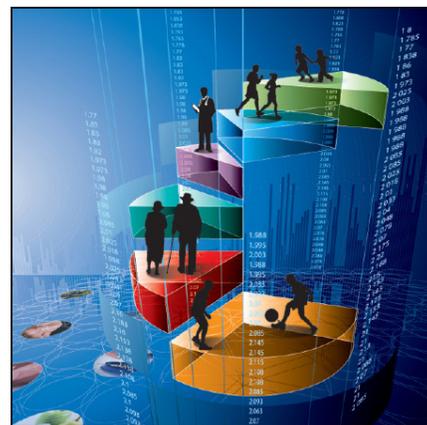


## Health Reports

# Population health impact of statin treatment in Canada

by Deirdre A. Hennessy, Peter Tanuseputro, Meltem Tuna,  
Carol Bennett, Richard Perez, Margot Shields, Dennis T. Ko,  
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- <sup>r</sup> revised
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# Population health impact of statin treatment in Canada

Deirdre A. Hennessy, Peter Tanuseputro, Meltem Tuna, Carol Bennett, Richard Perez, Margot Shields, Dennis T. Ko, Jack Tu and Douglas G. Manuel

## Abstract

**Background:** Statins are prescribed to treat dyslipidemia (abnormal amount of lipids such as cholesterol and/or fat in the blood) and reduce cardiovascular disease (CVD) risk. This study describes the CVD risk profile of Canadians aged 20 to 79, compares current treatment patterns with guideline recommendations, and investigates the population health impact of statin treatment.

**Data and methods:** The baseline CVD risk of the Canadian population aged 20 to 79 was estimated by applying population-weighted risk factor data from the 2007 to 2011 Canadian Health Measures Survey (CHMS) to the Framingham Risk Score. Estimates of statin effectiveness from the literature were applied to baseline risk to assess the number of CVD events avoided owing to actual (CHMS-reported) and recommended (2012 Canadian Cardiovascular Society guidelines) statin treatment.

**Results:** An estimated 2.8 million Canadian adults (about 1 in 10) were treated with statin drugs. The mean 10-year CVD risk of those treated was 27%. Assuming optimal adherence, it was estimated that statin treatment avoided around 18,900 CVD events annually and yielded a number-needed-to-treat (average number of patients treated to prevent one additional CVD event) of 15 over 10 years. In comparison, 6.5 million Canadian adults (about 1 in 4) were recommended for treatment under the 2012 guidelines. The mean 10-year CVD risk of those recommended for treatment was 24%, which translates into a number-needed-to-treat of 17 over 10 years, or approximately 38,600 CVD events avoided annually. The largest gaps in treatment and potential CVD events avoided were among people at high and intermediate risk for CVD.

**Interpretation:** Canadians' CVD risk could be lessened with enhanced targeting of statin treatment to individuals at high and intermediate risk. Such a strategy would likely require additional investments.

**Key words:** Cardiovascular disease, clinical guidelines, risk assessment, risk reduction

Statins—drugs used to lower cholesterol—have been shown to improve survival and reduce the risk of cardiovascular disease (CVD) events among individuals across the spectrum of CVD risk.<sup>1-3</sup> As a result, statins are one of the most frequently prescribed classes of drugs in Canada, and constitute the leading drug cost in all provincial drug programs,<sup>4-6</sup> with direct drug costs totalling almost \$2 billion annually.<sup>6</sup> The prescribing of statins has not been without controversy. New guidelines on CVD risk assessment and statin treatment from the American College of Cardiology and American Heart Association and from the National Institute for Clinical Evaluation in the United Kingdom have brought the issue into the headlines.<sup>7-11</sup>

Owing to the frequency of statin use and the considerable resources allocated to treatment, an examination of the population health impact is warranted. It is important to understand who takes statins; how these individuals are distributed along the spectrum of CVD risk; whether the medication is not taken when it is recommended and vice versa; and how effective the medication is in preventing disease events.

In contrast to the myriad data available from meta-analyses and clinical trials to support inclusion of statin drugs in provincial formularies, little evidence is available to inform the population health perspective. The Canadian Health Measures Survey (CHMS) offers the first opportunity in more than 25 years to examine the population health impact of statin medications. In

addition to evaluating medication use, the CHMS data allow for an assessment of treatment guidelines and adherence to targets such as the Canadian Heart Health Strategy.<sup>12-14</sup>

This study uses the latest CHMS data to describe the CVD risk profile of Canadian adults and investigate the population health impact (CVD events prevented) of statins. To reveal treatment gaps and potentially inform health policy related to CVD risk reduction, current treatment patterns reported in the combined cycles of the CHMS are compared with the 2012 Canadian Cardiovascular Society's (CCS) lipid guidelines.

