The 2006 Canadian dyslipidemia guidelines will prevent more deaths while treating fewer people – but should they be further modified?

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DG Manuel, S Wilson, S Maaten. The 2006 Canadian dyslipidemia guidelines will prevent more deaths while treating fewer people – but should they be further modified? *Can J Cardiol* 2008;24(8):617-620.

BACKGROUND: When clinical guidelines affect large numbers of individuals or substantial resources, it is important to understand their benefits, harms and costs from a population perspective. Many countries' dyslipidemia guidelines include these perspectives.

OBJECTIVE: To compare the effectiveness and efficiency of the 2003 and 2006 Canadian dyslipidemia guidelines for statin treatment in reducing deaths from coronary artery disease (CAD) in the Canadian population.

METHODS: The 2003 and 2006 Canadian dyslipidemia guidelines were applied to data from the Canadian Heart Health Survey (weighted sample of 12,300,000 people), which includes information on family history and physical measurements, including fasting lipid profiles. The number of people recommended for statin treatment, the potential number of CAD deaths avoided and the number needed to treat to avoid one CAD death with five years of statin therapy were determined for each guideline.

RESULTS: Compared with the 2003 guidelines, 1.4% fewer people (20 to 74 years of age) are recommended statin treatment, potentially preventing 7% more CAD deaths. The number needed to treat to prevent one CAD death over five years decreased from 172 (2003 guideline) to 147 (2006 guideline).

CONCLUSIONS: From a population perspective, the 2006 Canadian dyslipidemia recommendations are an improvement of earlier versions, preventing more CAD events and deaths with fewer statin prescriptions. Despite these improvements, the Canadian dyslipidemia recommendations should explicitly address issues of absolute benefit and cost-effectiveness in future revisions.

Key Words: Death; Health care delivery; Lipids; Myocardial infarction

Les directives canadiennes de 2006 sur les dyslipidémies préviendront plus de décès tout en traitant moins de gens, mais doivent-elles être encore modifiées?

HISTORIQUE : Lorsque des directives cliniques touchent beaucoup d'individus ou sollicitent des ressources substantielles, il est important d'en comprendre les avantages, les inconvénients et le coût, du point de vue des populations. Les directives de nombreux pays sur les dyslipidémies tiennent compte d'une telle perspective.

OBJECTIF : Comparer l'efficacité et l'efficience des directives canadiennes de 2003 et de 2006 sur le traitement des dyslipidémies au moyen des statines, pour ce qui est de réduire le nombre de décès d'origine coronarienne dans la population canadienne.

MÉTHODES : Les directives canadiennes de 2003 et de 2006 sur les dyslipidémies ont été appliquées à des données de l'Enquête canadienne sur la santé cardiovasculaire (échantillon pondéré de 12 300 000 personnes), incluant des renseignements sur les antécédents familiaux et certains paramètres physiques, notamment, les profils lipidiques à jeun. Pour chaque directive, les auteurs ont déterminé le nombre de personnes à qui le traitement par statines a été recommandé, le nombre potentiel de décès d'origine coronarienne évités et le nombre de patients à traiter pour éviter un décès d'origine coronarienne au moyen d'un traitement par statine d'une durée de cinq ans.

RÉSULTATS : Comparativement aux directives de 2003, on note une réduction de 1,4 % du nombre de personnes (de 20 à 74 ans) chez qui un traitement par statine a été recommandé, ce qui potentiellement préviendrait 7 % plus de décès d'origine coronarienne. Le nombre de patients à traiter pour prévenir un décès d'origine coronarienne sur une période de cinq ans est passé de 172 (directives de 2003) à 147 (directives de 2006).

CONCLUSIONS : Du point de vue des populations, les recommandations canadiennes de 2006 sur les dyslipidémies constituent une amélioration par rapport aux versions antérieures, puisqu'elles permettent de prévenir plus d'incidents et de décès coronariens au moyen d'un moins grand nombre d'ordonnances de statines. Malgré ces améliorations, lors des futures révisions, les recommandations canadiennes sur les dyslipidémies devraient expressément tenir compte des bénéfices et de la rentabilité absolus des interventions.

