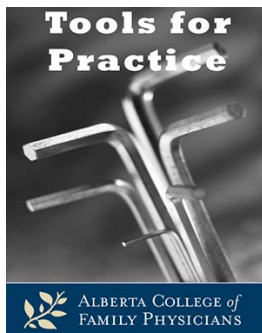


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Evidence Updated: New evidence
Bottom Line: Slight change
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Statin-Induced Diabetes: Too Sweet a Deal?

Clinical Question: Do statins increase the risk of diabetes, and does this worsen outcomes?

Bottom Line: Statins modestly increase blood glucose, which leads to an extra one in 250 patients crossing the “diabetic threshold” over 4 years. This should not change statin prescribing, as they reduce cardiovascular events and all-cause mortality in appropriate patients.

Evidence:

Statin versus no statin:

- Meta-analysis¹ of 13 Randomized Controlled Trials (RCTs) with 91,140 patients with, or at high risk for, cardiovascular disease:
 - New diabetes over four years: Statins 4.9%, control 4.5%, Number Needed to Harm (NNH)=250.
- Similar results in meta-analysis of 15 RCTs (91,828 patients):² odds ratio 1.11 (95% confidence interval 1.03-1.20).

High versus low/moderate dose statin (e.g. atorvastatin 80 mg versus 10 mg):

- Meta-analysis³ of five RCTs with 32,752 patients with cardiovascular disease:
 - New diabetes over five years: High-dose 8.8%, low/moderate-dose 8%, NNH=125.

Observational studies confirm increased diabetes diagnosis with statin versus no statin,⁴⁻⁶ and higher versus lower statin dose or potency^{7,8} seen in RCTs.

Context:

- Diagnosis of type 2 diabetes is largely based on crossing an arbitrary laboratory threshold, like fasting plasma glucose (FPG) ≥ 7.0 mmol/L:⁹
 - Baseline FPG 6.0-6.9 mmol/L is a risk factor for developing diabetes with statins.¹⁰

- In an observational study, FPG increased by 0.1 mmol/L at 2 years in non-diabetics taking statins.¹¹
- Thus, the increase in diabetes diagnoses in statin users is mostly from patients with borderline glucose levels crossing the diagnostic cutoff.
- Genetic studies showed that having mutations that impair HMG-CoA reductase activity is associated with greater FPG and higher incidence of type 2 diabetes.²
 - Confirms that risk of diabetes with statins tied to their LDL-lowering potency.
- Despite the increase in blood glucose, statins reduce important clinical outcomes including mortality in patients with an appropriate indication:^{5,12}
 - In the Heart Protection Study:¹² for every one person newly diagnosed with diabetes due to statin use over five years, statins prevented five deaths, six non-fatal myocardial infarctions and four strokes.
- Thiazides and beta-blockers also increase the risk of diabetes versus placebo or other antihypertensives.¹⁴
 - Both classes^{15,16} provide net benefit in appropriate patients.

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