achieve larger and more diverse cohorts, could be unified under umbrella organisations to drive national rare disease registries.

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i PDCD: Pyruvate dehydrogenase complex deficiency
ii LHON: Leber hereditary optic neuropathy
iii MELAS: Mitochondrial encephalomyopathy, Lactic acidosis, and stroke-like episodes

WORK THAT WILL CONTRIBUTE TO THE VISION

The Australian Government must support efforts towards a national approach to rare disease registries.

Health systems and government agencies must continue work to develop systems and frameworks for consistent, high-quality health data collection and sharing across sites and between jurisdictions.

The international mito community must continue collaborative efforts on patient registries, including standardising data models and supporting data sharing.

MITO FOUNDATION'S COMMITMENT

Mito Foundation will actively track global developments, including patient registries, natural history and prevalence studies for mito and other rare diseases. This will complement work to strengthen the current Mito Registry. Ongoing monitoring will inform a future strategy for establishing a high-fidelity, genetics-enabled national registry (or a network of registries) designed to improve patient identification, strengthen recruitment confidence, and attract industry investment.

Continuing work beyond industry-led trials, such as investigator-led trials, outcome measures and translational research

KEY INSIGHTS

Investigator-led studies can play an important role in therapeutic development and equitable access for the mito community.
Research that is not sponsored by industry can play an important role in evaluating and providing access to low-cost therapies for mito. These include repurposed medicines, dietary supplements, and exercise interventions. Investigator-led studies could also provide access to innovative therapies for mito patients that have not been prioritised in industry-led trials. Mito Foundation's horizon scan identified 10 investigator-led clinical trials for mito, with no Australian involvement. Successful implementation of this plan will lead to increased clinician research capacity, mito community readiness, and collaboration. These outcomes will also support non-industry-led trials.

Continued progress in genetic diagnosis is an enabler of clinical trials.
Most trials for mito have required a confirmed genetic diagnosis of mito. Genetic diagnosis of mito is relatively accessible in Australia. Ongoing work on detecting early symptoms of mito and increasing the diagnostic yield of genetic testing and pre-symptomatic diagnosis, such as through newborn screening, will also increase the number of trial-ready mito community members.

Other types of mito research play an important role.
Therapeutic development is enabled by discoveries made through discovery research into mitochondrial biology and the mechanisms of disease. Natural history studies will help to identify intervention windows, support outcome comparison between treatment and non-treatment groups, and inform decisions on future registration and reimbursement. Long-term efforts to develop and validate outcome measures, including clinical assessment tools and patient-reported outcome measures, may also contribute to clinical trials.

WORK THAT WILL CONTRIBUTE TO THE VISION

Governments and philanthropists need to support investigator-led studies, including Australian participation in international investigator-led projects.

There are particular opportunities for studies exploring low-cost interventions, including repurposed medicines, supplements, and dietary and exercise interventions.

Researchers must continue work to improve genetic diagnosis, including through discovering and validating new genes and using newer technologies like proteomics, RNA sequencing, and other advanced techniques.

Health systems must prioritise translating innovations in genetic diagnosis into clinical practice, including expanding current funding for genetic testing for mito. These decisions should consider the benefits of clinical trial participation that a genetic diagnosis can enable.

MITO FOUNDATION'S COMMITMENT

Mito Foundation will support this by funding research and tracking international projects to identify opportunities for Australian involvement.

There is a role for Mito Foundation to continue its support of these types of research and encourage others to also support this work.

Preparing for the future through proactive work towards registration and reimbursement in Australia

KEY INSIGHTS

Industry stakeholders highlighted market access as a critical factor in determining whether Australia is considered a viable location for clinical trials.
For industry, commercialisation pathways — including regulatory approval and government subsidy of successful therapeutics — are key incentives for investing in clinical trials. Ensuring that domestic clinical trial data is integrated into health technology assessment (HTA) processes strengthens the case for reimbursement and therefore enhances Australia's attractiveness as a trial site. Industry views on Australia's ability to commercialise therapeutics remain mixed, with some uncertainty about whether government subsidy pathways offer sufficient incentive for the significant investment associated with establishing clinical trial sites here.