## Methods

### Data source

From 2007 through 2011, the CHMS, a population-based survey, collected physical measures (including blood samples, blood pressure, weight and height) from 11,999 respondents aged 3 to 79. Details about the survey have been described in detail elsewhere.<sup>15-18</sup>

Briefly, the CHMS has a household and a clinic component. Data were collected at 15 sites across Canada in cycle 1 and at 18 sites in cycle 2. Estimates using the combined file reflect the average Canadian household population during the study timeframe (2007 to 2011). The CHMS is representative of 96% of the Canadian household population aged 3 to 79. It excludes

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residents of Indian Reserves, Crown lands, institutions and certain remote regions, and full-time members of the Canadian Forces. The response rates, calculated as the product of response fractions for the household (69.6%), the household questionnaire (88.3%), and the mobile examination centre component (84.9%), with an adjustment for the sampling strategy, were 51.7% for cycle 1 (2007 to 2009) and 55.5% for cycle 2 (2009 to 2011). During an in-home interview, respondents completed a questionnaire covering socio-demographic characteristics, medical history, current health status, prevalent conditions, and health-related behaviours. Ethics approval for the CHMS was obtained from Health Canada's Research Ethics Board. Written consent was requested from respondents before participation.

### Study sample

Of the total number of respondents ( $n = 11,999$ ) in the combined CHMS cycles, a subsample ( $n = 5,427$ ) provided fasting blood samples. This enabled a full lipid profile, which was necessary to calculate CVD risk. Of this subsample, adult respondents (20 or older and not pregnant) were selected for analysis ( $n = 3,512$ ). Special survey weights calculated for the fasting sample were applied to represent the Canadian population.<sup>19</sup>

### Covariates

The baseline CVD risk of Canadians aged 20 to 79 was examined by socio-demographic and CVD risk factor variables. Information about medication use was collected during the in-home interview, and also during a subsequent appointment at a mobile examination centre (MEC).

Drug identification numbers (DINs) were taken from medication containers during the home interview and verified during the MEC appointment, which typically occurred within two weeks of the home interview. The CHMS recorded up to 15 medications for each respondent. *Statin use* was defined as any statin medication taken in the past month. Medications reported in current use by respondents were assigned

codes from the Anatomical Therapeutic Chemical (ATC) Classification System.<sup>20</sup> Statin-users were identified with two ATC codes—C10A and C10B. These codes also identified users of non-statin lipid-lowering medications like fenofibrate. Respondents who reported only non-statin medications were classified as non-users. The small number of respondents who were using statin combination drugs were classified as statin-users.

The CVD risk of Canadian adults was examined by sex, age group (20 to 39, 40 to 59, and 60 to 79) and cardiovascular risk factors. The cardiovascular risk factors included: low-density lipoprotein (LDL) cholesterol level in mmol/L (less than 2; 2 to less than 3.5; 3.5 to 5; and more than 5); total cholesterol to high-density lipoprotein (HDL) cholesterol ratio in mmol/L (less than 5; 5 or more); smoking (respondents who reported smoking daily or occasionally were categorized as smokers); diabetes status (respondents were categorized as having diabetes if their measured blood glucose was greater than or equal to 7 mmol/l and/or had an audited use of glucose-lowering medication [ATC codes A10] and/or a self-reported health-care-provider diagnosis of diabetes); and mean systolic blood pressure (SBP) in mmHg, measured with the BpTRU™ BP-300 device at the MEC.<sup>21-23</sup> The use of blood pressure medications was also considered: beta blockers (ATC codes C07, excluding C07AA07, C07AA12 and C07AG02); agents acting on the renin-angiotensin system (ATC codes C09); thiazide diuretics (ATC codes C03, excluding C03BA08 and C03CA01); calcium channel antagonists (ATC codes C08); and miscellaneous antihypertensives (ATC codes C02, excluding C02KX01). Finally, family history of premature (younger than 60 in a first-degree relative) heart disease and stroke was investigated as a cardiovascular risk factor.

For risk-stratification, high-risk individuals were defined as having high-risk hypertension; that is, they had three or more of the following risk factors: male, older than 55, smoker, total cholesterol to

HDL-C ratio greater than 6, or a family history of premature CVD and chronic kidney disease.<sup>24</sup>

