

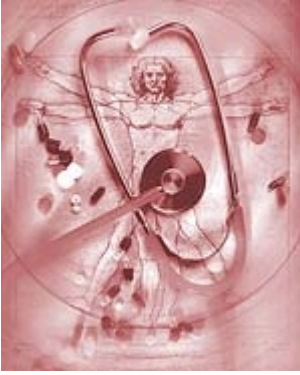
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REPORT

Cholesterol & Statin Drugs

Separating Hype from Reality

By William Davis, MD, FACC



You have seen the glitzy ads for cholesterol-lowering drugs. Advocates call the statin drugs the “new aspirin,” to be taken by everyone, every day. Here is the real story.

The pharmaceutical companies are waging a war.

The battleground: treating your cholesterol. This single sector of the health care market is reaping tens of billions of dollars in revenues for these multinational companies. They must be manufacturing great drugs. Or are they?

Supporters are so enamored of statin drugs that some have even proposed putting them in the water supply. Critics object that the statins are another thalidomide story for the drug industry, with ill effects not yet fully understood.

No matter what you believe, the statins—or more properly, HMG-CoA reductase inhibitors—are a huge success story. As one investment reporter put it, statin drugs “turn cholesterol into money.” Lipitor® alone brought Pfizer \$9.2 billion in 2003, more than the company earned over several years in the early 1990s.¹ Industry estimates put total annual spending on statins at more than \$22 billion. It is no wonder the pharmaceutical companies are hyping these drugs. The question is, what are we getting for our \$22 billion?

The Science Behind Statins

The statins are tailor-made to reduce cholesterol. They inarguably lower total cholesterol and LDL by 30-50%, and considerable clinical trial evidence proves it. No one disputes this point.

It is also well established that the risk of heart attack is reduced by around 30% over five years of treatment. In the widely publicized Scandinavian Simvastatin Survival Study, 4,444 participants took the simvastatin drug (Zocor®) or a placebo. Heart attacks and death decreased from 28% in the placebo group to 19% in the simvastatin group.²

The Scandinavian study and similar trials solidly bolster the argument that statins reduce LDL and thereby lower the risk of heart attacks in people who have suffered prior heart attacks, as well as in people at risk for a first heart attack. Over the years, some have voiced concern that statins might raise cancer risk, but the evidence solidly refutes that notion. In studies involving tens of thousands of participants, statins did not increase the risk of cancer.³⁻¹²

Unfortunately, the statins' success in lowering cholesterol has led many people to believe they represent a cure-all for cholesterol and heart disease risk. They are not, however, a cure-all. To get at the truth about statins, we need to dig deeper.

Statin Side Effects

The drug companies will tell you that the likelihood of side effects from statins is low: approximately 1-2% for serious muscle damage and liver dysfunction (usually represented as an increase in liver enzyme laboratory tests). Nevertheless, many physicians who prescribe these drugs—and their patients who take them—may tell you otherwise.

In many physicians' practices (including my own), muscle aches and weakness occur in approximately 30% of patients who take statins. The companies and clinical investigators roundly deny this, claiming that even people who take placebo experience muscle aches and weakness at a similar rate simply because humans are prone to such ailments.

Like many of my colleagues, I have hundreds of patients who, when they take a statin agent, develop annoying, sometimes incapacitating muscle aches and weakness that abruptly stop when they discontinue use of the drug, and return when drug use is resumed. The association appears clear.



Are the symptoms progressive and will they lead to some sort of irreversible damage? While there are no data to guide us, the recent observation that muscle biopsies reveal distinct structural abnormalities lends scientific credibility to the suspicion that the muscle aches are real. This observation and early research on statins demonstrating that they deplete cellular coenzyme Q10 suggest that CoQ10 replacement may have a role in treating these symptoms.

I have found the use of CoQ10 supplementation to be indispensable for these symptoms. A daily dose of 100 mg of CoQ10, preferably in an emulsified oil base rather than powdered form, relieves the symptoms of muscle aches and weakness in four of five instances, usually within five days of starting the supplement. These views are, of course, not supported by the drug manufacturers.¹³⁻¹⁵ (Should you suffer muscle aches or weakness, always discuss them with your doctor first, in the event that they do in fact represent serious muscle injury.)

