

Statins work better at higher doses in patients with coronary heart disease

Research question Standard doses of statins save lives and prevent cardiovascular events in patients with coronary heart disease. Do high doses work any better?

Answer Yes. High doses prevent more cardiovascular events, including heart attacks and strokes

Why did the authors do the study? The clinical benefits of standard doses of statins are well established, but doubt remains over the potential benefits of increasing the dose. Several large trials have been done comparing the two approaches, but results have been mixed.

What did they do? These authors searched systematically for all randomised trials comparing standard dose with high dose statins in patients with coronary heart disease. They included only those trials that were big enough to study clinical outcomes such as heart attacks, strokes, and deaths. They found four large trials, two in patients with stable coronary heart disease and two in patients with a recent acute coronary syndrome. The trials compared standard doses of pravastatin (40 mg), atorvastatin (10 mg), or simvastatin (20–40 mg) with high doses of atorvastatin (80 mg) or simvastatin (40–80 mg) over two or five years of treatment. They included a total of 27 548 patients.

By pooling data from all four trials, the authors calculated the relative odds of four different outcomes—heart attack or death from coronary heart disease, any cardiovascular event or death from coronary heart disease, stroke, and death from any cause.

What did they find? Patients treated with higher dose statins were significantly less likely to die a coronary death or have a heart attack (9.4% *v* 8.0%, odds ratio 0.84 (95% CI 0.77 to 0.91)), to die a coronary death or have any cardiovascular event (32.3% *v* 28.8%, 0.84 (0.8 to 0.89)), or to have a stroke (2.8% *v* 2.3%, 0.82 (0.71 to 0.96)) than patients treated with standard doses. A higher dose had no significant impact on all cause mortality (6.2% *v* 5.9%, 0.94 (0.85 to 1.04)), although the authors found a trend towards a lower odds of cardiovascular death (3.8% *v* 3.3%, 0.88 (0.78 to 1.00)). There were few serious side effects in any trial.

What does it mean? This meta-analysis suggests that higher doses of statins work better than standard doses in patients with coronary heart disease, largely by preventing more non-fatal cardiovascular events such as heart attacks and strokes. These benefits are over and above those already conferred by standard doses. A higher dose doesn't seem to save any more lives overall, but there is a suggestion here that increasing the dose could help prevent cardiovascular deaths. Although this meta-analysis included many thousands of patients, the authors say it was underpowered for the mortality outcomes. A fifth large trial is on the way, which should help provide a more definitive answer. In the meantime, the case for high dose statins is getting stronger. These authors estimate that, compared with a standard dose, high dose statins would prevent an extra 35 000 cardiovascular events for every million patients treated for five years—which gives a number needed to treat of just 29.

Cannon et al. Meta-analysis of cardiovascular outcomes trials comparing intensive versus moderate statin therapy. *J Am Coll Cardiol* 2006;48:438-45

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Editor's choice

Whither medicine?

In his introduction to *The Cambridge History of Medicine*, Roy Porter outlined the great paradox of 20th century medicine: better health and longer life have been accompanied by ever greater medical anxieties. Medicine, he argued, has become a victim of its own success. It has conquered many of the gravest diseases, but power and effectiveness have brought unrealistic expectations, critical scrutiny, distrust, and loss of direction. The second half of the 20th century in particular brought us, among other things, penicillin, the contraceptive pill, steroids, transplant surgery, and, in the United Kingdom, the creation of the NHS, perhaps the most important manifestation of medicine as a social utility. Writing in the *BMJ* in 1949, on the brink of this unprecedented progress, the distinguished physician Lord Horder exuded the uncomplicated confidence of the time. "Whither medicine?" he asked. "Why, whither else but straight ahead." As Porter says, "Today, who even knows where 'straight ahead' lies?"

The *BMJ* has been called the mirror of medicine, so you would expect it to reflect this disquiet and doubt. In this week's journal, Jack Fairhead and Peter Rothwell find that the people most at risk of transient ischaemic attacks and minor strokes—patients more than 80 years old—are just as likely to benefit from treatment as younger patients but are far less likely to be investigated and treated (p 525). In an accompanying editorial, John Young says that ageism will always prosper when resources are inadequate for the target population (p 508). A Cecile Janssens tries to dampen unrealistic expectations that there will soon be a genetic test for type 2 diabetes and urges us instead to focus on applying what we already know to prevent diabetes and its complications (p 509).

Lambert Schuwirth and Cees van der Vleuten ask how we can make medical education more effective in the face of shorter working hours and patients' understandable unwillingness to serve as learning objects (p 544). And Andrea Akkad and colleagues find that one of the pillars of patients' autonomy, written consent for treatment, is seen by most patients as a means of allowing doctors to take control (p 528).

But none of these complexities should blind us to the astounding successes of modern medicine—what Porter calls "the dependable ability to vanquish life threatening disease on a vast scale." Medical advances may in fact account for more than 75% of improved human survival (see Richard Lehman's journals blog on bmj.com). To coincide with next January's relaunch of the *BMJ*, with new content and a new design, we want to celebrate what medicine and health care have achieved since the *BMJ* was founded in 1840. As Trevor Jackson explains (see Contents, 10.1136/bmj.38965.474363.F7), we are asking *BMJ* readers to nominate the medical, scientific, and social innovations that have done most to benefit mankind and from which we have most to learn for the future.

Roy Porter himself died young by today's standards and before the beginning of the new millennium. But he left us some advice: "The task facing medicine in the 21st century will be to redefine its limits even as it extends its capacities."

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