

Do Cholesterol Drugs Do Any Good?
Research suggests that, except among high-risk heart patients, the benefits of statins such as Lipitor are overstated

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by John Carey

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Cholesterol-lowering drugs called a statins are the "best-selling medicines in history, used by more than 13 million Americans and an additional 12 million patients around the world, producing \$27.8 billion in sales in 2006. Half of that went to Pfizer for its leading statin, Lipitor."

However, critical review of the evidence for the benefits of statin drugs show that they can be life-saving in patients who already have suffered heart attacks, somewhat reducing the chances of a recurrence that could lead to an early death. But for the majority of patients who don't have heart disease, statin drugs offer "no benefit in people over the age of 65, no matter how much their cholesterol declines, and no benefit in women of any age."

The reduction in the number of heart attacks for middle-aged men taking statins in clinical trials is small. "But even for these men, there was no overall reduction in total deaths or illnesses requiring hospitalization—despite big reductions in 'bad' cholesterol."

Most people taking statin drugs have no chance of benefit and a risk of harm.

"Americans are bombarded with the message from doctors, [drug] companies, and the media that high levels of bad cholesterol are the ticket to an early grave and must be brought down. Statins, the message continues, are the most potent weapons in that struggle. The drugs are thought to be so essential that, according to the official government guidelines from the National Cholesterol Education Program (NCEP), 40 million Americans should be taking them. Some researchers have even suggested that the medications should be put in the water supply, like fluoride for teeth."

Statins are sold by:

Merck	Mevacor and Zocor
AstraZeneca	Crestor
Bristol-Myers Squibb	Pravachol
Pfizer	Lipitor

Many researchers harbor doubts about the need to drive down cholesterol levels.

On January 14, 2008, statin drug makers Merck and Schering-Plough revealed results of a trial in which a two-drug combination succeeded in forcing down patients' cholesterol further than with just the statin alone, "but even with two years of treatment, the further reductions brought no health benefit."

When Lipitor ads claim a dramatic 36% reduction in heart attacks, it means that "3% of patients taking a sugar pill or placebo had a heart attack compared to 2% of patients taking Lipitor."

In the Lipitor study, for every 100 people in the 3 1/3 year-long study, three people on placebos and two people on Lipitor had heart attacks.

This means there was one fewer heart attack per 100 people over a period of 3 1/3 years. "So to spare one person a heart attack, 100 people had to take Lipitor for more than three years. The other 99 (99%) got no measurable benefit."

This useful statistic is known as the **Number Needed to Treat (or NNT)**. To benefit one person, Lipitor had to be taken by 100 people for 3 1/3 years. This NNT, 100, is exceedingly high.

The NNT for antibiotic therapy to eradicate ulcer-causing stomach bacteria *H. pylori* is 1.1. Give the drugs to 11 people, and 10 will be cured. This is a low NNT.

There are reasons to believe the overall benefit for many patients taking statin drugs is even less than what the NNT score of 100 suggests. This is due to potential biases that were determined in a drug industry-sponsored trial, which carefully selected patients with multiple risk factors, including high blood pressure or smoking. "The only large clinical trial funded by the government, rather than [drug] companies, found no statistically significant benefit at all."

Experts claim that an "NNT of 50 is worse than a lottery ticket."

"Several recent scientific papers peg the NNT for statins at 250 and up for lower-risk patients, even if they take it for five years or more."

"What if you put 250 people in a room and told them they would each pay \$1,000 a year for a drug they would have to take every day, that many would get diarrhea and muscle pain, and that 249 would have no benefit? And that they could do just as well by exercising? How many would take that?"

Statin drugs have been in use now for 20 years, and the NNT does not decrease the longer people take the drug.

The statin trials of people without existing heart disease showed no reduction in deaths or serious health events.

"We should tell patients that the reduced cardiovascular risk will be replaced by other serious illnesses," says Dr. John Abramson, clinical instructor at Harvard Medical School and author of *Overdosed America*.

10% to 15% of statin users suffer side effects, such as muscle pain, cognitive impairments, and sexual dysfunction, and they cost billions of dollars per year.

"What would work better? Perhaps urging people to switch to a Mediterranean diet or simply to eat more fish. In several studies, both lifestyle changes brought greater declines in heart attacks than statins."

"The things that really work are lifestyle, exercise, diet, and weight reduction." Their cost is much less than drugs and they have benefits for quality of life.

"Difficult risk-benefit questions surround most drugs, not just statins. One dirty little secret of modern medicine is that many drugs work only in a minority of people."

"Beta-blockers are seen as essential in treating congestive heart failure. Yet studies show that an average of 24 people must take the drugs for seven months to prevent one hospitalization from heart failure (thus, an NNT of 24). And 40 people must take it to prevent one death (NNT of 40)."

The diabetes drug Avandia, increases the risk of heart attacks and does not prevent heart disease, strokes, and kidney failure in diabetic patients. "Its NNT is close to infinite." Yet it sells \$2.6 billion per year.

"Many drugs are most effective in relatively small subgroups of sufferers. With statins, these are the patients who already have heart disease. But that's not a blockbuster market. So companies have every incentive to market their drugs as being essential for wider groups of people, for whom the benefits are, by definition, smaller. What the shrewd marketing people at Pfizer and the other companies did was spin it to make everyone with high cholesterol think they really need to reduce cholesterol. It was pseudo-science, never telling you the bottom-line truth, which is that the drugs don't help unless you have pre-existing cardiovascular disease."

Drug companies "make sure that the researchers and doctors who extol the benefits of medications are well compensated." "It's almost impossible to find someone who believes strongly in statins who does not get a lot of money from the industry."