## Analyses

### CVD risk profile of Canadians

Figure 1 illustrates the steps used to stratify the population aged 20 to 79 according to CVD risk (steps 1 to 4) and calculate the number of CVD events potentially avoided (steps 5 and 6). First, high-risk individuals were identified based on self-reported and measured diagnosis of heart disease, diabetes (aged 40 or older, 30 or older with at least 15 years' duration of diabetes or with microvascular disease),<sup>25</sup> chronic kidney disease, and high-risk hypertension. For respondents reporting pre-existing heart disease, stroke or acute myocardial infarction, baseline CVD risk was calculated using the Framingham Risk Score (FRS) for recurrent coronary heart disease.<sup>26</sup> For respondents who did not automatically fall into the high-risk category, baseline CVD risk was calculated using the FRS for total CVD events over 10 years, as recommended in the 2012 CCS guidelines.<sup>25</sup> Total CVD events predicted included coronary death, myocardial infarction, coronary insufficiency, angina, cerebrovascular events (including ischemic stroke, hemorrhagic stroke, and transient ischemic attack), peripheral artery disease (intermittent claudication), and heart failure over 10 years.<sup>27</sup> The risk factors included in the algorithm were age, total cholesterol, HDL cholesterol, SBP, treatment for high blood pressure, smoking, and diabetes. Risks were calculated separately for men and women.

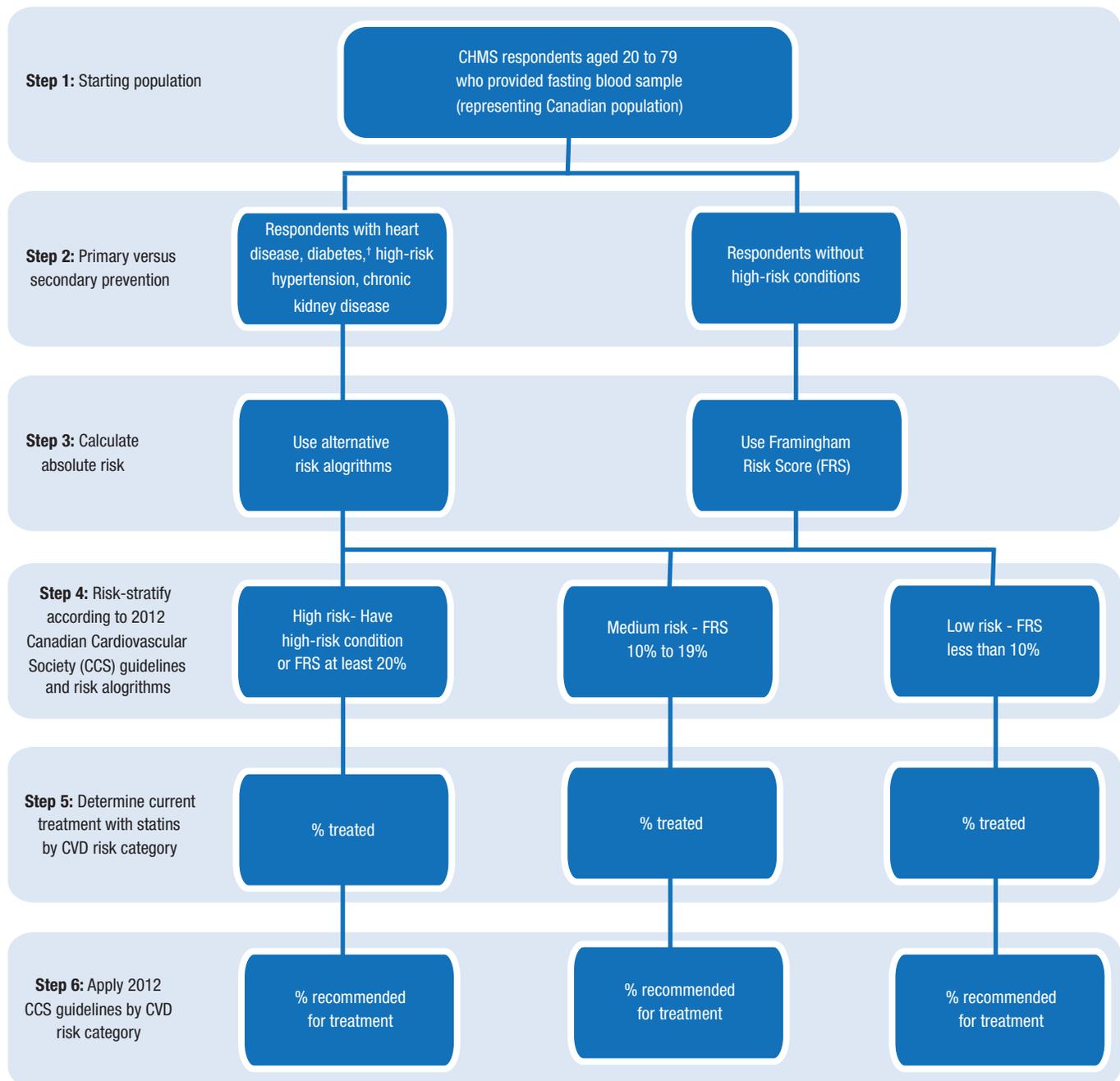
To improve risk stratification, the CCS guidelines recommend doubling the calculated baseline CVD risk for people with a family history of CVD. This inflates the estimate of population baseline risk and results in poorly calibrated population risk estimates.<sup>28</sup> To avoid this bias, baseline risk among those with a family history of CVD was not doubled; instead, a sensitivity analysis was conducted to show how many more people would be recommended for treatment based on a positive family history of CVD (Appendix A).

