GET TO KNOW HoFH

Your guide to homozygous familial hypercholesterolaemia (HoFH)
Welcome

You’re receiving this educational guide because you or someone in your family has been diagnosed with homozygous familial hypercholesterolaemia, or HoFH. HoFH is a serious condition, but the good news is that there are ways to manage it.

Inside you’ll find a lot of helpful information about what makes HoFH unique. Keep this guide handy so that you can refer to it when needed.
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What is HoFH?

Homozygous familial hypercholesterolaemia (HoFH) is an uncommon condition inherited from both parents that leads to high levels of cholesterol in your blood. That’s because the liver of someone with HoFH has trouble removing unused cholesterol from the blood.

See pages 10-11 to learn more about how your liver is different.

It can take a while to diagnose HoFH because it is uncommon—even among those with high cholesterol.

Homozygous familial hyper-what?

- **Homozygous (Ho)** means you inherited the condition from both of your parents.
- **Familial (F)** means the condition runs in your family.
- **Hypercholesterolaemia (H)** is a pretty big word that means high cholesterol.

“\[My grandfather, mother, and uncle had all struggled with high cholesterol. When I learned that HoFH was inherited—in that moment, my stubborn cholesterol levels made sense. It was earth shattering!\]

Mary // diagnosed with HoFH in 2013
HoFH is inherited

There are different types of familial hypercholesterolaemia (FH). HoFH is the least common and most severe form of FH that happens when both parents pass on the problem genes. Family members on both sides of your family may have FH, but you may be the only one with HoFH. An example of FH inheritance is shown below.
HoFH: the uncommon high cholesterol

While high cholesterol is common, HoFH is not.

- High cholesterol may be caused by a number of genetic (inherited) and/or lifestyle (bad diet, lack of exercise) factors.

- HoFH is the most severe form of high cholesterol. It is much less common because it must be inherited from both sides of your family, meaning each parent must pass on a specific problem gene that causes the condition.
Signs and symptoms of HoFH

Your doctor most likely diagnosed your HoFH based on a combination of physical symptoms, family history, and test results. Signs of HoFH may vary from person to person.

Blood tests can reveal what you don’t see or feel

- High cholesterol isn’t something you can typically feel, so doctors routinely check cholesterol through a simple blood test
- Even if you are taking cholesterol-lowering medicines, they may not be good enough for someone with HoFH. See page 13 to find out why.

Importance of family history

- In HoFH, both parents pass on the problem genes that cause the condition. It is also likely that your parents and other relatives have high cholesterol or heart disease
- Knowing your family history can be very helpful to diagnose inherited conditions such as HoFH
- Genetic tests may also be conducted using a blood sample to identify the faulty genes. While a positive result will confirm HoFH, a negative result will not rule out HoFH as the faulty genes cannot be identified in some patients

What you might see or feel physically

- Skin: Yellowish spots or bumps on the body (xanthomas) or around the eyes (xanthelasma)
- Eyes: A whitish ring around the cornea (the clear outermost layer of the eye), known as arcus cornealis
- Heart: Chest pain, shortness of breath, or fatigue, which may be early signs of heart disease
- Physical signs of HoFH vary from person to person; some people do not have any physical symptoms
Cholesterol for HoFH: the good, the bad, the target

Cholesterol isn’t all bad. Your body needs cholesterol to stay healthy. However, too little of one type and too much of another can cause health problems.

There are different types of cholesterol. High-density lipoprotein (HDL) is known as “good” cholesterol, while low-density lipoprotein (LDL) is known as “bad” cholesterol. Together, HDL and LDL make up the majority of your total cholesterol. Made by the liver and found in some foods, cholesterol circulates in the bloodstream.

The good

High levels of good (HDL) cholesterol can reduce your risk of heart disease. Most people can raise their good (HDL) cholesterol by exercising more and eating certain foods and fats in their diet.

The bad

Bad (LDL) cholesterol can build up in arteries, creating plaque that narrows your blood vessels and puts you at greater risk for developing serious health problems including heart disease.

The problem for someone with HoFH is that your liver has trouble removing unused cholesterol from the bloodstream. This means it may be harder for you to lower your bad (LDL) cholesterol.

See pages 10-11 to learn more about how your liver is different.
The treatment target for HoFH

Based on guidelines, doctors generally recommend that

- Total cholesterol be less than 200 mg/dL or 5.0 mmol/L*
- Bad (LDL) cholesterol be less than 100 mg/dL or 2.5 mmol/L*, and less than 70 mg/dL or 1.8 mmol/L for people with HoFH and who have signs of heart disease

As a person living with HoFH, it’s important for you to know your current cholesterol level and the target level your doctor has set for you.

Note your cholesterol numbers below either on your own or with your doctor.

*Different units of measurement of cholesterol levels are used in some countries.
A non-HoFH liver works differently from an HoFH liver

Normally, unused bad (LDL) cholesterol in the bloodstream is brought back to the liver and broken down.

- **A** The liver produces bad (LDL) cholesterol and releases it into the bloodstream.
- **B** Some of the bad (LDL) cholesterol is used up by the body.
- **C** Unused bad (LDL) cholesterol is picked up by the liver’s receptors. Receptors act like magnets, attaching to the unused LDL and bringing it back to the liver to break it down.

