

The Voice of the Patient



Summary report resulting from an *externally led*
Patient-Focused Drug Development Meeting,
a parallel effort to the
U.S. Food and Drug Administration's (FDA's)
Patient-Focused Drug Development Initiative

FRIEDREICH'S ATAXIA (FA)

Externally Led Public Meeting: June 2, 2017
Report Date: August 20, 2017



The Voice of the Patient

Summary report resulting from an Externally Led Patient-Focused Drug Development meeting, a parallel effort to the U.S. Food and Drug Administration's (FDA's)

Patient-Focused Drug Development Initiative

Friedreich's Ataxia

Externally Led Public Meeting: June 2, 2017

Report Date: August 20, 2017

Hosted by:

Friedreich's Ataxia Research Alliance, Muscular Dystrophy Association, National Ataxia Foundation, and Cure FA Foundation



Submitted to:

Center for Drug Evaluation and Research (CDER) &
Center for Biologic Evaluation and Research (CBER)
U.S. Food and Drug Administration (FDA)

This report represents the summary report composed by patient advocacy organizations as a result of an Externally Led Patient-Focused Drug Development meeting, a parallel effort to the FDA's Patient Focused Drug Development Initiative. This report reflects the host organization's account of the perspectives of patients and caregivers that participated in the public meeting.

Table of Contents

Table of Contents	2
Introduction:.....	3
Overview of Friedreich’s Ataxia:	3
Meeting Overview:	4
Report Overview and Key Themes:.....	5
Topic 1: Living with Friedreich’s Ataxia	7
Disease Symptoms:.....	8
Disease Symptoms: Balance and Walking	8
Disease Symptoms: Fatigue.....	9
Disease Symptoms: Manual Dexterity.....	10
Disease Symptoms: Speech and Hearing.....	10
Disease Symptoms: Vision	11
Disease Symptoms: Cardiomyopathy	11
Disease Symptoms: Other.....	11
Everyday Life with FA	12
Topic 2: Patient Perspectives on Current and Future Approaches for Treating FA.	14
Symptom Management: Medications	14
Symptom Management: Scoliosis.....	15
Symptom Management: Cardiac.....	15
Symptom Management: Other Surgeries	16
Symptom Management: Other Interventions	16
Perspectives on Clinical Trials.....	17
Perspectives on Future Treatments	18
Conclusions:.....	20
References:.....	20
Appendix 1: Incorporating Patient Input into a Benefit-Risk Framework for Friedreich’s Ataxia	21
Appendix 2: Meeting Agenda	23
Appendix 3: Meeting Panelists	25
Appendix 4: Discussion Questions	26
Appendix 5: Polling Questions	30
Appendix 6: Full Results from Polling Questions	36
Appendix 7: Patient / Caregiver Testimonies	55

Introduction:

On June 2nd 2017, The Friedreich's Ataxia Research Alliance (FARA), Muscular Dystrophy Association (MDA), National Ataxia Foundation (NAF), and Cure FA Foundation co-sponsored an Externally Led Patient-Focused Drug Development meeting for Friedreich's Ataxia (FA). The goal of the meeting was to give FA patients, their families and caregivers a forum to discuss their perspectives on living with the disease: what symptoms they experience, how it affects their lives, what concerns them about the disease, their opinions on current and future treatment options, and experiences with research studies and clinical trials. The meeting was formatted in a manner similar to the FDA-led Patient-Focused Drug Development Meetings, which were set up to more systematically gather patients' perspectives on their condition and available therapies to treat their disease (<https://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm>).

Overview of Friedreich's Ataxia:

Friedreich's ataxia (FA) is a debilitating, life-shortening, progressive degenerative neuromuscular disorder that affects approximately 1 in every 50,000 people in Caucasian populations of Europe, the Middle East, South Asia (Indian subcontinent) and North Africa. Incidence is very rare in other ethnic groups¹. Although rare, it is the most common form of inherited ataxia. FA is an autosomal recessive, single gene disorder, caused by mutations in the frataxin gene. In most cases, it is caused by an expanded GAA triplet repeat in intron 1 of the frataxin gene but, in about 4% of cases, patients have a triplet repeat expansion on one allele and a point mutation in the frataxin gene on the other allele². Diagnosis is typically by genetic testing, which detects about 99% of all cases. About 75% of patients are diagnosed between 6 and 20 years of age, while about 22% are diagnosed after 21 years of age.

Loss of balance and coordination is the most common presenting symptom, typically beginning between the ages of 5 and 15 years with progression of symptoms leading to loss of ambulation and independence of all activities of daily living. Adult or late-onset FA is less common and occurs after the age of 25. Patients with point mutations may have slightly different disease course than those with two expanded repeats.

FA is multi-systemic, affecting the neurological system – e.g., balance, fine motor skills, sight, and hearing – and also the heart, skeletal muscle, skeleton (scoliosis, pes cavus), and digestive system (diabetes). While neurological features of the disease are fully penetrant, affecting 100% of those diagnosed, other systems are not affected in all patients. Two thirds of patients develop cardiomyopathy, more than half develop severe scoliosis and the incidence of diabetes is between 10 and 40%.³ The *mean age at death is 35 years*, due to cardiac complications in greater than 50% of individuals.⁴

The first symptom identified is frequently ataxia - loss of coordination and balance - but, in some cases, cardiomyopathy or scoliosis may precede onset of neurological disease. Symptoms such as vision impairment, hearing loss, swallowing difficulties and urinary disturbances are generally more prominent in late-stage disease. On careful examination, however, signs of these symptoms are often detectable in patients early in progression. By end-stage disease, about 95% of patients will have myocardial involvement. Shinnick *et al* reported that FA patients also have a higher incidence than unaffected people of certain other diseases, such as ulcerative colitis, Crohn's disease, inflammatory bowel disease and growth hormone deficiency⁵. However, incidence of these conditions is still low in the FA population.

The progressive loss of coordination and muscle strength leads to motor incapacitation and the full-time use of a wheelchair, typically within 10-15 years of diagnosis. Most young people diagnosed with FA require mobility aids such as a cane, walker, or wheelchair by their teens or early 20s. Intelligence of people with FA remains completely intact, although subtle differences in cognition can be detected. There are no approved therapies for FA.

Meeting Overview:

The meeting provided the FDA and drug developers with an opportunity to hear from patients, caregivers, family and friends about FA, how FA affects patients' lives, and how patients treat the disease now, in the absence of any disease-specific therapies. Patients and caregivers also offered their perspectives on what they would find most valuable from future treatments, and how they would weight risk and benefit of such treatments. The two major topic areas were "Living with Friedreich's Ataxia" and "Current & Future Approaches to treating Friedreich's Ataxia" (see Appendix 2, meeting agenda).

Approximately 200 people attended the meeting in person, with about 200 more participating online, providing comments and taking part in the live polling. The in-person attendees included 145 patients and caregivers, representing 70 families, 10 representatives of patient advocacy groups, 25 representatives of drug development companies and approximately 20 FDA representatives. This is believed to be the largest gathering of FA patients and families that has ever occurred.

The meeting began with opening remarks and an FA overview by FARA's Executive Director and FARA's Co-Founder/Founding President, and FDA welcoming remarks by the Director of the FDA/CBER Office of Tissues and Advanced Therapies. The meeting moderator then previewed the agenda, conducted demographic polling of the in-person and remote participants and showed a brief video about living with FA. The central portion of the meeting consisted of two panel discussions on the major topic areas, in which a total of 10 patients and caregivers presented prepared testimony. Each panel was followed by a series of polling questions, with data collected in real time from both online and in-person patient and caregiver attendees (see Appendix 4, polling questions), followed by facilitated discussion of each topic to include all in-person patient and caregiver attendees, who were provided with the topic areas prior to the meeting. All patients and families attending in-person and online were encouraged to submit additional comments electronically. In addition, those who could not participate at all were

notified about the meeting and the topics so that they could electronically submit their thoughts before or after the meeting (within 30 days) in order to ensure that experiences of as many patients as possible were included. Written testimonies were received from 22 individuals (Appendix 7).

Patients and caregivers represented on each panel were chosen so that the disease spectrum was covered as fully as possible (see Appendix 3). This included patients with an early age of onset (severely affected) and those with later-onset disease, who typically have a milder course. In the discussion, patients with an expanded genetic repeat and a point mutation, who typically have a different disease course and symptom profile from those with two expanded repeats, were also represented. Patients who had FA symptoms that are not fully penetrant (e.g. scoliosis, cardiomyopathy, diabetes) were also represented on the panels and in discussions. A short video entitled “*Our Life with FA- Always Changing*” was included so that the testimony of patients with very advanced disease, who were unable to travel to the meeting, as well as patients who had passed away from the disease, were represented. The organizers of the meeting recognize that the panels likely under-represented those at very early stage of disease due to age, and those in very late stage of disease due to severe disability.

Polling showed that about half of the 145 respondents were patients, with the remaining 50% being caregivers of patients. Respondents came from around the US, with 35% from the Northeast; there were a small number of responses from outside the US. Approximately 55% of respondents lived in suburban areas, with the remaining responses coming equally from patients in urban and rural areas. Patients of all ages were represented in the polls, either by answering themselves or by having caregivers or others respond for them. However, only 8 patients under the age of 10 were represented (5.5%), and 15 over the age of 50 (10%). Over half of the responses were for patients between ages 20 and 40. Many patients had been living with the disease for significant periods of time, including 24 patients who had lived with FA for over 21 years (17%). Twelve patients (8%) had been diagnosed within the last year. Represented patients covered the spectrum of disability levels, but about 40% described themselves as not able to walk but able to perform some activities, and only 4% and 10% responded that they have minimal disability or severe disability, respectively.

Recordings of the meeting and the video “*Our Life with FA – Always Changing*” may be viewed at <https://www.youtube.com/watch?v=Va1D4SqrSfw&feature=youtu.be>.

Report Overview and Key Themes:

This report summarizes the input provided by patient and caregiver panelists and audience comments from the meeting, responses to the polling questions from people in the room and viewing the meeting online, and testimonials sent to FARA before and after the meeting in response to a request for submissions. As much as possible, the authors have used the patients’ and caregivers’ own words, so as to represent their feelings as closely as possible, rather than to interpret their comments. This report represents the perspectives of individuals who provided their input for the meeting; it may not represent the thoughts and feelings of all patients

throughout the disease community. Additional groups of patients may have not been represented, and the demographics of the group was limited as noted above.

The main themes that came out in the meeting, polling and testimonies were as follows:

- Friedreich's Ataxia is a devastating multisystem progressive disease. Patient symptoms include pervasive issues with loss of balance/coordination, issues with ambulation and falls, loss of manual dexterity and fatigue. These occur in nearly all patients. Over 50% of polling respondents also reported scoliosis, cardiac concerns, dysarthria and spasticity, with other symptoms represented in lower numbers of patients.
- The disease has an enormous effect on quality of life, with younger patients discussing the social and physical concerns of navigating life with a disability, and older patients discussing how progression of specific symptoms limited their ability to work, have families and pursue hobbies. Loss of independence was noted as the greatest concern for patients, particularly as the disease progresses.
- The progressive nature of the disease is very concerning to patients. Several noted they had adapted to where they are in the course of the disease, but that the constantly changing adaptations they must make are very challenging, both physically and mentally.
- While the majority of patients noted that balance, dexterity and fatigue affected their lives the most now, most patients' greatest concern for their future is the development/ progression of cardiomyopathy in the future because it is life limiting.
- The majority of patients take supplements (e.g. vitamins) and almost all have exercise regimes to help keep their muscles strong and attempt to slow progression, but strongly desire disease modifying therapies. Some have undergone surgeries for scoliosis or cardiac issues, and it was noted that the surgeries were difficult for patients and recovery time was prolonged. Many noted that their current interventions take significant time and have significant cost, but they felt that they helped slow progression a little.
- Patients expressed that while a cure for the disease as a whole is needed, short of a cure they would find a slowing or stopping of disease progression to be very valuable. Even treatment of individual symptoms, particularly cardiomyopathy, and treating balance issues, fine motor skills, and speech, were seen as advantageous, and maintaining their current status in terms of either disease progression as a whole or in terms of individual symptoms would be perceived as making an improvement in quality of life.
- Patients expressed a great willingness to take part in clinical research and to seek treatments and cures for the disease. Many had already taken part in clinical trials or research studies, and most were willing to accept some risk associated with using a novel treatment. Many reported positive outcomes in trials or with supplements, e.g. less fatigue and other aspects of the disease not captured with existing endpoints.

The patient input on these topics will help the FDA and drug developers more fully to understand the disease, its symptoms and specific therapeutic effects that would be meaningful to patients short of a cure. It will inform the field of new areas of investigation into potential therapies for specific disease symptoms that are most important to the FA community, and may provide insights into the development of new endpoints to measure drug effects on these symptoms. It will also inform the benefit-risk calculus for proposed new therapies (see Appendix 1), demonstrating how patients feel about what outcomes would represent a meaningful benefit from

a treatment, and what risks they may be willing to accept in order to modify the course of the disease.

Topic 1: Living with Friedreich's Ataxia

The first topic of discussion involved living with FA: the symptoms patients exhibit, how they feel about those symptoms, and how the disease affects their lives. The panel included three patients at different stages of disease, the mother of a younger patient with significant cardiac symptoms, and the mother of two older patients, one of whom is deceased due to FA. Patients and caregivers were chosen to represent a range of experiences of symptoms, and patients with both early and later disease onset (which correlates with symptom severity). As one panelist put it:

“There are two ends of the spectrum you can come from if you're an FA patient. Either you've had it since you were younger, most likely suffering the more severe symptoms-they've known FA their whole life. OR- the place I come from, which is having the later onset of symptoms, living a 'NORMAL LIFE' and slowly watching my body deteriorate and struggle to do things I once did with ease.... Whatever way you look at it, both ends of the spectrum are completely devastating.”

During the discussion, some patients noted that they had a point mutation along with a triplet repeat expansion, and that this causes a form of FA that differs somewhat from classical FA, which is associated with two triplet-repeat expansions:

- *“My daughter, Chelsea, was diagnosed at the young age of 4 ½. Not only did we win the lottery with a diagnosis so rare, but she also had an extremely rare point mutation, W155R. Her progression was rapid and we knew because of her rare point mutation, she wouldn't be here on this earth too long with us. She lived a short 19 years, but in those 19 years she truly touched so many lives.”*
- *“I have a point mutation, so my symptoms are a bit different to classic FA. I have a spastic gait, not an ataxic gait, and my coordination is not particularly affected. I have a lot of fatigue.”*

As a genetic disease that is often not diagnosed in the first few years of life, many families had multiple children with FA. This presents families with novel challenges, particularly living with uncertainty until younger siblings are tested, and for younger siblings seeing first-hand what progression may look like. One patient explained, *“Life was pretty normal until I turned 6 and my older brother was diagnosed with FA.... We discovered that I could have a 1 in 4 chance of also having this disease, and sure enough 2 years later it was confirmed. My clumsiness during this time became defined as FA – a fear we had tried to ignore during this 2-year period.”*

A mother of five children, two with FA, talked about how hard it was for her younger child to see what his sister was experiencing, believing he had the same disease *“Our 12-year-old was recently diagnosed, and we are waiting on diagnosis for one of my younger children....The six-year-old boy sees his sister who was once independent now in a chair – knowing he has many of the same issues she had when she was younger, prior to diagnosis. He is angry and scared and frustrated.”*

Disease Symptoms:

FA is a multisystemic disease, with significant variability, even within families, and is associated with many different symptoms that affect some or all patients as the disease progresses:

“We quickly learned that in addition to gait and balance issues, there were many other aspects to the disease: cardiomyopathy, scoliosis, fatigue, and even vision and hearing loss at later stages.”

Patients described a spectrum of disease symptoms. Almost all reported issues with balance and walking (86%), hand coordination (81%) and fatigue (92%). 66% reported having dysarthria; 56% scoliosis; 55% spasticity or cramping; and 51% reported cardiac conditions. 40-50% of patients experienced symptoms including choking and swallowing problems, urinary and bowel issues, and pain. A smaller proportion of the patients polled had vision and hearing loss, which typically develop later in disease. Diabetes was experienced by 14% of those polled. Of all the symptoms described, fatigue (63%), balance (66%) and coordination (63%) were most often described as the three that most affected daily life, followed by dysarthria (25%) which was a prevalent concern in later stage patients.

Patients noted that as disease progresses, new symptoms emerge and life becomes increasingly difficult – a mother of a deceased patient described her daughter’s later years: *“[By the time she left college] she could barely type, had begun having difficulty with the enunciation of words and the ability to control her breath when speaking. She began choking and strangling and had to have thickener in her liquids. She required 12 hours of sleep and never had much energy. ...She became unable to bathe and dress herself, brush her teeth or hair, put on make-up, and take care of her toileting needs. Rather quickly, she also lost the ability to feed herself and hold a cup. She soon was not able to roll over in bed or adjust her position during the night, and couldn’t scratch when she itched....”*

Disease Symptoms: Balance and Walking

“My saddest memory is the day I realized our home no longer embraced the comforting sound of footsteps of my children.”

Issues with balance and walking were pervasive among patients, with nearly 90% reporting these symptoms. 50% of the patients surveyed could no longer walk. Patients explained that these symptoms had a profound impact on their lives.

During discussion, a mother described her son’s experience with the loss of balance caused by FA, and how this affects his ability to socialize with other children: *“... the worst part is the loss of ability to walk. He is left behind.... It is hard to see him getting to where the other kids are, but by then the kids are going somewhere else. He just wants to fit in.”*

Another patient described going through high school while his balance was getting progressively worse: *“Progression in high school changed my walking and talking-- like I had a little too much tequila-- just imagine a giraffe in high heels on a windy day.”* He went on to tell a story where he was called into the principal’s office after being accused of being drunk by the parent of

another student, a story that resonated with other FA patients. In written testimony another patient explained *“Through junior high and high school I was bullied by not only other kids but teachers & the principal, thinking that my staggered steps/falls/struggle to climb the stairs were due to me being drunk and drug use.”*

A later-onset patient described a slower decline in balance and walking, which still affects her life significantly: *“... I was still walking but holding on to my husband and walls for support. Stairs and curbs became my enemy. I made the decision to get a service dog. It was a difficult decision, but she gave me back my independence... After my dog retired, I started using a walker for bilateral support. This was another loss, another downhill slide.”*

In written testimony, another patient described how the frequency of falls, accompanied by fatigue, prevents her from participating in activities of normal life: *“Physical impairment and frequent falls, combined with fatigue, is detrimental. When I fall, it takes anywhere from 5 minutes to 2 hours to get back up. Sometimes I still can't get up myself and have to call for help. Most of the time, I am hot, sweaty, and shaking from exhaustion once I get up, and then it takes me half an hour or more to recover my energy.”*

Disease Symptoms: Fatigue

“My biggest problem is transferring to bed and lying down when I need to, because I am fatigued all the time.”

Fatigue was the most commonly reported symptom in the polling questions, throughout the course of disease (92%). Patients describe the fatigue both as needing to sleep more than other people, but also muscle fatigue and slow recovery: *“One thing that holds me back is fatigue - not only feeling tired but muscle fatigue during exercise. My daily workouts include yoga, weights, recumbent bike, and keeping up with the activities of my 3 children. My muscles become so fatigued they cramp and shake making my workouts limited. Safety becomes a concern and it takes a while for my muscles to recover and steady. I feel like I am constantly thinking ahead to plan on how much energy I need to get through my day and often need rest periods to recharge my batteries.”*

Fatigue was described by patients as pervasive, and having a large effect on activities of daily living, as some patients frequently cannot get through a regular day.

One young man explained that, *“My biggest problem with FA is fatigue, simply because it affects everything I do, every day. Fatigue really affects my school attendance, and I often miss a full or half day of school. On a day when I'm feeling really good, I can get through what most kids would think was a pretty boring day. I can manage my short class schedule and then do either therapy or homework at night, but never both. On my worst days, I don't make it to school at all and try to catch up with my teachers through email. Just this year, I've missed 184 class periods. I try, but caffeine only goes so far.”*

Patients also noted that fatigue affects their other symptoms, making them harder to deal with: *“...when Anna gets fatigued, her balance becomes extremely unsteady, she falls more often, experiences an increased heart rate, and migraine headaches. Upon returning from a recent trip*

out of town to participate in a clinical drug trial, she was so unsteady, she held onto my arm for about a week when walking and asked for a walker to keep at home."

Disease Symptoms: Manual Dexterity

Issues with manual dexterity affect nearly 90% of patients surveyed. This is manifested in many ways, and profoundly affects how patients interact with their environment.

Patients talked about the challenges of simply picking up small items: *"It took me TWO whole minutes to pick up a bobby pin off of my bathroom floor the other day because I am slowly losing control over my hips and arms."* Other patients reported frustration trying to button their clothes, dress, eat and apply make-up. Several patients talked about how messy eating and drinking has become.

Patients also discussed the challenges of typing and writing - several noted how hard it is to keep up in school because using a pen or computer keyboard is so difficult and slow. This in turn affects career choices and future lives: *"I can't type, which means that I can't get my PhD, which means I can't get my ideal job,"* explained one patient.

Patients also talked about the hardship of having to give up hobbies that are important to them - building rifles, playing computer games and musical instruments, and tying flies for fishing were some examples of skills lost to disease. *"I see my fine motor skills getting worse every day when I play video games like Call of Duty. While my friends are getting better, my K/D stats are decreasing."* *"I grew up playing music and continue playing piano, saxophone and guitar to maintain finger dexterity. Unfortunately, it can be a frustrating chore as I continue getting worse due to my FA progression"*.

Disease Symptoms: Speech and Hearing

"The most common word I hear is "huh" thanks to my dysarthria, and I barely hear that due to hearing loss."

Slurring of speech, or dysarthria, was another symptom cited by many as an important aspect of disease progression, particularly in later stage patients. The combination of speech and hearing concerns means that many patients have only limited ways to communicate and connect with other people. As a consequence, many are made to feel bad or treated as if they are less intelligent because of FA. One stated, *"I'm often talked down to or belittled because of how I speak."* This often negatively affects self-worth and further isolates patients from the world.

Furthermore, loss of speech and hearing affects career choices for many FA patients: A teacher explained, *"I can't filter out the background noise to focus on the topic, and I can't hear students at the back of the class,"* while a college professor said, *"I teach college online. I can no longer teach live as my speech is too slow and too hard to understand to cover the material in time."* A speech pathologist with FA noted that, *"I truly enjoy working with others to improve their communication, but having dysarthria myself, it is incredibly taxing... When the voice and speech are impaired, as it is in FA, it is often laborious and fatiguing to communicate with others."*

Disease Symptoms: Vision

“Without vision you have nothing - isolation from the world is complete.”

Loss of vision typically occurs later in disease course, which is perhaps reflected in the polling questions where it was not listed as a major concern. However, statements from patients suggest that as vision is lost, it has profound effects on their lives: *“My optic nerve degeneration has affected my vision so much, that I cannot see objects that are further than a couple inches from my face. Vision is such a powerful sense, and it’s frightening to know I may never be able to enjoy life through my own eyes again.”*

Patients noted that loss of vision is particularly frightening when it comes on top of loss of other capabilities, *“I am most worried about losing my vision because of FA. I feel if I lose my vision, I will lose my remaining link to the world. It would take even more of my independence away...”*

Disease Symptoms: Cardiomyopathy

“The cardiomyopathy is the biggest stress. It is an unknown – how will it progress? That is what kills.”

The polling questions revealed that 51% of patients had a cardiac condition, while 60% worried about progression of cardiac health the most. About 33% were taking some type of medication to treat cardiac issues. Cardiac dysfunction is the eventual cause of death for approximately 60% of FA patients.

Patients note that cardiomyopathy can limit activity: *“One of my biggest problems is dilated cardiomyopathy. This makes it very hard staying active for any long period, especially if I am in a hot and humid environment.”* He went on to describe activities, such as fishing, which have become limited for him.

Sharing the experiences and views of her newly diagnosed 5th grade daughter with FA, a mother explained, *“She doubts her ability to swim laps for swim team and keep up with lacrosse teammates during basic drills, due to her inconsistent heart beat.”*

Patients are also all too aware that cardiomyopathy can kill: *“My heart is on the losing side of this battle. A premature death, that you hear in all the literature, is becoming apparent. I’m not scared of it, but I’m sure my family worries every single day.”*

Disease Symptoms: Other

In addition to the symptoms described in the sections above, patients reported other issues and concerns. They include scoliosis, diabetes, pain and anxiety/depression which are common features of FA. More than half of patients develop severe scoliosis requiring painful surgery to fasten metal rods to the spine to straighten it. Between 10 and 40% develop diabetes. Other symptoms include pain (44%), and diagnosed depression or anxiety (40%). These may have

significant impact on daily life. One FA patient explained, *“I live my life in constant pain whether it’s my muscle spasms, chest pain, headaches or the extreme fatigue”*.

