

Waisman Center
University of Wisconsin – Madison

Advancing knowledge of human development, developmental disabilities, and neurodegenerative diseases.

Study on Family Adaptation to Fragile X Syndrome



Report 7: Identifying the Health Needs of Individuals with FXS Across the Lifespan

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If you would like to read other family reports or research papers from our research group, please visit the study website:

<https://family.waisman.wisc.edu/fxs-fmr1-associated-conditions/>

For more information about FXS and related disorders, please visit the NFXF website: <https://fragilex.org/understanding-fragile-x/fragile-x-101/>

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Section I: Introduction

This is the 7th Family Report we are sharing with families of our *Family Adaptation to Fragile X Syndrome* study. In our past reports, we have shared information about daily life experiences, health, emotional well-being, education, and vocational activities of adolescents and adults with fragile X syndrome (FXS) and their families. We are very grateful to you and all of the other families who have provided us with this in-depth information during the past 15 years about the lives of adolescents and adults with FXS and other family members.

Recently, the 18th International Fragile X Conference, the National Fragile X Foundation (NFXF) presented our team with a 2022 NFXF Research Award for outstanding contributions to the understanding of FXS. The award honors and thanks individuals who have made a significant impact on the FXS community. We share this award with our participating families. We could not have done the work without your continued contributions to the research.

Within this report, we will share new research carried out by our study team members. In contrast to previous Family Reports, this one is *not* based on data collected from families participating in our longitudinal study, but rather focuses on a different study of FXS that we have conducted. We have used electronic health record data from people diagnosed with FXS in the state of Wisconsin. We are very grateful to Arezoo Movaghar, PhD, who led this research. The Family Report is based on the following published study:

Movaghar A, Page D, Scholze D, Hong J, DaWalt LS, Kuusisto F, Stewart R, Brilliant M, Mailick M. (2021). Artificial intelligence-assisted phenotype discovery of fragile X syndrome in a population-based sample. *Genetics in Medicine*. DOI: 10.1038/s41436-021-01144-7 -01144-7

We hope that this research continues to help medical professionals, service providers, and advocates understand the experiences of families with FXS. This information may be used to inform services, therapies, and supports for individuals with FXS and their families.

Section II: Identifying health needs of individuals with FXS

It is important to identify the health needs of individuals with FXS across the lifespan in order to provide appropriate and timely care and treatment. Past research has shown that people with FXS may have a variety of medical conditions. While many individuals with FXS are very healthy, others have health problems that can have a significant impact on their daily lives. Symptoms of certain conditions can differ, especially based on age, sex, and other factors. Some individuals with FXS may have difficulty communicating their needs and sharing their symptoms with care providers. A major goal of our research is to identify those conditions for which individuals with FXS are at greater risk compared to the rest of the population, so that families and health care providers can look for these conditions if health problems arise.

Using electronic health records in research on FXS

In recent years, health care systems have “digitized” patient medical data, and now health records can be accessed by computerized records. Without knowing the identity of patients, researchers can study digitized patient data to understand diseases and plan treatments. In this report, we describe what we have learned based on the electronic health records for over one million people who were served by the Marshfield Clinic, a health-care system in Wisconsin, of whom 55 individuals have a diagnosis of FXS.

The Marshfield Clinic is a large not-for-profit, multispecialty health-care system, serving patients from Northern and Central Wisconsin. It was one of the first US institutions to use electronic health records and the clinic has over 40 years of health data on each patient.

How electronic health records data were collected and examined

For this study, we examined electronic health records from 1,301,358 patients who had three or more medical visits in their lifetime at the Marshfield Clinic Health System. Fifty-five of the patients had a diagnosis of FXS (11 females and 44 males) who are the focus of this report. To protect the privacy and confidentiality of patients, the Marshfield Clinic removed all information that would reveal the identity of individual patients from the electronic health record data shared with our research team.

The purpose of this study was to gain an understanding of the health characteristics of people diagnosed with FXS. Specifically, we studied the electronic health records of people with FXS to learn about:

- physical health conditions across the lifetime
- mental and neurological conditions
- how to identify individuals who might need to be tested for FXS

Physical health conditions linked with FXS

We studied the entire medical records of patients in the Marshfield Clinic Health System and found that 39 specific physical health conditions were more common in those who have FXS compared to those in the general population. The table on the next page shows the most frequent physical health conditions found. For example, heart valve disorders were five times more often recorded in the electronic health records of patients with FXS compared with the general population.

Note that the frequency of the conditions shown in Table 1 varies greatly, and some individuals with FXS do not have any of these conditions.

