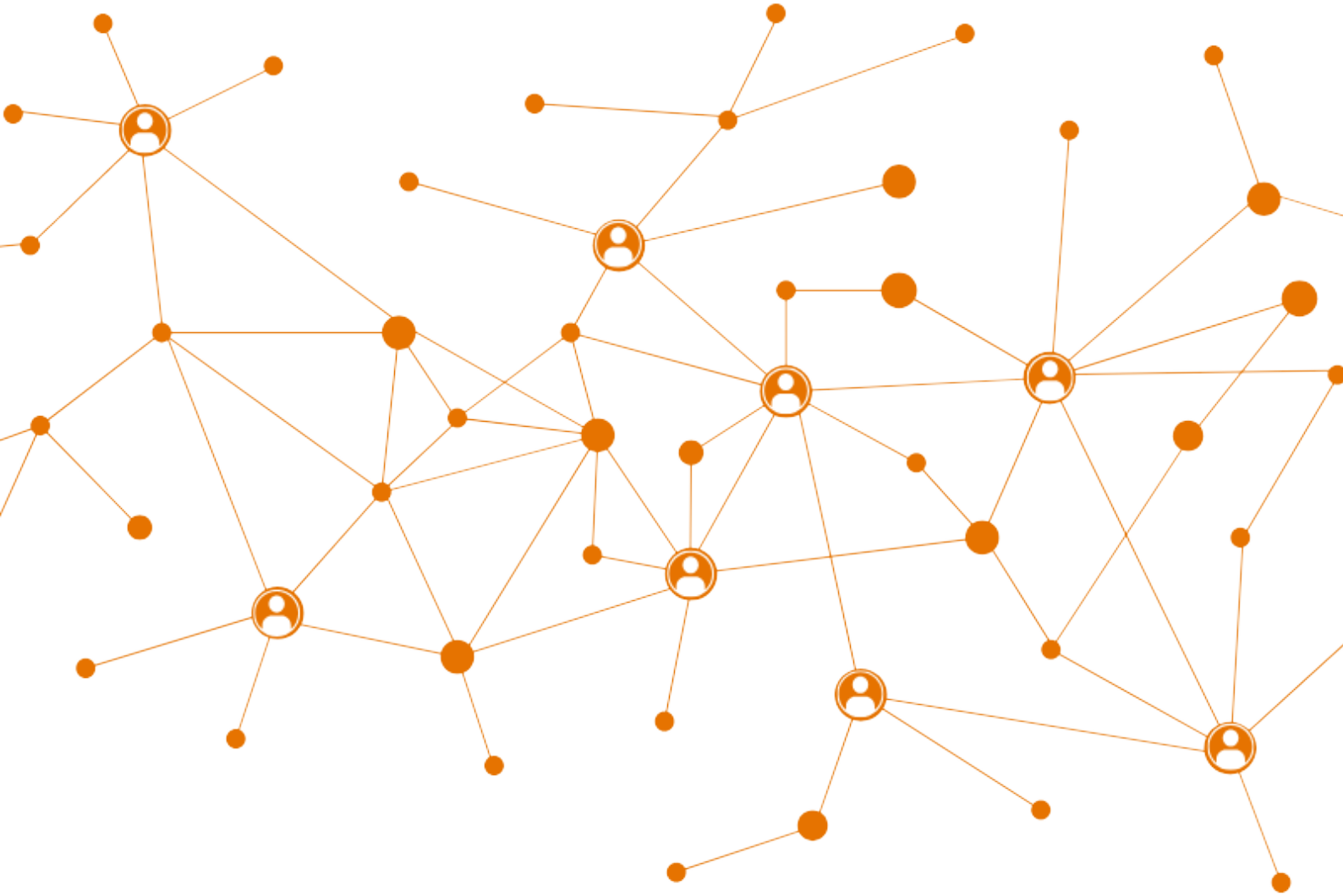


Stakeholder consultation summary

Increasing clinical trial activity in mitochondrial disease in Australia

mito FOUNDATION
Hope for mitochondrial disease

RESEARCH AUSTRALIA
Championing Australian health & medical research & innovation

Mito Foundation and Research Australia

April 2025

The action plan

A series of stakeholder consultation activities was conducted as part of a collaborative effort between Research Australia and Mito Foundation to develop an action plan aimed at increasing clinical trial activity for mitochondrial disease (mito) across Australia and New Zealand. This summary offers insights to inform efforts to boost clinical trial activity for mito and other rare diseases, both nationally and internationally.

Consultation activities overview

Consultation activities included:

1. **qualitative interviews** with stakeholders experienced in mito or other rare disease clinical trials (Table 2)
2. **online surveys** to gather insights from 3 key stakeholder groups: the mito community, clinicians and researchers, and industry representatives [i] (Table 3)
3. **stakeholder workshops** at the 2024 AussieMit conference and Mito Community Summit to gather insights from clinicians, researchers, and the mito community.

Each activity built on the findings from previous activities. All activities were also informed by an analysis of recent clinical trials for mito [ii] and a literature review to understand the barriers and enablers to conducting clinical trials for mito in Australia.[1]

[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.

[ii] Pending publication by Mito Foundation

Overview of consultation topics

Table 1 outlines the major themes from each stakeholder group's consultations.

Table 1. Consultation topics

Stakeholder group	Consultation topics
Mito Community	• Awareness of clinical trials and patient registries • Motivations and barriers to participation in trials and registries • Referral pathways and information sources • Support needs to improve participation and retention • Priorities for the clinical trials action plan
Clinician Researchers	• Participation in clinical trials for mito • Recruitment and referral pathways for clinical trials • Current enablers and barriers for mito/rare disease clinical trials in Australia • Collaboration preferences among stakeholders • Priorities for the clinical trials action plan
Industry	• Factors impacting decision-making for establishing Australian sites • Current enablers and barriers to trial setup in Australia • Collaboration preferences among stakeholders • Priorities for the clinical trials action plan

Consultation scope and considerations

The low response rate from New Zealand-based clinicians, researchers and mito community members limited the scope of these consultation activities, resulting in the clinical trials action plan focusing primarily on Australia. However, the findings from this consultation may be useful to guide efforts to increase clinical trials for mito in New Zealand and the wider region by identifying key enablers and barriers.

1. Qualitative interviews

Methodology

Mito Foundation identified interview participants through its knowledge of the sector and relevant stakeholders. Participants were contacted by Mito Foundation or Research Australia and informed about the project before scheduling virtual meetings.

Both Mito Foundation and Research Australia conducted the interviews as schedules allowed. They used a semi-structured interview format using an interview guide (Appendix 1), allowing open conversation and specific prompts. Each interview lasted 45 – 60 minutes, and interviewers took notes. Most interviews were recorded; 2 participants declined recording.

Table 2. Qualitative interviews overview

Participant type	N
Australian clinician researcher	7
mito-specific	5
other rare disease	2
Overseas clinician researcher	2
Australian patient organisation (other rare disease)	1
Overseas patient organisation (mito)	1
Industry representative	1
An Australian clinical trials network organisation	1
Mito community member [i]	1
Total	**14**

[i] This story was collected as part of the Mito Stories Project, Mito Foundation's formal lived experience research project which gathers, analyses and shares insights from the mito community.[2]

Key themes

Australia's strengths in clinical trials

Australia was generally viewed as an attractive location for clinical trials. The reasons cited included the relatively high quality of Australian health data, clinical trial governance, and a highly skilled and capable research workforce. Participants also discussed the current strengths and opportunities for mito and rare disease clinical trials in Australia. These focused on activities, systems, and processes that support trial activity in these or other therapeutic areas.

Identified key strengths

- **There are some well-established trial sites that exist in relatively well-resourced and supported clinics that have the expertise to attract, develop, and coordinate trials.** This includes the Neuroscience Research Australia (NeuRA) clinic in Sydney, referenced by 2 of the clinician researchers, and other sites in Melbourne and Adelaide.
- **Some sites studying other diseases have gained relevant experience with therapeutic advancements that may be applicable to future mito therapies and are becoming proficient in establishing related trials.** An example includes separate ethics panels for gene therapy trials, which can be leveraged for other emerging therapies.
- **Advocacy groups like Mito Foundation play a crucial role** in mobilising patient networks, providing direct access to patient populations and insights, funding research, and supporting patients who may be considering participation in clinical trials.
- **Networks of dedicated mito clinicians are forming**, enhancing collaboration and connection with patients through mutual referrals to trials by clinicians within the network.

Current barriers to increased mito clinical trial activity

The interviews mainly focused on barriers to increasing clinical trial activity for mito in Australia. Key topics included attracting trials, recruiting patients,

improving accessibility, establishing multi-site trials, and supporting clinician researchers. These barriers are grouped thematically below, with some overlap between individual barriers.

Barriers to attracting clinical trials

Many clinician researchers provided insights on the barriers to attracting clinical trials to Australia.

- **Market considerations:** Industry often focuses on larger US and European markets, though some stakeholders noted a shift with Australia's achievements in certain rare disease areas attracting international attention, such as in spinal muscular atrophy.
- **Operational barriers:** Trials for precision therapies, particularly for rare diseases, face challenges due to limited registries, complex logistics, and an already stretched healthcare system.
- **Translating trials into approved therapies:** Transitioning from trials to approved therapies is challenging for rare diseases because of high manufacturing costs that hinder scaling and translation, and potential issues with health technology assessment processes for market access.

Funding gaps

Clinician researchers provided insights on current funding models that may not support the sustainability of future trials in mito and other less common diseases.

- **Pre-trial funding needs:** Significant unfunded activities occur prior to trial approval. These include contributions to feasibility studies, patient screening, partnership and non-disclosure agreements, and coordination meetings. Moving towards "pre-trial establishment" funding, possibly through block funding from industry or contributions from alternate funding bodies, was suggested as a potential solution.
- **Sustainable models:** 2 clinician researchers indicated that the standard per-visit funding model from industry is not sustainable. There was support for a more stable funding structure, such as a percentage of

salary over a fixed period (e.g., 25% of a clinician's time over 3 years), particularly for rare disease trials that frequently see very low patient numbers enrolled at any given site.

Barriers to implementation

Clinician researchers were highly motivated to become involved in mito clinical trials. However, they articulated several barriers to implementing trials.

- **Lack of dedicated research time and support**: Many clinician researchers identified limited time and support as primary reasons for not participating in clinical trials, highlighting the significant challenge of balancing research and practice demands within frequently over-stretched systems. The time burden of trial setup and administration was reiterated often, with these time constraints preventing specialists from taking on the role of trial investigators. Participants reinforced the need for support roles dedicated to trial logistics.
- **Infrastructure barriers**: Insights from other rare disease clinical trials suggested that the demand for essential clinical services such as anaesthesia, MRI, and other clinical monitoring can be access barriers, particularly in the context of already stretched services in some public hospitals.