These and other problems can sometimes be managed with standard therapies, although their use may not be optimized for the FA community. Patient experience with these symptoms is described, below, under Topic 2 regarding existing therapies, as the patient experience of the symptoms is also tied in with how they treat the symptoms.

Some FA patients experience a range of other concerns. One mother explained that, *“When my daughter gets sick – a virus is so much worse for her than for her friends. It lasts longer, or she gets terrible leg pains. Any surgery is terrible for her – a lot of pain - extra fatigue and pain in recovery.”* Several other patients and parents expressed similar concerns.

A mother whose daughter was deceased due to FA explained that, *“She could no longer think clearly and was unable to focus. The depression worsened and then the most painful symptom raised its ugly head. She began experiencing attacks of intractable spasticity which struck with no warning, causing excruciating pain. She would have to go to bed with these attacks, because her body became completely rigid and we could not keep her in the wheelchair.”*

Everyday Life with FA

“All I’ve ever wanted was to be involved, be accepted, contribute to society. FA makes that almost impossible.”

Patients eloquently described their struggle to complete every-day activities and their fear of progression and the unknown:

“All of us are just sitting and uncontrollably shaking the magic 8 ball to see what symptoms and how severe they will be in our progression. Slurred speech? Diabetes? Scoliosis? Loss of coordination in everything from your finger tips to your toes? Or eventually becoming fully dependent on someone else for help on living your life, just to name a few. We don’t know and that is absolutely terrifying.”

Responses to polling questions related to activities of daily living reflected the experiences of the panelists, on-line participants, and those in the room. About 87% of respondents noted that being able to move independently and safely was one of their top three activities of daily life that were limited by FA, and the importance of this was confirmed by the fact that 60% of patients felt that loss of independence was one of the three most significant effects of disease.

One patient summarized these concerns as, *“Instead of developing and growing into a competent, independent adult, it seems I have been going backwards. Rather than developing autonomy and initiative when a normal school-age child would have, I developed more and more dependence and doubt.”*

Patients described frustration with FA symptoms and how they rob them of their independence. Loss of independence, and a desire to retain independence was a common theme both for earlier and later onset patients.

“My fear is of the future. My husband is my caregiver. He is loving and trustworthy. We do not have children or extended family. I don’t want to rely on anyone for my basic functions. Today, I can transfer on my own, go to the bathroom, shower, dress myself and feed myself on my own. Will I always? What if something happens to my husband? Will I end up in a nursing home, dependent upon others for every basic need?”

Many patients mentioned their dependence on others as disease progresses, and their concern about the affects this had on friends and family.

“[My daughter] often expressed how sad it was for her that we were having such a difficult time caring for her. She knew we were hurting too in not being able to protect her. We tried as hard as we could to keep her as comfortable as possible. I will always wonder whether our care kept her alive too long and prolonged her suffering.”

About a quarter of patients listed loss of a job or inability to get a job as a concern, and several expressed frustration with this limitation, as FA does not affect intellect.

“Typing difficulty exclusively keeps me from earning my Ph.D., the one degree I still need to achieve my ideal job as a professor and researcher” while another notes “I just graduated from a respected research university with a 3.6, after winning numerous awards and scholarships. I am currently looking into graduate programs. I am smart. Many of us with FA are. And yet, we are prohibited from being productive and benefiting society because of FA.”

Many patients noted that they were doing well now – they had adjusted their lives to their current status, but fear of progression was pervasive, and many patients and caregivers talked about the mental stress of dealing with a constantly changing disease:

“If I stay where I am now and don’t get worse, I can learn tricks to make my life easier. As it is now, I learn tricks, and then they become obsolete as my disease progresses.”

“It took 10 years just accepting myself as wheelchair bound. Now, add not hearing well when I once could, seeing well when I once could, then losing my ability to be understood, and it’s a recipe for feeling worthless.”

About 40% of respondents noted that they experienced depression as one of their top three concerns, and 32% experience frustration as a major corollary of the disease. Social isolation caused by the disease was recognized as an important factor in about 40% of patients. Particularly in children, friends have a hard time understanding the disease. One parent said *“The emotional drain on our family is something I never imagined. Sam, diagnosed at 8, is now 30. As Sam moved through school, there were struggles as friends became aware of the progressive stages of the disease. Between middle school and high school Sam pretty much lost most friends.”* Another patient said, *“I’ll never forget the day my mom first brought me to school in my wheelchair, and the isolation I felt from my former friends who didn’t understand the progressive nature of my disease.”*

In older patients, the isolation increases due to lack of mobility and increased disease symptoms. One mother explained coming to visit her distraught son at college, *“Sam explained a planned trip failed to include an accessible bus. Sam was left behind. The combination of anger and hopelessness on that face was heart-wrenching.”*

The social isolation extends beyond the patient to the family as a whole: *“When you face a diagnosis with no cure, most of life you once knew disappears. Family and old friends just can’t bear the burden of FA, they fade away.”*

Topic 2: Patient Perspectives on Current and Future Approaches for Treating FA.

The second topic of the meeting focused on what patients are doing to treat their symptoms now, and what they would like to see from future treatments. The panel included three patients with FA, each at different stages of disease; a father of two younger daughters with FA; and a mother with an adult son and daughter with the disease. They discussed their experiences with current treatments, participation in clinical trials and research studies, and their hopes for future treatments.

There are no FA-specific or disease-modifying approved therapies available at this time but, for treating some cardiac issues, diabetes, spasticity, pain and other individual symptoms, patients utilize therapeutics approved generally for those conditions. For example, many patients have undergone surgeries to help with scoliosis or cardiac concerns, take standard pain medications, take supplements and do physical therapy or exercise programs to build strength and try to help slow progression, and FA diabetics take insulin shots.

Symptom Management: Medications

“I have boxes of vitamins and supplements, constantly tweaking them. Hoping the right combination will help a little by possibly stopping the loss of speech or allowing Sam and Alex to possibly feed themselves again.”

Although no medications are approved to reduce the rate of FA progression, much less halt or improve it, many patients use supplements, particularly antioxidants and compounds thought to boost mitochondrial performance. One father explained *“We also began to look at the various dietary supplements, etc. that may be beneficial to FA. We’ve tried a lot; currently the girls take, vitamin E; sulforaphane; idebenone, and curcumin. We hope that these can impact mitochondrial function, reduce oxidative stress, and reduce inflammation. All said and done, the girls each take over 20 pills a day.”* In the polling questions, 63% said they take idebenone or CoQ10, and 46% take vitamin E, while lower proportions took B vitamins or other supplements.

Patients and families acknowledge that they do not know the extent to which these supplements help, but most continue to take them. One patient noted that *“I can’t be sure idebenone is helping, but I believe it is and have no side effects so I continue. It is my fear at what might be*

the irreversible damage done if I stop idebenone that keeps me from participating in a clinical trial.” Another felt that idebenone did help him, “Idebenone does help. I have issues with bladder control that go away with idebenone, and it does help with fatigue. However, I have seen the most progression this year. I started vitamin B3 recently and increased exercise – I feel a little improvement.” In written testimony, another patient explained that she found that supplements and exercise helped symptomatically only, “Self-medicating has given me more quality in my daily life by providing me with more energy and strength. While I cannot stop the progression, I have found exercises to keep my body moving/not tightening.”

Some patients noted that they are spending significant money on therapies with uncertain value, *“Idebenone, CoQ10 in amounts that are considered therapeutic add up. When I went back and thought about how much we have spent on supplements – when we don’t know if they work – we could have bought a second home for the cost.”*

In addition to supplements, many patients are on a cocktail of prescription drugs to help with symptoms. About a third of all patients surveyed took cardiac drugs, 20% took pain drugs, muscle relaxants and anti-anxiety medications. One patient explained that he finds medical cannabis helpful in managing pain and helping him sleep.

Symptom Management: Scoliosis

Scoliosis is a common symptom of FA. Many parents of younger patients talked about the embarrassment children face by wearing braces to reduce scoliosis: *“She is...more strongly objecting to wearing her brace for scoliosis a prescribed 22 hours a day. While the hope is that the brace minimizes her scoliosis progression, her curvature has increased by 9% in the last year and half, and wearing the brace makes it difficult for her to stay active.”*

Parents also talk about the time spent on therapies to try and slow progression of scoliosis. One said, *“To manage scoliosis, we focused on prevention through physical therapy. That has meant nearly 4 years of twice-weekly, hour-plus-long drives to Cherry Hill, NJ plus twice yearly drives to Washington DC for scoliosis braces. Nearly 400 hours a year just on managing scoliosis.”*

Approximately 27% of patients have had spinal fusion surgery or placement of rods to treat scoliosis. Surgery is challenging, and there are significant consequences. *“Over time, it became apparent I needed spinal fusion surgery to stabilize my spine; where the doctors were going to insert a titanium rod into my spine and screw it into place making my spine virtually unable to curve. However, this benefit would come at the cost of most of my upper body mobility.”*

Symptom Management: Cardiac

Patients explained that when they are diagnosed with cardiac issues, they are typically put on a range of therapies thought to help with symptoms, which sometimes work at least in the short term. These therapies have not been tested specifically in an FA population, but are used based on their effects in other forms of heart disease. One patient stated that, *“[I have medications to help manage my] cardiomyopathy symptoms such as increased heartrate, abnormal pacing, and high blood pressure. These treatments for my cardiomyopathy, as well as an ICD implant treat symptoms which aren’t even very noticeable to me, and that is frightening in and of itself.”*

However, on other occasions FA patients do not respond to treatment as expected. One mother of a deceased patient explained, *“About 4 years before her death, Becca developed a blood clot in her heart. Her health declined even more rapidly and she started taking powerful blood thinners. We had to buy a ceiling lift and rent a larger wheelchair because of the amount of fluid she retained.”*

In surveys, 33% of patients reported taking cardiac medications and 7% had had cardiac-related surgeries.

Symptom Management: Other Surgeries

“And if the emotional challenges aren’t enough, the medical management of FA is frightening.”

In addition to surgery related to scoliosis and cardiac issues, FA patients often undergo other surgeries to try and improve specific symptoms, such as deformed feet (pes cavus) and tight tendons (10% of those surveyed), and to implant medication pumps to control cramping and spasticity. Surgery and hospitalizations are challenging. One mother told this story of her daughter’s decision to have a baclofen pump implanted:

“She had maxed out on oral dosages [of baclofen] but had had so many problems during two prior spinal fusions she was understandably afraid to undergo another surgery with associated risks...It was difficult drilling through her spinal fusion to get a catheter through to her spinal canal. A one-hour surgery turned into five hours; an overnight stay into two weeks. I watched in horror when a resident just didn’t know how to manage Alex’s fluid balance. Her labs were off and they felt IV fluid boluses would help bring her labs up...Because they kept administering the boluses, which her heart could not handle, the fluid became too much. Alex had a horrible drop in blood pressure. Things became critical so quickly. The end result was a pulmonary edema which nearly proved lethal... I wish I could say that we have only been through this once, but that’s not the case.”

Other patients told similar stories of surgeries proving to be much more involved and painful than expected, and with long recoveries.

Symptom Management: Other Interventions

“Without these self-directed treatments, I would have much more difficulty accomplishing some of the things that I want to accomplish.”

About 80% of the patients surveyed do some form of exercise to help manage their FA symptoms. About 60% do physical therapy and stretching. Many patients feel that this helps them retain function. The programs chosen by patients vary, however, and are often limited by fatigue: *“I exercise at least 3 hours per week, aside from daily living which can prove to be a workout on its own. I have always been very active and have done what was possible to manage symptoms. I work 1-on-1 with a trainer at a CrossFit gym.”* A parent said, *“The girls do physical*

therapy for scoliosis twice weekly; as well as 1 to 2 days at the gym for strength training, and both girls do therapeutic horseback riding once per week. In the summer, they swim.”

In addition to exercise, 60-70% of patients report that they use adaptive devices or home modifications. Mobility aids include walkers, scooters and wheelchairs, and use of these drives a need for wheelchair accessible house, in addition to use of grab bars and bannisters to limit falls. Several later onset patients noted using hand controls to drive. One patient *explained “My father who is 65 and retired has to install handrails around my house to minimize my falls. Watching that happen, knowing the rails are for me and not him is extremely hard to process. Handicap placards and a countdown on the time I have to drive with my feet are now everyday thoughts. Accepting that I have physically more in common with my 80-year old grandmother and her friends than I do with my own 24-year-old friends is honestly mind blowing. Having her push me in a wheelchair knowing it should be the other way around has been hard to experience as well.”*

Although the majority of FA patients are taking supplements, prescription drugs, undergoing surgeries, and actively pursuing lifestyles to slow progression of their disease, 48% of poll respondents felt that these interventions only helped somewhat, and a further 20% felt there was no benefit, or were not sure if there was a benefit.

Perspectives on Clinical Trials

The FA community is highly motivated to take part in clinical trials, and about 15% of the poll respondents reported they were currently taking an experimental drug. One panelist explained that, *“The studies were transparent with me, allowing me to evaluate my own risk associated with participating. But I found the greatest risk to be not participating. With no approved treatment or even lifestyle choices known to slow progression or improve prognosis, living with FA is a constant race against the clock.”*

Several parents explained their desire for more pediatric trials: *“She hasn’t participated in clinical trials because most of them aren’t available to children her age. We would like to see broader criteria for participation in clinical trials, especially because our daughter’s condition is severe.”* *“Given that FA is typically diagnosed between 5 and 15 years of age, I would very much like to see more pediatric trials in FA and strong support from the FDA for interventional trials at early stage, in pediatric populations.”*

However, patients also noted that there are challenges associated with participating – *“The last trial I was a part of required 36 trips to California – 7 trips in 6 weeks,”* and some patients and parents noted that there were no trials available for them or their family member, either because of the mutation causing their disease (e.g. a point mutation) or their age (e.g. if very young), or their stage in progression, or other symptoms.

Of those who had taken part in trials, the feelings were generally positive, and several patients experienced benefits, particularly improvements in fatigue, which were not necessarily measured by the trial endpoints:

- *“Being on actimmune gave Mekayla her life back. We witnessed her hiking up a mountain (Diamond Head in Hawaii) while on actimmune during her Make A Wish trip.*

Now being off actimmune for several months, Mekayla really struggles going about her daily tasks. Her energy levels being off actimmune have been very depleted.”

- *“In the middle of my school semester I had full course load, a part-time job, and a social agenda that involves little sleep, but I was on a medicine that allowed me to make this my lifestyle. So now, two months without the medication, I wake up feeling more tired and weak than the day before and wonder how I am going to make it through the day”*
- *“Sometimes there are unexpected side effects – in the first trial I saw a part of my legs turned from their usual maroon and purple color to flesh color.”*

In the polling questions, patients were asked what risks they might be concerned with in trying a new treatment. The most highly ranked concern by a large margin was the risk of significant side effects – 82% of patients listed this as something they would take into account in making a decision to try a therapy. In contrast, only 10% felt that minor common side effects would stop them from considering a treatment (e.g., headaches, stomach upset etc.). Cost and the time associated with traveling were also prevalent concerns - 54% and 26% of respondents, respectively. Another 23% felt that the method of delivery of a therapy would impact their decision (e.g. intravenous, oral, or intrathecal delivery). About 7% of those polled said that nothing would influence their decision to try a new medication, they would participate regardless of the potential risks.

Perspectives on Future Treatments

“It would be very meaningful to slow progression. If 35 years of progression could be 25 she would still be walking, instead of using a wheelchair”

While patients clearly would like a cure for the disease, there was robust discussion of what a meaningful treatment might be short of this outcome. One father of two FA patients explained that, *“Different stages of the disease present different desires in terms of expectations for a therapy. For Samantha, I’d like to maintain her ability to walk & to improve her fine motor skills – for example, being able to handwrite an essay in school or keep notes independently in class. Angelina has largely lost the ability to walk - and her cardiomyopathy is worse - so I am more interested in a therapeutic that could stop progression or reverse her cardiac disease so that she does not die from cardiac failure in the coming years. For both, medicine that reduces fatigue or stops progression of scoliosis would be highly desirable. For us, there is clear benefit to a drug that slows, stops or reverses progression of any aspect of the disease - whether it be scoliosis, fatigue, ataxia, heart, speech, vision, hearing, or diabetes.”*

Many patients noted that slowing progression would be of significant value (80% of those polled ranked slowing or stopping progression as the most valuable outcome short of a cure), which agreed with earlier comments about fear of progression and the difficulties in planning ahead due to the unpredictable nature of the disease. On the whole, patients felt they could live as they were, meaning no new symptoms and halting of progression of existing symptoms. *“Life would be wonderful if we were able to stop this tireless race against time and sustain life as it is today.”* Another patient explained, *“Short of a cure, being able to objectively slow or stop progression would be invaluable to me. I want to plan my life, with confidence; to be able to rely*

on my current abilities in the future, and without the fear of devastating complications such as diabetes, stroke, or cardiomyopathy. This coupled with a sustained energy level would allow me to continue doing everything I do now... I can adapt my life to current symptoms to stay active and engaged, but fear of what I know the future holds, continues to cripple me, especially on an emotional level.”

Patients are realistic about treatment, and understand that one drug may not treat all aspects of the disease – *“FA affects many bodily systems and every patient slightly differently, so I do not think a single drug will solve all symptoms or help everybody. I think a drug cocktail, which will be tailored to each specific patient, is our solution. So, I do not believe discarding a drug for not producing universal benefits is an effective way to solve the problem of FA.”*

Patients also discussed which symptoms would be most important to treat. About 20% ranked a gain in function as more valuable than stopping progression. Consistent with the most troublesome symptoms, when asked to choose the top three symptoms that would be most meaningful to treat, about 55% of respondents chose improved balance and improved walking, and similar numbers chose improving fatigue. However, patients found it hard to choose. One panelist explained, *“A cure is something all affected will look to. It is a difficult task to consider what would be my preference to treat short of that. To me, the most important thing would be to walk freely and for long distance, to stand and address a jury, to walk up the steps in front of the U.S. Capitol, to chase the children that I hope to have one day.”*

Several patients explained that it would be meaningful to them to improve their manual dexterity in order to be able to pick up small objects, button clothes, type, write and complete other activities that require fine motor skills. One patient noted his frustration with his hobbies, *“Tying fishing hooks is a big frustration. Improving this would be meaningful.”*

Other patients noted that improvements in other symptoms would also have value:

- *“A treatment that would improve my hand dexterity would help drastically. Being able to type words at a normal speed would help communication. Being able to move my chair normally would allow more simple travel. Hand improvement would allow me to eat food without assistance, and without worry. One symptom would help.”*
- *“It is my hope that soon there are effective treatments that directly improve the speech and communication abilities of people with FA.”*
- *“Reducing spasticity or fatigue would be very meaningful.”*
- *“... if a treatment improved pa-ta-ka performance, I would be encouraged. This would mean that I could speak more clearly, be understood when placing an order in a noisy restaurant, chew my food without biting my tongue, teach, be a speech pathologist again, and defend my dissertation more fluently.”*
- *“...if my balance could improve somewhat so I could do a somewhat-standing transfer, my life would be so much easier and I would be so much more independent.”*

During the discussion, one mother noted that treating cardiomyopathy was only ranked as important by 35% of respondents. She felt that this reflected disease progression, and how perception of what is important changes with disease stage: *“When Sean was diagnosed, we saw*

the ataxia. Early in disease this was the fear – loss of walking. Later, even as his heart got worse – the worry was looking for a neurological cure. As his cardiomyopathy progressed, however, we realized that while being in a wheelchair is not great, the cardiomyopathy is what kills them. Slowing anything is worth it, and might improve the quality of life now.”

Conclusions:

This Externally Led Patient Focused Drug Development Meeting for Friedreich’s Ataxia provided patients and caregivers the opportunity to tell FDA, first-hand, about their experiences with FA, and what they would value in a treatment. It was clear that patients are resilient and adapt to their current state, but fear the uncertain progression of the disease, and suffer from severe social isolation and often depression and anxiety as the disease progresses. Patients worry about progression of cardiomyopathy, which is the eventual cause of death of most patients, while issues with balance, walking, manual dexterity and speech affect them more on a daily basis. Fatigue is a significant burden for most patients. Patients are very willing to take part in clinical research, and are eager for treatments that have the potential to reverse, halt, or even slow the progression of any aspect of this multi-faceted disease, and feel that there are aspects of their disease that are important and have not been measured in previous clinical trials.

References:

1. [Unique origin and specific ethnic distribution of the Friedreich ataxia GAA expansion.](#) Labuda M, Labuda D, Miranda C, Poirier J, Soong BW, Barucha NE, Pandolfo M. *Neurology*. 2000 Jun 27;54(12):2322-4.
2. [Friedreich Ataxia.](#) Bidichandani SI, Delatycki MB. In: Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean LJH, Bird TD, Ledbetter N, Mefford HC, Smith RJH, Stephens K, editors. *GeneReviews*[®] [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2017. 1998 Dec 18 [updated 2017 Jun 1].
3. Cross-sectional analysis of glucose metabolism in Friedreich Ataxia. Greeley et al. [Journal of the Neurological Sciences](#). [Volume 342, Issues 1–2](#), 15 July 2014, Pages 29-35
4. [Mortality in Friedreich ataxia.](#) Tsou AY, Paulsen EK, Lagedrost SJ, Perlman SL, Mathews KD, Wilmot GR, Ravina B, Koeppen AH, Lynch DR. *J Neurol Sci*. 2011 Aug 15;307(1-2):46-9. doi: 10.1016/j.jns.2011.05.023. Epub 2011 Jun 8.
5. [Comorbid Medical Conditions in Friedreich Ataxia: Association With Inflammatory Bowel Disease and Growth Hormone Deficiency.](#) Shinnick JE, Schadt K, Strawser C, Wilcox N, Perlman SL, Wilmot GR, Gomez CM, Mathews KD, Yoon G, Zesiewicz T, Hoyle C, Subramony SH, Yiu EM, Delatycki MB, Brocht AF, Farmer JM, Lynch DR. *J Child Neurol*. 2016 Aug;31(9):1161-5. doi: 10.1177/0883073816643408. Epub 2016 Apr 12.

Appendix 1: Incorporating Patient Input into a Benefit-Risk Framework for Friedreich’s Ataxia

In 2013, the FDA developed a plan for a structured approach to benefit-risk assessment in regulatory decision making. This framework calls for assessing five factors for each potential therapeutic under consideration for approval: Analysis of Condition, Current Treatment Options, Benefit, Risk, and Risk Management. In each specific use case, this framework summarizes each decision factor and explains how it influences the FDA’s rationale for its regulatory decision.

The input from the FA patient community at the Externally Led Patient Focused Drug Development Meeting for FA, compiled in this report, can inform such a framework. Here we offer an example of the first two factors, which can be derived from the information presented at the meeting. This sample framework is likely to evolve over time, and should be incorporated into a benefit-risk assessment framework for a drug under review.

