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REPORT

Do Your Really Need Maximum-Dose Lipitor®?

By Jay S. Cohen, MD (Introduction by William Faloon)

In an effort to boost profits, Pfizer is convincing doctors to prescribe the strongest, riskiest, and most expensive dose of Lipitor® to more and more patients—despite concerns about its safety and efficacy.

In recent years, the use of "statin" cholesterol-lowering drugs has elicited tremendous controversy. Doctors who believe in natural approaches to disease prevention have suggested that statin drugs are poison that should be avoided altogether. Pharmaceutical company-influenced cardiologists, on the other hand, have stated that virtually everyone over age 40 should be on a statin drug.

Life Extension advocates a common-sense approach to maximize benefit and minimize risk (and cost) by selecting a statin drug dose that fits your individual needs. We believe that no one should take a statin drug unless warranted by both clinical history (such as being at high risk for heart attack) and a blood test documenting unacceptable cholesterol-LDL levels.

In this article, one of the world's foremost experts on statin drugs, Jay S. Cohen, MD, reveals how today's sordid system works against the medical and economic interests of patients—and what you can do to avoid being victimized.

If your doctor recommends the maximum, 80-mg dose of Lipitor® for you at your next visit, do not be surprised. Better yet, be prepared for it, because Pfizer has launched an intensive marketing campaign to convince doctors to prescribe maximum-dose Lipitor® to everyone at risk of a heart attack or stroke. Many doctors are following Pfizer's lead, yet Pfizer's own studies raise serious concerns about the safety of maximum-dose (also called "intensive-dose") Lipitor®. Here is the story of maximum-dose Lipitor ®—including its marketing, the recent studies, and what you should know and do.

THE MAXIMUM-DOSE LIPITOR® CAMPAIGN BEGINS

Lipitor® (atorvastatin) is the best known of a popular group of cholesterol-lowering drugs called statins. The statin class of drugs includes Lipitor® (atorvastatin), Zocor® (simvastatin), Pravachol® (prava-statin), and others (see Table 1). Lipitor® is the best-selling prescription drug in the United States and worldwide. In 2005, Pfizer sold $8.4 billion worth of Lipitor® in the US and $12.2 billion worldwide; still, the company is angling to sell even more. The main thrust of Pfizer's current marketing campaign is to persuade doctors to prescribe more maximum-dose Lipitor®.

The campaign began in earnest in 2005, after a study of maximum-dose Lipitor® for reducing heart attacks was published in the *New England Journal of Medicine*.[1] The study, known as the Treating New Targets (TNT) study, was funded by Pfizer, and it received glowing coverage from newspapers and news programs that described maximum-dose Lipitor® as if it was a medical breakthrough. Unfortunately, it was not. Yet the coverage made a strong impression, and so began the campaign to persuade doctors to medicate ever more patients with the most powerful, expensive dose of Lipitor® available.

As doctors prescribe more maximum-dose Lipitor® than ever, serious questions remain about maximum-dose Lipitor®. Is it effective? Is it worth the high cost? Is it safe? Statins are important drugs. Some people require strong statin treatment. Yet the great majority of people with elevated cholesterol do not need high doses of strong statins. The risk of side effects is greater with stronger doses than with milder ones. There is no scientific basis for using more medication than needed for any medical condition, and this applies particularly to the use of statin drugs. Treatment should be individualized. Safety should be emphasized. Overmedication should be avoided. Side effects should be prevented. These are fundamental principles of medical science. The indiscriminate, widespread, "shotgun" use of maximum-dose Lipitor® violates all of them.

HOW EFFECTIVE IS MAXIMUM-DOSE LIPITOR®? THE TNT HEART STUDY

In the 2005 TNT study, 10,001 people with stable heart disease received either maximum-dose 80-mg Lipitor® or a standard

dose of 10-mg Lipitor® daily.[1] Maximum-dose Lipitor® reduced levels of harmful low density lipoprotein (LDL) to an average of 77 mg/dL. This represented a substantial reduction in LDL. In comparison, standard-dose Lipitor® reduced LDL to an average level of 101 mg/dL, which was also a good result.[1]

