The Canadian lipid guidelines are difficult to model quantitatively

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In this month's issue of *The Canadian Journal of Cardiology*, Manuel et al (pages 617 to 620) present a mathematical analysis of the 2006 Canadian guidelines for lipid management (1), as they had previously done (2,3) for the 2003 guidelines (4). The results of their work suggest that Canadian guidelines continue to be less 'favourable' than those of Britain and New Zealand from the perspective of the number of coronary artery disease (CAD) deaths prevented over a five-year period and the number needed to treat (NNT) to prevent one death over the same period.

To judge the results of this work, it is essential that the reader be aware of the assumptions the authors have made. First, the model assumes that all persons whose lipid levels are above the guideline thresholds associated with their Framingham risk score (FRS) category are immediately prescribed a statin medication. For example, a patient at low (less than 10%) Framingham risk and low-density lipoprotein cholesterol (LDL-C) higher than 5.0 mmol/L or a total cholesterol to high-density lipoprotein cholesterol ratio higher than 6 would automatically receive a statin prescription. Unfortunately, this is not a representation of reality. The guidelines' term 'treatment' is in no way intended to be translated 'automatic prescription of statin medication'. Under the section of the guideline labelled 'Treatment', the first paragraph is entitled 'Lifestyle' and the first sentence reads: "Lifestyle interventions remain the cornerstone of CAD prevention strategies...and are the first step in risk factor intervention for individuals in the low- and intermediate-risk categories" (1). The rest of the section discusses smoking cessation, dietary modification, weight loss and exercise. In other words, the flagship treatment is omitted from the model. When it finally comes to pharmaceutical intervention in the low-risk category, in fact, the guideline ultimately returns the decision to the clinician: "Clinical judgment may be used regarding the initiation of pharmacological therapy for patients in the lowest FRS category" (1). Similarly, medications are not universally recommended for young patients with diabetes. So, we have two immediate problems: neither lifestyle intervention nor clinical judgment has been modelled – naturally, because they are very difficult phenomena to model.

The second assumption is that the only prescribable medication is a statin. Although statins are the most commonly prescribed pharmaceutical for lipid management, they are by no means the only drugs used. There are a number of other medications available with different modes of action and utility based on the pattern of dyslipidemia. For example, in the case of isolated hypoalphalipoproteinemia, which will raise the total cholesterol to high-density lipoprotein cholesterol ratio, the clinician may choose to use pure or extended-release niacin.

A third assumption, acknowledged by the authors, is that their 18-year-old input data, taken from the 1990 Canadian Heart Health Survey, is applicable in 2008. Their justification for the use of an old data set is that there is "no strong evidence" that CAD risk has changed in this time period and that the incidence of CAD is stable. To our knowledge, this is not the case. In fact, the trend between 1978 and 1997, based on Canadian data, suggests that CAD risk, prevalence and mortality are probably falling (5), but, of course, the absolute number of cases of CAD is increasing (6). Similar observations have been made in the United States (7). Therefore, the choice of input data is questionable.

Finally, we would like to acknowledge the authors' observation that the NNT to prevent a case of CAD in the very low-risk group over a five-year period is extremely high (NNT=1940). This is precisely the reason that the guidelines do not recommend reflex prescription of medications to all low- and moderate-risk individuals who are not meeting their lipid targets. On the other hand, the clinician must remember that atherosclerosis is a slow, continuous process, and lifestyle changes do not always adequately improve the lipid panel. It has been shown that if two or more major cardiovascular disease risk factors have developed by the time a patient enters the sixth decade of life, there is a marked increase in cardiovascular disease risk (8). This long-term perspective is what motivates all risk reduction efforts (first lifestyle and, if need be, medication) for persons at lower risk.

A quantitative investigation of the efficacy of a clinical guideline is noble to attempt, but because accurate quantitative modelling of the effectiveness of the recommendations is impossible, the Canadian guidelines will continue to be called 'guidelines' for many years to come, and their efficacy should be judged with data produced after their inception. In summary, neither the assumptions nor the input data of the authors' model represent the current reality, and in that sense, we are unsure about the veracity of the conclusions.

CONFLICTS OF INTEREST: Jiri Frohlich is, or has been, a member of medical advisory boards for Merck Frosst, Pfizer, Astra Zeneca and Forbes Meditec, and has received research grants from all of these companies.

REFERENCES

- McPherson R, Frohlich J, Fodor G, Genest J; Canadian Cardiovascular Society. Canadian Cardiovascular Society position statement – recommendations for the diagnosis and treatment of dyslipidemia and prevention of cardiovascular disease. *Can J Cardiol* 2006;22:913-27. (Erratum in 2006;22:1077).
- Manuel DG, Kwong K, Tanuseputro P, et al. Effectiveness and efficiency of different guidelines on statin treatment for preventing deaths from coronary heart disease: Modelling study. *BMJ* 2006;332:1419-23.
- Manuel DG, Tanuseputro P, Mustard CA, et al. The 2003 Canadian recommendations for dyslipidemia management: Revisions are needed. *CMAJ* 2005;172:1027-31. (Erratum in 2005;173:133).
- Genest J, Frohlich J, Fodor G, McPherson R; Working Group on Hypercholesterolemia and Other Dyslipidemias. Recommendations for the management of dyslipidemia and the prevention of cardiovascular disease: Summary of the 2003 update. *CMAJ* 2003;169:921-4. (Erratum in 2003;169:1149).
- Chen J, Millar WJ. Are recent cohorts healthier than their predecessors? *Health Rep* 2000;11:9-23.
- Heart and Stroke Foundation of Canada. The growing burden of heart disease and stroke in Canada. Ottawa, 2003.
- Ford ES, Ajani UA, Croft JB, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. *N Engl J Med* 2007;356:2388-98.
- Lloyd-Jones DM, Leip EP, Larson MG, et al. Prediction of lifetime risk for cardiovascular disease by risk factor burden at 50 years of age. *Circulation* 2006;113:791-8.

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