Challenges establishing multiple trial sites

Clinician researchers offered insights on challenges they've encountered in trials they've been involved in establishing, both for mito specifically and other comparable rare diseases.

- **Differing site capacity:** Variability across sites was noted, with some already equipped for complex trials (e.g., advanced therapies) and others requiring extensive setup.
- **Limited access to dedicated clinical trial teams:** Successful models, such as those at NeuRA in Sydney, the PARC Clinical Research Unit in Adelaide (being used for other metabolic conditions), and internationally at the Children's Hospital of Philadelphia, demonstrate the benefits of

dedicated clinical trial teams. These teams — comprising specialised clinical trial coordinators, clinicians, and administrative staff — provide essential support for trial operations. However, similar support structures do not appear to be widely available to all mito specialists. This lack of dedicated teams may contribute to the limited number of mito clinical trial sites outside Sydney and Melbourne.

- **Governance and regulation delays**: Multi-site trials face delays due to varied legal, ethics, and governance procedures across sites, often extending setup times, particularly with sites in different states and territories. However, there was no consensus on the overall significance of these delays as a significant barrier.

Patient population challenges

Clinician researchers highlighted several factors related to patient populations as critical challenges that impact prospective trial activities.

- **Small patient population with high geographic spread:** Australia's small population and geographic spread present challenges for patients accessing trial sites, as physical limitations can impact travel. However, there were differing opinions on how significant this barrier is. Not all interviewees viewed the geographic spread of patients as a major recruitment challenge; some clinician researchers noted that patients often travel willingly for trials. Additionally, some stakeholders mentioned that many industry partners even sponsor patient travel from nearby countries, such as New Zealand, to centralised trial sites, thereby reducing logistical barriers.
- **No formal, comprehensive patient registry:** Knowledge of patient locations is mostly informal, relying on clinician knowledge and incomplete local or regional registries. Industry feedback similarly highlighted the need for a confident and accessible patient population for trial site selection. There was minimal awareness of Mito Foundation’s Mito Registry.

- **Disease heterogeneity:** The diverse nature of some mito conditions is a barrier to trial standardisation and recruitment, and eligibility criteria for trials is often complex.
- **Limited number of patients with genetic diagnoses:** A clinician researcher highlighted the lack of genetic diagnoses as a key barrier to future clinical trial activity, with many patients having only a clinical diagnosis of mito. They underscored the importance of increasing the availability and uptake of genetic testing and diagnosis for mito as a critical enabler for trials.

Patient access and support

Patient support emerged as a major theme in interviews with clinician researchers. While recruitment was not identified as a significant barrier, these insights highlight opportunities to enhance future clinical trial participation and reduce attrition through improved wrap-around services.

- **Concentration of expertise:** Centralised centres for trials provide essential expertise and infrastructure but place burdens on families, who may need to travel or relocate without guaranteed eligibility or outcomes. Clinician researchers emphasised the physical and emotional toll of this uncertainty.
- **Psychosocial and practical support:** Several clinician researchers stressed the lack of integrated psychosocial support in trials that is usually not incorporated into a trial budget. They advocated for dedicated funding to help families manage the emotional and logistical challenges of high-risk treatments. One clinician researcher additionally stressed the need for better accommodations for participants with physical impairment(s).
- **Communication barriers:** Confidentiality restrictions and limited communication channels often delay open discussions about trials until official approval is granted. Challenges in the mito space include a lack of awareness and dedicated collaborative networks, making it difficult for mito specialists to refer eligible patients. Additionally, health professionals

who treat mito patients but are not specialists may struggle to access referral pathways for clinical trials led by specialist clinician researchers.

Additional challenges

Interviews highlighted several additional challenges.

- **Patient-reported outcome measures (PROMs):** There is a need for improved tools to measure quality of life and treatment outcomes specific to mito.
- **Biomarkers for mito:** A deeper understanding of mitochondrial biomarkers is needed, particularly those that indicate disease progression when clinical signs are subtle. High testing costs pose a barrier for patients, though some industry and investigator-led natural history studies are addressing this by covering patient expenses.
- **Limited opportunity for investigator-led trials:** Investigator-led trials in Australia remain scarce due to their time-intensive nature and financial constraints. Without institutional funding or grants, exploring novel therapies can often be impractical.
- **Central stewardship and collaboration:** Some stakeholders stressed the need for more central coordination of prospective trial activity. A more integrated approach across clinical registries and genomic data repositories — similar to the TREAT-MITO initiative in the US — could streamline access for therapeutic companies and foster collaboration.

Areas for action

Participants were also asked to imagine and propose potential areas for action to increase mito clinical trial activity in Australia. These suggestions are described below.

Improving clinician research-readiness and capacity

- **Education and capacity-building:** Strengthening clinician research-readiness requires equipping clinicians with the skills and knowledge needed to participate in trials. A particular focus on early and mid-career

clinician researchers could help build a sustainable workforce. Additionally, clinicians are more likely to engage in trials when they believe in the research and the potential benefits of the therapy being tested.

- **Support:** Practical resources — such as reducing clinical workload through additional support roles (e.g., nurses, genetic counsellors) — were suggested to enable clinicians to dedicate more time to trial involvement.
- **Embedding clinical trials in medical training:** Integrating clinical trial experience into medical education was identified as a key strategy for making trials a standard part of rare disease care. A notable example is the University of Sydney's initiative to involve junior doctors as sub-investigators in trials, helping them gain experience in patient monitoring, safety event reporting, and trial administration. This hands-on involvement could strengthen future clinical trial capacity.

Strengthening partnerships

- **Stronger collaboration:** Fostering closer ties between consumer groups, peak bodies, and professional associations was a strong recommendation. Models that have seen relative success in cerebral palsy and multiple sclerosis were referenced.
- **Sustained industry relationships:** Ongoing engagement with industry is essential for trial activity, enhancing awareness of pipeline trials and Australia's role as a trial destination. Clinician researchers highlighted the importance of global networking opportunities, particularly at international conferences, though funding remains a barrier — especially for early and mid-career researchers. A potential solution is funding conference scholarships, with a suggested role for patient organisations like Mito Foundation.
- **Role of patient advocacy:** Advocacy groups can play a vital role in connecting patient communities with trial sponsors, leveraging lived experience to drive participation and improve trial design. Families often

advocate more effectively than clinicians for government support, using personal stories to amplify urgency. These organisations can also help raise trial awareness, gather patient feedback, and refine care models.

National collaboration and pooling of resources

- **Collaboration in paediatric trials:** National collaboration is particularly valuable for complex treatments like gene therapy, allowing sites to share expertise and resources. However, additional bureaucracy can sometimes slow progress.
- **Education and support structures:** Programs like the Kids Advanced Therapeutics Initiative[3] provide interdisciplinary support, such as nursing training for gene therapy, which could be expanded nationally to enhance capacity for advanced therapies.
- **Ensuring high-quality trials:** National cooperation was highlighted as key to maintaining the highest trial standards, and crucial for keeping Australia attractive to industry partners and avoiding resource wastage.
- **Specialised trial sites:** Some treatments, such as gene therapy, require specialised resources available only at select sites. Several clinicians recommended centralising expertise rather than spreading trials across multiple locations to maintain quality and efficiency.

Clinical trial processes and design

- **Innovative rare disease trial models:** The clinical trials network respondent referenced a developing 'rapid trial model' for rare diseases and cancers, which streamlines governance and enables faster site activation when a suitable patient presents. Both adult and paediatric consortia are piloting this model; this could inform future mito trials.
- **Improving accessibility:** While most patients travel to primary trial centres, there is growing interest in home nursing for trial assessments, which could be explored further for mito trials.
- **Transparent and effective communication:** Rapid recruitment is critical for many trials, particularly when early treatment significantly impacts

quality of life. More transparent and timely communication was recommended to improve recruitment efficiency.

- **Drug repurposing:** Given the challenges of developing novel therapies, repurposing existing drugs could provide faster treatment access and slow disease progression while awaiting new therapies.

Building data infrastructure

- **A national patient registry:** There was strong consensus on the value of patient registries. Mito Foundation's Australian contact registry exists, but international models like mitoSHARE demonstrate the benefits of comprehensive registries that integrate genetic data and longitudinal tracking. Expanding the registry could improve industry confidence in Australian trial sites by offering better insights into the patient population and recruitment potential.

Establishing sustainable funding models

- **Pre-trial funding:** To cover trial establishment costs, models such as industry block funding or contributions from alternative funding bodies.
- **Stable funding structures:** A more predictable funding model, such as allocating a percentage of a clinician's salary over a fixed period (e.g., 25% over 3 years), was suggested to support rare disease trials with low enrolment numbers.
- **Advocacy-driven funding:** Some interviewees spoke about the role that advocacy and patient organisations can play in directly funding clinical trials, or the resources and infrastructure related to running clinical trials.

Supporting patients on trials

- **Psychosocial support frameworks:** Future efforts could focus on integrating psychosocial assessments and support into trials, ensuring families understand and manage the risks and burdens of participation.

2. Online surveys

Online surveys were developed (Appendices 2, 3, and 4) and deployed using Mito Foundation and Research Australia communication channels to gather insights from 3 key stakeholder groups: the mito community, clinicians and researchers, and the pharmaceutical industry. The surveys were distributed via email through the Mito Foundation and Research Australia mailing lists, as well as through direct outreach to known contacts. The survey was also distributed by one research group in New Zealand to clinician researchers and known mito community members in New Zealand.

Table 3. Survey respondents overview

Respondent type	N
Mito community members	**38**
Respondent had a confirmed or suspected diagnosis	17
Respondent was a family member or friend of a person with a confirmed or suspected diagnosis	17
Both of the above	4
Clinicians and researchers	**9**
Clinician researcher	3
Member of clinical trial team(s), not investigator	1
Other health professional involved in the care of mito patients	5
Industry representatives	**6**
Clinical researchers	5
Executive	1

Key survey findings and analysis of the differences and similarities between different stakeholder groups' priorities for the clinical trials action plan are presented below.