Over the five years of the study, 434 people (8.7%) in the 80-mg group experienced another cardiovascular incident (such as a heart attack or stroke) versus 548 people (10.9%) in the 10-mg group. This was an improvement of 2.2%, which meant 104 fewer cardiovascular incidents with maximum-dose Lipitor® compared with standard-dose Lipitor®. Twenty-nine fewer deaths from cardiovascular causes (126 versus 155) occurred with maximum-dose Lipitor®. These were also good results. However, this improvement in deaths was completely offset when 31 more people taking maximum-dose Lipitor® died from other causes. Overall, maximum-dose Lipitor® did not reduce the number of deaths in comparison with low-dose Lipitor®. In fact, the total number of deaths slightly increased in those taking maximum-dose Lipitor®. This startling fact means that maximum-dose Lipitor® increased the risk of death due to non-cardiovascular causes! This included 10 more deaths from cancer in the maximum-dose Lipitor® group versus the 10-mg group.[1]

TABLE 1. STATIN MEDICATIONS

BRAND NAME	GENERIC NAME	CHOLESTEROL- LOWERING POTENCY	GENERIC AVAILBLE
Lipitor®	Atorvastatin	High	No
Zocor®	Simvastatin	High	Yes
Crestor®	Rosuvastatin	High	No
Pravachol®	Pravastatin	Moderate	Yes
Mevacor®	Lovastatin	Moderate	Yes
Lescol®	Fluvastatin	Moderate	No

Was there a reason that people taking maximum-dose Lipitor® died more often from other causes? The study did not address this critical question. Yet Dr. Bertram Pitt, the expert who wrote the editorial accompanying the maximum-dose Lipitor® study in the *New England Journal of Medicine pointed out the obvious: "Although the risk of coronary heart disease events was reduced by treatment with 80 mg of atorvastatin per day, the overall risk of death was not… it is a matter of concern."*[2]

After reviewing the results of the study, Dr. Pitt advised caution: "*We need further reassurance as to the safety of this approach*."[2] Dr. Pitt suggested that if doctors want to achieve very low LDL levels with their patients, they should do so with methods other than maximum-dose statins.

The TNT was an important study because it was the first to test the hypothesis that a LDL of 70 mg/dL is better than a LDL of 100 mg/dL in people with heart disease. Although the results were not reassuring, Pfizer found enough in this study to launch its campaign to convince doctors to prescribe maximum-dose Lipitor to more patients. To boost the campaign, another study of maximum-dose Lipitor® was published a year later.

HOW EFFECTIVE IS MAXIMUM-DOSE LIPITOR®? THE STROKE STUDY

STATIN DRUGS: WHAT YOU NEED TO KNOW

- The cholesterol-lowering statin drugs have become a major topic of debate in recent years.
- Recent studies have shown that high-dose Lipitor® helps prevent secondary heart attack and stroke, leading some experts to recommend aggressive cholesterol-lowering strategies. A closer look at the data, however, reveals that while high-dose Lipitor® did decrease the risk of death due to heart attack or stroke, it was associated with an increased risk in death due to non-cardiac causes.
- These alarming findings about high-dose Lipitor® highlight the need for individualized strategies to protect cardiovascular health.

- To maximize health while minimizing adverse effects, work with your doctor to find the lowest dose of statin medication needed to achieve optimal lipid levels. Also consider incorporating nutritional strategies such as fish oil and coenzyme Q10 in order to maximize your heart health and reduce your need for medications.

In August 2006, the *New England Journal of Medicine* published a large study of maximum-dose Lipitor® for people with a recent stroke. Despite results that were barely better than placebo, the authors of this Pfizer-funded study concluded that all people who suffer a stroke should receive maximum-dose Lipitor®.[3] Why would the authors suggest such an extreme, unproven, expensive approach? Perhaps it was because every one of the eleven authors was either a Pfizer employee or a Pfizer consultant.

After all, medicating large numbers of stroke patients with maximum-dose Lipitor® would boost sales by billions of dollars. Each year, approximately 15 million people worldwide suffer a stroke. About 5 million of these strokes occur in people in affluent countries, including 700,000 strokes in the US. Overall, about 5.4 million Americans and 55 million people worldwide have had a stroke.[4,5] If it could be shown that maximum-dose Lipitor® could reduce the risk of another stroke in people who had already sustained one, the marketing opportunity was huge.

