Improving post-diagnosis management and communication for people with mitochondrial disorders

Insights from Mitochondrial Disorder Specialist Services in Australia and people living with mito

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Improving post-diagnosis management and communication for people with mitochondrial disorders: Insights from Mitochondrial Disorder Specialist Services in Australia and people living with mito

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Contents

Summary

Mitochondrial respiratory chain disorders (hereafter mito) are a rare and diverse group of conditions. Mito can affect all ages with childhood presentations tending to be most severe and adult onset milder but chronic. As with many other rare diseases, practices can vary between small, isolated specialist centres.

This report summarises findings from a review of current general management practices in nine specialist mito disorder clinical services in Australia, and focus groups with 20 people with, or who were a parent of a child with mito. We developed detailed graphics combining patient pathway, resources and practices, and quotes from all sources to define elements of best practice. We present recommendations for specialist mito services and anyone involved in the care of people with mito around best practice after a person has been diagnosed:

Recommendations

Specialist mito disorder clinical services are recommended to:

1. Provide a diagnosis letter to the GP. This was reported as standard practice and indisputably useful for people/parents of children with mito.
2. Provide copies of the diagnosis letter to the person or parent. This removes significant barriers to accessing appropriate care.
3. Provide diagnosed people or parents with written information on mito. This assists with recall and is highly valued.
4. Introduce diagnosed people/families to the Mito Foundation. This is an important link for them to access key resources and knowledgeable social support. PDF materials can be downloaded from mito.org.au
5. For diagnosed people at risk of acute episodes: provide a patient-held letter, wallet card and/or emergency management plan, including diagnosis, and clear instruction on which clinician or clinical team should be consulted if the attending doctor is unfamiliar with the condition. This can facilitate timely and appropriate treatment of acute episodes.
6. Identify people with mito through flags or alerts on their medical notes. This can prevent delays through inappropriate triage or assessment for Emergency presentations requiring time-critical treatment.

7. Liaise with health services in regional or remote areas to set up an alert on their system for local people with mito at risk of acute episodes.

8. Consider making a business case for increased specialist clinical capacity so mito specialist teams can be contacted directly for real-time advice in emergency situations. If this is not feasible, identify the appropriate on-call service on the patient's notes (e.g., metabolic, endocrine, neurology).

9. Mito specialist services in collaboration with Mito Foundation and/or researchers, should develop national emergency plan templates for management of different types of mito.

10. For diagnosed people with a low risk of acute episodes, who rely on GPs for their health care, provide a general management plan.

11. Mark up the Mito Foundation infographic for patients/GPs to provide tailored, summarised information and management advice. PDF infographic can be downloaded from mito.org.au

12. Provide a management plan to the patient (or parent) and the GP. This is an important tool to support people with mito to negotiate to receive the care they need from health providers, including other specialist health providers.

13. Provide tailored information in letters for allied health professionals (e.g., exercise physiologists, physiotherapists, dieticians).

Primary Health Networks are recommended to:

14. Consider how to upskill and support GPs who have patients with mito.

Mito Foundation is recommended to:

15. Development of a directory of mito-aware GPs and allied health professionals.

Health services researchers in partnership with clinicians and consumers are recommended to:

16. Collate data on emergency management of patients with mito through survey of patients, audit of emergency records and focus groups or interviews with Emergency Staff. This would allow standardisation of care and identification of areas for improvement.

17. Develop standardised outcome and process measurements for people with mito so helpful practices can be compared and shared across sites, and optimal management be further defined.

Background

Mitochondrial respiratory chain disorders (hereafter mito or mito disorders[1]) are a rare and diverse group of conditions with an incidence for severe mito disorders of 1 in 5,000 births (Thorburn 2004). Most of these disorders present during infancy, with a median survival rate of 12 years (Darin, Oldfors et al. 2001). Childhood presentations tend to be more severe and acute, while adult cases often are milder but chronic conditions. Mito disorders can affect any organ, with highly variable clinical presentations, usually involving multiple systems (Pfeffer and Chinnery 2013).

Mito disorders are diverse and the initial health issues that patients face are variable, usually differing in paediatric and adult-onset forms of the disorder. Clinical features evolve over time, further complicating approaches to management. It is therefore not surprising that the approaches to management can vary considerably from one clinical centre to another. To address this variability, and the possible sub-optimal care that may result, an international consortium of experts developed recommendations for the management of people with mito based on best available evidence and consensus of experts (Parikh, Goldstein et al. 2017; Sue, Balasubramaniam et al. 2021).

A major research project in Australia is developing a rapid genetic diagnostic process for mitochondrial conditions using next generation sequencing technologies (Australian Genomics Mitochondrial Flagship) (Stark, Boughtwood et al. 2019). However, an issue that remains is how best to manage people once a diagnosis has been established. This challenge is commonly encountered by others with a rare disease.

This report summarises findings from a review of current general management practices in nine specialist mito disorder clinical services in Australia, focus groups with 20 people with, or who were a parent of a child with a diagnosed mito condition (Long, Best et al. 2021). We combine the findings into a graphic of patient pathway, resources and quotes from the different sources. From this we make recommendations for best practice and for future research.

Methods

Health professionals from adult and paediatric mito disorder clinical services from hospitals across Australia, including eight services already working together in the Australian Genomics Mitochondrial Flagship project, were invited to participate. Three services saw only adults, four only paediatric and one saw both. The group did not include all expert clinicians providing health care for people with

[1] We note that while the preferred term for consumers is 'mito,' medical specialists commonly use the more exact 'mitochondrial respiratory chain disorders'.

mito but sought to include one representative from each public health service providing mito specialist care in Australia.