Dimensions	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition	<p>-Friedreich’s Ataxia is an autosomal recessive disorder caused by reduced levels of frataxin protein. Most patients have two expanded GAA repeat sequences in the frataxin gene; about 4% have a repeat expansion on one allele and a point mutation on the other. Longer repeats correlate with less frataxin, earlier onset and more severe disease.</p> <p>- Disease is typically diagnosed in patients age 5-25, although later onset forms exist. Signs and symptoms are usually present long before diagnosis</p> <p>- Patients all exhibit progressive motor symptoms – ataxia, poor balance and poor manual dexterity. Almost all also have issues with fatigue and about two thirds have dysarthria. Many patients have or develop cardiac issues (cardiomyopathy and cardiac rhythm issues), and lose some sight and hearing over time. Diabetes, scoliosis, pes cavus and other symptoms are not fully penetrant, but common in FA patients.</p> <p>- As disease progresses, patients lose the ability to walk, lose fine motor coordination, develop significant dysarthria and many lose sight and hearing in later stages of disease. This causes them to become dependent on others for all activities of daily living. Patients expressed frustration with loss of independence and loss of ability to socialize and take part in life due to loss of ability to communicate. Depression and anxiety rates are high.</p> <p>-Patients fear progression of disease, especially as relates to cardiomyopathy and increased dependency on others.</p> <p>The unpredictability of which symptoms will emerge and</p>	<p>Friedreich’s Ataxia is a serious, progressive, debilitating and eventually fatal disease. FA is multisystemic, with different patients having different spectrums of disease. Neurological symptoms- loss of balance and reduced manual dexterity - and fatigue are fully penetrant. As disease progresses, many patients develop fatal cardiac effects, dysarthria emerges or progresses, and patients develop more significant vision and hearing problems. Scoliosis, pes cavus and diabetes are also common in this population. Patients fear progression and emergence of new symptoms, as well as loss of independence over time, and most fear development of cardiomyopathy and early death.</p>

	<p>when causes stress and difficulty in life-planning.</p> <p>-Average life expectancy is 35 years, with most deaths caused by cardiomyopathy.</p>	
<p>Current Treatment Options</p>	<p>-No treatments are approved for Friedreich’s Ataxia</p> <p>-Patients use standard treatments for specific symptoms (e.g. diabetes, cardiac disease) as required.</p> <p>-Patients use a variety of supplements and vitamins, particularly anti-oxidants, in attempting to manage disease symptoms (e.g., fatigue).</p> <p>-Scoliosis surgery and surgery to treat foot and ankle issues is common; cardiac surgery and implantation of baclofen pumps are also used.</p> <p>-Most patient use exercise and physical therapy in attempting to manage disease symptoms.</p> <p>-Patients spend significant time and money pursuing treatments that have not been proven to help, are very active in clinical trials, and willing to accept risk.</p>	<p>Patients can partially treat or manage some symptoms of FA, but there are no treatments available for the underlying disease. Patients express a great desire for treatments that would slow or stop progression. Value is also seen in being able to treat specific symptoms individually, particularly if they address cardiomyopathy, balance, fine motor skills, fatigue or speech. There is a great unmet need to find treatments that can delay onset, slow progression or treat symptoms in FA.</p>

Appendix 2: Meeting Agenda.



[CLICK HERE FOR LIVE WEBCAST](http://curefa.org/fda_meeting)
curefa.org/fda_meeting

Agenda For Externally Led Patient-Focused Drug Development Meeting Friedreich Ataxia

- | | |
|------------------------|--|
| 7:30 a.m. – 8:30a.m. | Registration |
| 8:30 a.m. – 8:50a.m. | Opening Remarks & Overview of FA - <i>Jennifer Farmer, Executive Director, FARA & Ronald Bartek, Founding President and Co-founder, FARA</i> |
| 8:50 a.m. – 9:10 a.m. | FDA Welcoming Remarks - <i>Wilson Bryan, MD, Director of Office of Tissues and Advanced Therapies, CBER.</i> |
| 9:10 a.m. – 9:20a.m. | Meeting Overview - <i>James Valentine, JD, MHS, Associate, Hyman, Phelps and McNamara, P.C. Moderator</i> |
| 9:20 a.m. – 9:30 a.m. | Audience and Remote Polling: Demographic Information Collecting Patient Input |
| 9:30 a.m. – 9:40 a.m. | Video: “Our Life with FA - Always Changing” |
| 9:40 a.m. – 10:05 a.m. | Patient Panel 1: Living with Friedreich’s Ataxia – <i>Frankie Perazzola, Jack DeWitt, Kristin Morrow, RJ Mercure, Nelda Van Schoick</i> |

Topic 1 Questions:

1. Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life (Examples may include difficulty moving, issues with balance, issues with sight or hearing, lack of energy etc.)
2. How do your symptoms and their negative impacts affect your daily life?
3. Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition?
4. What worries you most about your condition, and the progression of your condition?

10:05 a.m. -10:45 a.m. Topic 1 facilitated audience discussion & audience and remote polling.

10:45 a.m.-11:00 a.m. Break

11:00 a.m. – 11:25 a.m. Patient Panel 2: Current & future approaches to treating Friedreich's Ataxia – *Patrick Ritschel, Nicholas Carbone, Emily Young, Alex Fielding, Mary Caruso*

Topic 2 Questions:

1. What are you currently doing to manage your symptoms? (examples might include scoliosis surgery, cardiac drugs, physical therapy, over the counter antioxidants, etc.)
2. How well do these treatments treat your symptoms?
3. How well do these treatments improve your ability to do specific activities that are important to you in your daily life?
4. What specific things would you look for in an ideal treatment for your condition, short of a complete cure?

11:25 a.m.- 12:05 a.m. Topic 2 facilitated audience discussion & audience and remote polling.

12:05 p.m. – 12:20 p.m. FDA Concluding Remarks - *Jonathan Goldsmith, MD, Associate Director for Rare Diseases, CDER*

12:20 p.m. – 12:30p.m. Closing Comments & Next Steps - *FARA*

Appendix 3: Meeting Panelists

Patients and caregivers represented on each panel were chosen so that the disease spectrum was covered as fully as possible. This included patients with an early age of onset (severely affected) and those with later onset disease, who typically have a milder course. Patients who had FA symptoms that are not fully penetrant (e.g. scoliosis, cardiomyopathy, diabetes) were also represented on the panels and in discussion.

Panel 1:

- Frankie Perazzola. Patient with relatively early stage disease, moderate onset. Age: 24, Age of diagnosis: 22.
- Jack DeWitt. Patient with mid stage disease, early onset. Age: 17, Age of diagnosis: 10.
- Kristin Morrow. Mother of a child with early onset disease and cardiomyopathy. Age: 11, Age of diagnosis: 9.
- RJ Mercure. Patient with later stage disease and early onset. Age: 31 Age of diagnosis: 12.
- Nelda Van Schoick. Mother of two daughters with FA, one deceased. Discussed one daughter primarily: Age: deceased at age 33, Age of diagnosis: 14.

Panel 2:

- Patrick Ritschel: Father of two daughters with FA at different stages in progression, one with cardiomyopathy, Age: 15/ 13 Age of diagnosis: 11/9.
- Nicholas Carbone: Patient with FA, Age: 30 Age of diagnosis: 10, Emily Young: Patient with FA, manifest with scoliosis, Age: 21, Age of diagnosis: 10.
- Alex Fielding: Patient with later onset FA, Age: 29 Age of diagnosis: 26.
- Mary Caruso: Mother of two children with FA in later stage disease, Age: 27 and 30, Age of diagnosis: 7 and 8.

Appendix 4: Discussion Questions



Friedreich's Ataxia Patient Focused Drug Development Meeting Discussion Guide

Panel 1: Living with Friedreich's Ataxia

The purpose of this panel is to describe what it is like to live with FA, symptoms, what hurdles you encounter and what concerns you. Questions in this panel:

1. *Of all the symptoms that you experience because of your condition, which 1-3 symptoms have the most significant impact on your life? (Examples may include difficulty moving, issues with balance, issues with sight or hearing, lack of energy etc.)*
 - a. Which symptoms really affect you now?
 - b. Which ones were the most significant at other times in your life?
 - c. How have your feelings about specific symptoms changed over time?
2. *How do your symptoms and their negative impacts affect your daily life?*
 - a. Can you give a real-world example of how disease affects your daily life?
 - b. When was a time that having FA really prevented you doing something you really wanted to do?
 - c. How do you feel about doing things with FA that others find easier/faster?
 - d. Has anxiety or depression impacted your ability to live as you want to?

3. *Are there specific activities that are important to you but that you cannot do at all or as fully as you would like because of your condition?*
 - a. How does this affect your relationships/friendships with other?
 - b. How does it affect how you live your life (e.g. have you given up hobbies)?
 - c. How has it changed the trajectory of your life (schooling, jobs, relationships, living situation etc.)?
 - d. If you could do one activity that currently limits you, what would it be?
4. *What worries you most about your condition, and the progression of your condition?*
 - a. If you could correct one symptom of your condition, which would it be and why?
 - b. Would stopping or slowing progression be meaningful to you (e.g. preventing or slowing loss of mobility, vision loss, development of further cardiac symptoms)?

We have heard the panelists discuss how slowing of progression would be meaningful and some of them are quite descriptive in saying that slowing of progression allows you to adapt and function where you are – might want to dig into this a bit more with the audience in terms of **how** slowing of progression would improve their QOL or function.

Panel 2: Current & future approaches to treating Friedreich's Ataxia

1. *What are you currently doing to manage your symptoms? (examples might include scoliosis surgery, cardiac drugs, physical therapy, over the counter antioxidants, etc.)*

Other surgeries/interventions might include tendon release for pes cavus, botox for spasticity. We will likely hear more about vitamins and supplements and exercise.

If we hear that pain is a major symptom then we might want to dig into type of pain (neurological pain or muscle/spasticity pain) and management of pain

- a. What was your decision-making strategy in deciding to manage your symptoms in this way (e.g. why did you decide to do scoliosis surgery when you did, why do you take specific supplements, or how did you settle on a specific exercise regime)?
 - b. How does your current management strategy impact the time that you have for other activities?
2. *How well do these treatments treat your symptoms?*
- a. Do symptoms improve?
 - b. Are there specific activities that a treatment allows you to do?
 - c. Do you think they improve symptoms, or slows progression?
 - d. How do you measure the effect of these treatments (e.g. perception of fatigue, ability to do an activity, distance you can walk, how you perform exercises or other activities)?
 - e. Does the treatment affect you negatively in any way (e.g. side effects, time to complete, cost)
3. *What specific things would you look for in an ideal treatment for your condition, short of a complete cure?*
- a. What does treatment look like to you short of a complete cure?
 - b. What symptoms do you think are worth treating independent of a treatment for the disease as a whole?
 - c. What risks are you willing to assume in looking at a potential treatment?
 - d. Would a slowing of progression be meaningful to you in the absence of improvement?
4. *Have you ever participated in a clinical trial or research study?*
- a. If yes, did you encounter any unexpected challenges?
 - b. If yes, did you observe any benefits?

- c. If yes, what was measured in the trial/study and if you improved on that measurement, how did it directly relate to helping you do activities of daily living?
- d. If you have not participated in a trial/study, would you consider it? How would you weigh the risks and benefits?

Appendix 5: Polling Questions

Questions not for public response

What is your name?

What is your email address?

Demographic Questions

1. Where do you currently reside?

- A. Northeastern US
- B. Southeastern US
- C. Midwestern US
- D. Southwestern US, incl. Texas
- E. California
- F. Northwest US, not including California
- G. Canada
- H. Mexico
- I. Outside of North America

2. Do you live in:

- A. A city
- B. A rural area
- C. A suburban area

3. Which of the following best describes you?

- A. I have FA
- B. I am the parent or caregiver for someone with FA

4. At what age were you diagnosed with FA? Emphasize answering for patient

- A. 0-5 yrs
- B. 6-10 yrs
- C. 11-15 yrs
- D. 16-20 yrs
- E. 21-30 yrs
- F. >30 yrs

5. How long ago were you diagnosed with FA? Emphasize answering for patient

- A. <1 yr
- B. 1-2 yrs
- C. 3-5 yrs
- D. 6-10 yrs
- E. 11- 20 yrs
- F. >21 yrs
- G. Not sure

6. How old are you? Emphasize answering for patient

- A. 0-10 yrs
- B. 11-20 yrs
- C. 21-30 yrs
- D. 31-40 yrs
- E. 41-50 yrs
- F. > 50 yrs

Topic 1 Polling Questions

7. Please select the answer that best describes your stage of disability

- A. Minimal disability. Able to run or jump.
- B. Symptoms present but mild, able to walk and capable of leading independent life.
- C. Symptoms are overt and significant. Require regular or periodic holding on to wall or another person for stability and walking.
- D. Walking requires a walker or other aid such as a service dog. Can perform several activities of daily living.
- E. Not able to walk, confined to wheelchair. Can perform some activities of daily living that do not require standing or walking.
- F. Severe disability, dependency on others for assistance with all activities of daily living.

8. Which of the following FA-related health concerns do you/the person you care for have currently? Select ALL that apply:

- A. Issues with balance / walking / regular falls
- B. Coordination in hands and arms and manual dexterity – e.g. difficulty grasping/gripping/holding objects, or fine motor skills
- C. Fatigue
- D. Diabetes
- E. Scoliosis (curvature of the spine)
- F. Cardiac condition – e.g., Cardiomyopathy, shortness of breath, chest pain, arrhythmia or dysrhythmia (abnormal, irregular or fast heartbeat)
- G. Choking and/or swallowing issues
- H. Vision loss
- I. Hearing loss
- J. Dysarthria/slurred speech
- K. Incontinence and/or other urinary issues and /or any bowel issues
- L. Spasticity (cramping or stiffness in legs)

- M. Pain
- N. Other

9. Select the FA symptoms *that most impact* your daily quality of life [select up to 3].

- A. Issues with balance / walking / regular falls
- B. Coordination in hands and arms and manual dexterity – e.g. difficulty grasping/gripping/holding objects, or fine motor skills
- C. Fatigue
- D. Diabetes
- E. Scoliosis (curvature of the spine)
- F. Cardiac condition – e.g, Cardiomyopathy, shortness of breath, chest pain, arrhythmia or dysrhythmia (abnormal, irregular or fast heartbeat)
- G. Choking and/or swallowing issues
- H. Vision loss
- I. Hearing loss
- J. Dysarthria/slurred speech
- K. Incontinence and/or other urinary issues and /or any bowel issues
- L. Spasticity (cramping or stiffness in legs)
- M. Pain
- N. Other

10. As disease progresses, development or progression of which of the following symptoms worries you the most? Select up to 3

- A. Balance/ ability to stand
- B. Issues with walking / regular falls
- C. Coordination in hands and arms and manual dexterity – e.g. difficulty grasping/gripping/holding objects, or fine motor skills
- D. Fatigue
- E. Diabetes
- F. Scoliosis (curvature of the spine)
- G. Cardiac condition – e.g, Cardiomyopathy, shortness of breath, chest pain, arrhythmia or dysrhythmia (abnormal, irregular or fast heartbeat)
- H. Choking and/or swallowing issues
- I. Vision loss
- J. Hearing loss
- K. Dysarthria/slurred speech
- L. Incontinence and/or other urinary issues and /or any bowel issues
- M. Spasticity (cramping or stiffness in legs)
- N. Other

11. What specific activities of daily life are most important to you that you are NOT able to do because of FA? Select TOP 3

- A. Moving around independently and safely, walking and standing.
- B. Manipulating small objects (e.g., a key, picking up items)
- C. Writing and typing
- D. Sitting unaided
- E. Driving

- F. Feeding oneself, cutting food and handling utensils
- G. Personal Hygiene, taking a shower, bathing or dressing independently
- H. Transferring independently (e.g. from wheelchair/scooter to bed, toilet, etc.)
- I. Communication – speaking with others and being understood
- J. Understanding conversation in noisy settings
- K. Reading books, seeing a computer screen or phone
- L. Other

12. As a result of living with FA, which of the following social, emotional or economic consequences are most significant to you? Select up to 4

- A. Depression and/or Anxiety
- B. Social isolation
- C. Loss of job or inability to get a job
- D. Modified work/school hours
- E. Trouble building or maintaining relationships
- F. Frustration
- G. Lack of hope for the future
- H. Loss of independence
- I. Financial difficulties
- J. Communication issues
- K. Loss of hobbies or activities
- L. Other

Topic 2 Polling Questions

**13. What medications or supplements do you take now to treat symptoms of FA?
Select ALL that apply**

- A. Idebenone or CoQ10
- B. Vitamin E
- C. Vitamin B3, Nicotinamide or Niacin
- D. Other supplements or vitamins not listed
- E. Muscle relaxants (e.g. Baclofen, Chlorzaxazone, Botox, medical marijuana etc.)
- F. Pain medications (e.g. Neurontin/gabapentin, Cymbalta, Lyrica, opioids etc.)
- G. Heart medications (e.g. beta blocker, ACE-inhibitor, calcium channel blocker, diuretic, anti-arrhythmic, anti-coagulant)
- H. Diabetes medications
- I. Antidepressants or anti-anxiety medications
- J. Experimental medications as a part of a clinical trial
- K. Other
- L. Nothing

14. What are you currently doing to help manage FA or FA symptoms? Select ALL that apply

- A. Physical therapy, including aqua or hippo therapy
- B. Stretching
- C. Exercise (cardio or strength training)
- D. Bracing (back brace for scoliosis, leg or foot braces, AFOs)
- E. Occupational therapy
- F. Speech therapy
- G. Modifications/accommodations at work/in school/at home
- H. Mental health services
- I. Use of adaptive devices
- J. Choice of diet
- K. Other
- L. Nothing

15. Have you undergone surgery to treat or manage symptoms of FA? Select all that apply

- A. Spinal fusion or placement of rods for scoliosis
- B. Tendon release or surgery on feet and ankles
- C. Cardiac surgery (e.g. ablation) or implanted cardiac assist device (ICD, pacemaker, LVAD)
- D. Placement of baclofen pump
- E. Other surgery
- F. No surgery

16. In general, how much do the medications, surgeries or lifestyle changes used improve your quality of life:

- A. No benefit
- B. Helped somewhat
- C. Helped a lot
- D. Significant benefit
- E. Not sure

17. Which outcomes would be meaningful to you for a possible drug treatment? Select ALL that apply

- A. Slowing/stopping of progression (even if no gain in function, symptoms won't get worse)
- B. Gain in function (e.g. energy, strength, mobility, dexterity, cardiac function, speech)
- C. Prolong life
- D. Other

18. Which outcome is most important for a possible FA treatment? Select ONE option

- A. Slowing/stopping of progression (even if no gain in function, symptoms won't get worse)
- B. Gain in function (e.g. energy, strength, mobility, dexterity, cardiac function, speech)
- C. Prolong life
- D. Other

19. Which ability or symptom would you rank as *most* important for a *possible* drug treatment today? Select up to THREE options

- A. Improved balance / walking / fewer falls
- B. Improved arm/hand function, manual dexterity
- C. Reduced fatigue
- D. Fewer diabetic issues
- E. Reduced scoliosis (curvature of the spine)
- F. Improved cardiac symptoms
- G. Improved choking and/or swallowing issues
- H. Improved vision
- I. Improved hearing
- J. Improved dysarthria/slurred speech
- K. Improved incontinence and/or other urinary issues and /or any bowel issues
- L. Reduced spasticity
- M. Reduced pain
- N. Other

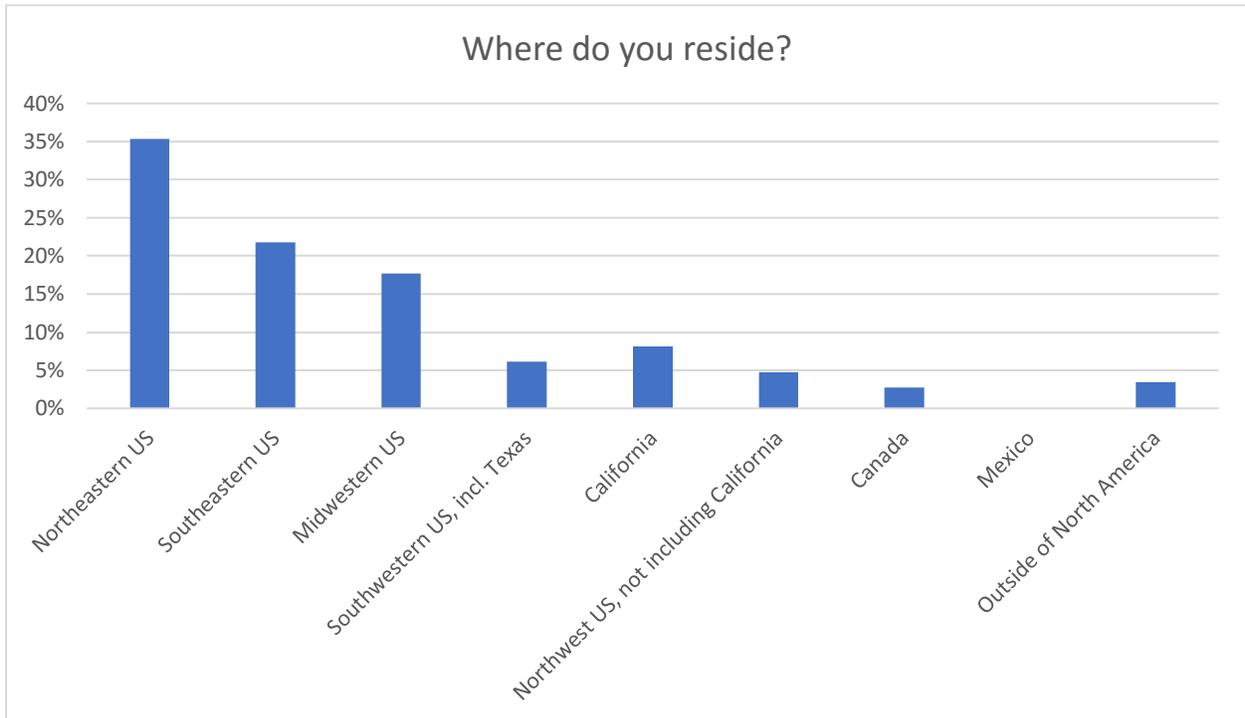
20. Which of the following factors would influence your decision to take a new medication or participate in a clinical trial or research study? Select ALL that apply

- A. Significant risks of serious side effects such as cardiac or kidney issues
- B. Common side effects of the treatment, such as nausea, loss of appetite, headache etc.
- C. The way that treatment is administered (for example, orally, intravenously, subcutaneous, injection into the spinal cord),
- D. How long the treatment takes, whether it requires hospitalization, required doctor's visits, etc.
- E. The burden of administration, such as the need for anesthesia, radiation exposure, surgical procedure, etc.
- F. Changing my current treatment or management plan (stopping a medication or supplement, stopping exercise)
- G. Cost
- H. Travel
- I. Other
- J. None of these

Appendix 6: Full Results from Polling Questions

Where do you currently reside?