In the study of maximum-dose Lipitor® for stroke, all of the 4,731 subjects had experienced a recent stroke. Of these, 2,365 people received maximum-dose Lipitor® and 2,366 received placebo. Of those receiving maximum-dose Lipitor®, 11.2% had another stroke. Of those receiving placebo, 13.1% had another stroke. Thus, maximum-dose Lipitor® reduced the frequency of a second stroke by 1.9%, a modest improvement over placebo. This result did not support the widespread use of maximum-dose Lipitor® for all stroke patients.[3] Instead, it suggested the need for further studies to confirm that the improvement was due to maximum-dose Lipitor® rather than chance.

The stroke study revealed other problems with maximum-dose Lipitor®. One of them was a serious increase in hemorrhagic strokes, which are characterized by bleeding in the brain. Fifty-five people taking maximum-dose Lipitor® sustained a second hemorrhagic stroke, whereas only thirty-three people taking placebo sustained a second hemorrhagic stroke. In effect, the incidence of second hemorrhagic strokes increased 67% with maximum-dose Lipitor® compared with placebo.[3] This raises the question of whether maximum-dose Lipitor® was responsible for the increase in hemorrhagic strokes, and it is a warning to doctors to be cautious and selective in prescribing maximum-dose Lipitor® to stroke patients.

Another worrisome finding was that maximum-dose Lipitor® did not reduce the number of deaths overall. The drug reduced the number of fatal strokes, but this benefit was offset by an increased number of deaths from other causes. Two-hundred-sixteen of the 2,365 (9.1%) people taking maximum-dose Lipitor® died. Two-hundred-eleven of 2,366 (8.9%) people taking placebo died. Overall, the total number of deaths was higher with maximum-dose Lipitor®.[3] In other words, the risk of death among these subjects was slightly greater with the Lipitor® than with placebo.

This finding was similar to that of the 2005 TNT heart study. Both studies showed that maximum-dose Lipitor® increased deaths from other causes. This was a very disturbing finding. It was so troubling that when the 2005 study had been published, Dr. Pitt warned against the use of maximum-dose Lipitor®. Unfortunately, with the publication of the 2006 stroke study, similar words of caution were not seen. Instead, the author of the accompanying editorial, who was also a consultant to Pfizer, called for the widespread use of Lipitor® in stroke patients.[6]

My view is that Dr. Pitt's warning still stands. Until medical science can explain why so many people in these studies died from other causes while receiving maximum-dose Lipitor®, the safety of this medication should not be assumed.

LIVER INJURIES—A STRONG WARNING SIGN

Side effects from statin drugs can be serious. Side effects include muscle pain, muscle degeneration, joint pain, memory impairment, depression, gastrointestinal discomfort, kidney injury, kidney failure, and liver injury.[7,8] These and other side effects may be mild or severe. According to Dr. William Davis, a cardiologist, "The drug companies will tell you that the likelihood of side effects from statins is low. Nevertheless, many who prescribe these drugs—and their patients who take them—may tell you otherwise. 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."[9]

The risk of liver injury with statin drugs is dose-related.

The risk of liver injury with statin drugs is also dose-related. Liver injuries with statins can be dangerous. Cases of liver failure and death with statin drugs have been reported to the FDA. In the TNT heart study, only nine subjects developed significant liver injury (liver enzymes more than three times normal on two consecutive measurements) with low-dose Lipitor®, yet such findings occurred in 60 people receiving maximum-dose Lipitor®. In the stroke study, 51 people developed liver injury with maximum-dose Lipitor®, while only 11 developed liver injury with placebo.[1] These are worrisome findings.

Severe liver injury has led to the withdrawal of several drugs—after scores of people died from liver failure. When the drug Rezulin® (troglitazone) was introduced in 1997, we were told that the drug caused modest liver enzyme elevations in a small percentage of patients. Soon, cases of liver failure and death with Rezulin® were reported to the FDA. In 1999, we learned that the manufacturer had withheld vital information from doctors and patients about the drug's liver toxicity. Subjects receiving Rezulin® during studies had developed dangerous elevations of liver enzymes.[10,11] By the time Rezulin® was pulled from the market in 2000, nearly 100 people had died.

Is maximum-dose Lipitor the new Rezulin®? It could be, but it is difficult to tell. In the heart and stroke studies, the authors withheld information about the degree of liver injuries occurring in people taking maximum-dose Lipitor®. We do not know whether the liver injuries were mild or severe.