Table 1. Conditions that are frequently reported in individuals with FXS

Category	Condition
Circulatory system disorders	Heart valve disorders
	Atrioventricular (AV) block
	Hypotension (low blood pressure)
Digestive issues	Disorders of function of stomach
	Intestinal obstruction
	Irritable Bowel Syndrome
Dental problems	Gingival and periodontal diseases
	Diseases of the teeth and supporting structures
Endocrine/ Metabolism problems	Short stature
	Abnormal weight gain
	Lack of normal physiological development
	Disorders of fluid, electrolyte, and acid-base balance
Genitourinary disorders	Retention of urine
	Urinary incontinence
	Other symptoms/disorders of the urinary system
Diseases of sense organs	Otitis media (inflammation or ear infections)
	Other disorders of middle ear and mastoid
	Dizziness and giddiness (Light-headedness and vertigo)
Other conditions	Diseases of nail
	Cancer, suspected or other

We want to clarify that although these conditions were statistically more prevalent among those with FXS, no one person with FXS is vulnerable to all of these conditions or at risk for poor health. **Your family member with FXS might not have any of these conditions – this is important to keep in mind.** But if he or she has one of these health problems, you might share this report with his or her physician.

Mental Health and Neurological Conditions linked with FXS

In addition to the physical health conditions that we studied, 28 mental health and neurological conditions were diagnosed more often in patients who had FXS compared to the general population. The following conditions were more frequently diagnosed in people with FXS:

- Autism spectrum disorders
- Developmental delays and disorders
- Attention Deficit Hyperactivity Disorder
- Speech difficulties
- Schizophrenia and other psychotic disorders
- Anxiety
- Phobias
- Dissociative disorders
- Epilepsy
- Recurrent seizures
- Convulsions

Section III: Finding patients who may need to be tested for FXS

It is well known that FXS is the most common inherited cause of intellectual disability and autism. Although doctors may recommend genetic testing for FXS when a child shows development or language delays, it can take months or even years before a person gets the genetic testing needed to confirm FXS.

Early diagnosis of FXS is important for patients and families and allows for timely intervention and better medical care. Even though there has been an increased emphasis on identifying individuals with FXS, it is still underdiagnosed.

Finding patients who may need to be assessed for FXS

In our study of the Marshfield electronic health records, people received a diagnosis of FXS at many different ages - ranging from 6 months to 92 years (see figure below). Genetic testing for FXS first became available in 1991. The first case in the Marshfield Clinic was diagnosed in 1994. The good news is that over time, patients with FXS have been diagnosed at younger ages.

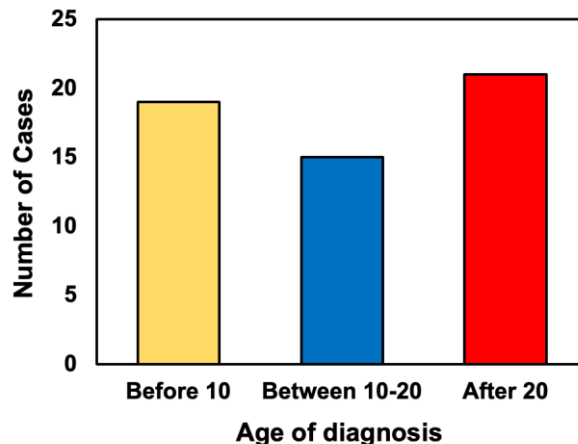


Figure 1. The age of diagnosis in individuals with FXS at the Marshfield Clinic

The figure above shows that many people (65 percent) did not receive a diagnosis of FXS until their teens or adult years. In order to possibly accelerate the method of FXS diagnosis, our research team searched the electronic health records of those diagnosed after age 10 to discover if there were predictable patterns of diagnoses given BEFORE FXS was diagnosed. In other words, for this part of our study, we focused on late-diagnosed cases. We were able to create a timeline of when other diagnoses were made **before** someone receives an actual FXS diagnosis. The timeline showed that patients who eventually were diagnosed with FXS were initially diagnosed with:

- Speech/language disorder around the age of 3
- Developmental delay at age 3
- ADHD at age 5.5
- Anxiety disorder at age 12
- Intellectual disability at age 13.5

In Figure 2 below, our research discovered that late-diagnosed cases eventually received the FXS diagnosis at an average of 23.5 years old. By using our own method to analyze electronic health records, our team discovered that we were able to successfully find people that needed to be assessed for FXS five years before they actually received a clinical diagnosis of FXS.

