Section 3 Symptoms and diagnosis

Section 3: Experience of symptoms and diagnosis

Symptoms at diagnosis

- The first question was in the online questionnaire and asked participants to recall all of the symptoms that they experienced and their quality of life while experiencing those symptoms. The most commonly reported symptoms were muscle symptoms by (such as muscle weakness, exercise intolerance, pain, fatigue, cramps and low muscle tone), noted by 47 (94.00%) participants, followed by fatigue (n=45, 90.00%), digestive tract symptoms (n=36, 72.00%), problems with eyes (n=34, 68.00%), central nervous system symptoms (n=32, 64.00%), and hearing problems (n=24, 48.00%). The symptoms that had the lowest average quality of life were central nervous symptoms (mean = 2.28; n=32, 64.00%), muscle symptoms (mean = 2.52; n=47, 94.00%), heart symptoms (mean = 2.53; n=15, 30%) and digestive tract symptoms (mean = 2.64; n=36, 72.00%).
- In the structured interview, participants were asked to describe the symptoms that actually led to their diagnosis, as opposed to all the symptoms that they could recall. There were 14 participants (28.00%) that described fatigues and/or a lack of stamina and 11 participants (22.00%) that described having gastrointestinal distress ranging from nausea, diarrhoea to constipation. The next most common symptoms leading to diagnosis were failing to thrive as an infant (n=8, 16.00%), weakness in the legs or not being able to use their legs (n=7, 14.00%) and migraines that were sometimes also described as being stroke-like (n=7, 14.00%).
- In relation to sub-group variations, participants from a low socio-economic area (26.09%) and those with a low general health (25.00%) reported having severe migraines more frequently compared to the general population (14.00%), while those with a high general health reported this less frequently (0.00%). In relation to gastrointestinal distress, participants who had a high school or trade education reported this less frequently (11.54%) while those with a university education (33.33%) and those that are hearing impaired (37.50%) reported this more frequently than the general population (22.00%). Participants with a university education (20.83%) and participants with hearing impairment (20.83%) reported diabetes being a condition that led to their diagnosis more frequently than the general population (1000%). Participants with high physical function (40.91%) reported experiencing fatigue and/or lack of stamina more frequently than the general population (28.00%) while those with low physical function reported this less frequently (17.86%). Participants with high social function (40.00%) also reported experiencing fatigue and/or lack of stamina more frequently than the general population (28.00%).
- As part of the structured interview analysis in relation to symptoms that lead to diagnosis, there were 13 participants (26.00%) that noted a hereditary component that led to their diagnosis. In some cases it was a known hereditary link while in others, the hereditary link was identified as part of the diagnostic process.

Support at diagnosis

- In the questionnaire, participants were asked whether they felt supported at the time of diagnosis. There were 36 participants (72.00%) that indicated that they had no support at diagnosis, while 3 participants (6.00%) noted that they had enough support. An additional 11 participants (22.00%) indicated that they had some support but that it was not enough.
- In relation to sub-group variations, participants with no eye problems reported having no support at diagnosis more frequently than the general cohort (81.25% compared to 72.00% in the general cohort),. Participants that had higher general health reported that they had no support at diagnosis, more frequently than the general cohort (86.36% compared to 72.00% in the general cohort), and reported less frequently than the general cohort that they had some support but it wasn't enough, (13.64% compared to 22.00% in the general cohort)

Genetic/biomarker tests

- Participants were asked whether they had ever had a discussion about genetic tests or tests to see if there were biomarkers that might be relevant to their condition or treatment. Six participants (12.00%) indicated that they had brought up the topic for discussion with their doctor, 15 participants (30.00%) reported that their doctor had brought up the topic for discussion, 29 participants (58.00%) had no discussion about genetic tests.

- In relation to sub-group variations, participants with higher social functioning indicated that their doctor brought up the topic of biomarker/genetic testing, more frequently than the general cohort and those with lower social functioning less frequently (higher social functioning 45.00%; lower social functioning 20.00%, compared to 30.00% in the general cohort). Participants with no eye problems indicated that no one brought up the topic of biomarker/genetic testing, more frequently than the general cohort (68.75%, compared to 58.00% in the general cohort).
- Participants were asked about their interest in this type of test if it was available, the majority noted that they had not had this test, but would like to (n=26, 52.00%), 8 participants (16.00%) reported having this test and not paying out of pocket for it, 8 had this test as part of a clinical trial (16.00%), and two paid for this test themselves (4.00%). There were 6 participants (12.00%) indicated that they had not had this test and were not interested in it.
- In relation to sub-group variations, participants that had hearing problems, no eye problems and that were university educated indicated that they had not had this test but would like to, less frequently than the general cohort (41.67%, 31.25% and 33.33% respectively compared to 54.00% in the general cohort), while participants that did not have hearing problems, had no eye problems and had high school or trade qualifications indicated that they had not had this test but would like to, more frequently than the general cohort (61.54%, 61.76%, and 69.33% respectively, compared to 54.00% in the general cohort).
- In the structured interview, participants were also asked to talk about their understanding of genetic or biomarker testing. Some of the descriptions included understanding that the test is used for diagnosis of mitochondrial disease; understanding that the test cannot help them but may help others in the future; and understanding that the test cannot target treatment as there are no treatments available or that there was no clinical indication following the test.

Understanding of condition at diagnosis

- Participants were asked how much they knew about mitochondrial disease at diagnosis. There were 31 participants (62.00%) that described knowing nothing about mitochondrial disease and this was the most common response. There were also eight participants (16.00%) that described knowing about mitochondrial disease by the time they were diagnosed because the time to diagnosis was relatively long, giving them time to educate themselves.

Understanding of prognosis

- Participants were asked whether anyone talked to them about prognosis. The most common theme noted by 26 participants (52.00%) was prognosis had not been clearly discussed. The next most common theme was that participants understood that mitochondrial disease came with a poor prognosis that was primarily related to physical decline and this was noted by 9 participants (18.00%). There were seven participants (14.00%) that described the need for ongoing management of their condition and this included the management of exacerbations. The final theme in relation to understanding of prognosis was that mitochondrial disease came with a poor prognosis, including reduced life expectance and/or a rapid disease progression. This was noted by six participants (12.00%).

Experience of symptoms before diagnosis

Participants were asked to recall the symptoms that they noticed in themselves that led them to pursue further investigation with a clinician. This question was asked both in an online questionnaire and as part of the structured interview. Responses from both sources of information were cross-validated to compile these results.

The first question was in the online questionnaire and asked participants to recall all of the symptoms that they experienced and their quality of life while experiencing those symptoms. Quality of life was rated on a Likert scale from one to seven, where one is "Life was very distressing" and seven is "Life was great". Table 3.1 describes symptoms and quality of life due to symptoms. Muscle symptoms include muscle weakness, exercise intolerance, pain fatigue, cramps and low muscle tone. Nervous system symptoms include developmental delays, mental retardation or regression, dementia, seizures, coma, neuro-psychiatric disturbances, atypical cerebral palsy, myoclonus, movement disorders, ataxia, migraine and strokes. Problems with eyes include drooping eyelids, inability to move eyes and vision loss. The most commonly reported symptom was muscle symptoms (such as muscle weakness, exercise intolerance, pain, fatigue, cramps and low muscle tone), these were experienced by 47 (94.00%) of participants. Other commonly experienced symptoms included fatigue (n=45, 90.00%), digestive tract symptoms (n=36, 72.00%), problems with eyes (n=34, 68.00%), central nervous system symptoms (n=32, 64.00%), and hearing problems (n=24, 48.00%). The symptoms that had the lowest average quality of life were central nervous symptoms (mean = 2.28; n=32, 64.00%), muscle symptoms (mean = 2.52; n=47, 94.00%), heart symptoms (mean = 2.53; n=15, 30%) and digestive tract symptoms (mean = 2.64; n=36, 72.00%).

