THE PEOPLE'S PHARMACY
The People's Perspective on Medicine

Cholesterol Control & Heart Health

Introduction

Heart disease is still the number one killer in America today, despite the billions spent annually on cholesterol-lowering drugs. More than 800,000 people will have a heart attack this year–and over 650,000 will die from a "coronary event." That's about one every minute. And nearly half of all heart attack sufferers have normal cholesterol levels.

Americans have been hearing about the evils of cholesterol for at least 60 years. In the early 1960s, the American Heart Association (AHA) warned people that saturated fat was the culprit behind elevated cholesterol levels. We were told that cholesterol in general, and "bad" LDL cholesterol in particular, would clog our arteries and that would lead to heart attacks. If we would just stop eating eggs, red meat, butter, cheese and other full-fat dairy products, we would reduce our risks of cardiovascular disease.

For decades, cardiologists and nutrition experts encouraged their patients to substitute margarine for butter. Anyone who regularly consumed eggs

Americans were advised that a heart healthy breakfast would include pancakes or waffles with margarine and syrup. No cholesterol or saturated fat! Just lots of carbs, which were considered heart healthy. Cereal was recommended as a much better choice than eggs. No matter that many of our favorite cereals were loaded with sugar. If people used skim milk on their cereal, they got a pat on the head and a thumbs up. Yogurt was OK, as long as it was no-fat or low-fat yogurt, which generally meant that there would be a generous dollop of fruit jam at the bottom of the carton.

Nuts were verboten. They were high in fat and we were repeatedly told that fat was the enemy. Other foods on the no-no list included avocados (also too high in fat) and shrimp (high in cholesterol). We could go on, but by now you get the drift. The bottom line was: fat would make you fat *and* clog your coronary arteries.

By now, the problems with most of this advice have been revealed. Margarine is NOT better than butter, and eating eggs a few times a week does NOT raise cholesterol. Although cholesterol is still considered an important risk factor, there are many, many others that may be equally strong.

Some Risk Factors

- High level of C-reactive protein (**CRP**)
- Smoking
- Hostility or anger
- High LDL cholesterol
- Low HDL cholesterol
- High level of very low-density (**VLDL**) cholesterol

- Being overweight
- High homocysteine
- Too much iron
- High blood pressure
- Lack of physical activity
- Genes & family history
- Diabetes & insulin resistance
- High uric acid level
- Depression
- Lack of a social network
- Socio-economic status
- Stress & anxiety
- Hormone Replacement Therapy (HRT)

Dietary Flip-Flops

Many of the so-called heart-healthy foods were not that good for us and many of the vilified items have turned out to be just fine. We will provide documentation momentarily. If it seems as if we have been on a roller coaster ride when it comes to heart health, strap in! It's about to get even more complicated.

The American Heart Association (**AHA**) carries a lot of weight with doctors and consumers. It is perceived as a highly objective and trustworthy organization by many people. Here is what the AHA still recommends when it comes to dairy fat:

> **"AHA Recommendation**

and older adults should have four.
• For dessert or snacks, choose ice milk, frozen or fruited low-fat or nonfat yogurt, sherbet, sorbet or low-fat puddings.

"Choose from:

• Fat-free, zero-fat, no-fat or nonfat milk
• ½–1% low-fat or light milk
• Nonfat or low-fat dry milk powder
• Evaporated fat-free milk
• Buttermilk made from fat-free or 1% fat milk
• Fat-free or low-fat yogurt
• Frozen fat-free or low-fat yogurt
• Drinks made with fat-free or 1% fat milk and cocoa (or other low-fat drink powders)
• Low-fat cheeses (dry-curd or low-fat, cottage cheese, low-fat natural cheeses or processed cheeses made with nonfat or low-fat milk with no more than 3 grams of fat per ounce and no more than 2 grams of saturated fat per ounce)
• Fat-free or low-fat ice cream (no more than 3 grams of fat per 1/2 cup serving)"

This is the old way of thinking but it is still firmly entrenched. You are supposed to substitute fruited nonfat yogurt or sherbet for dessert. The trouble with such desserts or snacks is that they are high in carbs in the form of sugar! We now know that sugar may be a bigger problem than dairy fat.

Trans Fats vs. Dairy Fat:

cardiovascular health because there was no cholesterol. We now know that was a horrible idea. Substituting hydrogenated margarine for butter probably caused more heart attacks than it prevented.

There is increasing evidence that a low-fat diet may not be as heart protective as doctors once imagined. But old habits die hard.

The Guardian (Oct. 9, 2015) offers these stats:

> "Between 1975 and 2014, sales of whole fat milk have decreased by nearly 61%, while sales of 2% milk have increased nearly 106%. Sales of 1% and skim milk have increased by around 170% and 156%, respectively, according to data from the USDA."

The Pros and Cons of Dairy Fat:

Despite the AHA's admonition to avoid dairy fat and saturated fat, here is some science dating back more than a decade:

An article in the *American Journal of Clinical Nutrition* (March, 2010) provides a shot across the bow of the AHA.

The authors analyzed data over 5-23 years involving 347,747 subjects:

> "**Results**: During 5-23 y of follow-up of 347,747 subjects, 11,006 developed CHD [coronary heart disease] or stroke.

> "**Conclusions**: A meta-analysis of prospective epidemiologic studies showed that there is no significant evidence for concluding that dietary saturated fat is associated with an increased risk of CHD or CVD."

In 2012 researchers published a study of "**the consumption of dairy fat and high-fat dairy foods, obesity, and cardiometabolic disease**" (*European Journal of Nutrition*, July 19, 2012):

> "**Results**: In 11 of 16 studies, high-fat dairy intake was inversely associated with measures of adiposity. Studies examining the relationship between high-fat dairy consumption and metabolic health reported either an inverse or no association. Studies investigating the connection between high-fat dairy intake and diabetes or cardiovascular disease incidence were inconsistent.
>
> "**Conclusions**: The observational evidence does not support the hypothesis that dairy fat or high-fat dairy foods contribute to obesity or cardiometabolic risk, and suggests that high-fat dairy consumption within typical dietary patterns is inversely associated with obesity risk."

We apologize for being obvious. *Inverse* means that eating dairy fat did *not* make people fat. If anything, it was associated with *less* obesity.

> "**Conclusion**: A high intake of dairy fat was associated with a lower risk of central obesity and a low dairy fat intake was associated with a higher risk of central obesity."

These results were confirmed in the Luxembourg Study (Nutrition Research, Nov. 2014):

> "Participants in the highest tertile of whole-fat dairy intakes (milk, cheese, yogurt) had significantly lower odds for being obese; abdominal obesity, compared with those in the lowest intake tertile, after full adjustment for demographic, lifestyle, dietary, and cardiovascular risk factor variables. Increasing consumption of dairy foods may have the potential to lower the prevalence of global and abdominal obesity."

Not all of the research is decades old. A recent review of prospective studies on major health outcomes found that people eating cheese frequently were less likely to die prematurely, develop heart disease or experience a stroke (*Advances in Nutrition*, Sep. 2023).

The authors of this study conclude

> "Our findings suggest that cheese consumption has neutral

Saturated Fat and Heart Disease:

In 2014, a study was published in the highly regarded *Annals of Internal Medicine* (March 18, 2014). The authors reviewed 72 studies. There were more than 600,000 participants in these studies:

The conclusions challenged the AHA's attack on dairy fat and love affair with polyunsaturated fatty acids. Those are the fats found in vegetable oils like safflower oil, peanut oil and sunflower oil.

The investigators wrote:

> "**Conclusion**: Current evidence does not clearly support cardiovascular guidelines that encourage high consumption of polyunsaturated fatty acids and low consumption of total saturated fats."

You can read more about this study and other recent studies that contradict the AHA at this link:

Has the Flip-Flop on Saturated Fat Made Your Head Spin?

One risk factor associated with heart disease is metabolic disruption in the form of diabetes or prediabetes. Not long ago, Austrialian scientists completed a twelve-year long study observing nearly 5,000 people (*Journal of Nutrition*, June 2023). All the participants had normal glucose tolerance at the beginning of the study. They answered questions about their diets at a few points during the study and also had their blood glucose measured.

The investigators note:

> "In this large Australian cohort, protective associations were found for high-fat dairy types, whereas neutral associations were seen for low-fat dairy types. Studies with more detail on sugar content of types of dairy foods and products eaten with dairy foods (e.g., cereals or jam), and studies into potential causal mechanisms of the health effects of dairy intake are required."

Saturated Fat vs. High-Carb Foods:

Remember how we suggested that the old "heart-healthy" breakfast of pancakes, waffles or sugary cereals was worse than a breakfast high in dairy fat? The PURE (Prospective Urban Rural Epidemiology) study collected dietary data from 135,000 people. It confirmed this concept.

After seven years, the people who followed a high-carb diet were more likely to have died or developed health problems than those consuming a high sat-fat diet. Read about this and other contradictory data at this link:

Just How Scary Is Saturated Fat?

What About Olive Oil?

By now you have heard that adding olive oil to the diet benefits the heart. Did you know that olive oil is **14% saturated fat**? The low-fat gurus continue to insist that olive oil is unhealthy.

Cardiology (January 18, 2022).

In the Nurses' Health Study, 60,582 women completed questionnaires about their diets, their activities and their health every few years between 1990 and 2018. During the same time frame, the Health Professionals Follow-up Study collected that information from 31,801 men.

In total, 36,856 of these 92,383 volunteers died in the course of the study. People consuming more olive oil were *less* likely to die, even after adjusting for age. By comparing the extremes–people who ate the most olive oil to those who ate the least–the investigators determined that olive oil lovers were 19 percent less likely to die of heart disease.

How Much Olive Oil Is Heart Healthy?

Those at the highest level of consumption were getting at least 7 grams of olive oil daily. How much, you may wonder, is that? It turns out that a tablespoon of olive oil comes in just under 14 grams, so 7 grams is a bit more than *half a tablespoon*.

Besides cardiovascular health, people eating more olive oil were also less likely to die of cancer (17 percent), neurodegenerative disease (29 percent) or respiratory disease (18 percent). The scientists calculated whether people would benefit by substituting olive oil for margarine, butter or other dairy fat. They suggest that olive oil is more healthful than animal fats.