In order to obtain this vital information, I published a letter expressing concern about the high number of liver injuries occurring with maximum-dose Lipitor® in the stroke study. I requested information on the actual liver enzyme elevations that occurred in individuals receiving the drug.[12] Unfortunately, this information was still not released.

This has raised my level of suspicion. Why would the authors refuse a simple request for information about the elevations in liver enzymes that occurred in their study? One would think they would be eager to show that maximum-dose Lipitor® is safe. Why the secrecy? If the authors are reluctant to reveal the data, why? What does it show? Interestingly, this is very similar to what occurred with Rezulin®. The key information was kept from the public for years until the FDA stepped in—two years too late for some unfortunate people.

Did the FDA learn the lesson with Rezulin®? Will it now investigate the safety of maximum-dose Lipitor® before people are harmed? Not likely. Recent investigations reveal that the FDA's ability to identify risks and ensure drug safety is severely compromised. The FDA pours far more money and manpower into rushing new drugs to the marketplace than into assuring the safety of our medications. So should we expect the FDA to investigate when an intensely marketed, highly potent, maximum-dose drug causes significant increases in liver injuries in two major studies? In a healthy system, yes. In the current system, no.

Until a thorough investigation is done, we must assume that maximum-dose Lipitor® may have the potential to cause serious, life-threatening liver injuries. Doctors should prescribe maximum-dose Lipitor® with appropriate care, checking patients' liver enzyme levels regularly.

PROFITS OVER SAFETY?

When you have been a doctor for a while, you begin to see how things work in the medical-pharmaceutical system. For instance, it is patently obvious that when a drug company undertakes large, expensive studies for already-approved drugs, it has an agenda. With maximum-dose Lipitor®, Pfizer's agenda seems clear: push the drug for as many heart and stroke patients as possible. Expand the market. Increase sales. Ignore the safety concerns. Dismiss the higher risk of serious side effects. Downplay the questionable benefits and high costs. Emphasize the positive, disregard the negative. Ply doctors with samples so they can get patients started—and then stuck—on the product. Remember, ultimately, it's not about science; it's about sales.

If this sounds cynical, consider what Pfizer itself reported about Lipitor® sales, according to Bloomberg News:

"Pfizer said Wednesday that it had increased second-quarter revenue from its Lipitor® cholesterol pill by persuading doctors to prescribe more expensive doses of the drug, the best-selling prescription medicine. Pfizer, the world's biggest drug maker, said it sent thousands of sales people to doctors' offices to tout studies showing that higher doses cut the risks of heart attack, stroke and death better than do other cholesterol drugs... The number of patients taking the highest doses of Lipitor® in June rose by more than 10% compared with May, analysts said."[13]

This was the agenda all along: publish large studies, obtain favorable news coverage, and then send in the sales reps. The strategy seems to be working. While sales of many drugs have been dropping, sales of maximum-dose Lipitor® are up. In 2005,

Lipitor® generated 40% of Pfizer's profits, and the 2006 numbers will probably be higher.

Why push maximum-dose Lipitor® instead of a lower dose? Because the 80-mg pill is more expensive than lower doses. A 80-mg pill of Lipitor costs about $3.93 per day, 34% more than the 10-mg pill, which costs $2.61 per day. The $1.32 extra per pill of maximum-dose Lipitor® adds up,13 especially when one considers that the active ingredient (atorvastatin) costs relatively nothing. A year's supply of 10-mg Lipitor® costs about $954. A year's supply of maximum-dose, 80-mg Lipitor® costs more than $1,400. Now multiply this by a few million patients, and it adds up to billions.

THE UNDERLYING STRATEGY

TABLE 2. STATIN DRUGS: COST COMPARISONS

By purchasing generic statin medications from the Life Extension Pharmacy, you can save a tremendous amount of money. The price comparisons below show how much less costly it is to obtain statin drugs through the Life Extension Pharmacy:

Zocor® (simvastatin) 20 mg, 90 tablets

Zocor® (brand name): $405.09 (Walgreens)

Simvastatin (generic): $249.69 (Walgreens)

Simvastatin (generic): $20.15 **(Life Extension Pharmacy)**

Pravachol® (pravastatin) 40 mg, 90 tablets

Pravachol® (brand name): $435.59 (Walgreens)

Pravastatin (generic): $203.89 (Walgreens)

Pravastatin (generic): $36.96 **(Life Extension Pharmacy)**

Lipitor® (atorvastatin) 80 mg, 90 tablets

Lipitor®: $353.89 (Walgreens)

Lipitor®: $327.95 (Life Extension Pharmacy)

No generic available

Why has Pfizer launched the maximum-dose Lipitor® campaign now? Because its top competitor, Zocor® (simvastatin), recently became available as a lower-cost generic drug.