Table 3.1: Symptoms experienced and mean QoL

Symptom	Symptom experienced	n=50	%	QOL mean	QOL SD
Muscle symptoms	Yes	47	94.00	2.52	0.96
	No	3	6.00		
Fatigue	Yes	45	90.00	2.96	1.17
	No	5	10.00		
Digestive tract symptoms	Yes	36	72.00	2.64	1.13
	No	14	28.00		
Problems with eyes	Yes	34	68.00	3.15	1.60
	No	16	32.00		
Central nervous system symptoms	Yes	32	64.00	2.28	1.11
	No	18	36.00		
Hearing problems	Yes	24	48.00	2.71	1.04
	No	26	52.00		
Heart symptoms	Yes	15	30.00	2.53	0.99
	No	35	70.00		
Fatty lumps in skin	Yes	11	22.00	3.73	0.79
	No	39	78.00		
Diabetes	Yes	10	20.00	3.50	0.85
	No	40	80.00		
Excess body hair	Yes	9	18.00	3.33	1.22
	No	41	82.00		
Kidney problems	Yes	7	14.00	2.67	1.37
	No	42	84.00		
Liver failure	Yes	2	4.00	3.00	
	No	48	96.00		
Underactive thyroid or parathyroid	Yes	2	4.00	3.50	
	No	48	96.00		

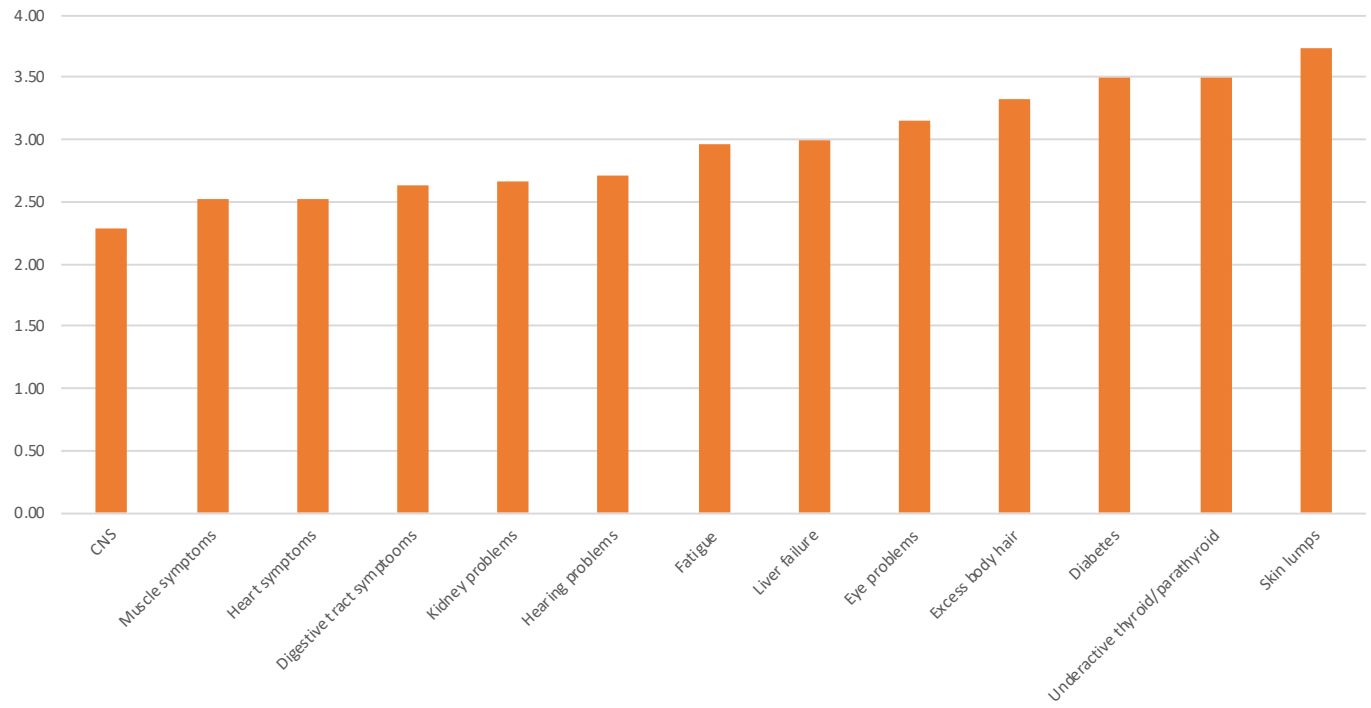

Figure 3.1 Symptoms and mean quality of life scores

Symptoms leading to diagnosis

In the structured interview, participants were asked to describe the symptoms that actually led to their diagnosis, as opposed to all the symptoms that they could recall. There were 14 participants (28.00%) that described fatigues and/or a lack of stamina and 11 participants (22.00%) that described having gastrointestinal distress ranging from nausea, diarrhoea to constipation. The next most common symptoms leading to diagnosis were failing to thrive as an infant (n=8, 16.00%), weakness in the legs or not being able to use their legs (n=7, 14.00%) and migraines that were sometimes also described as being stroke-like (n=7, 14.00%).

In relation to sub-group variations, participants from a low socio-economic area (26.09%) and those with a low general health (25.00%) reported having severe migraines more frequently compared to the general population (14.00%), while those with a high general health reported this less frequently (0.00%). In relation to gastrointestinal distress, participants who had a high school or trade education reported this less frequently (11.54%) while those with a university education (33.33%) and those that are hearing impaired (37.50%) reported this more frequently than the general population (22.00%). Participants with a university education (20.83%) and participants with hearing impairment (20.83%) reported diabetes being a condition that led to their diagnosis more frequently than the general population (10.00%). Participants with high physical function (40.91%) reported experiencing fatigue and/or lack of stamina more frequently than the general population (28.00%) while those with low physical function reported this less frequently (17.86%). Participants with high social function (40.00%) also reported experiencing fatigue and/or lack of stamina more frequently than the general population (28.00%).

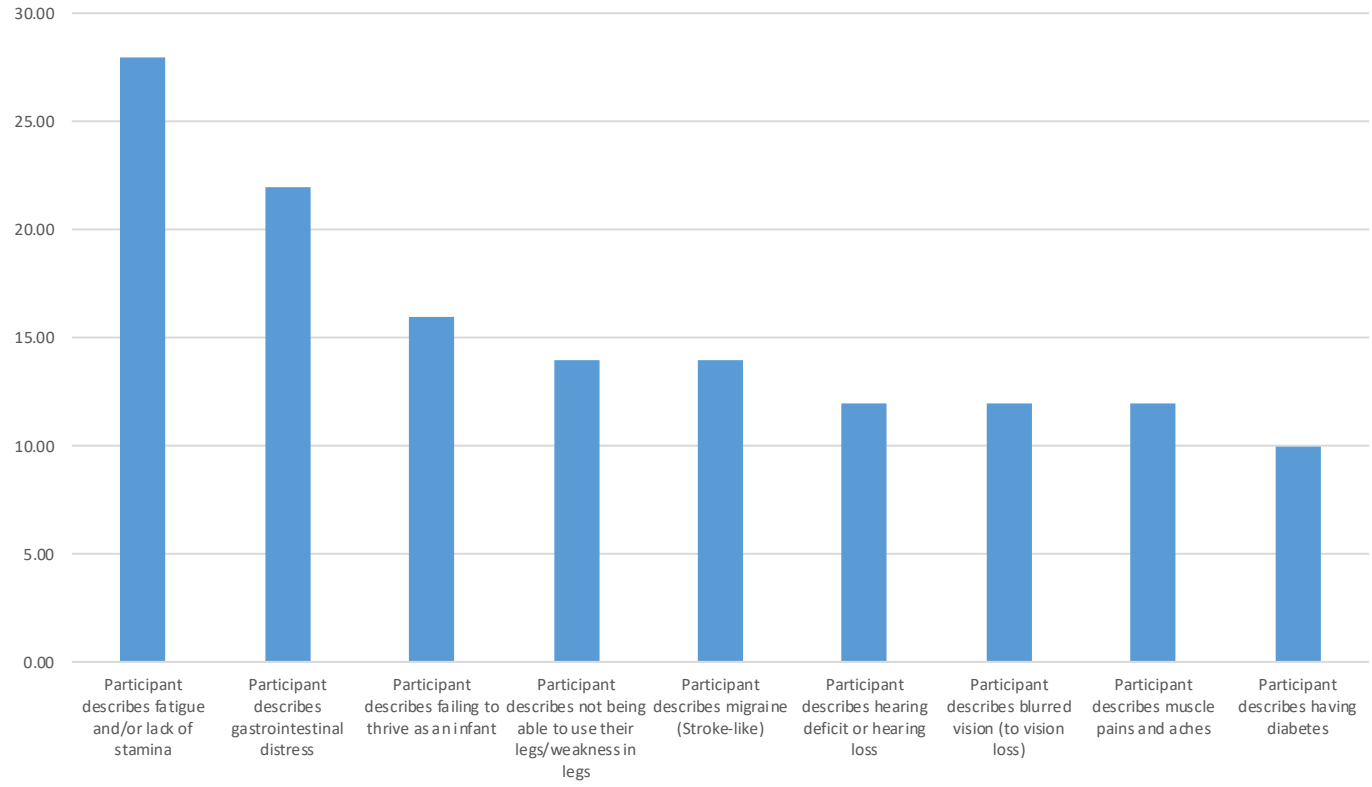

Figure 3.2: Symptoms leading to diagnosis (Percentage of all participants)

