With statin co-administration, drugs designed to increase HDL have no impact on cardiovascular outcomes

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Context
Decreasing low-density lipoprotein (LDL) cholesterol with statin treatment reduces cardiovascular disease (CVD) incidence. The National Institute for Health and Care Excellence (NICE) has recently recommended that first-line statin treatment in primary prevention should be atorvastatin 20 mg daily and in secondary prevention atorvastatin 80 mg daily, doses which typically decrease LDL cholesterol by 43% and 55%, respectively. In many patients this will leave little scope to reduce residual CVD risk by additional LDL lowering. Attention is therefore drawn to the epidemiological inverse association between HDL cholesterol and CVD risk. This is widely exploited in the prediction of CVD risk, but is HDL cholesterol also ‘good cholesterol’ in the sense that raising its level therapeutically can prove beneficial? Three lipid-modifying drug classes are known to raise HDL: niacin (nicotinic acid), fibrates and cholesteryl ester transfer protein inhibitors (CETP-i’s).

Methods
In this systematic review, an extensive search of published and unpublished randomised controlled trials (RCTs) of niacin, fibrates and CETP-i’s revealed 11 RCTs of niacin (35,301 participants), 20 of fibrates (46,099 participants) and 8 of CETP-i’s (36,011 participants) with all-cause mortality as an outcome. These were subjected to meta-analysis. Secondary end points included coronary heart disease (CHD) mortality and non-fatal myocardial infarction (MI).

Results
None of the drug classes was associated with reduction in all-cause or CHD mortality. Niacin and fibrates were investigated both in patients receiving statins and those not on statins, whereas CETP-i’s were tested only against a background of statin therapy. Non-fatal MI occurred less frequently on niacin alone versus placebo (HR 0.69; 0.56 to 0.85, p<0.001, n=4991), but in combination with a statin it had no significant effect. Similarly, fibrates alone decreased the incidence of non-fatal MI (HR 0.78; 0.71 to 0.86, p<0.001, n=32,086), but statistical significance was lost with statin co-administration.

References