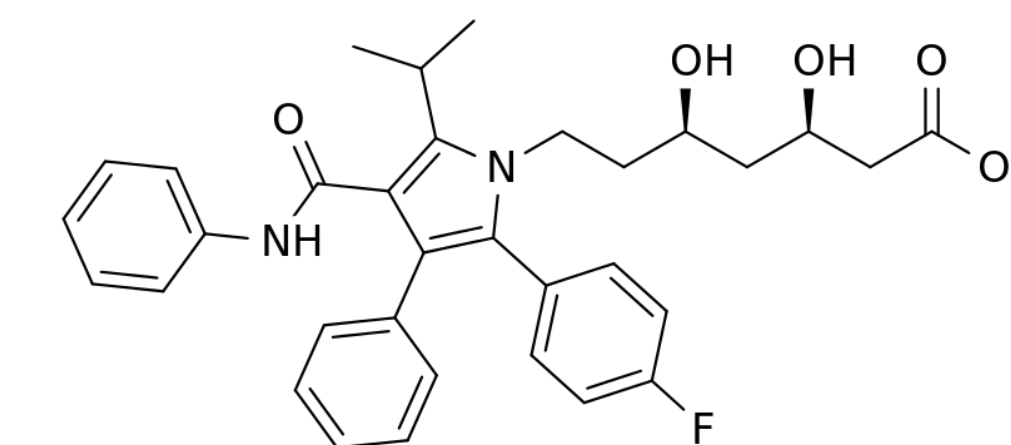


A RISK WORTH TAKING?

Investigating the potential link between statins and new-onset diabetes mellitus

Camille Andrzejewski, Erica Blimkie, Salma Ibrahim, Lauryn Dingwall
University of Ottawa, Faculty of Health Science



INTRODUCTION

•HMG-CoA reductase inhibitors (Statins) are a group of pharmaceuticals administered to lower cholesterol levels by inhibiting the HMG-CoA reductase enzyme, which plays a key role in cholesterol synthesis within the liver.

•Statins are effective in reducing cardiovascular events related to atherosclerosis. They are the most widely prescribed pharmaceutical in the world, and it is estimated that 3 million Canadians take statins daily.

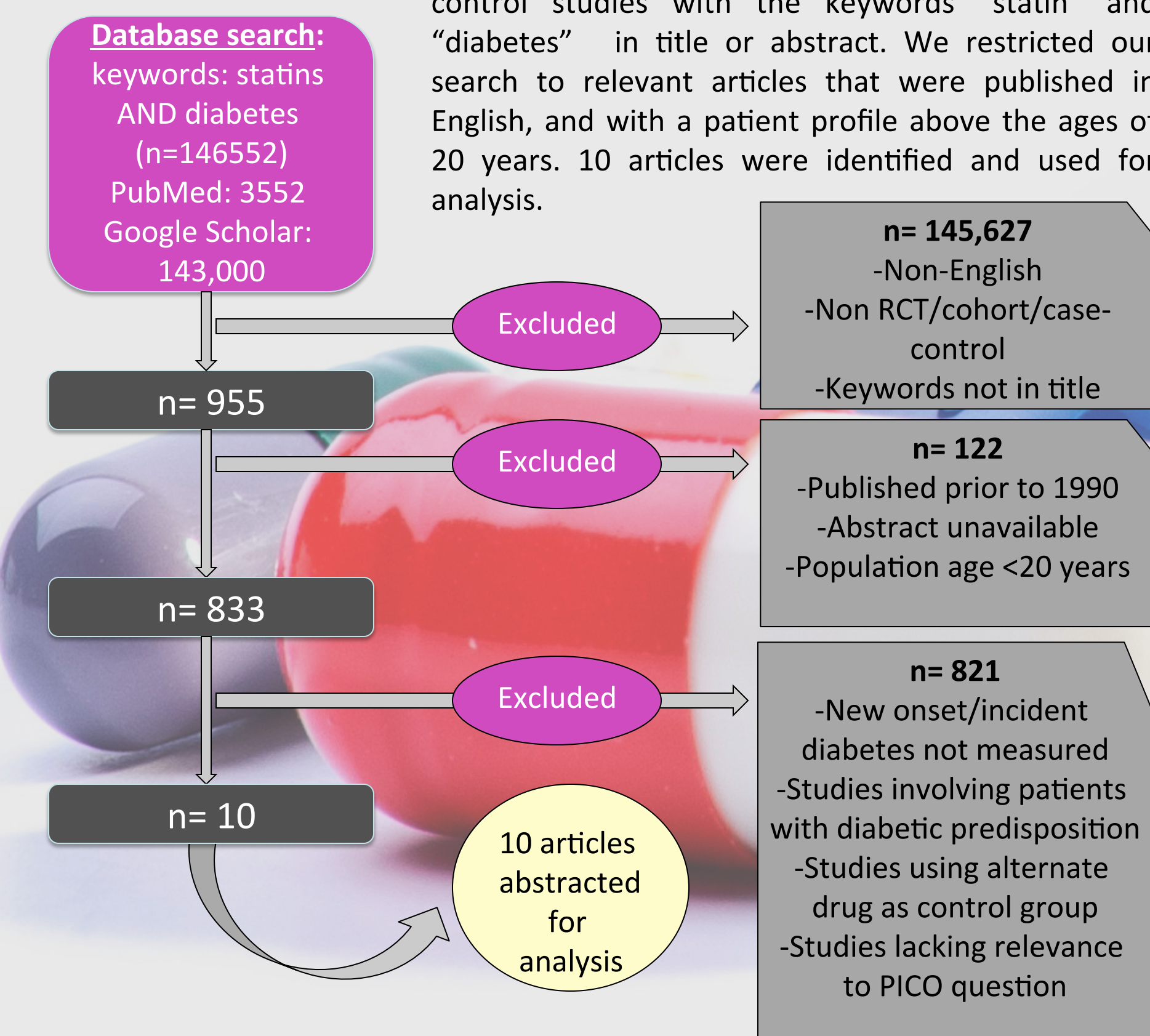
•The literature presents conflicting findings regarding the potential association between statin-use and new onset type-II diabetes mellitus (NOD).

