

Clinical Management Guidelines for Friedreich Ataxia

Chapter 3.3. Strength, balance, mobility and reduction of falls in non-ambulant individuals with Friedreich ataxia

Contents

3.3.1 Disturbance of strength, balance and mobility in Friedreich ataxia, functional consequences and falls risk	3
3.3.1.1 Mobility	3
3.3.1.2 Muscle strength	3
3.3.1.3 Balance	4
3.3.1.4 Falls	4
3.3.2 Management of strength, balance, mobility and reduction of falls	5
3.3.2.1 Monitoring	5
3.3.2.2 Management with rehabilitation, allied health therapies and exercise interventions	5
3.3.2.3 Evidence base for management recommendations	6
Best practice statements	8
Recommendations	9
Lay summary	11
Author details	12
References	13

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These Guidelines are not intended to replace clinical judgment and other approaches to diagnosing and managing problems associated with Friedreich ataxia which may be appropriate in specific circumstances. Ultimately, healthcare professionals must make their own treatment decisions on a case-by-case basis, after consultation with their patients, using their clinical judgment, knowledge and expertise.

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3.3 Strength, balance, mobility and reduction of falls in non-ambulant individuals with Friedreich ataxia

Sarah C. Milne, Manuela Corti and Massimo Pandolfo

This chapter describes the effects of Friedreich ataxia on strength, balance and mobility and risk of falls, the functional consequences of these effects, and strategies for managing disturbance of strength, balance and mobility and reducing falls risk, specifically in those who are non-ambulant. In making recommendations for management, the authors were tasked with answering the question:

For individuals with Friedreich ataxia who are not ambulatory, what management strategies could be implemented for disturbance of strength, balance, mobility and reduction of falls?

3.3.1 Disturbance of strength, balance and mobility in Friedreich ataxia, functional consequences and falls risk

3.3.1.1 Mobility

Over the course of the disease, walking ability diminishes until the individual with FRDA becomes wheelchair dependent (1). As a result, other issues related to de-conditioning and nonuse also occur, which can further impact functional independence.

Mobility loss has a profound impact on all domains of quality of life (2, 3). Key transitional events regarding mobility are recognition of symptoms, fear of falling and changes to mobility status (1). These transition events are related to disease severity and can be divided into three subgroups: people who are ambulant, people transitioning from walking to wheelchair and, people who are wheelchair dependent (2). Changes in mobility status may represent the final transition within the FRDA experience (1). As gait deteriorates, use of walking aids may be confined to home use and wheelchair for community activities. Some individuals with FRDA may choose to only use a wheelchair due to perceived social stigma, which reduce acceptance and contribute to abandonment of walking aids.

The transition from walking to using a wheelchair may be associated with increased freedom and independence as mobility is safer and not as physically or mentally exhausting (1). Earlier disease onset correlates significantly with faster progression to the use of a wheelchair and transition to a wheelchair is more likely to occur earlier in females (4). Klockgether and colleagues (4) suggest faster progression to a wheelchair may in part be related to an inability to cope with the physical disability and not just the biological cause alone.

For wheelchair-dependent individuals, functional independence is influenced by progressive loss of standing and transfer ability. This may result in an increased use of assistive aids (such as a hoist) or significant help from other people for transferring.

3.3.1.2 Muscle strength

Two studies have specifically evaluated muscle weakness in FRDA (5, 6). Sival and colleagues (5) examined whether muscle weakness has an impact on ataxia assessment by the International Cooperative Ataxia Rating Scale (ICARS). The authors tested 12 children with an average disease duration of eight years and 12 age-matched children without FRDA. The ambulation status of individuals was not reported. Significant muscle weakness in children with FRDA was found, more

pronounced in proximal than in distal muscles and with greater impairment of leg than arm muscles. Muscle ultrasound density “was homogeneously increased in the biceps, quadriceps, and tibialis anterior muscles (median 4SD) in children with FRDA”, suggesting subclinical myopathy. The authors concluded that in children with FRDA, ataxia scales based on ICARS are confounded by muscle weakness (5). Beauchamp and colleagues (6) reviewed 170 muscular assessments in 33 individuals with FRDA. This study preceded the availability of molecular diagnosis for FRDA. A consistent pattern of slowly progressive and symmetrical loss of strength affecting mainly the lower limbs, and more specifically the pelvic girdle muscles was found. Significant weakness was observed initially in the hip extensor group, followed in a variable fashion by other muscle groups of the lower limb. Upper limb and trunk muscles remained relatively spared until late in the disease process. Use of a wheelchair began at a mean age of 18.2 years, at which time the lower-limb strength averaged 70% of normal. Patients became totally unable to walk at a mean age of 20.5 years, with a further decline in lower limb strength to 56% of normal (6). These findings are consistent with a recent study examining FRDA progression where only mild weakness was detected before loss of ambulation, but by one year later it was significantly worse (7).

