PHIP-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 PHIP-related syndrome.
What is PHIP-related syndrome?

PHIP-related syndrome happens when there are changes to the PHIP gene. These changes can keep the gene from working as it should.

**Key role**
The PHIP gene plays a key role in cell growth.

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

- Intellectual disability or developmental delay
- Behavior issues, including autism
- Obesity
- Vision issues
What causes PHIP-related syndrome?

Our genes contain the instructions, or code, that tell our cells how to grow, develop, and work. Every child gets two copies of the PHIP gene: one copy from their mother, from the egg, and one copy from their father, from the sperm. 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.

Sometimes a random change happens in the sperm or egg. 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 PHIP plays a key role in development, de novo changes in this gene can have a meaningful effect.

Research shows that PHIP-related syndrome is often the result of a de novo change in PHIP. Many parents who have had their genes tested do not have the PHIP gene change found in their child who has the syndrome. In some cases, PHIP-related syndrome happens because the gene change was passed down from a parent. This is called dominant inheritance.

**Dominant inheritance**

Children have a 50% chance of inheriting the genetic change

Parent has the genetic change

**Child with dominant genetic change in autism gene**
Why do I or my child have a change in the PHIP gene?

No parent causes their child’s PHIP-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 PHIP-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 PHIP-related syndrome depends on the genes of both birth parents.

- If neither birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is on average 1 percent. This 1 percent chance is higher than the chance of the general population. The increase in risk is due to the very unlikely chance that more of the mother’s egg cells or the father’s sperm cells carry the same change in the gene.

- If one birth parent has the same gene change found in their child, the chance of having another child who has the syndrome is 50 percent.

For a symptom-free sibling, a brother or sister, of someone who has PHIP-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 PHIP-related syndrome.

- If one birth parent has the same gene change found in their 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 PHIP-related syndrome is 50 percent.

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

As of 2020, about 50 people in the world with changes in the PHIP gene had been described in the medical literature. Scientists expect to find more people who have the syndrome as access to genetic testing improves.

Do people who have PHIP-related syndrome look different?

People who have PHIP-related syndrome may look different. Appearance can vary and can include some but not all of these features:

- High forehead
- Curved pinky finger
- Full eyebrows
- Upturned nose
- Large ears
How is PHIP-related syndrome treated?

Scientists and doctors have only just begun to study PHIP-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 PHIP-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: www.epilepsy.com/learn/types-seizures.
PHIP-related syndrome is very rare. Doctors and scientists have just recently begun to study it. As of 2020, studies described fewer than 50 people who have PHIP-related syndrome.

This section includes a summary of information from two 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 PHIP-related syndrome

**Learning**
So far, everyone who has PHIP-related syndrome has some level of intellectual disability or developmental delay.

![35 out of 35 have intellectual disability or developmental delay](image)

**Behavior**
Most people have behavior issues. This can include hyperactivity, aggression, features of autism, anxiety, or depression.

![28 out of 34 have behavior issues](image)
Medical and physical concerns linked to PHIP-related syndrome

Eyes and eyesight
More than two-thirds of people who have PHIP-related syndrome have issues with their eyes or eyesight.

Growth
Almost two-thirds are overweight.

Fatigue
More than one-half have fatigue.

Muscle tone
Almost one-half have low muscle tone.

Feeding and digestion issues
Some infants who have PHIP-related syndrome have feeding issues.
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 200 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](http://www.simonssearchlight.org) and click “Join Us Today”.

- Learn more about Simons Searchlight
  [www.simonssearchlight.org/frequently-asked-questions](http://www.simonssearchlight.org/frequently-asked-questions)

- Simons Searchlight page on PHIP
  [www.simonssearchlight.org/research/what-we-study/phip](http://www.simonssearchlight.org/research/what-we-study/phip)

- Simons Searchlight PHIP Facebook community:
  [www.facebook.com/groups/436264670311297](http://www.facebook.com/groups/436264670311297)
Sources and References

The content in this guide comes from published studies about PHIP-related syndrome. Below you can find details about each study, as well as links to summaries or, in some cases, the full article.

  www.ncbi.nlm.nih.gov/pmc/articles/PMC5839042

  www.ncbi.nlm.nih.gov/pmc/articles/PMC6672026