Mito community survey

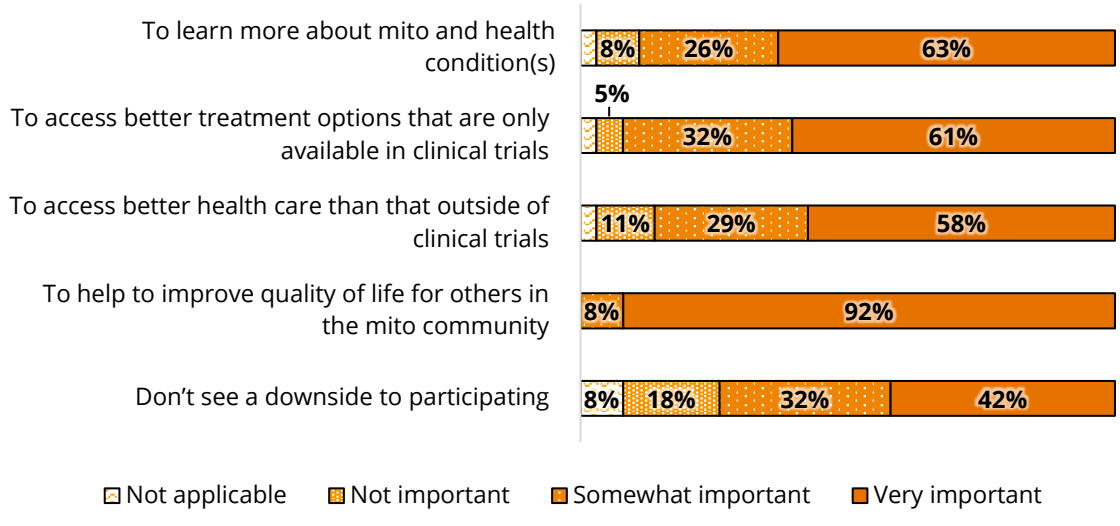
Clinical trial awareness and participation

- Awareness of clinical trials for mito and related conditions varied among respondents. Main sources of trial information included patient organisations, health care teams, and online sources.
- Interest in clinical trials was high, with nearly a quarter of respondents having previously participated and none expressing a lack of interest in participating.

Motivations for participating in clinical trials

Respondents ranked the importance of various factors influencing their motivation to participate in clinical trials (Figure 1 below). The top priority was improving the quality of life for the mito community as a whole. Other key drivers included gaining knowledge and accessing better treatments and health care.

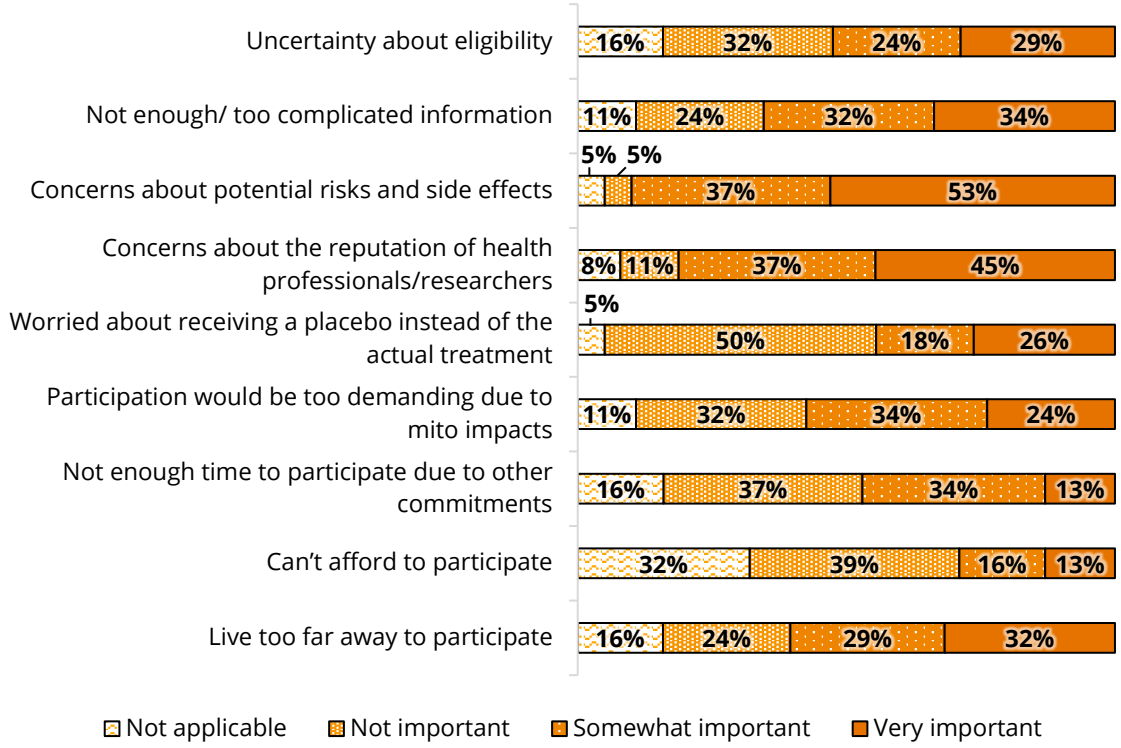
Figure 1. Mito community's motivations for participating in clinical trials (N=38)



Barriers to participating in clinical trials

Respondents also ranked their most significant barriers to participating in clinical trials (Figure 2 below). The most significant barriers included concerns about potential risks and side effects, the reputation of health professionals and researchers, and logistical issues such as distance from the clinical trial site.

Figure 2. Mito community's barriers to participating in clinical trials (N=38)



Patient registries

- Most respondents were aware of and had joined Mito Foundation's contact registry (n=23), but awareness of other mito-related registries was low.
- Most common **motivations for joining** patient registries included staying informed about medical and research updates (n=10), helping with research to find treatments or cures (n=8), and connecting with community and supporting others (n=8).

- Most common **reasons for not joining patient registries** included lack of awareness about their existence (n=6) and lack of interest/awareness from health professionals (n=2).

Mito community recommendations for information and resources to improve understanding of clinical trial opportunities

Respondents were asked to suggest what information or resources would help them better understand clinical trials and participation opportunities. Their suggestions included:

- provide clear, simple information about clinical trial eligibility and safety (n=10)
- regular communication through personal contact, email, social media, newsletters, and information sessions (n=9)
- an online portal or resource pack (n=5)
- availability of local trials (n=1)
- more details on patient registries (n=1)
- accessible information (e.g. audio information) (n=1)
- active information sharing by health professionals (n=1).

2 respondents were satisfied with their current knowledge, while some (n=7) were unsure of what could be improved.

Mito community recommendations to improve clinical trial participation

Respondents were asked to provide suggestions on how clinical trials for mito could be made easier to join and participate in. Their suggestions included:

- better communication about trial availability and eligibility, along with easy-to-understand information and personal contact (n=7)
- remote trial opportunities, such as home treatment options, couriered blood tests, and video consultations (n=4)

- practical support, including funding for out-of-pocket expenses like transport (e.g., taxi vouchers or transport from rural or regional areas) (n=7)
- improved genetic testing affordability (n=1)
- help with joining overseas trials (n=1)
- international patient inclusion in Australian trials to improve recruitment numbers (n=1)
- more funding to support clinical trial centres (n=1)
- reduced eligibility restrictions based on gene mutations (n=1).

Clinician and researcher survey

This survey had a low response rate (n=9), which limits the generalisability of the findings. The responses are unlikely to fully capture the perspectives of clinicians and researchers across different states, healthcare settings, or specialties involved in mito and related conditions. The small sample size may not reflect the full diversity of experiences, challenges, and priorities in clinical trial involvement.

Overview of respondents

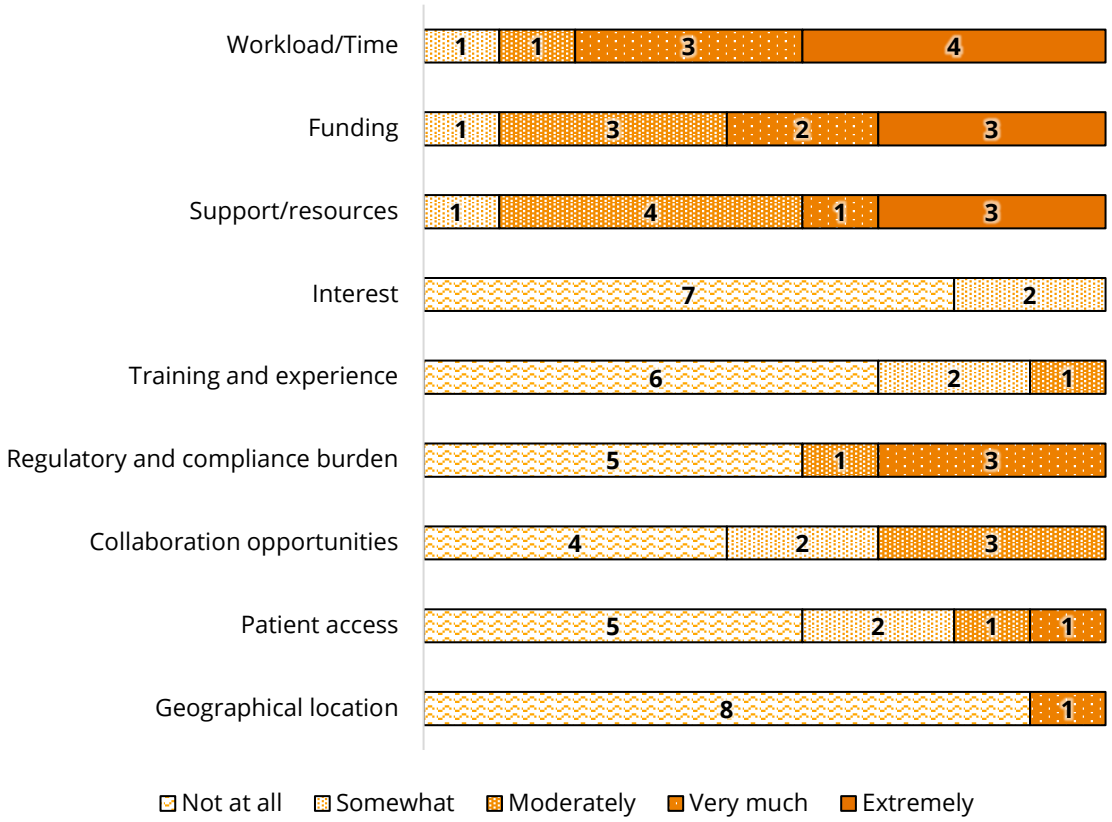
- The majority of respondents were based in New South Wales (n=4), and Victoria (n=4) . All 9 respondents worked in public hospitals; 2 respondents were also active in private practice.
- 5 respondents primarily cared for children and adolescents, 2 worked with adults only, and 2 worked with all age groups.

Involvement in clinical trials

- One-third of respondents were/had been involved in clinical trials for mito, another third for non-mito conditions, and the remaining had no trial experience in Australia or New Zealand.
- Main barriers to involvement in clinical trials (Figure 3 below) included workload and time constraints (77%) and funding issues (55%). Institutional support and resources also posed challenges (44%).

Regulatory burdens were less significant, and most did not consider professional interest, training, patient access, or location as major barriers.

