

# Statin-induced diabetes: too sweet a deal?

Ricky Turgeon G. Michael Allan MD CCFP

## Clinical question

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

## Bottom line

Statins modestly increase blood glucose levels, which leads to 1 in 250 or so patients crossing the “diabetic threshold” in a 5-year period. Pre-existing elevated blood glucose levels, other diabetes risk factors, or higher statin doses might slightly increase the risk. This should not change statin prescribing, as statins reduce cardiovascular events and all-cause mortality in appropriate patients.

## Evidence

- Statin vs no statin: meta-analysis<sup>1</sup> of 13 RCTs with 91 140 patients at high risk of or with cardiovascular disease.
  - New diabetes over a mean of 4 years: 4.9% of those taking statins vs 4.5% of the control patients; number needed to harm was 250.
- High vs moderate- or low-dose statin (eg, 80 mg vs 10 mg of atorvastatin): meta-analysis<sup>2</sup> of 5 RCTs with 32 752 patients with cardiovascular disease.
  - New diabetes over a mean of 5 years: 8.8% of those in the high-dose group vs 8.0% in the moderate- or low-dose group; number needed to harm was 125.

## Context

- Diagnosis of type 2 diabetes is largely based on crossing an arbitrary laboratory threshold, like fasting plasma glucose (FPG) of 7.0 mmol/L or greater.<sup>3</sup>
  - Elevated baseline FPG is a risk factor for developing diabetes with statins.<sup>4</sup>
  - In an observational study, FPG increased by 0.1 mmol/L at 2 years in those without diabetes taking statins.<sup>5</sup>
  - Thus, the increased diagnoses of diabetes in statin users are likely, in good part, from patients with borderline glucose levels crossing the diagnostic cutoff.
- Despite the increases in blood glucose, statins reduce important clinical outcomes including mortality in patients with appropriate indications.<sup>6</sup>
  - In the Heart Protection Study (mostly secondary prevention),<sup>7</sup> for every 1 person newly diagnosed with diabetes due to statin use, 5 deaths, 6 nonfatal myocardial infarctions, and 4 strokes were prevented in 5 years.
- Similar pooled RCT evidence shows an increased risk of diabetes with thiazides and  $\beta$ -blockers vs placebo or other antihypertensive medications.<sup>8</sup>
  - Thiazides<sup>9</sup> and  $\beta$ -blockers (in appropriate patients)<sup>10</sup> also provide net benefit.

## Implementation

Patients concerned about the increased risk of diabetes with statins should have the risk put in context. Statins increase the risk of diabetes by about 11%, while hypertension and obesity increase diabetes risk by approximately 100% and 200%, respectively.<sup>1,11,12</sup> Alternatively, it might be explained (using data from the JUPITER trial) that patients receiving statins are diagnosed with diabetes on average about 5 weeks sooner than nonusers.<sup>13</sup> Most important, for every person diagnosed with diabetes due to a small increase in blood glucose they will not feel, 2 to 15 patients (depending on risk) will avoid serious outcomes like stroke, heart attack, and death.<sup>7,13</sup>

**Mr Turgeon** is a pharmacist currently completing an additional training residency year in Vancouver, BC. **Dr Allan** is Associate Professor in the Department of Family Medicine at the University of Alberta in Edmonton.

The opinions expressed in Tools for Practice articles are those of the authors and do not necessarily mirror the perspective and policy of the Alberta College of Family Physicians.

## References

1. Sattar N, Preiss D, Murray HM, Welsh P, Buckley BM, de Craen AJ, et al. Statins and risk of incident diabetes: a collaborative meta-analysis of randomised statin trials. *Lancet* 2010;375(9716):735-42. Epub 2010 Feb 16.
2. Preiss D, Seshasai SR, Welsh P, Murphy SA, Ho JE, Waters DD, et al. Risk of incident diabetes with intensive-dose compared with moderate-dose statin therapy: a meta-analysis. *JAMA* 2011;305(24):2556-64.
3. American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2013;36(Suppl 1):S67-74.
4. Waters DD, Ho JE, DeMico DA, Breazna A, Arsenault BJ, Wun CC, et al. Predictors of new-onset diabetes in patients treated with atorvastatin: results from 3 large randomized clinical trials. *J Am Coll Cardiol* 2011;57(14):1535-45.
5. Sukhija R, Prayaga S, Marashdeh M, Bursac Z, Kakar P, Bansal D, et al. Effect of statins on fasting plasma glucose in diabetic and nondiabetic patients. *J Investig Med* 2009;57(3):495-9.
6. Wilt TJ, Bloomfield HE, MacDonald R, Nelson D, Rutks I, Ho M, et al. Effectiveness of statin therapy in adults with coronary heart disease. *Arch Intern Med* 2004;164(13):1427-36.
7. Heart Protection Study Collaboration Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high-risk individuals: a randomised placebo-controlled trial. *Lancet* 2002;360(9326):7-22.
8. Elliott WJ, Meyer PM. Incident diabetes in clinical trials of antihypertensive drugs: a network meta-analysis. *Lancet* 2007;369(9557):201-7. Erratum in: *Lancet* 2007;369(9572):1518.
9. ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002;288(23):2981-97. Errata in: *JAMA* 2004;291(18):2196, *JAMA* 2003;289(2):178.
10. Ko DT, Hebert PR, Coffey CS, Curtis JP, Foody JM, Sedrakyan A, et al. Adverse effects of beta-blocker therapy for patients with heart failure: a quantitative overview of randomized trials. *Arch Intern Med* 2004;164(13):1389-94.
11. Conen D, Ridker PM, Mora S, Buring JE, Glynn RJ. Blood pressure and risk of developing type 2 diabetes mellitus: the Women's Health Study. *Eur Heart J* 2007;28(23):2937-43.
12. Lindström J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. *Diabetes Care* 2003;26(3):725-31.
13. Ridker PM, Pradhan A, MacFadyen G, Libby P, Glynn RJ. Cardiovascular benefits and diabetes risks of statin therapy in primary prevention: an analysis from the JUPITER trial. *Lancet* 2012;380(9841):565-71.



Tools for Practice articles in *Canadian Family Physician* (CFP) are adapted from articles published on the Alberta College of Family Physicians (ACFP) website, summarizing medical evidence with a focus on topical issues and practice-modifying information. The ACFP summaries and the series in CFP are coordinated by Dr G. Michael Allan, and the summaries are co-authored by at least 1 practising family physician and are peer reviewed. Feedback is welcome and can be sent to [toolsforpractice@cfpc.ca](mailto:toolsforpractice@cfpc.ca). Archived articles are available on the ACFP website: [www.acfp.ca](http://www.acfp.ca).