Participant describes fatigue and/or lack of stamina

So my earliest symptoms were two, then I had always problems with the cold, given my body temperature. Trouble exercising, I couldn't do what the other kids do. I just couldn't keep up, but I damn well tried. I just had to rest a lot, go to bed early. Which I didn't think anything of, and nobody else did then either. Participant 24

Okay. Well, I guess early on it was fatigue and also knowing that I was just hopeless at sports. Whereas, I've got five siblings who were all quite well coordinated and good at sport. I wasn't, which was quite embarrassing sometimes, but I was supposedly normal…My teachers in primary school and in secondary school, two different teachers at different times said to me, you need an earlier bed time, you must be staying up too late. I was embarrassed to tell them actually I went to bed at the same time as my younger sister. I wasn't staying up too late. That wasn't why I was tired. Participant 34

Yep. I was born with it. I was a little bit delayed in comparison to everybody else. Sorry. I always lacked the energy that everybody else had and that I noticed from around the time I was about 14, 15. And then, growing up, I just didn't have the stamina. Of course, I was working … I was always constantly … I would always need like ten hours sleep. Otherwise, I didn't feel well. Participant 40

Participant describes gastrointestinal distress

I thought the symptoms for those is celiac disease, because I was actually diagnosed with celiac disease. I suddenly got all these symptoms of gut problems. I was sure I've gotten rid of all the gluten out of my diet and I was having all these symptoms. Participant 21

I was also getting really fatigued, and then I also had this weird diarrhoea, like before my menopause, I went into menopause about 55, and I'm now 60. Before my menopause every time I had my period I would get diarrhoea, just a sudden cramping, and have to go to the toilet in a hurry and then within five years that diarrhoea became more and more problematic. Then before I retired, I had to retire my work because I couldn't maintain it, I was having diarrhoea maybe 10 times a week, unexpectedly. Now it's back to just maybe just once a month. Participant 36

Starting to see problems with bowel and bladder and so forth. She'd already started to get issues with her stomach, feeling sick in the mornings. Participant 47

Participant describes failing to thrive as an infant

It's my son with mitochondrial disease and it was around seven months of age, six, seven months of age, and he wasn't sitting up, and he wasn't responsive to a lot of ... I pretty much had noticed that other mothers, you know, mothers group and all the rest of it, children weren't doing the same things. He wasn't reaching the same milestones. At that point in time, and I think for my son, NAME, I had to express my concern with the community nurse. It was the GP and they thought it might have just been muscular dystrophy and I think NAME was around that time, around the six, seven-month mark he had his first cold and that's where he went down. He just slept, and slept, and slept and slept. Still, at that point, no alarm bells where kind of going off other than I remember the GP suggesting that perhaps it might be a muscular thing, the lack of sitting up and being to hold things. That it might be best to go and see the paediatrician. At that point, I had the referral. I made the appointment to the local paediatrician. ...I remember my husband arriving home and I was in tears thinking there is something wrong here. Anyhow, I went to our appointment armed with a list of questions, and feedback, and on that list was that NAME would do this strange hiccupping thing, and then just fold into himself, and I'd only witnessed him do that four times and for whatever. As soon as I mentioned that the paediatrician guy, I saw the look on his face and he kind of just went, can you tell me more about that? Then on queue for whatever reason, NAME proceeded to have what I now know was an infantile spasm. Participant 45

So, right from birth. So we didn't know that it was mito at the time, but it was poor feeding, failure to thrive, that sort of thing. Participant 46

She was really, really lethargic before she was born. This is my third child, so I noticed that she was significantly inactive and I kept having to go onto those monitors. This is 18 years ago so they were built. To try and trace movement, they traced very light movement only and then when she was born, she had problems with feeding; just no strength to suck. Then she was just lethargic, so I had to develop and then quite a long way behind. At 12 months, she still wasn't rolling over and things like that. She had no head control. There's a lot of those developmental muscle that's not ranged in that 12 months. Participant 49.

Participant describes not being able to use their legs/weakness in legs

Well, I wasn't born with it but I noticed it in early 2012. I was at lunch with my wife and young kids and I sat down at the table. As we finished our lunch, we went to get up and go and I was on my lunch break at work and I couldn't get out of the chair. I was very surprised with that. I thought, "What's the matter with my legs?" I can't push myself up and struggled when I got up. I had problems from there. Participant 6

I felt as though it came in cycles, that my fatigue would get a lot worse for a while and then I would have all these muscle problems in my legs, my thighs and that went on for 40 years, I suppose, almost. Participant 34

Well I've been OCCUPATION, and probably about seven or eight years ago I started to notice that I was having trouble doing some of the exercises that I normally do, particularly squats, getting up from the floor. It started off that I had to use my hands to push up from the floor, and then that gradually increased over a number of years to being having to put the right foot forward, and having these and particular arrangements, the left leg back and blah, blah, blah. Then I was up to the point where I have to get a chair, and push up from the chair rather than from the floor and stuff and- ... have my legs in a certain arrangement and ... Yeah, so the difficulty getting up from the floor or out of chairs has got increasingly worse. Participant 36

Participant describes migraine (Stroke-like)

My first noticeable symptoms that I remember are at aged 8 suffering from chronic migraines and cyclical vomiting. Participant 30

As far as I know I was born with it. I had a lot of different symptoms through my early childhood with constipation, migraine and things like that. But it wasn't until later and it wasn't until I had a stroke like migraine that it came out, that was in Christmas, December 2015. Through various doctors, neurologists and things like that and they did a muscle biopsy. I'm still in the process of being diagnosed of actually which mitochondrial disease it is. Participant 35

It wasn't until my late forties…I kept getting constant migraines, and I'd get vomiting episodes, and like, auras, and feeling like I had a stroke. So, they sent me up to get a brain MI. Participant 40

Participant describes hearing deficit or hearing loss

Yeah. I think probably the first thing is that there wasn't a stage of mito. What happened to me is I've got, just remembering, the A genes would be the G gene or whatever, so my hearing started going in my 20th decade, and now I've actually linked it to mito. What happened was, my hearing started to go in my 20th, about 23, 24, and no one could explain it, and then why that started to happen. Participant 15

I noticed that my hearing had really deteriorated. I had noticed before 2004 that I was asking people to repeat themselves a lot but had seen an ear, nose and throat specialist and seen a audiologist who said yes, your hearing's not great but it's not time for any intervention then. Participant 20

Well, what I noticed first was hearing loss, really. I guess that was the first symptom for me. Participant 26

Participant describes blurred vision (to vision loss)

Yes, sure. I was diagnosed about three years ago. In the preceding couple of years, I'd started to notice when I was reading, particularly when I was tired I would get a separation of the lines that I was reading, almost like a double vision just of that line. I thought it was bad contacts or bad reading glasses. Basically, I ended up going to a different optometrist who then went, "Something's not right". They sent me off to a specialist, and he said, "You got CPEO", which is obviously part of the mitochondrial thing, and then from there I've had other issues develop in that time since then. I was having reading issues. It was Dr. NAME at the LOCATION, and I don't know what the tests were called. There was a whole barrage of eye tests that they did. He also sent me off to have neurological. and they got me to do an MRI on my brain to make sure it wasn't a tumour that was causing it. I also went and saw another specialist who did tests on my legs and things like that. Participant 2

I lost my central vision in YEAR, so age eight. Participant 13

On and off and that was peculiar, what happened to me, but nobody ever put it down to anything in particular of course. It wasn't until I was query about my eyesight, which only happened 18 years ago. I was living in LOCATION. I was having trouble, I couldn't see in the dark. I found it hard finding things in a handbag and things like that, if anything was dark. When I went to get a new prescription for glasses, I was told, "Well, there's these strange pigments on your retinas and do you have trouble seeing in the dark?" and I said, "Yes." I knew that I had a nephew who'd been diagnosed with something to do with retinitis pigmentosa and so I said so, "Well I want to follow it up." I was sent to LOCATION Eye Hospital because we were living in LOCATION at the time. They said, "It's very rare what we're seeing in your eyes. We've only seen once or twice before and it's probably a mitochondrial disease." I said, "What's that?". Participant 34

Participant describes muscle pains and aches

Sorry, I was diagnosed as an adult. I guess my experience is a bit…There might have been times that I showed symptoms as a child, but who knows now, whether or not, because I have this random stuff. If looking back on my time, because I've written it down…it was a couple of times in 2014 and then in 2015, I have about these pains, so like I'd pain all through, like....all around my joints. I had in my hand, and then it just felt like I had pain in my elbows and my knees. It felt like it was in my joints at the time I rested and went to my doctor and he said like it might be a viral thing, so he gave me steroids. I stayed home for like a few weeks and have the steroids and it kind of went away after a while. After

trying maintaining parameters and stuff; and then it came back again, did the same thing. Then it came back in, November 2015. The pain, I could feel more in my legs, not just in my joints anymore. It really like spread and then really understood then it was muscular, not joints I had the pain come back again, but it never went away this time. I tried the steroids, I tried different drugs and nothing happened. I went to rheumatologist for a long time. Participant 5.