The fact is, statins are pretty good drugs, considering that they are intended for long-term use. Imagine taking an antibiotic for 10 years! Even 10 days of antibiotic treatment can leave you with stomach aches, diarrhea, and opportunistic infections that emerge after elimination of the original infectious organism. In this respect, most people who take statin drugs year after year fare pretty well.

The fundamental flaws in focusing on cholesterol and statin agents are the perceptions that cholesterol identifies hidden heart disease and that lowering cholesterol is the way to a future free of heart attacks. Both perceptions are untrue.

Do Statins Cure Heart Disease?

A 30% reduction in death and heart attacks over five years is one thing. But can statins claim to cure coronary heart disease?

The answer is a clear “no.” The risks of heart attacks and death are reduced, not eliminated, by treatment. In other words, for every 100 people who participated in the Scandinavian study on Zocor®, 9 heart attacks were prevented (reducing the number of those suffering a heart attack from 28 to 19). Nevertheless, 19 heart attacks still occurred. Why does lowering LDL with statin drugs result in such limited success? Are there other ways to reduce the risk of heart attacks so that the 19 of 100 people destined to suffer a heart attack can avoid one?

We must step back for a moment and recognize that statin therapy for high cholesterol is just one piece of a bigger picture. Heart disease has many other risk factors, and there are many other ways to reduce risk and identify people at risk.



Lowering Cholesterol Naturally

It may be better to regard statin therapy as a solution only after other natural alternatives have been exhausted. The problem is that many people are unaware of many of the strategies that work.

For example, if you follow the American Heart Association's diet, you might enjoy a 7% drop in cholesterol.¹⁶ That is certainly an improvement, but still not good enough. If you follow an ultra low-fat diet (deriving no more than 10% of your total calories from fat), your cholesterol may drop, but you will also reduce HDL and increase triglycerides, sometimes dramatically.¹⁷ The net effect can be an increased risk of heart disease and diabetes.

The following are some healthy strategies that truly help lower total cholesterol and LDL.

Raw almonds. A handful (1/4-1/2 cup) of raw almonds daily not only lowers cholesterol, but also lowers the dreaded genetic risk factor for coronary disease, lipoprotein(a). Almonds also blunt abnormal spikes in blood sugar after eating and help prevent diabetes. They are tremendously filling and are great for sugar addicts who need to snack, since almonds take the edge off your sweet tooth.^{18,19}

Soy protein powder. Soy products are a source of many beneficial substances, such as isoflavones. Eating soy protein powder (sold in one-pound canisters) is a tremendous way to reduce cholesterol through soy's tendency to suppress the liver's production of cholesterol particles. Even the FDA, ordinarily charged with reviewing drugs, has endorsed the value of soy protein powder. Three tablespoons a day in fruit smoothies, protein shakes, or blended with yogurt or other foods will lower LDL by around 12%.^{20,21}

Pectin. Found in apples and the rinds of citrus fruits, pectin is a natural fiber that lowers cholesterol; the same foods also provide flavonoids that yield broad health-promoting effects. Pectin is also available in powdered form (for example, Life Extension's Apple Pectin Powder).^{22,23}

Flavonoids. A large and diverse collection of naturally occurring substances that lower cholesterol, flavonoids provide antioxidant benefits, lower blood pressure, possess anti-inflammatory properties, and prevent cancer. Sytrinol™, a new, patented complex of citrus bioflavonoids is a convenient way to lower LDL by as much as 15% while obtaining all the other benefits of

Tocotrienols. Isolated vitamin E, or d-alpha tocopherol, has shown disappointing results in lowering the risk of heart attacks. Yet a growing body of research suggests that the four tocotrienols (which are cousins to the vitamin E family) lower cholesterol and have potent chemopreventive effects, much like flavonoids.^{27,28}