Two surveys were completed by the clinical representative from each unique service. The first survey (February 2020) collected details of each participant's service, e.g., number of patients, members of the clinical team. The second survey (October 2020) collected details of current clinical practice on diagnosis of a mito disorder in a patient, asking specifically about communication with General Practitioners (GPs) and specialists, and the resources they provided for patients or parents.

Interviews were then conducted with members of eight of the mito disorder specialist clinics (February – March 2021). Details were elicited from the information provided in the survey about management strategies and resources for diagnosed people, parents and non-specialist health providers.

Focus groups were conducted with 20 participants drawn from five Australian states in June-September 2020: 14 adults with a Mito disorder, three of whom also had a child with a Mito disorder, and six of whom cared for a child with a Mito disorder. Questions elicited experiences of receiving information specific to their condition and management advice after diagnosis.

Ethical approval was given by Royal Children's Hospital Human Research Ethics Committee (61859/RCHM-2020).

Results

A graphic was constructed from the results of the clinician surveys (shown on p8) summarising current practice for specialist Mito services from when a person is diagnosed with a Mito disorder.

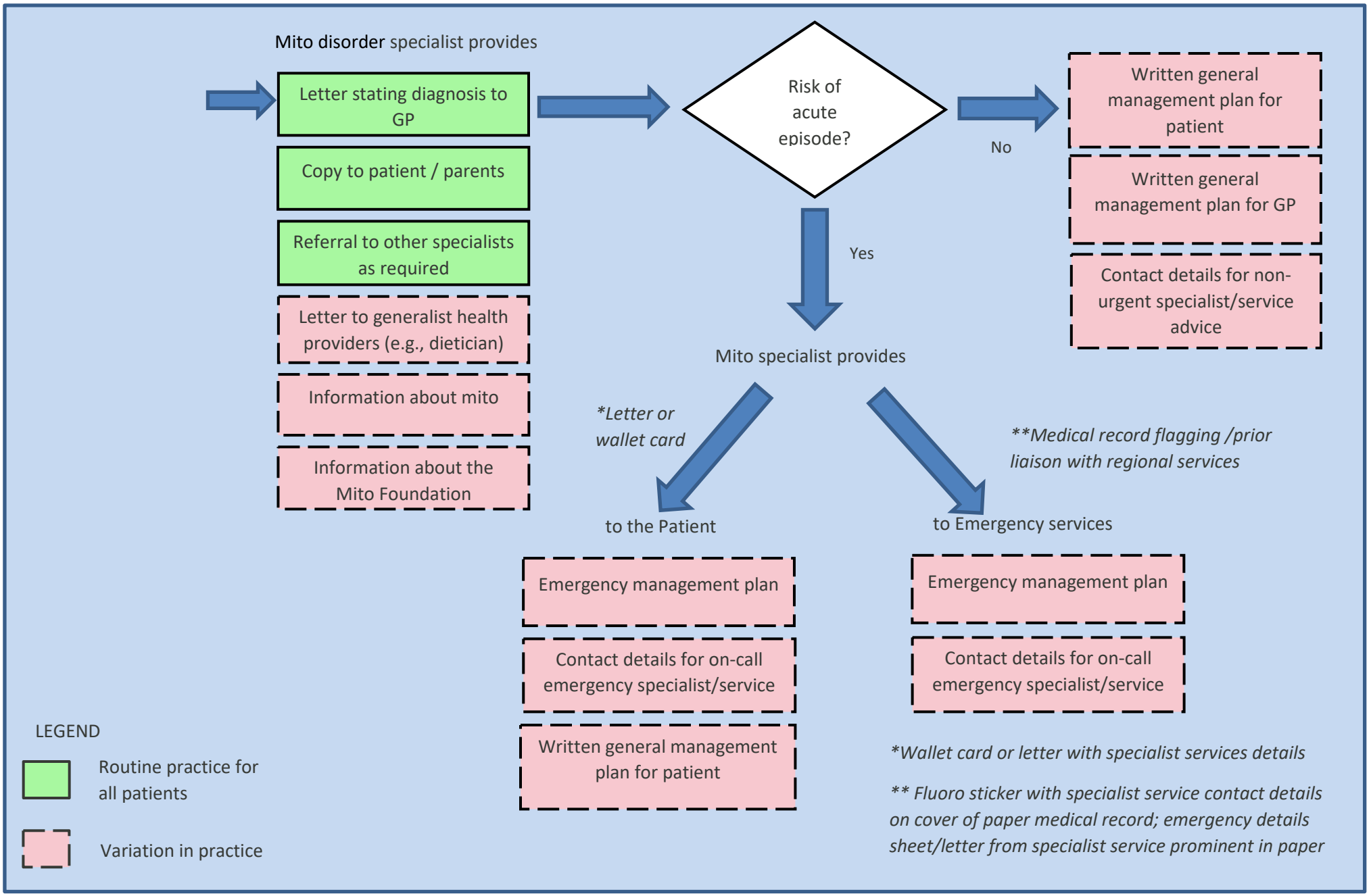
It starts on the top left corner with the person receiving a diagnosis. Resources that are mentioned by Mito specialist clinicians and by focus group participants as being provided at that consult are listed. Resources that all Mito specialist clinicians say are provided are signified by green. Those that are only provided by some services and not others are signified by pink colour and a dotted border.