Yes. It was January in 2012. I just woke up one morning, I was fine, went to work the day before. A little bit cold not fluey, like I had head cold coming on but nothing else. I woke up the next morning and my feet were so swollen, I couldn't walk on them. My hands were swollen and wouldn't move. My whole body from head to toe just the pain that was crossing through my body was just unbelievable. Participant 18

I was sent to a specialist arthritis doctor, Dr. NAME down at LOCATION. After three visits to him, he looked at me and he said, "I'll see you in six months." I said, "No you won't doctor, I'm sorry. You're not listening to me, I said I have not got joint pain, I have got muscular pain. It's in my thighs mainly and my calves. When I hang washing out I hurt. It's just muscular." Anyway, we came back and they were just giving me painkillers and things like that…. When I look back to when I'm young, we lived at LOCATION for 21 years, I used to work at PLACE and I'd walk, which would be almost both half a mile. For all the walking, playing squash, doing exercise and everything that I did in my younger days, I always had very sore legs, sore shins and I just took that as life. Everyone must have be like that, I never talked about it, I didn't asked questions and other little odd things that I used to get pains, unexplained. I'd put up with them for a week and I'd go to the doctor and they'd send me to scans. Nothing would be wrong with me, you forget about it and the pain eventually would go, that still happens. Anyway, that's it. Participant 31

Hereditary conditions noted in relation to diagnosis

As part of the structured interview analysis in relation to symptoms that lead to diagnosis, there were 13 participants (26.00%) that noted a hereditary component that led to their diagnosis. In some cases it was a known hereditary link while in others, the hereditary link was identified as part of the diagnostic process.

No. A lot of different things had happened. What happened was I had a MRI done and the specialist that I was seeing initially, he actually was treating my sister. When he was just looking at my MRI he went, "Hang on, I've seen similar." He got my sisters in my eyes and put them together and there was all these white lesions on our brain and that kind of thought that's when we got in touch. Participant 1

My mum was there at that time and she probably had a memory flash up because my…I have found a file and that someone had been diagnosed with LHON which we were never actually told about. She didn't really know anything about it, but it just rang a bell for mom. She went home, looks for documentation and saw that her mother, my grandmother or my brother's grandmother had been diagnosed with this condition. I took it straight back to this ophthalmologist who said, "Well, really sorry to tell you but it's genetic. It's inherited on the maternal line. You need to get tested but it's pretty much 100% certain already. That's what this is or at least that you carry it and given the similarities, that would be it manifesting." Participant 8

Yes, I've inherited it from my mum but I didn't know I had it until I had the muscle biopsy and I didn't have any conditions then, I do now. Participant 16

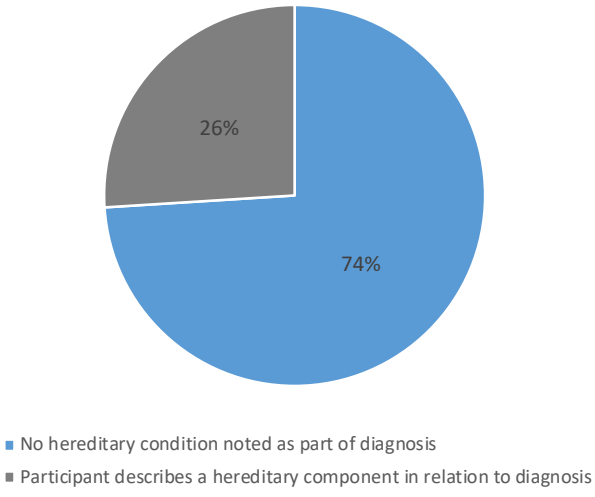

Figure 3.3: Hereditary condition noted as part of diagnosis

Misdiagnosis and other conditions suspected

During the description of their diagnosis, there were a number of participants that noted that they were misdiagnosed or another condition was suspected before their mitochondrial disease diagnosis including multiple sclerosis, muscular dystrophy, fibromyalgia and chronic fatigue.

Table 3.2: Conditions misdiagnosed or suspected at diagnosis.

Conditions misdiagnosed or suspected before diagnosis	All participants	
	n=50	%
Muscular dystrophy suspected or misdiagnosed	3	6.00
Rheumatoid arthritis suspected suspected or misdiagnosed	3	6.00
Diagnosed through other investigation or treatment/therapy regime	2	4.00
Multiple sclerosis suspected suspected or misdiagnosed	1	2.00
Fibromyalgia suspected or misdiagnosed	1	2.00
Chronic fatigue syndrome suspected or misdiagnosed	1	2.00

Multiple sclerosis suspected

I was reading a book one night and I was like, "Oh, I'm shutting one eye to read." I tried to not shut my eye to read and I realized that I couldn't because I was getting double vision. That's when I realized there must have been something wrong. I went and saw another neuro-ophthalmologist then. I was living in LOCATION at that point, went and saw another neuro-ophthalmologist who thought that I had MS. He sent me for testing for MS. Then when that came back all clear, he sent me for a blood test and I remember hearing the word mitochondrial, but he never explained what it was, never really said what he was doing or looking for or anything. Participant 10

Muscular dystrophy suspected

I pretty much had noticed that other mothers, you know, mothers group and all the rest of it, children weren't doing the same things. He wasn't reaching the same milestones. At that point in time, and I think for my son, NAME, I had to express my concern with the community nurse. It was the GP and they thought it might have just been muscular dystrophy and I think NAME was around that time, around the six, seven-month mark he had his first cold and that's where he went down. He just slept, and slept, and slept and slept. Participant 45

Fibromyalgia suspected

He tried to figure out what it was, almost diagnosed me with fibromyalgia, but then it didn't really add up. This is fatigue and everything else, and she referred me to a neurologist who did a muscle biopsy. Participant 5

Chronic fatigue suspected

Well, I think first, I was diagnosed as having chronic fatigue after I had a diagnosis of-- What's it called? (Glandular fever) Glandular fever. Yes. That's it. When I was 21 and well, I didn't get chronic fatigue diagnoses until about, I don't know about 15 years later or something. Participant 34

Diagnostic pathway

Participants noted in the questionnaire the approximate date when they first noticed symptoms and then the approximate date when they were diagnosed. From the information reported, from those participants were an approximate time lapse could be made (n=44), the range of time between symptoms and diagnosis was from 1 month to 58 years. Almost half of the participants were diagnosed within two years of noticing symptoms (n=19, 43.18), a quarter of participants were diagnosed between 3 and 5 years from noticing symptoms (n=11, 25.00%), and approximately a third of participants were diagnosed more than six years after experiencing symptoms (n=14, 31.81%).

Table 3.3: Time from symptoms to diagnosis

Approximate time between noticing symptoms and diagnosis (n=44)	N=	Percentage of participants
< 1 year	4	9.09
1-2 years	15	34.09
3-5 years	11	25.00
6-10 years	3	6.82
10-20 years	7	15.91
>20 years	4	9.09

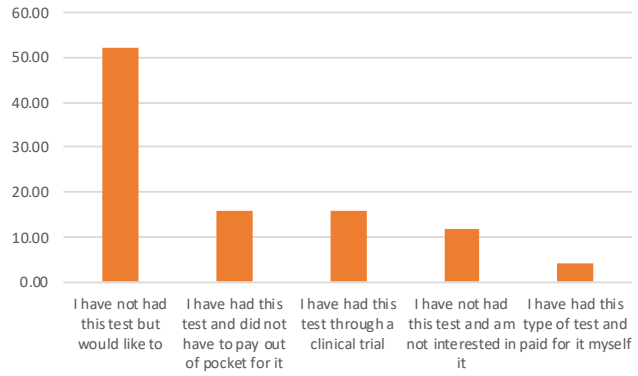

Figure 3.4: Time from symptoms to diagnosis (Percentage of all participants)

As noted, in the structured interview, participants were asked about symptoms leading to diagnosis and how the participant came to be diagnosed. As reflected in the results above, there were some participants that had a relatively straight forward diagnosis and others that had a long and complicated pathway to diagnosis. The following quotes are provided to demonstrate these variations:

Long, complicated diagnosis

I thought the symptoms for those is celiac disease, because I was actually diagnosed with celiac disease. I suddenly got all these symptoms of gut problems. I was sure I've gotten rid of all the gluten out of my diet and I was having all these symptoms and realized they were the symptoms my daughter was getting. My daughter and I compared symptoms and I went to a dietitian and she said, "Have you done this? Have you done this? Have you done this?" I've done all those things and yet I was still sick. I was going to a gastroenterologist who said, "It must be psychological." No, you're far out. This is exactly happened with the daughter. At the same time I was seeing the psychiatrist, I didn't get that far. I don't think I did. I was seeing the gastroenterologist and he said, "Well, if it was for your daughter having the same symptoms, I would have said it was psychiatric, because if some daughter being sick and da-da-da." He said, "But I've noticed this NAME in LOCATION." At the same time, my GP said, "I've heard of this NAME in LOCATION."…she's a professor at LOCATION…. Participant 21

