RESEARCH AMERICA
DISCOVERY. INNOVATION. HEALTH.

LASKER FOUNDATION

If you think research is expensive, try disease.

INVESTMENT IN RESEARCH SAVES LIVES AND MONEY

Friedreich's Ataxia (FA)

Friedreich's Ataxia (also known as FRDA or FA) is a genetic disorder that progresses over time. It is a multisystem disease that presents as a neurodegenerative movement disorder, meaning that nervous system damage from the disease, such as loss of sensation in the arms and legs, causes problems with movement.[1] Initial symptoms include unsteady posture, frequent falling, difficulty walking, and problems coordinating voluntary movements. Other characteristics of FA include cardiomyopathy (decreased ability of the heart to pump blood to the rest of the body), scoliosis, fatigue, and slowed or slurred speech. Those with later stages of FA may also develop hearing and vision loss. The disorder does not impair intellect or cognitive ability. Symptoms most often present during childhood between five and 15 years of age. Most patients require mobility aids such as a cane, walker, or wheelchair by their teens or early 20's.[3] FA is caused by a mutation in the frataxin gene (*Fxn*). The parents of a child with FA have one mutated gene each. People with only one mutated gene are called carriers. Carriers do not develop the disease or display any symptoms, but there is a 25% chance that their child will have FA.[1,2]

TODAY

FA affects approximately **1 in 40,000** people of European origin.[1,2] In the U.S., the prevalence is **1 in 50,000** people.[1,3]

Incidence of diabetes in FA patients ranges from **6% to 19%**.[4] Cardiac abnormalities occur in about **75%** of people with FA.[5]

Most individuals lose the ability to walk about **10 to 12 years** after onset of symptoms.[6]

COST[7]

$118,000: Average annual costs to FA families in the U.S., including direct medical costs such as physician and therapist services, laboratory analyses, emergency room visits, prescription medicines, and long-term care facility costs.

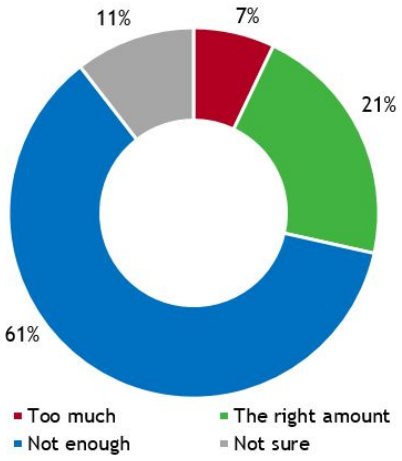
Individuals with FA obtain bachelor's degrees at almost **twice the rate** of the average U.S. citizen, yet the disease adversely affects their employment outcomes, likelihood of marriage, and housing status.[8]

Research Delivers Solutions

As FA progresses, coordination and balance are impaired, which leads to **loss of ambulation (LoA)**. This transition to becoming fully wheelchair-bound is a critical aspect of the disease. One study examined 1,021 patients with FA to try and predict when LoA starts. FA patients who were diagnosed with FA before 15 years of age typically became fully wheelchair dependent 11.5 years after onset of first symptoms. These study results help to predict risk and timing of LoA and facilitate treating patients based on their progression.[6]

FA is caused by the silencing, or "turning off," of the *Fxn* gene, severely reducing production of the frataxin protein. This silencing is caused by a mutation in the *Fxn* gene where sequences of **GAA nucleotides** (the building blocks of DNA) repeat many times. Without appropriate amounts of this protein, the **mitochondria** (the powerhouses of the cell) are severely impaired. Extensive biochemical studies documented that these expanded repeats have unusual DNA structures and epigenetic silencing. Advances in gene therapies show promise for repairing or replacing the broken Fxn gene. In one pre-clinical study, scientists were able to prevent and reverse the onset of cardiac disease in an experimental model by using a virus to implant the correct version of the *Fxn* gene into cells' DNA.[9,10] Understanding the cause of the disease and the downstream consequences at a cellular level has led to identification of multiple potential targets and approaches for therapy. Several therapies in development targeting mitochondrial function and frataxin replacement are currently in clinical trials.

The U.S. spends about 5 cents of each health dollar on research to prevent, cure and treat disease and disability. Do you think that this is too much, the right amount or not enough?