3.3.1.3 Balance

With disease progression, individuals with FRDA may lose their ability to sit independently, firstly relying on their upper limbs to provide balance, then eventually being unable to use their upper limbs to support upright sitting. This can result in the requirement for an extra supportive wheelchair, as well as extra assistance from others to complete activities of daily living. There are no studies specifically examining sitting balance in individuals with FRDA, but a sitting balance item is part of ataxia scales such as the SARA, used in the EFACTS clinical study (7). This item shows late progression in deterioration of balance, mostly after loss of ambulation (7). Four studies have examined standing balance (8-11), of which some of the findings may be extrapolated to non-ambulant individuals. These studies suggest individuals with FRDA are highly reliant on vision during tasks requiring postural stabilization, and this is likely related to the spinocerebellar tract and proprioceptive impairment seen early in the disease course (9, 10). In non-ambulant individuals with greater disease duration and severity, progressive cerebellar neuropathology, proximal muscle weakness (5, 6), lower limb spasticity, vestibular pathology, and scoliosis (12) are all likely to further contribute to impaired balance.

3.3.1.4 Falls

There have been no publications reporting the incidence or frequency of falls in individuals with FRDA. However, frequent falling is commonly reported by individuals with FRDA (as observed in clinical practice). Frequent falling, together with the increased presence of osteopenia or osteoporosis in individuals with FRDA, may result in common fall-related fractures. Data from the FRDA Clinical Outcome Measures (FA-COMS) registry found 9.7% of individuals (107/1104) had reported a fracture in the year prior. Individuals with FRDA have also identified a fear of falling as a key transitional event related to mobility decline (1). This fear typically arises from a previous fall or near fall and can limit participation in activities and cause anxiety about social stigmatization (1).

3.3.2 Management of strength, balance, mobility and reduction of falls

3.3.2.1 Monitoring

An annual multidisciplinary review can identify and address the changing needs of an individual with FRDA. Monitoring should include a functional review and an impairment-based assessment to establish the contributing factors to functional decline. A thorough assessment will allow treatment and management to be appropriate for each individual. Individualization of therapy ensures the rate and stage of decline, contribution of impairments to functional decline, impact on daily activities, individual goals, preferences and enjoyment, and pro-active and reactive needs are considered.

3.3.2.2 Management with rehabilitation, allied health therapies and exercise interventions

Rehabilitation and physiotherapy interventions may be applicable to people with FRDA at varying ages and stages of the disease and may be beneficial both proactively and reactively in delaying or maintaining functional decline or improving function for the individual with FRDA (13, 14). Physical activity and exercise are encouraged throughout the lifespan and can be divided into three categories: continuous/maintenance exercise and physical activity; short-term intensive rehabilitation; and targeted therapy. Intensity, type and amount of clinician support may vary between each category, as summarized below.

Continuous/maintenance exercise and physical activity

Daily exercise is designed to maintain physical function and prevent any complications caused by de-conditioning. Several studies have reported the importance of regular and frequent ongoing training and exercise to maintain improvement in function achieved with short-term rehabilitation (15, 16). Continuous rehabilitation is particularly beneficial if the demands of usual daily activities are not sufficient to maintain or improve physical capabilities (17). Continuous rehabilitation may comprise a home exercise, gym, hydrotherapy (15), standing and swimming, if they can be completed safely and are enjoyable. However, there is no published literature examining the effect of these activities.

The level of clinician support provided may vary and is dependent on finances, physical distance from suitable venues and/or clinicians, and individual preferences. Individualized and regularly reviewed exercise programs (by a qualified clinician such as physical therapist and/or exercise physiologist) are important to ensure the activities and exercise undertaken are targeted appropriately for each individual. Prescribed programs should consider individual goals, motivation, enjoyment and preferences (18), the disease stage, and presenting impairments.