Australia's HTA system is undergoing major reform, presenting an opportunity to improve the assessment of rare disease therapeutics.
The current HTA review aims to enhance the timeliness, transparency, and flexibility of HTA processes, which is particularly relevant for small patient populations like mito, where traditional evidence requirements can pose barriers to registration and reimbursement. Adaptive approaches, such as the use of real-world evidence, patient-reported outcome measures, and surrogate endpoints, will be critical to ensuring rare disease treatments can be more effectively assessed.

WORK THAT WILL CONTRIBUTE TO THE VISION

HTA reform must consider the needs of rare diseases to ensure that mito therapeutics are considered in policy discussions and decision-making. The 2024 HTA Policy and Methods Review contained several recommendations that should be implemented by the Australian Government to ensure that rare disease therapeutics in areas of high unmet need are prioritised in future HTA processes. These include:

- Establish a unified HTA pathway and committee approach for all Australian Government funding of health technologies.
- Reduce time to access life-saving drugs for patients with ultra-rare diseases through the Life Saving Drugs Program.
- Develop a comprehensive approach to identify therapeutic areas of high unmet clinical need and support the introduction of health technologies addressing these needs. This includes proactive pre-HTA processes and prioritising therapies with high therapeutic value for the Pharmaceutical Benefits Scheme listing.
- Enhance methods for assessing consumer evidence to ensure patient perspectives are integral to HTA evaluations, leading to more patient-centred outcomes.

MITO FOUNDATION'S COMMITMENT

Mito Foundation will continue to build its capacity to contribute to HTA processes for mito health technologies. This will build on previous work, including involvement in Medicare listing decisions (e.g. funding of genetic tests for mito),[15] other mito community driven campaigns (e.g. the successful mitochondrial donation legislative change campaign),[16] and qualitative research capabilities (e.g. the Mito Stories Project).[17]

As successful clinical trials complete, Mito Foundation will encourage and work with industry to pursue registration and reimbursement in Australia.

Mito Foundation will also actively monitor and contribute to HTA reform to ensure that mito therapeutics are considered in policy discussions and decision-making.

Long term improvements through policy change

KEY INSIGHTS

Mito Foundation plays a critical role in advocating for systemic change and reform to enable and incentivise clinical trial activity in Australia.
Stakeholders highlighted the value of patient organisations in mobilising patient communities, creating a collective voice for change, and engaging with governments to support and incentivise clinical trials. Mito Foundation has demonstrated success in shaping legislative change, most notably in advocating to allow mitochondrial donation by highlighting the needs of the mito community. Mito Foundation has a highly engaged community and strong internal expertise in policy, advocacy, and research.

It is essential that Australia's clinical trial and health research policies explicitly consider the needs of rare diseases.
Australia is at a pivotal moment to strengthen its clinical trial ecosystem and establish itself as a global leader in trial activity. The national "One Stop Shop" for clinical trials,[11] currently in development, represents a key opportunity to streamline trial processes and reduce barriers to set up. It is critical that rare diseases like mito are prioritised in the design and implementation of this initiative.

Beyond the "One Stop Shop," several ongoing policy reforms present further opportunities to advocate for systemic change, including:

- Efforts to increase consistency between different Human Research Ethics Committees to reduce variation in practice and facilitate easier multi-site approval processes.
- The National Health and Medical Research Strategy, which will shape the future direction of research funding and infrastructure.
- Health Technology Assessment reform, which could improve market access, and therefore incentivise industry to consider Australia for trial sites based on the likelihood of eventual government subsidy.
- The Medical Research Future Fund (MRFF) 10-year Investment Plan, which now consolidates rare cancers, rare diseases, and unmet clinical needs under the Clinical Trials Activity initiative.