For years, while Lipitor® has been the best-selling drug in the world, Zocor®'s sales were close behind. Now that Zocor® is available as a lower-cost generic, Lipitor®'s top standing is at risk. So, an unspoken goal of the maximum-dose Lipitor® studies and the marketing campaign has been to convince doctors that Lipitor® possesses some magical power to reduce heart attacks and strokes that other statins lack. If doctors can be convinced of this, they will continue to prescribe expensive, brand-name, maximum-dose Lipitor® instead of other statin drugs that are now far less costly.

Three statin drugs are now available as generics—Mevacor® (lovastatin), Pravachol® (pravastatin), Zocor® (simvastatin)—but Zocor® is the first major threat to Lipitor's dominance. Zocor® is nearly as potent as Lipitor®, and doctors have confidence in Zocor® as a high-potency statin. Now that generic Zocor® is available, individuals and health insurance organizations will often choose it over high-cost Lipitor®.

For example, the state employees' health insurance commission in Massachusetts isn't buying the "more Lipitor®" campaign. Instead, the commission is promoting the generic therapies. Regarding maximum-dose Lipitor®, Bob Carey, a spokesman for

the commission, said, “the vast majority of people don’t need that megadose.”[14]

When you think about it, the maximum-dose Lipitor® campaign is prompting doctors to break several basic principles of optimal treatment. The Pfizer campaign suggests that doctors should prescribe maximum-dose Lipitor®, with its greater risks and costs, to all heart disease and stroke patients. Yet medical science and the FDA advise that statin treatment should be individualized. Statin drugs and doses should be selected based on the individual needs of different people.

If doctors begin prescribing maximum-dose Lipitor® to all cardiovascular patients, many will become overmedicated, side effects will ensue, and people will leave treatment. As it is, many people already find statins difficult to take. Already more than two-thirds of the millions of people placed on statin drugs eventually discontinue treatment. This situation will worsen if doctors follow Pfizer’s advice to ignore cholesterol levels; ignore patients’ age, size, and state of health; and prescribe maximum-dose Lipitor® indiscriminately to all heart and stroke patients.

REPORT

Do Your Really Need Maximum-Dose Lipitor®?

By Jay S. Cohen, MD (Introduction by William Faloon)

QUESTIONS AND ANSWERS: WHAT SHOULD I DO IF I AM TAKING LIPITOR®?

If you are doing well on Lipitor®, you don't have to change anything. If Lipitor® has helped you reach your cholesterol goals, and it is not causing any side effects, you are getting a good result.

TABLE 3. CURRENT MEDICAL GUIDELINES FOR LOW-DENSITY LIPOPROTEIN (LDL) LEVELS
Just how low you should seek to decrease your LDL level depends on your state of health and your current cardiovascular risk factors. Those at higher risk should strive to achieve lower LDL levels than those who have no risk factors for cardiovascular disease.
HIGH RISK
People with a history of heart attack, coronary artery disease, angina, abdominal aortic aneurysm, stroke, or diabetes. **LDL Goal:** below 100 mg/dL for high risk patients, and at or below 70 mg/dL for very high risk situations, such as immediately after a heart attack or a procedure for unstable angina. **WHEN TO CONSIDER DRUG THERAPY:** If your LDL is 130 mg/dL or above (or for people with very high risk, 100 mg/dL or above; nutritional interventions should be employed, too.)
MODERATE RISK
People who do not have heart disease or diabetes, but have multiple other risk factors (e.g., low HDL; male over 44 or female over 54; high blood pressure; cigarette smoking; premature coronary artery disease, heart attack, or stroke in a parent or sibling). **LDL Goal:** 130 mg/dL or lower **WHEN TO CONSIDER DRUG THERAPY:** LDL 160 mg/dL or above (nutrition and lifestyle interventions should be tried first)
LOW RISK
People with 0 or 1 risk factors. **LDL Goal:** 160 mg/dL or lower **WHEN TO CONSIDER DRUG THERAPY:** LDL 190 mg/dL or above (nutrition and lifestyle interventions should be tried first)
LIFE EXTENSION GUIDELINES: ALL RISK CATEGORIES
LDL Goal: below 100 mg/dL **WHEN TO CONSIDER DRUG THERAPY:** LDL of 100 mg/dL or above. Nutritional and lifestyle interventions should be tried first, then natural cholesterol-lowering agents. Statins may sometimes be necessary; lower, safer doses should be considered to start.

