

Individual Participant Data Meta-Analysis of New-Onset and Worsening Diabetes Mellitus in Large-Scale Randomized Double-Blind Trials of Statin Therapy

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Background: Meta-analyses of trial data have shown that statins increase the risk of new-onset diabetes. However, these studies were based on summary data and used inconsistent definitions. Therefore, they could not reliably quantify the relative and absolute risk of new-onset diabetes, nor establish whether the risk is consistent over time and whether any increase in risk occurs only in particular groups of people. It is also unclear whether statins increase the risk of glycemic deterioration in those with diabetes.

Methods: Individual participant data were obtained for 19 large randomized double-blind trials of statin vs placebo (123,940 participants, 21% with diabetes, 4.3 years median follow-up) and 4 randomized double-blind trials of more vs less intensive statin therapy (30,724 participants, 17% with diabetes, 4.9 years median follow-up). Meta-analyses were conducted of the effects of statin therapy on new-onset diabetes (defined as an adverse event of diabetes, initiating glucose-lowering therapy or biochemical evidence of diabetes, in those with diabetes at baseline); and worsening diabetes (defined as an adverse event of complications of glucose control, initiating/escalating glucose-lowering therapy or an HbA1c increase of at least 0.5%, in those with diabetes at baseline).

Results: Trials of statin vs placebo provide >6700 cases of new-onset diabetes and >12,500 cases of worsening diabetes. Trials comparing more to less intensive statin therapy provide >2900 cases of new-onset diabetes and >3000 cases of worsening diabetes. Final analyses are underway and unblinded results for these outcomes will be presented at AHA 2022. Along with detailed results (overall and in various subgroups of participants), we will present data on the risks of new-onset diabetes and worsening diabetes over time. Finally, we will explore whether any observed increases are due to generalized increases in measures of glycemia.

Conclusions: These analyses of individual participant data by the Cholesterol Treatment Trialists' Collaboration will reliably establish the impact of statin therapy on new-onset diabetes and worsening diabetes.