

Growing Doubt on Statin Drugs: The Problem of Drug-Lifestyle Interaction

John Mandrola | July 02, 2014

Editor's Note: *This blog entry originally posted at drjohnm.org*

My mind is changing about [statins](#). I'm growing increasingly worried about the irrational exuberance over these drugs, especially when used for prevention of heart disease that is yet to happen.

An elderly patient called my office last week to tell me thank you . . . not for a successful procedure or surgery, but rather for helping with a problem that had dogged her for a decade. How did an electrophysiologist help a patient without doing a procedure?

I stopped her statin.

A few weeks later, the patient said, her muscle and joint pain were gone. "I thought it was arthritis. I'm walking now. I haven't felt this good in years. I've even lost five pounds."

So why was this elderly patient on a statin?

It was being used to lower cholesterol in the hopes that it would lower the risk of a future heart attack or stroke. This is called primary prevention. The patient had no vascular disease but had a high cholesterol level.

The problem, of course, is that statins have not been well-studied in elderly women. Her doctor and the medical establishment writ large have extrapolated findings of clinical trials on younger, mostly male, patients to all patients with high cholesterol levels. This is a striking jump to make, given that low cholesterol levels in the elderly are associated with higher death rates.

Anecdotes are not evidence, but this one moved me to review some of the statin evidence. And to think (again) about treating [people vs disease](#).

As always, let's start with the truth — absolute, not relative values. Then I will move on to some new revelations about statins, and then an interesting theory of why potent cholesterol-lowering drugs have such painfully small effects on overall cardiovascular outcomes.

The Truths

When statins are used in low-risk patients without heart disease (primary prevention) there is no mortality benefit. That's right. Your chances of dying are the same on or off the drug, regardless of how much the statin lowers the cholesterol level.

When statins are used for primary prevention, there is a small lowering of future vascular events (stroke/heart attack) over five to 10 years. The absolute risk reduction is in the range of seven per 1000. That means you have to treat 140 patients with a statin (for five years) to prevent one event. Or this: for 99.3% of statin-treated patients, there is no benefit. I like to call this the PSR, or percent same result.

There is also general agreement that statins increase the risk of developing diabetes, especially in women, and that risk is about the same as preventing a stroke or heart attack, approximately 1%.

Another fact is that patient-level (raw) data from the industry-sponsored cholesterol trials have not been independently analyzed. Systematic reviews from the Cochrane group have analyzed only published data rather than the raw data.

There is likely a [difference](#) ^[1].

There is great debate about the incidence of statin side effects, such as muscle pain, cognitive issues, decreased energy, sexual problems, and kidney and liver injury, among others. In the industry-sponsored randomized controlled clinical trials, discontinuation of statins was not significantly different from placebo. [Observational data](#) and the observations of any clinician provide a different picture^[2].

No statin drug has ever been compared with lifestyle interventions for the prevention of cardiovascular disease.

New Revelations

A [study](#) presented in April 2014 at the **Society of General Internal Medicine** meeting in San Diego showed that individuals prescribed statin therapy for high cholesterol consumed more calories and more fat than nonstatin users. And, not surprisingly, this increase in calories paralleled an increase in BMI in statin users.

An [analysis](#) of a prospective cohort study of men (published in *JAMA Internal Medicine*) revealed that physical-activity levels were "modestly" lower among statin users compared with nonusers independent of other cardiac medications and of medical history.

Possible Connecting Theory: Drug-Lifestyle Interaction

These two recent studies are troublesome. As pointed out in the [excellent coverage](#) from [heartwire](#) journalist **Michael O'Riordan**, there may be an interaction between medication and lifestyle. Namely, if statin users consume more calories, gain weight, and exercise less, it becomes easy to see why cardiovascular benefits are so small.

It's been really hard to explain why the striking reductions in LDL cholesterol—up to 30% to 50%—from statins haven't translated into significant future benefit.

One possibility is that cholesterol levels are a lousy surrogate for outcomes. That surely seems true in the elderly, but what about in younger patients and those with familial high cholesterol? These patients are definitely at increased cardiovascular risk. So cholesterol levels are surely not unimportant. There are convincing data, for instance, that higher HDL levels are associated with lower CV risk.

Another possibility for lack of statin benefit is analogous to AF rhythm control and high blood-pressure issues. As in, yes, it's better to be in regular sinus rhythm and have normal blood pressure, but getting to those goals with pills isn't the same as being there naturally. With rhythm-control and blood-pressure drugs, the achievement of the desired outcome is muted by side effects from the drugs. Perhaps it's the same with statin drugs?

You don't have to posit malfeasance on the part of big pharma here. All you have to do is think past the disease-specific mind-set of modern-day medicine. We are much more than our cholesterol level. A statin drug, like so many drugs that block enzyme pathways far upstream in major cellular pathways, is going to have much more biologic action than just moving an easily measured cholesterol level.

When you step back and look at medications as chemical modifiers of cellular processes in complex biologic systems like our body, it's easy to understand that health comes not from pills. Not even statins.

JMM

References

1. Wieseler B, Wolfram N, McGauran N, et al. Completeness of reporting of patient-relevant clinical trial outcomes: Comparison of unpublished clinical study reports with publicly available data. *PLoS Med* 2013; DOI:10.1371/journal.pmed.1001526. [Abstract](#)
2. Zhang H, Plutzky J, Skentzos S, et al. Discontinuation of statins in routine care settings: A cohort study. *Ann Intern Med* 2013; 158:526-534. [Abstract](#)

© 2014 WebMD, LLC

Cite this article: Growing Doubt on Statin Drugs: The Problem of Drug-Lifestyle Interaction. *Medscape*. Jul 02, 2014.