Well it took a long time. I'd seen lots of different specialists. Finally, they picked up rheumatoid arthritis marker, so I was sent to a Rheumatologist, and when I went to him he had a ... What do you call it? A locum or somebody had come up from I think it was LOCATION, and he actually noticed how I was getting out of the chair in the waiting room, and asked me about it. He was the first one who actually put his hands on and tested my muscles and went, "Oh, yeah they are weak." Even though I'd been telling multiple- ... specialists the same story for a long time, I was fobbed off for a long time. Like, "Oh, you don't exercise enough." Which I knew was wrong. I was also getting really fatigued, and then I also had this weird diarrhoea, like before my menopause, I went into menopause about 55, and I'm now 60. Before my menopause every time I had my period I would get diarrhoea, just a sudden cramping, and have to go to the toilet in a hurry and then within five years that diarrhoea became more and more problematic. Then before I retired, I had to retire my work because I couldn't maintain it, I was having diarrhoea maybe 10 times a week, unexpectedly. Now it's back to just maybe just once a month….Then I got referred to a neurologist who did muscle biopsies in my leg and my shoulder. They had ragged red fibres, so he suspected it was mitochondrial and referred me to NAME in LOCATION. Participant 36

Well it took a long time. I'd seen lots of different specialists. Finally, they picked up rheumatoid They took a ... it was a very, very long process. Probably two and a half years. Was a muscle biopsy and blood test. And they went to the Netherlands, and it was basically a point mutation. Yeah so it was a.... I forgot what they call it, but yeah it was a mutation…But that was the very final one. Participant 46

Relatively straight forward diagnosis

Okay. So the major symptom was just ptosis. Pretty slight ptosis on the left side. Yes, I don't know if this is relevant. But I just recently started using Snapchat and I was taking a lot of selfies. Yes I just, I guess when you take a lot of selfies you sort of notice things that weren't really there before. That would be the first symptom, and I went to see an ophthalmologist. Just to ask what was up with the ptosis, and expecting just him to say that it is just a bit of a lazy eye. But no, then he did a couple of really simple tests, just test my bilateral eye movements. Stuff like that and that it was lacking- he ask, how long have I had double visions or stuff like that. He essentially diagnosed. It was a very quick diagnosis, mitochondrial disease. Then obviously I have to get like biopsy and stuff just to confirm. Participant 11

I took my mum for an appointment to see a neurologist NAME and he said, "Oh, looking at your daughter " Straight away just looking at her, said, "Oh, I feel you got Mitochondrial myopathy." She had muscle biopsy and then he said, "Looking at the daughter, I feel she's showing the signs of it too." That would have to do with the ptosis of the eyes. Participant 16.

I was diagnosed in 2003. It all came about because my mother who also had it was in hospital…. They couldn't work out why she wasn't getting better. Based on some other family information, they tested her for mitochondrial disease. It turned out that she had it. At the same time, I was having a lot of symptoms with fatigue and headaches, and just not being able to do as much as I used to. I got tested as well. That's how that came about. I had started with a muscle biopsy. I was officially diagnosed by a muscle biopsy. Probably what I've just described. There were some other family members that were suspected to have it. I went to my GP and she referred me to a specialist who organized a muscle biopsy. Participant 43

Costs at diagnosis

In the questionnaire, participants were asked to estimate the amount of out of pocket expenses they had for diagnostic tests and medical consultations. Twenty-one participants (42.00%) had no out of pocket expenses, 13 participants (26.00%) spent more than $1000, 8 participants spent $1000 or less (16.00%), the remaining 8 participants were unable to recall how much they spent (16.00%).

Table 3.4: Costs of diagnosis

Cost	N=50	Percent
0	21	42.00
$0-500	2	4.00
$501-1000	6	12.00
>$1000	13	26.00
Not known/can't recall	8	16.00

The participants were then asked on the online questionnaire if the amount they spent was a burden, for half of the participants (50.00%), it was no burden at all, 14 participants found it extremely or moderately significant (28%), and 11 participants found it with somewhat or slightly significant (22.00%).

Table 3.5 Cost of diagnosis – level of burden

Cost a significant burden	N=50	Percent
Extremely significant	6	12.00
Moderately significant	8	16.00
Somewhat significant	5	10.00
Slightly significant	6	12.00
Not at all significant	25	50.00

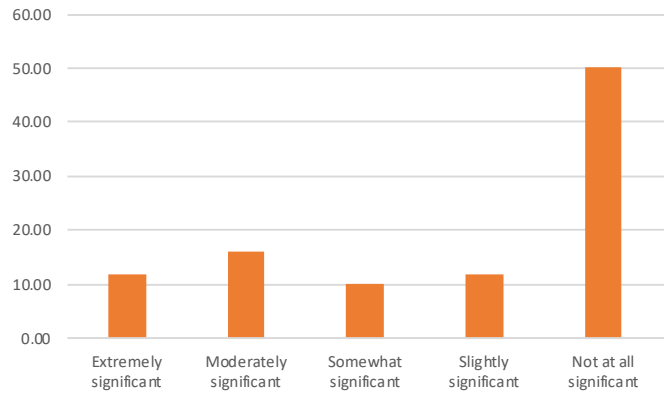

Figure 3.5 Cost of diagnosis – level of burden
(% of all participants)

Understanding of disease at diagnosis

Participants were asked how much they knew about mitochondrial disease at diagnosis. There were 31 participants (62.00%) that described knowing nothing about mitochondrial disease and this was the most common response.

Participant describes knowing nothing about mitochondrial disease at diagnosis

I didn't know anything about it before then. I've never heard of it. Completely new...shocked. I did hit the books so I did a lot of research. I helped inform my family a bit when we couldn't get to the doctors. I took that on myself a little bit. I ended up getting involved with AMDF. You've probably been in touch with them then. Participant 8

No, I never understood because I had my mum living with me for 10 years. I never understood why mom was always tired and basically, she'd look like she was sleeping all the time when she wasn't because of her. She had really bad ptosis over the eyes but she was always in bed by five o'clock, six o'clock in the evening. I never understood the condition where now, I understand the condition because I'm always ready for my bed at six o'clock. Participant 16

We didn't know anything, but it was good to get an answer about everything. Yes, because as I say, I was getting lots and lots of migraine headaches and just having lots of time off work, just getting so sick. Everything wasn't going down a normal pathway of diabetes treatment. It was good just to get an answer, but then there was nobody... It took us a while to find someone that actually knew what it was. Now, I'm under neurology. I see Dr. NAME down there. He's been helping us go through and somehow, we found out about the Mitochondrial Foundation and get the newsletters but no, we didn't know anything about it. It was very unknown and still is very unknown. Participant 19

There were also eight participants (16.00%) that described knowing about mitochondrial disease by the time they were diagnosed because the time to diagnosis was relatively long, giving them time to educate themselves.

Participant describes knowing about mitochondrial disease as the time to diagnosis was relatively long, giving them time to educate themselves

Well, by that point I did know a bit because there had been a bit of time between when I first had the word mentioned to me to when I got a diagnosis. I had a bit of time to get on to doctor Google and read up about it and because the neuro-ophthalmologist that I saw initially, he clinically diagnosed me with Kearns-Sayre syndrome from my vision loss and everything that I've got. Then I had a narrowed field, so then I could have a look and research that. By the time I got a diagnosis, I was pretty up there with what was happening and what it was. Participant 10

When I was diagnosed, I knew a little bit because I had spoken to the ophthalmologist about it. Well he said that mitochondrial disease so I did a research myself, so I guess I did not entirely know the cause or much about any treatment or anything like that but I would say I had like a decent amount of knowledge by the time I was diagnosed, because it was kind of ongoing process as well. Okay, right. So I was just going to say that because I think there was about an extended gap, like a two-year gap between when I first saw the ophthalmologist and when I got diagnosed, saying between that two years, I was sort of looking up more or less everything I could about it. To learn a little bit. Participant 11

Well, we actually bought it up with the doctors because I've been an inpatient for four or five months at that point. We were getting literally nowhere. I bought it up. Then, it took us another three months to get a consult with the metabolic team. Well, I guess that's why we've been really onto this because my symptoms fit very well....Everything else has been excluded at that point. We didn't really understand why all of these bodily systems were malfunctioning. It does makes sense....In actual fact, as I kept telling them at the time, "A...teenager sitting in bed, in your hospital, has pretty much diagnosed herself." Because she literally had every single symptom listed on the website. We couldn't explain it with anything else. It just seemed to be the most obvious. Participant 47

Table 3.6: Understanding of disease at diagnosis

Understanding of disease at diagnosis	All participants	
	n=50	%
Participant describes knowing nothing about mitochondrial disease at diagnosis	31	62.00
Participant describes knowing about mitochondrial disease as the time to diagnosis was relatively long, giving them time to educate themselves	8	16.00
Participant describes knowing very little about mitochondrial disease at diagnosis	7	14.00
Participant describes knowing about mitochondrial disease before diagnosis (scientific background)	2	4.00
Participant describes no-one knowing much about mitochondrial disease and the uncertainty of the diagnosis	2	4.00

Support at diagnosis

In the questionnaire, participants were asked whether they felt supported at the time of diagnosis. There were 36 participants (72.00%) that indicated that they had no support at diagnosis, while 3 participants (6.00%) noted that they had enough support. An additional 11 participants (22.00%) indicated that they had some support but that it was not enough.

