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# Patient education: High cholesterol and lipid treatment options (Beyond the Basics)

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#### INTRODUCTION

A high cholesterol level (also called "hypercholesterolemia") can significantly increase your risk of developing chest pain, heart attack, and stroke. Fortunately, a number of effective treatment options are available.

Cholesterol levels can almost always be lowered with a combination of diet, weight loss, exercise, and medications. As your level decreases, so does your risk of developing cardiovascular disease (CVD), including disease of the blood vessels supplying the heart (coronary artery disease), brain (cerebrovascular disease), and limbs (peripheral vascular disease). This results in a decrease in your risk of having a heart attack or stroke. Even if you already have established CVD, it's not too late to lower your risk. In fact, in this case, lipidlowering treatment can be lifesaving.

An explanation of what cholesterol is, how it affects your health, and when a level should be measured is available separately (see <u>"Patient education: High cholesterol and lipids (Beyond</u>

<u>the Basics)</u>"). This topic will discuss when treatment is recommended, the available treatment options, and the risks, benefits, and effectiveness of each approach.

#### DO I NEED TREATMENT FOR HIGH CHOLESTEROL?

The decision to start cholesterol-lowering treatment is made on a case-by-case basis. Health care providers consider current lipid levels, the presence or absence of cardiovascular disease (CVD), and other risk factors.

**People with CVD** — Studies have shown that in people with coronary heart disease (in which the arteries that supply blood to the heart get clogged or blocked), taking medication to significantly lower the level of "bad" cholesterol, called low-density lipoprotein (LDL) cholesterol, is beneficial. Many health care providers recommend treating anyone with CVD (including people who have coronary heart disease or have had a stroke) with high-dose statin therapy (see <u>'Statins'</u> below). After starting statin therapy, the LDL cholesterol is rechecked; a second medication may be suggested if the level is higher than 70 mg/dL (1.81 mmol/L). Studies have found that if the LDL cholesterol is reduced to less than 70 mg/dL, the size of the plaques can get smaller.

People who have been hospitalized following a heart attack (also called a "myocardial infarction" or MI) or after a coronary intervention procedure (eg, stent placement or bypass surgery) are started on cholesterol-lowering medication before going home from the hospital; they are also advised to make lifestyle changes related to improving their diet and exercise habits, regardless of their LDL cholesterol level. (See <u>"Patient education: Heart attack recovery (Beyond the Basics)"</u>.)

If you have CVD, your health care provider can talk to you about the different ways to manage your cholesterol and which approach is best for your situation.

**People without CVD** — People without a history of CVD also benefit from cholesterol-lowering therapy, although the goal is generally not as aggressive as in people with CVD. The decision of whether to start treatment is based on your individual risk for developing heart disease. Calculators are available that can estimate this risk based on your age, sex, medical history, and other characteristics (see <u>"Patient education: High cholesterol and lipids (Beyond the Basics)", section on 'Calculating your risk of cardiovascular disease</u>'). Some clinicians recommend treatment at a particular level of risk (such as a 7.5 or 10 percent risk of developing CVD over 10 years), while others place more focus on a person's individual preferences with regard to taking medication. Sometimes a calcium score test is done to see if plaque is present in the heart

arteries; if so, then treatment is recommended. As with people who already have known CVD, when the decision is made to start medication, the first choice is usually a statin. (See <u>'Statins'</u> below.)

#### **Other special groups**

**People with high triglyceride levels** — Triglycerides, like cholesterol, are a type of lipid. High triglycerides (called "hypertriglyceridemia") are also associated with an increased risk of heart disease. These need to be assessed on a fasting blood test.

Dietary interventions and exercise are usually effective in lowering triglycerides. The dietary interventions include limiting intake of refined carbohydrates, excess calories, and alcohol.

For reducing cardiovascular risk, the first step is to reduce the LDL to below the target level (see <u>'Statins'</u> below) and then check the fasting triglyceride level. If it is >150 mg/dL, then additional treatments may be needed. A trial has found that in some patients, a high dose of a purified, EPA-only omega-3 preparation, <u>icosapent ethyl</u> (not the over-the-counter fish oil), was effective in reducing risk of heart attack, stroke, need for stents, and cardiac death. This treatment also lower triglyceride levels, but the benefit goes beyond just the lowering of the triglyceride level. Some clinicians may offer a specific form of omega-3 fatty acid (derived from fish oil) to some people with high triglycerides and increased cardiovascular risk. (See <u>'Omega-3'</u> below.)