OBJECTIVE

This study aims to provide a comprehensive and systematically synthesized review of the current literature on statin use and incident diabetes by answering the question: **Does the use of statin medications create a heightened risk of developing new-onset type II diabetes mellitus in adults over the age of 20 since the year 1990?**

METHODS

Figure 1. Flow-chart depicting methodology for selecting studies to include in structured review. We searched PubMed and Google Scholar databases from 1990 to 2014, for RCT, Clinical trials, cohort and case-control studies with the keywords “statin” and “diabetes” in title or abstract. We restricted our search to relevant articles that were published in English, and with a patient profile above the ages of 20 years. 10 articles were identified and used for analysis.



RESULTS

- Individuals prescribed statins were found to be at a slightly increased risk of new onset diabetes
- Among the different types of statins, atorvastatin seems to have the highest association with NOD compared to other statin types.

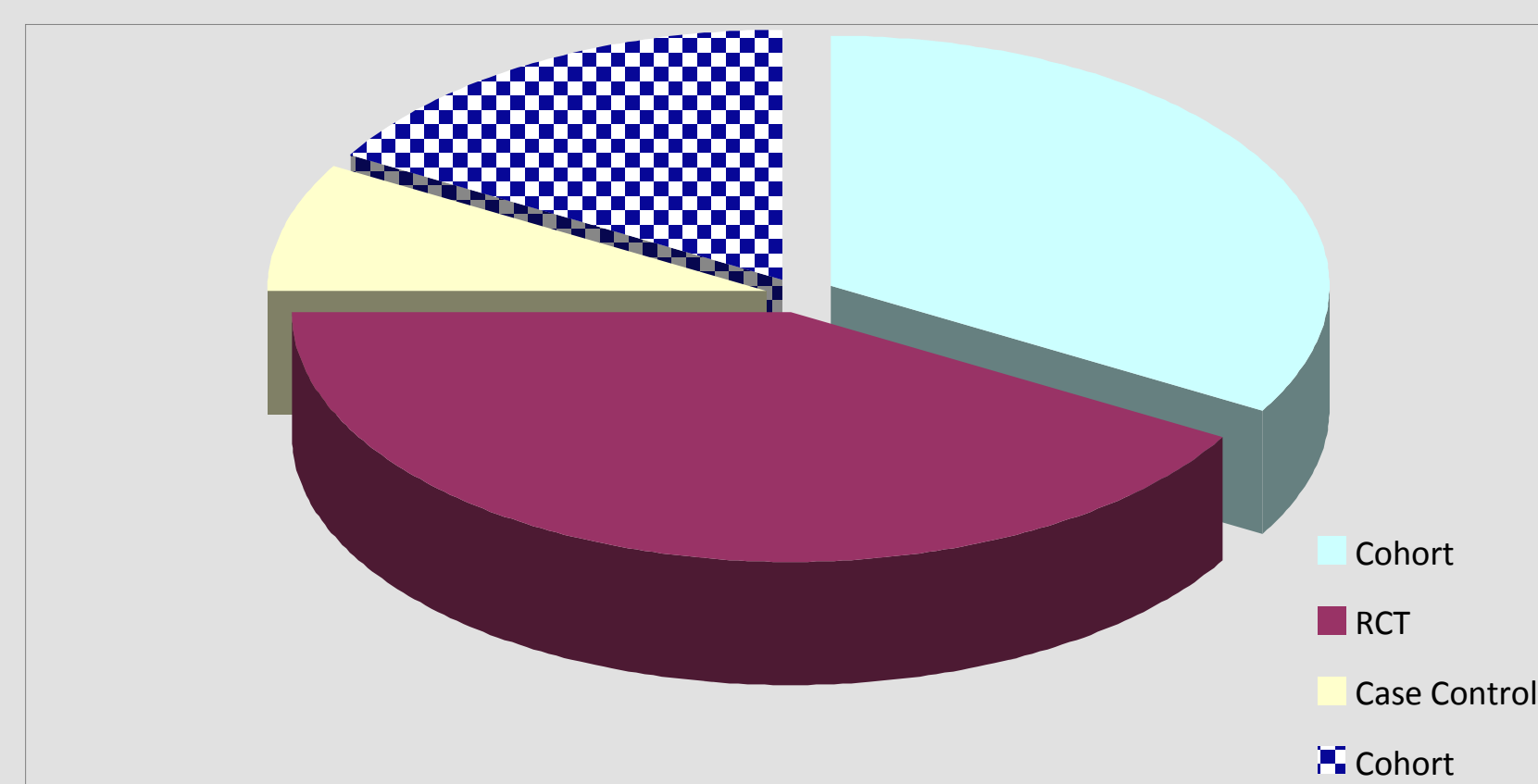


