Cardiovascular disease (CVD) is a major cause of mortality accounting for 27% of deaths in the UK in 2014 and is a great cost to the UK economy, estimated to be £15.2 billion in 2015. Lipid modification is important as there is a positive correlation between the incidence of CVD and cholesterol levels. There is substantial evidence of benefit in prescribing statins to all patients for secondary prevention of CVD and for primary prevention in many of those patients with higher CVD risk. A Cochrane review in 2013 included 18 randomised controlled trials of statin prescribing for primary prevention and reported a reduction in all-cause mortality odds ratio (OR) 0.86, 95% confidence interval (CI) = 0.79 to 0.94, with the number needed to treat to prevent one death over 5 years being 96 and an acceptable cost-effectiveness. The Cholesterol Treatment Trialists’ Collaboration (CTTC) trial performed a meta-analysis of individual patient data from 27 randomised controlled trials and reported in 2012 that statin therapy reduces the risk of major vascular events even in patients with 5-year CVD risks of <5%. The National Institute for Health and Care Excellence (NICE) guidance recommends the use of the QRISK2 tool to assess CVD risk, and treatment with statins at a >10% 10-year risk of developing CVD. This guidance was revised from a >20% risk in 2014 and a >30% risk in 2010. If the current NICE guidance was fully implemented in the UK, it has been estimated that 21% more men aged 40–75 years and 25% more women aged 55–75 years would be receiving statins after 10 years of monitoring. Virtually all individuals >75 years will have a >10% risk of developing CVD in 10 years, as the average 10-year risk of CVD without risk factors for males is 25.7%, and for females 19.6%. Despite this evidence base and these guidelines, primary care prescribing rates of statins for primary prevention are lower than predicted. Why might this be?

The causes of variations in the rate of statin prescribing in primary care are multifactorial and influenced by both clinician and patient factors. Qualitative research has identified several factors that include perceived reduced cost-effectiveness, excess workload, patient reluctance to take medication when they are asymptomatic, potential side effects, and medicalisation of healthy individuals. Other research has identified substantive overuse of statins in patients with low CVD risk and conversely underuse in those with high CVD risk. Some of these variations are thought to be influenced by single risk factors such as age >65 years, diabetes, and hypercholesterolaemia. An understanding of how GPs arrive at a decision to make primary prevention interventions is critical. GPs have reported concern about the clarity of the evidence base and a reluctance to prescribe at lower primary prevention thresholds. There is sparse literature regarding the views of GPs and further qualitative work within our department aims to explore this complex issue.

Barriers to prescribing statins for those at lower CVD risk include the transferability of the evidence from research into practice and the potential for side effects, especially diabetes. Regarding the transferability of the evidence, the majority (14/18) of the studies included in the Cochrane review included high-risk patients such as those with diabetes, hypercholesterolaemia, and hypertension. The CTTC study used a risk scoring system that is not reproducible in primary care patients, unlike QRISK2 or Framingham. The majority of randomised controlled trials using statins are of <5 years’ duration, whereas patients are started on statins with the intention of it being lifelong. Regarding the risk of diabetes, the Cochrane review reported an increased relative risk of 1.18 (95% CI = 1.01 to 1.39), although only two of the 18 studies in this meta-analysis reported the risk of new cases of diabetes. A meta-analysis of 17 randomised controlled trials has reported an increased risk of diabetes (OR 1.09, 95% CI = 1.02 to 1.17), with no differing treatment effects between statins.

How do we solve this mismatch between the guidelines and evidence base which supports the use of statins in lower-risk primary prevention individuals and prescribing behaviour of GPs, who appear reluctant to prescribe statins for primary prevention to low-risk individuals? First, there should be longer-term follow-up of participants in existing trials for both adverse and beneficial outcomes, and trial datasets made available. Second, large randomised controlled trials are needed examining the effectiveness of statins in primary prevention that should be powered to look specifically at side effects. Third, high-quality observational data are needed to investigate if the treatment effects of statins reported within the trials are reproducible in a typical low-risk primary care population. These suggestions should be complemented by research exploring patient-centred care and shared decision making for asymptomatic patients who are recommended statin therapy. There is some evidence that patients will heed the advice of their doctor and it is therefore essential that doctors have an adequate and transferable evidence base on which

“If 96 patients with similar risks … were to take a statin tablet [for primary prevention] every day for 5 years then one life might have been saved. However, those patients taking statins are more likely to develop diabetes.”
“Given this evidence, it may not be surprising that many patients choose not to take statins for primary prevention where benefit appears marginal and there is a risk of diabetes.”

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