More Support for Olive Oil:

This is not the first study to conclude that olive oil can help heart health. One famous trial was known as **PREDIMED** (*New England Journal of*

One group followed a Mediterranean-style diet rich in vegetables, fish and legumes, to which they added **four tablespoons** of extra-virgin olive oil daily. Another group also consumed a Mediterranean diet, but instead of olive oil, they added an ounce of almonds or hazelnuts to their daily fare. The third group served as a control and followed a low-fat cardiologist-recommended diet to the best of their ability.

People in both the olive oil and the nut dietary groups were significantly less likely to have a heart attack, stroke or death from a cardiovascular cause. In addition, women in the olive oil group were less likely to be diagnosed with breast cancer (*JAMA Internal Medicine*, Nov. 2015).

If olive oil and a Mediterranean diet were pills, doctors would prescribe them for everyone and the drug companies would charge a lot of money. And when I say a lot of money I mean thousands of dollars a month! Instead, you can help yourself to health at your local grocery store or farmers' market by eating real food.

Deaths from Heart Disease

The good news is that deaths from heart disease have been dropping for decades. And cholesterol levels have also been coming down. But, we shouldn't break out the party hats and confetti prematurely, because the news could be a lot better. According to the CDC, heart disease is still the number one cause of death in America. That is despite the American Heart Association's dietary recommendations and its guidelines encouraging statin use in almost anyone with "risk factors." Here are the scary CDC stats:"

- About 659,000 people in the United States die from heart disease each year—that's 1 in every 4 deaths.
- In the United States, someone has a heart attack every 40 seconds.
- Every year, about 805,000 people in the United States have a heart attack. Of these,
    - 605,000 are a first heart attack
    - 200,000 happen to people who have already had a heart attack
    - About 1 in 5 heart attacks is silent—the damage is done, but the person is not aware of it."

The Heart Disease Dilemma:

There is no doubt that heart disease remains a huge health problem in the US. There is still a lot of confusion and contradiction. What used to be written in stone has crumbled. The connection between cholesterol and heart disease may be far more complicated than we've been led to believe.

The manufacturers of cholesterol-lowering drugs like **Lipitor** (atorvastatin), **Livalo** (pitavastatin), **Crestor** (rosuvastatin), and **Zocor** (simvastatin) would certainly like us to think that high cholesterol causes heart attacks, and conversely that by lowering cholesterol, one eliminates the risk of a major coronary event. They seem to have convinced a lot of people: these drugs have been among the most profitable in the history of pharmaceuticals. We would like nothing more than if popping a pill could prevent a heart attack with no adverse side effects. Unfortunately, the reality is a bit fuzzier.

As it turns out, the cholesterol dogma may be wrong in all kinds of ways. For one thing, the notion that eating a diet high in cholesterol–full of eggs, meat, and fats–is a cardinal cholesterol sin, sure to send you straight to the

weight loss, reduction in serum triglycerides, and an increase in good HDL cholesterol than a low-fat diet.

Higher-fat diets seem to raise good HDL cholesterol better than low-fat diets, which may help explain why they also seem to give those following them better scores on heart-disease risk factors than those on Dean Ornish-style low-fat, carbohydrate-heavy diets.

And contrary to the medical community's long-held belief that low-fat = good health, several high-profile studies, including the Women's Health Initiative with over 48,000 female participants over 50 years old, have demonstrated no statistically significant benefit to a low-fat, high-veggie diet for lowering the risks of heart attack, stroke, breast cancer and colorectal cancer.

Another startling discovery to come out of studies on cholesterol is that daring to push it as low as you can go may indeed be a gamble. Some people are very surprised to learn that our bodies need cholesterol to function: it's the building block for things like vitamin D and sex hormones such as estrogen and testosterone. It's also vital for our nervous systems, particularly in the brain. When there isn't enough cholesterol in your body, synapses (the way neurons communicate with other neurons) break down. As you might imagine, then, having too little cholesterol may also be a bad thing.

At least two studies have provided evidence that there may be a link between very low cholesterol and the risk of bleeding stroke, especially for women with high blood pressure. One study of Japanese-American men found that those with the lowest cholesterol levels were more likely to die earlier. Those with cholesterol in the 188-209 range seemed to fare better.

lowering cholesterol in an older woman will extend her life expectancy significantly.

Of course, none of this is meant to suggest that we shouldn't pay attention to our lipid levels, or that we should gorge on hot dogs and hot fudge sundaes. Cholesterol that is too high is clearly dangerous and can lead to an increased risk for heart attack. But what has become clear through the haze of cholesterol confusion is that how *much* fat you eat matters much less than *what kind*.

Lp(a): The Best Kept Secret in Cardiology

The REALLY BAD Lipid Most Doctors Never Mention

Your eyes may have missed one of the important risk factors for heart disease listed above (just under triglycerides). It's referred to as **lipoprotein (a)** and is abbreviated **Lp(a)**. People in the know call it "**Lp little a**" but it is rarely, if ever, mentioned to patients. That is why you have probably never heard of it and almost assuredly have never had your level measured. That is hugely disappointing because Lp(a) could be the best kept secret in heart disease!

Ask most people about their risk factors for heart disease and they will likely mention high total cholesterol (**TC**), high **LDL-C** ("bad") cholesterol and low **HDL-C** ("good") cholesterol. Sometimes people even include triglycerides (**TG**) and **VLDL** (very low-density lipoprotein cholesterol. Chances are very good they have never heard about **Lp(a)**. Yet it is a key player in heart disease and it could be contributing to many preventable heart attacks.

What is Lp(a)?

cholesterol-protein particle in genetically susceptible people. When levels of Lp(a) are high they clog arteries. The sticky nature of of this protein makes it harder for the body to naturally dissolve blood clots.

Elevated Lp(a) levels may also lead to the calcification of aortic valves (aortic valve stenosis or **AVS**). This is a *very* serious heart condition (*Biomolecules*, Dec. 2019).

According to these authors:

> "Aortic valve stenosis (AVS) is the most prevalent valvular heart disease in the Western World with exponentially increased incidence with age. If left untreated, the yearly mortality rates increase up to 25%…Lipoprotein(a) [Lp(a)] has been implicated as a pivotal player in the pathophysiology of calcification of the valves. Patients with elevated levels of Lp(a) have a higher risk of hospitalization or mortality due to the presence of AVS. Multiple studies indicated Lp(a) as a likely causal and independent risk factor for AVS."

Here is the bottom line. High levels of Lp(a) are bad for coronary arteries *and* heart valves.

What Happens When Lp(a) Is Too High?

When you read about an unlikely candidate for heart disease–someone who is very fit, eats healthy food, has low cholesterol levels and doesn't

in the family. Statins probably *won't* prevent this kind of cardiovascular "accident."

Doctors almost always ask about family history. If grandpa, dad, aunt Martha and Uncle Charlie all died at a relatively early age of heart disease or stroke, suspect Lp(a) as a potential factor. When there is such a genetic history, we think it is imperative that doctors order a blood test to check for elevated Lp(a)!

If a cardiologist learns about a history of heart disease in a family, the chances are pretty good that a statin will be recommended. That might make sense, but *only* if Lp(a) has been ruled out as a risk factor. Something many cardiologists may not realize is that statins might make matters worse. More about that shortly.

Most healthcare professionals are unfamiliar with lipoprotein(a). And yet this independent risk factor was identified six decades ago as a key player in coronary heart disease (*Clinical Biochemist Review*s, Feb. 2004).

Lp(a) and Heart Disease:

It has been estimated that at least one fifth of the population has inherited high levels of lipoprotein(a) (*Scientific American*, Nov. 4, 2019). This independent risk factor is comprised of a lipid-protein compound. Part of it is like "bad" LDL-C and part of it is a combination of apo B100 and apo(a). The combo known as **Lp(a)** can be deadly.

That's because levels greater than **50 mg/dL** [or **>100 nmol/L**] increase the risk of heart attacks and strokes. What makes this lipid fraction so toxic is its ability to clog arteries *and* promote the formation of blood clots. Lp(a) can also lead to calcification of the aortic heart valve. That is not good, as it

palpitations.

Why Have You Never Heard of Lp(a) Before?

This may sound cynical, but the reason we suspect that ***Lp little a*** has flown below the radar is because there is, as yet, no pricey pharmaceutical to lower this risk factor for heart disease. There has been no motivation for drug companies to encourage doctors to measure **Lp(a)** because there was no money in it. As a result, blood tests for this heart attack risk factor are rarely, if ever, performed.

The accepted dogma has been that diet and exercise have little to no impact on this risk factor. Perhaps that's because cutting back on eggs, butter and red meat doesn't reduce this cholesterol-transport protein.

That explains why some people who exercise regularly, follow a low-fat or vegan diet and take statin-type cholesterol-lowering drugs can still end up with heart disease. But there is one dietary intervention that might make a difference! More about that shortly.

We suspect that many cases of hereditary heart attacks may be linked to Lp(a). Because many physicians have not been educated about this risk factor, it goes unmeasured, unreported and untreated.

This reader describes just such a situation:

> "I forget where I first heard of Lp(a) but it worried me, so I had mine tested. I had to cajole my family doctor, who didn't know about it. To get it covered by insurance, she referred me

> "As it turns out, my Lp(a) is very high, despite years of good diet and lots of exercise. My LDL is borderline high, my HDL is high (good) and my triglycerides are low (also good). The cardiologist and I sat together at his computer researching Lp(a).
>
> "I won't take statins. He did recommend baby aspirin. He still evaluated my risk of heart disease at 3 percent over ten years. What else can I do?"

More about what people can do shortly.

Heresy: Statins Raise Levels of Lipoprotein(a)

Shortly after statins were introduced in the U.S. in the late 1980s, a drug company researcher contacted us. He had been involved in statin research and was concerned that these drugs might raise a little-known lipid fraction called lipoprotein(a).

He was in favor of *lowering* LDL cholesterol with a statin. But he thought that also *raising* Lp(a) with a statin might be a little like pushing a boulder up a steep mountain. Remember the *Myth of Sisyphus*?

Many healthcare professionals are unaware that statins can raise levels of Lp(a). Here is what the authors of an article in the (*European Heart Journal*, June 21, 2020) wanted to know:

Aims:

study aimed to assess the effect of statins on Lp(a) levels."