Figure 2. Summary of results from systematic review grouped by study design. Solid fill indicates studies in which a heightened risk of NOD was found. Pattern fill indicates studies with no significant increase in risk of NOD.

Study #	Population		Association P<0.05, CI= 95%	Heightened risk of NOD?	
	Demographic	n			
1	M/F (35-75)	15,056	2012	HR=1.24	Yes
2	M/F (66+)	471,250	1997-2010	HR=1.22	Yes
3	M/F (65+)	23,710	2004-2010	13% NOD in statin users	No
4	M/F (20-84)	16,027	2006-2009	HR=1.29	Yes
5	M (45+)/ F(55+)	42,060	2000-2003	2.4% in statin users vs. 2.1% in non users	Yes
6	M/F (40-60)	32,086	2006-11	HR=3.31	Yes
7	F (40+)	11,715	2013	OR= 8.0*	No
8	M/F (65+)	15,637	2004-2009	HR=0.77	Yes
9	M/F (66+)	3798	1997-2010	HR=1.10	Yes
10	M/F (66+)	3803	1997-2010	HR=1.44	Yes
11	M/F (66+)	18,885	1997-2010	HR=1.16	Yes
12	F (50-79)	153,840	1993-2005	HR=1.71	Yes

Table 1. Summary of findings. Association between statins and the development of diabetes is shown for each corresponding study compared to control or placebo (HR=hazard ratio, OR=odds ratio). Development of new onset diabetes (NOD) is also indicated.

