ThinkFA

FACT:

You can make a difference when you ThinkFA

Biogen

FACT:

Friedreich ataxia is a progressive, incapacitating neurodegenerative disease[1]

Friedreich ataxia (FA) is the most common form of inherited ataxia, but its true impact is difficult to know[2-4]

Incidence of FA is often estimated at around 1 in 50,000 births. **In the United States, approximately 5000 people or more live with FA.**

Furthermore, FA is highly variable in both age of onset and rate of progression, adding complexity to symptom identification and diagnosis.

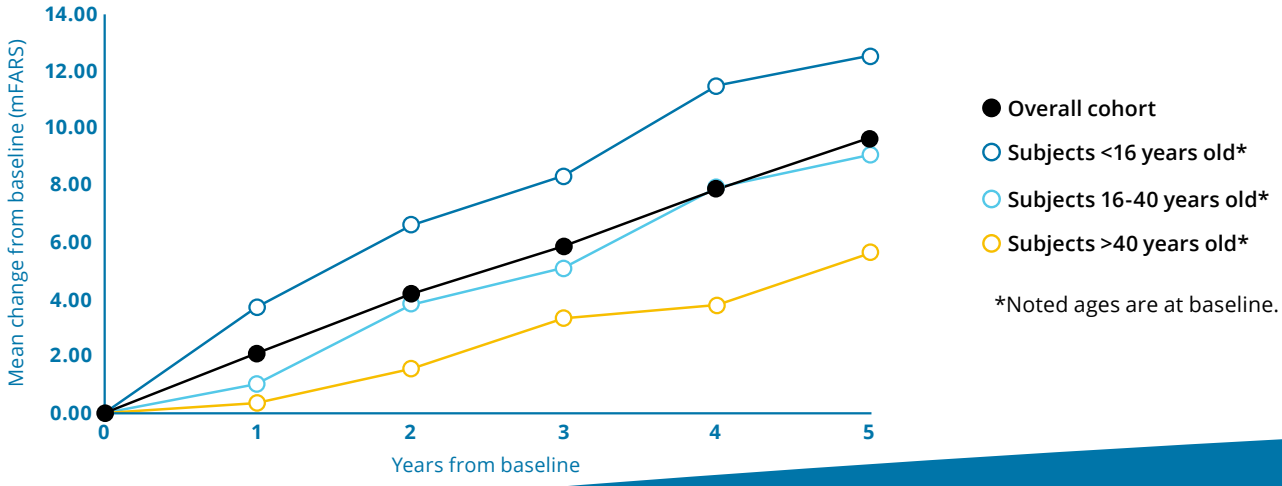
Time is function for patients with FA

While each person's experience is unique, every patient with FA progresses down a neurodegenerative path toward loss of ambulation. By the time they are diagnosed, many patients will have already lost some of their functional abilities, particularly those related to standing and mobility.[5]

The progression of FA can be measured using the modified Friedreich Ataxia Rating Scale (mFARS), a clinically validated neurological assessment that provides an evaluation of a patient's status. As FA progresses, a patient's mFARS score will worsen (increase). A natural history study of untreated patients found that as FA progresses, a patient's mFARS score increases (worsens) by ~2 points per year on average.[6,7]

An increase in mFARS scores could indicate further loss of function that may affect everyday tasks such as speaking clearly, swallowing, or brushing teeth.[7,8]

Typical mFARS progression by age group[7]



FACT:

Non-neurological complications may arise as FA progresses

Additional symptoms may develop over time

As FA progresses, symptoms such as dysarthria and loss of upper limb coordination often become more pronounced. Non-neurological symptoms such as diabetes, scoliosis, and cardiomyopathy are also common among patients with FA.[2,9]