Discussion:

> "This individual-patient-data analysis demonstrates that Lp(a) levels increase significantly in patients started on statin therapy and that the findings were directionally consistent among most statins studied. Cell culture studies revealed a time and dose-dependent, statin-mediated increase in *LPA* mRNA expression and apolipoprotein(a) production, suggesting the mechanism is at least in part related to increased Lp(a) production. Whether statin-mediated increases in Lp(a) contribute to residual risk in patients treated with statin therapy should be evaluated in future studies."

A review in the journal Biomedicines (Aug. 9, 2021) states:

> "Statin treatment does not lower but may even increase the level of Lp(a) by 10-20%"

This is *not* welcome news. That's because many physicians believe that statins are one-stop-shopping when it comes to heart health. The idea that drugs such as atorvastatin, pravastatin, rosuvastatin or simvastatin could

Please do not take our word for this. The review in the *European Heart Journal*, (June 21, 2020) notes that:

> **"This meta-analysis reveals that statins significantly increase plasma Lp(a) levels."**

Unexplained Heart Attacks!

Despite a concerted effort by the American Heart Association and over 30,000 cardiologists, heart disease is still our number one killer. According to the CDC:

> **"Every year, about 805,000 people in the United States have a heart attack."**

Put another way:

> **"One person dies every 36 seconds in the United States from cardiovascular disease."**

The Cardiologist's Formula for Preventing Heart Disease:

Ask most health professionals how to prevent heart attacks and you will likely be told that people should:

3) Keep blood pressure below 120/80

4) Exercise regularly

5) Lose weight if you are over the recommended range

6) Keep blood sugar under control

7) Take a statin daily to lower cholesterol.

The Statin Statistics:

Many people do their best to follow these recommendations. Just take statins as one example.

At last count, nearly 50 million Americans received 219 million prescriptions for statin-type cholesterol-lowering drugs such as atorvastatin, simvastatin, pravastatin, rosuvastatin, lovastatin or pitavastatin. If each prescription has *only* 30 pills, that would equal **6.6 billion** pills annually. Over a decade that represents tens of billions of statins swallowed.

And yet the CDC states that:

> "About 659,000 people in the United States die from heart disease each year—that's 1 in every 4 deaths."

How Do Cardiologists Explain This Sad Story?

We read about a doctor who specialized in heart attack prevention. He was a dedicated athlete and in fabulous shape. Because there was heart disease in his family, this middle-aged physician was taking a statin.

cath lab found one artery that was almost completely blocked. Interventional cardiologists opened the blockage and inserted a stent to keep the artery open.

This doctor survived his prolonged cardiac arrest because of excellent cardiopulmonary resuscitation. Paramedics arrived on the scene promptly and shocked his heart to get it beating again. At a nearby hospital, the emergency cardiac team was able to get blood flowing to the heart muscle within a relatively short period of time. Most people are not so fortunate.

But the key question is: **why did this heart attack happen in the first place?** A physician who was doing everything right *and* taking a statin should *not* have experienced such a life-threatening event.

The James Fixx Heart Attack:

There are other examples. James Fixx was a renowned runner. He had lost 60 pounds, stopped smoking and written a bestseller titled *The Complete Book of Running*.

Nonetheless, James Fixx died of a heart attack at age 52 during his daily run. Like the physician above, he too had a coronary artery that was almost completely blocked.

Our Friend:

Let's call our friend Bob. We have known him for more than 40 years. He has always been an avid exerciser. He used a Nordic Track before such equipment became popular. He is a walker and a swimmer and he has always been very thoughtful about his diet. He is not a smoker and he has taken a atorvastatin for years.

Bottom line: Bob should *not* have had such blocked heart arteries. He was doing everything right! We are awaiting word about his Lp(a) levels.

Is Lp(a) Contributing to Mysterious Heart Attacks?

If a middle-aged overweight man who smokes, doesn't exercise and eats a lot of burgers and fries for lunch has a heart attack, most doctors nod knowingly. If there was a history of heart disease in the family, they chalk it up to bad genes *and* bad lifestyle…a deadly combination.

But how do cardiologists explain heart attacks in seemingly healthy people with "normal" cholesterol levels, no smoking history, a good diet and a regular exercise program? When a cardiac event occurs in a person who is taking statins, people often shrug is astonishment. It happens more often than most cardiologists would like to admit.

We don't know the details of the personal medical history of either case we described above. All we know are the facts that have been publicly reported. But there is growing evidence that one risk factor might help explain these and many other mysterious cardiac deaths.

Why Don't Doctors Consider Lp(a) Contributing to Heart Disease?

Doctors rarely test for Lp(a), even when they are trying to determine a patient's risks for heart disease. Perhaps that is because they have been told that there isn't much, if anything, they can do to lower Lp(a). Exercise doesn't appear to change it significantly, and neither does a conventional heart-healthy low-fat diet. And as we have pointed out, statins may actually raise Lp(a) levels.

An Inconvenient Truth: Lp(a) Contributing…?

(June 21, 2020)? These same authors wrote an article titled **"Statins and Increases in Lp(a): An Inconvenient Truth That Needs Attention"** (*European Heart Journal*, Jan. 1, 2020):

> "We feel that the importance of our study is that it points out a unique limitation of statin therapy, primarily in patients with elevated Lp(a), that must be understood pathophysiologically and studied for impact on residual risk. It may come across as an inconvenient truth that statins lower LDL-C but can raise levels of Lp(a). Our duty is to report these data to allow the clinical community to replicate them and allow clinicians to obtain experience in their practice for better-informed decision making and risk evaluation in their patients with elevated Lp(a)."

Can Doctors Lower Lp(a)?

As we have pointed out, researchers have known for decades that Lp(a) is an independent risk factor for heart disease. Doctors have been told that they **1)** do not have to measure Lp(a) and **2)** they can't do anything about it even if it is elevated. We're not so sure that is correct.

In our book, Graedons' Best Medicine (Bantam Books, 1991) we wrote that:

> "New research suggests that the blood fat lipoprotein(a), abreviated Lp(a), may be the most important marker of coronary heart disease. Unfortunately, most of the lipid-

> artery-clogging compound is niacin, though fish oil may also be beneficial."

We had discovered an article in the *New England Journal of Medicine* (May 24, 1990). It nailed the dangers of Lp(a):

> "We conclude that an elevated level of lipoprotein(a) is a strong risk factor for CHD [coronary heart disease] in patients with familial hypercholesterolemia, and the increase in risk is independent of age, sex, smoking status, and serum levels of total cholesterol, triglyceride, or high-density lipoprotein cholesterol."

The authors noted that niacin could be beneficial against Lp(a).

Niacin (aka nicotinic acid or vitamin B3) vs. Lp(a):

More than two decades ago we wrote about the benefits of niacin in the book, *Graedons' Best Medicine*. We noted that niacin must be considered a drug because doctors were prescribing a whopping dose (three grams a day). In those days niacin was surprisingly popular with cardiologists and family physicians. That's because:

> "…niacin lowers bad LDL cholesterol 15 to 40 percent and raises good HDL cholesterol 10 to 20 percent (*Drugs*, March,

Doctors liked niacin because it was shown to actually reduce the risk of repeat heart attacks. One of the most impressive and long-lasting studies was called the Coronary Drug Project (*Journal of the American College of Cardiology*, Dec. 1986). It was:

> "…conducted between 1966 and 1975 to assess the long-term efficacy and safety of five lipid-influencing drugs in 8,341 men aged 30-64 years with electrocardiogram-documented previoius myocardial infarction (heart attack)."

The researchers tested two estrogen formulations, dextrothyroxine (a thyroid hormone drug) and clofibrate. The hormones were stopped early because of adverse reactions and clofibrate did not work. Niacin demonstrated "modest benefit" in reducing repeat heart attacks during the study. The really exciting news, though, was that the follow-up produced unexpectedly impressive results.

> "…nearly 9 years after termination of the trial…mortality in the niacin group was 11% lower than in the placebo group. This late benefit of niacin, occurring after discontinuation of the drug, may be a result of a translation into a mortality benefit over subsequent years of the early favorable effect of

Could this long-lasting benefit of niacin have been as a result of its ability to lower Lp(a)?

Niacin Lowers Lp(a):

Doctors have known for a long time that niacin reduces levels of Lp(a). A meta-analysis of extended-release (ER) niacin reported some fascinating results (*Metabolism*, Nov. 2016). The authors reviewed 14 randomized, placebo-controlled clinical trials published between 1998 and 2015:

> "In this meta-analysis of randomized placebo-controlled clinical trials, treatment with nicotinic acid was associated with a significant reduction in Lp(a) levels."

At a dose of around 2,000 mg daily of extended-release niacin, the reduction in Lp(a) was about 23%.

Even though there is evidence that niacin lowers Lp(a) levels, most physicians have moved away from this drug. That may be in part becuase statins have completely dominated the lipid-lowering landscape for over two decades, even though they likely raise Lp(a) levels.

Niacin can also be a hard drug to manage. Even extended-release niacin can cause uncomfortable flushing (an uncomfortable burning, tingling, redness, and itching that often spreads down from the face and neck to the rest of the body). The flush can start within 15 minutes to two hours after

If the dose is started quite low and is very gradually increased over several weeks the body may adjust, especially if the drug is taken with food. Some doctors recommend a small dose of aspirin 30 minutes prior to taking niacin. This may also reduce the flushing.

Niacin should *only* be taken under a doctor's supervision! Other less common reactions may include an increase in liver enzymes, nausea, aggravation of stomach ulcers, blood sugar fluctuations and irregular heart rhythms. People with a history of gout, glaucoma, liver disease or diabetes should avoid niacin. Periodic liver function tests are essential.

L-Carnitine vs Lp(a):

You may have heard of L-carnitine for weight loss or to improve exercise performance. We won't get into those claims here. Your body makes this nutrient from the amino acids methionine and lysine. This dietary supplement is important for energy production within the mitochondria. These are the energy factories of each cell. More to the point here, L-carnitine supplementation might help lower Lp(a).

