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Statins rarely cause serious side effects

Research question Are statins safe?

Answer Yes. Serious side effects such as rhabdomyolysis, myopathy, and peripheral neuropathy are rare. There's little or no evidence that statins cause liver disease, renal disease, or cognitive decline

Why did the authors do the study? Statins are widely used and are generally considered safe. But well documented concerns over two drugs in this class—cerivastatin and rosuvastatin—prompted these authors to review the published safety data on all statins. Cerivastatin was withdrawn from the market in 2001.

What did they do? They systematically searched for data on the side effects of any statin from four sources: randomised controlled trials, cohort studies, voluntary notifications to regulatory authorities, and case reports. They combined data where possible to estimate the risks of muscle disease (rhabdomyolysis, myopathy), liver disease, renal disease, and neurological disease associated with taking statins. They estimated the class effect, the effects of individual statins, and any additional risks associated with combining statins with other drugs, especially the fibrate gemfibrozil.

What did they find? The estimated incidence of rhabdomyolysis was 3.4 (95% CI 1.6 to 6.5) per 100 000 person years of treatment with any statin other than cerivastatin. This estimate was based on two large cohort studies and 20 randomised controlled trials. Combining a statin with gemfibrozil resulted in a 10-fold increase in the risk of rhabdomyolysis. Drugs metabolised by cytochrome P450, such as simvastatin and atorvastatin, were slightly more likely than other statins to cause rhabdomyolysis (4.2 per 100 000 person years), particularly when combined with a fibrate. Rosuvastatin had the weakest safety data.

Statins were also associated (rarely) with myopathy (11 per 100 000 person years), and peripheral neuropathy (12 per 100 000 person years estimated from four cohort studies and case reports), but the authors found no convincing evidence of a link with hepatobiliary problems including liver failure. Data from three randomised trials and the adverse events reporting system of the US Food and Drug Administration, suggest that the risk of liver failure associated with statins is about 0.5 per 100 000 person years of treatment, which is no greater than the risk in the general population. These authors found no evidence at all that statins damage renal function or accelerate cognitive decline in older people.

What does it mean? Simvastatin, atorvastatin, lovastatin, pravastatin, and fluvastatin are widely used and seem safe. Serious side effects can occur but are rare. The well established benefits of these drugs outweigh the risks. Rosuvastatin has the weakest safety record simply because few data have been published on this statin.

Most cases of rhabdomyolysis in this study were associated with drug interactions, usually between simvastatin, lovastatin, or atorvastatin and another drug metabolised by cytochrome P450, such as erythromycin or azole antifungal drugs. In a fifth of rhabdomyolysis cases, the patient was taking a statin and a fibrate (usually gemfibrozil). The authors conclude that many cases could be prevented by avoiding these kinds of interactions.

Law M, et al. Statin safety: a systematic review. *Am J Cardiol* 2006;97(suppl):52-60C

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Editor's choice

Improving on improvement

Last week, members of a small but increasingly confident tribe of healthcare enthusiasts gathered in Prague for their annual meeting, the Forum on Quality Improvement in Health Care. Run jointly by the BMJ Publishing Group and the Institute for Healthcare Improvement (www.ihi.org/ihi), the forum is in its 11th year and, according to the feedback we've received, its best year yet.

Discussions in the sessions and over lunch—and through the evening in Prague's many bars—were wide ranging: what has happened to clinical leadership, what can happen when you learn to think like a designer, the importance of directly observing what goes on in hospitals and primary care, how to achieve sustainable change within a complex adaptive system, and whether quality improvement should be seen as research. There was also some eye opening gossip on who's on the way up and who's on the way out, or should be.

Participants talked alot about the problem of getting their work published. Journals treat quality improvement as research and wonder why there's no ethics committee approval. But often the work began simply as an effort to improve health care locally; the fact that it came up with a generalisable message that might merit publication is a bonus. And many, perhaps most, ethics committees are still unclear what to do with quality improvement proposals ("unclear" is a euphemism for "ill informed" and "in disarray"—the words I scribbled down at the time).

Over lunch I talked to Frank Davidoff, former editor of *Annals of Internal Medicine* and now working with IHI, about why so little of this work gets published. The Quality Improvement Report format, pioneered by *Quality and Safety in Health Care* and adopted by the *BMJ*, has helped, but there are still significant barriers. Last year in an effort to tackle the problem, he and Paul Batalden developed draft publication guidelines (*Quality and Safety in Health Care* 2005;14:319-25). But they don't think quality improvement should be seen as research or subjected to the bureaucracy of review by ethics committees or institutional review boards. From conversations I heard in Prague, this is still a live debate and one on which we would welcome your views.

The meeting was judged a success by the 1000 delegates who attended, including me and our two bloggers, Jane Smith and Jenny Kowalczuk whose accounts you can read on bmj.com. But the real test will be how much of the enthusiasm filters through to normal practice. The improvement scientists will have to work hard to dispel the notion that improving health care locally means you have to join a club and get a badge—conferring special skills, privileged knowledge, and expert blessing. That'll be a challenge for next year's forum: Barcelona, 18-20 April 2007. Book your place now.

Fiona Godlee *editor (fgodlee@bmj.com)*

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