For those already taking statins, the calculated FRS was based on adjusted levels of cholesterol. Cholesterol levels were adjusted back to pre-treatment

levels with a meta-analysis that provided estimates of statin effectiveness by type and dose (Appendix B).<sup>29</sup> Failure to make this adjustment would have underesti-

mated baseline CVD risk. All estimates of CVD risk, the number needed to treat (NNT), and CVD events avoided were based on pre-treatment cholesterol levels.

**Figure 1**  
**Risk-stratifying household population aged 20 to 79 and determining current and recommended statin treatment, Canada excluding territories, 2007 to 2011**



<sup>†</sup> among diabetics aged 40 or older or 30 or older with at least 15 years' duration of diabetes, or among those with microvascular disease

**Current and guideline-recommended treatment**

Once individuals were stratified by baseline CVD risk, the percentage currently taking statins and being treated at target was estimated (Figure 1, step 5). The CCS guidelines were applied to estimate the numbers who would be screened and treated if the guidelines were fully implemented. Screening criteria recommended by the guidelines that were measured in the CHMS were applied to the population. Men older than 40 and women older than 50 (or postmenopausal women of any age) were considered for screening. In addition, respondents (regardless of age) who had diabetes, hypertension, family history of premature CVD, chronic kidney disease, HIV infection, chronic obstructive pulmonary disease, obesity (BMI greater than 27) or were current cigarette smokers would be screened.

According to the CCS guidelines, individuals screened were considered for treatment based on their risk stratum. Low-risk individuals were considered for treatment, along with lifestyle modification, if their LDL cholesterol was at least 5.0 mmol/L. Intermediate-risk individuals were considered for treatment if their LDL-cholesterol was at least 3.5 mmol/L or their non-HDL cholesterol was at least 4.3 mmol/L. All high-risk individuals were considered for treatment. “Successful” treatment was defined as meeting the targets of LDL cholesterol of no more than 2.0 mmol/L or non-HDL cholesterol of no more than 2.6 mmol/L for individuals in intermediate- or high-risk groups, and a 50% reduction in LDL cholesterol for the low-risk group.

**Population health impact**

To assess the population health impact of statins, the total number of CVD events potentially avoided was calculated for two groups: 1) people currently treated with statins identified in the CHMS (Figure 1, step 5), and 2) people who would be recommended for statin treatment according to the CCS guidelines (Figure 1, step 6).

The absolute risk reduction was calculated by multiplying the mean 10-year baseline risk in the risk group (treated or recommended for treatment) by a relative risk reduction of 25%, obtained from the latest meta-analysis of clinical trials of statin treatment.<sup>1</sup> The inverse of the absolute risk reduction, multiplied by 100 and rounded to the nearest whole number, is the number-needed-to-treat (NNT—the average number who need to be treated to prevent one additional CVD

event). The total number of CVD events avoided was calculated by dividing the number treated by the NNT for those currently treated and performing the same calculation for those recommended for treatment according to the CCS guidelines.<sup>13</sup> Confidence intervals were obtained for the number of CVD events avoided by completing the same calculations on the 95% variance estimates of the number treated and recommended for treatment by risk group.

**Table 1**  
**Prevalence of cardiovascular disease (CVD) risk, by sex, age and cardiovascular risk factors, household population aged 20 to 79, Canada excluding territories, 2007 to 2011**