WORK THAT WILL CONTRIBUTE TO THE VISION

Ongoing policy reform by the Australian Government, along with states and territories, particularly:

- Increased support and investment in the clinical workforce to participate in research.[18]
- Health data reform to facilitate data sharing to improve patient identification and trial recruitment.
- Regulatory reforms to streamline trial establishment and approval processes.
- Improved market access pathways, particularly for patients with high unmet needs, to ensure clinical trial outcomes translate into real-world treatment options.
- Financial incentives and funding for international clinical trials to consider Australian sites in rare disease trials.[7]

MITO FOUNDATION'S COMMITMENT

Mito Foundation will continue to make clinical trials and clinical research key priorities in its systemic advocacy work. Activities will include engaging in government consultations on policy reforms, collaborating with other organisations representing rare diseases to strengthen advocacy efforts, and monitoring the policy landscape to identify emerging opportunities for reform.

IMPLEMENTATION AND NEXT STEPS

TIMEFRAMES

This clinical trials action plan is designed as a 10-year vision of activity required to increase clinical trial activity for mito in Australia.

ROLES AND RESPONSIBILITIES

Mito Foundation
Consultation highlighted the essential role of Mito Foundation as a patient organisation. Its current contributions include direct research funding, advocacy, mito community engagement, providing support to mito community members, and the dissemination of resources and information to patients and families. Mito Foundation has opportunities to expand its impact by providing direct support to researchers, fostering greater collaboration, collecting and leveraging mito community insights to drive advocacy and change, and working collaboratively to enhance data quality and accessibility.

Collective ownership of actions
The action plan is designed to provide the entire sector, including the research community, industry, patient organisations, the mito community, and government(s), a collectively owned blueprint towards increased mito clinical trial activity.

MONITORING PROGRESS AND MEASURING SUCCESS

Monitoring the progress of the action plan against its objectives is critical to ensuring its effectiveness. As policies, practices, and global conditions evolve, the plan may need to be adjusted, funding or focus reallocated, or strategies adapted to meet new needs.

Continued regular horizon scanning will identify emerging therapeutics and clinical trial opportunities. Appendix 4 lists the key metrics the Mito Foundation will gather through engagement with the community, researchers, and industry. These metrics will help measure the success of the action plan in achieving its objective of increasing clinical trial activity.

This ongoing benchmarking and reporting process will use the evaluation metrics outlined in the action plan to track key success indicators, measure progress, and identify challenges and opportunities.

WHERE TO FROM HERE

Realising our vision of Australia as a global leader in mito clinical trials will require sustained commitment across research, industry, and government. The actions outlined in this plan provide a roadmap to strengthening clinical research capacity, improving trial accessibility, and fostering collaboration. This will help to ensure clinical trials deliver meaningful outcomes for people living with mito. Our sense of urgency to take action is fuelled by a rapidly advancing global pipeline of mito therapeutics, offering new hope to the mito community. This presents Australia with a critical opportunity to lead and shape the future of mito clinical trials.

Investment and financial support are essential to advancing this work. Government support will play an important role. Philanthropic contributions will be crucial to bridging gaps where government and industry funding alone are insufficient. Strategic investment can accelerate progress, support clinician researchers, enhance patient engagement, and ensure the sustainability of initiatives.

Mito Foundation remains committed to its advocacy, working to remove systemic barriers and readying the Australian mito community for trial participation. It is also committed to funding clinical research directly, and tracking and responding to global progress in mito therapeutic development. We will use regular benchmarking, and reporting on the success indicators in this plan will ensure accountability, drive continuous improvement, and position Australia at the forefront of mito research.

Through collaboration across research, industry, and the mito community, we can build a future where clinical trials are not only possible but become a recognised tool to deliver life-changing advancements to those affected by mito. We invite our partners to join us in making this vision a reality.