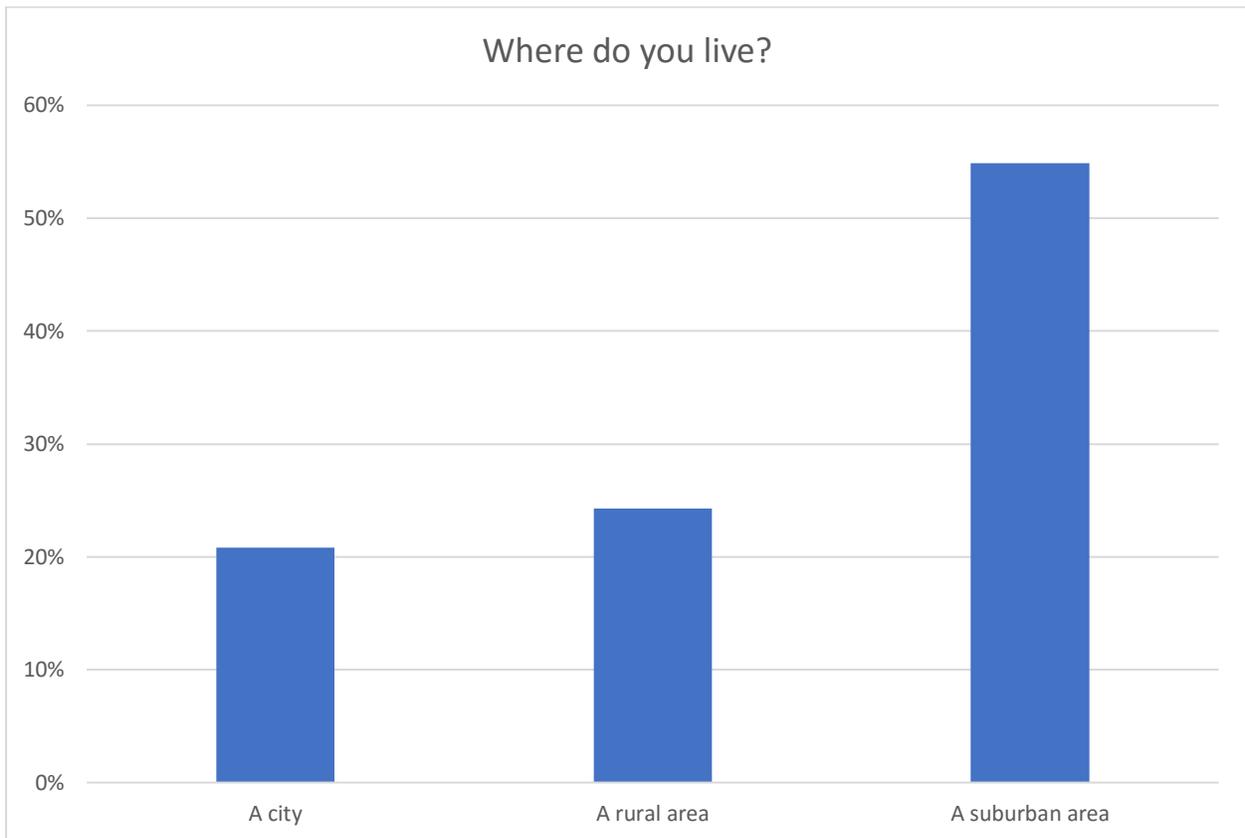
Total Responses	147	
Unique Participants	147	
Response options	Count	
Northeastern US	52	35%
Southeastern US	32	22%
Midwestern US	26	18%
Southwestern US, incl. Texas	9	6%
California	12	8%
Northwest US, not including California	7	5%
Canada	4	3%
Mexico	0	0%
Outside of North America	5	3%



Do you live in:

Total Responses 144
Unique Participants 144

Response options	Count	
A city	30	21%
A rural area	35	24%
A suburban area	79	55%

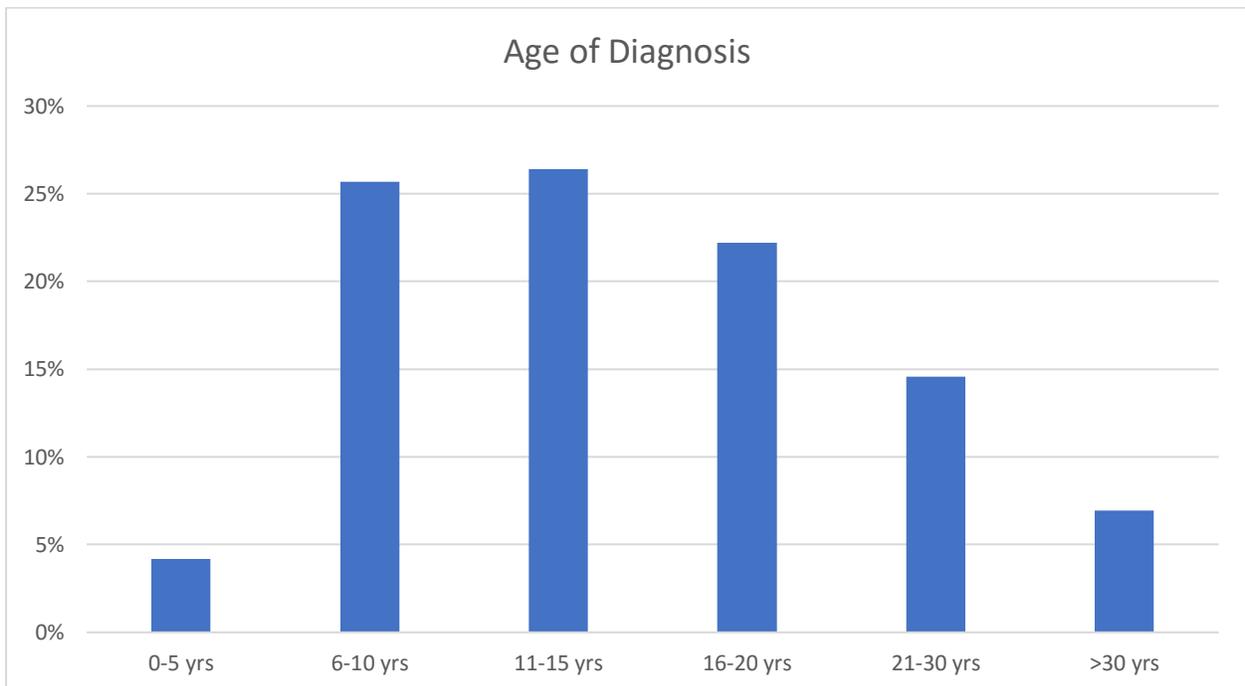


Which of the following best describes you?

Total Responses	143	
Unique Participants	143	
Response options	Count	
I have FA	67	47%
I am the parent or caregiver for someone with FA	76	53%

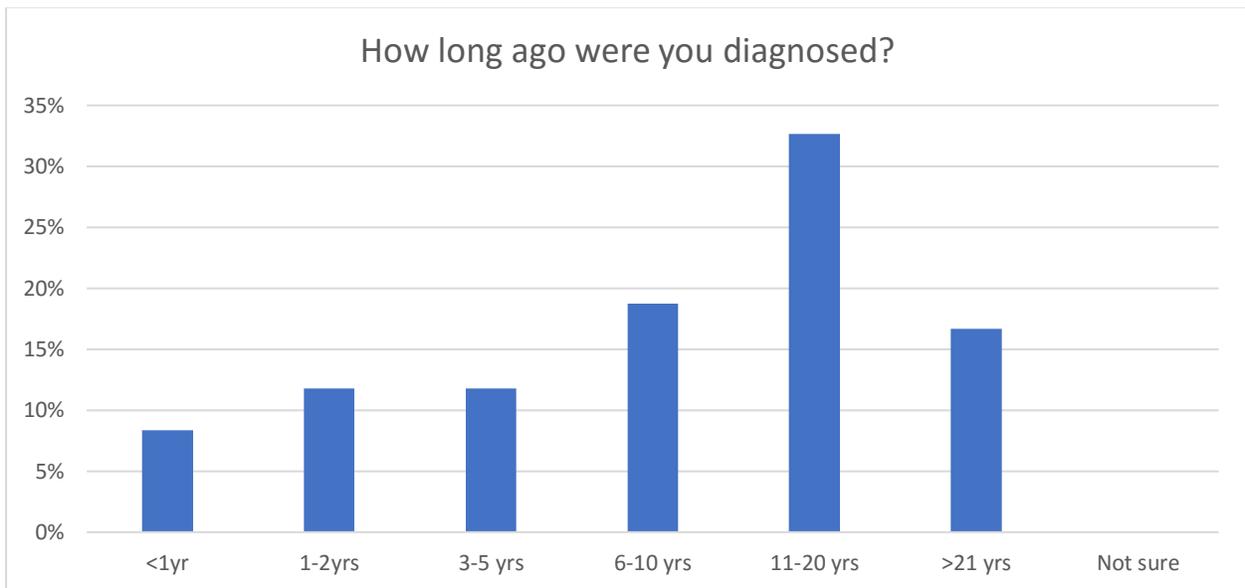
At what age were you diagnosed with FA?

Total Responses	144	
Unique Participants	144	
Response options	Count	
0-5 yrs	6	4%
6-10 yrs	37	26%
11-15 yrs	38	26%
16-20 yrs	32	22%
21-30 yrs	21	15%
>30 yrs	10	7%



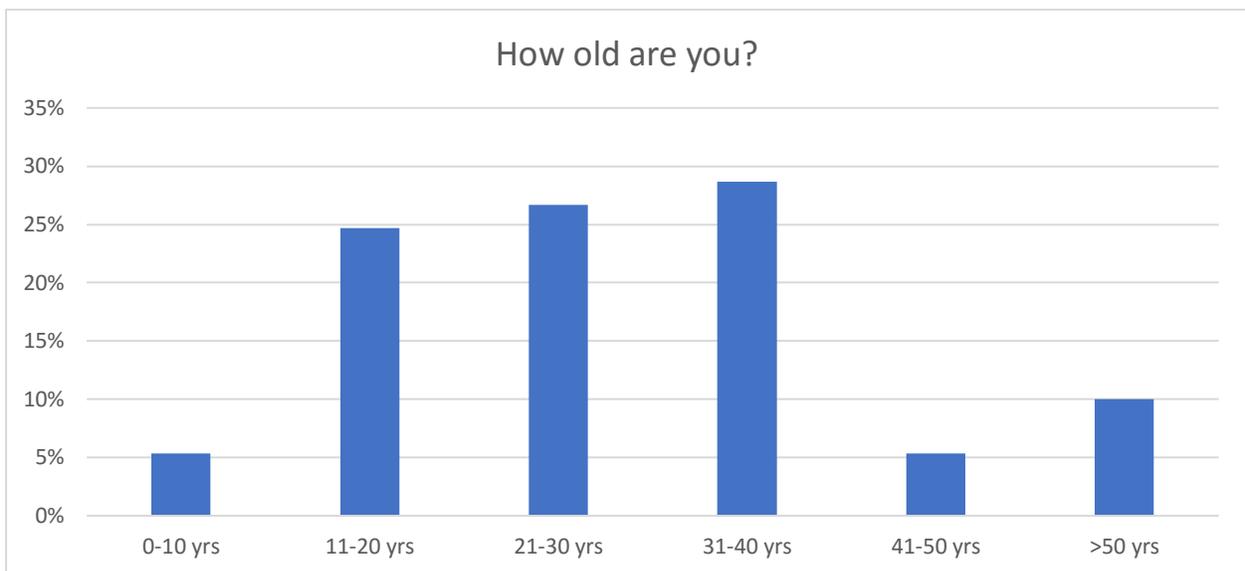
How long ago were you diagnosed with FA?

Total Responses	144	
Unique Participants	144	
Response options	Count	
<1yr	12	8%
1-2yrs	17	12%
3-5 yrs	17	12%
6-10 yrs	27	19%
11-20 yrs	47	33%
>21 yrs	24	17%
Not sure	0	0%



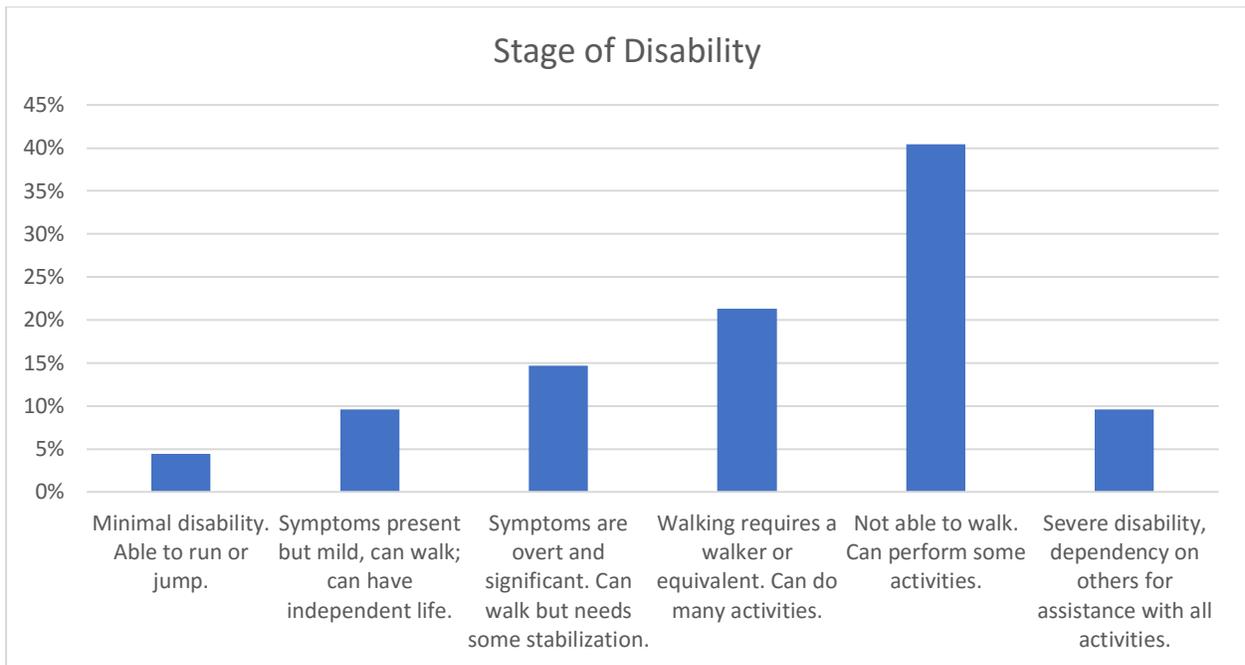
How old are you?

Total Responses	151	
Unique Participants	150	
Response options	Count	
0-10 yrs	8	5%
11-20 yrs	37	25%
21-30 yrs	40	27%
31-40 yrs	43	29%
41-50 yrs	8	5%
>50 yrs	15	10%



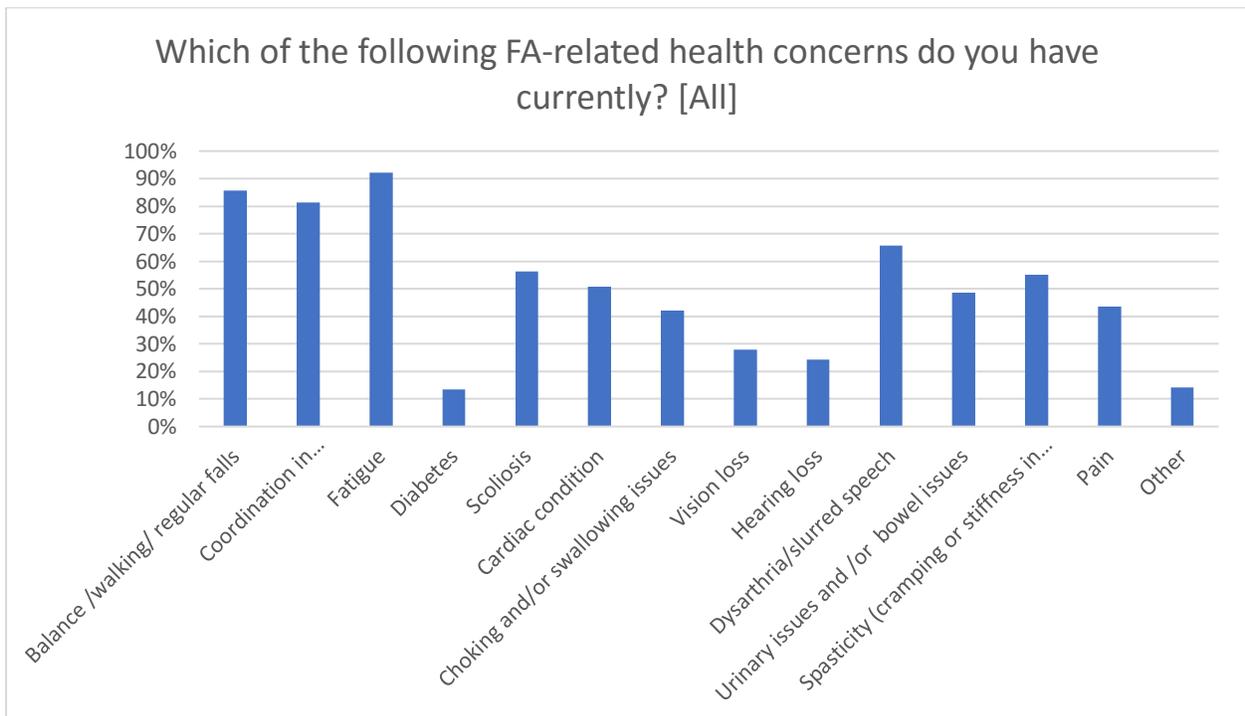
Please select the answer that best describes your stage of disability:

Total Responses	136	
Unique Participants	136	
Response options	Count	real percent
Minimal disability. Able to run or jump.	6	4%
Symptoms present but mild, can walk; can have independent life.	13	10%
Symptoms are overt and significant. Can walk but needs some stabilization.	20	15%
Walking requires a walker or equivalent. Can do many activities.	29	21%
Not able to walk. Can perform some activities.	55	40%
Severe disability, dependency on others for assistance with all activities.	13	10%



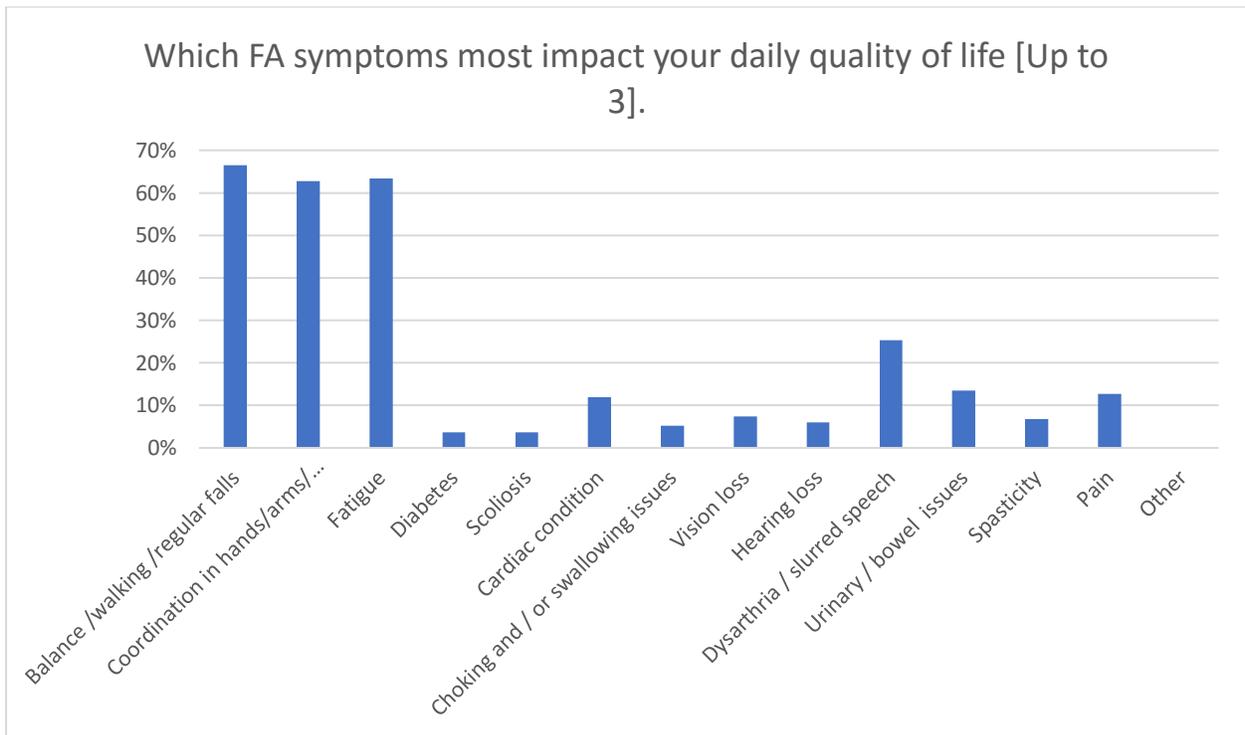
Which of the following FA-related health concerns do you have currently? [All]

Total Responses	982	
Unique Participants	140	
Response options	Count	
Balance /walking/ regular falls	120	86%
Coordination in hands/arms/manual dexterity	114	81%
Fatigue	129	92%
Diabetes	19	14%
Scoliosis	79	56%
Cardiac condition	71	51%
Choking and/or swallowing issues	59	42%
Vision loss	39	28%
Hearing loss	34	24%
Dysarthria/slurred speech	92	66%
Urinary issues and /or bowel issues	68	49%
Spasticity (cramping or stiffness in legs)	77	55%
Pain	61	44%
Other	20	14%



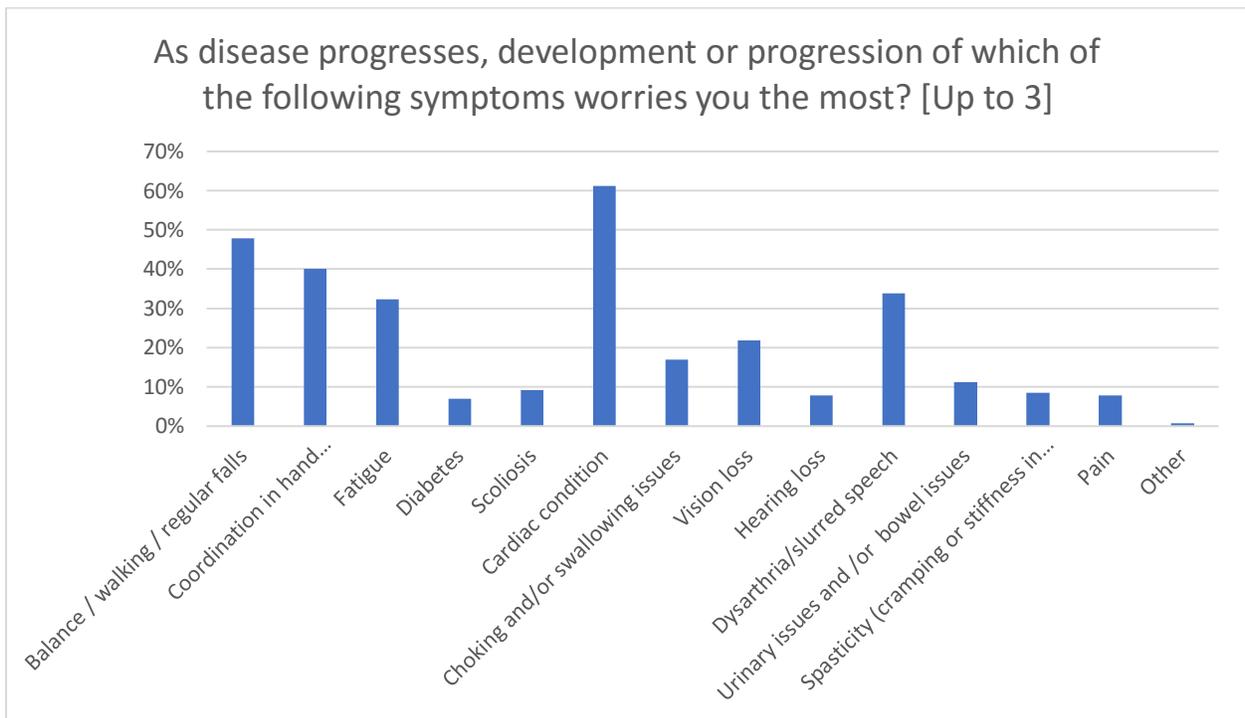
Which FA symptoms most impact your daily quality of life [Up to 3].