FA reduces life expectancy

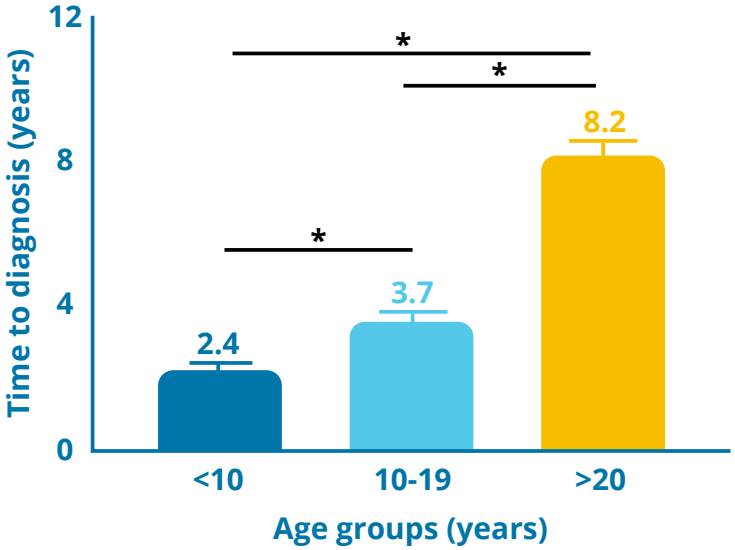
The average life expectancy for someone living with FA is 37.5 years. The most common cause of death among FA patients is cardiomyopathy.[2,10]

The path to diagnosing FA is often long and frustrating

FA typically goes undiagnosed for several years after symptoms first appear, with time to diagnosis influenced by the patient's age at the time of onset.[11]

Because early symptoms can be vague, it is common for patients to see 4 or more doctors before a diagnosis is made. Even after years of searching for an answer, it is estimated that overall, about one-quarter of patients with FA receive an incorrect diagnosis.[11]

Average time to an FA diagnosis[11]



*P<0.05 determined by one-way analysis of variance (ANOVA), Dunn's correction.

Time to diagnosis in older patients with FA can be >8 years, more than double the time to diagnosis in younger patients.[11]

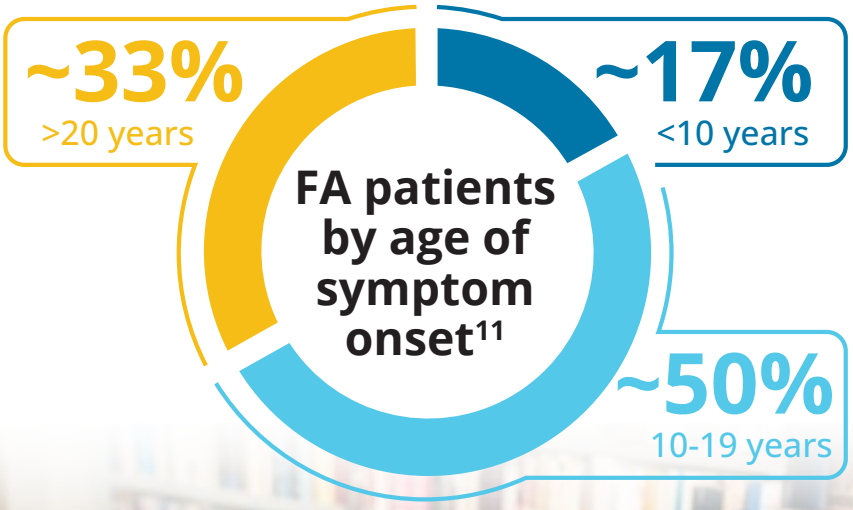
FACT:

When you think FA FIRST, you can shorten the time to diagnosis and connect patients to care sooner

Signs of FA typically appear between the ages of 10 and 15 years, but symptoms can emerge at nearly any age[2]

Patient age at symptom onset strongly correlates with FA severity. Patients who experience symptom onset at a younger age have more rapid disease progression, while patients who experience later-onset FA may never even need to use a wheelchair.[4]

Even so, every patient diagnosed with FA will see a progressive loss of mobility and physical ability.[5]



FACT:

