

NON-STATINS

Written by Jeff Whittle, MD, MPH

There are a lot of drugs that affect cholesterol. Unfortunately, not all of them seem to prevent heart disease. In fact, when scientists first studied the effect of lowering cholesterol with drugs, some of the drugs seemed to INCREASE risk of death even though they lowered cholesterol. For example, men were given estrogen, and they had more heart attacks and blood clots than those who got a placebo. A drug called clofibrate lowered cholesterol even more than the estrogens, but it caused enough gall bladder problems that it is hardly ever used any more.

Several cholesterol drugs besides the statins have been proven to prevent heart attacks, at least in some people. No other drug has nearly as much proof as the statins, so doctors almost always reach for statins first. Nevertheless, there are several other drugs that most people agree will prevent heart attacks for at least some groups of people. These include:

Niacin

Niacin was the first drug proven to reduce deaths from heart attacks, at least in people who had already had one heart attack. It is still widely used. It is a B vitamin, but the doses we use for treating cholesterol are much, much higher than what occurs in your diet or in a standard vitamin pill. Side effects include a flushing sensation that comes on 15 minutes to an hour after the pill is taken. The flush can be reduced by taking niacin with food or by taking a baby aspirin just before the niacin. It also predisposes people to gout and can make blood sugar run higher. A very uncommon but more dangerous side effect is liver damage. Some of the over the counter versions of slow release niacin are particularly prone to causing this, so check with your doctor before you take niacin for your cholesterol.

Cholestyramine (Questran) and Colestipol (Colestid)

These are drugs that stay in the intestine and keep cholesterol from being absorbed. Unfortunately, they tend to cause constipation and are unpleasant to take. They are a powder that needs to be stirred into liquid then swallowed quickly, before the powder settles to the bottom. A variation called **colesevelam (Welchol)** is a pill and is easier to take, but quite expensive. On the plus side, cholestyramine was carefully studied back in the days when we did not have very many choices. It did reduce the number of heart attacks in people with high levels of bad cholesterol, so doctors are pretty confident that it is helpful, if the patient can stand to take it.

Gemfibrozil (Lopid)

Gemfibrozil is widely used because it is easy to take and has been available as a generic for many years. Like most cholesterol-lowering drugs, it can cause liver damage, but this

is very rare. It does not have a very big effect on bad cholesterol, but it does raise good cholesterol and also lowers triglycerides. Most importantly, it has been shown (in a VA-sponsored study) to reduce heart attacks in men with known heart disease who had low levels of good cholesterol. A newer cousin, **fenofibrate (Tricor)**, seems to have an even better effect on cholesterol and triglycerides, but so far it has not been shown to prevent heart disease. Tricor is still quite expensive, since there is no generic version.

Ezetimibe (Zetia)

Ezetimibe is the newest cholesterol-lowering drug. It is popular because it is an easy-to-take pill that has few side effects. It lowers the bad cholesterol pretty well—about 15% on average. This is nowhere near as high as the 50%-60% drop you can get with certain statins—for example atorvastatin (Lipitor) or rosuvastatin (Crestor)—but it is significant and it seems to add to the effect of the statin. So if you drop your bad cholesterol from 200 to 100 with Lipitor, you might be able to drop it all the way to 85 by adding ezetimibe. But there are no studies that show that ezetimibe decreases heart attacks, either alone or when added to a statin. So most doctors don't use it unless a person can't tolerate the cholesterol-lowering drugs that we are pretty sure reduce heart attacks. During 2007 and 2008, there was some publicity that perhaps Zetia could cause cancer, but more recent studies seem to show that it was a false alarm. It is probably pretty safe, but we don't know if it is useful for reducing heart attacks.

Fish Oil

Fish oil is one of the most popular treatments for cholesterol among patients, since you can get it without a prescription and it is generally safe. A very well known study of fish oil was done in Italy about 20 years ago among men who had had a heart attack. Those who took fish oil were less likely to have another heart attack than those who did not. Because of this study, many doctors recommend fish oil to their patients with heart disease, or are at risk of heart disease. However, the actual effect on cholesterol is very small, so it is not clear how fish oil works. Since the original study was done before there were treatments for cholesterol—and even before aspirin was routinely used—it is not clear that fish oil adds anything if someone is taking the more routine treatments. The bottom line is that it might help, but we don't know, so lots of people decide to take it.

Combinations

The simple truth is that no combination of drugs is widely accepted to work better than single drug therapy to reduce heart attacks and strokes, although there is pretty good evidence for the combination of niacin and certain statins. Unfortunately, our best non-statin drugs seem to interact with statins to make the risk of muscle injury get higher. This applies to gemfibrozil and niacin in particular. So when you start using multiple drugs for cholesterol, different doctors are likely to make different recommendations. Hopefully, your doctor will involve you with the decision, since it is a place where the science of medicine does not allow us to give clear answers.