Abbreviations and glossary

Term	Explanation
Centres of expertise	Specialised healthcare facilities with expertise in diagnosing, managing, and researching rare or complex diseases, often serving as referral hubs and contributing to clinical research and trials. **Alternative terms:** Centres of excellence, specialist clinics.
Mitochondrial donation	An assisted reproductive technology that allows women with mitochondrial DNA mutations to have biological children without transmitting the disease, by using healthy mitochondria from a donor egg. Mito Foundation led the campaign to legalise mitochondrial donation in Australia.
Clinical assessment tools	Standardised instruments or tests used to evaluate a patient's health status, symptoms, or functional abilities, often employed in clinical trials and routine health care. **Alternative terms:** Clinical outcome assessments, diagnostic tools.
Clinical study	Research involving human participants, aimed at gaining knowledge about health, diseases, or medical treatments. These include observational (no intervention) or interventional (involving specific medical interventions like drugs, devices, or therapies). **Alternative terms:** Medical study, clinical research study.
Clinical trial	A specific type of clinical study focused on testing the safety, efficacy, or effectiveness of a medical intervention, such as a drug, device, or procedure. Clinical trials are interventional studies and often follow strict protocols in phases (e.g., Phase I-IV). **Alternative terms:** Drug trial, intervention trial, therapeutic trial.
Clinical trial network (CTN)	A collaborative group of research centres, healthcare providers, and/or institutions that work together to conduct clinical trials. These networks aim to streamline the process of designing, conducting, and analysing clinical trials, often across multiple sites, to increase efficiency and improve the quality of data collected. Clinical trial networks can focus on specific diseases or treatments, facilitating large-scale studies with broader participant pools. **Alternative terms:** Clinical research network, collaborative trial network.
Clinical trial readiness	The ability of a patient or patient community to participate in clinical trials, influenced by factors such as disease awareness, access to genetic testing, engagement with healthcare providers, and availability of trial sites. **Alternative terms:** Trial preparedness, patient trial eligibility.
Clinical trial units (CTUs)	Dedicated facilities or teams within hospitals, research institutions, or specialised centres that conduct and manage clinical trials, ensuring regulatory compliance and patient safety. **Alternative terms:** Clinical research units, trial coordination centres.
Clinician researchers	Health professionals, often physicians or specialists, who also conduct medical research, including clinical trials and translational studies, to improve patient care. **Alternative terms:** Physician-scientists, clinical investigators.
Clinicians	Health professionals, such as doctors, nurses, and allied health practitioners, who diagnose, treat, and manage patient care. **Alternative terms:** Healthcare providers, medical practitioners.

Term	Explanation
Gene therapies	Gene therapies aim to correct genetic defects by introducing functional genes, often using viral vectors or techniques to modify mitochondrial DNA directly.
Genetic testing	The analysis of an individual's DNA to identify genetic mutations or variations associated with diseases, aiding in diagnosis, treatment selection, and risk assessment. **Alternative terms:** Genomic testing.
Health technology assessment (HTA)	A process that systematically evaluates the properties, effects, and impacts of health technologies to determine their value and inform decision-making in health care. In Australia, HTA is used as a part of decisions on which medicines are funded through the Pharmaceutical Benefits Scheme and which services are funded through Medicare.
Horizon scan	A systematic process of identifying and assessing emerging health technologies (such as diagnostic tools, treatments and medical devices).
Industry-led clinical trials	Companies involved in the research, development, manufacturing, and commercialisation of therapeutics. This publication uses this term to be inclusive of pharmaceutical companies and biotechnology companies. **Alternative terms:** Industry organisations, pharma, pharmaceutical industry, medicine companies, pharmaceutical companies, biopharmaceutical industry
Investigator-led clinical trials	Clinical studies initiated and managed by independent researchers, typically affiliated with academic or medical institutions. **Alternative terms:** Academic clinical trials, investigator-initiated studies
Mito	Mitochondrial disease, a group of genetic disorders that impair mitochondria, which are essential for producing energy in cells. **Alternative terms:** Primary mitochondrial disease.
Mito community	This term describes: • People impacted by mito, even if their diagnosis is uncertain or preliminary • People supporting people impacted by mito. This includes parents, spouses, other family members, and friends. We also include people who have supported someone who has since passed away. **Alternative terms:** Mito patients, consumers.
Mito Registry	Mito Foundation's contact registry of people with diagnosed or suspected mito. This registry collects general demographic data, contact information, and details about diagnosis.
Mito specialist centres	Clinics or healthcare facilities dedicated to the diagnosis, management, and treatment of mito. These centres may bring together a multidisciplinary team of specialists to provide care tailored to the needs of mito patients. **Alternative terms:** Mito clinics, centres of expertise, centres of excellence, specialist clinics.
Natural history studies	Observational research tracking the progression of a disease over time without intervention, helping to understand disease mechanisms and identify outcome measures for clinical trials. **Alternative terms:** Longitudinal studies, disease progression studies.