In relation to sub-group variations, participants with no eye problems reported having no support at diagnosis more frequently than the general cohort (81.25% compared to 72.00% in the general cohort),. Participants that had higher general health reported that they had no support at diagnosis, more frequently than the general cohort (86.36% compared to 72.00% in the general cohort), and reported less frequently than the general cohort that they had some support, but it wasn't enough, (13.64% compared to 22.00% in the general cohort).

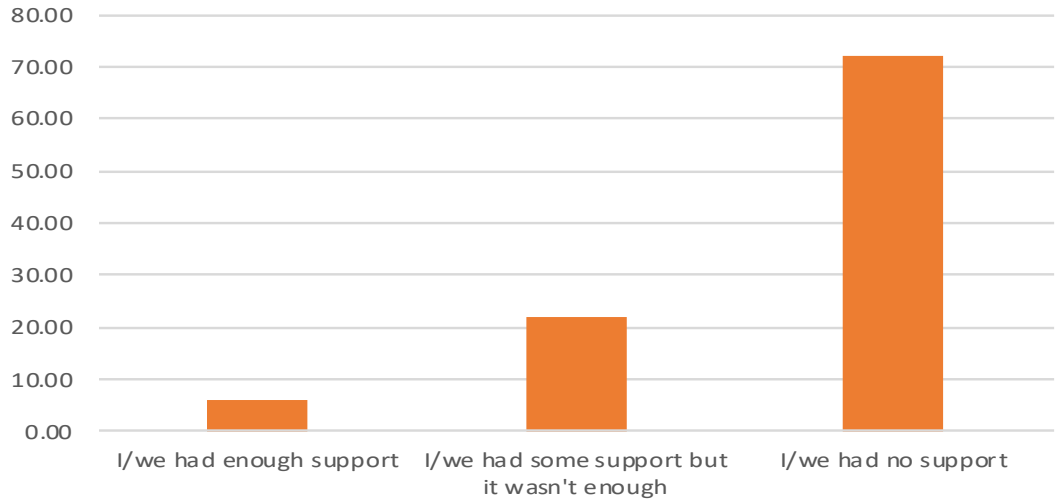

Figure 3.6: Support at diagnosis (% of all participants)

Table 3.7 Support at diagnosis

			General Health		Physical function		Emotional well-being	
Support at diagnosis	N=50	Percent	Higher N=22	Lower N=28	Higher N=22	Lower N=28	Higher N=26	Lower N=24
I/we had enough support	3	6.00	1 (5.00%)	2 (7.14%)	1 (4.45%)	2 (7.14%)	1 (4.55%)	2 (6.67%)
I/we had some support, but it wasn't enough	11	22.00	4 (20.00%)	17 (25.00%)	4 (18.18%)	7 (25.00%)	4 (18.18%)	7 (23.33%)
I/we had no support	36	72.00	15 (75.00%)	19 (67.86%)	17 (77.27%)	19 (67.86%)	17 (77.27%)	21 (70.00%)

	Social functioning		Hearing impairment		Eye/visual impairment	
Support at diagnosis	Higher N=20	Lower N=30	No hearing problems N=26	Hearing problems N=24	No eye problems N=16	Eye problems N=34
I/we had enough support	0 (0.00%)	3 (10.71%)	1 (3.85%)	2 (8.33%)	0 (0.00%)	3 (8.82%)
I/we had some support, but it wasn't enough	3 (13.64%)	8 (28.57%)	5 (19.23%)	6 (25.00%)	3 (18.75%)	8 (23.53%)
I/we had no support	19 (86.36%)	17 (60.71%)	20 (76.92 %)	16 (66.67%)	13 (81.25%)	23 (67.65%)

	Location		Education		SEIFA	
Support at diagnosis	Metropolitan N=30	Regional N=20	School/ Trade N=26	University N=24	Higher N=27	Lower N=23
I/we had enough support	1 (3.33%)	2 (10.00%)	2 (7.69%)	1 (4.17%)	1 (3.70%)	2 (8.70%)
I/we had some support, but it wasn't enough	6 (20.00%)	5 (25.00%)	6 (23.08%)	5 (20.83%)	5 (18.52%)	6 (26.09%)
I/we had no support	23 (76.67%)	13 (65.00%)	18 (69.23%)	18 (75.00%)	21 (77.78%)	15 (65.22%)

Diagnostic tests

Participants were asked on the online questionnaire what tests that they had received leading up to their diagnosis with mitochondrial disease. The majority of participants had blood tests (n=43, 86.00%), medical history (32, n=64.00%), genetic tests (n=31, 62.00%), muscle or tissue biopsies (n=31, 62.00%), eye tests (n=30, 60.00%), urine tests (n=27, 54.00%) and family history (n=26, 52.00%).

Table 3.8: Diagnostic tests

Diagnostic test	N=50	Percent
Blood tests	43	86.00
Medical history	32	64.00
Genetic tests	31	62.00
Muscle/Tissue biopsy	31	62.00
Eye tests	30	60.00
Urine tests	27	54.00
Family history	26	52.00
Hearing test	24	48.00
Hair tests	9	18.00
Imaging(Ultrasound, MRI, CT, X-ray)	5	10.00
Nerve conduction tests	5	10.00
Skin cell tests	5	10.00
Lumber puncture	2	4.00
Electroencephalography	1	2.00
Endoscope	1	2.00
Exercise testing	1	2.00

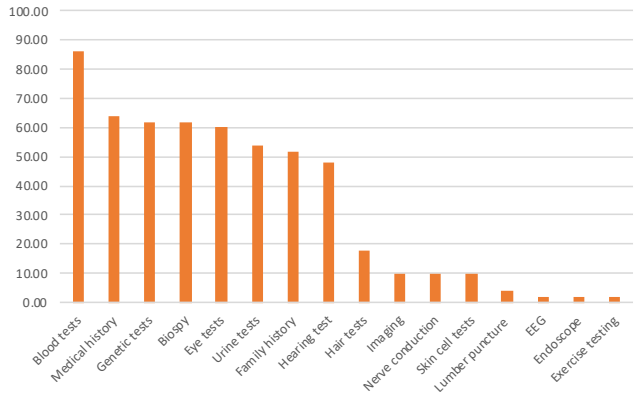

Figure 3.7: Diagnostic tests (% of all participants)

Time from diagnostic tests to diagnosis

Participants were asked on the online questionnaire about the amount of time from diagnostic test until they received a diagnosis. The time ranged from less than one week to 27 years. The majority of participants described the time in months (n=28, 56.00%), others described the time in weeks (n=11, 22.00%), years (n=8, 16.00%) or not known/still waiting for diagnosis (n=3, 6.00%).

Table 3.9: Time to diagnosis

Time from tests to diagnosis	n=50	Percent
< 1week	2	4.00
1-2 weeks	1	2.00
2-3 weeks	7	14.00
3-4 weeks	1	2.00
>4 weeks	36	72.00
Don't know	3	6.00

Diagnosis delivery

Participants were asked who gave them their diagnosis and where the diagnosis was given. The majority were diagnosed by a neurologist (N=23, 46.94%), followed by a geneticist (n= 9, 18.37%) and mitochondrial specialist (n= 7, 14.00%).

Table 3.10 Diagnosis provider

Health professional who gave diagnosis	N=49	Percent
Neurologist	23	46.94
Geneticist	9	18.37
Mitochondrial specialist	7	14.29
Eye specialist	4	8.16
Ophthalmologist	2	4.08
Functional medicine specialist	1	2.04
Gastroenterologist/Digestive system specialist	1	2.04
Neuro-ophthalmologist	1	2.04
ophthalmologist + ENT specialist	1	2.04

Most participants received their diagnosis at a specialist clinic (n=24, 48.98%), followed by the hospital (n=18, 36.73%).