After diagnosis, the management pathway of the person is split into those people who are at risk of acute episodes needing medical intervention and those that are at a low risk of this. Following the not at high risk ("no") pathway across to the right top corner, resources to assist day-to-day management are listed as reported to us via the Mito specialist clinicians and focus group members. Following the path for people at high risk ("yes"), resources are split into patient held resources to the left, and resources for the emergency clinicians to the right. We note that general management plans are also desirable for this cohort of people but were not specifically mentioned.

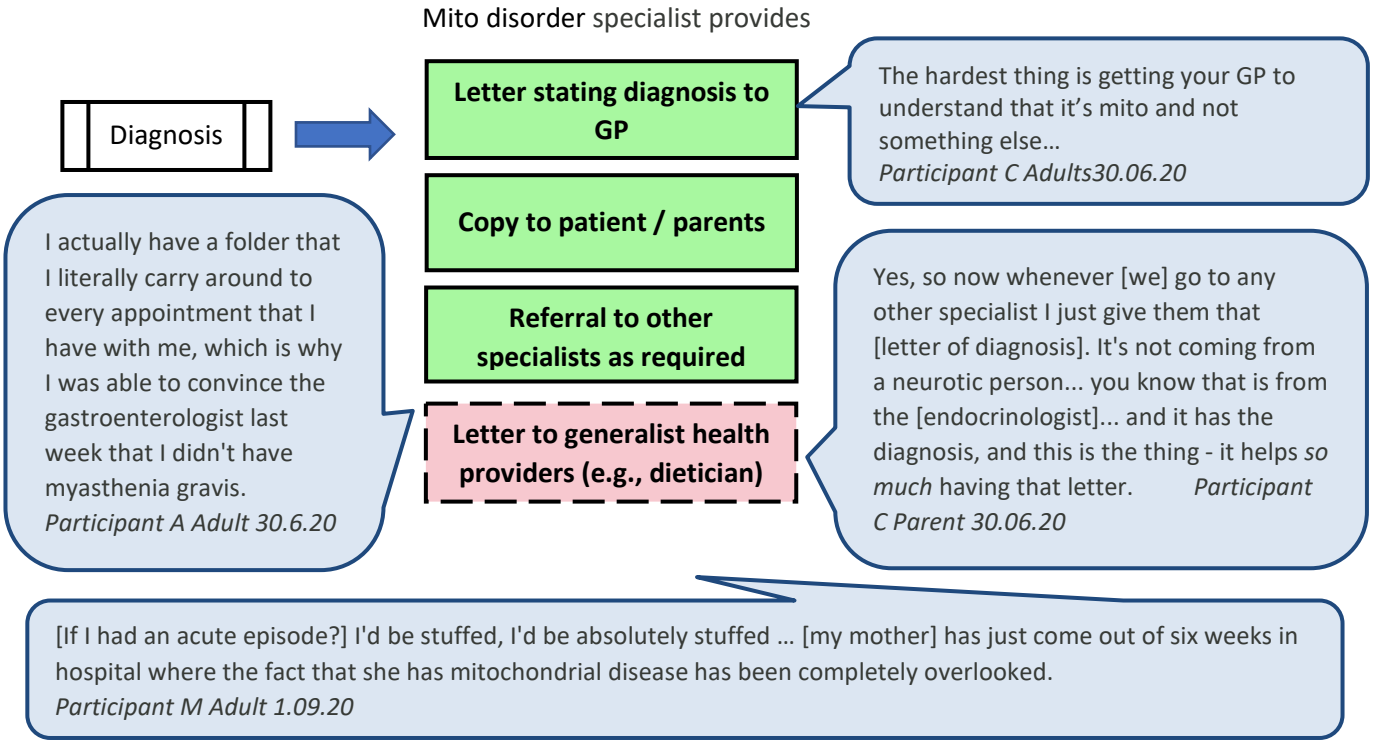
Individual sections of the pathway are examined in the subsequent pages as we focus on segments of the graphic in turn. Quotes from diagnosed people or parents in the focus groups, clinician interviews

and free text survey responses have been added as appropriate. This data is then discussed, and next steps proposed.

Elements of best practice and resources provided by Mito disorder specialist services on diagnosis.



Letter stating diagnosis to the GP, specialists and other generalist health providers with a copy for the patient / parent.



On diagnosis, mito disorder specialist services reported they provided their patients with a letter to their GP and referral letters to any medical specialist services they required, clearly stating the diagnosis of a mito disorder. All clinics stated that they provided a copy to the patient or parent. Less common was the routine provision of a letter for generalist services such as dieticians, or physios.