Soluble fibers. Among the best soluble fibers is oat bran. Containing twice as much beta-glucan as oatmeal, oat bran is a versatile source of soluble fiber that can lower cholesterol by around 10-15% while also reducing blood sugar and providing roughage for bowel health. Beta-glucan is also available as a nutritional supplement. Starchy beans such as black, pinto, Spanish, red, and kidney beans provide significant soluble fiber that can lower LDL. Consuming one-half cup of these beans each day in one or more meals is an easy way to lower cholesterol. Note that fibers like the wheat fiber found in whole wheat bread and raisin bran cereals do nothing for your cholesterol.²⁹⁻³¹



Phytosterols. These soybean derivatives lower cholesterol by 12-15%.^{32,33}

PGX™ A relatively small amount (one to three grams before each meal) of this highly viscous fiber blend of glucomannan, xanthan, and alginate may help lower LDL and total cholesterol. Even more important may be its ability to limit sugar absorption and the subsequent after-meal insulin spike. High after-meal blood glucose and insulin levels increase the risk of heart attacks significantly.³⁴⁻⁴³ When study subjects took just one gram of glucomannan before each meal, total cholesterol was reduced by 21.7 mg/dL and LDL was lowered by 14 mg/dL.^{44,45}

What cholesterol levels should you aim for? There is broad consensus that, in the absence of known heart disease, an LDL level below 100 mg/dL is desirable. In our program for coronary plaque regression, once plaque is identified, we aim for an LDL of 60 mg/dL or less. We achieve this by using statins when necessary but after natural alternatives have been attempted.

HOW TO SAFELY TRANSITION FROM STATINS TO NATURAL THERAPIES

If your doctor advises you to begin taking a statin drug, suggest a lower dose or a delay in initiation of the drug until you have had two to three months to try natural cholesterol- and LDL-lowering agents. Patient involvement in treatment decisions is commonplace today, and most physicians will work with you. A rough rule of thumb: adherence to a low-fat, high-fiber diet (that eliminates processed foods), along with some of the nutritional supplements discussed in this article, will lower LDL cholesterol by as much as 30%. Keep this in mind when starting your program. For example, if your LDL is a very high 250 mg/dL, nutritional therapy alone will not lower your LDL to a safe target level. In this case, a statin agent is a necessity and should be used along with natural therapies.

To illustrate situations that are more common: say your LDL is 140 mg/dL and your target LDL is 100 mg/dL (the "ideal" level in the absence of known heart or vascular disease, according to the national Adult Treatment Panel III). You could suggest to your doctor that a trial of raw almonds, soy protein powder, psyllium seed, oat bran, and a preparation like Sytrinol™ might be attempted first. A follow-up lipid panel to assess your results could be used two to three months later to decide whether a more intensive diet and supplement program is in order or a statin drug is necessary. Alternatively, if your LDL is 190 mg/dL and your target is less than 70 mg/dL because you have a history of coronary disease, you will likely need the statin agent, but include the supplements to minimize your need for the statin and to perhaps get by using a lower dose of it.

If you are already taking a statin agent, do not stop using the drug. Doing so abruptly carries a small but real risk of activating previously silent coronary plaque. Instead, add the natural supplements while you are taking the statin agent. The only significant interaction between supplements and statin drugs is with red yeast, which contains tiny amounts of several naturally occurring statins and can add to the liver and muscle side effects of the statin. Do not use red yeast and a statin agent without discussing it with your physician.

Anyone taking a statin drug should have a lipid panel (including total cholesterol, LDL, HDL, and triglycerides) and liver enzymes (ALT and AST) every three to six months. All of these tests are included in Life Extension's comprehensive CBC/Chemistry blood panel.

You and your doctor can then discuss whether the results produced through dietary modifications and supplement use justify lowering the dose of or even discontinuing the statin drug. This makes the transition smooth and safe, while providing precise feedback on the success of your dietary modifications and use of supplements.

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What the Doctor Does Not Tell You

Cholesterol is nothing more than one of many risk factors for coronary heart disease, and just one of the contributors to the silent growth of plaque. Lowering cholesterol is still a good idea, but should be viewed in the proper perspective. Cholesterol does not reliably identify all people with hidden heart disease, nor does lowering it cure you of heart disease.