	CVD risk category											
	Total			High			Intermediate			Low		
	Number ('000)			Mean 10-year risk of CVD event			95% confidence interval			95% confidence interval		
	%	from	to	%	from	to	%	from	to	%	from	to
<b>Number ('000) (% distribution)</b>	24,033.9 (100.0%)			4,729.6 (19.7%)			2,167.6 (9.0%)			17,136.8 (71.3%)		
<b>Mean 10-year risk of CVD event</b>	8.9%			27.9%			14.0%			2.9%		
<b>Sex</b>												
Men	49.7	49.5	50.0	63.9	60.2	67.4	67.4	59.6	74.3	43.6	42.4	44.9
Women	50.3	49.9	50.6	36.1	32.6	39.8	32.6	25.7	40.4	56.4	55.1	57.7
<b>Age group</b>												
20 to 39	37.3	36.9	37.8	F	...	...	F	...	...	51.9	50.7	53.1
40 to 59	41.1	40.7	41.4	34.2	28.4	41.3	46.8	39.8	54.0	42.2	40.8	43.6
60 to 79	21.6	21.4	21.8	64.0	57.5	70.1	53.0	45.9	60.1	5.9	5.0	6.9
<b>Cholesterol - LDL-C†</b>												
Less than 2	13.7	11.6	16.1	20.5	16.6	24.9	4.3 <sup>E</sup>	2.5	7.2	13.0	10.5	16.1
2 to 3.5	56.4	53.1	59.6	45.6	40.2	51.1	45.3	38.5	52.3	60.8	57.2	64.2
3.5 to 5	26.7	24.3	29.2	25.4	19.7	31.9	45.0	37.7	52.5	24.7	22.2	27.4
More than 5	3.3	2.5	4.2	8.6 <sup>E</sup>	5.8	12.6	5.4 <sup>E</sup>	3.4	8.5	1.5 <sup>E</sup>	0.9	2.4
<b>TC/HDL-C</b>												
Less than 5.0	82.4	79.8	84.7	71.4	65.8	76.5	72.7	64.1	79.8	86.7	83.9	88.9
5.0 or more	17.6	15.3	20.2	28.6	23.5	34.2	27.4	20.2	35.9	13.4	11.0	16.1
Current smoker	21.8	19.1	24.7	23.6	17.8	30.5	27.7	21.9	34.3	20.6	17.5	23.9
Diabetes	6.5	5.3	8.0	30.7	24.9	37.2	F	...	...	0.7 <sup>E</sup>	0.0	1.3
<b>Mean systolic blood pressure (mm Hg)</b>	112.3	111.2	113.3	124.3	122.5	126.1	122.9	121.3	124.6	107.6	106.6	108.6
<b>Taking blood pressure drugs</b>	17.5	15.9	19.3	61.2	55.8	66.4	25.4	18.7	33.4	4.4	3.5	5.7
<b>Family history of premature CVD</b>												
Heart disease	18.2	15.8	20.8	25.1	21.4	29.1	22.4	17.4	28.5	15.8	13.0	18.9
Stroke	5.1	3.9	6.4	7.0 <sup>E</sup>	4.8	10.2	6.1 <sup>E</sup>	3.6	10.1	4.4	3.3	5.8

... not applicable

<sup>E</sup> use with caution

F too unreliable to be published

<sup>†</sup> adjusted to pretreatment levels for those treated with statins (Appendix B)

LDL-C = low-density lipoprotein cholesterol

TC/HDL-C = total cholesterol/high density lipoprotein cholesterol

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

All analyses were weighted using the CHMS combined cycle survey weights for the fasting subsample. The weighted sample represented the community-dwelling population aged 20 to 79.<sup>19</sup> To account for survey design effects, variance estimates were calculated using the bootstrap technique with 24 degrees of freedom, as appropriate for the CHMS. Analyses were conducted using SAS 9.1 and Stata 11.

## Results

### CVD risk profile of Canadians

For the population aged 20 to 79, the 10-year risk of a CVD event was 8.9% or approximately 2.1 million events over 10 years (about 210,000 each year) (Table 1). Around 20% of adults were classified as high-risk, 9% as intermediate-risk, and 71% as low-risk. The mean 10-year risk of a CVD event was 28% for high-risk, 14% for intermediate-risk, and 3% for low-risk adults.

### Current statin treatment

Almost 2.8 million Canadians aged 20 to 79 (12%) reported being treated with statin drugs during the period from 2007 to 2011 (Table 2). The mean 10-year CVD risk of those treated was 27%, which translates into an NNT of 15 over 10 years, or about 18,900 total CVD events avoided annually (188,700 in 10 years), assuming full adherence to statin therapy (Table 2). Approximately 2.1 million high-risk individuals with an average 10-year risk of 32% were treated with statins; this potentially avoided 17,000 CVD events annually (90% of all CVD events avoided). An estimated 323,600 intermediate-risk individuals with an average 10-year risk of 15% were treated with statins, potentially avoiding almost 2,000 CVD events annually. Around 360,000 low-risk individuals, whose average 10-year risk was 7%, were treated, potentially avoiding 600 CVD events annually. Of those

treated, 1.1 million (40%) had achieved recommended target lipid levels (data not shown).

### Guideline-recommended lipid screening and statin treatment

About 19 million 20- to 79-year-olds (79%) met the CCS recommendations for lipid testing and risk assessment (data not shown). Of those eligible for lipid testing, 6.5 million (27% of the total population) would be recommended for statin treatment (Table 2). The mean 10-year CVD risk of those recommended for treatment was 24%, which translates into an NNT of 17 over 10 years, or 38,600 CVD events avoided annually, assuming full adherence to statin therapy (Table 2).

