Publication

Association between change in high density lipoprotein cholesterol and cardiovascular disease morbidity and mortality : systematic review and meta-regression analysis

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OBJECTIVE: To investigate the association between treatment induced change in high density lipoprotein cholesterol and total death, coronary heart disease death, and coronary heart disease events (coronary heart disease death and non-fatal myocardial infarction) adjusted for changes in low density lipoprotein cholesterol and drug class in randomised trials of lipid modifying interventions. DESIGN: Systematic review and meta-regression analysis of randomised controlled trials. DATA SOURCES: Medline, Embase, Central, CINAHL, and AMED to October 2006 supplemented by contact with experts in the field. STUDY SELECTION: In teams of two, reviewers independently determined eligibility of randomised trials that tested lipid modifying interventions to reduce cardiovascular risk, reported high density lipoprotein cholesterol and mortality or myocardial infarctions separately for treatment groups, and treated and followed participants for at least six months. DATA EXTRACTION AND SYNTHESIS: Using standardised, pre-piloted forms, reviewers independently extracted relevant information from each article. The change in lipid concentrations for each trial and the weighted risk ratios for clinical outcomes were calculated. RESULTS: The meta-regression analysis included 108 randomised trials involving 299 310 participants at risk of cardiovascular events. All analyses that adjusted for changes in low density lipoprotein cholesterol showed no association between treatment induced change in high density lipoprotein cholesterol and risk ratios for coronary heart disease deaths, coronary heart disease events, or total deaths. With all trials included, change in high density lipoprotein cholesterol explained almost no variability (<1%) in any of the outcomes. The change in the quotient of low density lipoprotein cholesterol and high density lipoprotein cholesterol did not explain more of the variability in any of the outcomes than did the change in low density lipoprotein cholesterol alone. For a 10 mg/dl (0.26 mmol/l) reduction in low density lipoprotein cholesterol, the relative risk reduction was 7.2% (95% confidence interval 3.1% to 11%; P=0.001) for coronary heart disease deaths, 7.1% (4.5% to 9.8%; P<0.001) for coronary heart disease events, and 4.4% (1.6% to 7.2%; P=0.002) for total deaths, when adjusted for change in high density lipoprotein cholesterol and drug class. CONCLUSIONS: Available data suggest that simply increasing the amount of circulating high density lipoprotein cholesterol does not reduce the risk of coronary heart disease events, coronary heart disease deaths, or total deaths. The results support reduction in low density lipoprotein cholesterol as the primary goal for lipid modifying interventions.

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