Let's dispel some popular statin and cholesterol myths:

MYTH 1

"High cholesterol (and LDL) is the number-one cause of heart disease in this country."

Dead wrong. High cholesterol is among the risk factors for heart disease, but is not the leading risk factor. The most prevalent risk factor is low HDL, along with small LDL particles, which commonly occur together. In fact, of every 100 people with coronary heart disease, 60-70 will have low HDL and small LDL particles, but fewer than 30 will have high LDL. If this is the case, why do we not hear more about low HDL and small LDL particles? The answer is simple: because treating these is not as profitable for drug companies. But just wait—when a profitable drug becomes available to treat this more prevalent risk factor for heart disease, we can expect to hear about an "epidemic" that will justify billions of dollars in new drug expenditures.⁴⁶⁻⁴⁹



What qualifies as low HDL? National guidelines say it is a level of less than 40 mg/dL for men and less than 45 mg/dL for women.⁵⁰ In fact, a level of less than 60 mg/dL is probably very significant.⁵¹

HDL is already a standard measure in everyday cholesterol panels. Small LDL particles, on the other hand, need to be measured specifically. The medical world focuses on statin therapy for LDL, while the most prevalent risk factor for heart disease goes untreated in the great majority of cases.

MYTH 2

"If I take a statin agent, I won't have a heart attack."

This is simply untrue. Lowering cholesterol (even to rock-bottom levels) reduces, but does not eliminate, the risk of heart attacks. Many heart attacks still occur in people with low cholesterol levels, whether or not they take cholesterol-lowering drugs.⁵² We must consider that there are other risk factors for heart disease besides cholesterol, such as small LDL particles, low HDL, lipoprotein(a), homocysteine, and high insulin levels. Results from the most recent National Health and Nutritional Survey show that 47 million US adults have metabolic syndrome (low HDL, high triglycerides, high blood pressure, excess abdominal fat), which substantially heightens the risk of heart disease even in the presence of low cholesterol levels.⁵³

MYTH 3

"I feel fine and my stress test was normal. My doctor says I don't have heart disease."

This is among the most widely propagated fallacies spread by many primary care physicians and even cardiologists. First, lack of symptoms should not be reassuring, as most heart disease is silent—without symptoms and undetectable by conventional means such as electrocardiograms and cholesterol testing. Second, stress testing is a miserable failure for screening asymptomatic people. Most future deaths and heart attacks, in fact, occur in people with normal stress tests (when symptoms are not present). This is why you will hear about your neighbor passing a stress test on Tuesday, only to drop dead from a heart attack on Thursday. The net result of this misperception is that most future heart-attack victims are walking around now, feeling fine and unaware of their risk.⁵⁴ Cholesterol can be high, low, or in between, but all too frequently fails to shed light on this murky situation.



Giving the Paradigm Shift a Shove

Really lowering your risk for heart disease requires a dramatic shift in focus. Cholesterol is one way to reduce risk, but there are others as well.

Let us discuss the most prevalent risk factor for heart disease: low HDL and small LDL particles. Testing for HDL is included in any standard lipid (or cholesterol) panel, along with testing for LDL, total cholesterol, and triglycerides. Small LDL particles, on the other hand, need to be specifically measured.

Generally, the lower your HDL level is below 60 mg/dL, the more likely you are to also have small LDL particles, and the greater your risk for hidden coronary disease. Both abnormalities are also strongly associated with

insulin resistance (i.e., an inability to respond to your own insulin) and risk for diabetes. Low HDL and small LDL particles respond to the same treatments and lifestyle changes, and the risks associated with each are hugely magnified by excess weight. With 47 million adults with metabolic syndrome in the US today, low HDL and small LDL are epidemic.

Weight loss (if you are overweight) is the most powerful and healthy way to correct the entire picture. Losing even the first 10 pounds of excess weight can raise HDL, suppress the small LDL pattern, and enhance insulin response. Some people will, however, require dramatic weight loss before full correction is seen, depending on genetic factors and their amount of excess weight. Carbohydrate restriction (eliminating or minimizing flour products such as pasta, bread, cookies, cakes, and other processed foods) is an effective way to lose some weight when you have these patterns.