Lipitor® and other statins are important drugs that help millions of people. I support the use of statin drugs when they are used

appropriately. Even maximum-dose Lipitor® has its uses, but it should be reserved for people who have a very high risk of cardiovascular disease or who do not obtain adequate LDL reduction with lower statin doses.

What should I do if I am experiencing side effects with Lipitor®?

Tell your doctor and ask about reducing the dose. This often solves the problem. If your side effects involve serious muscle or abdominal pain, call your doctor right away.

It is very important for doctors to handle statin side effects quickly and effectively. Side effects are a main reason that so millions of people discontinue statin treatment. The fact that this occurs is a failure of the medical system. When statins are used carefully, starting with lower, safer doses, fewer side effects occur and more people stay in treatment. If a lower dose is not strong enough, it can then be increased.

My doctor wants to switch me to another statin. Is that okay?

When side effects occur, the choice is either to reduce the dose of the current statin or to switch to another. Either approach is fine, but if you are switched, make sure your doctor prescribes a lower, milder dose of the new statin. For example, if your doctor is switching you from maximum-dose 80-mg Lipitor® to Zocor®, make sure that he drops the Zocor® dose down, perhaps to 40 or 20 mg. Or he can switch you to another statin such as Pravachol® or Mevacor®. High-potency statins such as Lipitor® and Zocor® are not needed by everyone with elevated cholesterol. Many people get good results with milder statins, which have a lower risk of side effects.

I am doing well on Lipitor®, but it is very expensive. What do you think of switching to a generic?

Cost is an important consideration in choosing a statin medication. Today, three statin drugs are available as generics: lovastatin, pravastatin, and simvastatin. Simvastatin is the closest of the three to Lipitor® in its cholesterol-lowering potency.

Be sure to shop around, because prices of generic statins vary widely from pharmacy to pharmacy. Significant savings can be achieved using generic pharmaceuticals, particularly when purchased from the Life Extension Pharmacy (see Table 2).

My total cholesterol is 160 mg/dL and my LDL is 110 mg/dL. Because I have coronary artery disease, my doctor says I should be on a statin. Do you agree?

The current guidelines for LDL goals are most stringent for people at high risk. These include people with a history of heart attack, angina, coronary artery disease, or diabetes. The current goal for high-risk people is a LDL below 100 mg/dL, and in some cases below 70 mg/dL. Because your LDL is only 110, you may be able to accomplish this with a low-dose statin. Indeed, you may not need a statin at all if you adopt a heart-healthy nutritional program as well soluble fiber, fish oil, CoQ10, plant phytosterols/ stanols, small amounts of red wine (1-2 glasses daily), regular exercise, and stopping smoking.

My total cholesterol is 180 mg/dL and my LDL is 120 mg/dL. I am completely healthy and have no family history of heart disease or stroke. My doctor says I need to take a statin to lower my LDL. Do you agree?

Current guidelines state that for people at low risk, cholesterol below 200 mg/dL and LDL lower than 160 mg/dL is fine. A LDL of 160 mg/dL or above should be lowered, but treatment should start with nutritional and lifestyle changes rather than with prescription drugs. Natural therapies can also be very helpful in reducing a moderately elevated LDL.

Life Extension believes that most people should seek to keep LDL below 100 mg/dL. In the case presented above, however, the total cholesterol is already low, so attempts to reduce the LDL lower could also reduce the total cholesterol too much (below 150 mg/dL). A LDL of 120 mg/dL may be acceptable, yet anyone with a LDL reading near 160 mg/dL or above should seek to reduce it with natural approaches, and if necessary, a standard-dose statin.

Life Extension recommends obtaining a VAP® (vertical auto profile) cholesterol analysis to assess LDL particle size, lipoprotein (a) levels, and other factors that indicate atherogenic potential. It is also critical to address other cardiovascular risk factors besides cholesterol, such as triglycerides, homocysteine, fibrinogen, CRP, elevated fasting plasma glucose, obesity, and hypertension—ALL of which are important risk factors for heart attack and stroke.