DISCUSSION

Potential Limitations/Biases of this Investigation:

- Limited to Pubmed and Google Scholar databases.
- Limited to English.
- Limited to studies reporting on incident diabetes.
- Interventions varied between studies (e.g. doses)
- Statin type varied between studies.
- Demographic heterogeneity between studies.
- Diagnostic criteria of NOD may vary between studies.

Potential Limitations/Biases of Studies Reviewed

- Self-report of statin use/ dose.
- The populations studied (statin-users) are generally older, display higher rates of cardiac disease, and have higher body mass indices which may skew results.
- Residual confounding effects: possible protective factors in control/placebo group may account for differences between groups.

Suggestions for future research

- Statin-induced NOD morbidity, mechanisms of action

Clinical implications:

- Increased clinical follow-up of statin-users (e.g. monitoring early signs of diabetes onset such as irregular glucose levels).
- Rigorous evaluation of risk-factors for diabetes prior to statin-prescription.

CONCLUSION

The use of HMG-CoA reductase inhibitors is associated with a heightened risk of incident type-II diabetes mellitus in adults over the age of 19. **However, the overall benefit of reduced cardiovascular events gained by statin use outweighs the potential risk of NOD.**

REFERENCES

- 1) Waters, D.D., Ho, J.E., Boehkhardt, S.M., DeMicco, D.A., Kastelein, J.J.P., Messig, M., Breazna, A., & Pedersen, T.R. (2012). Cardiovascular event reduction versus new-onset diabetes during atorvastatin therapy: effect of baseline risk factors for diabetes. *J Am Coll Cardiol* 61 (2), 148-5.
- 2) Carter, A.A., Gomes, T., Camacho, X., Juorink, D.N., Shah, B.R., Marmiani, M.M. (2013). Risk of incident diabetes among patients treated with statins: population based study. *BMJ*. 346.
- 3) Ko, D.T., Wijeyesundara, H.C., Jackevicius, C.A., Youssef, A., Wang, J., & Tu, J.V. (2013). Diabetes mellitus and cardiovascular events in older patients with myocardial infarction prescribed intensive-dose and moderate-dose statins. *Circ Cardiovasc Qual Outcomes*. 6(3), 315-22.
- 4) Ma, T., Tien, L., Fang, C.L., Liou Y.S., & Jong, G.P. (2012). Statins and new-onset diabetes: a retrospective longitudinal cohort study. *Clin Ther*. 34(9), 1977-83
- 5) Wang, K.L., Liu, C.J., Chao, T.F., Huang, C.M., Wu, C.H., Chen, S.J., Chen, T.J., & Chiang, C.E. (2012). Statins, risk of diabetes, and implications on outcomes in the general population. *J Am Coll Cardiol* 60(14), 1231-8
- 6) Currie, O., Mangin, D., Willman, J., McKinnon-gee, B., & Brifford, P. (2013). The comparative risk of new-onset diabetes after prescription of drugs for cardiovascular risk prevention in primary care: a national cohort study. *BMJ Open*. 3
- 7) Chen, C.W., Chen, T.C., Huang, K.Y., Chou, P., Chen, P.F., & Lee, C.C. (2013). Differential impact of statin on new-onset diabetes in different age groups: a population-based case-control study in women from an asian country. *PLoS One*, 8 (8).
- 8) Ma, T., Chang, M.H., Tien, L., Liou, Y.S., & Jong, G.P. (2012). The long-term effect of statins on the risk of new-onset diabetes mellitus in elderly Taiwanese patients with hypertension and dyslipidaemia: a retrospective longitudinal cohort study. *Drugs Aging*. 29 (1), 45-51
- 9, 10, 11) Water, D.D., Ho, J.E., DeMicco, D.A., Breazna, A., Arsenault, B.J., Wun, C.C., Kastelein, J.J., & Barter, P. (2011). Predictors of new-onset diabetes in patients treated with atorvastatin: results from 3 large randomized clinical trials. *J Am Coll Cardiol*, 57 (14), 1535-45
- 12) Culver, A.L., Ockene, I.S., Balasubramanian, R., Olendki, B.C., Sepavich, D.M., Wactawski-Wende, J., Manson, J.E., & Ma, Y. (2012) Statin Use and Risk of Diabetes Mellitus in Postmenopausal Women in the Women's Health Initiative. *Arch Intern Med*, 172 (2), 144-52