People with very high triglyceride levels (above 886 mg/dL [10.0 mmol/L]) may be started on treatments to lower the risk of pancreatitis (inflammation of the pancreas that leads to damage over time). People who have already had triglyceride-related pancreatitis may be treated at lower levels. In these situations, a class of medication called fibrates are usually the first line of treatment.

**People with diabetes** — People with diabetes (type 1 or 2) are at high risk of heart disease. A moderate- or high-intensity statin is recommended in most adults with diabetes. (See <u>"Patient</u> education: Type 2 diabetes: Overview (Beyond the Basics)".)

**Older adults** — The decision to treat high cholesterol levels in a person over the age of 75 depends upon the individual's "chronologic age" (age in years) as well as their "physiologic age" (which takes into account their health and fitness level). A person with a limited life span and underlying illness may not need to receive drug therapy. On the other hand, an otherwise healthy older adult should not be denied drug therapy simply on the basis of age alone. In general, the treatment goals discussed above apply for people of all ages.

#### HIGH CHOLESTEROL TREATMENT OPTIONS

You can help lower your lipid levels with lifestyle changes, medications, or a combination of both. In certain cases, a health care provider will recommend a trial of lifestyle changes before recommending a medication. The best approach for you will depend on your individual situation, including your lipid levels, health conditions, risk factors, medications, and lifestyle.

**Lifestyle changes** — If you have high low-density lipoprotein (LDL) cholesterol, you should try to make some changes in your day-to-day habits, including reducing the amount of total and saturated fat in your diet, losing weight (if you are overweight or obese), getting regular aerobic exercise, and eating plenty of fruits and vegetables. (See <u>"Patient education: Exercise (Beyond the Basics)"</u> and <u>"Patient education: Diet and health (Beyond the Basics)"</u>.)

The benefits of these lifestyle changes usually become evident within 6 to 12 months. However, the success of lipid lowering with lifestyle modification varies widely, and health care providers sometimes recommend beginning medication sooner.

**Medications** — There are many medications available to help lower elevated levels of LDL cholesterol. Each category of medication varies in how it works, how effective it is, and how much it costs. Your health care provider will recommend a medication or combination of medications based on your blood lipid levels and other individual factors.

**Statins** — Statins are one of the best-studied classes of medications and the most commonly used drugs for lowering LDL cholesterol. They are the most effective drugs for prevention of coronary heart disease, heart attack, stroke, and death. Available statins include <u>atorvastatin</u> (brand name: Lipitor), <u>rosuvastatin</u> (brand name: Crestor), and several other similar medications (<u>table 1</u>). Statins decrease the body's production of cholesterol and increase removal of cholesterol by the liver, so they reduce LDL cholesterol levels by as much as 25 to 55 percent. In addition, they can lower triglycerides. Statins may also reduce inflammation and may prevent heart attacks and strokes through this mechanism.

While most people tolerate statins well, there are some potential side effects, mainly muscle pain, aches, or weakness. Changing statins and using low doses often can avoid these issues, but if not, non-statin medications can be used to lower LDL cholesterol.

It is important to closely follow the dosing instructions for when to take statins; some are more effective when taken before bedtime while others should be taken with a meal. In addition, some foods, such as grapefruit or grapefruit juice, can increase the risk of side effects of statins.

Most manufacturers recommend that people who take <u>lovastatin</u>, <u>simvastatin</u>, or <u>atorvastatin</u> consume no more than one-half of a grapefruit or 8 ounces of grapefruit juice per day.

**Ezetimibe** — <u>Ezetimibe</u> (brand name: Zetia) impairs the body's ability to actively transport cholesterol from food as well as cholesterol that the body produces internally. It lowers LDL cholesterol levels by 20 to 25 percent and has relatively few side effects. It is usually prescribed in combination with a statin but is also used alone in patients who cannot tolerate a statin. When used in combination with a statin after an acute coronary syndrome (eg, heart attack), ezetimibe provides a small additional reduction in the risk of having another cardiovascular event.

**PCSK9 inhibitors** — PCSK9 inhibitors are a newer class of drug that lower LDL cholesterol levels. The PCSK9 inhibitors include <u>alirocumab</u> (brand name: Praluent) and <u>evolocumab</u> (brand name: Repatha) ( <u>table 1</u>), which are given by injection every two to four weeks. They can reduce LDL cholesterol by as much as 60 percent. They reduce cardiovascular events (such as heart attack or stroke) and potentially death. Aside from mild skin reactions at the site of injection, they have few side effects. However, they are expensive and their use is limited to patients treated with maximal tolerated statins and <u>ezetimibe</u> who have persistent elevations of cholesterol. Specifically, these treatments are used in patients with known heart and vascular disease and those with familial hypercholesterolemia.