Once FA symptoms are identified, genetic testing can confirm a diagnosis

Be the one to break the cycle of delayed or missed diagnosis. If you suspect FA, take these steps to quickly confirm a diagnosis:

1 When you see any combination of these symptoms, think FA FIRST[12,13]

Falls (gait ataxia)

Imbalance (poor proprioception)

Reflex loss (areflexia)

Sensation loss (neuropathy)

Tiredness (fatigue)

2 Consider non-neurological signs that may also be present early in the course of disease[2]

- Scoliosis may be an initial indicator of FA when you also see imbalance or other neurological signs
- Cardiomyopathy may be more common at presentation among younger patients with more severe early-onset FA

3 Order a genetic test that includes a GAA triplet-repeat expansion analysis[2]

- A genetic test can be conducted at the same time as other diagnostic tests, potentially speeding the time to diagnosis
- Patients may be eligible for free genetic testing through the Biogen-sponsored FA Identified program

Remember: ~33% of FA patients first experience symptoms in adulthood. Patients who are older at the time of symptom onset may be more difficult to identify because of their age and slower rate of disease progression.[4,11]

FACT:

The most common form of inherited ataxia is commonly misdiagnosed

Early symptoms of FA often overlap with other similar ataxias and neurological disorders[2]

Because FA typically presents with nonspecific symptoms such as balance and coordination disturbances, misdiagnosis is common.[9]

Other conditions with symptoms that may overlap with FA include[2,11]:

- Multiple sclerosis - ICD-10 G35
- Charcot-Marie-Tooth (CMT) - ICD-10 G60
- Cerebral palsy - ICD-10 G80.9
- Ataxia with oculomotor apraxia - ICD-10 G11.8
- Ataxia-telangiectasia - ICD-10 G11.3

As many as 1 in 4 patients with FA have been misdiagnosed.[11]

Misdiagnosis is common regardless of age at symptom onset[11]:

FACT:

Atypical symptoms for FA may signal the need for a genetic test

Certain atypical signs of FA may also contribute to a misdiagnosis[9,14]:

Later onset (>20 years)

Spasticity

Retained reflexes

Chorea

Severe optic atrophy

Think FA for your differential diagnosis if[1]:

- Ataxia is sporadic or recessive
- MRI reveals cervical spinal cord atrophy
- Nerve conduction and electrogram indicate loss of sensitivity

Any patient with a G11 diagnostic code can be considered for genetic testing to identify FA

Patients with other forms of hereditary ataxia may benefit from genetic testing if they have not had their diagnosis confirmed with a genetic test. Unspecified ataxia diagnostic codes G11.9 and G11.10 are especially important to look out for.

