

Byrne P, Cullinan J, Smith A, Smith S. Statins for the primary prevention of cardiovascular disease: an overview of systematic reviews

Supplementary Appendix 3: Analyses from the Included Systematic Reviews that were not included in Overview

Supplementary Appendix 4: Interpretation of Composite Outcomes Reported in Included Systematic Reviews

Supplementary Appendix 5: Calculation of the Absolute Risk Benefit of Statins

Supplementary Appendix 3: Analyses from the Included Systematic Reviews that were not included in Overview

Mora reported outcomes from three ‘exclusively primary prevention trials’ as well as from ‘predominantly or exclusively primary prevention trials’. We did not include outcomes reported in this SR from analyses of ‘predominantly or exclusively primary prevention trials’.

Some outcomes reported by CTT were results of analyses that included RCTs of more versus less statin and those that included secondary prevention participants and these were not eligible for our overview.

Appendix 4: Interpretation of Composite Outcomes Reported in Included Systematic Reviews

Review	Composite outcome	Definition	Does the review describe proportion of each outcome comprises composite outcome?
CTT	Major coronary events	Non-fatal myocardial infarction or coronary death	No
	Major vascular events*	The first occurrence of any major coronary event, coronary revascularisation or stroke	No
Mora	Total CVD**	Predominantly myocardial infarction, angina/revascularization, stroke, and CVD death, with some of the trials including peripheral vascular events (AFCAPS & JUPITER) and 1 trial including ischemic congestive heart failure (AFCAPS).	
Ray	N/A	N/A	N/A

* Abramson et al. (Should people at low risk of cardiovascular disease take a statin? BMJ 2013;347:f6123) noted that 35% the composite outcome 'major vascular events' comprised coronary revascularisations. This was calculated from Figure 1 of CTT 2012 by summing the number of events reported for 'major coronary events', 'any stroke' and 'coronary revascularisation' and calculating the proportion of this total sum that comprised 'coronary revascularisation'. By this method we can calculate that 'any stroke' comprised 27% of the composite outcome and 'major coronary events' 38%. However, the outcome 'major vascular events' as reported in Figure 1 reported *first occurrences* major coronary event, coronary revascularisation or stroke and we cannot ascertain the proportion of each component of this outcome from the figure.

** Mora notes that when the components of the composite outcome 'total CVD' in women are analysed in one large trial included in his analysis, women had a significant reduction in revascularisations and unstable angina but not in other components, including stroke, of the composite outcome.

Appendix 5: Calculation of the Absolute Risk Benefit of Statins

Reduction in risk of CVD outcomes is presented in these reviews as relative risk reductions. However, for an individual patient knowing their absolute risk reduction is more relevant when making a decision to take a statin. We used two theoretical patients to illustrate this point. One is a 65-year old man who smokes, does not have heart disease but who has high total cholesterol levels and elevated blood pressure. The second is a 45-year old woman who does not smoke, has elevated total cholesterol levels and slightly elevated blood pressure. Based on the ACC/AHA Risk calculator, the man has a 38% risk of having a major coronary event in the next ten years; the woman, a 1.4% risk. Risk reductions were reported by CTT stratified by baseline risk categories; (<5% risk RR 0.57 (CI 0.36 to 0.89); ≥5% to <10% risk RR 0.61 (CI 0.50 to 0.74); ≥10% to <20% risk RR 0.76 (CI 0.69 to 0.85); ≥20% to <30% risk RR 0.78 (CI 0.71 to 0.85); ≥30% risk RR 0.78 (CI 0.72 to 0.84)). According to those reported risk reductions, statin therapy would reduce the man's relative risk of major coronary events by 22% (≥30% risk RR 0.78 (CI 0.72 to 0.84)) and the woman's relative risk by 43% (<5% risk RR 0.57 (CI 0.36 to 0.89)). However, the man could expect an *absolute* risk reduction of about 8.4% ($38\% \times 0.22 = 8.4\%$) (Number Needed to Treat of 12); the woman by 0.6% ($1.4\% \times 0.43 = 0.60\%$) (Number Needed to Treat of 166).