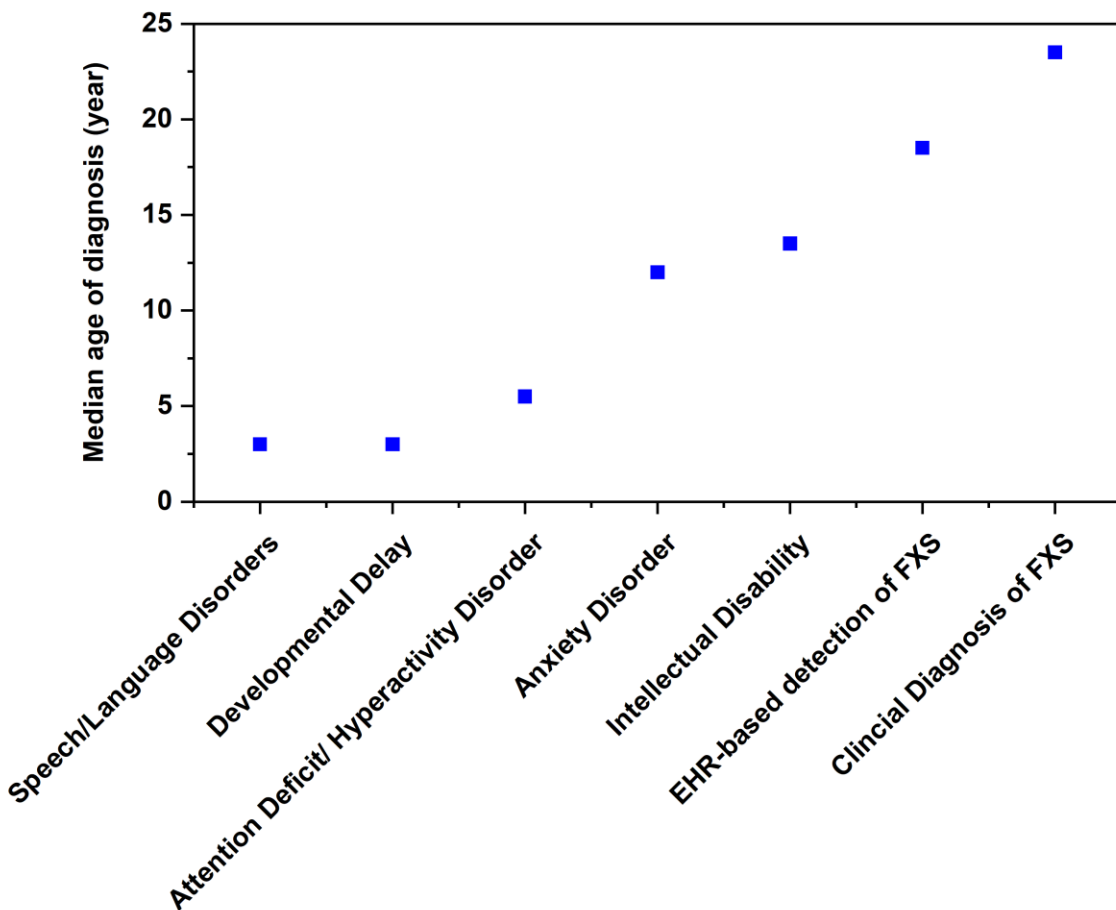


Figure 2. The median age of diagnosis for key conditions in late diagnosed cases (i.e., individual diagnosed with FXS after age 10)

Section IV: Conclusions

Through the use of electronic health records, our research team studied health conditions in people with FXS and compared them to the general population. We found that there were many health conditions that people with FXS had more often than people in the general population. These results show researchers and health care providers that FXS is linked with a wide range of physical and mental health conditions. Knowing that some health conditions may be more likely to occur for individuals with FXS will help families work with their health care providers to plan healthcare visits and treatments. The results of this study will also give useful information to share with professionals and policy makers to improve services and supports for individuals with FXS and their families. Below are some examples of important health findings.

- Our examination of electronic health records shows that people with FXS are more likely to have heart conditions than the general population, and that these conditions can begin at a much younger age. Therefore, regular screening for heart disease is important for people with FXS.
- Dental and gum problems were also seen at higher rates for people with FXS in this study. Knowing this, families and care providers can take a close look at dental health and can advocate for FXS family members to get access to preventive dental care as needed.
- Several mental health and neurological conditions were identified in our examination of health records. Families might want to seek evaluation by a professional for mental health concerns that may be more difficult to diagnose for people with FXS such as anxiety or ADHD.

Children, youth, and adults with FXS have unique physical health needs. Although many individuals with FXS are very healthy, some may have an increased risk for developing some of the conditions mentioned above. Being aware of the health conditions that may be linked to FXS can help service providers understand the needs of their patients with FXS. It may also improve the treatment and services offered to families.

Getting an early diagnosis and intervention for FXS is an important public health goal. Understanding the complicated health profile of FXS and how to support the well-being of patients and their families will improve current clinical practice and the quality of life for people with FXS. The study of electronic health records can help health-care providers find families affected by FXS at a faster rate and allow them to get the treatments that addresses their complex needs.

Section V: Next Steps

In this report we outlined the findings from our recently published study examining longitudinal health records from more than one million individuals in Wisconsin to determine the health characteristics of patients who had a diagnosis of FXS. We identified physical and mental health diagnoses that occur more frequently in those with FXS and looked at health diagnosis patterns that may precede a diagnosis of FXS. Although we often think of FXS as a neurological diagnosis, the information from this study indicates that there are a wide range of medical conditions that can be associated with FXS including circulatory, endocrine, digestive, genitourinary, and mental and neurological disorders. Next steps for this work include replicating these findings in other health care systems. We hope this information will be useful for families and healthcare providers.

We are grateful for the continued support of families for participating in our research. We hope to have more reports in the future and plan to stay connected with you. We intend to continue to analyze the data you have shared with us in order to understand the health and well-being of individuals with FXS and their families. Our future plans also involve continuing our study of families who have members with FXS. We hope to receive a new round of funding for this study, which will focus on how life changes for adults with FXS and their families as they age. We hope you will continue your participation in this study and we will be in touch with you about future interviews. As always, we are so very grateful to you for your contributions to this research.