Even though I’d been doing everything my doctor had recommended, my cholesterol levels were still high.

Stacee // diagnosed with HoFH in 1991
In an HoFH liver, the receptors or magnets are faulty and do not work well and so the liver can’t remove excess bad (LDL) cholesterol from the bloodstream and break it down the way a non-HoFH liver can. This means that the LDL cholesterol levels become very high.

- The HoFH liver also produces bad (LDL) cholesterol and releases it into the bloodstream for the body to use.
- However, because the HoFH liver’s receptors (magnets) aren’t working right, they cannot remove and break down all of the unused cholesterol in the liver.
- As a result, unused bad (LDL) cholesterol builds up in the bloodstream.

Since HoFH liver receptors don’t work properly, bad (LDL) cholesterol can build up in your bloodstream if left undertreated.
What happens when bad (LDL) cholesterol is high in HoFH?

Too much bad (LDL) cholesterol in your arteries is bad for your health.

When cholesterol is at a healthy level, blood flows freely through your arteries.

Unhealthy levels of cholesterol can cause a buildup of cholesterol and other substances inside your arteries (plaque).

Over time, this buildup can lead to narrowing and hardening of your arteries (atherosclerosis), which limits the flow of blood to organs and other parts of your body.

Limited or blocked blood flow may cause serious health problems.

Talk to your doctor about what you can do to lower your bad (LDL) cholesterol and manage your HoFH.
Have you struggled to lower your cholesterol?

You are not alone. Often, people with HoFH who are taking commonly prescribed cholesterol-lowering therapies and following their doctor’s eating and exercise recommendations still have trouble lowering their cholesterol to a healthy level.

Why does this happen?
Most commonly used cholesterol-lowering medicines available today work to increase the number of receptors in the liver. Receptors act like magnets, attaching to the unused bad (LDL) cholesterol and bringing it back to the liver to be broken down. Since people with HoFH have receptors that don’t work properly, increasing the number of receptors may not be enough to reach their cholesterol goals.

See pages 10-11 to learn more about how your liver is different.

Also, while healthy eating habits and regular exercise are important, they are often not enough to help people with HoFH lower their cholesterol.

Another treatment that is often used to lower LDL cholesterol in HoFH patients is apheresis, a process where your blood is passed through a machine which filters your blood to remove the LDL cholesterol. However, as soon as you eat, the LDL cholesterol levels build up again and your average cholesterol may not be kept at a healthy level despite the process being repeated at weekly or alternate week intervals.

What else can I do?
Your doctor may recommend adding newer medicines for HoFH to your treatment plan to try to help you achieve your LDL target levels. Your doctor may also recommend the testing of other members of your family to identify those who may also have raised cholesterol.
My HoFH record and cholesterol levels

**WHERE I’VE BEEN**

Age that I was first told I had high cholesterol:

Cholesterol-lowering treatments I am no longer taking:

<table>
<thead>
<tr>
<th>WHERE I’VE BEEN</th>
<th>WHERE I AM NOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age:</td>
<td>Age:</td>
</tr>
<tr>
<td>Cholesterol-lowering treatments:</td>
<td>Cholesterol-lowering treatments:</td>
</tr>
</tbody>
</table>

Highest cholesterol level(s) I can remember:

<table>
<thead>
<tr>
<th>WHERE I’VE BEEN</th>
<th>WHERE I AM NOW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current cholesterol level(s):</td>
<td>Current cholesterol level(s):</td>
</tr>
<tr>
<td>TOTAL</td>
<td>TOTAL</td>
</tr>
<tr>
<td>LDL</td>
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As a person living with HoFH, it’s important for you to know your current cholesterol level and the target level your doctor has set for you. Note your cholesterol numbers below either on your own or with your doctor. Discuss your progress with your doctor.

HOW I SEE MY FUTURE

Cholesterol target levels:

TOTAL

LDL
When I had my first bypass surgery, my doctor told me that I had to start paying attention to my health and get my cholesterol under control.

Darrell // diagnosed with HoFH in 2012

My biggest lesson learned from my HoFH diagnosis is that I am in control of the changes I make. If you are ready and have the right support, you can be too. You may have HoFH, but it doesn’t have you.

Fran // diagnosed with HoFH in 2013
After more than 25 frustrating years of not responding to treatment and feeling like a failure—when I was finally diagnosed with HoFH—I felt like a weight had been lifted from my shoulders.

Holly // diagnosed with HoFH in 2012
Let’s review

1. HoFH is different because I inherited it from both sides of my family.

2. My liver cannot remove enough of the unused bad (LDL) cholesterol from my blood because I have HoFH.

3. The buildup of excess cholesterol may lead to serious health problems over time.

4. Medicines typically used to lower cholesterol in the general population may help, but may not be enough for people like me because my high cholesterol has a different cause that those medicines may not address.

5. Optimising my cholesterol treatments and lifestyle changes may help me reach my cholesterol goals.
Living with HoFH can be a challenge at times, but here are some steps you can take to feel more in control of your condition:

1. Know your cholesterol level and set an individual target level with your doctor.
2. Ask your doctor about what else you can do to lower your cholesterol.
3. Learn about treatments for people with HoFH.