My doctor seems to want to reduce every patient's LDL to 70 mg/dL. Is this a good idea?

Although there is evidence that aggressive LDL reduction is helpful for people with heart disease, current guidelines do not support the aggressive treatment of healthy people. The push for stronger and stronger statins for everyone stems from intensive marketing campaigns, as seen with the maximum-dose Lipitor® onslaught.

This has led to a great deal of confusion among doctors and patients. Many people are put on statins although they do not really need them. Others receive far stronger statins than they need and become overmedicated. To avoid these problems, you should ask your doctor some questions if he or she recommends a statin for you. Why do you think I need a statin? What is my LDL goal? I would prefer to start with a milder statin dose in order to avoid side effects—what do you think? What about trying nutritional approaches for reducing LDL first? Is my HDL okay?

My cholesterol numbers are good, except that I have a low HDL. Should I be concerned?

Some experts believe that the most important cholesterol test is neither your total cholesterol nor your LDL, but instead your level of HDL, the beneficial blood lipid. Studies suggest that in women, a low HDL is a more worrisome risk factor than a high LDL.

Dr. Davis states, “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. Why do we not hear more about low HDL and small LDL particles? Because treating these is not as profitable for drug companies.”[9]

My doctor says that LDL is only one of several risk factors that should be considered before prescribing anything. Do you agree?

Your doctor is one of many who now recognize that LDL is only one of several important risk factors for heart disease. In recent years, an elevated C-reactive protein level has been identified as a sign of arterial inflammation. Elevated fibrinogen can lead to sticky platelets and an increased risk of heart attacks, especially in women. Triglycerides are waxy substances that increase your risk; if elevated, control of carbohydrate intake is required. As mentioned previously, the VAP® test can identify your level of small particle LDL, which defines whether your LDL is dangerous or not. The VAP® will also determine your level of lipoprotein(a), which some experts consider as important a cardiovascular risk factor as elevated LDL.

TABLE 4. HIGH-DENSITY LIPOPROTEIN (HDL) LEVELS

HDL carries cholesterol away from the arteries and to the liver for elimination. This helps keep cholesterol from building up in walls of arteries. Higher levels of HDL confer greater cardiovascular protection.

HDL LEVEL	EFFECT
Less than 40 mg/dL	Increased risk of heart disease
40 to 59 mg/dL	Some benefit
60 mg/dL and above	Protective against heart disease

A low HDL is defined as a level below 40 mg/dL in men and below 45 mg/dL in women, but levels above 50 mg/dL are preferred. A HDL of 60 mg/dL or higher reduces the risk of cardiovascular disease. Statins are not particularly effective at raising HDL. In contrast, niacin not only reduces LDL, but also can raise HDL substantially. Mainstream doctors usually recommend prescription Niaspan®, which is expensive and can cause side effects. Instead, you might first try plain niacin. Taking niacin with food and a baby aspirin (81 mg) seem to reduce the unpleasant “niacin flush”. Best results are usually obtained by working with an experienced integrative practitioner. The goal is to raise the HDL level to 60 mg/dL or higher. Olive oil, raw nuts, omega-3 fatty acids, a daily glass of red wine, and exercise can all help boost artery-protecting HDL.

Tests for these factors should be performed on people with cardiovascular disease or at high risk of developing it. Testing should also be done on anyone interested in knowing about possible risks for cardiovascular disease.

I often encounter side effects with medications. How can I avoid side effects with a statin?

Most statin side effects are dose-related. The higher the dose, the greater the risk. This was seen in both the TNT heart study and the stroke study, in which maximum-dose Lipitor® caused more side effects, more liver injuries, and more deaths from non-cardiovascular causes. Maximum-dose Lipitor® also caused more people to discontinue treatment. This is a huge problem in medical care today: side effects are one of the reasons that millions of people quit statin treatment each year.

If you want to avoid side effects, ask your doctor about starting with a low dose. You should also ask about starting with a moderate-potency statin, such as pravastatin, instead of a high-potency statin.

Studies show that some people obtain excellent responses to small doses of statins and do not need a higher dose. For example, in a study using just 2.5 mg of Zocor®, 18 people obtained LDL reductions of 40% or greater.[15] This was an unexpected yet excellent result.