A study in *Scientific Reports* (Jan. 12, 2016) assessed:

> "…the impact of L-carnitine on plasma Lp(a) concentrations through systematic review and meta-analysis of available RCTs…The meta-analysis showed a significant reduction of Lp(a) levels following L-carnitine supplementation…In conclusion, the meta-analysis suggests a significant Lp(a) lowering by oral L-carnitine supplementation. Taking into account the limited number of available Lp(a)-targeted

required to fully elucidate the clinical value and safety of oral L-carnitine supplementation."

Aspirin and Lp(a):

It will come as a surprise to most health professionals to learn that the lowly aspirin might also be helpful against high Lp(a) levels. A review in the journal *Drugs in Context* (Sept. 4, 2019) offers these tidbits:

"In a small trial in Japan, which included 70 patients with CAD [coronary artery disease] or cerebral infarction, low-dose aspirin therapy (81 mg daily) for 6 months led to a significant reduction of Lp(a) levels by 18.3% in the subset of patients with a baseline Lp(a) level >30 mg/dL.

"In another small trial of 25 patients with ischemic stroke in northern India, 4 weeks of daily treatment with 150 mg of aspirin provided similar favorable results, as it lowered Lp(a) plasma values by 46.24%."

"Based on the previous discussion, aspirin therapy may be an option for patients with elevated levels of Lp(a) and high risk for or established CVD, as it is commonly administered

Diet and Lp(a):

Most health professionals have written off diet as a way to lower Lp(a). They shouldn't have given up so soon. A study in the *American Journal of Clinical Nutrition* (Jan. 2022) reports that a low-carb diet lowered Lp(a). If you don't want to wade through that article (and we do not blame you if you don't), why not listen to our interview with David Ludwig, MD, PhD? He is an endocrinologist and researcher.

Dr. Ludwig is a Professor of Pediatrics at Harvard Medical School and Professor of Nutrition at the Harvard T.H. Chan School of Public Health. He is also a primary author of the article above and discusses the impact of a low-carb diet on Lp(a) during our interview. Here is a link to the podcast. You can listen to the streaming audio by clicking on the arrow inside the green circle under Dr. Ludwig's photo or download the free mp3 file.

Once statins became the dominant drugs in cardiology, aspirin and niacin were mostly abandoned for cardiac prevention. These inexpensive, old drugs may help against high Lp(a). Perhaps it's time doctors made this risk factor a priority. If there is a history of heart disease in your family, you may want to ask your doctor to consider a blood test for Lp(a). If your level is elevated, inquire about strategies to lower it.

Nondrug Approaches to Lowering Cholesterol

Before making a beeline for the cholesterol-lowering drugs available at the local pharmacy, we think it's prudent to consider some nondrug approaches to heart health, including dietary and lifestyle changes.

There are all kinds of fats floating around in the American diet, and some are far better for us than others. Walter Willett, MD, DrPH, MPH, chair of the Department of Nutrition at Harvard's School of Public Health and one of the leading nutrition experts in the world, equates trans fats (hydrogenated vegetable oil) with poison.

There's also no denying that Americans eat too much omega-6, found in vegetable oils like corn, safflower and sunflower oils, and not even close to enough omega-3 fat, which can be found in some fish, and in walnuts and flaxseed. Avoiding omega-6 and trans fats while you up your omega-3 intake and consume healthier forms of fat is one excellent first step on the road to a healthier heart.

As we have already described above, olive oil in particular is a superlative fat. High in monounsaturated fatty acids, it brings down total cholesterol, bad LDL cholesterol, and blood pressure, as well as lowering the risk of atherosclerosis; extra-virgin olive oil may also reduce the risk of blood clots and some types of cancer.

Looking for healthy oils other than olive? Try almond, avocado, canola, and walnut oils.

Cholesterol-lowering spreads

For those who can't live without bread, the best thing to put on it is olive oil. But now there are also some spreads that will treat your heart much better than the trans-fatty margarines of old. Try Benecol, Promise, Take Control, or Smart Balance if you can't live without bread spread. Benecol and Take Control in particular have been designed to include cholesterol-lowering ingredients called stanols.

One indicator of heart health that many patients– and doctors–fail to fully consider is the level of C-reactive protein (CRP), a measure of inflammation that may be even more relevant than cholesterol for predicting heart-disease risk. You can be tested for $20 or less. If your number is between one and three, your risk for cardiovascular disease is moderate; a number of one or below is good, while any number above three is very dangerous.

There are a few different ways to lower your CRP numbers. The Stanford School of Medicine did a study that indicated diet may have an effect on CRP numbers. Specifically, those who adhered to a Mediterranean diet (full of fruits, vegetables, nuts, grains, seeds, beans, oils and alcohol) had lower CRP numbers. People who consume a lot of vitamin C and fruit also have good CRP levels.

Other foods, including fish oil and many fish, can also help control CRP. (See list at left.) Aspirin can bring down CRP, as can statins. So can regular exercise, keeping your midsection trim, controlling blood sugar levels, and drinking tea and moderate amounts of alcohol.

Anti-Inflammatory Foods

- Wild salmon
- Bluefish
- Tuna
- Sardines
- Fresh or ground ginger
- Garlic
- Olive oil
- Broccoli

- Pomegranates
- Strawberries
- Blueberries

Fish Oil

Our championing of fish oil for cardiovascular health was considered strange and even radical twenty years ago; now, however, it's the ace up many cardiologists' sleeves and there's even a prescription-strength version of fish oil available, Lovaza.

The cardiovascular benefits of fish oil are many. Fish oil is full of good omega-3 fatty acids, which help combat inflammation and can beat back the buildup of atherosclerotic plaque. And they can also help reduce the chances of a blood clot, which might lower the risk of a heart attack or stroke.

Fish oil also helps decrease triglyceride levels— by as much as 45% when taken at doses of 4 grams per day. Also, unlike most medications prescribed to fight heart disease, it's able to raise good HDL cholesterol by up to 9%. And fish oil can also help reduce the ratio between your triglyceride and HDL levels: the lower the TG/HDL number, the better, just like your CRP number. Not only that, but fish oil can bring down blood pressure, too, and improve blood-vessel flexibility. It also slows your heart rate, stabilizes the electrical activity of your heart, and can cut back on the chance of abnormalities in heart rhythm.

We also like fish oil because its benefits may extend to arthritis and decreasing the likelihood of Alzheimer's, asthma, and depression. The only

Nuts

We're nuts for nuts. Walnuts in particular are packed with heart-helping goodness. Four or five servings of walnuts each week (of 2 to 3 ounces each) can bring down the risk of coronary artery disease by 30-50%, and can also do positive things for blood lipids. (Those are the kinds of results you might hope to get from medications.)

Walnuts can also bring total cholesterol, bad LDL, and triglycerides down while it brings good HDL up; it can help prevent plaque buildup in coronary arteries; and it can also improve flexibility in blood vessels and circulation in people who have high cholesterol. Other great seeds and nuts include almonds, pecans, pistachios, macadamia nuts, peanuts and cashews. Just make sure that increased calories are compensated for in other ways, like by cutting back on sugars and starches.

Alcohol

For those who like to sip a nut-brown ale in the evenings, or linger over a glass of Chardonnay at dinner, the next news flash may appeal to you: there's a great deal of evidence that suggests a moderate daily consumption of alcohol significantly benefits the heart. One large study indicated that men who had one drink 4 or 5 times a week could decrease their risk of heart attack by as much as 30-50%. And you can pick your poison: it didn't matter whether the drink consumed was wine, beer, or spirits. (One drink = 12 ounces of beer, 4 ounces of wine, or 1 1/2 ounces of liquor.)

Drinking alcohol in moderation—and moderation is key—may have other benefits as well: decreased risk of ischemic (clotting) strokes, type 2

But you should only drink, of course, if it's something you already enjoy in moderation. We don't recommend starting to drink as a way to improve health, and there are of course many people who shouldn't and can't drink, including alcoholics. Alcohol can also interact with many medications, so you should carefully consult your physician about possibly dangerous combinations. Remember that there are many other ways to treat your heart right.

Grape Juice

If you don't like the heavy stuff, you can always try sipping its non-alcoholic cousin: good, oldfashioned grape juice. A lot of the antioxidant flavonoids found in red wine are also abundant in grape juice, and its cardiovascular benefits are almost as impressive: it can bring down bad cholesterol, prevent the oxidation that leads to plaque buildup, help keep blood vessels flexible and blood pressure down, increase blood flow, and help prevent the likelihood of blood-clot formation. It might even give your immune system a bump.

So stop worrying about the purple mustache and take a swig of your favorite grape juice. And adding Certo (plant pectin) to your grape juice may have special anti-inflammatory benefits, helping not only your heart, but maybe your joints, too, in the process. Many with arthritis pain have reported excellent results from this winning combination. Try 1 packet Certo in 64 ounces of grape juice, and drink 6 to 8 ounces of the mixture daily.

Pomegranate Juice

alcohol and grape juice, and it may also have a few hidden boons, too. It might help fight cancer and arthritis, for instance, and possibly also erectile dysfunction. We recommend drinking 8 ounces daily.

One important side note: there's some initial evidence that suggests pomegranate might interact with some drugs (including statins) in harmful ways similar to grapefruit. It might increase the chance for pharmaceutical side effects. Pomegranate juice might also cause constipation. And it can be pricey. You might want to try juice from concentrate to cut back on costs. One supplier that we like is www.healingfruits.com.

Chocolate

What your mother always told you about chocolate may not be true: it's looking more and more likely that small quantities of dark chocolate may actually be very good for your health. Chocolate has been shown to bring down blood pressure, help improve insulin response, and boost bloodvessel flexibility. It might also help prevent the formation of clots, raise good HDL cholesterol, and keep LDL cholesterol from generating atherosclerosis.

But the real test revolves around the question of whether or not it can prevent heart attacks—and the results are in. A study from the Netherlands indicated that men over 65 who ate chocolate (around 10 grams—or a bit less than one of those small Ghiradelli squares) were 50% less likely to die of a heart attack than those who didn't indulge their sweet tooth daily. So go ahead and try a nibble of the good stuff. Just remember once again to cut your calories somewhere else.

Cinnamon

some data reveals it might lower cholesterol, too. It brings down rat cholesterol and triglyceride levels better than the drug lovastatin.