"The National Cholesterol Education Program's 2004 guideline update garnered headlines by recommending lower targets for bad cholesterol, which would put more Americans on the drugs. But there was also a heated controversy in the medical community over the fact that 8 of the 9 experts on the panel had financial ties to the industry. Thirty-five experts sent a petition of protest to the National Institutes of Health, saying the evidence [for the benefit of lowering cholesterol with statins] was weak and the panel members were biased by their ties to [statin drug] companies."

Dr. Howard Brody, professor of family medicine at the University of Texas Medical Branch at Galveston states "I now see it as myth that everyone should have their cholesterol checked."

Cholesterol is just one of the risk factors for coronary disease. Spaniards have cholesterol levels similar to Americans', but less than half the rate of heart disease. The Swiss have higher cholesterol levels than Americans, but their rates of heart disease are lower. Australian aborigines have low cholesterol but high rates of heart disease.

Cholesterol-lowering medications other than statins do not prevent heart attacks or strokes, indicating that statins do not work because they lower cholesterol. Recent evidence indicates that statins probably work (as poorly as they do] because they reduce inflammation in arteries called Rho-kinase.

Experts conclude "Cholesterol lowering is not the reason for the benefit of statins."

"For anyone worried about heart disease, the first step should always be a better diet and increased physical activity."

"If the drugs were used more rationally, drugmakers would take a hit. But the nation's health and pocketbook might be better off."

"The way our health-care system runs, it is not based on data, it is based on what makes money."

KEY POINTS FROM DAN MURPHY

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- 1) Cholesterol-lowering drugs called statins are the "best-selling medicines in history, used by more than 13 million Americans and an additional 12 million patients around the world, producing \$27.8 billion in sales in 2006. Half of that went to Pfizer for its leading statin, Lipitor."
- 2) Statin drugs offer "no benefit in people over the age of 65, no matter how much their cholesterol declines, and no benefit in women of any age."
- 3) The reduction in the number of heart attacks for middle-aged men taking statins in clinical trials is small. "But even for these men, there was no overall reduction in total deaths or illnesses requiring hospitalization—despite big reductions in 'bad' cholesterol."

- 4) Most people taking statin drugs have no chance of benefit and a risk of harm.
- 5) Statin drugs are thought to be so essential that the official government guidelines from the National Cholesterol Education Program, claim that 40 million Americans should be taking them and they "should be put in the water supply, like fluoride for teeth."
- 6) When Lipitor ads claim a dramatic 36% reduction in heart attacks, it means that "3% of patients taking a sugar pill or placebo had a heart attack compared to 2% of patients taking Lipitor," and this occurred over a period of 3 1/3 years. This means there was one fewer heart attack per 100 people over a period of 3 1/3 years. "So to spare one person a heart attack, 100 people had to take Lipitor for more than three years. The other 99 (99%) got no measurable benefit."
- 7) This useful statistic is known as the **Number Needed to Treat (or NNT)**. To benefit one person, Lipitor had to be taken by 100 people for 3 1/3 years. This is a very high NNT, 100.
- 8) There are reasons to believe the overall benefit for many patients taking statin drugs is even less than what the NNT score of 100 suggests. This is due to potential biases that were determined in a drug industry-sponsored trial, which carefully selected patients with multiple risk factors, including high blood pressure or smoking. "The only large clinical trial funded by the government, rather than [drug] companies, found no statistically significant benefit at all."
- 9) Experts claim that an "NNT of 50 is worse than a lottery ticket."
- 10) "Several recent scientific papers peg the NNT for statins at 250 and up for lower-risk patients, even if they take it for five years or more."
- 11) The statin trials of people without existing heart disease showed no reduction in deaths or serious health events.
- 12) 10% to 15% of statin users suffer side effects, such as muscle pain, cognitive impairments, and sexual dysfunction, and they cost billions of dollars per year.
- 13) "What would work better? Perhaps urging people to switch to a Mediterranean diet or simply to eat more fish. In several studies, both lifestyle changes brought greater declines in heart attacks than statins."
- 14) "The things that really work are lifestyle, exercise, diet, and weight reduction." Their cost is much less than drugs and they have benefits for quality of life.
- 15) "Difficult risk-benefit questions surround most drugs, not just statins. One dirty little secret of modern medicine is that many drugs work only in a minority of people."

16) "Many drugs are most effective in relatively small subgroups of sufferers. With statins, these are the patients who already have heart disease. But that's not a blockbuster market. So companies have every incentive to market their drugs as being essential for wider groups of people, for whom the benefits are, by definition, smaller. What the shrewd marketing people at Pfizer and the other companies did was spin it to make everyone with high cholesterol think they really need to reduce cholesterol. It was pseudo-science, never telling you the bottom-line truth, which is that the drugs don't help unless you have pre-existing cardiovascular disease."

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18) "The National Cholesterol Education Program's 2004 guideline update garnered headlines by recommending lower targets for bad cholesterol, which would put more Americans on the drugs. But there was also a heated controversy in the medical community over the fact that 8 of the 9 experts on the panel had financial ties to the [drug] industry. Thirty-five experts sent a petition of protest to the National Institutes of Health, saying the evidence [for the benefit of lowering cholesterol with statins] was weak and the panel members were biased by their ties to [statin drug] companies."

19) Cholesterol-lowering medications other than statins do not prevent heart attacks or strokes, indicating that statins do not work because they lower cholesterol. Statins probably work (as poorly as they do) because they reduce inflammation in arteries called Rho-kinase. "Cholesterol lowering is not the reason for the benefit of statins."

20) "For anyone worried about heart disease, the first step should always be a better diet and increased physical activity."

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