If a low statin dose does not reduce your LDL adequately, your doctor can gradually increase the dose until you reach your LDL goal. This "start low, go slow" method is recommended by the FDA, especially for older people starting a statin.[16] A "start low" approach works anyone who wants to emphasize safety with statin drugs.

Cardiologists have reported that their patients who concomitantly use coenzyme Q10 with statin drugs seem to suffer fewer drug side effects such as muscle aches and pains. This observation is supported by a recent study that found that 30 days of treatment with coenzyme Q10 decreased muscle pain related to statin medications by a dramatic 40%.[17]

I do not like taking medications. Are there natural alternatives that reduce LDL?

Start with nutrition. A heart-healthy diet (reduced saturated fat and simple sugar intake) can lower cholesterol levels as much as a moderate-strength statin.

Supplements for reducing LDL include red yeast rice (do not use with a statin), niacin (which lowers LDL and raises beneficial HDL), and plant sterols (which block cholesterol absorption from the intestine).

Other supplements to consider for heart health are magnesium and coenzyme Q10. Regular consumption of wild salmon or sardines, or daily fish oil capsules, can reduce the risk of death from a heart attack as much as a statin drug.[18]

If you are interested in using non-drug therapies, work with a health care professional who is knowledgeable about natural approaches and products.

I have heart disease, and my doctor wants to prescribe maximum-dose Lipitor®. What alternatives do I have?

As Dr. Pitt suggested in his editorial against maximum-dose Lipitor®, substantial LDL reduction can be accomplished with a moderate dose of a statin combined with other therapies. These include Zetia® (ezetimibe) and Welchol® (colesevelam), which block cholesterol absorption in the intestine, and a similar effect can be obtained with natural plant sterols. Or ask your doctor about combining modest doses of a statin and a niacin product.

Many people think statins provide 100% protection against heart attacks, but the effect is about 30%. In other words, if 100 people likely to have a heart attack are placed on statins, about thirty will avoid the heart attack. Seventy will not. No treatment, natural or prescription, provides full protection against heart disease. This is why people need to use all of the therapies—nutritional, natural and, if necessary, medications—to reduce their risk as much as possible. Your treatment should be individualized. Treatment may differ from person to person because different people have different risks and goals, and thus need different therapies. Shotgun, one-size-fits-all therapies should be avoided. If your doctor insists that maximum-dose Lipitor® is the only solution, get a second opinion.

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COENZYME Q10 AND STATIN DRUGS

In an effort to prevent the progression of dangerous atherosclerosis, millions of Americans now take cholesterol-lowering statin drugs daily. These drugs dramatically lower harmful cholesterol and LDL, and some even raise levels of beneficial high-density lipoprotein (HDL). But these drugs are not without risk. Potentially serious side effects, including liver damage, chronic muscle pain, muscle wasting, and even death have been associated with their use.[7,8]

In 2001, Bayer announced the withdrawal from the market of its statin drug, Baycol®. This withdrawal of a potential blockbuster drug, which was conducted with the FDA's support, was prompted by the deaths of 31 people due to rhabdomyolysis, a severe form of muscle damage. The deaths were attributed to Baycol® use. Although Baycol® is no longer available, rhabdomyolysis is a potential side effect, albeit rare, of statin drugs.[19]

While statin medications effectively lower cholesterol and LDL levels, they also can induce a coenzyme Q10 deficiency. Although the conventional medical establishment has been painfully slow to embrace this association, the scientific literature supports this conclusion.[20-24] For many years, Life Extension has alerted the public to the need for supplementation with coenzyme Q10 when taking statins, to prevent depletion of this important antioxidant/mitochondrial cofactor. CoQ10 is involved in the production of ATP, the basic unit of energy used to power cellular functions throughout the body. For years, manufacturers have remained inexplicably silent on this issue, despite the fact that the first manufacturer of a statin drug filed a patent for a co-formulation of their statin with CoQ10.

"The depletion of the essential nutrient CoQ10 by the increasingly popular cholesterol lowering drugs…(statins), has grown from a level of concern to one of alarm," wrote scientists in the British medical journal, Biofactors. "With ever higher statin potencies and dosages, and with a steadily shrinking target [LDL], the prevalence and severity of CoQ10 deficiency is increasing noticeably."[25] More recently, the same team wrote: "We conclude that statin-related side effects, including statin cardiomyopathy, are far more common than previously published."[26]

—Dale Kiefer

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