When clinical guidelines affect large numbers of people or substantial resources, such as the Canadian dyslipidemia recommendations, it is important to understand their benefits, harms and costs from a population perspective. Currently, hundreds of thousands of Canadians take statins, at a direct drug cost of approximately \$2 billion, or more than 1% of total health care expenditures (1). We previously assessed the 2003 Canadian recommendations from a population perspective (2) and

found that they performed worse than those of other countries' recommendations. We now provide an updated assessment for the most recent (2006) changes to the Canadian recommendations (3). A detailed description of our methodology, including the assumptions of our model, can be found in the accompanying Appendixes 1 to 3.

The most recent recommendations decreased low-density lipoprotein (LDL) target levels for high-risk people (from 2.5 mmol/L to

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Figure 1 Number of coronary artery disease (CAD) deaths avoided per 100,000 population over five years versus the percentage of Canadian population 20 to 74 years of age treated with statins based on the 2000 to 2006 Canadian dyslipidemia guidelines. *The optimal community effectiveness curve shows the number of CAD deaths avoided if the highest-risk people were treated first. A – The effectiveness gap or the difference between the potential deaths avoided by the guideline recommendations compared with the optimal number of deaths avoided if the highest-risk people were recommended treatment. B – The efficiency gap or the difference between percentage of the population recommended statin treatment compared with the minimum population who could be treated to avoid the same number of deaths. NNT Number needed to treat to prevent one CAD death over five years

2.0 mmol/L) and increased LDL targets for low-risk people (from 4.5 mmol/L to 5.0 mmol/L). We assessed these changes with respect to three population characteristics – the number of people recommended statin treatment, the potential community effectiveness (defined as the potential number of deaths from coronary artery disease [CAD] prevented if all Canadians were screened, treated and compliant according to the guidelines) and the guideline efficiency (defined as the number of deaths from CAD prevented in relation to the number of people recommended statin treatment and measured by the overall number needed to treat [NNT]).

As with our previous assessment, we used the 1990 Canadian Heart Health Survey (CHHS), the last national population health survey that included physical measures such as cholesterol levels and blood pressure (2,4,5). The 2006 Canadian population had an older age distribution compared with 1990, which will likely result in an underestimation of the number of individuals in the moderate and high-risk groups. However, the CHHS is well-suited to estimate the potential effectiveness of statins because its measurements pre-date the widespread adoption of statin therapy in Canada. Furthermore, there is no strong evidence that the risk of CAD among Canadians has appreciably changed in the intervening period, given that the incidence of CAD is stable (6) and, aside from smoking, risk factors are either unchanged or have shown small prevalence increases (7). The CHHS methods have previously been described in detail (8). We applied the screening and treatment recommendations to each survey respondent, as described by the guidelines. We included only respondents who were questioned about their family history of heart disease to allow for comparison with our assessment of other national and international guidelines. CHHS respondents were allocated to risk groups based on their 10-year probability of a ‘hard’ CAD event, as determined by the Framingham-based risk point scoring system used in the Canadian guidelines. The Framingham

risk index is an accurate and discriminating tool for the estimation of CAD risk, but it cannot be substituted for the history and physical examination taken by the clinician, which may aid in the detection of less common causes of dyslipidemia. For example, our model did not account for the small number (9) of individuals with monogenic dyslipidemias, such as familial hypercholesterolemia, who may be inappropriately labelled as low-risk by the Framingham risk algorithm alone. Finally, we assumed that individuals would be recommended statin therapy if their LDL level exceeded the target level set for their particular risk category (Appendixes 1 to 3).

We found that compared with the 2003 guidelines, the latest updates recommend statin treatment to 1.4% fewer people (a decrease from 16.6% to 15.2% of Canadians 20 to 74 years of age) while potentially preventing 7.0% more deaths from CAD (an increase from 96 to 103 CAD deaths prevented per 100,000 Canadians) (Figure 1). The recommendations’ overall efficiency improved by 14.5% (NNT from 172 to 147), or equal to approximately \$290 million in direct drug cost savings at the national level given current expenditures (14.5% of \$2 billion equals \$290 million).

