AFF2-related syndrome
This guide is not meant to take the place of medical advice.

Please consult with your doctor about your genetic results and health care choices. The information in this guide was up to date at the time it was written in 2020. But new information may come to light with new research. You may find it helpful to share this guide with friends and family members or doctors and teachers of the person who has AFF2-related syndrome.
What is AFF2-related syndrome?

AFF2-related syndrome happens when there are changes to the AFF2 gene. These changes can keep the gene from working as it should. The AFF2 gene is also called FMR2 or FRAXE.

**Key role**
The AFF2 gene plays a key role in brain development.

**Symptoms**
Because the AFF2 gene is important in the development and function of brain cells, many people who have AFF2-related syndrome have:

- Intellectual disability
- Developmental and speech delays
- Autism or features of autism
- Hyperactivity and attention difficulties
- Behavior issues
What causes AFF2-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Genes are arranged in structures in our cells called chromosomes. Chromosomes and genes usually come in pairs, with one copy from the mother, from the egg, and one copy from the father, from the sperm.

We each have 23 pairs of chromosomes. One pair, called the X and Y chromosomes, differs between biological males and biological females. Biological females have two copies of the X chromosome and all its genes, one from their mother and one from their father. Biological males have one copy of the X chromosome and all of its genes, from their mother, and one copy of the Y chromosome and its genes, from their father.

In most cases, parents pass on exact copies of the gene to their child. But the process of copying genes is not perfect. A change in the genetic code can lead to physical issues, developmental issues, or both.

The AFF2 gene is located on the X chromosome, so changes in this gene can affect biological males and biological females in different ways. Biological males who have changes in this gene will likely have AFF2-related syndrome. Biological females will likely have AFF2-related syndrome if they have changes in both copies of the gene.

Biological females who have one working copy of the gene and one non-working copy of the gene are called ‘carriers’. This means that they may not have signs or symptoms of the syndrome, but they can pass it along to their children.

Research shows that some cases of AFF2-related syndrome are inherited.
In other cases, it results from a random change in the AFF2 gene in the sperm or egg during development. This change to the genetic code is called a ‘de novo’, or new, change. The child can be the first in the family to have the gene change.

De novo changes can take place in any gene. We all have some de novo changes, most of which don’t affect our health. But because AFF2 plays a key role in development, de novo changes in this gene can have a meaningful effect.

Some people have a small change within the AFF2 gene itself. Others have too many copies of a small segment of DNA within the gene. When this happens, it is called Fragile XE syndrome, because it causes parts of the person’s DNA to appear fragile under a microscope.

Fragile XE syndrome was first identified through screening programs for a more common and more severe condition called Fragile X syndrome. Although the two syndromes share some similarities, Fragile X syndrome is caused by changes to a different gene, called FMR1.
Why does my child or I have a change in the AFF2 gene?

No parent causes their child's AFF2-related syndrome. We know this because no parent has any control over the gene changes that they do or do not pass on to their children. Please keep in mind that nothing a parent does before or during the pregnancy causes this to happen. The gene change takes place on its own and cannot be predicted or stopped.
What are the chances that other family members or future children will have AFF2-related syndrome?

Each family is different. A geneticist or genetic counselor can give you advice on the chance that this will happen again in your family.

The risk of having another child who has AFF2-related syndrome depends on the genes of both birth parents.

- If biological females who have changes in the AFF2 gene are pregnant with a daughter, the child has a 50 percent chance of being a carrier. If they are pregnant with a son, the child has a 50 percent chance of having the syndrome.

For a symptom-free sibling, a brother or sister, of someone who has AFF2-related syndrome, the risk of having a child who has the syndrome depends on the symptom-free sibling’s genes and their parents’ genes.

- If neither parent has the same gene change found in their child who has the syndrome, the symptom-free sibling has a nearly 0 percent chance of having a child who has AFF2-related syndrome.

- If the mother has the same gene change found in her child who has the syndrome, the symptom-free sibling has a small chance of also having the same gene change. If the symptom-free sibling has the same gene change as their sibling who has the syndrome, the symptom-free sibling's chance of having a child who has the genetic change is 50 percent. A son with the genetic change will have AFF2-related syndrome, whereas a daughter is likely to be a carrier.

For a person who has AFF2-related syndrome, the risk of having a child who has the genetic change is about 50 percent.
How many people have AFF2-related syndrome?

Researchers estimate that about 1 in 25,000 to 1 in 100,000 newborn males have AFF2-related syndrome. There are likely many more undiagnosed people who have the syndrome. As of 2020, doctors had described about 46 people in the world with changes in the AFF2 gene. The first case of AFF2-related syndrome was described in 1993. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have AFF2-related syndrome look different?

People who have AFF2-related syndrome typically do not look different from others.
How is AFF2-related syndrome treated?

Scientists and doctors have only just begun to study AFF2-related syndrome. At this point, there are no medicines designed to treat the syndrome. A genetic diagnosis can help people decide on the best way to track the condition and manage therapies. Doctors can refer people to specialists for:

- Physical exams and brain studies
- Genetics consults
- Development and behavior studies
- Other issues, as needed

A developmental pediatrician, neurologist, or psychologist can follow progress over time and can help:

- Suggest the right therapies. This can include physical, occupational, speech, or behavioral therapy.
- Guide individualized education plans (IEPs).

Specialists advise that therapies for AFF2-related syndrome should begin as early as possible, ideally before a child begins school.

If seizures happen, consult a neurologist. There are many types of seizures, and not all types are easy to spot. To learn more, you can refer to resources such as the Epilepsy Foundation’s website: epilepsy.com/learn/types-seizures.
AFF2-related syndrome is very rare. Doctors and scientists have not been studying this condition very long. As of 2020, studies had described about 46 people who have AFF2-related syndrome.

This section includes a summary of information from major published articles. It highlights how many people have different symptoms. To learn more about the articles, see the Sources and references section of this guide.

**Behavior and development concerns linked to AFF2-related syndrome**

**Learning**
Most people have some degree of intellectual disability and learning difficulties.

**Speech**
Many have language difficulties.

**Behavior**
Many people have autism or show features of autism, such as social difficulties, excessive hand flapping, and restricted interests. Many also have attention difficulties, hyperactivity, and impulsivity.
Medical and physical concerns linked to AFF2-related syndrome

There are no known medical or physical concerns linked to AFF2-related syndrome as of this writing.

Simons Searchlight is another research program sponsored and run by the Simons Foundation Autism Research Initiative, also known as SFARI. As part of the next step in your research journey, Simons Searchlight offers you the opportunity to partner with scientists and other families who have the same gene change. Simons Searchlight is a registry for more than 150 genetic changes that are associated with neurodevelopmental conditions, including autism spectrum disorder. Simons Searchlight makes it easier for researchers to access the information they need to advance research on a condition.

To register for Simons Searchlight, go to the Simons Searchlight website at www.simonssearchlight.org and click “Join Us Today”.

- Learn more about Simons Searchlight
  www.simonssearchlight.org/frequently-asked-questions

- Simons Searchlight webpage with more information on AFF2
  www.simonssearchlight.org/research/what-we-study/aff2

- Simons Searchlight Facebook group
  www.facebook.com/groups/2330706373860379
Sources and References

The content in this guide comes from published studies about AFF2-related syndrome. Below you can find details about each study, as well as links to summaries.