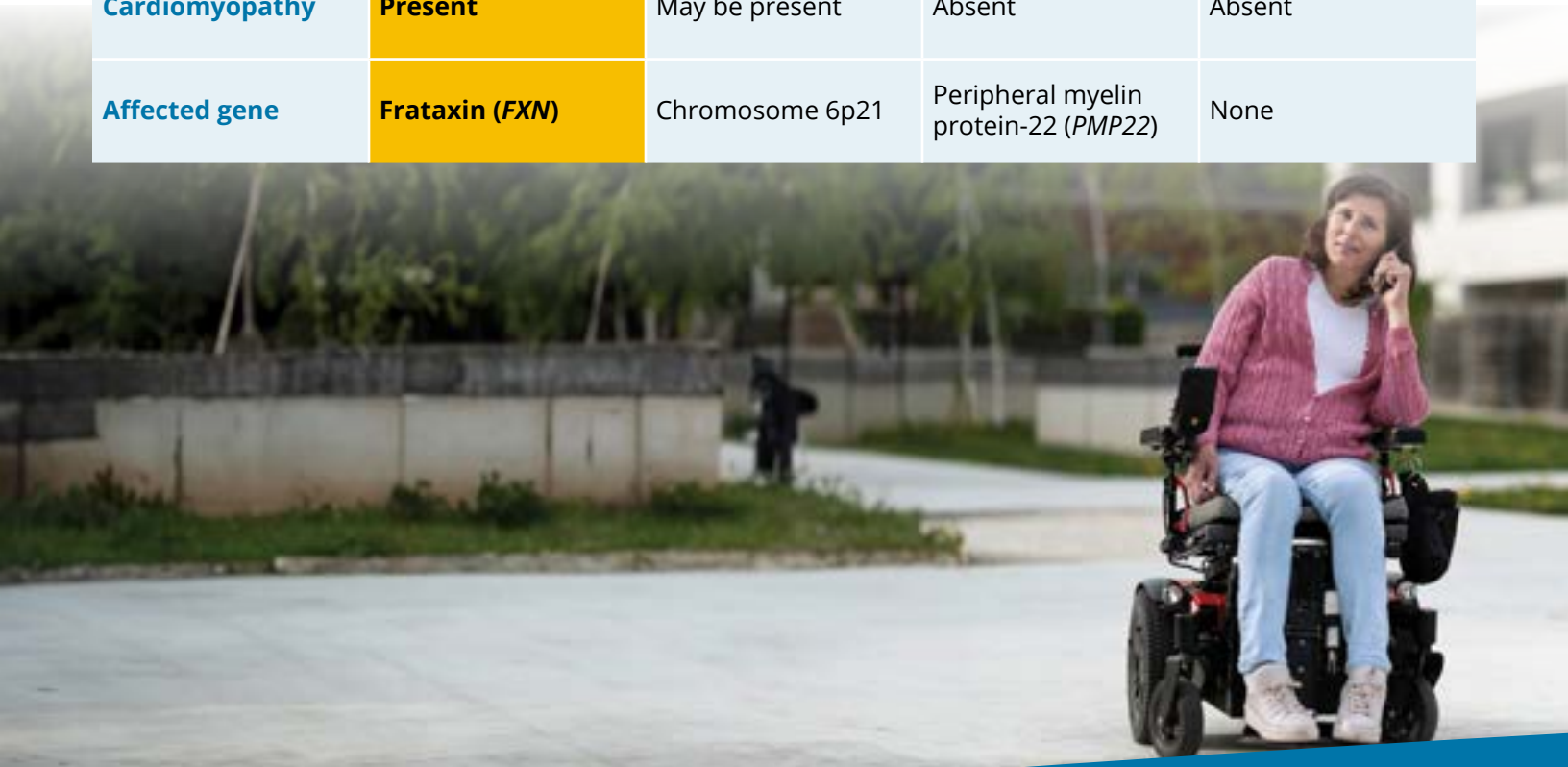
Patients may be eligible for no-cost genetic testing through the Biogen-sponsored FA Identified program. Visit **FAidentified.com** to learn more.

FACT:

There are many overlapping symptoms to consider in a differential diagnosis for patients with ataxia

Comparing FA to commonly misdiagnosed conditions[1,15-22]

Feature	Friedreich ataxia	Multiple sclerosis	Charcot-Marie-Tooth	Cerebral palsy
Age of onset	**~10 to 15 years (range: ~2 to 50 years)**	~20 to 40 years (range: any age)	~5 to 25 years	~1 year
Cerebellar atrophy	**Advanced cases only**	Frequent	Rare or absent	5% to 10% of cases
Pyramidal signs	**Frequent**	Present	Present	Frequent
Peripheral neuropathy	**Present (sensory axonal)**	May be present	Present	Absent
Cardiomyopathy	**Present**	May be present	Absent	Absent
Affected gene	**Frataxin (*FXN*)**	Chromosome 6p21	Peripheral myelin protein-22 (*PMP22*)	None



FACT:

Mutation of the frataxin gene is a primary indicator for differential diagnosis

Comparing FA to similar types of ataxia[1,23-25]