Term	Explanation
Outcome measures	Specific criteria or endpoints used in clinical trials and research to assess the effectiveness of treatments, often including patient-reported, functional, or biomarker-based measures. **Alternative terms:** Clinical endpoints, health outcomes.
Patient-centred	A health care and research approach that prioritises the needs, preferences, and experiences of patients in decision-making, care delivery, and study design. **Alternative terms:** Patient-focused, person-centred.
Patient organisations	Not-for-profit groups that advocate for and support individuals affected by a particular disease, often involved in research funding, policy influence, and patient education. **Alternative terms:** Patient advocacy groups, health consumer organisations, support organisations, advocacy groups.
Patient registry	A system specifically designed to collect and maintain information about patients with a particular disease and/or condition(s). Patient registries collect clinical and genetic data used for research, improving care, and facilitating clinical trial recruitment. **Alternative terms:** Disease registry, patient database.
Patient-reported outcome measures (PROMs)	These are tools used to collect information on patient's perceptions of their own health status, quality of life, and functional outcomes directly from the patients themselves.
Pharmaceutical Benefits Scheme (PBS)	The Pharmaceutical Benefits Scheme (PBS) is an Australian government program that subsidises the cost of a wide range of prescription medicines for eligible patients. Medications, medical products and medical devices listed on the PBS are reviewed for their clinical effectiveness, safety, and cost-effectiveness, with updates made regularly to include new treatments.
Preclinical data	Experimental findings from laboratory and animal studies used to evaluate the safety, efficacy, and mechanism of action of a potential therapy before human trials. **Alternative terms:** Non-clinical data, preclinical evidence.
Professional organisations	Associations or societies that represent and support professionals within a specific field, providing education, advocacy, networking opportunities, and guidelines for best practices. For mito in Australia, relevant professional organisations include the Australasian Society for Inborn Errors of Metabolism (ASIEM), Australian and New Zealand Association of Neurologists (ANZAN), and the Mito Medical Network. **Alternative terms:** Professional societies, industry associations, scientific associations.
Proteomics	The large-scale study of proteins, including their structure, function, and interactions, often used to identify disease biomarkers and therapeutic targets. **Alternative terms:** Protein analysis, systems biology.
Real-world evidence (RWE)	Data collected outside of controlled clinical trials, derived from routine health care settings, patient registries, electronic health records, or observational studies to assess treatment effectiveness and safety in diverse populations. **Alternative terms:** Real-world data, observational evidence.
Registration and reimbursement of health technologies	The process of obtaining regulatory approval for new medical treatments and securing funding or insurance coverage to ensure patient access. **Alternative terms:** Market access, Health technology assessment (HTA).