Figure 2 compares current treatment levels with those recommended by the CCS guidelines, by risk group. Figure 3 compares total CVD events avoided, by risk group, for current treatment levels

Table 2

Prevalence of statin treatment, recommended statin treatment, risk of cardiovascular disease (CVD) events, number needed to treat (NNT) and CVD events avoided, by CVD risk category, household population aged 20 to 79, Canada excluding territories, 2007 to 2011

	CVD risk category															
	Total				High				Intermediate				Low			
	Number ('000)	% or number	95% confidence interval		Number ('000)	% or number	95% confidence interval		Number ('000)	% or number	95% confidence interval		Number ('000)	% or number	95% confidence interval	
<b>Total population</b>	24,033.9	100.0	...	...	4,729.6	19.7	17.9	21.6	2,167.6	9.0	7.6	10.7	17,136.0	71.3	69.5	73.1
Currently treated	2,785.5	11.6	9.9	13.5	2,101.9	44.4	38.8	50.3	323.6 <sup>E</sup>	14.9 <sup>E</sup>	9.7	22.3	360.0	2.1 <sup>E</sup>	1.5	2.9
Recommended <sup>†</sup> for treatment	6,518.2	27.1	25.3	29.1	4,729.6	100.0	...	...	1,467.2	67.7	60.8	73.9	321.4 <sup>E</sup>	1.9 <sup>E</sup>	1.2	2.9
<b>Mean 10-year risk (%) of CVD event</b>																
Currently treated	...	27.1	...	...	...	32.4	...	...	...	14.7	...	...	...	6.9	...	...
Recommended <sup>†</sup> for treatment	...	23.7	...	...	...	27.9	...	...	...	13.9	...	...	...	5.6	...	...
<b>NNT to prevent one CVD event over 10 years</b>																
Currently treated	...	15	...	...	...	12	...	...	...	27	...	...	...	58	...	...
Recommended <sup>†</sup> for treatment	...	17	...	...	...	14	...	...	...	31	...	...	...	71	...	...
<b>Total CVD events avoided over 10 years ('000)</b>																
Currently treated	...	188.7	159.5	217.9	...	170.3	139.6	200.9	...	11.9	6.5	17.2	...	6.2	4.1	8.3
Recommended <sup>†</sup> for treatment	...	386.2	357.7	414.7	...	329.9	298.7	361.1	...	50.9	40.5	61.4	...	4.5	2.6	6.4

... not applicable

<sup>E</sup> use with caution

<sup>†</sup> according to 2012 Canadian Cardiovascular Society guidelines

NNT = number needed to treat

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

versus total CVD events avoided under the CCS guidelines. In the high-risk group, 2.6 million more people would be treated with statins if the guidelines were fully implemented, potentially avoiding 16,000 more CVD events each year. Among intermediate-risk individuals,

treatment would be recommended for 1.1 million more, potentially avoiding 3,900 more CVD events annually. In the low-risk group, the numbers currently treated and recommended for treatment were similar (Table 2, Figure 2).

## Discussion

Using data from the largest population-based survey of physical measures since the 1992 Canadian Heart Health Survey,<sup>30</sup> this study reports the distribution of CVD risk and the current and potential health impact of statin treatment in Canada. The results reveal a gap between current and guideline-recommended treatment. About 1 in 10 people aged 20 to 79 were treated with statins—substantially fewer than the approximately 1 in 4 who, according to CCS guidelines, would be recommended for treatment. Specifically, these results show a gap in statin treatment among high- and intermediate-risk Canadians.

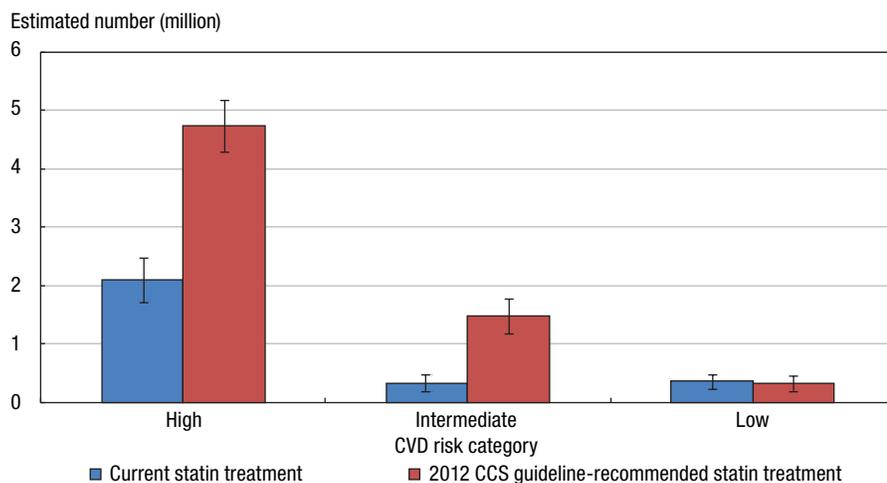
Most (90%) of the current population benefit of statins is attributable to high-risk individuals. Treatment of this group has more than twice the efficacy (measured by NNT) of treating the intermediate-risk group, and four times the efficacy of treating the low-risk group. The current study shows that, according to the CCS guidelines, almost 20% of 20- to 79-year-olds would be classified as high-risk, 9% as intermediate-risk, and 71% as low-risk of a CVD event.