At face value, the New Zealand Guidelines Group (6) and the Joint British Societies (7,8) continue to have more favourable population characteristics than the Canadian recommendations, mainly because they do not recommend statins to low-risk people unless they have very high cholesterol levels. For example, the 2003 New Zealand dyslipidemia guidelines recommended statins to low-risk individuals (10-year CAD risk of less than 10%) only if the total cholesterol is greater than 8 mmol/L or if the total cholesterol to high-density lipoprotein cholesterol ratio is greater than 8. The 1998 and 2005 Joint British Societies’ dyslipidemia guidelines (7,8) do not use lipid targets for statin therapy for people at low risk of CAD. In the 1990 Canadian population, low-risk people comprised 8.4% of the population recommended statin therapy, or 1.3% of Canadians 20 to 74 years of age, according to the 2006 recommendations. People at very low risk (0% to 5% 10-year risk of CAD) comprised 3.3% of the population recommended statin therapy.

Statin recommendations for people at low and very low risk for CAD are debated for two reasons. First, meta-analyses and reviews reach different conclusions about whether statins are efficacious, in terms of relative benefit, in low- and very low-risk groups. There are no statin intervention trials in very low-risk people, with differing views on whether the (same) relative benefit that is observed in high-risk groups holds for low- and very low-risk groups, including low-risk people whose lipid levels are above the Canadian targets. Second, there is no consensus on whether absolute benefit, cost-effectiveness and resource implications should be considered when developing clinical recommendations and guidelines. The Canadian recommendations do not explicitly include these perspectives, but other countries’ guidelines do. Even if statins have a favourable relative benefit for very low-risk groups, the absolute benefit is very small. We estimated the mean 10-year CAD risk for the very low-risk group to be 1.2%, which equals an absolute benefit of 0.05% (NNT=1940) for five years of statin therapy to prevent CAD.

CONCLUSIONS

From a population perspective, the 2006 Canadian dyslipidemia recommendations are an improvement over earlier versions. The updated guidelines have the potential to prevent more CAD events and deaths with fewer statin prescriptions. However, the Canadian guidelines should be further discussed. Recommending treatment to very low-risk people appears to be neither an efficient nor effective way to reduce cardiovascular outcomes, but has large resource and patient implications given the number of people in this group.

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APPENDIX 1**Screening criteria and classification of risk groups as defined in the 2003 and 2006 Canadian recommendations for the management of dyslipidemia as applied to the population of the Canadian Heart Health Survey (CHHS)**

Guideline recommendations		Application to CHHS dataset
Screening criteria according to the 2003 recommendations		
Age	Men >40 years of age, women >50 years of age or postmenopausal	Men >40 years of age, women >50 years of age
Risk factors	Presence of ≥ 1 risk factor for coronary artery disease (CAD)	Any of obesity (BMI ≥ 30 kg/m ²), hypertension (blood pressure higher than 140/90 mmHg) or smoking
Family history	Strong family history of premature CAD	Self-reported family history of CAD
Disease state	Presence of diabetes	Self-reported diabetes
	Presence of xanthoma or other stigmata of dyslipidemia	Previous myocardial infarction or angina
	Evidence of atherosclerosis	
Screening criteria according to the 2006 recommendations		
Age	Men >40 years of age, women >50 years of age or postmenopausal	Men >40 years of age, women >50 years of age
Risk factors	Presence of ≥ 1 risk factor for CAD	Any of obesity (BMI ≥ 30 kg/m ²), hypertension (blood pressure higher than 140/90 mmHg) or smoking
Family history	Strong family history of premature CAD	Self-reported family history of CAD
Disease state	Presence of diabetes	Self-reported diabetes
	Manifestations of hyperlipidemia	Previous myocardial infarction or angina
	Exertional chest discomfort, dyspnea or erectile dysfunction	
	Chronic kidney disease or systemic lupus erythematosus	
	Evidence of atherosclerosis	
Risk group definitions according to the 2003 recommendations		
High	10-year risk of 'hard' CAD event (CAD-related death, nonfatal myocardial infarction) $\geq 20\%$ or history of diabetes or any atherosclerotic disease	10-year risk of 'hard' CAD event (CAD-related death or nonfatal myocardial infarction) $\geq 20\%$ or self-reported diabetes or self-reported past myocardial infarction or angina
Moderate	10-year risk of 'hard' CAD event 11%–19%	10-year risk of 'hard' CAD event 11%–19%
Low	10-year risk of 'hard' CAD event $\leq 10\%$	10-year risk of 'hard' CAD event $\leq 10\%$
Risk group definitions according to the 2006 recommendations		
High	10-year risk of 'hard' CAD event (CAD-related death, nonfatal myocardial infarction) $\geq 20\%$ or history of diabetes or any atherosclerotic disease, and most patients with chronic kidney disease	10-year risk of 'hard' CAD event (CAD-related death or nonfatal myocardial infarction) $\geq 20\%$ or self-reported diabetes or self-reported past myocardial infarction or angina
Moderate	10-year risk of 'hard' CAD event 11%–19%	10-year risk of 'hard' CAD event 11%–19%
Low	10-year risk of 'hard' CAD event $\leq 10\%$	10-year risk of 'hard' CAD event $\leq 10\%$