Feature	Friedreich ataxia	Ataxia with oculomotor apraxia – type 1	Ataxia with oculomotor apraxia – type 2	Ataxia-telangiectasia
Age of onset	**~10 to 15 years (range: ~2 to 50 years)**	~7 years (range: ~2 to 20 years)	~10 to 22 years	~5 years (range: ~2 to 30 years)
Cerebellar atrophy	**Advanced cases only**	Present	Present	Present
Pyramidal signs	**Frequent**	Absent	Occasional	Present
Peripheral neuropathy	**Present (sensory axonal)**	Present (motor and sensory axonal)	Present (motor and sensory axonal)	Present (axonal)
Cardiomyopathy	**Present**	Absent	Absent	Absent
Affected gene	**Frataxin (*FXN*)**	Aprataxin (*APTX*)	Senataxin (*SETX*)	ATM serine/threonine kinase (*ATM*)

FACT:

Selecting the right genetic test is critical to accurately diagnosing FA

A genetic test that includes a GAA triplet-repeat expansion analysis is the only way to confirm an FA diagnosis[26]

FA is caused by a variant within the *FXN* gene called a GAA triplet-repeat expansion. Nearly all cases—96%—are caused by this variant, while about 4% are attributable to point mutations.[27]

Genetic testing not only confirms a diagnosis, it also informs prognosis

A greater number of GAA triplet repeats typically means[2]:

- Earlier disease onset
- More severe symptoms
- More rapid progression

PCR-based tests often do not show repeat sizes above the threshold for diagnosis, so a more detailed follow-up test may be needed to fully inform a prognosis.[26]

Representative ranges of FA severity by GAA expansion length[1,4]:

Normal range	Threshold for diagnosis	Late onset (24+ years)	Intermediate onset (15 to 24 years)	Typical onset (8 to 14 years)	Early onset (0 to 7 years)
<33 repeats	66 repeats	136 to 360 repeats	376 to 630 repeats	600 to 820 repeats	700+ repeats

Less severe with slower progression to more severe with more rapid progression

FACT:

Genetic testing is the key to connecting patients to the care and treatment they need

Genetic testing can confirm a diagnosis of FA even when nonspecific or atypical symptoms are present[10]

Despite similarities in presentation between FA and other ataxias, laboratory and genetic testing can quickly confirm a correct diagnosis. Because FA is often misdiagnosed, patients with ataxia diagnoses that have not been confirmed through genetic testing may benefit from a GAA triplet-repeat expansion analysis to confirm their diagnoses.

Even patients who have been genetically tested with a general ataxia panel may benefit from receiving testing that evaluates for a repeat expansion in the frataxin gene.

Genetic confirmation can help a patient's family know whether they are at risk

Because genetic testing may have implications for siblings, parents, and children of the patient, both patients and their family members should be encouraged to participate in genetic counseling.

If your patient and their family are interested in a genetic counselor, genetic counselors in your area can be found by visiting the website of the National Society of Genetic Counselors at FindAGeneticCounselor.org.

No-cost genetic testing may be available

Eligible patients who are suspected of having FA may qualify for **no-cost genetic testing** through FA Identified, a program sponsored by Biogen and offered through PreventionGenetics. Your patients may be eligible if they meet the following criteria:

- Are suspected of having or have a clinical diagnosis of FA
- Are 16 years old or older
- Reside in the United States or Puerto Rico

While Biogen provides financial support for these programs, at no time does Biogen receive identifiable patient information. The FA Identified program includes:

- Multiple testing and screening options
- Easy ordering of kits and DNA collection methods
- Results within ~3 weeks of testing, with expedited testing available

Specimen collection kits are provided along with a test requisition form. Simply complete the form and send it along with the collected specimen to PreventionGenetics for testing.

FA IDENTIFIED

Learn more about genetic testing for FA at FAidentified.com.

FACT:
Identifying FA depends on you

Be the one to break the cycle of delayed or missed diagnosis

Think FA FIRST when you see certain symptoms

Confirm a diagnosis with a genetic test

Connect patients to treatments and services to help manage FA

Learn more about identifying and diagnosing patients with FA at ThinkFA.com.

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