Readers have benefited from this nice spice. One woman told us that her high cholesterol dropped precipitously (from 290 down to 122) while eating just a quarter teaspoon of cinnamon a day. Cinnamon can cause heartburn in some people, though, so be careful. We also worry about the possibility of liver damage. To minimize that risk, it makes sense to use water-extracted cinnamon. As usual, it's best to consult your doctor before adding something new to your routine.

Grapefruit

It's long been believed that grapefruit has special weight loss-inducing powers. While those particular claims may be dubious—we've never seen any evidence to back it up—there is proof that grapefruit lowers cholesterol. In one Israeli study, eating red grapefruit each day for a month lowered the total cholesterol of people who had undergone heart bypass surgery by 15%.

Please be careful, though: grapefruit interacts dangerously with dozens of prescription medications, including certain cholesterol-lowering drugs.

Apple Cider Vinegar

There's no good science here, but one of our readers reported that after drinking a bit of apple cider vinegar per day, her good HDL was 63 and bad LDL was 61—and her total cholesterol had been 384 before the vinegar cure!

could be at risk.

Steps for Reducing Heart-Disease Risk

- Exercise regularly
- Eat sensibly
- Lose weight, especially around the midsection
- Get a good night's sleep
- Stop smoking
- Manage anger
- Marriage counseling
- Reduce stress, depression, and anxiety
- Foster a support network
- Lower blood pressure
- Bring down cholesterol and other lipids

Supplements

Niacin

We used to think vitamins B6 and B12 would lower the risk for a heart attack or stroke. Unfortunately, long-term studies haven't shown that these B vitamins offer a statistically significant benefit. But one form of B that really does boost your odds of beating heart disease is niacin, B3. And there are no doubts about its long-term effectiveness: it's been prescribed for more than 50 years.

Researchers still don't understand exactly how niacin manages to lower the risk of a heart attack. What they do know is this: it brings down triglycerides and bad cholesterol, and it pumps up the good kind. And it's cheap.

to effect a change in lipid profiles can have powerful side effects, and you should have your liver enzymes checked regularly. You'll also need to see your doctor to find out what the best dose is for you.

Some unpleasant reactions to niacin that have been reported include nausea, flushing, tingling, itching, fatigue, headache, dry eyes and skin, and muscle problems. Controlled-release formulations such as prescription Niaspan may diminish the effects of tingling and itching.

Red Yeast Rice

We've heard from a lot of readers who are really excited about red yeast rice. And we were initially excited, too, when we saw data from a UCLA School of Medicine study that was subsidized by a company called Pharmanex, which was using red yeast rice in one of its product. The results of the trial were impressive: they showed a 22% decrease in bad LDL cholesterol.

Pharmanex was forced to take red yeast rice out of its product, Cholestin. Red yeast rice contains natural statin compounds, including lovastatin, the ingredient in **Mevacor**. Big Pharma complained to the FDA that Cholestin was an "unapproved new drug," even though Chinese people have used red yeast rice for hundreds or even thousands of years in food. After a protracted legal battle with the FDA, the company replaced red yeast rice with policosanol, a complex of compounds derived from sugarcane wax or sugar beets. (Unfortunately, well-designed double-blind placebo-controlled clinical trials on policosanol do not support its ability to lower cholesterol significantly.)

on Pharmanex, FDA does not seem concerned about these products being sold as dietary supplements, which it does not generally regulate.

We suggest that people who would prefer to take red yeast rice rather than prescription cholesterollowering medicines discuss this with their doctors and check the quality of the supplement before purchasing it. Both *Consumer Reports* and ConsumerLab.com (www.consumerlab.com) occasionally test dietary supplements for contamination as well as whether the product contains what it claims to. The brand **HPF Cholestene** had red yeast rice and no toxic contaminant in the last test ConsumerLab. com did. Caveat emptor!

Many of our readers swear by red yeast rice and have used it to lower their cholesterol effectively. Just be advised red yeast rice, like statin drugs, may cause muscle pain and weakness as well as elevated liver enzymes in some people. It may also interact with some drugs including antibiotics, antifungals, antidepressants, immune-suppressants, anticoagulants, HIV/AIDS drugs, other cholesterol-lowering medications, and grapefruit. Take it only with medical supervision!

Psyllium

Another well-kept supplement secret is psyllium, the fiber in laxatives like Metamucil and Fiberall. Its effects on cholesterol are relatively modest—more modest than we had once hoped—but about 10 grams per day (or 3 tablespoons of Metamucil) can bring total cholesterol down by roughly 4%, and bad LDL by 7%.

We think psyllium might best be employed as part of a vegetarian "portfolio" diet:

- Eggplant
- Margarine (like Benecol)
- Oats
- Okra
- Psyllium
- Soy meat analogues (burgers, dogs, deli slices)

This diet might lower cholesterol nearly as much as statin-type medications, according to a Canadian study.

The standard dose of psyllium is 1 tsp in 8 ounces of water, three times daily before meals. There are a few drawbacks: most people think it isn't exactly delicious. It also may cause some bloating, gas, and other digestive discomfort.

Magnesium

Magnesium doesn't get much press; compared to sodium and potassium, it barely gets its 15 minutes. But it's essential to many of the most fundamental physiological processes: it helps control blood pressure and maintain bone strength; it keeps migraines at bay and improves regularity as well as cardiovascular health.

Our bodies are frequently low in this important mineral, and some of the same diuretics that diminish potassium also deplete magnesium. Studies have shown that having too little magnesium in your body can put you at risk of heart disease and heart attacks. Getting more magnesium in your diet reduces that risk. (See column at left for a list of high-magnesium foods.) People with the lowest levels of magnesium are also the most likely to have clogged coronary arteries. Increasing magnesium intake,

and diminishes cellular inflammation. It also ramps up coronary artery circulation, and keeps the heart beating regularly.

The recommended dose of magnesium is 300 to 500 mg a day. Loose stools means you're taking too much. Magnesium is dangerous for people with kidney disease or reduced kidney function.

High Magnesium Foods

- Almonds
- Cashews
- Halibut
- Oatmeal
- Peanuts
- Potatoes (baked)
- Soybeans
- Spinach

Drugs for Heart Health and Lower Cholesterol

While we always advocate trying nondrug approaches first—the risk of side effects, interactions, complications, and complacency are much lower when we don't depend on pharmaceuticals to do our bidding for us—sometimes we all need a little bit of extra help. This is also true when it comes to protecting the heart. And our first drug of choice for cardiovascular fitness and protection is aspirin.

Aspirin

of a year's supply totals around $5, if bought in bulk. When you think about that in comparison to some prescription statins, which can cost upwards of $3.50 per pill, or the blood thinner Plavix (clopidogrel), which can cost $4 per pill, aspirin truly seems like a steal—especially when you consider its results compared to these other drugs. One study published in *The New England Journal of Medicine* demonstrated that out of a population of 15,000 high-risk patients taking either Plavix with aspirin or aspirin by itself for 2 years, there was no difference in the rate of heart attack, stroke, or cardiovascular-related death between those taking the Plavix plus aspirin and those just on aspirin.

Aspirin's benefits are almost mind-boggling: not only does it significantly reduce the risk of stroke and heart attack, it also seems to fight cancer, lowering the risk of colon, rectum, prostate, pancreas, lung, skin, ovary, and breast malignancies. And if that weren't enough, it also appears to cut one's chances of developing diabetes and Alzheimer's disease. Not only that, but it also seems able to prevent a heart attack from doing major damage even after it's started: emergency rooms have a standard practice of giving aspirin to anyone who seems to be having a heart attack. And if they don't, it's considered a serious misstep.

All of these remarkable benefits of aspirin are probably due to its anti-inflammatory and anticoagulant properties. Another advantage of aspirin is that it's been around for a very long time, more than 100 years, so the medical community has become quite familiar with its long-term potential risks and side effects, particularly indigestion, gastritis and ulcers. Bleeding or perforated ulcers can be life-threatening. Many of the newer cholesterollowering and blood pressure medications just haven't been on the market long enough for a thorough assessment.

Aspirin's history is fascinating. It was developed in 1897 by the Bayer chemist Felix Hoffman, who was just trying to create a stable form of acetylsalicylic acid to relieve his father's painful rheumatism symptoms. He certainly couldn't have known then that his breakthrough would go on to save tens if not hundreds of millions of lives.

But it took some 50 years before the remarkable insights of another scientist, this time a doctor, brought aspirin's incredible life-saving potential to light. Lawrence Craven, MD, a general practitioner in California, began distributing Aspergum (just what it sounds like: a gum containing aspirin) to his tonsillectomy patients in 1948 when it was first introduced. This brought down their pain enough to allow them to eat and sleep. But it also caused a lot of people to develop hemorrhaging—sometimes so severe that they had to be hospitalized.

Instead of just giving up on the stuff, as many contemporary physicians might do, Dr. Craven realized that aspirin must have strong anticoagulant properties. He wondered if it would stop blood clots from forming in the coronary arteries. As early as 1950, he started recommending that all of his male patients ages 40 to 65 start taking the equivalent of about 1 or 2 tablets of aspirin per day. He wrote up his results six years later, after getting roughly 8,000 men to follow his advice. He reported that "not a single case of detectable coronary or cerebral thrombosis [heart attack or stroke] has occurred among patients who faithfully have adhered to this regime."

Unfortunately, it took rather a long time before cardiologists followed Craven's lead. But over the past half century, more and more data about aspirin's heart-saving abilities have accrued. Two major reviews in respected medical journals (the *British Medical Journal* and *Annals of*

And additionally, if more at-risk people took aspirin, a huge number of lives could be saved—40,000 more each year, according to the British scientists. Those who should especially consider aspirin therapy include: men over 40, post-menopausal women, smokers, and those with diabetes, high blood pressure, clogged arteries or angina. But aspirin is inappropriate for a lot of people, most notably those who are prone to gastric irritation or ulcers. Many individuals are allergic to aspirin and must avoid it for that reason. Aspirin may also interact with other medications, including blood thinners, NSAIDs or some blood pressure pills. Anyone on aspirin long-term should of course consult his or her physician.

What Is the Dose?