Source: A Research!America poll of U.S. adults conducted in partnership with Zogby Analytics in January 2020

Friedreich's Ataxia (FA)

Then. Now. Imagine.

THEN
FA's devastating effects were first described in the 1860s by Nikolaus Friedreich.[11] The mutation in the Fxn gene was discovered as the cause of FA in 1996.[12]

NOW
While there are currently no drug treatments for FA, research has advanced to the point of understanding the causes of the disease. As a result, new potential treatments are emerging and being evaluated in clinical trials.[3]

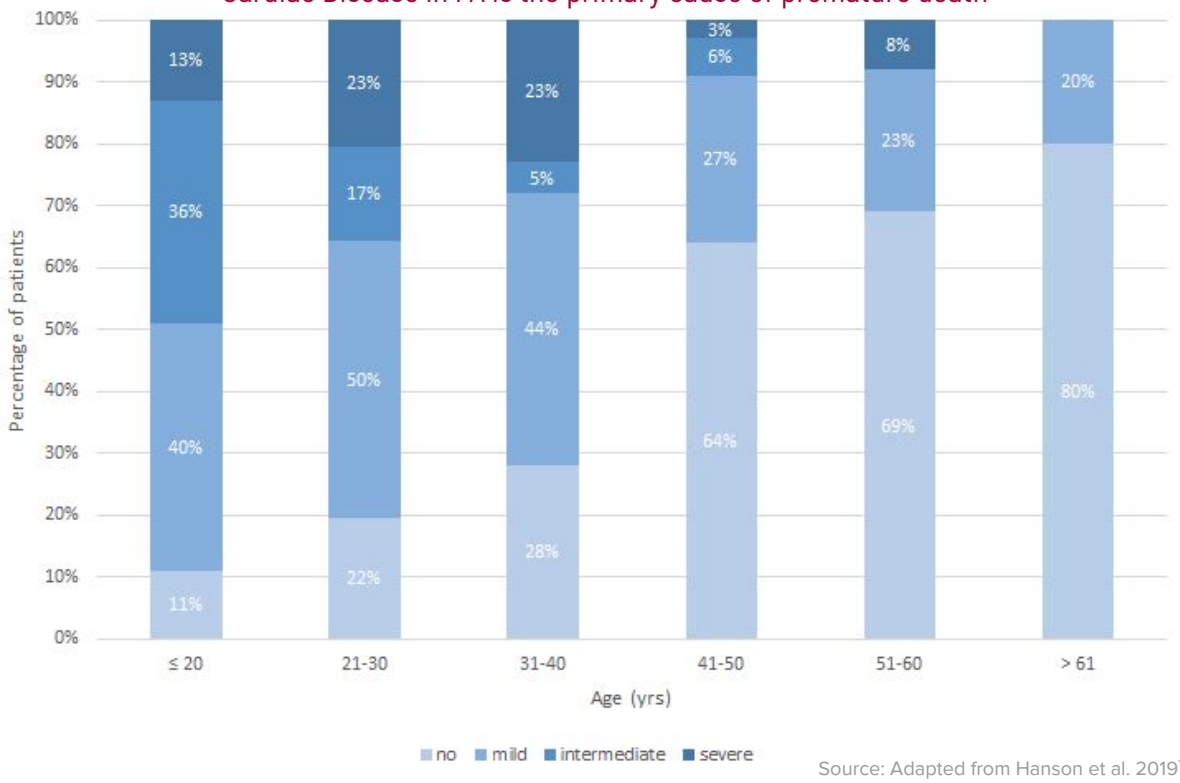
IMAGINE
A cure.

FA Global Patient Registry

The FA Global Patient Registry is the largest registry capturing patient reported data and outcomes from individuals with FA. Originally created by the **Friedreich's Ataxia Research Alliance (FARA)**, this registry is now an international collaboration with worldwide advocacy organizations. This registry is meant to serve the patient, physician, and research communities in connecting individuals with FA and providing updates from the medical world. As new therapies for FA are entering the clinical trial phase, patients with FA can be recruited for these studies. This registry works to provide updates, communication, and hope between patients and research.[13]

Proportion of patients according to severity of FA cardiomyopathy*

*Cardiac Disease in FA is the primary cause of premature death



Source: Adapted from Hanson et al. 2019[14]

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