BMI Body mass index

APPENDIX 2**Analysis of the 1992 Canadian population by risk group using the 2003 recommendations for the management of dyslipidemia*†**

Analysis	Low risk	Moderate risk	High risk	Total	High-risk subgroups		
					History of CVD	History of diabetes and age ≥ 30 , years	10-year risk of CAD $>30\%$
Estimated number (%) of individuals	10,200,000 (82.9)	790,000 (6.4)	1,330,000 (10.7)	12,350,000 (100.0)	500,000 (4.0)	390,000 (3.2)	430,000 (3.5)
Number (%) recommended for lipid testing	7,100,000 (69)	790,000 (100)	1,330,000 (100)	9,200,000 (75)	500,000 (100)	390,000 (100)	430,000 (100)
Number recommended for statin therapy	450,000	430,000	1,150,000	2,000,000	400,000	330,000	400,000
Percentage recommended statins of those screened	6	55	87	22	81	85	96
Number of CAD-related deaths prevented over 5 years [§]	300	1140	10,400	12,000	6360	1255	2800
NNT to prevent 1 CAD-related death over 5 years of statin therapy [§]	1477	380	111	172	64	265	148

Raw numbers (before rounding) were used to calculate all percentages and the number needed to treat (NNT). *The reference population included Canadians in 1992 20–74 years of age. Data from the Canadian Heart Health Survey were used to identify the risk categories of respondents; †See Appendix 1 for risk group definitions; §Calculated using Framingham study equations given a 24% relative efficacy of statins. CAD Coronary artery disease; CVD Cardiovascular disease

APPENDIX 3

Analysis of the 1992 Canadian population by risk group using the 2006 recommendations for the management of dyslipidemia*†

Analysis	Low risk	Moderate risk	High risk	Total	Very high-risk subgroups		
					History of CVD	History of diabetes, and age ≥30, years	10-year risk of CAD >30%
Estimated number (%) of individuals	10,200,000 (82.9)	790,000 (6.4)	1,330,000 (10.7)	12,350,000 (100.0)	500,000 (4.0)	390,000 (3.2)	430,000 (3.5)
Number (%) recommended for lipid testing	7,100,000 (69)	790,000 (100)	1,330,000 (100)	9,200,000 (75)	500,000 (100)	390,000 (100)	430,000 (100)
Number recommended for statin therapy	150,000	430,000	1,275,000	1,900,000	470,000	370,000	430,000
Percentage recommended statins of those screened	2	55	96	20	95	94	100
Number of CAD-related deaths prevented over 5 years§	155	1100	11,400	12,700	7200	1300	2900
NNT to prevent 1 CAD-related death over 5 years of statin therapy§	1011	380	112	147	66	283	148

Raw numbers (before rounding) were used to calculate all percentages and the number needed to treat (NNT). *The reference population included Canadians in 1992 20–74 years of age. Data from the Canadian Heart Health Survey were used to identify the risk categories of respondents; †See Appendix 1 for risk group definitions; §Calculated using Framingham study equations given a 24% relative efficacy of statins. CAD Coronary artery disease; CVD Cardiovascular disease

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