Remarkably, although aspirin has been around for over 100 years, there is still a great deal of debate about what the best daily dose ought to be for those taking it preventatively. One expert in the field has proposed 160 milligrams per day for prevention of heart attack and stroke. The Plavix/aspirin study utilized low-dose aspirin at between 75 and 162 milligrams daily.

Q & A

Q. I know that aspirin reduces the risk of heart attacks, strokes and cancer, but I am confused about the best dose. Some experts recommend a baby aspirin while others suggest a regular aspirin daily.

I am prone to stomach irritation from chronic NSAID use. How can I get the benefits of aspirin and minimize the risks? Is buffered aspirin better?

that aspirin can increase the risk of hemorrhagic stroke. That's why no one should undertake a lifelong aspirin program without medical supervision.

There is still a lot of confusion about the ideal dose. The cardiovascular benefits of aspirin are detectable at surprisingly low levels (40 mg), but some people are resistant and may need higher amounts.

Neither buffered aspirin nor enteric-coated aspirin provides complete protection against digestive tract damage. An acid-suppressing drug like Prilosec OTC might help. Doctors sometimes prescribe Cytotec (misoprostol) to prevent stomach ulcers.

Statins

There's no denying the power of statins; they have been the highest grossing pharmaceuticals in history, and there's a reason: they bring cholesterol down. But as we hope we've explained by now, cholesterol is not the only factor in determining heart health or heart attack risk—and may not even be the most important one. Statins also can cause some unpleasant side effects in many people, and some of their other quite serious potential downsides are just coming to light.

We don't mean to suggest that statins aren't helpful. They certainly do lower cholesterol, but the ability to prolong life is less clear. Before you reach for that bottle of pills as a quick fix for your cholesterol concerns, there are a few things you should know that may lead you to try some other approaches first.

How Low Can You Go?
What Statins Are and Do

lovastatin (**Mevacor**), pravastatin (**Pravachol**), rosuvastatin (**Crestor**), and simvastatin (**Zocor**). The annual sales of these drugs exceed tens of billions of dollars. About 50 million people globally take a statin each day. There's no other prescription medication in the world that even comes close to matching those kinds of sales or distribution rates.

And their track record with bringing down bad LDL cholesterol as well as total cholesterol is incontestable. One study out of the Cleveland Clinic showed that high-dose rosuvastatin could reduce LDL by 52-60%, which is astounding, and decrease coronary-artery plaque buildup by 9%.

Doctors advise any of their patients who are at a fairly high risk of heart attack but who have no history of heart disease to get their LDL down to 100. Those who are in the highest-risk category are often told to get their LDL below 70. And there are some cardiologists who'd like to see that number shrink even more. It's impossible to bring the numbers down that low without drugs—which is why so many people take them.

The category of people for whom statins are most effective is middle-aged men who have coronary heart disease. Those men who have bad LDL to HDL ratios and multiple other risk factors may also be able to benefit from statins. At this point, it's still unclear as to whether or not statins would benefit women and those over the age of 70 enough to outweigh their potential side effects. And in fact, even for those in the highest-risk group, there's some suggestion that statins may only be worth it for those whose heart-attack risk is 10% or more over 10 years.

Statins have unquestionably saved many lives by reducing patients' risk of heart attack and stroke. Their ability to bring down cholesterol, and their

But we also don't want to over-exaggerate their benefits. *The New England Journal of Medicine* published a book review that notes "two fish meals a week are as effective as statins in preventing death among patients with cardiac disease." And when you compare the results of taking aspirin to taking statins, their ability to prevent a first heart attack is remarkably similar.

One difference between statins and other methods for bringing down cholesterol, though, is that you can "cheat" while on statins—still getting impressive results on cholesterol tests without changing your diet or lifestyle. This is one reason many patients like the drugs as much as doctors, some of whom have (half) jokingly suggested putting statins in the water supply.

For a whole slew of reasons, though, we find this suggestion extremely troubling. Statins are associated with a number of side effects—including some that are incredibly grave, even fatal—that have only recently come to light. Some of these adverse reactions are still disputed by the pharmaceutical companies and many doctors.

The Dangers of Statins

Many people are able to take statins without experiencing any side effects from the drugs. But a significant number have reported major, debilitating, and in some cases life-threatening problems as a result of taking these medications. No drug is tolerated by everyone—even medicines as life-saving as penicillin or aspirin can harm or even kill certain individuals. That is why it's crucial for us to know all of the potential benefits and risks of any drug we are considering taking.

attributed to the drugs. At first, we weren't sure whether to lend any credence to reports of muscle pain, cramping and weakness—sometimes so severe that it left patients effectively paralyzed—memory loss, depression, sexual dysfunction, nerve damage, joint pain, and elevated liver enzymes. And for a long time, we didn't want to believe what our readers were telling us. It was, after all, totally at odds with what the literature and doctors were saying.

Over time, these reports really started to scare us, and little by little, the literature has also been catching up with what our readers have been saying for years. But awareness is still lagging in some doctors, and also many patients, about the degree and scale of the problem.

Many of the side effects—forgetfulness, for example, or joint pain—are often attributed to the normal aging process, even when they're drug-induced. (Stopping the medication often leads to reversal of the symptoms.) Other times, side effects come on so gradually, they're hard to associate with the medication. There may be a number of associated reactions that seem disparate and unrelated: sore muscles, depression, and sexual dysfunction might not seem like they all come from the same source. Unfortunately, many doctors have also been unwilling, until recently, to take these claims seriously—as has the FDA. While they've done some investigation, the problem hasn't been treated with the seriousness it requires.

Statins and Serious Muscle Problems:

Rhabdomyolysis:

Some of the most frightening reports that we have been receiving involve severe muscle damage. Many doctors will assume we are referring to

convinced it is really rare and not that big a deal. They do not always warn patients what to watch out for. Here is one example:

> **Q.** I've been experiencing illness that I think is related to **Crestor** prescribed by my primary care provider to lower cholesterol. I've had fever, fatigue and dark urine. I believe that even though I work out regularly, I have experienced muscle damage.
>
> Can this damage be reversed? I lead a healthy lifestyle and hope that I will be able to recuperate. What can you tell me about this medicine and its side effects?

A. Statins such as rosuvastatin (Crestor), atorvastatin (**Lipitor**), pravastatin (**Pravachol**) or simvastatin (**Zocor**) can cause a life-threatening condition called rhabdomyolysis. Although rhabdo is relatively rare, it occurs when muscles break down. This can lead to symptoms such as fatigue, muscle tenderness and weakness, dark urine (tea colored) and fever. Kidney failure can result.

Please notify your physician immediately! She will want to run tests for creatine kinase (CK), myoglobin, creatinine and potassium. You will likely be told to stop the statin immediately. If you do have rhabdo, and the drug is eliminated promptly, your muscles and kidney function should recover.

Statins and Other Muscle Damage (Myositis):

muscle symptoms). But not all muscle pain and weakness is created equal. *Myalgia* is very different from *myositis*!

Some health professionals may not be familiar with the adverse reaction called *inflammatory myositis*. This autoimmune muscle disease is supposed to be rare (purportedly occurring in approximately 3 people out of 100,000 taking a statin) but it is debilitating and potentially irreversible (*JAMA Internal Medicine*, Sept. 2018). We have received so many reports of myositis that we aren't completely convinced it is as rare as most health professionals believe.

Symptoms of this condition include difficulty doing normal activities such as walking up stairs, getting out of a chair or lifting arms. Muscle weakness and soreness that do not go away are other potential signs. There is no cure.

Physicians should have known about the statin-myositis link long ago. That's because it has been documented in the medical literature for years (*Journal of Clinical Epidemiology*, Aug. 2007).

The FDA and Statin-Myositis:

The FDA makes only passing reference to myositis in its prescribing information for atorvastatin (**Lipitor**), pitavastatin (**Livalo**) and rosuvastatin (**Crestor**). Here is how the agency lists this complication for atorvastatin. You will see that myositis is lumped together with lots of other scary side effects. It could easily be missed amidst the medical word salad:

"Postmarketing Experience

> "The following adverse reactions have been identified during post-approval use of atorvastatin calcium. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.
>
> "Adverse reactions associated with atorvastatin calcium therapy reported since market introduction, that are not listed above, regardless of causality assessment, include the following: anaphylaxis, angioneurotic edema, bullous rashes (including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis), rhabdomyolysis, **myositis**, fatigue, tendon rupture, fatal and non-fatal hepatic failure, dizziness, depression, peripheral neuropathy, pancreatitis and interstitial lung disease.
>
> "There have been rare reports of immune-mediated necrotizing myopathy associated with statin use."

Did your eyes glaze over? We would not be at all surprised if they did. But trust us when we say that ***myositis*** is way different than myalgia. Whenever you see *ITIS*, think inflammation. ArthrITIS is inflammation of the joints. GastrITIS is inflammation of the stomach. MyosITIS is inflammation of the muscles. There is no cure for myositis. Think of it as an incredibly debiliting condition that can lead to disability and/or death.

Symptoms of myositis may include:

- Difficulty getting up stairs

- Exhaustion after walking or even standing for awhile
- Breathing or swallowing complications

Here are a few stories about statins and myositis:

Deb wrote from the UK:

> "Statins have ruined my life. I can no longer work. I cannot walk very far, and I'm exhausted all the time. I can't cook, as I can't stand, and my arms are so weak I can't lift a pan, and I drop things. I've gained 3 stone from the prednisolone, and I no longer have an interest in going out. The worst is the pain that medication can't stop. I take morphine-based tablets as a back up."

MK developed inclusion body myositis:

> "I developed muscle weakness soon after starting Lipitor. When I complained to my doctor, he switched me to Vytorin [which contains simvastatin along with ezetimibe].
>
> "The muscle weakness continued even after being off the statins for 6 months. I was diagnosed with biopsy proven inclusion body myositis. My muscle strength continues to decline and my neurologist says that there is no effective treatment at this time."

> "My doctor prescribed simvastatin because I have had type 1 diabetes for 50+ years and it was supposed to be a preventative, although my cholesterol levels were great.
>
> "After just a short time the muscles in my legs became so weak I had a hard time coming up my basement stairs and getting out of a chair. I broke out in a very severe rash in my hair and around my eyes and nose and fingernails.
>
> "Eventually, blood work showed my CK levels were very high and the Dr took me off the medication. After a month my symptoms did not get better and I was eventually diagnosed with dermatomyositis. I under went high doses of prednisone to get them down and I still have a lot of muscle weakness. I am on Imuran now but I still can't do stairs without a handrail to help pull me up. Sad story!"