Among supplements, white bean extract is a great way to accelerate weight loss if you have the low HDL and small LDL pattern. White bean extract blocks intestinal carbohydrate absorption by 66% with minimal side effects, unlike its prescription counterpart (which causes abundant gas).^{55,56} Taking 1000 mg twice a day with meals can lead to 3-7 pounds lost in the first month.



Calcium pyruvate (2500 mg twice a day) is another weight-loss accelerator that is safe and free of ephedra. Calcium pyruvate has a two-pronged benefit. First, it accelerates weight loss (by a poorly understood mechanism), usually resulting in a few extra pounds of weight loss over several weeks. Second, it also has the interesting property of enhancing exercise by making it easier and less taxing, thus enabling you to exercise longer and harder with easier recovery. Exercise “highs” are achieved more easily with calcium pyruvate supplementation.⁵⁷

Supplementing with niacin (vitamin B3) is a direct, effective way to raise HDL and lower small LDL. Doses of up to 500 mg daily can be taken safely; higher doses of 1000 mg or more should be taken under medical supervision, as these occasionally result in liver dysfunction, elevation of blood sugar, stomach intolerance, and gout. Niacin typically causes a hot flush (usually of the chest, neck, and face) that is harmless though annoying. The flush usually can be inhibited by drinking plenty of water, taking niacin with solid food, and avoiding spices and alcohol when you take the tablet.^{58,59} Always take folic acid and vitamin B12 with niacin to protect against disruption of healthy methylation patterns. Folic acid and vitamin B12 also help to lower homocysteine, another important piece of the atherosclerosis puzzle.

Fish oil can also raise HDL and lower small LDL when taken in the form of a concentrated omega-3 preparation that provides at least 1400 mg of EPA and 900 mg of DHA per day. Fish oil has tremendous benefits beyond its lipid effects, including reduced mortality from heart attack, anti-inflammatory and mood-improving effects, and reduced cancer risk.^{60,61}

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Conclusion

Statin drugs do indeed help to lower cholesterol and LDL. Nevertheless, cholesterol reduction using a statin agent is far from the final word on reducing heart disease risk, as other risk factors for heart disease, such as low HDL and small LDL particles, are both independent of LDL and far more prevalent than high cholesterol. A number of interesting nutritional strategies are available to address total cholesterol, LDL, low HDL, and small LDL particles. The pattern of low HDL and small LDL particles responds powerfully to weight loss, as well as to treatment with supplements such as niacin and fish oil. These simple approaches will provide a far more effective approach to heart health than a reflex treatment of cholesterol with medication.

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Editor's note: The content of this article and the interpretation of study results are those of Dr. Davis. A consensus has yet to be reached concerning when statin drugs should be prescribed. We published this article because it articulates both sides of this issue very well.

*To read our lengthy protocol on preventing atherosclerosis, refer to the *Cardiovascular Disease: Comprehensive Analysis* chapter in *Life Extension's Disease Prevention and Treatment* book.*

Lipoproteins and the VAP™ Test

“My doctor said my cholesterol was fine... So why did I have a heart attack?”

If you want to know whether a heart attack is in your future, knowing your cholesterol level may not be enough.

An excessive quantity of small LDL particles is the most common risk factor contributing to heart-attack incidence in the US—far more common, in fact, than high cholesterol. It is a hidden danger that can be uncovered only when measured specifically. You can have small LDL particles with high, low, or in-between levels of cholesterol. Small LDL particles triple the risk of heart attacks. When they occur alongside other abnormalities, such as high total cholesterol or high C-reactive protein (a measure of inflammation), the risk of heart attacks increases sixfold.⁶²