The treatment gap for people at high and intermediate risk is consistent with previous studies. Evidence for both Canada and the United Kingdom suggests underuse of statins among the highest-risk individuals.<sup>31,32</sup> On the other hand, Van Staa et al.<sup>32</sup> reported overuse among low-risk individuals.

The moderate increase in the level of treatment of Canadians with dyslipidemia since the Canadian Heart Health Survey of the early 1990s<sup>33</sup> contrasts with dramatic improvements in the treatment and control of hypertension, largely owing to coordinated physician education efforts and public awareness.<sup>34</sup> The analyses in this study suggest a potential for gains in population health by targeting statin treatment toward high- and intermediate-risk groups.<sup>32</sup>

However, raising statin coverage to guideline-recommended levels has cost implications. Doubling the numbers treated would double the \$1.6 billion direct costs.<sup>6</sup> Recommendations to

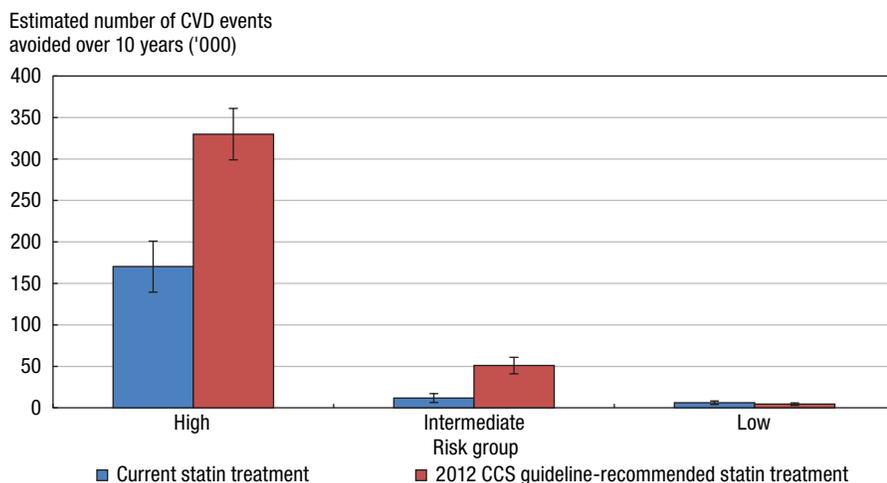
**Figure 2**  
**Number currently treated with statins and number who would be treated<sup>†</sup> according to 2012 Canadian Cardiovascular Society (CCS) Guidelines, by cardiovascular disease (CVD) risk category, household population aged 20 to 79, Canada excluding territories, 2007 to 2011**



<sup>†</sup> given complete (100%) adherence to guidelines  
 | 95% confidence interval

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

**Figure 3**  
**Number of cardiovascular disease (CVD) events avoided with current statin treatment and treatment recommended<sup>†</sup> in 2012 Canadian Cardiovascular Society (CCS) Guidelines, by CVD risk category, household population aged 20 to 79, Canada excluding territories, 2007 to 2011**



<sup>†</sup> given complete (100%) adherence to guidelines  
 | 95% confidence interval

Source: 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

increase statin eligibility in the U.S. and U.K. have triggered considerable controversy.<sup>7-11</sup> Under both sets of recommendations, the numbers eligible would rise substantially.<sup>11,35</sup> Concern has been expressed about the cost to indi-

viduals and the health care system of broader statin coverage, as well as about the medicalization of people who would be newly treated.<sup>10,11</sup> Critics in the U.K. have contended that increasing statin coverage would divert resources from primordial prevention.<sup>36</sup>

Compared with earlier versions, the 2012 guidelines classify more Canadians as high-risk (20%). Based on the 2009 guidelines, 13.7% of Canadians aged 20 to 79 would be high-risk,<sup>33</sup> an increase over the estimate based on the 2006 guidelines.<sup>37</sup> While the increase from the 2006 to 2009 versions likely resulted from updating the algorithm used to calculate baseline CVD risk,<sup>37</sup> the 2012 version broadened the definition of high-risk individuals.<sup>25</sup> It is difficult to determine whether the increase in baseline CVD risk reflects a true increase in CVD risk in the population, or whether the increase could be attributable to a poorly calibrated FRS or other measurement misclassification. The FRS may overestimate baseline risk,<sup>38,39</sup> a possibility supported by observed rates of Canadian CVD hospitalization and death below the rate estimated in this study using the Framingham Risk Score.<sup>40,41</sup> The trend toward classifying more people as “high-risk” may be appropriate for subpopulations such as those with renal disease, whose risk was updated in the CCS guidelines based on high-quality evidence,<sup>25</sup> but likely overestimates CVD risk in Canada overall. Validation and calibration of CVD risk-assessment tools specifically for the Canadian population are clearly warranted.