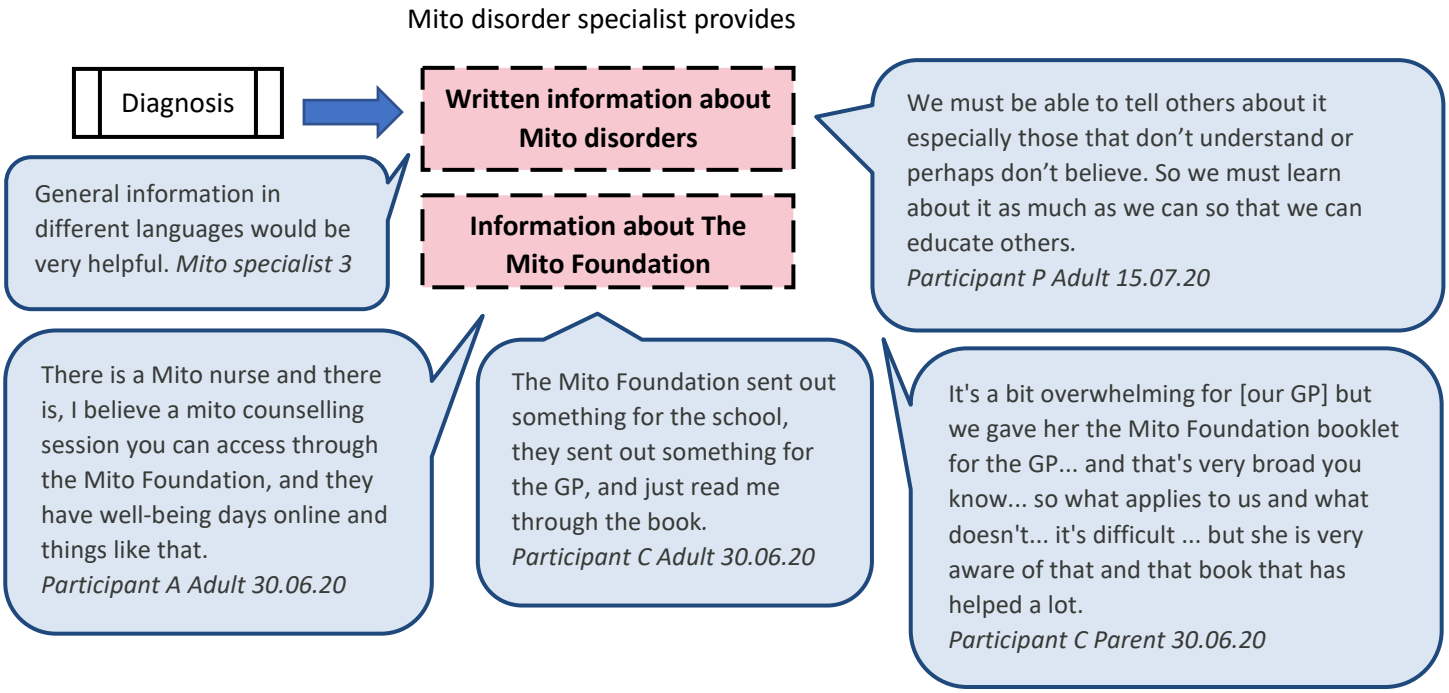
Focus group participants noted the huge utility of a letter stating their diagnosis. Though not a failsafe, this 'evidence' gave them credibility ("It's not coming from a neurotic person") and helped them access the appropriate care.

Recommendations for specialist mito services

1. Provide a diagnosis letter to the GP. This was reported as standard practice and indisputably useful for people /parents of children with mito.

2. Provide copies of the diagnosis letter to the person or parent. This removes significant barriers to accessing appropriate care.

Information about Mito disorders and connection to the Mito Foundation



There was no doubt that information from the mito disorder specialists delivered face-to-face was highly valued by patients, however, it could not cover all the issues, and it was difficult afterwards to remember all that was said. Written information was provided by six of the nine sites, with specific information tailored to their case. Some provided written information if appropriate on how to apply for NDIS support. Most clinics also noted that on diagnosis, patients have a session with a genetic counsellor who may also provide materials.

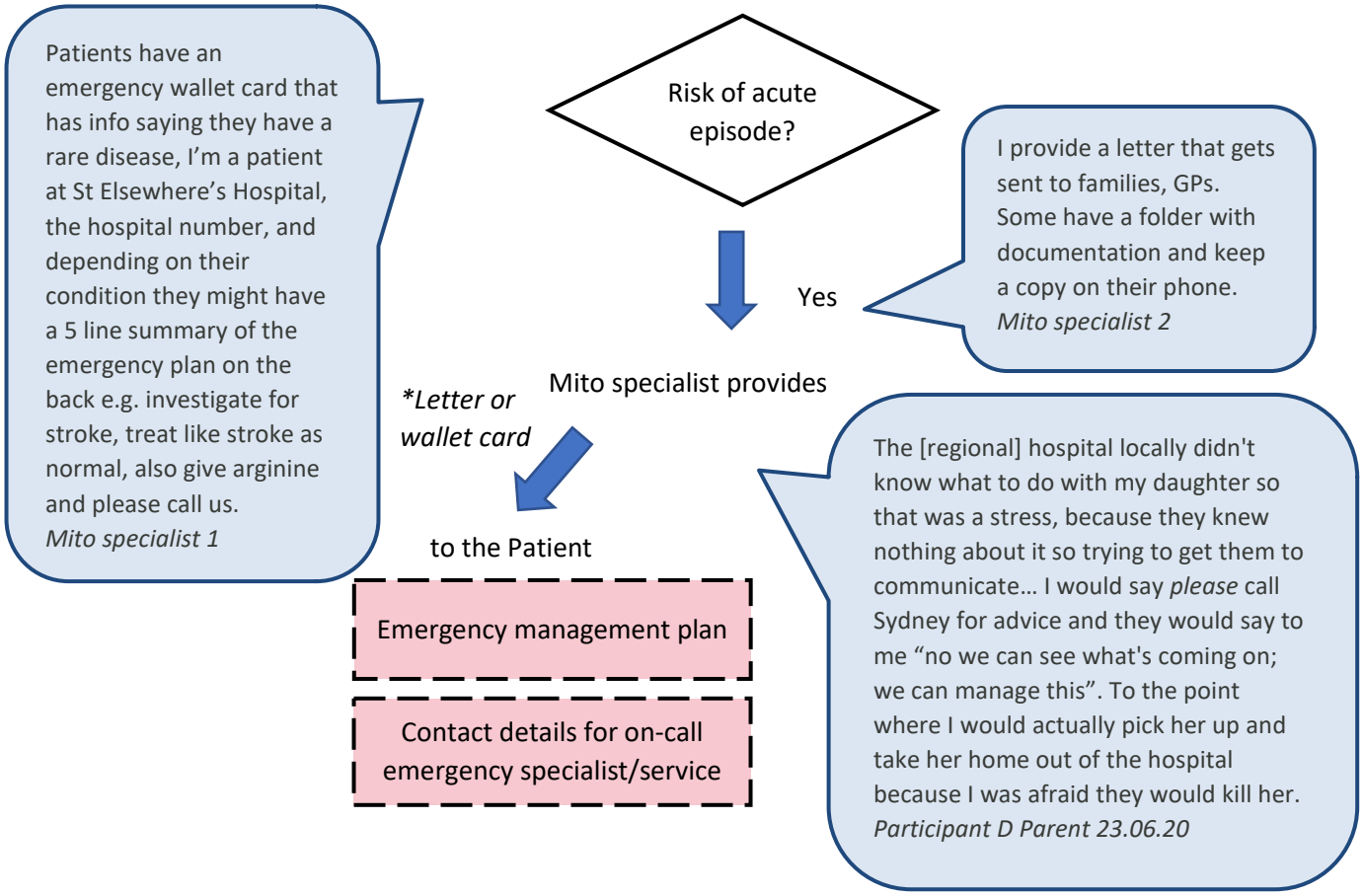
Focus group participants spoke highly of the resources available from the Mito Foundation especially those resources that assisted general health providers, schools and workplaces understand the condition. Resources for GPs can be found at: https://www.mito.org.au/maybe-its-mito-gp/. It was also noted that there was a lack of written resources in other languages.