Short-term intensive rehabilitation

A 4- to 8-week period of intensive rehabilitation (defined as 3 or more sessions per week) appears beneficial in improving function for non-ambulant people with FRDA and other degenerative ataxias (19). Theoretically the intensity is thought to provide stimulus to the neuromuscular system (20), but may be difficult to maintain for a longer period due to other life commitments. Rehabilitation may be provided in an inpatient, outpatient or community setting. The benefits of intensive rehabilitation appear to have some carryover into the community and may persist over time; however, there is evidence to indicate continuous ongoing exercise is required to maintain these benefits (13, 15, 20).

Targeted therapy

Targeted therapy is aimed at addressing specific concerns or problems that arise or are identified as immediate risks. They may be identified by a clinician or an individual with FRDA. Issues may include

but are not limited to falls, deterioration of function, losing capacity to transfer, deconditioning post medical or surgical event, pain, pressure care and musculoskeletal injury. Support to address the challenges with community, home or workplace access (due to mobility decline) may also be required. The therapy provided is dependent on the issue and the findings of a comprehensive assessment of function, and sensory and motor impairments. A neurologist, pediatrician, physical therapist, occupational therapist, podiatrist, orthotist, or a combination of clinicians, may be involved.

3.3.2.3 Evidence base for management recommendations

There is emerging and consistent evidence that rehabilitation, allied health therapies and exercise interventions are beneficial for individuals with FRDA (19). However, there is limited and minimal high-quality evidence to guide the type, duration and intensity. The recommendations in this topic aim to guide these aspects of therapy for individuals with FRDA. The following provides a summary of each of the interventions recommended:

Botulinum toxin, stretching (including standing machine) and prescription of ankle-foot orthotics

As the person with FRDA becomes more dependent on a wheelchair, calf spasticity and equinovarus deformity become more evident (21). Equinovarus deformity and spasticity interferes with a stable base on which individuals stand to transfer, leading to an increased dependency on equipment and others to ensure safety during transfers (22). Early treatment may prevent secondary complications and minimize the need for more drastic intervention (22).

Although they can be useful treatment options in isolation, combining focal spasticity management with gastrocnemius and soleus stretching and wearing of ankle-foot orthotics (AFOs) during weight-bearing tasks has shown beneficial effects in clinical practice. Focal spasticity management prior to stretching and/or wearing AFOs may allow improved posture, range of movement, improved comfort, reduced pain and may minimize the risk of pressure areas. For individuals who are no longer walking, prolonged standing in a standing machine for a weight-bearing stretch may be beneficial. A systematic review found standing machine stretches for 30 minutes, five days per week improved range of movement and activity for individuals with stroke and spinal cord injury, but there was mixed evidence for other neurological conditions, with no studies of individuals with FRDA (23). Other stretching options may include serial casting, eccentric strengthening (15) and standing balance re-training. There are no studies specifically looking at orthotic prescription for people with FRDA; however, there are multiple studies describing the benefits of AFO prescription in improving postural stability and movement, increasing weight-bearing percentage, improving knee control, reducing toe clawing and improving standing and balance in individuals with other neurological conditions such as stroke and spastic cerebral palsy (24-28). Prior to prescription of AFOs, the 'wearability' of the AFOs, including comfort during hot weather, aesthetic appearance and need for suitable shoes should be discussed and considered by the individual with FRDA.

Please refer to Chapter 3.4 for further detail on focal pharmacological interventions (including botulinum toxin) for lower limb spasticity in ambulant individuals with FRDA.

Sitting and standing balance exercises

Sitting balance exercises should be incorporated into all exercise programs with the aim of reducing dependence on the upper limbs to support sitting and balance during transfers and in the wheelchair. In individuals who are no longer walking, standing balance exercises should be aimed at maintaining unsupported standing for performance of activities of daily living, including transfers.

Balance exercise prescription should be at the appropriate balance exercise intensity for each person, to maximize benefit (29). Setting up the environment and/or physical assistance from a clinician, carer or family member can ensure the balance challenge is appropriate while exercises are completed safely. Scoliosis, past spinal surgery and pain, while generally not contraindicated for balance exercise, may limit an individual's ability to complete standing or sitting balance exercises. Therefore, careful assessment and prescription by a trained clinician, such as a physical therapist, is recommended.

Upper limb strengthening

For individuals who are no longer walking, upper limb function takes on an additional role in terms of assisting to transfer (30), sit, balance and wheelchair propulsion (31). Simultaneously, upper limb strength progressively declines in individuals with FRDA. This includes intrinsic hand muscle weakness (32), decreased muscle endurance of the forearms and reduced feelings of physical energy (33), and generalized upper limb weakness (although lower limb weakness is more severe and is present earlier in the disease) (5, 6). There is evidence that weakness linked to pyramidal tracts degeneration is a major contributor to upper limb motor dysfunction in advanced FRDA (34).