Statins and Memory:

Some people taking statins have also reported memory loss and difficulty remembering words—sometimes very severe. We became very alarmed when we heard the following story:

> "I am a retired family doctor and former astronaut. Two years ago at my astronaut physical at Johnson Space Center I was started on Lipitor. Six weeks later I experienced my first episode of total global amnesia lasting 6 hours. They couldn't

> "Other doctors and pharmacists were unaware of similar problems. Believing it must have been a coincidence, I restarted Lipitor a year later. After 6 weeks I landed in the ER with a 12-hour episode of total global amnesia."

This astronaut-physician was Duane Graveline, MD, who went by "Spacedoc." He described his experiences with statins, and total global amnesia—a temporary but total amnesia, during which he didn't even recognize his wife—in *Statin Drugs: Side Effects and the Misguided War on Cholesterol*, available at the website www.spacedoc.net.

Another of our readers, Michael K., a retired professor of business law and computer science, was diagnosed with probable Alzheimer's after going on Zocor. He even attended his 50th college reunion with a sign on his neck that said, "I'm Mike. I have Alzheimer's disease." After reading our column, however, he took himself off Zocor, and several months later regained his memory and cognitive function.

Statins and Cataracts:

This is one potential statin side effect that most physicians have never considered. The very first statin approved by the fda (July, 1987) was **Mevacor** (lovastatin). The official prescribing information in the early days noted that dogs treated with Mevacor developed cataracts and:

> "There was a high prevalence of baseline lenticular opacities in the patient population included in the early clinical trials

In other words, there was acknowledgment that clouding of the lens suggestive of cataracts occurred during the early human tests of statins. A large British study (*BMJ*, May 20, 2010) involving over 2 million patients detected a cataract signal associated with statin use.

In June 2013, a study was published in the journal *Drug Safety* titled: "Statin Use and Cataract Surgery: A Nationwide Retrospective Cohort Study in Elderly Ethnic Chinese Patients." The analysis of 50,000 individuals enrolled in the National Health Insurance Database of Taiwan suggested that people taking statins were approximately 20 percent more likely to undergo cataract surgery than those not taking such drugs.

There have been other studies linking statins to cataracts, but the medical profession seems unconcerned. That's because most people don't think twice about cataracts. But clouding of the lens is a primary cause of poor vision and blindness in the U.S. The annual cost is nearly $5 billion. And not all cataract surgery goes smoothly. Some people are left with poor vision even when everything goes according to plan.

Statins and Quality of Life:

Even for those experiencing the relatively "minor" side effects of muscle weakness, nerve damage or cramping, the effect on quality of life can be devastating. (Any muscle symptoms should be immediately reported to your doctor, as they could be a sign of life-threatening muscle breakdown, or rhabdomyolysis.)

Some statins (Lipitor, Zocor, Mevacor) can also interact with many drugs, as well as grapefruit, so check with your doctor and pharmacist to make sure that you're not getting into a dangerous drug-interaction situation.

You should never discontinue such medication on your own. Stopping statins could make your CRP and bad LDL cholesterol levels rise dangerously. But if you feel that you can't tolerate statins and that your quality of life is being affected by taking them, talk to your doctor about trying other alternatives for lowering cholesterol.

Readers' Statin Stories

"About 7 years ago, I was put on Lipitor. I didn't like the way it made me feel —extreme fatigue, dry cough, felt 100 yrs. old. I then refused to take it against my doctor's advice.

"I developed neuropathy (numbness) of my toes. Now 7 years later, this neuropathy has spread to include my whole foot. I went to a neurologist, who diagnosed neuropathy, but he also said it couldn't be due to Lipitor.

"I am a retired registered nurse and I KNOW that Lipitor caused my problem. Doctors are not admitting that the statin drugs are very dangerous. I hope I live long enough for the medical profession to admit statins are a dangerous group of drugs! Because I am sure this will eventually happen."

"This summer my father committed suicide. After his death we became aware of the possibility that his death might have been related to a little-known side effect of a medication he took to lower his cholesterol.

"My father began taking Zocor 2 years ago. Prior to that he had never been depressed. I have since met a patient who can directly attribute the start of depression with beginning on Zocor and its end with stopping the drug.

“My doctor insists I must take statins to lower my cholesterol even though I experience pain with all of them. Sometimes it gets so bad that I struggle not to cry when I walk down the hall of my child’s school.

“My doctor says I should accept what he calls ‘a little discomfort’ because studies show statins reduce heart disease. He says this pain is rare, but I know a lot of people who have had the same severe muscle pain.”

“My mother passed away 5 years ago from ALS. She had been put on Lipitor and started experiencing muscle weakness, falling, nerve damage, etc.

“When she contacted her physician to report the muscle weakness, he told her it could not possibly be from the Lipitor. He was very annoyed at my mother for even questioning him.

“My mother was an educated person who had a friend with ALS, and she did her research. To this day, we still believe the Lipitor had something to do with the ALS, as she was primarily a healthy person for her age (83 y.o.). She diagnosed herself and when the official diagnosis came back, she basically gave up, stopped eating or drinking, and lasted only 3 weeks after that.

“Physicians need to listen to their patients!”

Coenzyme Q10

Coenzyme Q10 (CoQ10), while no panacea for statin side effects, has reportedly helped some people with their symptoms, especially muscle pain and weakness. The recommended dose is often 200 to 300 mg for

Studies of statins and CoQ10 have produced mixed results. Some research does show that this dietary supplement can reduce statin-induced muscle pain. Other studies have not demonstrated benefit (*Antioxidants*, Aug. 29, 2022). Until there is more conclusive research, we suggest a try and see approach for people with statin-related myopathy.

CoQ10, which is in almost all our cells, is a strong antioxidant that enables many biochemical reactions. It may be helpful, in conjunction with other treatments, for gum disease, angina, congestive heart failure, Parkinson's, high blood pressure, and some irregular heart rhythms, as well as statin side effects.

CoQ10 may decrease the effectiveness of blood thinners like warfarin (Coumadin). It also may cause digestive tract upset in rare cases. It can be a bit expensive; oil gelcaps, which are the best way to take it, can cost $15 to $60 a month. The **Q-Gel** and **All-Q** brands seem to be the easiest to absorb.

Other Cholesterol-Lowering Drugs

Statins so totally dominate the cholesterollowering corner of the drug market that it may come as a surprise to you that there are other pharmaceuticals available for lowering cholesterol.

Zetia (ezetimibe)/Vytorin

One drug that might have a familiar ring is **Zetia** (ezetimibe). It's often prescribed with statins, and some people may think that it works in the same way, but it doesn't. Statins stop cholesterol synthesis, whereas Zetia keeps cholesterol from being absorbed by the small intestine.

statins, these numbers come down even more dramatically. **Vytorin** combines simvastatin and ezetimibe. It brings total cholesterol down by 34-37%, and LDL by 46-50%.

But Vytorin (and by extension Zetia) has become extremely controversial. Despite its ability to produce nice lab results, there are questions about long-term cardiovascular benefits. Studies have not shown that Zetia can reduce the risk of heart attacks and strokes or prolong life.

In Australia and Canada, drug regulators have issued warnings about a connection with hepatitis, pancreatitis, and depression. Concerns have also been raised that it may increase the risk of cancer. It's important to remember that cholesterol is only one out of more than 240 factors for determining heart-attack risk.

Zetia interacts with cyclosporine, and people also on warfarin (Coumadin) should monitor their INR levels carefully while on Zetia. There are also some rare side effects associated with Zetia, including diarrhea, abdominal pain, sinusitis, muscle pain, back pain, arthritis, fatigue, cough, allergic reaction, pancreatitis, and liver enzyme elevation.

Lopid (Gemfibrozil) and TriCor (Fenofibrate)

Fibrates are another class of cholesterol-lowering medication. These include **Lopid** (gemfibrozil), which has been on the market for more than a quarter century, and is now available at a fairly reasonable price generically ($15 to $20 per month); and **TriCor** (fenofibrate), which is a newer compound. Generic fenofibrate is also quite affordable from big box pharmacies like Costco, Walmart and Publix with a GoodRx coupon.

down, they also raise good HDL cholesterol, which many other cholesterol-lowering drugs can't do as effectively. They also break down small, dense particles of bad cholesterol into larger and less dangerous particles.

One long-term Finnish study on gemfibrozil showed that it reduced the risk of heart attack in men by about a third: 34%.

An Unexpected Fenofibrate Bonus:

Fenofibrate does a lot more than lower cholesterol. This compound also affects the brain in a surprisingly positive way. This gets technical, but we will try to keep it as simple as possible. The bottom line is that fenofibrate impacts PPARα (peroxisome proliferator-activator receptor alpha). Doing so seems to reduce oxidative damage and neuroinflammation. That in turn can have a positive impact on emotions and responses to stress.

A review of the research (*Biomolecules*, May, 2022) notes:

> "Stimulating PPARα signaling induces potent behavioral effects and may offer a suitable treatment strategy to improve both symptoms of depression and anhedonia [inability to experience pleasure] in patients."

Other investigators report (*British Journal of Pharmacology*, Jan. 2017):

> "The major findings of this study are as follows. Firstly, fenofibrate has antidepressant-like effects in the FST, TST and CSDS model. Secondly, the antidepressant-like effects of

> "Although fenofibrate is clinically used as a hypolipidaemic [cholesterol-lowering] drug, more and more reports have been demonstrating the effects of fenofibrate on the CNS. To the best of our knowledge, our study is the most comprehensive study showing that fenofibrate has beneficial effects against depression, a most burdensome neuropsychiatric disease worldwide. This finding is very interesting and exciting as it has identified a new potential antidepressant."

There is also some reason to believe that fenofibrate might have activity against neurodegenerative diseases involved in the development of dementia (*Neurochemical Research*, March 13, 2020). Much clinical research will need to be done before physicians get a green light to prescribe this drug to treat or prevent depression or dementia. Nevertheless, this cholesterol-lowering medicine just might have some surprisingly beneficial effects on the brain. You can listen to our interview with two renowned and innovative Harvard psychiatrists at this link. You will learn about fenofibrate for the treatment of depression in this podcast.