Recommendations for specialist mito services

3. Provide diagnosed people with written information on mito. This assists with recall and is highly valued.

4. Introduce diagnosed people/parents to the Mito Foundation. This is an important link for them to access key resources and knowledgeable social support. PDF materials can be downloaded from mito.org.au

Patient resources for acute episodes

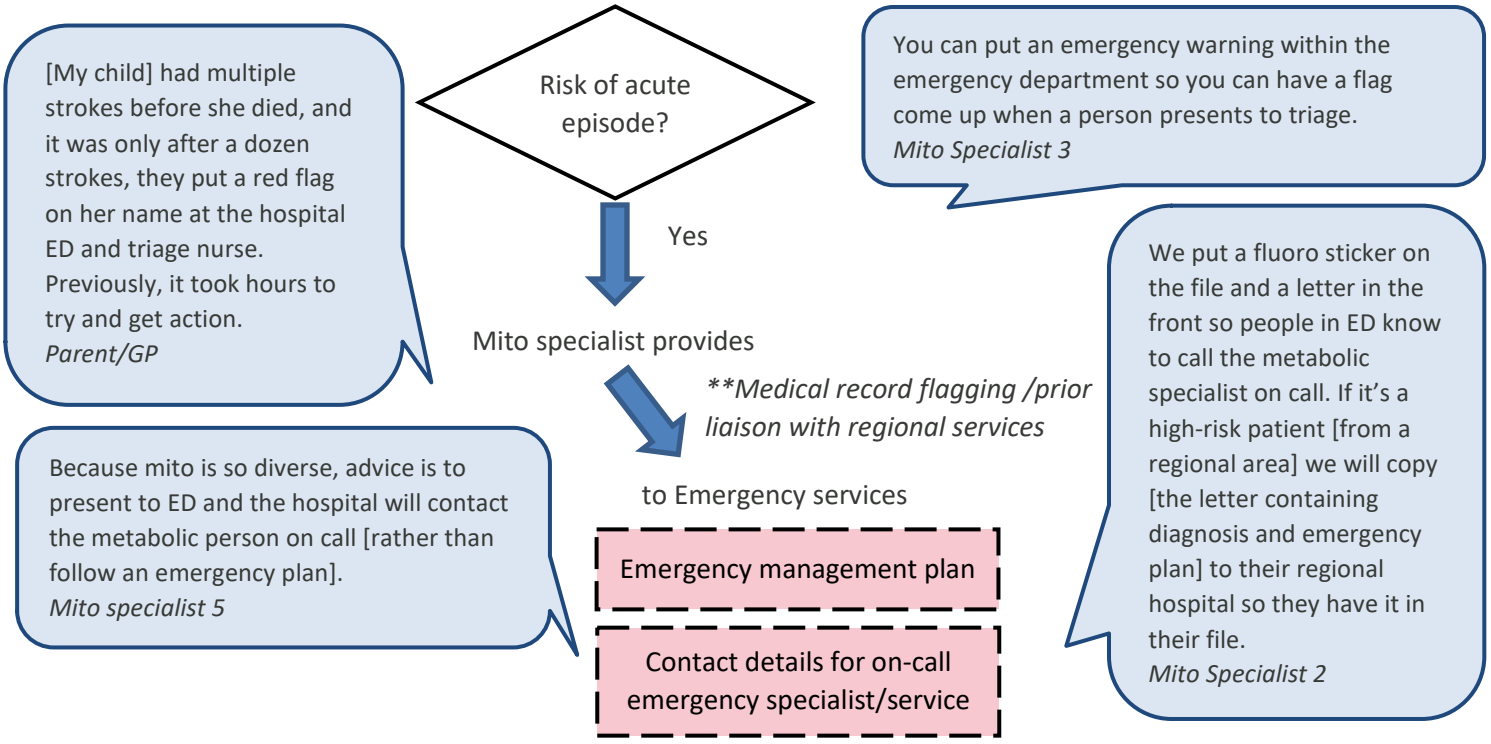


For the subset of people with mito who are at risk of acute episodes, there were two main approaches reported by the mito disorder specialist services. The first approach was to give a resource to the patient or parent. Most, but not all provided a letter, wallet card or other document to the patient or parent to show to the emergency staff on presentation. This again facilitated access to appropriate, timely treatment by giving credible evidence of a diagnosis of a mito disorder and contact details of the appropriate specialist; either the actual mito specialist team or a named appropriate on-call specialty (e.g., metabolic, neurology).

Recommendations for specialist mito services:

5. For patients at risk of acute episodes: provide a patient-held letter, wallet card and/or emergency management plan, including diagnosis, and clear instruction on which clinician or clinical team should be consulted if the attending doctor is unfamiliar with the condition. This can facilitate timely and appropriate treatment of acute episodes.

Clinician resources for acute episodes



The second approach for the subset of people with mito who are at risk of acute episodes is to develop a mechanism that allows the triage nurse or attending doctor not familiar with rare mito disorders to identify these at-risk individuals. Identification is through flags or alerts in electronic systems, or stickers or letters in the front of paper files. Some services supplied a one-page summary emergency management plan to guide assessment and management; others included emergency care in a standard complex management plan. Most also provided a link to the mito specialist service or appropriate on-call team to call for real-time advice (see more below). This flagging was most often and most reliably done in the hospital associated with the mito disorder specialist service (facilitated by the shared medical record). A similar identification prompt (placed on the patient's notes) was reported by some mito disorder specialists, who negotiated for people who live away from the specialist mito service and who may need to present to a regional or rural hospital.

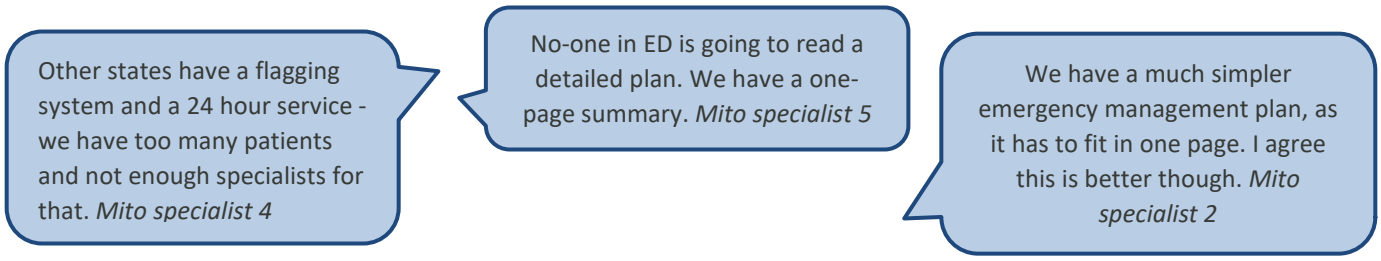
Recommendations for specialist mito services:

6. Identify people with mito through flags or alerts on their medical notes. This can prevent delays through inappropriate triage or assessment for Emergency presentations requiring time-critical treatment.