Total Responses	387	
Unique Participants	134	
Response options	Count	
Balance /walking /regular falls	89	66%
Coordination in hands/arms/ dexterity	84	63%
Fatigue	85	63%
Diabetes	5	4%
Scoliosis	5	4%
Cardiac condition	16	12%
Choking and / or swallowing issues	7	5%
Vision loss	10	7%
Hearing loss	8	6%
Dysarthria / slurred speech	34	25%
Urinary / bowel issues	18	13%
Spasticity	9	7%
Pain	17	13%
Other	0	0%



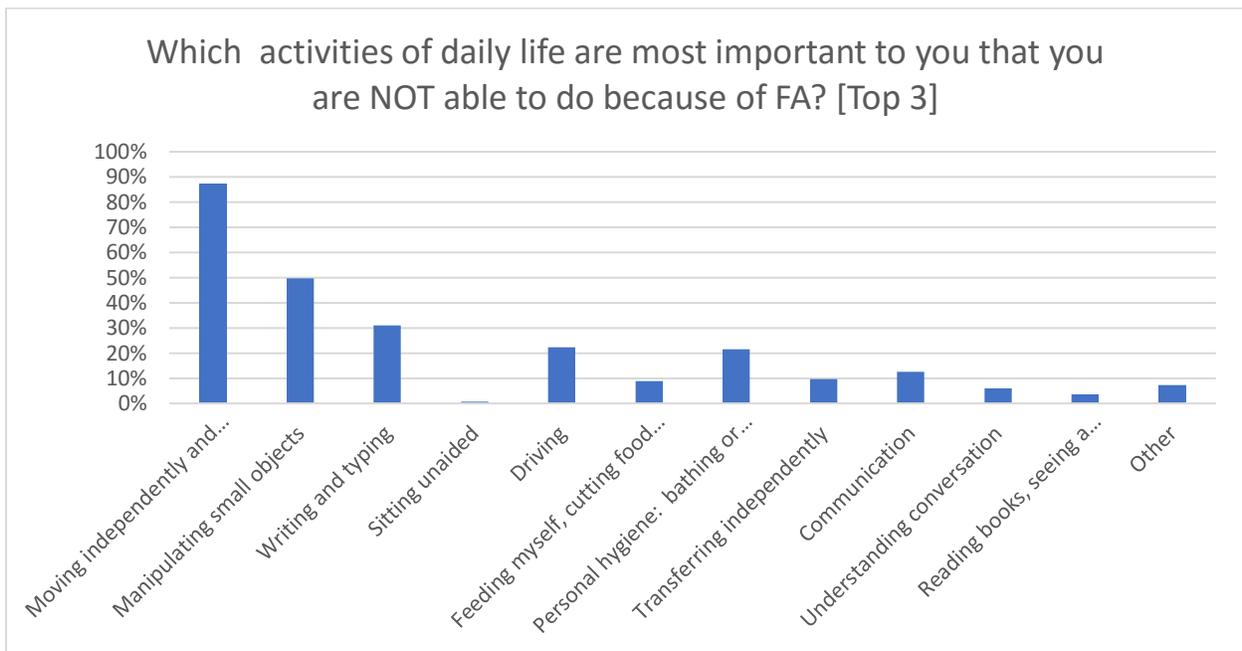
As disease progresses, development or progression of which of the following symptoms worries you the most? [Up to 3]

Response options	Count	
Total Responses	435	
Unique Participants	142	
Balance / walking / regular falls	68	48%
Coordination in hand /arms/dexterity	57	40%
Fatigue	46	32%
Diabetes	10	7%
Scoliosis	13	9%
Cardiac condition	87	61%
Choking and/or swallowing issues	24	17%
Vision loss	31	22%
Hearing loss	11	8%
Dysarthria/slurred speech	48	34%
Urinary issues and /or bowel issues	16	11%
Spasticity (cramping or stiffness in legs)	12	8%
Pain	11	8%
Other	1	1%



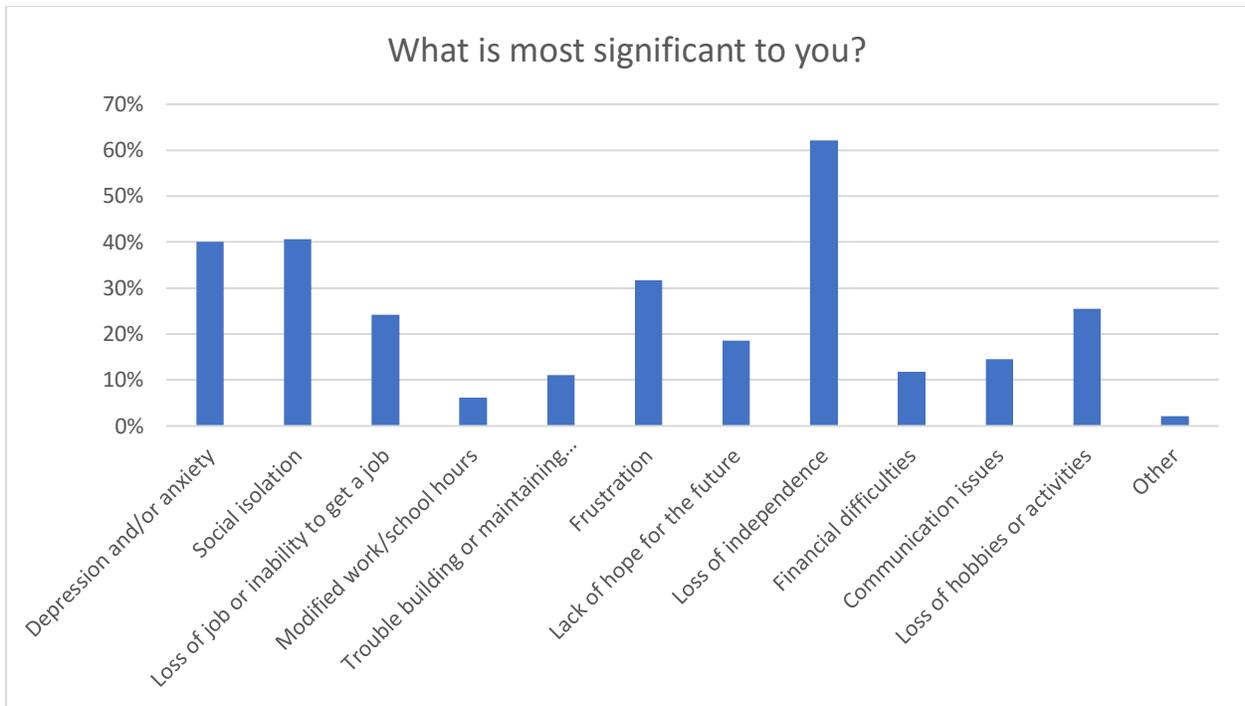
Which activities of daily life are most important to you that you are NOT able to do because of FA? [Top 3]

Response options	Count	
Total Responses	352	
Unique Participants	135	
Moving independently and safely, walking / standing.	118	87%
Manipulating small objects	67	50%
Writing and typing	42	31%
Sitting unaided	1	1%
Driving	30	22%
Feeding myself, cutting food and handling utensils	12	9%
Personal hygiene: bathing or dressing independently	29	21%
Transferring independently	13	10%
Communication	17	13%
Understanding conversation	8	6%
Reading books, seeing a computer screen or phone	5	4%
Other	10	7%



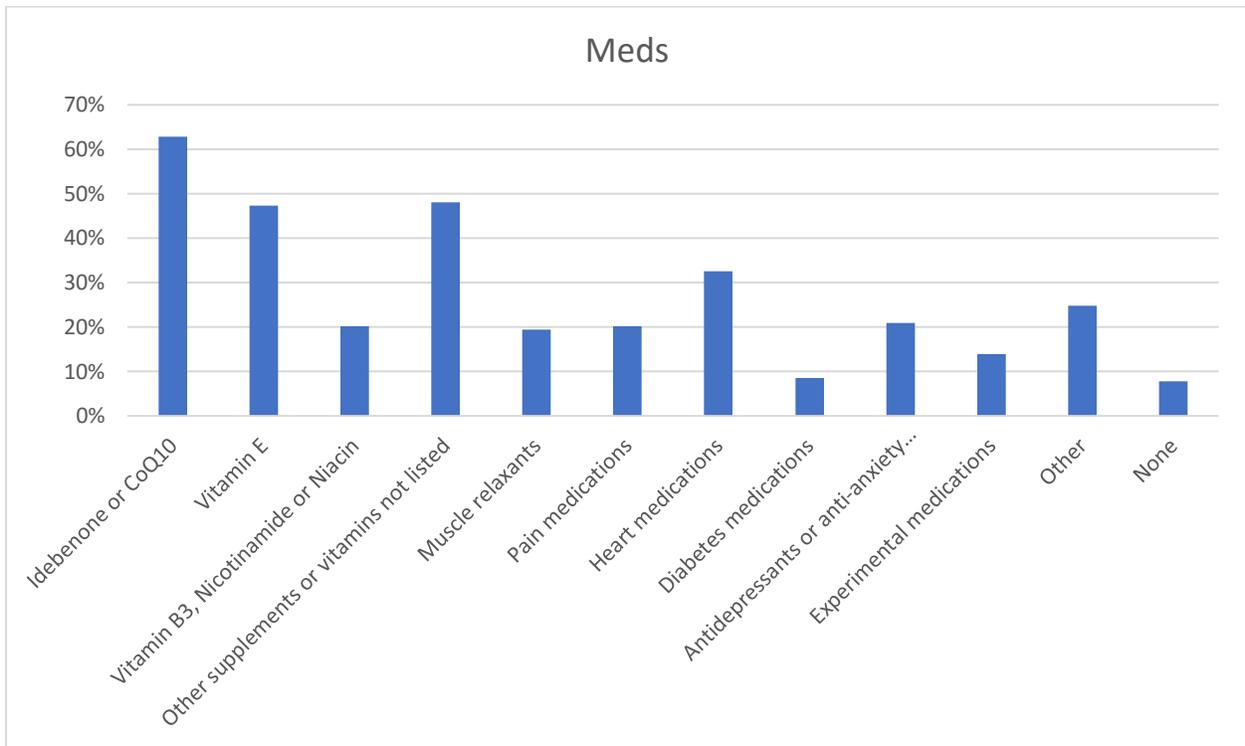
As a result of living with FA, which of the following are most significant to you? [Top 3]

Total Responses	418	
Unique Participants	145	
Response options	Count	
Depression and/or anxiety	58	40%
Social isolation	59	41%
Loss of job or inability to get a job	35	24%
Modified work/school hours	9	6%
Trouble building or maintaining relationships	16	11%
Frustration	46	32%
Lack of hope for the future	27	19%
Loss of independence	90	62%
Financial difficulties	17	12%
Communication issues	21	14%
Loss of hobbies or activities	37	26%
Other	3	2%



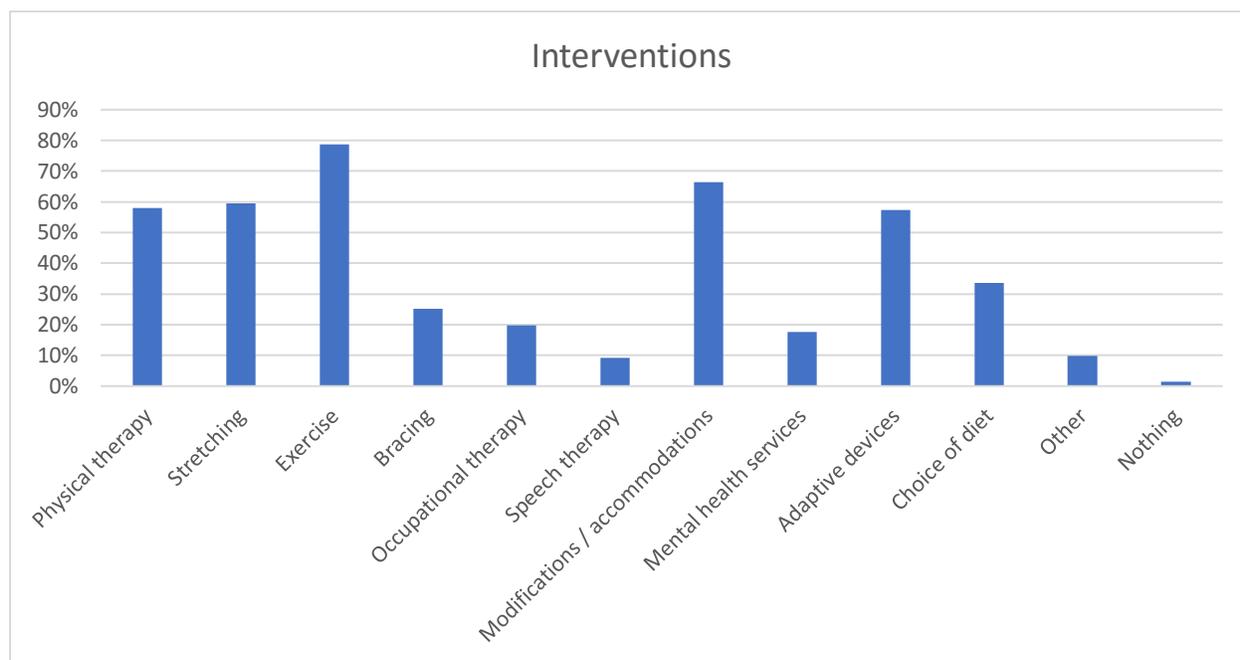
What medications or supplements do you take now to treat symptoms of FA? [All]

Total Responses	421	
Unique Participants	129	
Response options	Count	
Idebenone or CoQ10	81	63%
Vitamin E	61	47%
Vitamin B3, Nicotinamide or Niacin	26	20%
Other supplements or vitamins not listed	62	48%
Muscle relaxants	25	19%
Pain medications	26	20%
Heart medications	42	33%
Diabetes medications	11	9%
Antidepressants or anti-anxiety medications	27	21%
Experimental medications	18	14%
Other	32	25%
None	10	8%



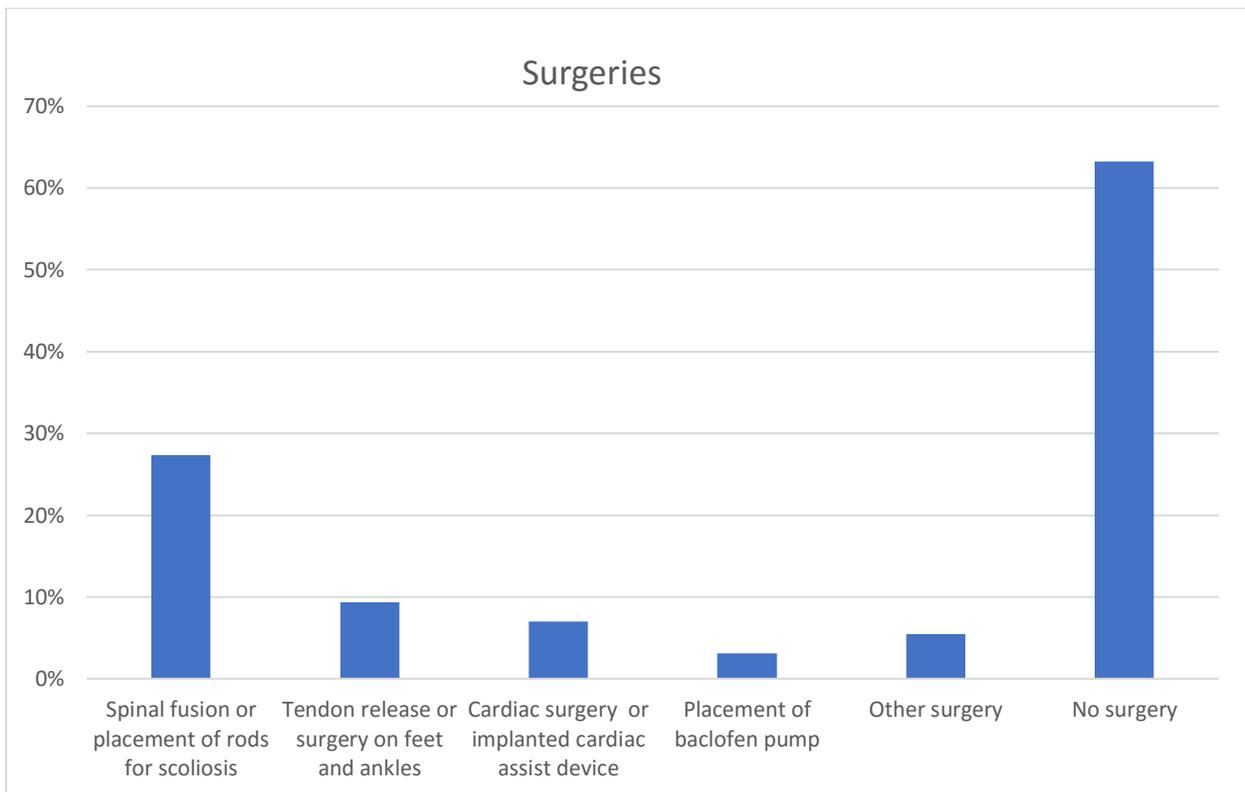
What are you currently doing to help manage FA or FA symptoms? [All]

Response options	Count	
Total Responses	572	
Unique Participants	131	
Physical therapy	76	58%
Stretching	78	60%
Exercise	103	79%
Bracing	33	25%
Occupational therapy	26	20%
Speech therapy	12	9%
Modifications / accommodations	87	66%
Mental health services	23	18%
Adaptive devices	75	57%
Choice of diet	44	34%
Other	13	10%
Nothing	2	2%



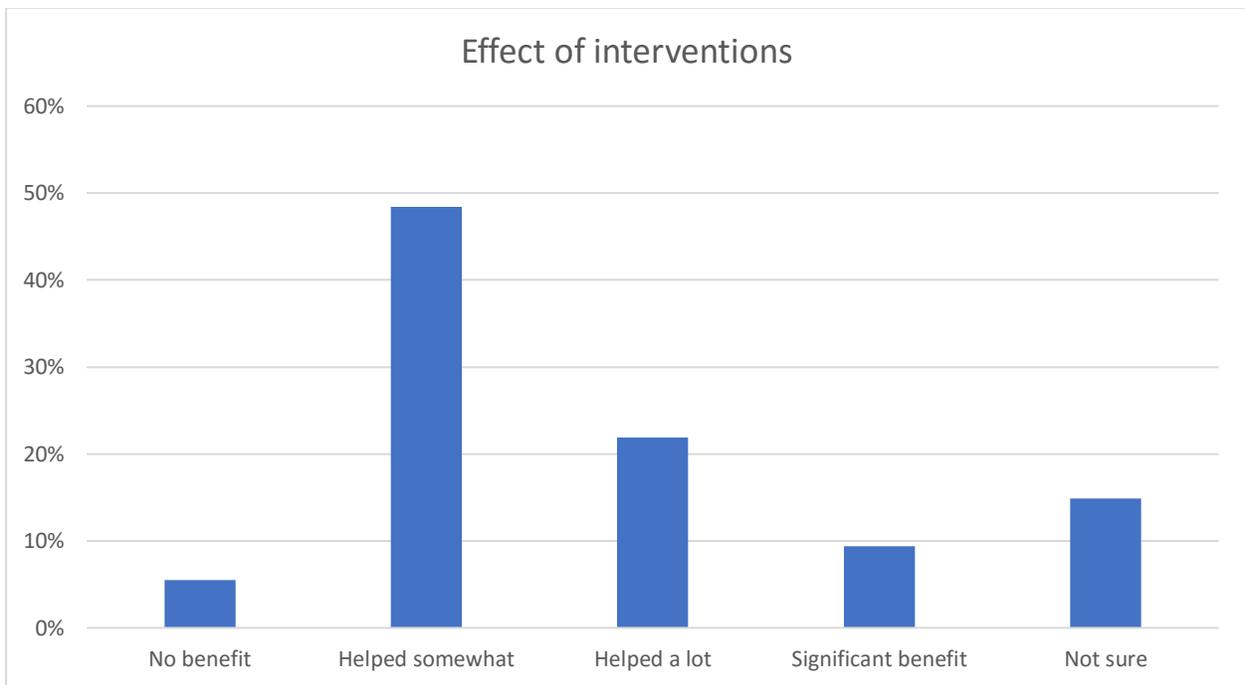
Have you undergone surgery to treat or manage symptoms of FA? [All]

Total Responses	148	
Unique Participants	128	
Response options	Count	
Spinal fusion or placement of rods for scoliosis	35	27%
Tendon release or surgery on feet and ankles	12	9%
Cardiac surgery or implanted cardiac assist device	9	7%
Placement of baclofen pump	4	3%
Other surgery	7	5%
No surgery	81	63%



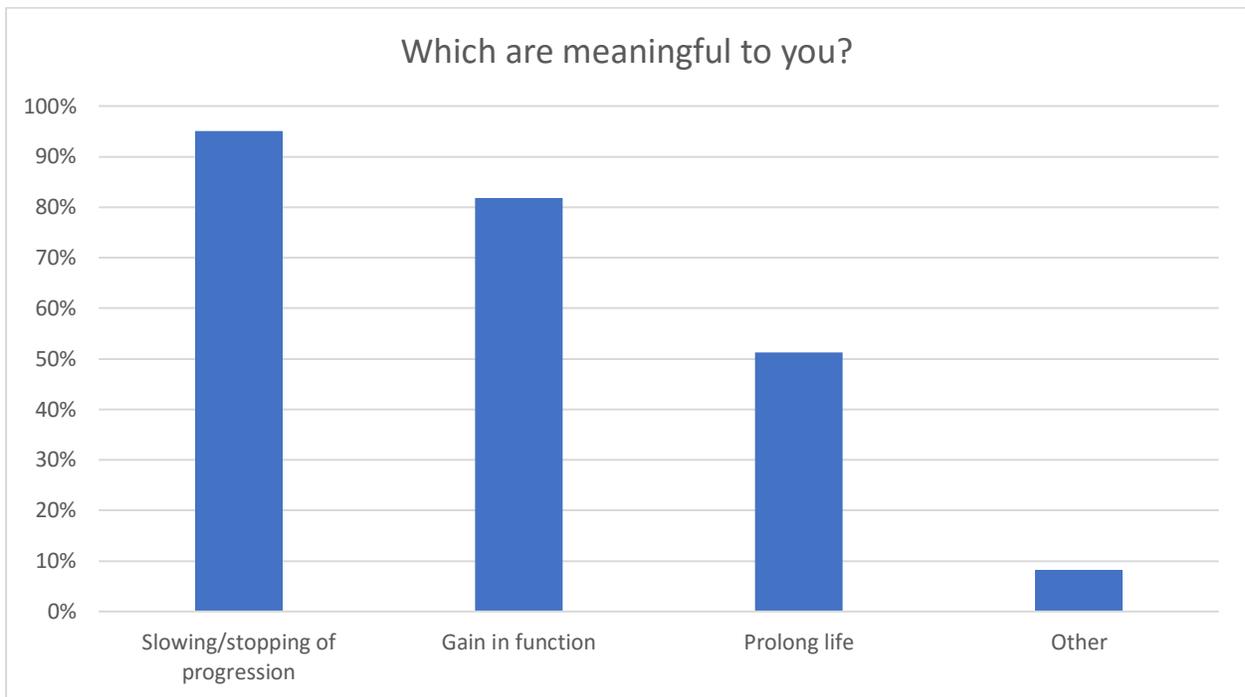
How much do the medications, surgeries or lifestyle changes used improve your quality of life?

Total Responses	128	
Unique Participants	128	
Response options	Count	
No benefit	7	5%
Helped somewhat	62	48%
Helped a lot	28	22%
Significant benefit	12	9%
Not sure	19	15%



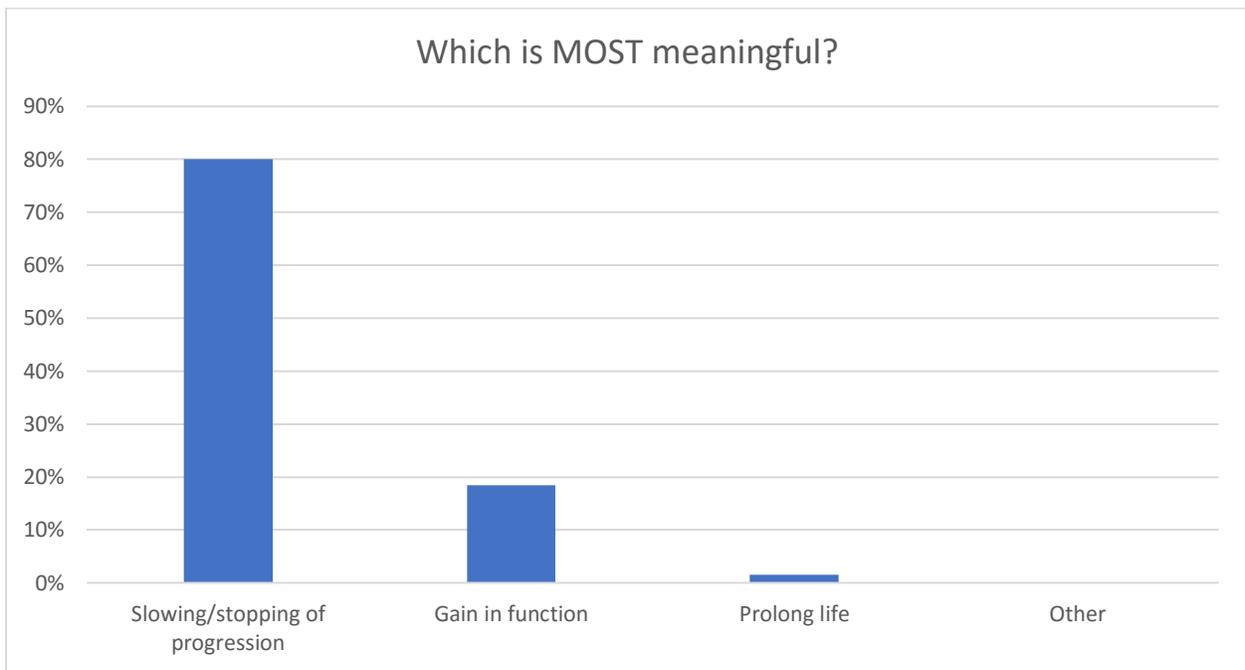
Which outcomes would be meaningful to you for a possible drug treatment? [All]

Total Responses	286	
Unique Participants	121	
Response options	Count	
Slowing/stopping of progression	115	95%
Gain in function	99	82%
Prolong life	62	51%
Other	10	8%



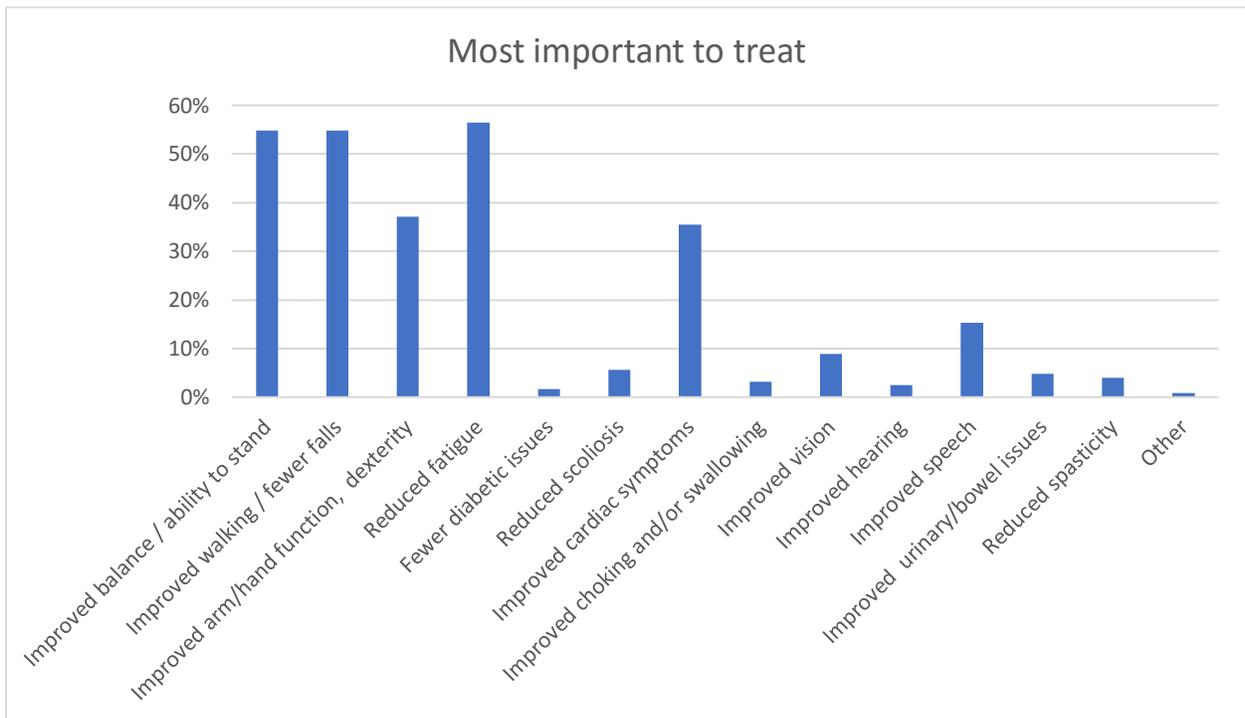
Which outcome is most important for a possible FA treatment?