Fibrate Side Effects:

There are also some drawbacks to these medications: gallstone formation may be more common while taking them, and they also may interact with the blood thinner Coumadin; very careful monitoring of INR levels is required while on either medication.

If you experience muscle pain while on these drugs, you must get a creatine kinase (CK) test right away. If fibrates are taken with statins, the risk of very serious muscle problems (rhabdomyolysis) is increased.

Bile Acid Binders

Another class of cholesterol-lowering medications includes the bile acid binders. Bile acids are the precursors to cholesterol.

These drugs, which include **LoCholest** (cholestyramine), **Cholestid** (colestipol), and **WelChol** (colesevelam), work by preventing cholesterol from being reabsorbed by the digestive tract. They may be a good option when other cholesterol-lowering medications are inappropriate for whatever reason.

Their ability to bring down cholesterol, relative to other cholesterol-lowering medications, is modest. They may also raise triglyceride levels.

People with high triglycerides should therefore avoid these drugs. They're also not for people who have difficulty swallowing. Cholestyramine and colestipol may also make the absorption of nutrients and many other drugs more difficult. Anyone on these medications should talk to his pharmacist about drug compatibility and the best time to take a dose.

Bile acid binders may cause digestive tract upset (heartburn, constipation, flatulence, gallbladder problems), headache or rash. Fatigue has been reported on cholestyramine.

The Latest Cholesterol-Lowering Drugs

PCSK9 Inhibitors (Praluent, Repatha)

then there are the names of these drugs: alirocumab (**Praluent**) and evolocumab (**Repatha**).

The FDA approved both Praluent and Repatha in 2015. These are monoclonal antibodies (MABs). We won't subject you to the back story on the discovery of these drugs. It's the sort of history that make's a pharmacologist like Joe get quite excited. We're talking about genetic modification, and yes, that means messing with Mother Nature. Chromosone 1 has PCSK9. Scientists figured out how to inhibit the gene that makes this enzyme. The bottom line on such medicationis is that they are exceptionally good at lowering LDL cholesterol.

As you will recall, this is the so-called "bad" cholesterol that most cardiologists blame for clogged coronary arteries and ultimately heart attacks. But wait just one second. Isn't that what statins are supposed to do? Absolutely! Statins do this by blocking a different enzyme (HMG-CoA reductase) that your liver depends upon to make cholesterol. And yes, statins are also messing with Mother Nature.

Why Not Just Stick with Statins?

The problem with statins is that they have side effects. Although many doctors try to downplay the adverse reactions, we have been collecting poignant stories for decades. For some people it's "just" muscle pain and weakness. Others experience elevated liver enzymes, memory problems, headaches, joint pain, blood sugar elevations, dizziness, insomnia, nerve pain, pancreatitis, cataracts or sexual problems.

Mainstream medicine has tried mightily to downplay such complications, but an article by one of the country's leading cardiologists, Steven Nissen,

(March 4, 2023). If patients complain that they cannot tolerate a statin, there are different options: Repatha or Praluent.

PCSK9 Are Added to or Substituted for Statins:

Many cardiologists and other physicians have decided that if a *little* LDL cholesterol lowering is good, then a *lottle* LDL cholesterol lowering is even better! Statins can often get LDL cholesterol below 100. Add a PCSK9 inhibitor and you can get LDL cholestesrol below 50. Some enthusiasts can even get LDL cholesterol below 25 mg/dL by prescribing high-dose statins together with a PCSK9 inhibitor like Repatha.

How Good Are PCSK9 Inhibitors?

There is no doubt that drugs like Praluent and Repatha can lower LDL cholesterol levels either on their own or in combination with statins. But do they reduce the risk of developing heart attacks and strokes. More to the point, do they prolong life?

We wish there were a nice simple answer to this question. One study published in the *New England Journal of Medicine* (May 4, 2017) was called **FOURIER**. There were 27,564 patients with diagnosed heart disease recruited for the trial. They were all receiving statin therapy. These high-risk individuals were randomized to receive either a placebo injection or a shot of Repatha (evolocumab) either every two weeks or once a month. Those getting Repatha lowered their LDL cholesterol to a median of 30. The authors report:

> **"Overall, 74 patients would need to be treated over a period of 2 years to prevent a cardiovascular death, myocardial**

In other words, regular Repatha injections "reduced the risk of cardiovascular events." But only 1 person out of 74 avoided a heart attack, stroke or death from heart disease. That is known as the number needed to treat. Many cardiologists would consider that a win. Others might say that many more patients *should* have benefited from such low LDL cholesterol numbers. We will let you draw your own conclusions.

A systematic review and meta-analysis of PCSK-9 inhibitors involving 41 studies and 76,304 patients was published in the journal *Cureus* (Oct. 6, 2023).The studies were conducted between 2010 and 2023. Nearly 50,000 high-risk patients were receiving Repatha in addition to statins. More than 27,000 high-risk patients were receiving Praluent in addition to statins. We were shocked to read the conclusions of this large review:

> **"Overall, no significant differences were observed in CV [cardiovascular] and all-cause mortality between PCSK9 inhibitors and controls."**

We would have expected a substantial reduction in deaths from heart disease in the patients getting these powerful LDL-cholesterol reducers.

There was a some good news, though. The authors of this review noted that patients taking Praluent had fewer overall deaths than controls. Patients on PCSK9 inhibitors did have fewer heart attacks, strokes and stents than the control patients. The authors of this review did not offer a number needed to treat, so we cannot tell you with any authority how many patients would need to take either Repatha or Praluent in order for one to avoid such

Another LDL-Lowering Drug: Inclisiran (Leqvio)

Doctors are prescribing other LDL-lowering medications. One that is being advertised is **Leqvio** (inclisiran). It is called a "small interfering RNA therapy." Like the PCSK9 inhibitors, inclisiran does a very impressive job lowering LDL cholesterol. It works differently from the PCSK9 inhibitors, but it has much the same overall effect.

Here is a link to a commercial for Leqvio. Some of the key messages are:

> "…lowering cholesterol can be hard. And diet and exercise add to the struggle. It can feel never ending. But today, it's possible to go from struggle to cholesterol success with Leqvio. Taken with a statin, Leqvio is proven to lower bad cholesterol by over 50%."

Then the announcer rushes through the potential adverse reactions:

> "Common side effects were injection site reaction, joint pain, urinary tract infection, diarrhea, chest cold, pain in legs and often shortness of breath."

What About the Data?

reducing heart attacks and death. Leqvio reduced LDL cholesterol by 40 to 50% in high-risk patients. Shockingly, people taking Leqvio were no less likely to have a heart attack or die prematurely than those on placebo. In the words of the reviewers:

> **"Among the Inclisiran treatment group, there were no significant differences in the overall risk of major adverse cardiac events compared with the control group…"**

You might imagine this disappointing result would make some cardiologists think twice about the importance of LDL cholesterol. The authors attribute the disappointing results to a lack of long-term data. We will be waiting to see what the number needed to treat is for Leqvio before we can make any recommendations about this injectable drug.

Will Nexletol (Bempedoic Acid) Replace Statins?

There is another cholesterol-lowering drug you should know about. The FDA approved **Nexletol** (bempedoic acid) in February, 2020. It is *not* a statin. And most cardiologists don't consider it for a couple of reasons.

First, it's *not* a statin! Physicians are in love with statins. At last count, more than 40 million Americans are prescribed medications like atorvastatin, simvastatin, rosuvastatin, lovastatin, fluvastatin, pitavastatin or pravastatin each year. Most of these drugs are now available generically, which means they are quite affordable.

And **third**, the cost is substantially higher than a statin. The last time we checked, the average retail price for a month's supply of Nexletol was listed around $460 on www.GoodRx.com. Even with a coupon, the cost could be over $400.

So why should anyone consider Nexletol instead of a statin? According to a study in the *New England Journal of Medicine* (March 4, 2023), bempedoic acid can lower LDL cholesterol for patients who cannot tolerate statins. The research was conducted on roughly 14,000 patients who were "statin intolerant."

The randomized controlled trial lasted more than three years. People taking Nexletol daily were 23% less likely to have a heart attack than those taking placebo pills. The absolute risk for a heart attack was **3.7%** in the bempedoic acid group compared to **4.8%** in the placebo group. That's the good news.

The bad news was that:

> "Bempedoic acid had no significant effects on fatal or nonfatal stroke, death from cardiovascular causes, and death from any cause."

In other words, Nexletol did not save any lives over the three plus years of the study. Some cardiologists will say that's not enough time to see a clinical benefit. Others point to fewer heart attacks and say that is good enough for them.

placebo. The difference was not statistically significant. It was also not reassuring.

Side Effects of Bempedoic Acid:

Uric acid levels were elevated in a substantial number of patients taking Nexletol (26%). That might increase the risk for gout attacks. Tendon rupture is a rare, but serious side effect. Other potential adverse reactions include:

- Elevated liver enzymes
- Muscle spasms
- Back pain
- Pain in an extremity
- Abdominal discomfort
- Benign prostatic hyperplasia (BPH)

Laurel Effel Shares Her Non-Drug Approach

Laura Effel's strategy for lowering her LDL cholesterol 44 points in 5 weeks

One of the listeners to our radio show, Laura Effel, called and later wrote in to us to tell us the remarkable story of how she used dietary changes to bring down her bad LDL cholesterol, and to keep it down.

Laura didn't want to take the Zocor her doctor had prescribed, as she'd heard some reports of people having bad reactions to statins, like muscle weakness. So with the help of a food scientist and the "skeptical" go-ahead from her doctor, she radically and permanently changed her diet. Here's what she did:

- Ate a high-protein breakfast
- Substituted olive oil for other fats
- Added soluble fiber to meals other than breakfast
- Focused on fish
- Drank green tea
- Consumed antioxidants
- Stopped eating before bed

After following this new dietary regimen, Laura's cholesterol not only dropped 44 points in five weeks, it continued to go down. We heard from her three months later, and her LDL had gone down a total of 70 points from its peak of 155.

This approach may not have the same dramatic effect for everyone as it did for Laura, but it certainly can't hurt to try it!

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