Term	Explanation
Researchers	Scientists conducting studies to expand medical knowledge, ranging from laboratory-based discovery science to clinical and translational research. **Alternative terms:** Biomedical scientists, research investigators
RNA sequencing	A laboratory technique used to measure and analyse RNA in a sample. It provides insights into which genes are active, how much they are expressed, and how they change in different conditions or diseases.
Small molecule therapies	Small molecule therapies use pharmacological agents to enhance mitochondrial function or improve energy production.
Surrogate endpoints	A biomarker or intermediate measure used in clinical trials as a substitute for a direct clinical outcome, helping to predict long-term treatment benefits more quickly. **Alternative terms:** Proxy endpoints, intermediate outcomes
Teletrials	Clinical trials conducted remotely using digital technologies, allowing participants to engage with the trial process without needing to visit the trial site in person. This approach can involve the use of telemedicine, digital health tools, video consultations, electronic data collection, and remote monitoring. **Alternative terms:** Virtual clinical trials, remote clinical trials, telemedicine trials, telehealth trials
Therapeutics	The branch of medicine focused on the study, development, and use of interventions designed to manage, treat, or cure medical conditions. It encompasses all types of healthcare approaches, including medications, therapies, surgical procedures, and other interventions aimed at improving health outcomes. **Alternative terms:** Therapies, treatments, interventions
Translational research	Research that bridges the gap between laboratory discoveries and clinical applications, aiming to develop new diagnostics, treatments, or healthcare interventions. **Alternative terms:** Bench-to-bedside research, applied medical research
Treatments	Specific interventions, methods, or procedures applied to a patient to manage, relieve, or cure a disease or medical condition. This includes medications, surgical procedures, physical therapies, and other practical measures used in clinical care. Treatments are part of a broader therapeutic approach and are designed to address an individual's specific health needs. **Alternative terms:** Therapeutic approaches, care strategies, interventions

Appendices

APPENDIX 1: How the action plan was developed

The project methodology was co-designed and implemented by both Mito Foundation and Research Australia. More information about consultation activities and key findings are available in the separate Consultation Summary report.[6]

A literature review:[18] Mito Foundation conducted a targeted, non-systematic, literature review to provide an overview of the available literature regarding rare disease clinical trials. It included publications that either focused on clinical trial activity for mito, clinical trial activity in other rare diseases, particularly diseases similar to mito, or clinical trial activity in Australia.

Horizon scan: Mito Foundation conducted a scan of emerging mito therapeutics. As a part of this work, Mito Foundation compared access to mito clinical trials in Australia compared to other countries.

Stakeholder interviews: Mito Foundation and Research Australia conducted semi-structured stakeholder interviews with individual Australian and international stakeholders across clinician researchers, industry, funders, and peak bodies. Interviews sought to understand current barriers, enablers, and opportunities to increase clinical trial activity.

Stakeholder survey: An online survey was developed and deployed to gather insights from 3 key stakeholder groups: mito community, clinicians and researchers, and industry. Results from these surveys were analysed by Mito Foundation and differences and similarities between different stakeholder groups' priorities provided considerations for the clinical trial action plan.

Consensus-building workshop at the 2024 AussieMit conference: A final consensus workshop was facilitated by Research Australia as part of a broader conference session about therapeutic developments and clinical trials. The workshop included a brief panel discussion, open discussion, and an online prioritisation exercise to rank pre-prescribed preliminary action areas as contained in an earlier survey.

Community workshop at the 2024 Mito Community Summit: This workshop aimed to gather insights from the mito community on their perspectives on clinical trials, including key priorities for the clinical trials action plan. The workshop focused on communication needs and preferences about clinical trials, and support needs during participation in clinical trials.

Data and insights collected from the above methods were then synthesised and analysed by Mito Foundation and Research Australia to compile the action plan.