Total Responses	130	
Unique Participants	130	
Response options	Count	
Slowing/stopping of progression	104	80%
Gain in function	24	18%
Prolong life	2	2%
Other	0	0%



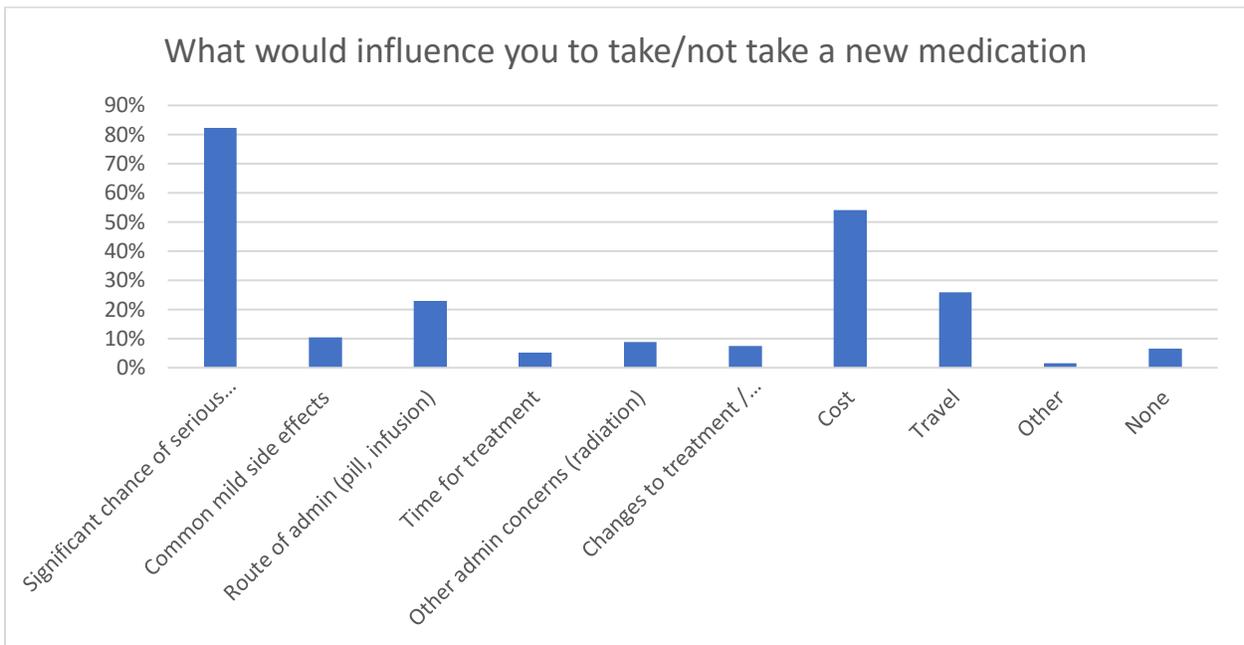
Which ability or symptom would you rank as most important for a possible drug treatment today? [Top 3]

Total Responses	354	
Unique Participants	124	
Response options	Count	
Improved balance / ability to stand	68	55%
Improved walking / fewer falls	68	55%
Improved arm/hand function, dexterity	46	37%
Reduced fatigue	70	56%
Fewer diabetic issues	2	2%
Reduced scoliosis	7	6%
Improved cardiac symptoms	44	35%
Improved choking and/or swallowing	4	3%
Improved vision	11	9%
Improved hearing	3	2%
Improved speech	19	15%
Improved urinary/bowel issues	6	5%
Reduced spasticity	5	4%
Other	1	1%



Which of the following would influence your decision to use a new treatment or take part in a trial? [All]

Total Responses	304	
Unique Participants	135	
Response options	Count	
Significant chance of serious side effects	111	82%
Common mild side effects	14	10%
Route of admin (pill, infusion)	31	23%
Time for treatment	7	5%
Other admin concerns (radiation)	12	9%
Changes to treatment / management	10	7%
Cost	73	54%
Travel	35	26%
Other	2	1%
None	9	7%



Appendix 7: Patient / Caregiver Testimonies

Testimonies included are done so with consent from the individual.

Panel 1 – Living with FA: Symptoms that most impact your life; What worries you most about your condition?

Frankie Perazzola

Hello and good morning. My name is Frankie Perazzola. I am 24 years old, born and raised in beautiful Los Angeles, California with a family the size of most elementary schools and an inconceivable love for the game of basketball. I've always had a passion for any sport really- especially now with an admiration and jealousy of all types movement. At the age of 22, one year after I graduated from Arizona State University (Go Devils) and my career set in sales for professional sports with dreams as high as being the first female GM of the NBA, I was diagnosed with Friedreich's Ataxia (FA). I was asked to talk about certain symptoms that affect me most and to be honest, ALL OF THEM shake me to my now unstable core. Remember years ago, the [Magic] 8 balls we asked questions to? You shook it and waited for the answer on that little triangle to pop up on the window? That is exactly how I feel about us FA patients. All of us are just sitting and uncontrollably shaking the [Magic] 8 ball to see what symptoms and how severe they will be in our progression. Slurred speech? Diabetes? Scoliosis? Loss of coordination in everything from your finger tips to your toes? Or eventually becoming fully dependent on someone else for help on living your life just to name a few. We don't know and that is absolutely terrifying. After years of questioning my body's declining capability of physically keeping up with my peers in softball, struggling to stay on Junior Varsity in High School, the inability to walk a few blocks after being able to cross ASU's main campus for 4 years, not being able to climb a set of stairs without white-knuckling the railing and the draining fatigue I would experience after simple tasks such as vacuuming, doing a load of laundry or mopping the kitchen, I finally had the answer. The diagnosis. Friedreich's Ataxia.

There are 2 ends of the spectrum you can come from if you're an FA patient. Either you've had it since you were younger, most likely suffering the more severe symptoms-They've known FA their whole life. OR- the place I come from which is having the later onset of symptoms, living a "NORMAL LIFE" and slowly watching my body deteriorate and struggle to do things I once did with ease. It took me TWO whole minutes to pick up a bobby pin off of my bathroom floor the other day because I am slowly losing control over my hips and arms. I would and will not let the bobby pin win. Ever. Whatever way you look at it, both ends of the spectrum are completely devastating. No one can teach you how to deal with an incurable disease or how to handle the sound of your parent's heart breaking as they watch your body get worse every day. My father who is 65 and retired has to install handrails around my house to minimize my falls. Watching that happen, knowing the rails are for me and not him is extremely hard to process. Handicap placards and a countdown on the time I have to drive with my feet are now everyday thoughts. Accepting that I have physically more in common with my 80-year old grandmother and her friends than I do, my own 24 y/o friends is honestly mind blowing. Having her push me in a wheel chair knowing it should be the other way around has been a hard to experience as well. Choosing between my cane, walker and wheel chair, depending on the event or activity and

noticing more wheelchair days than before is hard to accept and mentally debilitating most times. We need to address the progression and somehow slow it. Honestly, I haven't been this scared in my entire life and it's the only time I haven't had a solution for one of my problems. I can't begin to explain the fear of watching your body physically declining with birthdays now being markers of tracking my progression and how much worse I have gotten. It's time we break that magic 8 ball open and get some definite answers- we need to have some say in what happens to our bodies because after all, we didn't have a say with having FA. Thank you.

Jack Dewitt

Hi my name is Jack DeWitt. I'm 17 and I live in Howell, Michigan outside of Detroit. My parents first noticed I had balance problems when I was 5. By the time I was 9 I needed a walker and I was finally diagnosed with FA when I was 10. I had a scooter when I was 12 and couldn't walk anymore at all by the time I was 14 and had my spinal fusion surgery. I try to remain optimistic but I know my symptoms from FA will only continue to get worse without a treatment or cure.

My biggest problem with FA is fatigue, simply because it affects everything I do, every day. Fatigue really affects my school attendance, and I often miss a full or half day of school. On a day when I'm feeling really good, I can get through what most kids would think was a pretty boring day. I can manage my short class schedule and then do either therapy or homework at night, but never both. On my worst days, I don't make it to school at all and try to catch up with my teachers through email. Just this year, I've missed 184 class periods. I try, but caffeine only goes so far.

Now, I am 17 and my grandfather grew up in Kentucky. So it's no surprise I became interested in rifles. Now, as you become more interested in these rifles, you get to the stage where you start building them. This is not easy when FA affects your fine motor skills. I don't know if you've ever taken apart a rifle trigger group, but it has a lot of small parts that can go everywhere when your fingers don't cooperate. I've lost many springs and screws that I have to re-buy. It is very frustrating and incredibly demoralizing to have a hobby that I love taken away from me. I see my fine motor skills getting worse every day when I play video games like Call of Duty. While my friends are getting better, my K/D stats are decreasing.

Also because of FA, I've had to give up on driving. During drivers training I tried to drive with hand controls but I couldn't see well enough or react quickly enough. For example, I couldn't really see street signs because of the nystagmus that I get from FA and I would be half way through the intersection before I realized I needed to turn. I still do have posters of a Corvette and a Mustang in my room though because I am still a teenager from the Motor City. But I will always have to rely on others to get where I want to go.

Now I mentioned that I'm 17 and that's the age that you start getting calls that make your parents worry. About a month ago, I got my first call from a Marine recruiter. I had to turn him down on account of my condition even though I have always wanted to serve in the armed forces. I guess I have other battles to fight.

I am most worried about losing my vision because of FA. I feel if I lose my vision, I will lose my remaining link to the world. It would take even more of my independence away and I will lose more hobbies and activities I enjoy like hunting, video games and travel. I'd miss seeing my friend's goofy looks and even my brother's dorky face. Thanks for this chance to tell you how FA affects my life.

Kristin Morrow

Hello and thank you for the opportunity. My name is Kristin Morrow and my husband Ben and I are parents to our kind and delightful 11-year old daughter Anna, who was diagnosed with FA at age 9. As a 5th grader, Anna walks the half mile walk to and from school each day with her siblings and neighbors. This simple act, best represents the symptoms and challenges she experiences living with FA. When Anna experiences an increased heart rate many mornings during this walk, we now know that we just need to stop and take a break, and make sure that we provide ourselves with extra time. Heart rate inconsistencies, in addition to her staggering gait, lack of balance, and repeated falls, have led to her riding her recumbent trike to school beginning in April. When asked by friends and family how she is doing, we often reply, "She's doing great!" We know that this response is not entirely truthful. While we know she is in the early stages of symptoms, we have noticed some progression in the last year. This progression is especially pronounced when Anna gets fatigued. Her balance becomes extremely unsteady, falls more often, experiences an increased heart rate, and migraine headaches. Upon returning from a recent trip out of town to participate in a clinical drug trial, she was so unsteady, she held onto my arm for about a week when walking and asked for a walker to keep at home. 1

We recently traded bedrooms with Anna and her sister so she could be downstairs and not have to navigate the one flight of steps, as she has fallen numerous times. Anna's lack of balance is particularly more pronounced in the morning, as well as more frequent episodes of an increased heart rate, which occur several times a week, sometimes with no forewarning or correlation to her activity. This has frightened her to the point of tears, which has also lead to anxiety, especially when participating in sports. She doubts her ability to swim laps for swim team and keep up with lacrosse teammates during basic drills, due to her inconsistent heart beat and lack of balance. We often have to coax her to participate, many times without success. She sits out, upset with herself for not participating in something she loves to do, but just cannot bring herself to do so despite her strong desire to participate. She is becoming more and more self-conscious because of these difficulties, as well as more strongly objecting to wearing her brace for scoliosis, a prescribed 22 hours a day. While the hope is that the brace minimizes her scoliosis progression, her curvature has increased by 9% in the last year and half, and wearing the brace makes it difficult for her to stay active. We have discussed the importance of wearing the brace, in hopes that by doing so, will eliminate the need for an extensive spinal fusion surgery, a painful and multiple month long recovery. Anna, however, is dedicated to staying strong. Although it takes up much of her free time, she dedicates herself personal strength training sessions and aqua therapy several times each week, as well as daily rides on her trike.

Anna is not fully aware of what lies ahead. She knows that FA is causing her scoliosis and balance difficulties, and can affect her heart. She knows that she may have to use a wheelchair one day, but that is the extent of it. We live in a constant state of urgency, trying to fit as much into a day as possible, while retaining its normalcy.

- How much longer will she be able to walk to school?
- Will this be her last season of lacrosse?
- Will she need spinal fusion surgery?
- Will she be able to live independently in college?
- How long does she have?

Questions we hope to shield her from for as long as possible.

Anna has a heart that is brimming with kindness. However, our greatest worry about FA is that the mild thickening in her heart will worsen. We feel there are ways to modify her lifestyle and accommodate her changing needs. But the heart condition aspects are much more serious, as they can end her life, not just make it extremely challenging. The struggles she could face are almost unbearable to imagine. We know that by the time our daughter is my age, she could be develop vision and hearing loss, lose the ability to verbally communicate, and even feed herself. But the most unbearable would be that she is not with us at all, due to the life-threatening heart condition that often plagues those living with this vicious disease.

Anna is the strongest, yet most tender soul her dad and I have the privilege of knowing. We will stop at nothing to ensure she is able to live her life to its fullest, and we thank all who are doing the same for those living with FA.

RJ Mercure

Hi, my name is RJ Mercure. The most common word I hear is “huh” thanks to my dysarthria, and I barely hear that due to hearing loss. Thank you for this opportunity to give a voice to managing this lovely disease, Friedreich's Ataxia. I'm not one to be so negative; I love to smile; but today must be an exception. I'm 31 years old and was diagnosed almost 20 years ago, at the age of 12. Before high school, my only symptom that was noticeable was a stumble here and there, something only close family would catch. I was also diagnosed with life-shortening cardiomyopathy, but I never thought twice about it, as image was a big concern as a teenager. Progression in high school changed my walking and talking-- like I had a little too much tequila-- just imagine a giraffe in high heels on a windy day. The best way I can describe to you my early years of FA would be, if you were drunk all the time. Now don't get me wrong, you don't feel drunk but your physical reactions are ataxic, the definition of ataxia is “the loss of full control of bodily movements.” If that's not what you'd call drunk, what's your definition? That realization comes from a time in life I felt so good about not having to ride the bus with all the cruel comments from other kids anymore. One day in 11th grade sitting in my class feeling accomplished that I made it into school fine that morning and I'm called into the principal's office because a parent had called in reporting that I was drunk. My handwriting, eyesight and stamina were all weakening. After graduating, my stubbornness was forced to adapt, I had to use a wheelchair full-time.

If you asked me 10 years ago what symptoms I have the hardest time coming to terms with, my answer would constantly change, just like this disease. I am sick of always adapting as symptoms worsen. It is so exhausting. I now have nystagmus (my eyes are ataxic!) and it drives me crazy to not be able to focus. My heart is on the losing side of this battle. A premature death, that you hear in all the literature, is becoming apparent. I'm not scared of it, but I'm sure my family

worries every single day. But of all the symptoms that I experience, one that now has the most significant impact on my life would be my speech. Our most defining characteristic given to us is our voice. And to have that taken from anyone is awful. I'm often talked down to or belittled because of how I speak. Too many times to count, I've tried to explain to people why I'm in a wheelchair and they are just staring at me like they have no idea what just came out of my mouth. As you likely noticed, my poor muscle control causes slurring and breathlessness. It took 10 years just accepting myself as wheelchair bound. Now, add not hearing well when I once could, seeing well when I once could, then losing my ability to be understood, and it's a recipe for feeling worthless. I'm not asking how to adapt to this one. I'm painting a picture of patients just like me, losing the ability to communicate—losing individuality—losing independence. All I've ever wanted was to be involved, be accepted, contribute to society. FA makes that almost impossible. Being rare adds a lot of extra work and added loneliness. The clock is ticking and I am fighting against so much! We have to get this one.

Nelda Van Schoick

Thank you for this very important opportunity. Before I start, I would like to say those in our FA audience, that I do not wish to cause you pain with the details I am about to share. This is a rare occasion for me, to explain explicitly what happened in the last few years of our daughter's life. Please remember that no two cases of FA are the same.

One year ago, we lost our 33-year old daughter Rebecca to FA. Our oldest daughter Robbi who also has FA is here today, and our youngest daughter Katie is a carrier, and married with a one year old child.

Becca was a precocious little girl, who excelled at almost everything. FA symptoms started at about age 7 and by age 14, she was using a wheelchair. This was before genetic testing so it was a waiting game to see what she and her sister had. Despite worsening physical limitations, Becca was a hardworking student and made her mark in academics. Much to our concern, she set her sights on the University of Notre Dame. In 2001, she graduated as valedictorian of her high school class in Texas, and enrolled in Notre Dame, without being able to take a single step on her own. In 2005 she graduated on time, with two degrees, after having the time of her life for 4 years. The faith based, service-oriented environment at Notre Dame had helped her achieve her goals. Unfortunately, her health had been failing over this same period and by the time she graduated, the toll of FA was very apparent.

She could barely type, had begun having difficulty with the enunciation of words and the ability to control her breath when speaking. She began choking and strangling and had to have thickener in her liquids. She required 12 hours of sleep and never had much energy. She became unable to bathe and dress herself, brush her teeth or hair, put on make-up, and take care of her toileting needs. Rather quickly, she also lost the ability to feed herself and hold a cup. She soon was not able to roll over in bed or adjust her position during the night, and couldn't scratch when she itched. The last 5 years of Becca's life were very sad and very difficult for her and us. She developed heart failure, and took more and more medication to control the symptoms of shortness of breath, fatigue, low energy, and fluid retention.

These physical losses were accompanied by social isolation and depression. We had moved while she was in college and it was extremely difficult to make new friends. The academic environment which had given her life its drive for so many years had come to a screeching halt, and her alternatives were few. She could not make plans because she never knew how she would feel, but when she did feel ok, she would watch funny television shows, take her service dog to a library program called Read to Rover, hang out on our deck where she had an herb garden, and visit the farm of some close friends. It was being close to nature that gave her the most comfort.

About 4 years before her death, Becca developed a blood clot in her heart. Her health declined even more rapidly and she started taking powerful blood thinners. We had to buy a ceiling lift and rent a larger wheelchair because of the amount of fluid she retained. She developed gastric paresis, which caused great discomfort. We constantly tried to determine what she could eat and what medication she needed to handle the bloating and distention.

She could no longer think clearly and was unable to focus. The depression worsened and then most painful symptom raised its ugly head. She began experiencing attacks of intractable spasticity which struck with no warning, causing excruciating pain. She would have to go to bed with these attacks, because her body became completely rigid and we could not keep her in the wheelchair. Medication helped somewhat, but at therapeutic doses caused extreme drowsiness, slowed breathing, loss of lucidity, and psychotic episodes.

Becca often worried about the other families impacted by FA and helped us with fundraising. She knew that we were fortunate that I had physical therapy training and that we were able to provide her with good medical care, but she knew she was dying. She often expressed how sad it was for her that we were having such a difficult time caring for her. She knew we were hurting too in not being able to protect her. We tried as hard as we could to keep her as comfortable as possible. I will always wonder whether our care kept her alive too long and prolonged her suffering.

By the beginning of 2016, she was ready to go, and by the time we called in hospice, she lasted one week, taking her last breath on May 21, Friedreich's Ataxia Awareness Day. For her funeral service, which perfectly captured her spirit, we had to go back four years to find a photograph that looked like her.

Becca's last good day was a Monday in mid-May, just 5 days before she died. Kyle Bryant and Felicia DeRosa were in town for the screening of FARA's wonderful documentary *The Ataxian*. Becca was able to be up for about an hour, and although she couldn't really see, she knew that they were in our home, and was able to visit with them. She seemed serenely happy that day.

In closing, Becca would want you to appreciate the importance of learning everything we possibly can to help alleviate the suffering, in any way, for those with Friedreich's Ataxia. My hope is that her story will help to inspire any research that could one day lessen the impact of this tragic disease.

Submitted Comments - Panel 1 Topics

Paige Meyers

Physical impairment and frequent falls, combined with fatigue, is detrimental. When I fall, it takes anywhere from 5 minutes to 2 hours to get back up. Sometimes I still can't get up myself and have to call for help. Most of the time, I am hot, sweaty, and shaking from exhaustion once I get up, and then it takes me half an hour or more to recover my energy. Additionally, I can type okay, but being in college and being slower at typing is tricky. Essays, homework, and tests take me much longer and are more mentally exhausting than for other students. And of course, losing the ability to speak clearly and communicate effectively is huge. I just graduated from a respected research university with a 3.6, after winning numerous awards and scholarships. I am currently looking into graduate programs. I am smart. Many of us with FA are. And yet, we are prohibited from being productive and benefiting society because of FA. Molecular genetics are a love of mine, but it took one day of freshman bio lab to realize I do not have the coordination to set up a gel electrophoresis. Physical barriers—like the inaccessibility of many buildings—prevent us from taking other jobs. Speech difficulties add an additional barrier to yet other jobs. FA robs us from some of our best minds with otherwise enormous potential. Thank you for all you do! It's fantastic that we got this opportunity!

Sandy Lane

My daughter, Chelsea, was diagnosed at the young age of 4 ½. Not only did we win the lottery with a diagnosis so rare, but she also had an extremely rare point mutation, W155R. Her progression was rapid and we knew because of her rare point mutation, she wouldn't be here on this earth too long with us. She lived a short 19 years, but in those 19 years she truly touched so many lives. Many of her friends have continued on in the medical field, including her sister who is now a PICU nurse at UCLA. She taught those around us compassion, love, and how to maintain hope.

I'm not sure if I was naïve, but I truly believed and hoped that there would be a cure in her lifetime.

My plea to you is that you continue to support FARA in finding a treatment and a cure for our kids. This disease is a tragedy. While I was blessed to have been given an opportunity to have such a wonderful soul such as Chelsea, as a daughter, I wouldn't want any other parent to have to bury their child and feel the pain that accompanies such a loss. Please help us stop this disease!

Teresa Holm

Hi, my name is Teresa Holm and the mom of four, and two of my children have been diagnosed with Friedreich's Ataxia. The thing is, since being diagnosed two years ago, Hope is what we have clung too. As you glance around the room, most of the age of those afflicted are young. Where are the senior citizens? This disease is not a once and done. It is drawn out. We mourn each individual loss. Every day I wait for the next regression. I know what's coming. As FA parent's, we all do. As the aged neurologist first diagnosed the kids, he told us what he suspected with tears in his eyes. He knew what the future holds. I said but our daughter wants to be a pulmonologist (lung doctor) and he scolded me that she could still be a doctor in a wheelchair. But realistically, with an hourglass filling with sand faster than we'd like, those dreams have

ended. What 22 year old young man wants to use a walker to get around? Or call his parents that he got into an accident because his reaction time for his legs and stopping the car is gone. He hasn't driven since. How can we give these kids more time... How can we help them... How can we protect their hearts...