There is minimal evidence for isolated upper limb strength training in FRDA; however, a 2017 review found upper limb exercise reduced the cardiometabolic risk profile and precipitated neuromuscular upper limb overuse injuries in wheelchair users (35). The review also highlighted the need for assessment of wheelchair set-up to prevent injury. It is important when prescribing exercises that the following are considered: injury prevention; current functional involvement of the upper limbs; correct posture and movement patterns; balancing antagonist and agonist muscle strength; incorporating postural control where possible, maximizing mobility; and the psychosocial impact.

Lower limb strengthening

There is minimal evidence for isolated strength training in FRDA. Notwithstanding, three studies including non-ambulant participants have included strength training as one component of multi-faceted rehabilitation programs designed for individuals with FRDA (13, 15, 36). This suggests that clinicians believe strengthening may be beneficial for individuals with ataxia.

Several considerations may assist in guiding the strengthening program prescribed for individuals with FRDA:

- Maintaining correct movement patterns and eccentric control may concurrently address ataxia, coordination and strength impairments.
- Facilitation of postural control and/or alignment to isolate control for strengthening may concurrently address ataxia, coordination and strength impairments, as well as allow progressive resistance principles to be applied (37).
- Eccentric control and multi-joint muscle exercises should be considered as they may produce more substantial physiological adaptation of skeletal muscle (38).
- Although there is no published evidence examining isometric strength training, facilitated strengthening of the hip, spine and abdominal muscles may provide a beneficial effect on sitting balance and ability to maneuver in the wheelchair in individuals with significant muscle weakness.

Cardio-pulmonary exercise

For the general population, the *American Heart Association Physical Activity Guidelines for Americans* (39) recommends 150 to 300 minutes per week of moderate-intensity aerobic activity spread over the week for adults and 60 minutes per day for children aged 6 years and older. There is

no evidence to suggest the benefits to health and well-being would not be similar in individuals with FRDA and physical activity may also counteract secondary adaptations caused by decline in mobility and de-conditioning. As cardiomyopathy is present in around 40% of individuals with FRDA (12), a comprehensive assessment and advice from a cardiologist is recommended before commencing physical activity. Arm ergometers, reclined bicycles and swimming are just three options that may be utilized by non-ambulant individuals to achieve the recommended exercise intensity and duration.

Best practice statements

Facilitating ambulant mobility for as long as possible is advantageous to the overall health and well-being of the individual with Friedreich ataxia (40). During and after transition to full-time wheelchair use, it is essential that individuals with Friedreich ataxia maintain the capacity to transfer safely and independently for as long as possible, particularly as length of time since disease onset and time since full-time wheelchair use have been shown to be major indicators for severe deformity requiring intervention (22).

Core stability, defined as abdominal, gluteal, hip girdle, paraspinal, and other muscles working in concert to provide spinal stability, is imperative for initiation of functional limb movements. Any weakness or reduced motor control of these muscles can impact on a person's ability to mobilize and balance effectively and independently (41, 42).

People with Friedreich ataxia tend to have weakness in the core stability muscles which then causes problems with balance that can affect their ability to mobilize (6). Although there is no evidence directly examining core stability in individuals with Friedreich ataxia, numerous studies have found beneficial effects on trunk control and sitting and standing balance in stroke survivors (43, 44). Therefore, therapy for non-ambulant individuals should include core stability training as one component of their overall program.

Individuals who require a wheelchair for mobility should have these prescribed and customized by a trained clinician. Sensory loss, reduced mobility, scoliosis, diabetes and impaired balance need to be factored into the design and materials chosen to maximize function and minimize falls and pressure area injuries.

Please refer to Chapter 16 for further details on digital and assistive technologies.

Recommendations

Grading for strength of recommendation and level of evidence

For the rating of the **strength** of the recommendation, in addition to evidence from studies in FRDA, evidence from like conditions, clinical experience and expert consensus are taken into account when published evidence is not available.

The **level of evidence** is based on published evidence from studies in FRDA. If there is no published evidence in FRDA, evidence from other like conditions or clinical expertise may have been used to make the recommendation – this is graded as ‘very low’ or in some cases ‘low’ level evidence. See the table below for an explanation of the symbols used to grade recommendations.