7. Liaise with health services in regional or remote areas to set up an alert on their system for local people with mito at risk of acute episodes.

Different approaches to Emergency management plans based on capacity

"Provide diagnosed patients (especially those at risk of acute episodes or who have recurrent episodic crises) or their caregivers/ parents, with an emergency management plan for their MD including diagnosis, clinical symptoms, organ-specific symptoms, baseline cardiorespiratory function, special nutritional needs, medications, allergies, and contraindicated therapies. Include guidelines for management during critical illness or emergency along with contact details for the relevant MD physician. This document should be easily available in the patient's records and widely circulated amongst all teams managing the patient. It may be useful to have the patient's records labelled as "Mitochondrial disease" on their patient chart. Include the management plan in the patient's My Health Record file if it has been established." (Sue, Balasubramaniam et al. 2021)



Ways of dealing with acute presentations were closely linked to the capacity of the mito specialist service that cared for the patient. For services dealing with small numbers of patients at risk of an acute episode, flags that identified the patient included: contact details for either the treating mito disorder specialist, or an on-call specialist service (e.g., metabolic registrar; Queensland's Lifespan Metabolic Medicine Service). This was to encourage the attending medical officer to contact the service for real-time advice on how to proceed. Since mito disorders can affect a range of organs and systems, naming the appropriate on-call speciality (e.g., endocrine, neurology) can save confusion and delays connecting with the appropriate expertise.

All specialist mito disorder clinicians agreed that specialist on-call services were only manageable for relatively small cohorts of patients. The point was frequently made that patients with mito make up only a fraction of the case load for most metabolic or neurogenetic specialists. If a similar on-call service was offered for all patients with a complex or rare condition this quickly becomes untenable with the limited resources available at most centres. For these patients a written emergency management plan was considered best practice.

Recommendation for specialist mito services:

8. Consider making a business case for increased specialist clinical capacity so mito specialist teams can be contacted directly for real-time advice in emergency situations. If this is not feasible, identify the appropriate on-call service on the patient's notes (e.g., metabolic, endocrine, neurology).