Robbi Van Schoick

Of the great many symptoms [that] I have experienced, the two main symptoms that hinder me the most are my poor manual dexterity +and hearing loss. My manual dexterity is problematic for me, not only because I am no longer able to feed myself, but because I have severe difficulty typing. Typing difficulty exclusively keeps me from earning my Ph.D., the one degree I still need to achieve my ideal job as a professor and researcher. My manual dexterity problems make everything I do so exhausting and tedious, if not impossible, and are steadily getting worse. Being able to feed myself would greatly improve my quality of life, as far as not having to rely on paid help, and increase my personal freedom. I have done physical therapy for years until my ability to fully use my arms and hands eventually became impossible. Second in my perceived severity is hearing loss. Hearing loss, to me, means difficulty filtering out any noise going on in the background from a conversation I on which I want to focus. In my University of Georgia classroom. I have severe difficulty hearing the student, especially those who sit in the back of the class. I have noticed that my hearing loss extends beyond problem as with background noises, because I unfortunately miss certain words spoken by people in my daily life. My middle sister's death was incredibly heartbreaking and challenging for me personally. I could not help but think ahead to my own decline at the end of my life and the choices want to have made before my death. Living with Becca makes me realize how even sisters with the same disease are often affected by FA very differently. Becca's heart disease was more profound than mine is, but she experienced vision loss and severe spasticity, two symptoms I do not have.

Laura Arioto

Siena was diagnosed with Friedreich's ataxia one year ago when she was 7. We were told her disorder was progressive and that there was neither a treatment nor a cure. We were also told her condition was considered to be severe because she was diagnosed at such a young age and because the repeat of the frataxin genes were extensive.

The symptoms that have negatively affected Siena the most are her deteriorating balance and declining energy levels. She needs guidance when walking to the restroom at night to prevent her from falling. Her lack of stability is causing her to trip more and more. She can no longer ride her bike she got for her 7th birthday. The neighborhood girls her age don't stop at our house to see if she'd like to ride with them because she can't keep up on her recumbent bike. She loves to swim in our pool but now she spends more time hanging on the side because she loses her energy so quickly.

What worries us most about Siena's progression is that we'll have to bury our daughter before she's had time to experience all of the wonderful joys of life. If a cure is out of reach, I would hope for a treatment that could help her regain her balance and improve her energy level.

Katie Snead

Hi, my name is Katie Snead, I am 12 years old. I was diagnosed with Friedreich's Ataxia about three and a half years ago. With F.A. I haven't been able to do things I want to do and that other kids do such as track, and soccer. With F.A. I haven't been able to do athletic activities with my friends, I trip and get hurt a lot easier than most people. This affects my walking even more and because I have F.A. it takes longer to heal.

-Walking is very difficult

-I lose my balance very easily

-I miss school more than others for medical appointments

I travel a lot.

-I have been to Minnesota, Philadelphia, and UCLA taking time out of my summer to contribute to M.R.I. studies and I am here today missing school to help you see that we need your help to work towards a cure.

Donna Littell

My name is Donna Littell and I have Friedreich's Ataxia, FA. I am 59 years old and first showed symptoms in High School. I was never athletic, somewhat clumsy and my friends pointed out that my eyes would shift from left to right. There was nothing to be concerned about and I enjoyed childhood and my early twenties as any other 'normal' person. I am grateful for that time but it also makes it difficult to accept each progression because I remember walking and living a full life.

My symptoms became very noticeable in my late twenties. I developed issues with balance and an unsteady gait. My first diagnosis at the age of 29 was Arnold Chiari syndrome, the compression of bone on the cerebellum. I was referred to John Hopkins and had brain surgery to remove bone and vertebrae caps to relieve the pressure. After recovery, I convinced myself I was cured, however, the symptoms returned weeks later. I went back to Johns Hopkins for a week of inpatient testing which resulted in a diagnosis of Spinocerebellar Degeneration. The doctors looked as though they were giving me a death sentence and offered nothing to assist with my physical or mental well-being.

They did suggest contacting the National Ataxia Foundation. It was in one of the NAFs Generations newsletters that I read an article about a doctor at Hahnemann Hospital in Philadelphia. Since I lived close to Philadelphia, I wrote him a letter explaining that I was looking for a neurologist specializing in ataxia. He wrote back to explain he was a scientist, not a medical doctor but he worked with Dr. Fischbeck on ataxia research. I contacted Dr. Fischbeck at the University of Pennsylvania. My entire world opened up. He was knowledgeable and encouraged anything I mentioned to help – physical therapy, psychological therapy, etc. He also encouraged me to take the genetic testing for FA. He suspected I had late onset FA. The test came back that I did indeed have FA. Finally, I had a diagnosis.

Dr. Fischbeck left to go work for NIH and I saw his predecessor Dr. Lynch. By this time, I was still walking but holding on to my husband and walls for support. Stairs and curbs became my enemy. I made the decision to get a service dog. It was a difficult decision, but she gave me back

my independence. I continued to work full-time, attend college at night, did volunteer work and took therapeutic horseback riding. I was driven to live a very full independent life.

After my dog retired, I started using a walker for bilateral support. My dexterity and handwriting declined. This was another loss, another downhill slide. By this time, I was in my forties.

In my fifties, my driving was becoming dangerous when sometimes my foot could not find the brake pedal. I made the decision to stop driving until I went through training to drive with hand controls. I also decided after several bad falls with the walker, to go to a power chair full time. Another decline, another transition, another loss.

I am very blessed that my employer allows me to work from home full time. I enjoy the interactions with my colleagues and the work but it can be stressful and tiring. My latest battle is fatigue. My primary physician once warned me that I may use up my energy keeping the pace that I was. I fear she was right. I don't sleep well some nights because of the spasticity in my legs.

My fear is of the future. My husband is my caregiver. He is loving and trustworthy. We do not have children or extended family. I don't want to rely on anyone for my basic functions. Today, I can transfer on my own, go to the bathroom, shower, dress myself and feed myself on my own. Will I always? What if something happens to my husband? Will I end up in a nursing home, dependent upon others for every basic need? This is what haunts me as I approach 60. I am not eligible for drug trials and I wonder if treatments will be available to me. I am not expecting a cure for me, but I pray for a treatment to stop the progression so I will never end up in that nursing home.

Christine Battaglia

Hi: I'm Christie Battaglia. I'm 31 years old and was diagnosed 2 years ago but in retrospect my symptoms started when I was around 23-24. Having late onset FA I went 20ish years living a completely "normal" life, then in my mid-twenties things started to change. For years I thought I was just clumsy then around 27 we started to worry.

1 of the 1st things that alerted us something might be wrong was in Dec 2013, 9 months before I first went to the doctor, I was on my way to bring my mom dinner when I was pulled over for speeding. The officer noticed my slur and asked me if I had been drinking; I told him I hadn't, but he asked me to step out of the car. He asked if I had a speech impediment, mind you, I had no idea anything was "wrong" with me at this point. Or if I had taken any prescription drugs. After failing the field sobriety test, I was handcuffed, put in the back of the cop car and taken to the station for a breathalyzer, which I passed since, like I told him, I hadn't been drinking.

Fast forward to April 2016, now knowing I have FA. I was at court for a speeding ticket, yes, I have a lead foot, when an officer stopped me to tell me I shouldn't come to court drunk and hoped I wasn't driving when I left- embarrassed, I explained I hadn't been drinking but I have a neuromuscular disorder which the symptoms make it seem like I'm drunk. He quickly dismissed my explanation and reiterated that I should not be driving in my current state. I was aggravated with the encounter but more than that I felt humiliated and self-conscious.

My point is, having FA does mean people judge us and while it's easy for non-FA'ers to tell us not to care what other people think, in reality, the opinions of some, such as police officers, potential employers, etc. actually do matter and greatly affect us in multiple areas of our everyday lives. Every day, for everything I do, I have to decide if I want to visually appear to be an able bodied 31- year old and have outsiders wonder what's "wrong" with me or, more likely, JUDGE me for being a lush OR do I use my cane, to have an "excuse" for my slur and stumble, and appear as handicapped as I am and have outsiders PITY me for being disabled at 31.

Caroline Spencer

My name is Caroline Spencer. I am 28 years old and I was diagnosed with FA when I was 23.

When I was diagnosed, it really hit home professionally, as well as personally. I was in the middle of completing my Master's degree in speech pathology. I truly enjoy working with others to improve their communication, but having dysarthria myself, it is incredibly taxing.

Still, it gives me a deeper understanding of the power of communication. It's how we express our needs, emotions, thoughts, and ideas. When the voice and speech are impaired, as it is in FA, it is often laborious and fatiguing to communicate with others. Therefore, it is my hope that soon there are effective treatments that directly improve the speech and communication abilities of people with FA.

Beth Hanes

Fatigue: I have yet to give up my position as a teacher. Although I have moved to a different position so I am in charge of small groups that come to me throughout the day, I love to teach and desperately want to help provide for my family. I am exhausted after teaching all day and I come home to a 7-year-old daughter who has Autism, ADHD, and is starting to become involved in sports. Balancing her need with my own is a challenge. My mother comes each day for a few hours to cook and help with laundry. We are a very active family, going many places and experiencing as much as we can to provide exposure for my daughter, and memories for me.

Mobility: It is getting harder and harder to remain active and be independent due to my mobility. I am always thinking ahead on how I can do things in as few steps as possible. I have to think ahead about where I can park, if there are any steps to get there, if I can get around with my walker because I can't get my wheelchair out of my van. I am at the point where I have made the minimal amount of home modifications that I can, and wonder how I can financially manage major modifications when I can't rely on a walker anymore. I already damage our walls and door jams with the wheelchair I use when I am suffering from knee pain or severe exhaustion. I am also terrified that my days of being able to use a walker to perform my job are numbered.

Restless Leg Syndrome: I experience horrible restless legs. If I need to sit down to relax, I have to get back up because my legs shake so badly. I suck it up until I am able to take my first dose of Requip. I am already at the max dose and must do my best to take it in the evening. If I don't I will not sleep because of constant leg movement. I also have to plan any travel or trips in the car around my medicine time. Even when I take my medication, I often awake with my legs shaking and can't get back to sleep. Sleep is so important for me, especially when I go to work every day. Many days my restless legs only allow me 4-5 hours of sleep.

My symptoms make life not only physically, but mentally exhausting. I have to plan everything! Managing life as a mother when my husband also works is hard to do. When my daughter has a practice or event we need to attend, I always have to enlist help. For example, at her recent soccer practices, if my husband couldn't make it I had to have my Mom or Dad ride with me to walk her across the field to her practice. Although this is not a great risk now, she used to be a flight risk and she would take off running (something typical of Autism). Even if I could walk with her across the field, I would not have been able to catch her if she decided to take off.

There are many activities that I can't do because I am unable to go most places independently. When my daughter had cancer, a local organization BrAva, came to the aid of our family. I sought to join to group to help give back to other local families affected by childhood cancer. I was involved for two years, as my sisters were also members and could help me get to the meeting safely. As time passed, I was unable to attend night meetings, as I can't drive at night alone or when I am tired because I struggle to find the gas pedal. Although the committee members were understanding, I had to resign because I could no longer provide my services and didn't deserve the recognition the other got. I am only close with my family, as they are the only ones that truly understand my needs and how I feel, so I constantly feel left out of activities with friends and coworkers.

What worries me the most about FA is the progression of the disease. When I was first diagnosed with FA, I would put a timeline on things. I remember thinking that within five years most individuals with FA would be confined to a wheelchair. I thought to myself, "OK, my daughter will be going to Kindergarten and will not require as much help." I also remember that statistically, I would be alive long enough to see her walk down the aisle. When I experienced the positive effects of the drug trials I participated in, those thoughts seemed to have faded. Now, as I feel the progression speeding up, I am taking things one day at a time!

This question [of choosing one symptom to correct] is hard to answer. I am going to narrow it down to mobility, or my ability to walk. The hardest part of being diagnosed with FA is knowing that I have become a burden to those that are closest to me. I need help to perform the most basic functions of a wife and a mother. I have to give my Mom the credit of cooking, cleaning, and practically raising my daughter with special needs. My Dad has sacrificed so much time and money to help. My husband has had to pull double-duty when he gets home to make sure that my daughter's needs are met, and has been on the receiving end of many bursts of crying, anger, and frustration when I am too tired to regulate my emotions. My sister has had to be my means of transportation to doctor's appointments and clinical trials. I always took pride in my ability to take care of myself and my family, just as my parents raised me to be. I am crushed knowing that without a treatment or cure, I will never get to experience that again!

Anonymous

The best way to describe how the symptoms of FA impact my life is for me to look at how my hobbies and interests have had to change. As an example, before FA, I really enjoyed playing golf. I'm a competitive person and golf is a great way of competing. I would feel a real sense of accomplishment when practice paid off and I could feel like my efforts were being rewarded. Golf was also a great way to spend time with friends.

When I think about the effect that FA symptoms have had on my life, I realize that the biggest impact is not as simple as just "feeling tired more easily" or "a loss of coordination." These are definitely problems that I have and they are easily picked up on by a neurologist asking about symptoms, but the cumulative effect is not as easy to see. FA greatly limits the amount of hobbies and social opportunities that I have in life. Its impact is the loss of many small sources of enjoyment that most people take for granted.

Amanda Davis

My name is Amanda Davis. I am a 25 yr old mother of 2 healthy energetic kids, but unlike most mothers, I am battling an incurable disease called Friedreich's Ataxia. Friedreich's Ataxia is an inherited disease that causes progressive damage to the nervous system, as well as poor coordination and it can also lead to scoliosis, heart disease and diabetes, but does not affect cognitive function. At the young age of 12, I was diagnosed with FA after years of unexplained falls, low energy, muscle pain, and failing concentration. As a child, I was always an A & B student, soon after my symptoms began I became a straight F student. Through junior high and high school I was bullied by not only other kids but teachers & the principal, thinking that my staggered steps/falls/struggle to climb the stairs were due to me being drunk and drug use. The thought of attending school became very depressing between the judgement and my low energy and concentration. Due to the depression, I started self-harming and soon ended up in an inpatient rehab facility. At age 17, I met a guy that I quickly fell in love with and we moved into our own home, I then found out that I was pregnant. My doctor was stunned and referred us to go get the baby tested to find out if it was going to have FA. Since termination of the pregnancy wasn't even an option, I didn't follow through with the test but instead had the baby monthly monitored by my high-risk obstetrician and through ultrasounds by my cardiologist. September 2010, I gave birth to a beautiful healthy 7lb baby boy.

As exciting as it is to be a new mom, it's difficult even for able-bodied mothers, I was never able to carry him, I had to rely on his dad and my parents to carry him to the bath or bring me bottles or lay him down into his crib. Being a mother has changed me in more ways than one, but it also affected my FA. I could no longer walk without holding on to someone or something. Right before my son turned 1, I went to see my neurologist and he was still in shock about my ability to deliver my son and told me that if I planned to have another child, I would need to do it soon before my body lost any more strength. In July 2012, I gave birth, via emergency c-section, to my premature baby girl, she only spent 5 days in the NICU before she was healthy enough to come home. Shortly after her birth, I was wheelchair bound.

Now my children [are] 6 & 4, they are both extremely intelligent and creative. They are my entire life. I push myself every single day to try to do more or better than the last. I cook, I clean, I help with homework, read books, I play barbies, I build lego's, I even make crafts (like hand-painted shoes, hemming costumes, making their valentines boxes for class, etc.). I try my hardest daily to be a good memory for them to have. I live my life in constant pain whether it's my muscle spasms, chest pain, headaches or the extreme fatigue. I drink at least 5 or more cups of coffee each day just to make it through the day without a nap. My kids are getting older and beg to go outside to play and go swimming or riding bikes but my FA has gotten to the point that after I get done doing the things I have to do every day I am too tired to do anything extra. Their father & I have not been able to go out and spend time alone together in over a year due to my

lack of energy and the burden it is to leave the house. I have lost all of my friends in the past few years as a result of isolating myself.

I am very concerned about losing my ability to speak and loss of my sight. I am a very talkative person and if I feel if I lost my ability to speak and be understood, I would lose my whole personality. I am the type of person that will point out how beautiful the clouds are or how blue the sky is, I love watching the rain splash in a puddle, I love watching my dad and my husband play with my children, I love the look of excitement on my daughters face when she sees her brother after a long day at school, I love to see the beauty in small things like that and I try to soak it all in because I know the time will come when those memories are all I will have. My husband jokes about how many times a day I tell him and our kids "I love you" and "you are so gorgeous!". My days are limited so I don't ever want them to forget how important they are. The fear that courses threw my body every time one of my kids fall is almost unbearable, the thought of them possibly one day having to live with this disease kills me. There has to be a cure, and I have faith that it will be found whether in my lifetime or not, I would not wish this on my worst enemy. I would absolutely love if a cure was found, but short of a cure I would love to see a drug to help stop loss of eye sight, speech, pain management and fatigue. FA has changed every aspect of my life but I refuse to let it defeat me. Thank You for taking the time to read my story and Thank you for your interest!

Alex Bode

When I was eight years old I was diagnosed with Friedrich's Ataxia, which I had no idea what it meant. Later that day, my mom sat down with me and told me all about FA and the inevitable changes that I was going to experience. At this age, I vividly remember walking to my best friend's house to play on the swings and then we would stay at his house for dinner. With my new diagnosis, this would never be a typical day for me ever again. I was only 8 years old, so I had no idea what to expect but looking back, I realized my childhood life was an hourglass and time was running out.

I was an avid dancer since the age of 2, so eventually my dreams were crushed. As a toddler, I was just another playful, energetic child. I used to go down in our family's basement to play games, but the stairs to our basement became too difficult for me to manage. I also loved to help my father with yardwork, which was a joy stripped away as my walking abilities declined. Life was pretty normal until I turned 6 and my older brother was diagnosed with FA. For my family, the hardest concept to grasp was that no one knew what the gene clone for FA was, leading my mom to be a Founding Board member of the Friedrich's Ataxia Research Alliance. We discovered that I could have a 1 in 4 chance of also having this disease, and sure enough 2 years later it was confirmed. My clumsiness during this time became defined as FA – a fear we had tried to ignore during this 2-year period.

Instead of developing and growing into a competent, independent adult, it seems I have been going backwards. Rather than developing autonomy and initiative when a normal school age child would have, I developed more and more dependence and doubt. When I was 11, I needed a walker to help with my mobility. At 13, I had my first back surgery to correct scoliosis. When I was 14 or 15, I became dependent on my wheelchair. I'll never forget the day my mom first brought me to school in my wheelchair, and the isolation I felt from my former friends who didn't understand the progressive nature of my disease. In junior year of high school, I was

rushed to the emergency department because my heart went into atrial fibrillation. Every day things got more and more difficult, and the only thing that saved me was knowing the fact that I had a brother who had the same disease. I was lucky in the sense that he knew what I was going through but when I got older, I learned that Sam and I have different alleles and were affected in different ways. My speech and fine motor skills were more affected by FA. I also required multiple spinal surgeries for my scoliosis and needed a baclofen pump for muscle spasticity, all things which Sam didn't experience as severely.

As if high school with FA wasn't stressful enough, I continued onto college at Southern Connecticut State University and attempted living on campus. To briefly recap my struggles at college, I had to ensure that I had PCA help at all times since I was living alone. Aside from the typical college challenges of roommates, crammed class schedules and new environments, I experienced bigger issues due to my condition. On several occasions, the lack of accessibility on campus caused Emergency Department visits and detrimental emotional stress. When deciding a career path, I really wanted to do nursing because I wanted to help care for people, but I knew that was not going to be realistic. I thought maybe I could help people with my words, so I chose social work. I worked very hard to get my bachelor's and master's degrees, and although these were some of the best years of my life I began to lose many pertinent abilities over time. One of these abilities being my speech, which is a vital component to being a social worker. I cannot stress the urgency I feel to serve my community as a social worker, and the only hope I have is to participate in the drug trials that FARA has worked hard to establish.

The most frustrating symptom of my FA currently is my deteriorating vision. My optic nerve degeneration has affected my vision so much, that I cannot see objects that are further than a couple inches from my face. Vision is such a powerful sense, and it's frightening to know I may never be able to enjoy life through my own eyes again. Things I once was able to do alone, like take my service dog for a walk down the street, is no longer possible due to my vision problems. The little vision I do have left allows me to experience many of life's joys, but also reminds me I cannot be like my family and friends walking around, being independent people. With a heavy heart but determined mind, I have faith that my story can expedite the process of further FA treatment research. Knowing that I have done my best to contribute makes my limited days much more meaningful.

Panel 2 – Symptom management; How well do treatments work? What is an ideal treatment?

Pat Ritschel

Good morning. My name is Pat Ritschel, and I am the father of two girls with Friedreich's Ataxia. My daughter Angelina began having balance difficulties when she was 9, and was eventually diagnosed in 2013 at the age of 11. We then decided to test her younger sister, Samantha, who was unfortunately confirmed to have FA a few months later at the age of 9. When we received our diagnosis of FA, it was a bit overwhelming as the first message we heard was that there is not any approved treatment for FA. Still, we began to actively read and research the disease. We quickly learned that in addition to gait and balance issues, there were many other aspects to the disease: cardiomyopathy, scoliosis, fatigue (although we already seen the fatigue present with Angelina), and even vision and hearing loss at later stages.

We found that managing FA takes a lot of effort and time.

To manage scoliosis, we focused on prevention through physical therapy. That has meant nearly 4 years of twice-weekly, hour+ long drives to Cherry Hill, NJ., plus twice yearly drives to Washington DC for scoliosis braces. All in nearly 400 hours a year just on managing scoliosis

We also began to look at the various dietary supplements, etc. that may be beneficial to FA. We've tried a lot; currently the girls take vitamin E; sulforaphane; idebenone, and curcumin. We hope that these can impact mitochondrial function, reduce oxidative stress, and reduce inflammation. All said and done, the girls each take over 20 pills a day

Has there been a great result from these supplements? Clearly not - as both girls continue to progress. Angelina now uses a scooter to get around.

In addition to supplements, we manage the disease with exercise. The girls do physical therapy for scoliosis twice weekly; as well as 1 to 2 days at the gym for strength training, and both girls do therapeutic horseback riding once per week. In the summer, they swim. I am a strong believer in the benefits of exercise in Friedreich's Ataxia - while it cannot stop the progression, having stronger muscles does improve their ability to stand / transfer / compensate for lack of balance.

The girls are active participants in trials, both interventional and non-interventional. In the past two years, the girls have participated in a total of 10 non-interventional studies to help researchers understand the disease. Unfortunately, there are not many pediatric interventional trials that are available to FA patients – so only Samantha has participated in an interventional trial (and only 2 at that) over the past 4 years. Given that FA is typically diagnosed between 5 and 15 years of age, I would very much like to see more pediatric trials in FA and strong support from the FDA for interventional trials at early stage, in pediatric populations.

Due to the lack of trials, and based on preliminary results in an open label trial of interferon gamma, Angelina does use interferon gamma on an off-label basis. This has had a significant benefit for her with respect to fatigue – where she used to nap daily after school for hours, she no longer naps at all and is able to keep up with her schoolwork.

I recognize that we are still in the early stages of the disease and that while the girls have progressed, significant deterioration still lies ahead- while Angelina has lost her ability to walk independently, she can still transfer on her own and can "wall walk" for some distance but is no longer independent and needs some level of assistance with activities of daily living such as bathing and dressing. She has mild cardiomyopathy at this time. Samantha is at an earlier stage - she is still independently mobile and her primary issue is loss of fine motor skills - handwriting and eating are both slow and messy.

Different stages of the disease present different desires in terms of expectations for a therapy. For Samantha, I'd like to maintain her ability to walk & to improve her fine motor skills – for example, being able to handwrite an essay in school or keep notes independently in class. Angelina has largely lost the ability to walk - and her cardiomyopathy is worse - so I am

more interested in a therapeutic that could stop progression or reverse her cardiac disease so that she does not die from cardiac failure in the coming years. For both, medicine that reduces fatigue or stops progression of scoliosis would be highly desirable.

In a perfect world, it would be wonderful to have a therapeutic that would address all aspects of FA - or even reverse damage that has been done. But given the multi-system nature of the disease, this may not be likely. For us, there is clear benefit to a drug that slows, stops or reverses progression of any aspect of the disease - whether it be scoliosis, fatigue, ataxia, heart, speech, vision, hearing, or diabetes. I remain hopeful that in the coming years we will see therapies developed and approved that may help my daughters.

Nick Carbone

Good morning, members of the Food and Drug Administration, pharma and industry partners, researchers, parents, and friends. My name is Nick Carbone, I am 30 years old, and I am a patient living with Friedreich's Ataxia or FA. I am speaking with you today to give my perspective, how I manage symptoms, and what my hopes are for the future of FA research.

