Cardiovascular risk: use of statins for people at lower risk?

A large meta-analysis has shown that taking statins leads to a small absolute reduction in the risk of major vascular events among people at low risk of such events. However, the adverse effects of statins and other implications of their more widespread use need careful evaluation including health economic analysis. In the meantime, health professionals should continue to follow current NICE guidance on lipid modification.

Overview and current advice

The NICE clinical guideline on lipid modification recommends that statin therapy should be considered as part of the management strategy for the primary prevention of cardiovascular disease (CVD) for adults who have a 20% or greater 10-year risk of developing CVD. The current NICE guidance on lipids is being updated.

New evidence

A large meta-analysis of individual participant data from each randomised controlled trial within the Cholesterol Treatment Trialists’ (CTT) database modelled the effects of statin treatment among people with a lower risk of developing CVD. The authors calculated the relative risk (RR) of cardiovascular events per 1 mmol/litre reduction in LDL cholesterol, stratified by 5-year risk of major vascular events (defined as non-fatal myocardial infarction, coronary death, stroke or coronary revascularisation). This risk was modelled from data collected at trial baseline. (Note that this is different from using cardiovascular risk calculators such as QRISK or Framingham to estimate a person’s 10-year risk of CVD).

Among people with a 5-year risk of major vascular events of less than 5% (n=24,790), the RR of major vascular events was 0.62 (95% confidence interval [CI]: 0.47 to 0.81) per 1 mmol/litre reduction in LDL cholesterol in people taking a statin compared with those taking control. Applying this RR to the annual event rate in the control group suggests that a 1 mmol/litre reduction would reduce the number of these events from about 28 per 1000 to about 17 (95% CI 13 to 22) per 1000 over 5 years.
Among people with a 5-year risk of major vascular events of between 5% and 10% (n=28,362), the RR of major vascular events was 0.69 (95% CI 0.60 to 0.79) per 1 mmol/litre reduction in LDL cholesterol in people taking a statin compared with those taking control. This suggests a 1 mmol/litre reduction would reduce the number of these events from about 79 per 1000 to about 54 (95% CI 47 to 62) per 1000 over 5 years.

The meta-analysis showed a dose-related risk of myopathy and rhabdomyolysis (excess incidences of around 0.5 per 1000 and around 0.1 per 1000 over 5 years). The risks are low in absolute terms compared with the absolute benefits of statins, even in people at low risk of CVD. However, a review of observational studies suggests that myalgia occurs in 5–10% of people who take statins.

**Commentary**

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Health professionals should continue to follow NICE guidance, and use a systematic strategy to identify people aged 40–74 who are likely to be at high risk of CVD. They should offer statins to people who have a 20% or greater 10-year risk of developing CVD, and this should include an informed discussion about the risks and benefits of statin treatment. As the guidance says, the National Prescribing Centre decision aid may be helpful in this discussion. If health professionals are asked about statin therapy by people whose CVD risk is less than this, they should be prepared to discuss the pros and cons of treatment.

Questions remain about the implications for practice of the findings of this meta-analysis. In the UK, about 83% of men older than 50 years and 56% of women older than 60 years have a 10-year CVD risk of 10% or more. Some commentators have suggested that a pragmatic approach would be to offer statins to everyone over a certain age (say, 50 years), to avoid the costs involved in risk assessment. However, this would not take into account differences in risk between individuals, which are likely to be important when people are deciding whether they wish to take life-long statin treatment.

Adherence rates for statins are often low and in people without evidence of CVD disease, 2-year adherence rates might be as low as 25%. It is not known how widely accepted and adhered to statin therapy would be by people at low CVD risk once they have thought carefully about the pros and cons of treatment in the context of their individual circumstances.

When considering treatment options, one must consider not only treatment efficacy but also safety, cost (and cost effectiveness), and individual patient circumstances and preferences.

For example, despite finding a reduction in the net risk of stroke, the meta-analysis found an excess risk of haemorrhagic stroke of about 0.5 per 1000 people over 5 years per 1 mmol/litre reduction in LDL cholesterol. This might possibly be greater in some populations such as people of South Asian family origin. Statins may also cause adverse effects such as the muscle related events reported in the meta-analysis, as well as being associated with causing about a 10% relative increase in the risk of diabetes, which is greater at higher doses.

UK observational data suggest that statins are associated with small but statistically significant increases in risk of other adverse effects that are not considered in the meta-analysis reported here (including acute renal failure, moderate or severe liver dysfunction, and cataract). These observational data provide a lower standard of evidence than randomised controlled trial data, but still need to be considered carefully.

Currently, the annual cost to the NHS of prescribing simvastatin 40 mg daily, which will achieve a 1 mmol/litre reduction in LDL cholesterol in most people, is about £15–16 per individual treated. However, the costs would be significant if prescribing was extended more widely than is currently
recommended, or if a more expensive statin was used. There would also be costs arising from managing iatrogenic diabetes and other adverse effects requiring a health economic evaluation to assess the impact of using statins in this group of people.

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References

2. See http://guidance.nice.org.uk/CG/WaveR/123

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