Women in western countries are more likely to die from heart disease than from cancer. **Scott M Grundy** argues that the risks make preventive treatment essential, but **Malcolm Kendrick** believes the evidence of benefit is not strong enough

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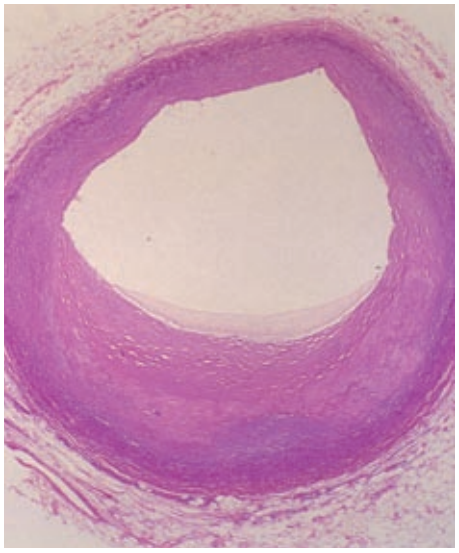
NO As no other cholesterol lowering drug has been shown to improve survival, this discussion is effectively about the use of statins. To date, none of the large trials of secondary prevention with statins has shown a reduction in overall mortality in women.[1] Perhaps more critically, the primary prevention trials have shown neither an overall mortality benefit, nor even a reduction in cardiovascular end points in women.[2] This raises the important question whether women should be prescribed statins at all.

I believe that the answer is clearly no. Not only do statins fail to provide any overall health benefit in women, they represent a massive financial drain on health services. This money could be diverted to treatments of proved value.

In addition to the lack of benefit and expense, statins carry a substantial burden of side effects.[3 4] Lifetime drug treatment can also create other problems. Firstly, women may falsely believe that they are being protected and may therefore be less likely to make beneficial lifestyle changes. Secondly, mass medicalisation is a dangerous road with many psychological and societal consequences.



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Atherosclerosis in a coronary artery

Lack of benefits

The Scandinavian simvastatin survival study found the biggest effects of all statin trials—in men. However, what is less publicised is that, overall, three more women died in the statin arm than in the placebo arm.[5] The more recent heart protection study was hailed as a major success for men and women, but despite the hype there was no effect on overall mortality in women.[6]

In the studies of primary prevention neither total mortality nor serious adverse events have been reduced.[7] A meta-analysis published in the *Lancet* found that statins even failed to reduce coronary heart disease events in women.[8] Of greater concern is that a further meta-analysis of statins in primary prevention suggested that overall mortality may actually be increased by 1% over 10 years (in both men and women).[9]

Sex differences

Perhaps it should not be a surprise that men and women respond differently to statins. In most countries cardiovascular disease strikes men at a much earlier age. Also, the relation of risk to cholesterol concentrations is not consistent. To quote from a major conference held in 1992 that looked at the data from 523 737 men and 124 814 women from 19 studies and trials: "Many findings for women were discrepant from those for men. Of particular importance in women was considered to be the essentially flat relation of TC [total cholesterol] to total mortality, total CVD [cardiovascular disease], and total cancer."[10]

What creates this difference is a matter of debate. However, when we know that such differences exist, and the results from the statin trials point to highly divergent end points, it seems inappropriate that the guidelines (and thus the advice on using statins) remain exactly the same for men and women. This seems to run directly contrary to the concept of evidence based medicine.

Costs

Statins currently represent the single greatest drug expenditure in the National Health Service. In 2006, the cost in England was £625m (€918m; $1.2bn).[11] Statin prescribing is increasing by 30% each year, which means that in 2007 the cost of statins could well reach £1bn. However, this is only the direct drug cost. Combining additional expenditure resulting from activities such as blood tests, dispensing costs, and increased general practice consultations, this figure could easily double to around £2bn.

Exactly how the costs break down between men and women is not clear. But we can be fairly sure that stopping prescribing statins to women would save the NHS hundreds of millions of pounds each year.

Side effects

Statins are generally considered to have few side effects, with most being mild and reversible.[12] However, some studies have suggested that side effects may be much more common than is recognised.[13] A study on athletes with familial hypercholesterolaemia found that only 20% could tolerate statins.[14] Furthermore, research by Golomb and McGraw found that doctors often dismiss most (probable) statin related events.[15] Patients who met the criteria for definite or probable adverse events reported that their doctors tended to dismiss symptoms, deny specific statins adverse events, and failed to appreciate the effect of the adverse reaction on their quality of life.

More definite evidence comes from the US Food and Drug Administration adverse event reporting system. Between November 1997 and May 2004 simvastatin was reported as a direct cause of 49 350 adverse events and 416 deaths.[4] Adverse events are greatly underreported, so the actual figures are likely to be much higher.

Of further concern, as statins are increasingly prescribed to younger women, is the potential for teratogenicity, with severe neurological abnormalities reported.[16 17] Spending millions on a treatment that has no proved benefit and may cause serious harm goes against the rationale of evidence based prescribing

Competing interests: MK is the author of The Great Cholesterol Con.

References are in the full version on bmj.com