APPENDIX 2: Stakeholders

The mito community — including individuals with a diagnosis or suspected diagnosis of mito, as well as their families and carers — are prospective participants in trials testing new therapies and interventions. These trials aim to improve quality of life, extend life expectancy, or better manage symptoms. Because mito is a rare disease, it has limited therapeutic options. In some cases, clinical trials represent the only viable way to access treatment for mito. To engage effectively, this group has distinct needs for information, education, support and access, alongside their own motivations to participate.

Clinician researchers are dual-role professionals who both treat mito and conduct research to develop and test innovative therapies. The types of clinicians involved, or who have the potential to be involved, in mito research are diverse due to the multiple professions that are tasked with treating mito and its related conditions. The most common specialties involved in mito clinical trials as lead and site investigators are neurologists, metabolic clinicians, and ophthalmologists. Others involved in health care and evaluation of outcomes include nurses, paediatricians, endocrinologists, dieticians, physiotherapists, and general practitioners.

Clinician researcher involvement in clinical trials typically includes identifying and recruiting patients, administering therapies, collecting data, and analysing outcomes, usually as part of a larger international research team. Other clinicians contribute by referring patients for recruitment or delivering additional healthcare services essential to trial protocols, e.g. a clinical trial nurse who may assist in monitoring and reporting side effects for a patient enrolled in a clinical trial.

Industry is a key driver of clinical trials, leading the development of potential therapeutics for mito. Their decisions about trial locations are influenced by the presence of skilled clinician researchers, access to eligible patient populations, and local market conditions — particularly the potential for government subsidies if a therapy proves successful. Most companies currently developing therapeutics for mito are based in North America and Europe, with no local presence in Australia.

Patient organisations are another vital stakeholder in the clinical trial ecosystem. They collaborate with industry and clinician researchers, engage with the mito community, and often contribute by directly funding research or providing resources essential for trial operations.

Academic and research institutes are key stakeholders in clinical trials. These organisations often have dedicated research ethics and governance mechanisms to regulate and monitor clinical trials.

Other funders of clinical trials, such as government agencies and non-governmental organisations, may provide full or partial funding for trials in high-priority clinical areas for low-cost and repurposed therapeutics.

Health systems and services play a critical role in supporting clinical trials, often providing the physical infrastructure needed, including clinical equipment, space, and staff. These systems typically have their own ethics and governance requirements, which can vary across jurisdictions. As a result, trials conducted in multiple regions may face duplicative regulatory processes.

Government policies also significantly influence clinical trials. These include funding streams for clinical research, legislation governing trial regulation and safety, financial policies such as tax incentives that impact the commercial viability of trials, and health technology assessment processes that affect the potential for subsidised access to therapeutics.

APPENDIX 3: Sector views

More detailed information about the consultation process and findings is available in the separate Consultation Summary report.[6]

Mito community perspectives

Awareness and information: Awareness of clinical trials for mito and related conditions varies widely amongst the community. Patient organisations and health care teams are key sources of information, although some individuals lack access to trial details, or knowledge of other enablers such as patient registries.

Interest and participation: Despite varied awareness and previous involvement, there is strong interest amongst the Australian mito community in participating in clinical trials.

Motivations: Key motivators include improving the quality of life for the broader mito community, gaining knowledge, and accessing better treatments. Additional drivers include contributing to research for future generations and staying updated on treatment developments.

Barriers: Participation challenges include concerns about risks and side effects, logistical difficulties such as travel requirements to get to trial sites, and trust issues with industry. Specific challenges like consent processes for older patients and behavioural difficulties in children are also factors.

Engagement with patient registries: Many individuals engage with patient registries to stay informed, support research, and connect with the community. However, barriers to joining include lack of awareness, perceived complexity, and data privacy concerns.

Clinician perspectives

Involvement in clinical trials: Participation in clinical trials varies, with some professionals having direct involvement in mito trials and others engaged in trials for conditions other than mito, whereas other clinicians have no current involvement in clinical trials.