Strength of recommendation	Symbol	Level of evidence	Symbol
Strong for intervention	↑↑	High	⊕⊕⊕⊕
Conditional for intervention	↑	Moderate	⊕⊕⊕○
Neither intervention nor comparison	—	Low	⊕⊕○○
Conditional against intervention	↓	Very low	⊕○○○
Strong against intervention	↓↓		

Monitoring

<i>Should monitoring at least once per year versus informal monitoring be used for non-ambulant individuals with Friedreich ataxia?</i>	Strength	Level of evidence
For individuals with Friedreich ataxia who are no longer ambulant, we recommend regular monitoring of mobility (including ability to transfer) and contributing physical factors for mobility decline (such as balance, strength, lower limb spasticity and environment set-up) at least once per year over less regular or informal monitoring.	↑↑	⊕○○○
Justification: Although there is no published evidence directly addressing the effectiveness of monitoring mobility for non-ambulant individuals with Friedreich ataxia, annual decline seen in clinical practice warrants regular monitoring (at least annual) and assessment of mobility. This recommendation is consistent with recommendations made in the Ataxia UK Medical Guidelines (45).		
Subgroup considerations: This recommendation is for non-ambulant individuals with Friedreich ataxia.		

Balance

<i>Should sitting and standing balance exercises versus no treatment be used for non-ambulatory with Friedreich ataxia?</i>	Strength	Level of evidence
For individuals with Friedreich ataxia who are no longer ambulant, we conditionally recommend standing and sitting balance exercises over no balance exercises. Balance exercises should be individually tailored to address each person’s specific impairments and functional goals and minimize risk of falls or fatigue.	↑	⊕○○○

Justification: A number of small studies indicate balance training can improve ataxia and assist in achieving functional goals (15, 46, 47). Clinical experience supports these findings.

Subgroup considerations: This recommendation is for non-ambulant individuals with Friedreich ataxia. Although there are no specific subgroup considerations, individualized balance exercises should be targeted at the appropriate level of mobility and sitting and standing balance control.

Lower limb strengthening

<i>Should lower limb strengthening versus no treatment be used for non-ambulant people with Friedreich ataxia?</i>	Strength	Level of evidence
We conditionally recommend lower limb strengthening over no lower limb strengthening for individuals with Friedreich ataxia who are no longer ambulant.	↑	⊕○○○
Justification: Although there is no published evidence examining the effects of lower limb strengthening on individuals who are non-ambulant, in clinical practice there appears to be a beneficial effect.		
Subgroup considerations: This recommendation is for non-ambulant individuals with Friedreich ataxia. There might be a greater benefit when a person first commences use of a wheelchair; however, this is unclear.		

Upper limb strengthening

<i>Should upper limb strengthening versus no treatment be used for non-ambulant people with Friedreich ataxia?</i>	Strength	Level of evidence
We recommend upper limb strengthening versus no upper limb strengthening in individuals with Friedreich ataxia who are no longer ambulant. Caution should be taken to not ‘over-exercise’, especially when there is reliance on the upper limbs to transfer or mobilize.	↑↑	⊕○○○
Justification: There is no published evidence for upper limb strengthening; however, benefits from upper limb strengthening are seen in clinical practice. Prescription of upper limb exercises should aim to maintain muscle balance, considering how the upper limbs are being used during everyday function. Strengthening can prevent or reduce the risk of shoulder or wrist injuries.		
Subgroup considerations: This recommendation is for non-ambulant individuals with Friedreich ataxia.		

Cardio-pulmonary exercise

<i>Should cardio-pulmonary exercise versus no exercise be used for non-ambulant people with Friedreich ataxia?</i>	Strength	Level of evidence
We conditionally recommend cardio-pulmonary exercise over no cardio-pulmonary exercise in individuals with Friedreich ataxia who are no longer ambulant. Gradual onset and increase in the level of activity, with monitoring for any adverse symptoms, is likely to be a safe approach in those with and without cardiac abnormalities.	↑	⊕○○○

Justification: There is limited published evidence and some uncertainty in clinical practice regarding the efficacy of this exercise focus. However, case studies have demonstrated beneficial effects without significant adverse effects (48, 49).

Subgroup considerations: This recommendation is for non-ambulant individuals with Friedreich ataxia.