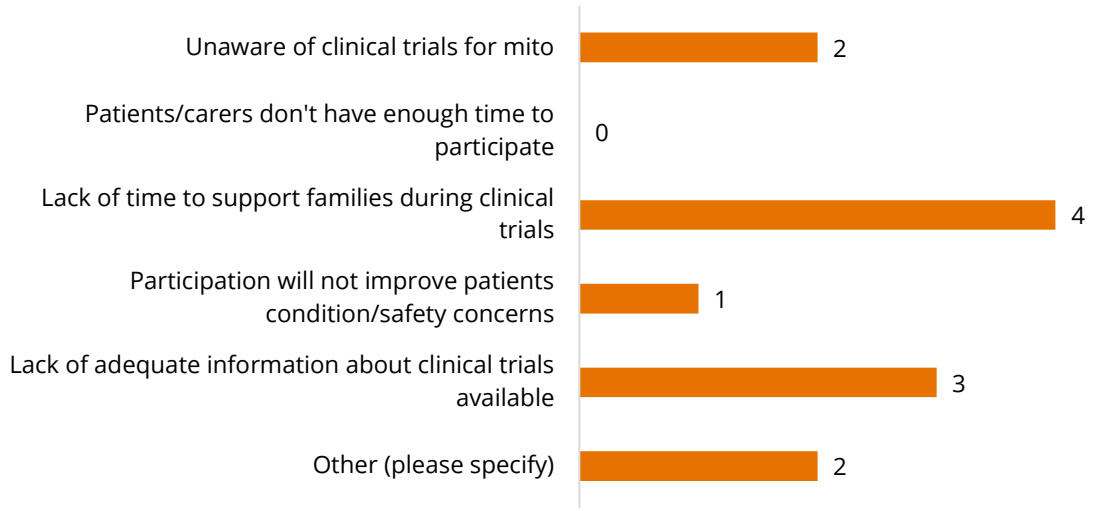
Figure 3. Factors impacting clinicians' and researchers' involvement in clinical trials (N=9)



Clinical trial referral and recruitment

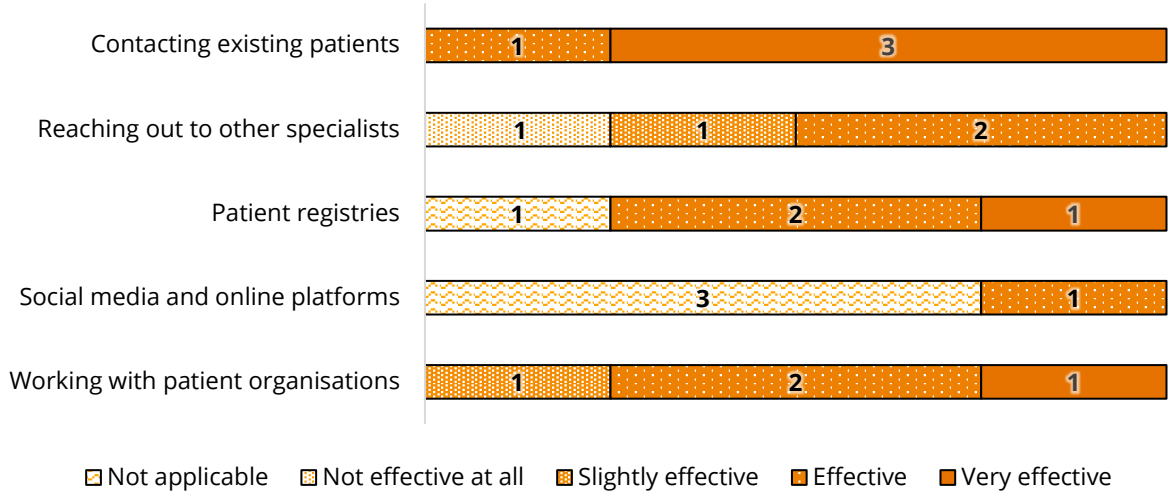
The primary factors affecting respondents' decisions to **refer** their patients to clinical trials included: limited time to support families during trials (n=4), insufficient information about clinical trials (n=3), and lack of awareness of clinical trials for mito (n=2).

Figure 4. Factors affecting clinicians' and researchers' decision to recommend clinical trials to patients (N=9)



Respondents ranked direct patient contact through their hospitals or clinics as the most effective recruitment method.

Figure 5. Effectiveness of patient recruitment strategies according to clinicians and researchers (N=9)



Ranking of current enablers and barriers for mito clinical trials in Australia/New Zealand

Respondents were asked to identify their top 3 aspects of mito clinical trials that they perceive as enablers and barriers (Table 4).

*Table 4. Summary of rankings for current enablers and barriers for mito clinical trials in Aus/NZ**

Factor	Enablers ranking	Barriers ranking
Patient engagement	1	8
Patient recruitment pathways	2	6
Trial design and methodologies	3	6
Support systems for participants	3	7
Training and experience of clinical trial workforce	4	5
Collaboration and partnerships between different stakeholders	5	3
Funding and resources	6	1
Infrastructure including access to the workforce, space, equipment needed to run trial	6	2
Regulatory and approval processes	7	4

**Rankings based on weighted scores for each aspect. 1 is the highest ranking, and 8 is the lowest. Weighted scores were calculated by assigning 3 points to top choices, 2 points to second choices, and 1 point to third choices.*

Industry representative survey

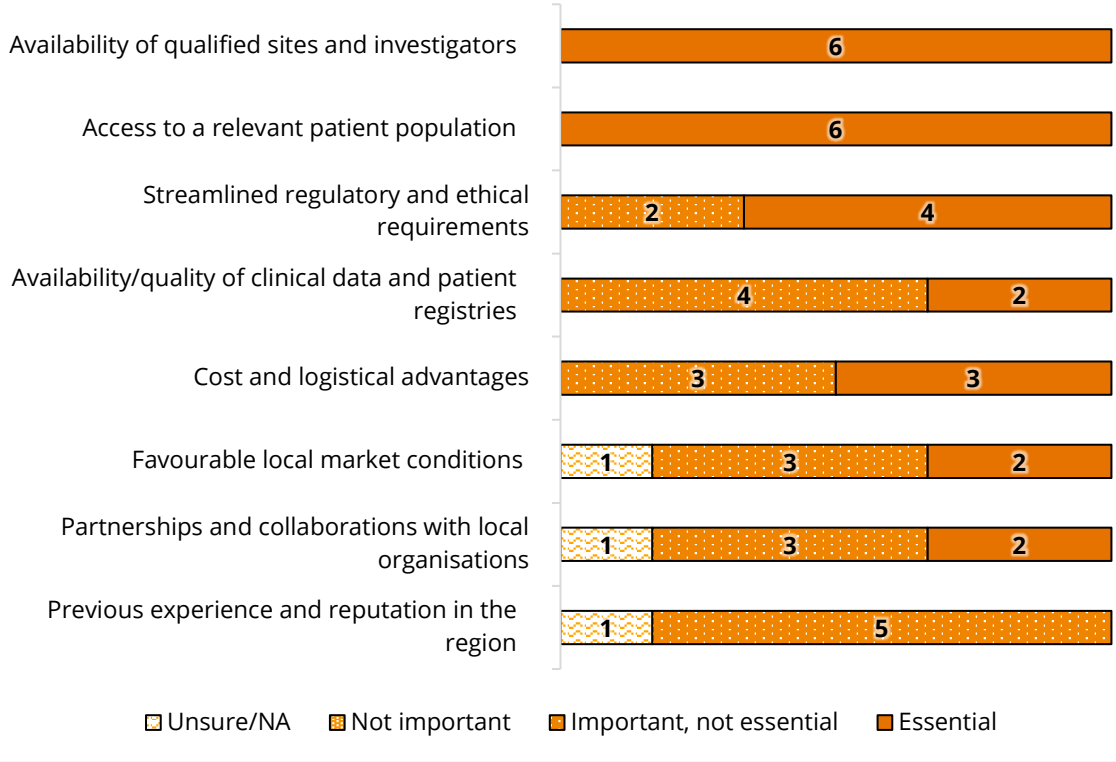
6 representatives from 6 different pharmaceutical and/or biotechnology companies responded to the survey. All respondents reported that their company had sponsored or was planning to sponsor clinical trial(s) for mito.

Key considerations for establishing clinical trial sites in Australia and New Zealand

Respondents highlighted several key factors when considering the establishment of clinical trial sites in Australia and New Zealand. 2 factors were identified by all respondents as essential: the availability of qualified sites and investigators, and access to a relevant patient population. 4 respondents additionally stressed the importance of the ability to access a sufficient patient population with methods to contact them. One respondent wrote:

"To motivate the time, cost and other resources to add a country for a trial, it is essential that sufficient numbers of patients can be included in the trial. This often requires at least 2 – 3 sites, preferably more, to motivate the trial set up."

Figure 6. Key considerations for industry in decisions to establish clinical trial sites in Aus/NZ (N=6)



Other less common considerations included:

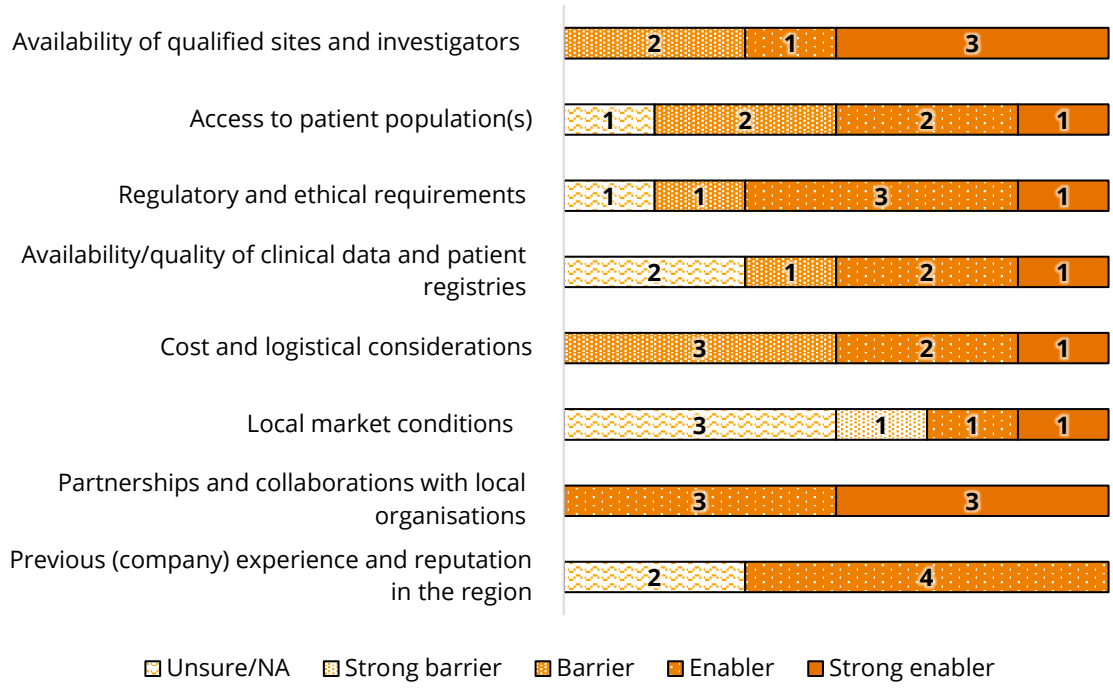
- turnaround time of site contracts (n=1)

- availability of sites (with capacity) to conduct studies (n=1). One respondent mentioned the importance of access to cell therapy manufacturing facilities for clinical trials involving advanced therapies.