Small LDL particles are a far more destructive force than their larger counterparts. They are like finely tuned weapons designed to wreak maximum damage. Smaller particles are better able to penetrate the cellular barrier and be deposited in the artery walls, creating atherosclerotic plaque. They also persist longer in the circulation, giving them greater opportunity to cling like little magnets to tissues within the arterial walls. Once residing in the arterial wall, small LDL particles are more prone to oxidation, stimulating the release of inflammatory and adhesive proteins.⁶³

The growing recognition of small LDL particles as a common and potent hidden source for heart disease has led to the availability of specialized tests from several laboratories. Life Extension is now making one such technology available through its VAP™ (Vertical Auto Profile) test. VAP™ is a method of separating blood proteins into component lipoproteins, or lipid carrying proteins. Dr. Jere Segrest, director of the Atherosclerosis Research Unit at the University of Alabama-Birmingham, developed the test, which reveals much more than simple cholesterol panels.

After you submit your blood for testing, a VAP™ report will be returned to you. LDL particle size is reported in a readily understandable format as pattern A (the less harmful large LDL) or pattern B (the dreaded small LDL). Intermediate-sized LDL particles are reported as pattern A/B. Pattern B poses maximum risk; pattern A/B poses an intermediate level of risk.

What does having pattern B, or an excess of small LDL particles, tell you? This one measurement holds a world of information. Not only is your risk for heart attacks three to six times higher, but also you are more resistant to insulin and more likely to develop the metabolic syndrome or even diabetes if you become overweight.⁶⁴ It also tells you that a low-fat diet (deriving less than 20% of total calories from fat) may paradoxically heighten your risk for heart disease.⁶⁵

Knowing that you are pattern B also points you toward treatment strategies that can effectively correct this hidden source of risk. Small LDL is very responsive to niacin (vitamin B3) treatment, usually disappearing with doses of 500-1000 mg per day (though long-term treatment will be necessary). Weight loss can be a very powerful treatment strategy if you are overweight. Fish oil in doses providing at least 1400 mg of EPA and 900 mg of DHA per day helps by reducing triglyceride levels, a necessary ingredient to create small LDL particles. Dietary strategies that slow or reduce sugar release (i.e., lower glycemic index) can be helpful, including eating high-fiber foods or supplements such as flaxseed, glucomannan, oat bran (beta-glucan), psyllium seed, raw nuts like almonds and walnuts, and the starch blocker white bean extract.

The VAP™ panel directly measures LDL. Many people are surprised to learn that the LDL reported to you by your doctor or hospital is calculated, not measured, and is commonly inaccurate by 30% or more.⁶⁶ Lipoprotein tests like VAP™ can be crucial, and perhaps lifesaving, for people who have already been diagnosed with coronary or vascular disease. It is not uncommon for heart-attack victims to have normal cholesterol levels and be told that there is no identifiable cause for their disease. VAP™ testing uncovers one, if not several, hidden risk factors in over 90% of people with heart disease.

The information provided through VAP™ lipoprotein testing provides far greater insight into heart disease risk factors than the offered by standard cholesterol testing, which will enable you to take greater control over your risk of heart disease.

The full VAP™ test measures:

Direct Measured Lipids	Targets of Therapy	Risk Factors	Clinical Considerations
<ul style="list-style-type: none"> • Low-density lipoprotein (LDL) • High-density lipoprotein (HDL) • Total very low-density lipoprotein (VLDL) • Total cholesterol • Triglycerides 	<ul style="list-style-type: none"> • Non-HDL cholesterol (LDL + VLDL) • Probable metabolic syndrome 	<ul style="list-style-type: none"> • Lipoprotein(a) • Remnant lipoprotein (IDL + VLDL 3) • LDL density pattern 	<ul style="list-style-type: none"> • HDL-2 • HDL-3 • Total HDL • VLDL 1+2 • VLDL 3 • Total VLDL • Intermediate-density lipoprotein (IDL) • Total cholesterol/HDL ratio

If your doctor is unfamiliar with or unwilling to order the VAP™ test and other tests discussed in this article, please call **800-208-3444** to order one yourself. VAP™ is normally a very expensive test, which is why it is not widely used. The retail price of the comprehensive VAP™ panel is ~~\$246.67~~. The test is available to Life Extension members for **\$185**.

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