**Bile acid sequestrants** — The bile acid sequestrants include <u>colesevelam</u> (brand name: Welchol), <u>colestipol</u> (brand name: Colestid), and <u>cholestyramine</u> (sample brand names: Prevalite, Questran) ( <u>table 1</u>). These medications bind to bile acids in the intestine, reducing the amount of cholesterol the body absorbs from foods. They are used only occasionally. They lower LDL only modestly (10 to 15 percent).

Side effects can be bothersome and may include nausea, bloating, cramping, and liver damage. Taking <u>psyllium</u> (a fiber supplement, such as Metamucil) can sometimes reduce the dose required and the side effects.

Bile acid sequestrants can interact with some medications, including as <u>digoxin</u> (brand name: Lanoxin) and <u>warfarin</u> (brand name: Jantoven), and with the absorption of fat-soluble vitamins (including vitamins A, D, K, and E). Taking these medications at different times of day can solve these problems in some cases.

**Omega-3** — Oily fish, such as mackerel, herring, bluefish, sardines, salmon, and anchovies, contain two important fatty acids called docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Eating a diet that includes one to two servings of oily fish per week can lower triglyceride levels and reduce the risk of death from coronary heart disease.

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Fish oil supplements, supplements with low-dose mixed fish oils (usually approximately 1 gram per day of combined DHA and EPA), had been thought to provide cardiac benefit, but large trials have found no significant benefit. As such, they are no longer recommended.

A specific high-dose preparation (4 grams per day of <u>icosapent ethyl</u> or 1800 mg per day of highly purified EPA) has been found to reduce the risk of heart attack, stroke, need for stent of bypass surgery, and cardiac death when used with a statin in people who have mild hypertriglyceridemia (149 to 500 mg/dL) and either established CVD or diabetes plus other cardiovascular risk factors. A second study of a high-dose agent which had both EPA and DHA failed to provide benefit, suggesting that the EPA only preparation at the 4 gram dose is important. This preparation is obtained through a prescription from your doctor.

**Nicotinic acid (niacin)** — Nicotinic acid is a vitamin that is available in immediate-release, sustained-release, and extended-release formulations (<u>table 1</u>). Nicotinic acid is rarely used for a high cholesterol. In most situations, <u>ezetimibe</u> or a PCSK9 inhibitor is tried before nicotinic acid. This agent used to be used to raise HDL levels, but that is no longer recommended. It is sometimes used for patients with high lipoprotein(a) levels.

Nicotinic acid is associated with many side effects, including flushing (when the face or body turns red and becomes warm), itching, nausea, numbness and tingling, and worsening of gout. This medication can also cause liver damage; people who use it require regular blood tests to monitor their liver function.

Due to these risks, the FDA no longer recommends its use with statins or cautious use.

#### **Nutritional supplements**

**Soy protein** — Soy protein contains isoflavones, which mimic the action of estrogen. A diet high in soy protein can slightly lower levels of total cholesterol, LDL cholesterol, and triglycerides and raise levels of high-density lipoprotein (HDL) cholesterol. However, normal protein should not be replaced with soy protein or isoflavone supplements in an effort to lower cholesterol levels.

Soy foods and food products (eg, tofu, soy butter, edamame, some soy burgers) are likely to have beneficial effects on lipids and cardiovascular health because they are low in saturated fats and high in unsaturated fats.

**Garlic** — Garlic has not been proven to be effective in lowering cholesterol.

**Plant stanols and sterols** — Plant stanols and sterols may act by blocking the absorption of cholesterol in the intestine. They are naturally found in some fruits, vegetables, vegetable oils,

nuts, seeds, and legumes. They are also available in commercially prepared products such as margarine (Promise Active and Benecol), orange juice (Minute Maid Premium Heart Wise), and rice milk (Rice Dream Heart Wise) as well as dietary supplements (Benecol SoftGels and Cholest-Off).

Despite lowering cholesterol levels, there are no studies demonstrating a reduced risk of coronary heart disease in people who consume supplemental plant stanols and sterols. There is some evidence that these supplements might actually increase risk in the long term. These products need to be studied more before they can be recommended.

#### STICKING WITH TREATMENT

The treatment of high cholesterol and/or triglycerides is a lifelong process. Although medications can rapidly lower your levels, it often takes 6 to 12 months before the effects of lifestyle modifications are noticeable. Once you have an effective treatment plan and you begin to see results, it is important to stay committed to the plan. Stopping treatment usually allows lipid levels to rise again and increases your risk for heart attack, stroke, or other cardiovascular problems.

