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Statins: underused by those who would benefit

But caution is needed for young people at low risk of cardiovascular disease

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The United States Food and Drug Administration has recently rejected proposals by the manufacturers of lovastatin and pravastatin to make these drugs available over the counter. Advisers to the Food and Drug Administration decided that physicians should probably determine who should get the drugs as well as monitoring them for side effects. The main arguments for allowing over the counter sales were summarised in a recent conference sponsored by the industry: statins are effective, easy to take, and relatively safe, and many people who should be taking these drugs are not doing so.[1]

The underuse of statins is most apparent in the secondary prevention of heart disease in patients with known atherosclerotic disease, for whom there is overwhelming evidence that statins are highly beneficial.[2 3] In one recent survey, for example, only 37% of patients with recent myocardial infarction and blood cholesterol concentrations above 2 g/l had been given drugs to lower their lipid concentrations and few had reached their target cholesterol concentrations.[4] Most patients with heart disease have concentrations of low density lipoprotein cholesterol that warrant treatment, and making statins available over the counter might increase their use (as has occurred with aspirin).[5]

Undertreatment is also a problem for the much larger population of people who do not have manifest atherosclerotic disease (primary prevention). There is no longer any doubt that treatment benefits those who are at substantial coronary risk. An updated meta-analysis in this issue of the *BMJ* (p 983) shows that drugs that lower lipid concentrations prevent nearly a third of myocardial infarctions and coronary deaths.[6] All cause mortality was not reduced significantly, but this is not surprising because statins affect only cardiovascular mortality,[2 3] and most of the deaths in people without heart disease were not due to cardiovascular causes.[7]

Practice guidelines have been devised to identify patients who need treatment.[8] The recently revised Sheffield table is easy to use and an excellent example. It provides cut-off points for ratios of total cholesterol to high density lipoprotein cholesterol (based on age, sex, diabetes, hypertension, and smoking) that identify people whose coronary risk exceeds 30% per decade.[9] The table also gives cut-off points for treating the larger numbers of people whose coronary risk exceeds 15% per decade "where resources permit."[9] This lower cut-off point has the virtue of more closely resembling the 10 year coronary risk of participants in trials of primary prevention.[6]

Age is the most important determinant of coronary risk,[10 11] and the two main primary prevention trials of statins both set the lower limit for enrolment at the relatively mature ages of 45 for men and 55 for women.[6] This decision made sense when designing these trials: younger participants would have too few coronary events to provide adequate power to detect an effect of treatment. But in clinical practice physicians may ask why not extrapolate these results and use statins to help prevent the few coronary events that do occur in younger people? Treating younger people may be reasonable if they have other strong risk factors, such as familial hypercholesterolaemia or diabetes. But the reasons for not doing so in most younger people are the remaining concerns about safety and the harsh realities of cost.

Statins do seem to be reasonably safe and are probably less likely to cause serious harm than aspirin. Earlier concerns that lipid lowering drugs might increase the risk of death from injuries were a false alarm.[2 3] Serious adverse effects such as liver failure and rhabdomyolysis are rare, and more common side effects such as myositis and raised serum transaminase activity are usually reversible. There remains the theoretical possibility that statins may have adverse effects years later. A recent follow up report from the first major trial of statins was reassuring on this point, showing trends towards continued benefits in survival and fewer cancer deaths for two years beyond the five years of randomised statin treatment.[12] The evidence for both safety and efficacy have led statins to outstrip other lipid lowering drugs and to eclipse the role of diet in coronary prevention (which has a far smaller effect on low density lipoprotein concentration and is resisted by many patients).[13] However, there are two caveats about the safety of these powerful drugs. Firstly, not every statin has been studied in large clinical trials with disease end points; use of the newer formulations is based on surrogate end points and analogy.[14] And secondly, seven years is not long enough to eliminate concerns about long term adverse effects such as cancer. While we await the findings of continued follow up of the statin trials, it is prudent to hold back from prescribing statins for patients who have a low risk of coronary events over 10 years.

Cost is the other reason to hesitate before recommending statins to people at low risk of heart disease. Coronary heart disease is so rare among

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young adults that starting drug treatment for life in people in their 30s costs up to £1m ($1.4) per year of life extended.[15] Until the price of statins comes down a lot, this is not a reasonable expenditure of medical resources.

Of course, people who are well off can ignore concerns of cost. In a world that allows statins to be bought over the counter, they could also bypass the need to persuade a physician to prescribe them. But the problems of deciding who should be treated and how to monitor adverse effects underscore the wisdom of the Food and Drug Administration's conclusion to leave decisions about taking statins in the hands of healthcare providers.

However, this does leave us with the obligation to do it right. Many people who could substantially benefit from statins are not getting them, perhaps due to a lack of understanding by physicians or to organisational and fiscal policies that do not support prevention.[4 16] It is time to get serious about identifying and removing these obstacles. Physicians must do a better job of following practice guidelines for using statins to treat undesirable cholesterol concentrations in people at substantial risk of coronary events over 10 years, including most patients with a history of coronary disease and a good many (mostly older) people who may soon develop it.

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Another look at visual standards and driving

Better tests are needed to determine driving ability

The law in the United Kingdom requires that a car driver must be able to read, in good daylight with the aid of corrective lenses if necessary, a vehicle number plate containing letters and figures 79.4 mm high at a distance of 20.5 metres. This is a test of binocular static visual acuity and corresponds to a geometric visual angle of 6/15 Snellen acuity. (In the United States this translates into the equivalent of the 20/20 notation, in which the measurement is expressed at a test distance of 20 feet rather than 6 metres as in the Snellen notation. In other parts of Europe people use both the Snellen notation and a system of expressing the visual angle as a decimal fraction—for example 6/6 = 1 6/12 = 0.5 6/60 = 0.1. The rest of the world uses the Snellen notation.) Because of differences in letter types the driving visual test is clinically similar to a Snellen acuity of approximately 6/10.[1]

These tests should be performed with both eyes open because the acuity of the better eye when tested separately is often different from the binocular visual acuity. This is the result of interactions in the visual cortex between the input from each eye. The lack of equivalence between performance in the Snellen acuity test and the number plate test is highlighted in the paper by Currie et al (p 990).[2] The paper also emphasises how this discrepancy causes different healthcare professionals to give drivers widely conflicting advice about their driving fitness based on measurements of visual acuity.

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The Royal College of Ophthalmologists in the United Kingdom has recommended that the minimum visual field permissible for safe driving is at least 120° on the horizontal meridian with no significant field defect within 20° of fixation. When a driver who is visually impaired fails to meet these standards and is advised to give up driving it is difficult to justify this restriction of freedom on the basis of scientific literature. Retrospective studies of large numbers of drivers show only a weak association between a reduction in static visual acuity[3–6] and increased crash rates. No significant increase in collision rates generally exists when 6/12 is used as a cut-off point to predict the ability to drive safely.[3 4 7]

Studies that have examined visual field loss and the history of drivers' crashes have also failed to show a significant relationship.[3 4 6–8] These negative findings may partly be explained by the unsophisticated methods used to assess the visual field,[3 4 8] poorly controlled testing conditions[8] and failure to adjust for the

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