Botulinum toxin, stretching and ankle-foot orthotics

<i>Should botulinum toxin, stretching (including standing machine) and prescription of ankle-foot orthotics versus no treatment be used for non-ambulant people with lower limb spasticity with Friedreich ataxia?</i>	Strength	Level of evidence
We conditionally recommend botulinum toxin injections, stretching, and prescription of ankle-foot orthoses for individuals with Friedreich ataxia who are no longer ambulant and who have spasticity and reduced length of the calf muscles. A comprehensive physiotherapy and medical assessment of impairments, mobility status and patient goals should be done to determine the appropriateness of this treatment.	↑	⊕○○○
<p>Justification: There is no published evidence examining the effect of this group of management strategies (either as single interventions or as a group) for individuals with Friedreich ataxia with lower limb spasticity. However, approximately 40-50% of clinicians who work with individuals with Friedreich ataxia have found beneficial effects from these treatments.</p>		
<p>Subgroup considerations: For non-ambulant individuals with Friedreich ataxia who have difficulty transferring due to foot placement and/or ankle or foot pain, treatment including botulinum toxin injections as an adjunct to stretching and orthotic prescription may warrant greater consideration. However, individuals who present with spasticity or muscle length changes who do not have difficulty transferring may warrant a conservative approach, including stretching and orthotic prescription, prior to trialing botulinum toxin injections.</p>		

Lay summary

Lay summary of clinical recommendations for strength, balance, mobility and reduction of falls in non-ambulant individuals with Friedreich ataxia

Why these recommendations?

The following recommendations are aimed at maximizing balance, strength and physical function in people with Friedreich ataxia who are no longer walking, as well as preventing any secondary consequences from reduced mobility and balance.

Monitoring: We recommend at least annual monitoring of physical function, sitting balance and posture, ability to transfer (move between a wheel-chair and other seating, bed or car) and independence in their chosen mobility device (i.e., wheel-chair), for all people with Friedreich ataxia who are no longer walking.

Management: There are a number of recommendations related to managing balance, strength and physical function in individuals who are not walking.

- We suggest strengthening exercises for the leg muscles as part of a regular exercise program. Strengthening exercises should concentrate on increasing resistance as well as correct movement patterns.
- We suggest strengthening exercises for the arm muscles as part of a regular exercise program. Strengthening exercises should target the muscles that are most likely to be

weakened due to the differing use of arms in daily activities. Care should be taken to not over-exercise frequently used muscles.

- If spasticity is present in the leg muscles and is affecting the ability to stand and/or transfer, the use of anti-spasticity medications given by injection, in combination with ankle braces and a stretching program, may be beneficial. Suitable medications may include botulinum neurotoxin or phenol injections. Appropriate treatment of spasticity should be carefully assessed by a neurologist and physiotherapist. The benefits and side effects of medication should be discussed.
- We suggest cardio-pulmonary exercise as part of a regular exercise program. Gradual onset and increase in the level of exercise, with monitoring for any adverse symptoms, is likely to be a safe approach.
- We recommend sitting and standing balance exercises as part of a regular exercise program. This should target maintaining your independence during daily activities and minimizing falls.

What does this mean for you as a person living with Friedreich ataxia or caring for someone living with Friedreich ataxia?

People with Friedreich ataxia who are no longer walking should have regular (at least once per year) monitoring and assessment by a clinician experienced in managing ataxia. There are subtle differences in how physical function is affected in each person with Friedreich ataxia; therefore, there is no one approach that will work for everyone. Regular contact with a healthcare provider will give you an opportunity to discuss the management options available to improve or maintain your independence and to work out which recommendation (or a combination of recommendations) may be best for you. Your healthcare provider/s will ensure that management is tailored specifically for you.

Who are these recommendations specifically for?

Regular monitoring is recommended for all non-ambulant individuals with Friedreich ataxia. There are subtle differences in how moving in and out of the bed, the wheelchair and the car is affected, and how sitting and standing balance changes in each person with Friedreich ataxia. Therefore, there is no one approach that will work for everyone.

The management recommendations are for all individuals with Friedreich ataxia who are no longer walking; however, we recommend discussing these with your healthcare provider/s to ensure they are tailored specifically for you.

Author details

Manuela Corti, P.T., PhD

Assistant Professor, University of Florida, Gainesville, Florida, USA

Email: m.corti@peds.ufl.edu

Sarah C. Milne, BPhysio, PhD

Physiotherapist, Murdoch Children's Research Institute, Melbourne, Victoria, Australia

Email: sarah.milne@mcri.edu.au

Massimo Pandolfo, MD

Professor (Clinical), McGill University, Montreal, Quebec, Canada

Email: massimo.pandolfo@mcgill.ca

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