Over the past several years, my routine, as far as the management of my symptoms has not changed significantly. The over-the-counter vitamins that I take have been part of my regimen for nearly 20 years: Approximately 400 milligrams of COQ-10 and 1,000 I.U. of vitamin E daily. I also take 10 milligrams of aspirin per day. The prescription drugs that I take are Sotolol and diltiazem for my cardiomyopathy symptoms such as increased heartrate, abnormal pacing, and high blood pressure. These treatments for my cardiomyopathy as well as an ICD implant treat symptoms which aren't even very noticeable to me and that is frightening in and of itself. The ICD activates when my heart beats abnormally and rapidly. It rarely happens due to the medications but I really have no warning when it happens and I don't feel very different as the pattern continues. Having the ICD has unfortunately disqualified me from several studies, despite my physical ability to complete all of the tests.

As far as physical activities to help manage my symptoms, I exercise at least 3 hours per week aside from daily living which can prove to be a workout on its own. I have always been very active and have done what was possible to manage symptoms. I work 1-on-1 with a trainer at a CrossFit gym. We spend a lot of time working on functional fitness movements, and adapting traditional CrossFit workouts. We also work on things that require my mental focus just as much as physical stamina such as walking, sitting up, and standing. This certainly helps with my activities of daily living as I currently live on my own and have to have enough energy and ability to accomplish things such as grocery shopping, cleaning, taking out the trash, and doing laundry.

My work is also something that helps me manage my symptoms. I am an attorney and local politician. The pressure and reliance that clients and residents have on me makes me feel important and also reminds me that I HAVE to keep working on myself and doing what I can to keep progression of my disease to a minimum.

All of these aforementioned 'quote on quote treatments' are how I proceed with my life, despite the lack of energy that I feel on most days. Without these self-directed treatments, I would have

much more difficulty accomplishing some of the things that I want to accomplish. With a treatment or cure resulting from increased clinical research and trials, my goals and accomplishments might come sooner and would increase in magnitude. Some of these goals are having a family, buying and remodeling a house, pursuing politics on a national scale, and traveling.

A cure is something all affected will look to. It is a difficult task to consider what would be my preference to treat short of that. To me, the most important thing would be to walk freely and for long distance, to stand and address a jury, to walk up the steps in front of the U.S. Capitol, to chase the children that I hope to have one day. That's where you come in. More must be done those affected by Friedreich's Ataxia. Thank you.

Emily Young

Hi, my name is Emily Young, I am 21 years old and I am a student at the University of Illinois. Members of the FDA, thank you for taking the time to meet with us.

In 2007, I met with a doctor who seemed to display little interest and time in what my mother and I had to say. "I have no reflexes" we explained, "that's normal" he said. He shortly diagnosed me with scoliosis and said I needed to wear a back brace to contain the curve.

In 2008 I was then diagnosed with Friedreich's Ataxia. My parents explained how it progressed [and] what would happen. However, the scoliosis was one of the only FA symptoms I was having, so I did not really understand how my body could just gradually become limited over time. The fatigue, the falling, the wheelchair, all of that sounded too far and unrealistic; I mean besides having a back brace, I was totally fine. I was all too scared of the adversity I'd begun to face, besides none of the other 13 year olds talked about losing the ability to walk.

Over time, it became apparent I needed spinal fusion surgery to stabilize my spine; where the doctors were going to insert a titanium rod into my spine and screw it into place. Making my spine virtually unable to curve, however this benefit would come at the cost of most of my upper body mobility.

In 2010, I had my first spinal surgery, at Shriner's. It was 7 ½ hours. When I woke up, the pain was worse than anticipated. But my nurses kept coming asking if I'm ready for a walk, and was thinking "I am honestly not sure my legs are even still attached to my body" I mean I was in so much pain.

As the week progressed, it is painful in every aspect. I mean your body hurts unimaginably, your family is trying to live in a hospital, no one is sleeping, meanwhile these nurses are still coming in on the daily asking if you are ready for your walk. But eventually I went home and faced a near 3-month recovery. I was still in a little pain but manageable, but I was getting ready to go into my freshman year of high school, no more back brace, just getting stronger.

At my next check-up, my doctors revealed that a screw had come loose in my back, but they assured me a quick and painless surgery could repair it. Knowing that "quick and painless" surgeries do not exist, we let my doctor's do the repair. The pain was less, but still extreme the

doctors added the rod up neck, stabilizing the lower portion of spine, but further immobilizing me. I was able to start high school on time, however I felt slightly less mobile than my peers and for the [first] time in my life, I felt restricted in what I could do.

Looking back on the experience now, I can say this was the first time I was limited with FA. This was my first big symptom. My first hurdle to overcome. And my first step in managing FA. Little did I know, it was one of the more easy-fixes than things I deal with now. As everything now does not have a clear and concrete solution. I spent the last 18 month trialing a drug I thought to be very beneficial, only to find it is not beneficial enough to be an approved treatment. In the middle of my school semester I had full course load, a part time job, and a social agenda that involves little sleep, but I was on a medicine that allowed me to make this my lifestyle. So now two months without the medication, when I wake up feeling more tired and weak than the day before and wonder how I am going to make it through the day? These are my symptoms of FA now and I am still looking for ways to manage them??

Alex Fielding

Good morning and thank you for allowing me to share my experiences living with Friedreich's Ataxia. My name is Alex Fielding and I am 29 years old living my life despite FA. At 26, I was given my genetically-confirmed diagnosis of late-onset FA after years of struggling up the stairs to my apartment and staggering through weekend hikes. To my friends with FA – I am lucky to be a late-onset patient with slower progression and the ability to walk. To my healthy family and friends – I am unlucky to battle an incurable disease that makes each waking day worse than the last. Some days I feel blessed. Other days I feel cursed. The only constant is keeping myself motivated to push through every day and live my life as normally as possible. With this attitude, I've earned my master's degree in Chemical Engineering, worked and lived independently across the country, purchased and now maintain my own house, and now serve as the Vice President of Operations in my family's 55-year old manufacturing company. These milestones in my life are not just accomplishments to be proud of; they have become integral parts of how I manage FA on a day-to-day basis.

Some of my best therapy occurs on the job. Work is a dangerous and exciting place for me. I'm constantly around moving machinery, working on tooling with my hands, and walking throughout the plant to manage all departments. For 8 to 10 hours per day, I am walking, moving my body in unique ways, using my hands, and most importantly, not mentally focusing on FA. These daily activities help preserve my motor coordination and engage me to keep from succumbing to depression. Unfortunately, all this activity is taking a toll on my body. My gait and posture have adapted to keep me walking and I feel it in my ankles, knees, hips, and lower back – they are all in constant stress and pain. Last year my neurologist identified minor scoliosis as a new symptom to watch. I now fight a mental battle to keep myself moving, knowing I am destroying my body while doing so.

For me, my motto has become "you'll lose it when you don't use it". This is why I try to cook for myself when possible since dicing vegetables and grilling food requires fine motor coordination and an increasing effort to focus and keep from slicing off a finger! I grew up playing music and continue playing piano, saxophone and guitar to maintain finger dexterity. Unfortunately it can be a frustrating chore as I continue getting worse due to my FA progression.

In the short time since my diagnosis, I have participated in several research studies and one clinical drug trial. I found these experiences extremely positive. The studies were transparent with me, allowing me to evaluate my own risk associated with participating. But I found the greatest risk to be not participating. With no approved treatment or even lifestyle choices known to slow progression or improve prognosis, living with FA is a constant race against the clock. Participating in studies allows research to move forward and renews my hope of a future without FA.

It's becoming harder to keep up with all my responsibilities at work and home, to keep doing the things I want to do. Earlier this year, we revised our two to five-year strategy for the business. It's already difficult planning ahead for a small business; it's nearly impossible when facing a degenerative disease that you know will continue pulling you back. Short of a cure, being able to objectively slow or stop progression would be invaluable to me. I want to plan my life, with confidence; to be able to rely on my current abilities in the future, and without the fear of devastating complications such as diabetes, stroke, or cardiomyopathy. This coupled with a sustained energy level would allow me to continue doing everything I do now; live independently, work a rewarding career, and contribute back to my community. I can adapt my life to current symptoms to stay active and engaged, but fear of what I know the future holds, continues to cripple me, especially on an emotional level.

Thank you for your time this morning.

Mary Caruso

Good Morning! My Name is Mary Caruso, I'm the mom of two amazing young adults who have lived more than half their lives fighting the disease Friedreich's ataxia. When I began gathering my thoughts about what I wanted to say, I quickly realized it was a struggle. I wrote, rewrote, took suggestions, and comments from those who know me best.

I just couldn't find the words to truly explain what life is like.

Then it came to me. I couldn't come up with the right words because I never allow myself to look at what life is like for our family living with this disease. As an optimist, I have chosen to deal with it and make the best of it. The reality however, is that life is unbearable in many ways. The anger and fear that embraces us is constant, I could never sustain this battle if I allowed myself to think about it. So yes, life as we knew changed the day a doctor wrote the words FRIEDREICH'S ATAXIA on a piece of paper and nothing was ever the same.

The emotional drain on our family is something I never imagined. Sam diagnosed at 8, is now 30. As Sam moved through school, there were struggles as friends became aware of the progressive stages of the disease. Between middle school and high school Sam pretty lost most friends. I kept his spirits up by promising college would be different, kids older and more accepting. Sam moved on to college eager to begin a new chapter. One night I got a call from him asking if I wanted to have pizza. Sensing something was off I immediately accepted the invitation, grabbed a pizza and made the drive. As I walked into Sam's dorm room I felt this immediate emptiness as Sam explained a planned trip failed to include an accessible bus. Sam was left behind. The combination of anger and hopelessness on that face was heart-wrenching.

We made it through the pizza, cried a little, then talked through the disappointment. Being able to manage the anger and emptiness that comes with FA is real and constant.

And if the emotional challenges aren't enough, the medical management of FA is frightening. Alex, 27 was diagnosed at age 7.

In her short life, [she] has had numerous hospitalizations. The fragility and complexity of this rare disease creates its own obstacles. Years ago, Alex anguished over the decision to have a baclofen pump implanted. Her spasticity was overwhelming, the pain too much. She had maxed out on oral dosages but had had so many problems during two prior spinal fusions she was understandably afraid to undergo another surgery with associated risks. For me, it was painful to watch her struggle with such a decision, but I let her decide and stood by to support her. After all, it was her body deteriorating. She decided on the surgery, during the hospital stay there were problems. It was difficult drilling through her spinal fusion to get a catheter through to her spinal canal. A one hour surgery turned into five hours an overnight stay into two weeks. I watched in horror when a resident just didn't know how to manage Alex's fluid balance. Her labs were off and they felt IV fluid boluses would help bring her labs up. Although I asked them to please consult FA experts my wishes were dismissed. Because they kept administering the boluses, which her heart could not handle, the fluid became too much. Alex had a horrible drop in blood pressure. Things became critical so quickly. The end result was a pulmonary edema which nearly proved lethal. Luckily the ability to fight and stand up for what I believe, saved her. It was a scary and horrifying. I wish I could say that we have only been through this once but that's not the case.

I never let myself think of what life would be like without FA. Instead I focus on the hope that there will be a cure. And if we can't find that cure, we can at least find a meaningful treatment to stop progression. Life would be wonderful if we were able to stop this tireless race against time and sustain life as it is today. I have boxes of vitamins and supplements, constantly tweaking them. Hoping the right combination will help a little by possibly stopping the loss of speech or allowing Sam and Alex to possibly feed themselves again. It's the simple things in life that are robbed by this disease, things that allow you to enjoy life as others do. Eating out in public restaurants is a thing of the past for us. There is no dignity in allowing someone else to feed you as others watch.

I take great joy in the wonderful accomplishments of Sam and Alex, the college degrees, the career paths, the laughter and the kindness they so genuinely display. But I also find loneliness in life with FA. When you face a diagnosis with no cure, most of life you once knew disappears. Family and old friends just can't bear the burden of FA, they fade away. My saddest memory is the day I realized our home no longer embraced the comforting sound of footsteps of my children.

Submitted comments: Panel 2 Topics

Rick Snead

I would like to see an option for patients that won't do needles and can't swallow pills such as an arm patch or a type that dissolves under the tongue.

Laura Arioto

Siena was diagnosed with Friedreich's ataxia one year ago when she was 7. We were told her disorder was progressive and that there was neither a treatment nor a cure. We were also told her condition was considered to be severe because she was diagnosed at such a young age and because the repeat of the frataxin genes were extensive.

The symptoms that have negatively affected Siena the most are her deteriorating balance and declining energy levels. She needs guidance when walking to the restroom at night to prevent her from falling. Her lack of stability is causing her to trip more and more. She can no longer ride her bike she got for her 7th birthday. The neighborhood girls her age don't stop at our house to see if she'd like to ride with them because she can't keep up on her recumbent bike. She loves to swim in our pool but now she spends more time hanging on the side because she loses her energy so quickly.

What worries us most about Siena's progression is that we'll have to bury our daughter before she's had time to experience all of the wonderful joys of life. If a cure is out of reach, I would hope for a treatment that could help her regain her balance and improve her energy level.

Jordan Howell

Hi, my name is Jordan. I am 37 years old and have been living with Friedreich's ataxia for 23 years. I believe finding a treatment that would improve my hand dexterity would help me drastically. Being able to type words at a normal speed on my keyboard would improve my overall communication. Being able to move my manual wheelchair at a normal speed because my hands are able to grasp the rims would allow me to travel much easier. My hand improvement would allow me to eat 100% of my food without any assistance and not having to worry about many issues would be huge. This would be a great example of how important it is to even just take care of one symptom.

Carrie Lempicki

Please include in FDA comments as we were not able to attend meetings.

As this disease is commonly diagnosed between ages 5 and 15, I would like to see more pediatric drug trials in this age group. I am the caregiver of two young six-year old girls and feel hopeless waiting for a treatment and not being able to participate. Allowing this could potentially solve multiple issues such as getting more participation, getting people who are still ambulatory and discover if the drug in question would work better earlier on in life.

There are several gene therapy companies working on fixing the FXN gene as well as other diseases. There is yet to be any gene therapies approved in the United States. My hope is that the FDA can help this new and very promising treatment type to get to trials and approved faster in the near future. Time is not on our side with Friedreich's Ataxia so anything we can do to speed up a working treatment as long as it is safe is important.

Finally, any treatment that buys more time for maintaining a quality of life is all I ask for. Being able to walk, write, see and hear are all important as well as being able to stay awake and not

having the horrible fatigue that comes with this disease. A quality life is much more important to our family. The better a person can function as close to a typical person without the disease, the better the quality. Thank you.

Caroline Spencer

My name is Caroline Spencer, I am 28 years old, and I was diagnosed when I was 23.

The topic of clinical research is near and dear to my heart. As a current doctoral student and future researcher myself, I love to push the boundaries of science. I've also been a participant in a clinical study of FA that assessed coordination of multiple modalities. For example, I had to rapidly say pa-ta-ka, over and over again.

Performance on this task reflects coordination of muscles needed for speech and for chewing and eating safely. In the context of future treatments, if a treatment improved pa-ta-ka performance, I would be encouraged. This would mean that I could speak more clearly, be understood when placing an order in a noisy restaurant, chew my food without biting my tongue, teach, be a speech pathologist again, and defend my dissertation more fluently.

Beth Hanes

I have participated in two clinical trials, EPI-743 and RTA-408, in the last three years.

I have tried many supplements to help manage my symptoms. I am a DoTerra wellness advocate and have tried numerous things to help manage my pain and restless legs. A few things that target energy production have shown that they can help but only for a few hours. I currently take Ropinirole and Gabapentin to help manage my restless legs.

My restless leg medications help the symptoms subside long enough to try to get some sleep, but start back in every day. The two clinical trials that I have participated in have been very promising. The first, EPI-743, lasted 2 years. After one year, my neurological scores improved by 10 points. This significant increase meant I could take a few steps on my own without assistance; whip my walker around in an instant with sufficient control; and I had sustained energy. I didn't notice the gradual improvements, living with the disease, but those who saw me daily noticed huge improvements! The second trial, RTA-408, showed great improvement in the three short months on the drug. While on the drug, I could cook dinner, clean up, do laundry and manage my very active 5-year-old, all without feeling like I had to crash on the couch at 6:00 pm! This was huge when my mother typically did all of that for me 5 days a week! I long to have that energy again and to be free of the worries of being dependent on a wheelchair! I could focus on my family and not on FA.

After taking the trial drugs, not only could I move around with improved stability and precision, manipulate items with better dexterity, and perform more tasks before becoming too tired, I felt more complete as a person. I could do more at home (cooking, cleaning, laundry, etc.) like a "normal" mother does. I did not have to accept or ask for as much assistance with daily tasks. I felt like my mind was able to give more time and energy to my daughter. She requires so much, being Autistic, having ADHD, and a 5-year cancer survivor! Between both of our medications,

Dr. appointments, and daily lives I didn't feel as if I were being swallowed by some giant beast living beneath the clay under our basement floor!

For my own medications and supplements, the financial burden [of the treatments I use now] is the only downside. When considering a clinical trial, the only downsides are being dependent on someone to get me there, distance to trial site, taking days off from work, and the financial burden that traveling can ensue. The time spent away from my daughter can be very hard to endure at times, but it all well-worth it in the end! If there is a possibility that my quality of life can be improved or lengthened, it is all well worth it! Treatments, and the future possibility of a cure, improve my total outlook on life, to focus on the positive, rather than dwell on the negative.

[An ideal treatment, short of a cure, would be] Anything to slow progression and give me more quality time with my family is a blessing! Managing my symptoms is a constant battle. I am perpetually stuck in that revolving door, with nothing to stop the door and nobody brave enough to wedge that stick that could slow it down long enough for me to escape! Treatments would help to restore my body to function more independently. I am at the point where my body is resisting the medication to help my restless legs. I need something to help improve communication with the limbs in my body so I am more mobile. Something that could supply my body with more energy to keep my ability to watch my daughter flourish, despite numerous roadblocks, could provide me the opportunity to one day say, "She got that fight from me!"

[Symptoms worth treating independent for a treatment for the disease as a whole]. As all people with FA are affected differently from this disease, no one symptom jumps out at me. We need help for all of them, and fast! Personally, I have been fortunate enough to have a late diagnosis, and a slower progression. Anything to keep these children from suffering is key! My daughter has not been tested for FA, as doctors did not feel the need unless symptoms appeared, but after seeing her battle cancer, Autism, and ADHD, her battling FA would be a devastating blow to any hope that I have!

[Risks willing to assume when evaluating a potential treatment]. I watched my 14-month-old have her kidney removed, toxic chemo put into her little body, millions of needles, thousands of tests, hundreds of hospital visits, biopsies, and her little helpless body cry for her Momma within the bars of a hospital bed as they wheel her off to surgery. I have built a tolerance of what I may have to physically and emotionally endure. Bring it on! I will do whatever possible to ensure that I can replace all the recollections of hard times, with memories of happiness and health! I will go to all end of the earth to foster HOPE! Any positive is a reason to keep fighting and remain hopeful [including a slowing of progression in the absence of improvement would be meaningful to me]! Of course!!

Anonymous

When I imagine the ideal treatment for FA, independence is an important goal. I value a treatment that would improve my mobility, energy, and fine motor skills. These symptoms obviously limit the amount of time it takes me to do everyday activities. I also end up having to

ask for help and coordinate that help with other people's schedules. Independence would help my self-esteem and save me time.

An important aspect of a meaningful treatment would be to remove the dependence I have on adapting my activities. I would want a treatment that minimally disrupts my life. Taking a pill once or twice a day would be ideal. Having to rely on a daily injection would be much more of an inconvenience. I know from experience that a restrictive diet or reliance on refrigerating medication would limit my independence when it comes to traveling or being away from home. My experiences with these kinds of restrictions have been temporary, but I would have a hard time wanting to comply with this indefinitely. Implanted medical devices or scheduling visits for regular infusions are examples of huge burdens that I would want to avoid. The benefits of a treatment should outweigh the costs. A meaningful treatment would give me greater independence with minimal disruption to my life.

Paige Meyers

I take many supplements, including idebenone, vitamin E, a vitamin B complex, a multivitamin, niacinimide, vitamin D, iron, an antidepressant, and a birth control pill (anemia makes me period unbearable). The idebenone trial was soon after my diagnosis and the first and only trial I've participated in. I have been taking it since. I had mild cardiomyopathy for a while, and currently have no cardiac issues. I can't be sure idebenone is helping, but I believe it is and have no side effects so I continue. It is my fear at what might be the irreversible damage done if I stop idebenone that keeps me from participating in a clinical trial. FA affects many bodily systems and every patient slightly, so I do not think a single drug will solve all symptoms or help everybody. I think a drug cocktail, which will be tailored to each specific patient, is our solution. So, I do not believe discarding a drug not producing universal benefits is an effective way to solve the problem of FA. Additionally, I have been told my speech is clearer after starting niacinimide. The symptom that really is most detrimental to me is balance loss and standing/walking difficulties. I have no ability to even stand unassisted anymore, and if my balance could improve somewhat so I could do a somewhat-standing transfer, my life would be so much easier and I would be so much more independent. If only one thing could be helped, stopping progression is huge. If I stay where I am now and don't get worse, I can learn tricks to make my life easier. As it is now, I learn tricks, and then they become obsolete as my disease progresses. Thank you for all you do! It's fantastic that we got this opportunity!

Submitted Comments that Cover Panel 1 and Panel 2 Topics

Tricia Maul

I attended the FDA meeting in June and wanted to share some of my experiences and thoughts. I am 37, still walking, and trying to stay as active as possible. One thing that holds me "back" is fatigue - not only feeling tired but muscle fatigue during exercise. My daily workouts include yoga, weights, recumbent bike, and keeping up with the activities of my 3 children. My muscles become so fatigued they cramp and shake making my workouts limited. Safety becomes a #1 concern and it takes a while for my muscles to recover and steady. I feel like I am constantly thinking ahead to plan on how much energy I need to get through my day and often need rest periods to recharge my batteries.

Something else that was not discussed (but I don't think it's just me) is the inability to maintain a constant body temperature. From a young age, I've felt that my thermostat is broken - it takes forever to regain warmth when feeling chilled and the heat/humidity makes me feel faint and shaky. This makes me reconsider outings and sometimes cancel based on weather that I don't think my body can tolerate.

I have not undergone any surgeries and do not intend to have any. I have seen the negative effect that spinal fusion has had on my sister's well-being and heard negative outcomes from others. Currently, I practice yoga, take a multi-vitamin high in B vitamins, take a supplement for focus and energy, and follow a gluten-free/high protein diet. Self-medicating has given me more quality in my daily life by providing me with more energy and strength. While I cannot stop the progression, I have found exercises to keep my body moving/not tightening.

My hope is to see my children become successful adults. My heart goes out to the young children diagnosed as their progression is more rapid and their ability to experience a normal life becomes minimalized.

Kim Welch

My name is Kim Welch- I'm 38 and I was diagnosed at 19. I kind of wanted to put a face on something that Jen touched on at the beginning- the 4% of FAers who have 1 GAA repeat and a point mutation. I have the g130v point mutation. My symptoms are a lot different from most FAers in that my speech and hand coordination aren't affected. I have a spastic gait as opposed to an ataxic gait so for me spasticity is one of my main symptoms and with that comes a lot of fatigue. So, I think for me, ideally for a treatment would be to either reduce the spasticity or fatigue but also a lot of the trials are for people with 2 GAA repeats so I'd just like to make sure that for future treatments that they would also benefit people with point mutations. Thank you!

Other Comments

Sean Baumstark

I shared one concern from the floor. Although not word for word, it's something like this: A concern I have as an ambulatory and independent FA patient, is my safety as it relates to other people who prey on weaker individuals. With this condition, I can't run and it doesn't take very much to push me over. While we wait for treatments or a cure, I'm constantly concerned for my own well-being whenever I'm out and about on my own.

Additional concerns (not shared at meeting):

1) Communication is so important, if my ability to talk, hear and even control my eyes continues to diminish, how will I express love and appreciation to those in my life? Saying "I love you" is something I want to be able to say to my children until I'm no longer breathing.

2) The financial pressure and burdens are extremely heavy. Our health care system continues to leave "pre-existing" conditions out in the pastures to suffocate and many disabled individuals cannot work nor collect enough income to support themselves, their equipment needs, or the 'health-maintenance' supplements/prescriptions. The "system" in the USA can't afford itself, how

are people expected to survive off that system? I am surviving outside the system today, but given my prognosis, I expect that the day will come where I am no longer competitively employed. Financial survival is a real concern.

The Voice of the Patient

FRIEDREICH'S ATAXIA (FA)

Cover Photography : Marshall Major

Graphic Support : Lawrence Phillips