Current barriers and enablers impacting clinical trial setup

Respondents evaluated various factors influencing the setup of mito clinical trials in Australia and New Zealand. Several key factors emerged as either enablers or barriers to establishing clinical trial sites (Figure 7). Responses varied widely, possibly reflecting differences in respondents' level of involvement with Australian and/or New Zealand trial infrastructure. Some respondents also expressed uncertainty or found certain factors inapplicable. To guide actionable insights, we focused on the strongest enablers and barriers — those that were perceived to have the most significant impact on trial setup. These key factors included the availability of qualified trial sites and investigators, partnerships and collaborations with local organisations, access to patient populations, availability and quality of clinical data and patient registries, as well as regulatory and ethical requirements.

Figure 7. Barriers and enablers for clinical trial setup for industry (N=6)



Perceptions of Australia's competitiveness in setting up clinical trial sites

Respondents were asked to consider the potential benefits and risks of setting up clinical trial sites in Australia compared to other countries. While there were mixed perceptions, several key differences were identified, both positive and negative, that impact the attractiveness of Australia as a location for clinical trials.

Potential benefits of Australia

- The presence of a strong patient advocacy group (Mito Foundation), with respondents acknowledging that Mito Foundation has strong connections to patients and a deep understanding of their needs (n=2).
- One respondent mentioned their positive interactions with regulatory bodies and Human Research Ethics Committees (HRECs), noting smooth processes for approvals.
- The presence of high-quality clinicians (n=1)
- The overall competitiveness of the Australian clinical trial landscape (n=1).

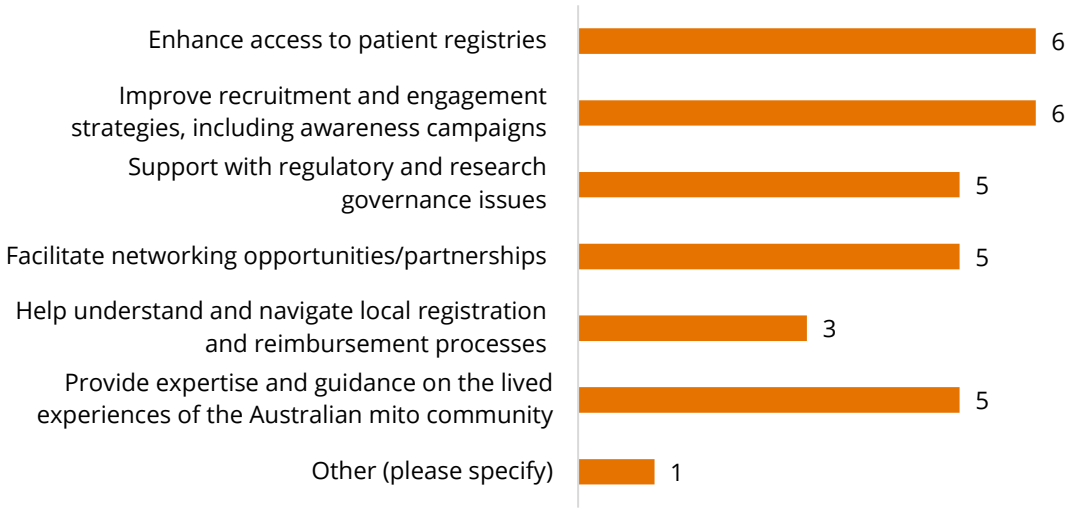
Potential risks of Australia

- Difficulty in recruiting patients for clinical trials and challenges with study start-up (n=1)
- Higher start-up costs and long start-up times, noting that additional requests for equipment and resources could make trials more expensive in Australia (n=2)
- Limited number of clinical trial sites (n=1)
- Geographic spread of patients makes Australia riskier than the US/EU in setting up clinical trials (n=1)
- Concerns over the low likelihood of therapies being reimbursed by the government (n=1).

Preferences for collaboration with Mito Foundation

Respondents highlighted several areas where collaboration with the Mito Foundation could enhance the setup of clinical trials in Australia and New Zealand.

Figure 8. Industry's preferences for collaboration with Mito Foundation (N=6)



Combined priorities for the clinical trials action plan

Table 5 below outlines the priority rankings for the clinical trials action plan as identified by clinicians and researchers, and industry. These differences reflect the unique roles and challenges each group faces in the clinical trial ecosystem, emphasising the need for a multi-faceted action plan that reconciles their perspectives.

Table 5. Overview of clinicians and researchers, and industry representatives' priorities for the clinical trials action plan

Actions	Clinicians and researchers' ranking	Industry's ranking
Making patient recruitment easier	6	1
Improving regulatory and governance processes	4	2
Increasing research funding	1	3
Growing the clinical research workforce	3	4
Improving support for clinician researchers	2	5
Fostering collaborations	3	5
Enhancing patient engagement and retention	5	5
Increasing mito community awareness and education	5	6
**Rankings based on weighted scores for each aspect. 1 is the highest ranking, and 8 is the lowest. Weighted scores were calculated by assigning 3 points to top choices, 2 points to second choices, and 1 point to third choices.*		

The differences in these priority rankings highlight the complementary but distinct focuses of clinicians and researchers, and industry. Clinicians and researchers emphasise upstream, foundational issues, such as funding, workforce development, and support for clinician researchers, which are critical for building a sustainable framework for future trials. Industry prioritise downstream, operational aspects like patient recruitment and regulatory efficiency, which directly affect trial feasibility and execution.

3. Stakeholder workshops

2 in-person consultation workshops were held in 2024 in Melbourne to capture diverse stakeholder perspectives:

a) AussieMit 2024 workshop for clinician researchers, industry representatives, and select mito community members [i]
b) Mito Community Summit 2024 workshop for mito community members

a) Aussiemit 2024 Workshop

Methodology

Held at the 2024 AussieMit conference in Melbourne, this workshop was facilitated by 2 staff from Research Australia, and engaged clinician researchers, industry representatives, and select mito community members to:

- present preliminary findings from the qualitative interviews and the surveys (Sections 1 and 2) to community members, clinician researchers, and industry stakeholders
- discuss emerging action areas and test their relevance
- facilitate a prioritisation exercise, where 73 participants ranked key action areas.

The workshop was approximately 55 minutes in duration. This workshop was contained within the AussieMit conference program within a day focused on topics most relevant to clinician researchers. The workshop followed a session that included short talks relevant to clinical trials for mito. The workshop consisted of a high-level presentation of preliminary consultation and survey findings, followed by a panel discussion. The panel included a clinician researcher, an industry organisation representative, and a mito community member. Following the panel discussion, open discussion was held involving some audience members, panellists, and facilitators. At the close of the

[i] These were predominantly members of Mito Foundation's Mito Community Advisory Panel (MCAP). The MCAP brings together mito community members from across Australia to provide feedback, share ideas, and guide Mito Foundation's work.

workshop, an online prioritisation exercise using the digital tool Slido, asking audience members (n=73) to rank the same action areas as used in the survey to industry representatives and clinician researchers (Table 4 and 5) to further test these results. Research Australia staff remained available throughout the day to capture additional input from conference attendees which are recorded below alongside insights from the workshop itself.

Audio recordings from the workshop discussions have been transcribed and compiled with facilitator notes by Research Australia. The main themes are described below.

Key themes

Clinical trial infrastructure and workforce

- Clinical trials require **robust infrastructure and a skilled workforce** to function effectively. Specialised facilities and well-equipped trial sites are essential to meet patient needs and regulatory standards.
- Having a **dedicated clinical trial team** in place significantly improves efficiency and reduces delays in setting up new trials.
- **Sites with a successful history of conducting trials** are more attractive to industry sponsors, as they demonstrate reliability in managing complex research protocols.

Patient engagement

- Building **strong relationships between patients and healthcare providers** is crucial to encouraging trial participation. Patients are more likely to engage when they feel a personal connection with the care team.
- **Comprehensive patient registries** connected to clinical teams is a critical pathway for effective trial recruitment, ensuring patients are matched with the right studies.

Clinical trial design

- While industry often focuses on speed and efficiency, **patient engagement and advocacy** are essential in designing practical trial protocols and fostering long-term commitment from participants.

- Traditional primary outcome measures may not fully reflect patients' day-to-day experiences. **Patient-reported outcomes**, such as the ability to perform daily tasks like brushing hair or shopping independently, may be more meaningful but are often excluded from regulatory assessments. Incorporating these broader measures could offer a more holistic understanding of treatment effectiveness from a patient-centric perspective.

Information sharing

- **Informed consent should be an ongoing process**, starting with initial contact and revisited regularly to maintain transparency and trust.
- Simplifying and tailoring consent and information materials can make the process more accessible for patients.
- **Closing the information loop post-trial** is valued by patients, providing clarity on the tested therapy, their data, and how the findings may inform their future care. Despite improvements in trial result transparency, significant gaps remain. Patient portals or other information resources could play a transformative role in improving transparency and facilitating data sharing.

Further actions to explore

During discussions with audience members and panellists, several additional focus areas were raised that could supplement and expand upon those highlighted in previous consultation activities:

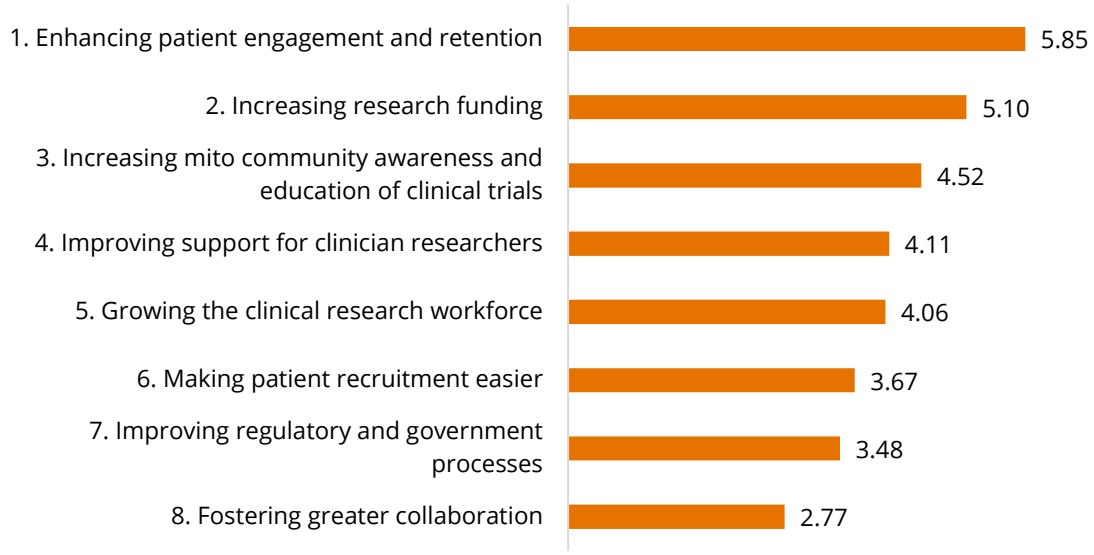
- **Developing a 'one-stop shop' directory of clinical services and trial sites** across states to improve visibility and access for sponsors and patients. This action could be explored by Mito Foundation.
- **Strengthening centres of expertise for mito**, in alignment with broader initiatives for rare disease centres at the federal level.
- Identifying and engaging **underserved or disconnected patients** to ensure equitable access to clinical trials.
- Advocating for **continuity of care** for trial participants, extending timely health care access beyond the trial period to improve long-term care.