Barriers: Key barriers to participation include heavy workloads, limited funding, insufficient institutional resources, workforce shortages, and challenges in fostering collaboration among stakeholders. Structural limitations, particularly in public hospitals, and delays in securing resources further complicate implementation and clinicians' ability to have a role in leading or participating in trials.

Patient referral and recruitment: Several factors influence professionals' decisions to recommend clinical trials, including time constraints for supporting families, lack of information about trial availability, and limited awareness of existing trials. Effective recruitment relies heavily on direct patient contact through established clinical relationships.

Enablers for clinical trials: Strong patient engagement and established recruitment pathways are significant enablers of clinical trials. Other factors, such as trial design and participant support systems, also contribute positively.

Industry perspectives

Barriers and enablers for site selection:

1. **Qualified sites and investigators:** While generally seen as a strength, gaps in site availability and investigator expertise can present challenges, especially in specialised trials requiring advanced capabilities.
2. **Patient recruitment:** Access to and engagement with suitable patient populations is pivotal but remains a challenge in rare diseases like mito, where recruitment pipelines can be limited. Access to high-quality patient data was highlighted as an enabler.
3. **Regulatory processes:** The regulatory environment is viewed as largely manageable, though opportunities for simplification exist to reduce delays in trial setup.
4. **Cost and logistics:** Opinions are mixed; some companies navigate these challenges successfully while others struggle with high costs and logistical complexities, including resource availability.
5. **Local market conditions:** Market conditions and long-term viability, particularly for therapies for chronic conditions, are increasingly critical factors for companies when considering trial investments in the region.
6. **Partnerships and collaborations:** Strong local collaborations, especially with patient organisations, are consistently identified as an enabler, supporting recruitment and trial visibility.

Competitiveness of Australia for clinical trials:

Australia offers several advantages, including strong patient advocacy networks, high-quality clinicians, and favourable regulatory processes. However, higher costs, limited site availability, and patient distribution challenges pose risks compared to other regions. Concerns about therapy reimbursement and long trial setup times also impact Australia's competitiveness.

APPENDIX 4: Evaluation metrics

Combined with continued regular horizon scanning, Mito Foundation will gather these key metrics to measure the success of the action plan.

Outcome area	Metrics sought	Input(s)	Frequency of data capture and reporting
Overarching	Number of mito clinical trials being run globally.	Horizon scan	6-monthly
	Number of mito clinical trials with sites in Australia, including benchmarking against other countries.	Horizon scan	6-monthly
	PBS/MBS listing of new mito therapeutics.	Horizontal scan	2-yearly
	Quality of life and life expectancy outcomes for mito in Australia.	Health data sources	5-yearly
Building clinical capacity and readiness	Number of clinician researchers involved in clinical trials in Australia, including their location.	Engagement with clinicians	Annually
	Clinician researcher experiences and perceptions of their capacity to engage with clinical trials.	Engagement with clinicians	2-yearly
Supporting the mito community to participate in clinical trials	Community-reported satisfaction with clinical trial participation, including availability of psychosocial and practical supports.	Survey/insight gathering from community	2-yearly
	Community-reported satisfaction in the knowledge and understanding of clinical trials available to them.	Survey/insight gathering from community	2-yearly
	Uptake of Mito Foundation resources containing clinical trial information.	Website and resource analytics	Annually
	Number of participants enrolled in the mito registry.	Mito Registry analytics	Annually
	Indicative retention/attrition rates for mito clinical trials in Australia.	Engagement with industry and researchers	2-yearly
Strengthening collaboration	Clinicians' perceptions of collaboration activity with peers.	Engagement with clinician researchers	2-yearly
	Number of international collaboration opportunities attended by Australian clinician researchers.	Engagement with clinician researchers/ desktop review	2-yearly
	Number of clinician researchers connected to a Clinical Trials Unit.	Engagement with clinician researchers	2-yearly
	Industry perceptions of Australia as a clinical trial site.	Engagement with industry	2-yearly

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