Table 3.11 Diagnosis location

Where was diagnosis given	n=49	Percent
Specialist clinic	24	48.98
Hospital	18	36.73
General practice	5	10.20
By letter	1	2.04
By phone	1	2.04

Table 3.12 Genetic and biomarker tests

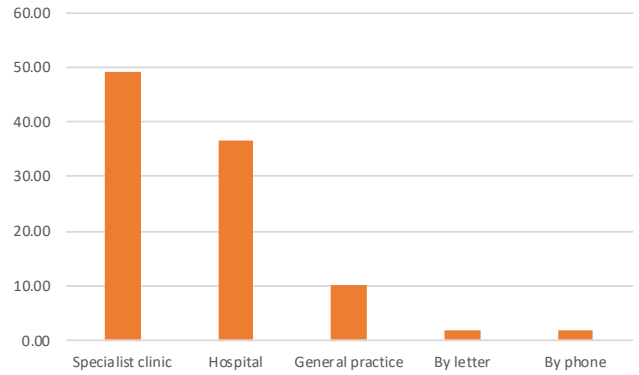

Figure 3.8 Diagnosis location

Genetic and biomarker tests

Participants were asked whether they had ever had a discussion about genetic tests or tests to see if there were biomarkers that might be relevant to their condition or treatment. There were 6 participants (12.00%) that indicated that they had brought up the topic for discussion with their doctor and 15 participants (30.00%) that reported that their doctor had brought up the topic for discussion. There were also 29 participants (58.00%) that indicated that no one had ever spoken to them about this.

In relation to sub-group variations, participants with higher social functioning indicated that their doctor brought up the topic of biomarker/genetic testing, more frequently than the general cohort and those with lower social functioning less frequently (higher social functioning 45.00%; lower social functioning 20.00%, compared to 30.00% in the general cohort). Participants with higher social functioning indicated that no one brought up the topic of biomarker/genetic testing, less frequently than the general cohort and those with lower social functioning more frequently (higher social functioning 40.00%; lower social functioning 70.00%, compared to 58.00% in the general cohort). Participants with no eye problems indicated that no one brought up the topic of biomarker/genetic testing, more frequently than the general cohort (68.75%, compared to 58.00% in the general cohort).

Genetic testing	All participant	% of all participants	General Health		Physical function		Emotional well-being	
	N=50	Percent	Higher N=22	Lower N=28	Higher N=22	Lower N=28	Higher N=26	Lower N=24
I brought up the topic with my doctor for discussion	6	12.00	1 (4.55%)	5 (17.86%)	2 (9.09%)	4 (14.29%)	3 (11.54%)	3 (12.50%)
My doctor brought up the topic with me for discussion	15	30.00	8 (36.36%)	7 (25.00%)	9 (36.36%)	7 (25.00%)	9 (34.62%)	6 (25.00%)
No one has ever spoken to me about this type of test	29	58.00	13 (59.09%)	16 (57.14%)	12 (54.54%)	17 (60.70%)	14 (53.85%)	15 (62.50%)

	Social functioning		Hearing impairment		Visual or eye impairment	
	Higher N=20	Lower N=30	No hearing problems N=26	Hearing problems N=24	No eye problems N=16	Eye problems N=34
I brought up the topic with my doctor for discussion	3 (15.00%)	3 (10.00%)	3 (11.54%)	3 (12.50%)	1 (6.25.00%)	5 (14.71%)
My doctor brought up the topic with me for discussion	9 (45.00%)	6 (20.00%)	7 (26.92%)	8 (33.33%)	4 (25.00%)	11 (32.35%)
No one has ever spoken to me about this type of test	8 (40.00%)	21 (70.00%)	16 (61.45%)	13 (54.17%)	11 (68.75%)	18 (52.94%)

	Location		Education		SEIFA	
	Metropolitan N=30	Regional N=20	School/ Trade N=26	University N=24	Higher N=27	Lower N=23
I brought up the topic with my doctor for discussion	2 (6.67%)	4 (20.00%)	3 (11.54%)	3 (12.50%)	2 (7.41%)	4 (17.39%)
My doctor brought up the topic with me for discussion	10 (33.33%)	5 (25.00%)	7 (26.92%)	8 (33.33%)	9 (33.33%)	6 (26.09%)
No one has ever spoken to me about this type of test	18 (60.00%)	11 (55.00%)	16 (61.45%)	13 (54.17%)	16 (59.26%)	13 (56.52%)

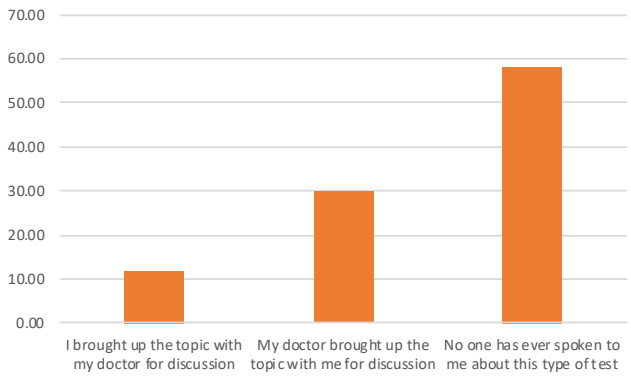

Figure 3.9: Genetic and biomarker tests (% of all participants)

Participants were also asked about their interest in this type of test if it was available. The majority of participants noted that they had not had this test, but would like to (n=26, 52.00%). There were 8 participants (16.00%) that reported having this test and not paying out of pocket for it, 8 had this test as part of a clinical trial (16.00%), and two paid for this test themselves (4.00%). There were 6 participants (12.00%) indicated that they had not had this test and were not interested in it.

In relation to sub-group variations, participants that had hearing problems, no eye problems and that were university educated indicated that they had not had this test but would like to, less frequently than the general cohort (41.67%, 31.25% and 33.33% respectively compared to 54.00% in the general cohort), while participants that did not have hearing problems, had no eye problems and had high school or trade qualifications indicated that they had not had this test but would like to, more frequently than the general cohort (61.54%, 61.76%, and 69.33% respectively, compared to 54.00% in the general cohort).

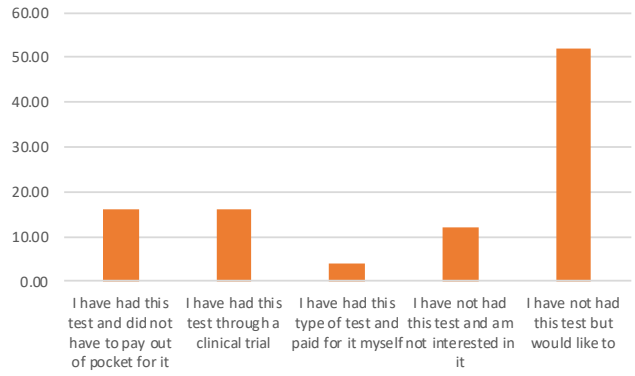

Figure 3.10: Interest in genetic and biomarker test (% of all participants)

Table 3.13: Interest in genetic and biomarker test

Genetic testing	All participants	All participants	General Health		Physical function		Emotional well-being	
	N=50	Percent	Higher N=22	Lower N=28	Higher N=22	Lower N=28	Higher N=26	Lower N=24
I have had this test and did not have to pay out of pocket for it	8	16.00	6 (27.27%)	2 (7.14%)	3 (13.64%)	5 (17.86%)	5 (19.23%)	3 (12.50%)
I have had this test through a clinical trial	8	16.00	3 (13.64%)	5 (17.86%)	5 (22.73%)	3 (10.71%)	5 (19.23%)	3 (12.50%)
I have had this type of test and paid for it myself	2	4.00	1 (4.55%)	1 (3.57%)	2 (9.09%)	0 (0.00%)	1 (3.85%)	1 (4.17%)
I have not had this test and am not interested in it	6	12.00	2 (9.09%)	4 (14.29%)	0 (0.00%)	6 (21.43%)	3 (11.54%)	3 (12.50%)
I have not had this test but would like to	26	52.00	10 (45.45%)	16 (57.14%)	12 (54.54%)	14 (50.00%)	12 (46.15%)	14 (58.33%)