Most people who stop treatment do so because of side effects. However, there are a wide variety of medications available today, which should make it possible for most people to find an option that works for them. Talk with your health care provider if a specific medication is not working for you; he or she can recommend alternatives that are compatible with your lifestyle and preferences.

#### WHERE TO GET MORE INFORMATION

Your healthcare provider is the best source of information for questions and concerns related to your medical problem.

This article will be updated as needed on our web site (<u>www.uptodate.com/patients</u>). Related topics for patients, as well as selected articles written for healthcare professionals, are also available. Some of the most relevant are listed below.

**Patient level information** — UpToDate offers two types of patient education materials.

**The Basics** — The Basics patient education pieces answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a

general overview and who prefer short, easy-to-read materials.

<u>Patient education: High cholesterol (The Basics)</u> <u>Patient education: High triglycerides (The Basics)</u> <u>Patient education: Can foods or supplements lower cholesterol? (The Basics)</u>

**Beyond the Basics** — Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are best for patients who want in-depth information and are comfortable with some medical jargon.

<u>Patient education: High cholesterol and lipids (Beyond the Basics)</u> <u>Patient education: Heart attack recovery (Beyond the Basics)</u> <u>Patient education: Type 2 diabetes: Overview (Beyond the Basics)</u> <u>Patient education: Exercise (Beyond the Basics)</u> <u>Patient education: Diet and health (Beyond the Basics)</u>

**Professional level information** — Professional level articles are designed to keep doctors and other health professionals up-to-date on the latest medical findings. These articles are thorough, long, and complex, and they contain multiple references to the research on which they are based. Professional level articles are best for people who are comfortable with a lot of medical terminology and who want to read the same materials their doctors are reading.

**Hypertriglyceridemia** Low density lipoprotein-cholesterol (LDL-C) lowering after an acute coronary syndrome HDL cholesterol: Clinical aspects of abnormal values Heart transplantation: Lipid abnormalities after transplantation Kidney transplantation in adults: Lipid abnormalities after kidney transplantation Lipid abnormalities in thyroid disease Lipid management with diet or dietary supplements Low density lipoprotein cholesterol lowering with drugs other than statins and PCSK9 inhibitors Lipoprotein classification, metabolism, and role in atherosclerosis Lipoprotein(a) Management of cardiovascular risk (including dyslipidemia) in patients with HIV Measurement of blood lipids and lipoproteins Mechanisms of benefit of lipid-lowering drugs in patients with coronary heart disease Screening for lipid disorders in adults Statins: Actions, side effects, and administration Treatment of drug-resistant hypercholesterolemia Management of elevated low density lipoprotein-cholesterol (LDL-C) in primary prevention of

cardiovascular disease

<u>Management of low density lipoprotein cholesterol (LDL-C) in the secondary prevention of</u> <u>cardiovascular disease</u>

The following organizations also provide reliable health information.

• National Library of Medicine

(www.nlm.nih.gov/medlineplus/healthtopics.html)

• National Cholesterol Education Program of the National Heart, Lung, and Blood Institute of the NIH

(www.nhlbi.nih.gov/health/health-topics/topics/hbc)

• American Heart Association

(www.americanheart.org)

• The Hormone Health Network

(<u>https://www.hormone.org/diseases-and-conditions/hyperlipidemia</u>, available in English and Spanish)

• The Framingham Heart Study

(https://framinghamheartstudy.org/)

[<u>1-5]</u>

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#### **GRAPHICS**

#### Lipid lowering medications

Generic name	Brand name
Statins	
Atorvastatin	Lipitor
Fluvastatin	Lescol, Lescol XL
Lovastatin	Mevacor, Altoprev
Pitavastatin	Livalo
Pravastatin	Pravachol
Rosuvastatin	Crestor
Simvastatin	Zocor
PCSK9 inhibitors	
Alirocumab	Praluent
Evolocumab	Repatha, Repatha SureClick
Cholesterol absorption inhibitors	
Ezetimibe	Zetia
Bile acid sequestrants	
Cholestyramine	Prevalite, Questran, Questran Light
Colesevelam	Welchol
Colestipol	Colestid
Niacin (nicotinic acid)	
Niacin immediate release	
Niacin extended release	Niaspan
Fibrates	
Fenofibrate	Fenoglide, Tricor, Triglide, others
Gemfibrozil	Lopid

Brand names listed are for medicines available in the United States and some other countries.

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