Suggested new resources

Not captured as part of the graphic, we also asked Mito specialists what resources they thought were missing or that would be useful for patients.

> [I'd like to see a] nationwide standard template for common diagnoses like for MELAS.
> *Mito specialist 3*

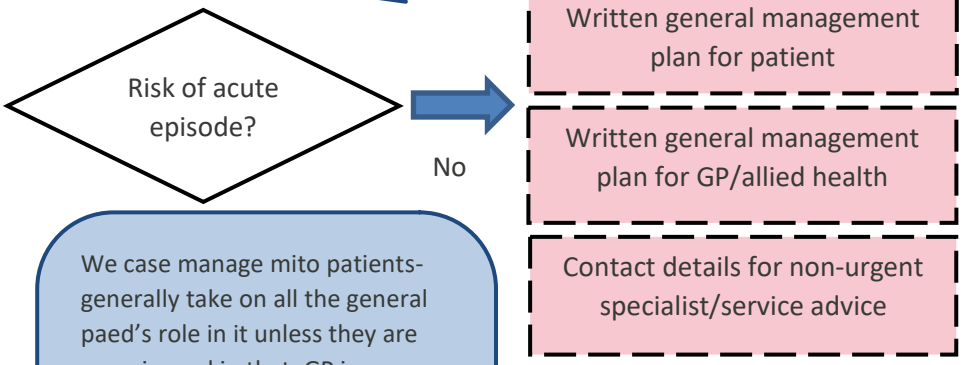
> [Writing an emergency management plan] takes considerable time ... It would be good to have uniform guidelines and a management template.
> *Mito specialist 4*

Recommendation for mito specialist services:

9. Mito specialist services in collaboration with Mito Foundation and/or researchers, should develop national emergency plan templates for management of different types of mito.

Resources for general management

The GPs, I'm going to say, are almost useless. We've been turned away several times. We'll go to the GP for little things like - I know metabolically he's pretty stable, I've had him for 7 years, so I know what unstable looks like. I need to know whether he's got an ear infection or a UTI. And they'll be like "no you have to go to the emergency." *Participant F Parents 03.07.20*



[The MRCD specialist] was the only one who really understands … in hindsight I would have loved if they could have educated... had an education zoom meeting with the therapists and the GP and the other people who were very dominant in [my child's] life to ... show them that this is what mito looks like, this is how it's different, you can't do intensive rehab with mito children. You can't do bursts of five days of therapy. You can't, it doesn't work that way… getting that across was quite challenging sometimes. *Participant P Parents 03.07.20*

We case manage mito patients- generally take on all the general paed's role in it unless they are experienced in that. GP is more peripheral and important for mental health and family and for milder presentations. We send a clinic letter summarising what's happened in the past 3-6 or 12 months and update the diagnosis and problem list and medication list - goes to GP or other specialists. *Mito specialist 6*

…with the GP and everything I've had to tell them read the last letter [from MRCD specialist]] ... and then they say yeah, I need to read that. Like it's not an instant click that there's something else they need to look at. Same with the anaesthesiologist. You have to constantly remind them about it. Don't forget about that, don't forget about that. *Participant C Adults 30.06.20*

Some people with complex and high-risk mito disorders report that they never see their GP and receive all their care from the specialist service or emergency department. Those who have a lower risk of acute episodes may rely only on a GP for day-to-day general management. Not all mito disorder specialist clinics provided a letter or management plan to assist with this. Patients who did get a letter found it helpful for highlighting key concepts (such as fatigue) and for reminding the GP to consider the presenting problem in the context of the mito disorder diagnosis. As seen previously, resources for GPs from the Mito Foundation were also noted as useful guides.

Recommendations for mito specialist services

10. For low-risk patients who rely primarily on GPs for their health care, provide a general management plan.

11. Mark up the Mito Foundation infographic for patients/GPs to provide tailored, summarised information management advice to the patient. PDF infographic can be downloaded from https://www.mito.org.au/maybe-its-mito-gp/

Approaches for patients with additional social or other needs dependent on capacity

> Parents can directly contact the metabolic consultant if something is wrong. This gives patients reassurance. Then they can tell the parents over the phone if their child requires a GP or hospital care. *Mito specialist 3*

Some of the mito disorder specialist services offered selected parents of paediatric patients direct access to them, e.g., a mobile number or email address for non-urgent questions. If a person was unsure what to do (e.g., if a child was vomiting) they could ring to find out what action to take. Those that offered this access said it was sustainable only if: (a) there was capacity in the system to match the number of patients, (b) parents were carefully selected based on an assessment of need, with a lack of social support, low health literacy or low self-efficacy being key considerations, (c) need was also assessed on severity of the condition and potential for time critical management advice, (d) inappropriate calls were addressed in a firm way. We make no recommendation, as we recognise this is not feasible for large services and may be inappropriate in others.

Resources for negotiating care

I've actually struggled to find a GP that is willing to take on mito. I've had two doctors turn around and say we're actually not interested in that, we'll manage [child's] other issues… even the current paediatrician we were seeing for [other condition] has made it very clear that mito doesn't come into play with how she treats my child. *Participant M Parents 010920*

I have a new GP and she's great, but I have been educating her and it's difficult. Fortunately, she is prepared to learn. I saw another doctor first and I gave her the [Mito Foundation] booklet [for GPs] and the next time I went back I said did you have any questions about that booklet? And she said "ah, I haven't read it, haven't got time for that." Changed to a new doctor, so it's like doctor shopping in the safest possible way. But this one is really good. *Participant C Adult 150720*

It was not unusual to hear from patients/parents that they had to "shop around" to find a GP, physio or other health professional willing to provide care in the context of their Mito disorder. This highlights the value of a letter or management plan in giving willing collaborators a place to start. It is worth noting that while many rare diseases have comprehensive information available on sites such as *Orphanet*, knowing the exact name of the disease is almost a pre-requisite to access it, as searching by signs and symptoms alone can throw up thousands of misleading hits.