	Social functioning		impairment		Eye or visual impairments	
	Higher N=20	Lower N=30	No hearing problems N=26	Hearing problems N=24	No eye problems N=16	Eye problems N=34
I have had this test and did not have to pay out of pocket for it	3 (15.00%)	5 (16.67%)	4 (15.38%)	4 (16.67%)	2 (12.5%)	6 (17.65%)
I have had this test through a clinical trial	5 (25.00%)	3 (10.00%)	3 (11.54%)	5 (20.83%)	1 (6.25%)	7 (20.59%)
I have had this type of test and paid for it myself	1 (5.00%)	1 (3.33%)	0 (0.00%)	2 (8.33%)	2 (12.50%)	0 (0.00%)
I have not had this test and am not interested in it	1 (5.00%)	5 (16.67%)	3 (11.54%)	3 (12.50%)	6 (37.50%)	0 (0.00%)
I have not had this test but would like to	10 (50.50%)	16 (53.33%)	16 (61.54%)	10 (41.67%)	5 (31.25%)	21 (61.76%)

	Location		Education		SEIFA	
	Metropolitan N=30	Regional N=20	School/ Trade N=26	University N=24	Higher N=27	Lower N=23
I have had this test and did not have to pay out of pocket for it	4 (13.33%)	4 (20.00%)	4 (15.38%)	4 (16.67%)	4 (14.81%)	4 (17.39%)
I have had this test through a clinical trial	5 (16.67%)	3 (15.00%)	2 (7.69%)	6 (25.00%)	4 (14.81%)	4 (17.39%)
I have had this type of test and paid for it myself	1 (3.33%)	1 (5.00%)	0 (0.00%)	2 (8.33%)	1 (3.70%)	1 (4.35%)
I have not had this test and am not interested in it	5 (16.67%)	1 (5.00%)	2 (7.69%)	4 (16.67%)	4 (14.81%)	2 (8.70%)
I have not had this test but would like to	15 (50.00%)	11 (55.00%)	18 (69.23%)	8 (33.33%)	14 (51.85%)	12 (52.17%)

Participants were asked if they had any particular mitochondrial disease biomarkers, the majority of participants (n=39, 78.00%) were not sure.

Table 3.14 Biomarkers

Biomarkers	n=50	Percent
I'm not sure	39	78.00
m.3232A>G	5	10.00
m 3243A>G	2	4.00
11778	1	2.00
FGF21,GDF15,m.3232A>G,	1	2.00
m.3302A>G	1	2.00
m 3113 A>G	1	2.00

In the structured interview, participants were also asked to talk about their understanding of genetic or biomarker testing. Some of the descriptions are provided below and include understanding that the test is used for diagnosis of mitochondrial disease; understanding that the test cannot help them but may help others in the future; and understanding that the test cannot target treatment as there are no treatments available or that there was no clinical indication following the test:

Participant understands that the test is used for diagnosis of mitochondrial disease

That it would just give me a name to at least put to and allow me to understand the cause of the vision loss, which was a good thing. Participant 13

The genetic treatment was, again, under NAME. I'm not too sure of the exact results, genetically speaking, but whatever it was, it was enough to confirm the diagnosis that they had been making through the years. Participant 23

It was partly for our peace of mind to know what was actually wrong with us. We weren't just fit or lazy, but there was actually a diagnosable illness. It was probably for our peace of mind. Participant 43

Participant understands that the test can not help them but may help others in the future

I didn't believe that there was anything that could help me because they keep saying there's no treatment, so basically, I was of the opinion that it was more for potential of assisting in the future for other people. Participant 2

I don't know whether they were going to help me. We were under the understanding they might help other people. Participant 41

Participant understands that the test can not target treatment as there are no treatments available or that there was no clinical indication following the test

Well, actually, they've got it wrong because there isn't anything they can do with it, there is only so…there is no treatment or I've had as much treatment as I can have. Participant 9

….so it wasn't until after his diagnosis that we sort of talked more about their use, which was kind of like a moot point kind of thing, really. Participant 46

Communication and understanding of prognosis

Participants were asked whether anyone talked to them about prognosis. The most common theme noted by 26 participants (52.00%) was prognosis had not been clearly discussed:

Participant describes prognosis not being discussed

No, nothing. All we've received is what I've said about Dr. NAME a couple of years ago. The name and I received some information from AMDF by Googling and NAME at AMDF. Also we went down recently to NAME Hospital and went to a clinic there, run by NAME. They took 15 vials of blood and 5 urine jars, and I've got to do further testing with them at the LOCATION Hospital. I did an Echocardiogram recently about two weeks ago. They got to do further tests and they're going to contact me in about six months, they said. Participant 6

No I can't because it's such a fickle thing…I think my neurologist who I have a great deal of respect for, would say it's very difficult to make a prognosis as indefinite things, such and such will happen at such a time, or even what organs might be affected. Participant 20

No, no. I mean, that's the nature of the condition is that it is very ... the fact that he's holding on there. I mean, he has absolutely shocked everyone. No one would have thought that the child ... generally, when a baby presents as he did, they generally don't make it through and he's low abnormal mitochondrial cell load is 95 to 100% effective. He's quite the miracle. That's why we just keep on going. Participant 45

The next most common theme was that participants understood that mitochondrial disease came with a poor prognosis that was primarily related to physical decline. This was noted by 9 participants (18.00%)

Participant describes poor prognosis - decline in physical function

I'm already experiencing a bit of what I've been told is a drop foot. I've also get a lactic acid build up very quickly when I walk. If I walk up two flights of stairs, I feel like I'm weak in my legs. I have periods where I become very lethargic. I'm going to lose the ability to like I get out in the garden on a Saturday and get everything done and then Sunday I would go and do family stuff. Now, it takes me a weekend what I used to do in three-quarters of a day, simply because of the lethargy of losing strength. I've definitely noticed that in my arms and legs. I suppose the drawback there, if you feel that when you're told you need to get into the gym but instead of being sore for one or two days after, you're sore for a week or seven days after, which means to go start doing it, you're going to be constantly sore. It's a bit of a mental thing to keep overcome. Participant 2

My main issues which really troubles me is my calf muscles. I'm finding it difficult to walk around. Difficulty getting up off a chair, that's hard. I've got to struggle. I'm finding it difficult to walk around. Simply get up off a chair is hard. I can't get up without using the arms on the chair to push myself up. Uneven ground is difficult for me to walk on. Going upstairs, I can still use stairs by using a handrail or else I'll fall over. Participant 6

In the last three years, it seems to have got worse. I'm just more tired and I have no energy and very...I've had to quit my job. It seems very unknown, but it seems to be getting worse. Participant 19

There were seven participants (14.00%) that described the need for ongoing management of their condition and this included the management of exacerbations:

Participant describes a ongoing management of their condition, often with exacerbations

The current prognosis is it remains the same. As I said, I see Dr. NAME, the neurologist, every six months. If I do have a really bad three or four days, I'll give her a call and she gets me into an earlier session, but there's no basic cure, there's no...except pain medication which tends to..at the...in the pain management center. Participant 23

It's mixed. There are some days that are really quite frightening and I guess you sort of reflect on what your family's gone through and the symptoms they had, then you assume that you are going to get the same thing which isn't an easy thing to go through. I guess it makes it more challenging in terms of starting a family as well. That was always something that we had assumed would just happen. That's now presented a whole lot of challenges as well and also how is my health going to be in a few years and will I be a productive mother if we do have a child. There's a lot of ups and downs. Participant 26

I'm supposed to be on managing the diabetes side because part of it I've got eye problems. That's being monitored annually by an Ophthalmologist. That's slightly deteriorating. I have diabetes. That's been monitored. I'm supposed to control that. I know I should better than I am. Exercising and the medication. I've had one medication to start with to control seizures. Then, after 12 months or so, they changed that to my current medication that I've been taking for about eight years now. Participant 29

The final theme in relation to understanding of prognosis was that mitochondrial disease came with a poor prognosis, including reduced life expectance and/or a rapid disease progression. This was noted by six participants (12.00%):

Participant describes poor prognosis - reduced life expectancy and/or rapid progression of disease

When I was diagnosed, NAME said, "It'll probably shorten your life." et cetera. He said we would just go along because as I said earlier he explained that there was no medication he could give me, only painkillers and things like that. He didn't seem to know a real lot about it. When I went to him, he only had one other patient that had been diagnosed with it. He's an MS specialist actually, I think that's what he really is noted for. That's about it. Participant 31

Not really, they just said it's ...they're thinking at the moment which is good because the fast progression means it will be terminal quickly....hoping that it's not going to be that. Participant 35

I've been told there is no cure. It's uncertain, I don't know, because it seems to have progressed more rapidly in the last five years. I don't know whether I'll stay as I am now for another 10 to 15 years, or whether it will continue to deteriorate at that rapid rate, I have no idea. Participant 36

Table 3.15: Understanding of prognosis

Understanding of prognosis	All participants	
	n=50	%
Participant describes prognosis not being discussed	26	52.00
Participant describes poor prognosis - decline in physical function	9	18.00
Participant describes a relatively stable disease/controlled (may have some exacerbations)	7	14.00
Participant describes poor prognosis - reduced life expectancy and/or rapid progression of disease	6	12.00