- Collaborating with sponsors and companies to refine **patient engagement and recruitment strategies**, making the trial experience more inclusive and patient-centred.
- Contributing to the expansion of measures used to assess trial effectiveness, particularly in the context of **Patient Reported Outcome Measures (PROMs**) and **Patient Reported Experience Measures (PREMs)**, and their role in trial design and regulatory processes.

Prioritisation results

Aggregate weighted responses to the Slido prioritisation exercise (73 responses) are presented below. While these results differ from those gathered from clinician researcher and industry respondents to the initial surveys (Section 2), there is some potential bias in results due to the results being shown live to the audience prior to closing the ranking activity, and one panellist expressing surprise that patient-related priorities did not rank higher.

Figure 9. Ranking action areas for the action plan



b) Mito Community Summit 2024 Workshop

Methodology

Held during Mito Foundation's annual Community Summit in Melbourne in November 2024, this workshop aimed to:

- Inform the mito community about the clinical trials action plan project and its progress
- Gather insights from the mito community regarding their perspectives on clinical trials, including key priorities for the clinical trials action plan.

The workshop focused on 2 specific topics. These were selected based on insights from previous consultation activities. Participants were asked to consider the following questions for each topic:

Topic 1: Communication needs and preferences about clinical trials

1. How have you learnt about mito clinical trials in the past?
2. How do you want to learn about mito clinical trials?
3. What can we do to help all mito community members learn about clinical trials? Please particularly think about mito community members who are not connected to Mito Foundation.

Topic 2: Support needs during participation in clinical trials.

Imagine there was an opportunity for you to participate in a clinical trial. What would an ideal experience of a trial include for you? You may like to consider:

1. *What would you like to know about the clinical trial?*
2. *How can you be supported to make a decision about whether to participate?*
3. *How much travel would be too much?*
4. *Is there any other practical or emotional support that you would like?*

35 community members participated in 4 groups. 6 of the 8 community members who attended the Aussiemit 2024 workshop also chose to attend this workshop. Each group discussed the 2 topics and recorded their thoughts on whiteboards. Following the group discussions, participants shared their insights as a group with the session moderators (Mito Foundation staff) during a report-back session.

The session was audio-recorded with permission from all participants. The audio transcript, along with moderator notes and whiteboard notes were compiled and the results are presented below.

Topic 1: Communication needs and preferences about clinical trials

How have you learnt about mito clinical trials in the past?

Community members identified the following key sources of information about clinical trials:

- Proactive outreach from:
  - clinicians and specialists (e.g. neurologists)
  - Mito Foundation and the Mito Registry
  - other patient registries (such as the Genomics of Rare Disease Registry)
- Community events, such as Mito Foundation's annual Community Summit
- Online, including websites like clinicaltrials.gov and patient organisation websites (e.g., Mito Foundation, United Mitochondrial Disease Foundation, Monash University for mitoHOPE pilot program).

How do you want to learn about clinical trials?

Community members emphasised the importance of accessible and proactive communication, including:

- clinicians and hospitals taking the lead by having information readily available and reaching out to patients, reducing the need for patients and their families to search for details themselves
- improved online visibility, such as optimising search engines (e.g., Google) so clinical trial information appears prominently in search results
- increased communication from Mito Foundation, particularly through the Mito Registry, including personalised information and connections to specific trials
- scientific conferences, such as AussieMit, as venues to disseminate clinical trial updates and opportunities

- accessible information through all possible channels, ensuring inclusivity and ease of access
- using General Practitioners (GPs) as a trusted source of information on clinical trials

What can we do to help all mito community members learn about clinical trials?

Community members suggested several strategies to ensure broader awareness and understanding of clinical trials across the mito community:

- Engage clinicians as a primary channel to reach community members by focusing outreach on trusted healthcare providers identified by the mito community, leveraging their established relationships with patients.
- Educate health professionals such as GPs, dentists, and other practitioners, to equip them with information about mito and clinical trials and referral pathways to Mito Foundation that can then provide information about clinical trials. Suggestions included creating informational booklets for distribution.
- Utilise social media to promote clinical trial opportunities and increase visibility.
- Advocate through community representatives to spread awareness within the mito community.
- Develop a clinical database that supports both self-enrolment and active recruitment for clinical trials.
- Use marketing strategies to make information about clinical trials more engaging and accessible beyond traditional scientific communication. One community member suggested, *"think like marketers and not scientists when it comes to getting clinical trial information out there. Do the science in the clinical trial, and before that, think like salespeople and marketers."*

Topic 2: Support needs during participation in clinical trials

What would you like to know about the clinical trial?

Community members emphasised the importance of receiving clear, comprehensive, and specific information about clinical trials. Key aspects included:

- comprehensive details about side effects, risks, privacy, and other critical aspects of participation
- clear and unambiguous information about the clinical trial's purpose, procedures and potential implications for participants — this includes information about whether participating in one trial may impact eligibility for future trials.

How can you be supported to make a decision about whether to participate?

Community members shared their preferences for the methods and resources that would help them feel more confident in whether to join a clinical trial. Suggestions included:

- sufficient time to process information before making a decision
- opportunities to hear directly from previous trial participants about their experiences, with the chance to ask questions during information sessions or similar events
- access to professionals who can explain technical information in plain language and answer follow-up questions — participants highlighted the importance of consistency in this point of contact throughout the decision-making process
- accessible information materials in formats such as plain language guides, written documents, and videos, allowing participants to revisit information as needed
- endorsements from trusted specialists, such as neurologists, to build confidence and trust in the trial.

How much travel would be too much?

Community members highlighted that travelling for clinical trials, especially from rural, remote, or regional areas, can be challenging. The need for repeated visits — sometimes as often as fortnightly — was described as "life-altering" for some, often imposing significant financial, physical, and emotional burdens. These visits can also disrupt work, education, and family life, with one community member noting that *"these appointments can consume your entire life."*

To help mitigate the impact of these visits, community members suggested:

- offering financial assistance to cover travel costs
- reducing the frequency of visits or consolidating them into blocks of time to minimise travel
- incorporating online options, such as telehealth, which, while not preferred over face-to-face interactions, would be highly valuable in reducing the need for travel.

Is there any other practical or emotional support that you would like?

Community members suggested the following forms of additional support to help improve their clinical trial experiences:

- mental health and emotional support for participants and their families, including:
    - regular check-ins during participation to address psychological wellbeing
    - care for individuals who are not selected for trials
    - support with balancing work, caring, and other responsibilities
- financial support to help participants and their families manage the costs and challenges of balancing work, travel, and accommodation etc.
- 24/7 access to nursing staff during the trial to provide round-the-clock medical advice and reassurance
- counselling embedded in trials to offer compassionate care, clear communication, and support for understanding complex medical information
- occupational therapy services available before, during, and after the trial

- more consideration for the human experience, such as consolidating procedures like drawing all required blood samples at once to reduce discomfort and disruption
- access to effective medications post-trial, ensuring participants can choose to continue treatments that yielded positive outcomes during the study
- follow-up care to provide ongoing support and monitoring after the trial ends, helping participants transition smoothly
- improved coordination among specialists to streamline the scheduling of routine health care tests and trial-related appointments, particularly for participants living in rural or regional areas, to minimise logistical challenges.

Appendix 1: Qualitative interview guide

Preamble/overview of project: Australia is globally competitive as a preferred location for clinical trials due to our excellent research community, strong healthcare system and diverse population. Despite this, there are challenges and barriers for mito trials. These can apply in similar ways or different ways for trials led by industry compared to trials led by clinician researchers.

Mito Foundation and Research Australia have partnered on a project aiming to increase access to clinical trials in Australia for people affected by mitochondrial disease. An outline of the project is as follows: To inform this project, Mito Foundation and Research Australia are conducting semi-structured interviews of identified key stakeholders who hold knowledge or experience that will be vital in identifying barriers, enablers, and ways forward.

[Where possible] we have provided you with a pre-reading briefing paper that consolidates an analysis of mito clinical trials in Australia, as well as a literature review synthesising existing barriers and enablers to clinical trials more generally in Australia. This informal interview will consist of approximately 10 questions.

[Check for consent to record]

Introduction:

- Can you briefly outline your area of specialty and your experience with clinical trials for mitochondrial disease or other conditions?

Involvement in clinical trials:

- Have you been involved in any clinical trials here in Australia [or in your respective location], either directly or indirectly?
    - *Direct involvement* could include being an investigator on a trial, assisting in recruitment, or trial administration.
    - *Indirect involvement* could include helping patients navigate information about relevant trials or advocating for trials in Australia (or your location).

- Based on your involvement, can you elaborate on your specific role and experiences?

Enablers:

- From your perspective and involvement in mito clinical trials, what is currently working well? What are the key enablers?
    - Participant recruitment and support through clinical trials
    - Clinical trial capacity (i.e. having the clinician researchers, supporting them to have the time and career incentives
    - Clinical data and registries
    - Consumer/patient engagement
    - The regulatory environment

Barriers:

- What are the main barriers you have encountered in mito clinical trials?
    - (This could include challenges in participant recruitment, resource limitations, lack of expertise or collaboration, absence of disease registries, clinical data issues, consumer engagement, or administrative burden.)
- Do you think there are different barriers and enablers between industry-led projects and others?
- Additional probing questions:
    - Are you aware of any clinical trials where industry groups were interested in having sites in Australia, but we did not have the site investigators available? Can you tell me more about what would have needed to be different for those trials to go ahead in Australia?
    - How would you describe the support you receive as a clinician researcher? How could this be improved to increase your capacity (or the capacity of others) to be involved in clinical trials for mito?
    - As a clinician researcher, what is your approach to recruiting participants for clinical trials? Is this different for mito compared to other conditions?