Letters for allied health professionals may need to be different in content compared to letters for other medical specialist or GPs. For example, they may need to address issues around temperature regulation, fatigue, and signposting to the best way to deliver exercise programs to people with mito in terms of muscle growth when addressing physiotherapists.

Recommendations to mito specialist clinics:

12. Provide a management plan to the patient (or parent) and the GP. This is an important tool to support people with mito to negotiate to receive the care they need from health providers, including other specialist health providers.

13. Letters for allied health professionals (e.g., exercise physiologists, physiotherapists, dieticians) will require tailored information.

The consistent message from the focus group participants about GPs who did not have any skills or knowledge around mito disease should prompt some targeted work by Primary Health Networks to upskill staff. People or parents of children with mito would benefit from a Directory of GPs or allied health practitioners knowledgeable about mito disease. Funding could be directed to developing a

Directory or a navigation service. Development of tools or resources that help people or parents of children with Mito advocate for their needs is also a wider recommendation arising from this work.

Recommendation for Primary Health Networks:

14. Primary Health Networks should consider how to upskill and support GPs who have patients with mito.

Recommendation for Mito Foundation

15. Development of a directory of mito-aware GPs and allied health professionals.

Discussion

Current practice in specialist mito clinics, although variable, aligned with what is generally considered high quality care (e.g., communication with GP, consideration of how to manage emergencies). A few areas for attention include providing written information about mitochondrial disorders and introducing every patient to the Mito Foundation. Mito Foundation resources were spoken of highly including assistance with applying for the NDIS, letters for a child's school, information for GPs and links to social support. Resources can be easily downloaded and printed from their website.

Emergency management for the small subset of patients who are risk of an acute episode showed the greatest variation across sites. Identifying patients as having a mito disorder was almost universal although methods varied. Once identified, action pathways differed; at one end of the spectrum, there were instructions given to liaise directly with the treatment team, at the other, a summary emergency plan was given to guide assessment and management.

A comprehensive emergency management plan as recommended in the Australian Patient Care Standards (Sue, Balasubramaniam et al. 2021) was not reported. Some clinicians had developed a tailored summary with specific actions to take for paediatric patients at risk of an urgent acute situation, while others had provided an excerpt of the Australian Patient Care Standards as more general guidance (for less severe presentations). The suggestion of a national template for emergency recommendations for patients with MELAS was met with caution.

A general management plan was valued by people that had less severe forms of the condition, many of whom only saw a mito specialist once a year or less. Negotiating care with allied health was a particular concern.

GPs and allied health professions that are willing to learn more about their patient's condition are given a head start if provided with a clear diagnosis and details of how the disorder is affecting the patient. They can then search more efficiently and find comprehensive information on Mito disorders through reputable sources such as *Orphanet,* the Mito Foundation*,* or journal articles. Since the presentations of Mito disorder can be so varied, a quick but useful practice is marking up the Mito Foundation's infographic for GPs to highlight particular issues that their patient faces.

This program of work had some limitations. The use of online focus groups may have limited participation of people or parents by those less digitally confident or equipped. There is also the possibility that the topic of the focus groups skewed representation to more proactive and informed people. We included clinicians from nine mito specialist clinics from across Australia but many sole practitioners (e.g., neurologists) are known to manage people with mito and the views of this group were not represented.

Next steps

This work has focused on general high level best practice by mito specialist services for patients with any presentation of mito disorder and has considered management of those at risk of an acute episode as well as those with a more chronic milder illness. We found there was a mismatch between specialist information and support provided, and consumer experience when presenting with an acute episode related to their mito at the Emergency Department.

The next step is to consider management of people with mito from the viewpoint of emergency service providers. There is currently very little data on this. Actual episodes of emergency management of patients with a Mito disorder could be identified through audit and assessed against "best practice" criteria and possibly matched to patients' accounts of the same episode of care. Focus groups or interviews with Emergency Staff could be added to the data so that shortfalls in care and barriers could be identified and addressed in a co-design process. Learnings from this process could provide transferable approaches for patients with other rare diseases to improve care there too.

Recommendation for: Health services researchers in partnership with clinicians and consumers

16. Data on emergency management of patients with mito could be identified through survey of patients, audit of emergency records and focus groups or interviews with Emergency Staff. This would allow standardisation of care and identification of areas for improvement.

Standardised outcome measures for people with mito have not yet been developed, nor have full models of care been defined. The work of the Australian Genomics Mitochondrial Flagship, the publication of the Australian Patient Care Standards, and this study lay the foundation for this work. Future collaborative research is needed to advance this. For example, the development of an audit tool for mito specialist services to either self-score or allow health services researchers to audit practice around recommended checks (e.g., audiology, cardiology), dietary advice, physical exercise advice and mental health screening could help identify areas that work well and ones requiring work.

Recommendation for: Health services researchers in partnership with clinicians and consumers

17. Develop standardised outcome and process measurements for people with mito so helpful practices can be compared and shared across sites, and optimal management be further defined.

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