    - Have there been mito clinical trials in Australia that have failed to recruit their expected numbers? What do we know about why this happened?
    - (if applicable) Have you been able to recruit participants from outside metro areas into mito (or other) clinical trials? Or interstate? What has enabled this and what could be improved?
    - Do you think there are different barriers and enablers between industry-led projects and others?
- **Consensus building:** As part of this project, Mito Foundation and Research Australia will be hosting a workshop at the end of the year as part of the AussieMit conference to share findings and build consensus on next steps. What considerations should we keep in mind when attempting to build consensus across the sector?
- **Implementation challenges:** Are there any specific implementation challenges or considerations that you think we should also be aware of?
- **Additional stakeholders:** Who else do you think needs to be included in this conversation?

Other possible questions (collaboration and partnerships):

- Can you provide examples of successful partnerships and collaborations in clinical trials and what made them effective?
- What role does data sharing play in effective clinical trial access and management?
- What innovations or technological advancements do you see as important for mitochondrial disease research and clinical trials?
- What is your view on the role of organisations such as Mito Foundation in driving change in access to clinical trials? (consider probing for roles related to providing funding, central coordination, consumer engagement, advocacy related to government/regulatory issues and funding)

Appendix 2: Mito community survey questionnaire

Title: Increasing clinical trial activity in mitochondrial disease in Australia and New Zealand

1. **Participant information sheet**

We are inviting you to take part in a short survey to help us understand your views and experiences related to clinical trials and patient registries. Your input will provide valuable insights to guide improvements in these areas by helping us decide priorities for the clinical trials action plan.

What is the clinical trials action plan?

Clinical trials are research studies that test the safety and effectiveness of medical treatments or devices. Participation can offer access to new therapies and help advance medical knowledge.

Patient registries are databases that collect and store information about people with specific conditions. This can help to improve what is known about the condition and connect people to research projects (including clinical trials).

The *clinical trials action plan* is a joint project between Research Australia and Mito Foundation. It aims to improve access to clinical trials for the Australians and New Zealanders who are impacted by mitochondrial disease (mito). By gathering your input, we can ensure that this plan addresses the needs and priorities of the Australian and New Zealand mito community.

Why is this survey important?

Your feedback will help us identify ways to increase the number of clinical trials for mito in Australia and New Zealand and make it easier for the mito community to participate in clinical trials.

Who can take part?

This survey is open to anyone in the mito community who lives in Australia or New Zealand. This includes:

- People who have a diagnosis of mito
- Parents, spouses, family members, or friends who support or have supported someone with mito
- People who have supported someone with mito who has since passed away.

How long will it take?

The survey will take around 10 – 15 minutes to complete.

Is it anonymous?

Yes, your responses will be anonymous, and all information will be treated confidentially in accordance with the privacy policies of Mito Foundation and Research Australia. Results from the survey will be published in a way that does not identify you.

Thank you for your time. Your participation is voluntary, and your insights will help make a difference in the future of clinical trials for mito in Australia.

Contact us. If you have any questions, please contact:

Dr Isabel Lopez Sanchez

Research Manager, Mito Foundation

Email: isabel.lopez@mito.org.au

2. Questionnaire

About you

1. Please select the statement that best describes you. (Choose all that apply)*

- I have mito or a suspected diagnosis of mito
- Someone I know has/had mito or a suspected diagnosis of mito. (E.g., family member, someone I care or used to care for etc.)

2. How would you describe your diagnosis of mito? If you do not have mito yourself, answer for the person you provide(d) the **most** care for. (Choose one)*

- Experiencing symptoms and suspect mito
- Undergoing tests with health professionals to confirm or rule out mito
- Clinical diagnosis of mito

- Genetic diagnosis of mito
- Prefer not to say

Awareness and participation in clinical trials

As a reminder, *Clinical trials* are research studies that test the safety and effectiveness of medical treatments or devices. Participation can offer access to new therapies and help advance medical knowledge.

3. On a scale of 1 to 5, how aware are you of opportunities to participate in clinical trials for mito or related conditions?
    1- Not aware at all
    2- Slightly aware
    3- Moderately aware
    4- Fairly aware
    5- Very aware
4. What are your main sources of information about clinical trials? (Select all that apply)*

- My health care team (for example, doctors, nurses and allied health professionals)
- Other mito community members (for example, other people with mito, their carers and/or family members)
- Through interactions with patient organisations and service providers (for example, mito organisations like Mito Foundation)
- Online (for example, through a Google search)
- Not applicable/ I don't get information about clinical trials
- Other sources (please specify)

5. Have you or the person you know with mito ever participated in clinical trials? (Select one)

- Yes, one or more
- No, applied but not eligible
- No, but interested to participate in the future
- No, and not interested to participate in the future
- Unsure

6. Imagine you, or the person you know with mito, are considering participating in a clinical trial. How important are the following reasons when deciding to participate? (Choice matrices)*

Reason	Not Applicable	Not Important	Somewhat Important	Very Important
So that I can learn more about mito and my health condition(s)				
So that I can access better treatment options that are only available in clinical trials				
So that I can access better health care than what I can get outside of clinical trials				
So that I can help to improve quality of life for others in the mito community				
Because I don't see a downside to participating				

7. Imagine you, or the person you know with mito are considering participating in a clinical trial. How important are the following reasons when deciding not to participate? (Choice matrices)*

Reason	Not Applicable	Not Important	Somewhat Important	Very Important
Being uncertain about whether I would be eligible				
Don't have enough information or there is too much complicated information				

Concerns about potential risks and side effects that could worsen symptoms				
Concerns about the credibility or reliability of health professionals and researchers				
Worried about receiving a placebo (a treatment that has no effect) instead of the actual treatment				
Participation would be too demanding given how mito impacts me/them (e.g. energy levels)				
Don't have enough time to participate due to other commitments (e.g., work, education, medical appointments)				
Can't afford to participate (e.g., due to time off work)				
Live too far away to participate				

8. Please share more details on your answers to questions 6 and 7 here. This can include other reasons for participating or not participating in clinical trials that are important to you but are not included above. (optional)

Free text box

Awareness and participation in patient registries

As a reminder, *Patient registries* collect and store information about people with specific conditions. This can help to improve what is known about the condition and connect people to research projects (including clinical trials).

9. How aware are you of the following registries, and have you, or the person you know with mito joined any of them?* (Choice matrix)

Patient registry	Unsure	Not aware	Aware, but not joined	Joined
Mito Registry (Mito Foundation)				
The North American Mitochondrial Disease Consortium (US National Institutes of Health)				
GENOMIT (E-Rare Programme 2015 and the European Joint Programmes on Rare Diseases (EJP RD) 2020 and 2023)				
mitoSHARE (United Mitochondrial Disease Foundation, USA)				
LHON registry (Royal Victorian Eye and Ear Hospital, Melbourne)				

10. If you or the person you know with mito has joined any other patient registries, or are aware of them, please provide details below. (optional)

Free text box

11. Tell us about your main reasons for choosing to join (or not to join) a patient registry?*

Free text box

Making clinical trials for mito better

12. What kinds of information or resources would help you better understand clinical trials and opportunities to participate?

Free text box

13. What other ideas do you have for how clinical trials for mito can be made easier to join and participate in?

Free text box

Appendix 3: Clinician and researcher survey questionnaire

Title: Increasing clinical trial activity in mitochondrial disease in Australia and New Zealand

1. Participant information sheet

Thank you for your interest in this survey. We are inviting healthcare professionals and researchers to share their experiences and perspectives on clinical trials related to mitochondrial disease (mito) and similar conditions in Australia. The survey aims to gather insights to help to develop a clinical trials action plan for mito in Australia and New Zealand.

What is the clinical trials action plan?

The *clinical trials action plan* is a joint project between Research Australia and Mito Foundation. It aims to improve access to clinical trials for the Australians and New Zealanders who are impacted by mito. Your expertise and experience will help us ensure that this strategy promotes efficient trial recruitment, optimises resources, and strengthens collaboration between researchers, clinicians, and other key stakeholders.

Who can take part?

We are inviting professionals involved in or may be interested in clinical trials for mitochondrial disease and related conditions, including:

- Clinician researchers
- Clinicians including allied health professionals
- Clinical trial coordinators and other professionals involved in clinical trials

How long will it take?

The survey will take around 10 – 15 minutes to complete.

Is it anonymous? Yes, our responses will be anonymous, and all information will be treated confidentially in accordance with the privacy policies of Mito Foundation and Research Australia. Results from the survey will be published in a way that does not identify you.

Thank you for your time. Your participation is voluntary, and your insights will help make a difference in the future of clinical trials for mito in Australia and New Zealand.

Contact us. If you have any questions, please contact:

Dr Isabel Lopez Sanchez

Research Manager, Mito Foundation

Email: isabel.lopez@mito.org.au

2. Questionnaire

Background information (this section for all participants)

1. Please indicate your primary role. (Select best option)*

- Clinician researcher
- Member of clinical trials team(s), but not an investigator
- Other health care professional involved in the care of mito patients

2. Where do you primarily work? (Dropdown fields)

Locations: New South Wales, Victoria, Queensland, South Australia, Western Australia, Tasmania, Northern Territory, Australian Capital Territory, Other Territories, New Zealand
Setting: Public hospital / Private practice / both public hospital and private practice

3. Who do you primarily work with? (Select one)

- Adults
- Children and adolescents (paediatrics)
- Both adults and children

Your involvement in clinical trials (this section for all participants)

4. Have you been involved in clinical trials (as a clinical investigator or member of clinical trial team) in Australia and/or New Zealand? (Select one)*

- Yes, for mitochondrial disease (mito)
- Yes, but only for non-mito conditions

- No, I have not been involved in clinical trials in Australia and/or New Zealand.

5. Please indicate how much each of the following factors will impact **your ability to become involved in or run clinical trials for mito in the future**. Select the option that best describes the impact of each factor. * (Choice matrix)

Factors	Not at all	Somewhat	Moderately	Very much	Extremely
Workload/Time: I have limited availability due to clinical or other professional responsibilities.					
Funding: I lack sufficient financial resources or incentives to support my involvement in clinical trials.					
Institutional Support/Resources: I have insufficient support from my institution, including administrative assistance and necessary resources.					
Interest: I have limited personal or professional interest in the specific trial or research area.					
Training and experience: I have insufficient access to the training, experience, or					

qualifications needed to participate in or lead clinical trials.					
Regulatory and compliance burden: I have difficulties navigating the ethical approvals, legal requirements, and compliance issues.					
Collaboration opportunities: I have limited opportunities for collaboration with industry, academia, or other stakeholders.					
Patient access: I have challenges accessing a sufficient patient population for a trial.					
Geographical location: I have issues related to proximity to trial sites or major medical centres, which affects my ability to be involved in clinical trials					

Referrals into clinical trials (this section only for those who have identified themselves as 'clinical investigators' or 'other healthcare professionals' in Q1)

This section focuses on how you, as a healthcare professional, may refer patients with mito to clinical trials.

6. Which of these factors affect your decision to recommend clinical trials for mito to your patients? (Select all that apply)

- I am not aware of any clinical trials for mito

- I don't think my patients (and their carers) have the time or resources to participate
- I don't have enough time to support families during the clinical trials
- I don't think the clinical trials will improve my patient's outcomes or I have safety concerns
- I don't have adequate information about the clinical trials available
- Other (please specify below)

6a. Which other factors affect your decision to recommend clinical trials for mito to your patients?

Recruitment for clinical trials (this section only for those who have identified themselves as 'clinical investigators' or 'member of clinical trial team' in Q1)

7. When you are recruiting patients into clinical trials, which of the following strategies have you found most effective? (Choice matrix)

Strategy	Not applicable	Not effective at all	Slightly effective	Effective	Very effective
Contacting existing patients (those in your own clinic or hospital)					
Reaching out to other specialists (directly or through other promotion)					
Patient registries					
Social media and online platforms					
Working with patient organisations on outreach and/or referrals					

8. Are there any other recruitment methods you have found effective for clinical trials? Please describe them. (Optional)

Free text box

Enablers and barriers for mito clinical trials *(this section for all participants)*

Below is a list of factors related to mito clinical trials in Australia and New Zealand. Please refer to this list to answer the following 2 questions.

- Infrastructure including access to the workforce, spaces, equipment needed to run the trial
- Funding and resources
- Collaboration and partnerships between different stakeholders (researchers, clinicians, pharmaceutical companies, patients and patient organisations, government)
- Regulatory and approval processes
- Training and experience of clinical trial workforce
- Patient recruitment pathways
- Trial design and methodologies
- Support systems for participants (e.g., financial, travel, psychosocial)
- Patient engagement
- Other (please specify in the questions below)

9. From the list above, please select the top 3 aspects that you think are currently working well for mito clinical trials in Australia and New Zealand and could be further developed. Explain why these aspects are effective and how they could be built upon:

Factor 1: Explanation:
Factor 2: Explanation:

Factor 3: Explanation:

10. From the same list, please select the top 3 challenges or barriers that in your opinion are currently faced in mito clinical trials in Australia and New Zealand. Explain why these are barriers and suggest ways to address them:

Factor 1: Free text
Factor 2: Free text
Factor 3: Free text

Priorities for the clinical trials action plan *(this section for all participants)*

Below we have a list of focus areas that have been identified as potentially important for the clinical trials action plan to address. The plan aims to improve the clinical trial system for mito and access to these trials for the mito community in Australia and New Zealand.

- **Increasing research funding**: This might include Government funding more clinical trials for mito or more philanthropic funds directed into clinical trial research.
- **Improving support for clinician researchers:** This may include funding for clinical trial coordinators or helping to build partnerships with existing clinical trial units/centres.
- **Growing the clinical research workforce:** This may include opportunities for mito clinicians to train with research groups in Australia or internationally.
- **Making patient recruitment easier:** This may include strengthening clinical registries and referral networks between mito specialist services

- **Fostering collaborations:** This may include establishing and supporting a formal clinical trial network for mito
- **Enhancing patient engagement and retention**: This may include understanding what can make participation easier for people with mito and seeking to design trials that accommodate these needs.
- **Increasing mito community awareness and education**: This may include education campaigns to improve the knowledge and understanding of clinical trials by people with mito and their families
- **Improving regulatory and governance processes**: This may include simpler approval processes or increased tax incentives for the pharmaceutical industry

11. In your opinion, which 3 focus areas are most important for the clinical trials action plan? please select the top 3 actions and explain why they matter most.*****

Choice 1 (Free text box)
Choice 2 (Free text box)
Choice 3 (Free text box)

12. If you have any specific ideas or suggestions on how the Mito Foundation could contribute to your top 3 choices, please let us know here.*****

Free text box

Appendix 4: Industry representative survey questionnaire

Title: Increasing clinical trial activity in mitochondrial disease in Australia and New Zealand

1. **Participant information sheet**

Thank you for considering our survey. We are seeking insights from pharmaceutical companies, CROs, and consultants involved in therapeutics to understand their experiences and priorities in the clinical trial landscape for mito in Australia and New Zealand. We welcome multiple responses from the same organisation, as different perspectives are valuable for understanding various aspects of the clinical trial landscape.

The survey will take around 10 minutes to complete. Responses will be anonymous, and all information will be treated confidentially in accordance with the privacy policies of Mito Foundation and Research Australia. Results from the survey will be published in a way that does not identify you.

What is the clinical trials action plan?

The clinical trials action plan is a strategy to enhance the clinical trial system for mito and improve access for the Australian and NZ mito communities. By gathering your input, we aim to develop a plan that addresses the unique needs and challenges of the Australian/NZ context. Your expertise will help ensure this strategy improves trial recruitment, optimises resources, and strengthens collaboration between researchers, clinicians, and other key stakeholders. Ultimately, our goal is to enhance access to high-quality clinical trials for the mito community.

Thank you for your time! Your participation is voluntary, and your insights will help make a difference in the future of clinical trials for mito in Australia and New Zealand.

Contact us:

If you have any questions, please contact:

Dr Isabel Lopez Sanchez

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2. Questionnaire

Background information

1. Company name: _____

   [We are asking for the name of your company or organisation solely to ensure diversity in responses and to avoid overrepresentation from any single source. This information will be used only for internal analysis and will not be shared or linked to any individual respondent.]

2. Which of the following best describes your role within the pharmaceutical industry? (Select best fit)*

- **Medical affairs**
- **Regulatory affairs**
- **Marketing or sales**
- **Patient engagement**
  - **Clinical research** (including working with and within a contract research organisation (CRO))
  - **Other** (please specify)

Involvement in mito clinical trials

3. How would you describe your company's involvement in clinical trials for mito? (Select all that apply)*

- Has sponsored/ is planning to sponsor clinical trial(s) for mito
- Has sponsored/is planning to sponsor clinical trial(s) for related rare genetic condition(s)
- Is not planning to sponsor a clinical trial for mito
- Unsure

Factors impacting clinical trial sites in Australia and New Zealand

4. Out of these factors, what key considerations does, or would your company prioritise when deciding to establish clinical trial sites in Australia and/or New Zealand? (Choice matrix)*

Factors	Essential	Important, not essential	Not important	Unsure/ Not Applicable
Availability of qualified sites and investigators				
Access to a relevant patient population				
Streamlined regulatory and ethical requirements				
Availability/quality of clinical data and patient registries				
Cost and logistical advantages				
Favourable local market conditions				
Partnerships and collaborations with local organisations				
Previous experience and reputation in the region				

5. Please provide more details on any of the factors listed above, or mention any additional considerations that are particularly relevant to your company when establishing clinical trial sites? (Optional)

Free text box

6. Please rate the following factors based on how they currently act as barriers or enablers when setting up clinical trial sites for mito or related conditions in Australia. (Select one option per factor)*

Factor	Strong enabler	Enabler	Barrier	Strong barrier	Unsure/ Not applicable
Availability of qualified sites and investigators					
Access to patient population(s)					
Regulatory and ethical requirements					
Availability/quality of clinical data and patient registries					
Cost and logistical considerations					
Local market conditions					
Partnerships and collaborations with local organisations					
Previous (company) experience and reputation in the region					

7. Please use the text box below to explain your responses above and/or include your reflections on additional factors not included above. (Optional)

Free text box

8. Considering the potential benefits and risks of setting up clinical trial sites, how do you think Australia compares to other countries?*

Free text box

Working with Mito Foundation

Mito Foundation is the main patient organisation for the mito community in Australia. Its current work includes providing support services, educating health

professionals about mito, funding research projects and advocating for systemic changes to benefit the mito community.

9. Looking ahead, how would you like to collaborate with the Mito Foundation or other patient organisations? Consider any past experiences you may have had with patient organisations as you respond. (Select all that apply)*

- Enhanced access to patient registries
- Improved recruitment and engagement strategies, including awareness campaigns
- Support with regulatory and research governance issues
- Facilitation of networking opportunities/partnerships
- Working with industry organisations to understand and navigate local registration and reimbursement processes
- Provide expertise and guidance on the lived experiences of the Australian mito community
- Other (please specify)

Priorities for the clinical trials action plan

Below we have a list of focus areas that have been identified as important for the clinical trials action plan.

- **Increasing research funding**: This might include Government funding more clinical trials for mito or more philanthropic funds directed into clinical trial research.
- **Improving support for clinician researchers:** This may include funding for clinical trial coordinators or helping to build partnerships with existing clinical trial units/centres.
- **Growing the clinical research workforce:** This may include opportunities for mito clinicians to train with research groups in Australia or internationally.
- **Making patient recruitment easier:** This may include strengthening clinical registries and referral networks between mito specialist services

- **Fostering collaborations:** This may include establishing and supporting a formal clinical trial network for mito
- **Enhancing patient engagement and retention**: This may include understanding what can make participation easier for people with mito and seek to design trials that accommodate these needs.
- **Increasing mito community awareness and education**: This may include education campaigns to improve the knowledge and understanding of clinical trials by people with mito and their families
- **Improving regulatory and governance processes**: This may include advocating for simpler approval processes or increased tax incentives for the pharmaceutical industry

10. In your opinion, which 3 focus areas are most important for the clinical trials action plan? Please select the top 3 focus areas and explain why they matter most.*****

Choice 1 Explanation (optional free text box)
Choice 2 Explanation (optional free text box)
Choice 3 Explanation (Optional free text box)

11. For the top 3 focus areas you selected above, what role do you see the Mito Foundation playing? If you have any specific ideas or suggestions on how the Mito Foundation could contribute to each of these focus areas, please let us know here.

Free text box

12. Do you have any additional comments or suggestions on how to improve clinical trial processes for mito in Australia?

Free text box

References

1. Mito Foundation. Literature review: Understanding the barriers and enablers to conducting clinical trials for mito in Australia. [Internet] Sydney (AU): Mito Foundation; 2025 [cited 2025 Apr 16]. Available from: https://www.mito.org.au/literature-review-clinical-trials-for-mito-in-australia/
2. Mito Foundation. Mito Stories Project [Internet]. Sydney (AU): Mito Foundation; [cited 2025 Mar 26]. Available from: https://www.mito.org.au/mito-stories/
3. New South Wales Government. Kids Advanced Therapeutics [Internet]. New South Wales (AU): New South Wales Government; [updated 2024 Oct 11; cited 2025 Mar 26]. Available from: https://kr.schn.health.nsw.gov.au/our-research/research-enablers/kat