## Limitations

The results of this study should be considered in the context of a number of limitations. The CHMS data describe statin use in the 2007-to-2011 period, which predates the 2012 CCS guidelines. As well, although combined survey cycles were used, some estimates were un-reportable due to small sample sizes. Because the CHMS was designed to produce national estimates, it was not possible to examine CVD risk and statin

use by province or among at-risk ethnic groups like South Asians.<sup>19</sup>

The overall response rate to the CHMS was 53.5%; applying the survey weights ensured that the sample was representative of the target population, but bias might exist if non-respondents differed systematically from respondents.<sup>19</sup>

Some of the variables in this analysis were self-reported; therefore, the prevalence of characteristics such as family history of CVD was likely underestimated.

Another limitation is that the study reflects treatment within a month of survey administration; respondents who started or discontinued treatment shortly after sampling are not included. In addition, the CHMS captured a maximum of 15 prescription medications; therefore, in extreme cases of polypharmacy, statin use may be underestimated.

A small number of respondents used other cholesterol-lowering drugs like fenofibrate; this study did not examine the population health effects of such drugs. The analysis was based on the assumption that everyone for whom statins were recommended took them as prescribed. In addition, it was assumed that statins yield a constant absolute risk reduction of 25% over the entire population,<sup>1</sup> which may be an overestimate, as the percentage is based on data collected from clinical trials, not “real-world” observational studies.

Because the CHMS excludes people aged 80 or older and residents of institutions, estimates of CVD risk and statin use are lower than they would have been had these populations been included.

## Conclusion

This analysis provides a population health perspective on current and guideline-recommended statin use in Canada. A treatment gap appears to have emerged for people at intermediate and high risk of CVD, which, if fully addressed, could avert an estimated 19,500 CVD events each year. While some of the gap may reflect patient intolerance and/or reluctance to accept treatment, the size of

## What is already known on this subject?

- Statins—drugs that lower cholesterol—have been shown to improve survival and reduce the risk of cardiovascular disease (CVD) events.
- Statins are one of the most frequently prescribed classes of drugs in Canada, and constitute the leading drug cost in all provincial drug programs.
- Little evidence is available to assess the population health impact of the use of statins.

## What does this study add?

- With data from the 2007 to 2011 Canadian Health Measures Survey, this study describes the CVD risk profile of Canadians aged 20 to 79, compares current treatment patterns with guideline recommendations, and examines the population health impact of statin treatment.
- An estimated 2.8 million Canadian adults (about 1 in 10) were treated with statin drugs.
- Assuming optimal adherence, statin treatment was estimated to have avoided around 18,900 CVD events annually, with a number-needed-to-treat (average number of patients treated to prevent one additional CVD event) of 15 over 10 years.
- A treatment gap emerged for people at intermediate and high risk of CVD, which, if addressed, could avert an estimated 19,500 CVD events each year.

the gap (more than 50% in the high-risk group) is considerable. On the other hand, the results show that the CVD risk among Canadians has increased under

the current CCS guidelines; validation and calibration of the FRS for use in Canada are needed to assess the degree to which CVD risk is overestimated.

Increased statin coverage requires accurately measuring risks and weighing the costs, opportunity-costs, and benefits of statin therapy. ■

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## Appendix

**Table A**

**Mean 10-year risk of cardiovascular disease (CVD) event, accounting for positive family history of CVD, and number and percentage recommended for treatment, by CVD risk category, household population aged 20 to 79, Canada excluding territories, 2007 to 2011**

	CVD risk category											
	Total			High			Intermediate			Low		
	95% confidence interval			95% confidence interval			95% confidence interval			95% confidence interval		
	% or number	from	to									
<b>Mean 10-year risk of CVD event†</b>												
% of population aged 20 to 79	9.6	9.1	10.1	29.2	27.7	30.7	15.5	14.8	16.3	3.5	3.3	3.6
% of population recommended for treatment	24.4	23.3	25.6	29.2	27.7	30.7	16.1	15.1	17.1	10.5	9.7	11.4
<b>Recommended‡ for treatment†</b>												
Number ('000)	6,948.7	...	...	4,729.6	...	...	1,515.7	...	...	703.4 <sup>E</sup>	...	...
% of risk category	28.9	26.8	31.1	100.0	...	...	69.9	62.9	76.1	4.1 <sup>E</sup>	2.8	6.1

... not applicable

<sup>E</sup> use with caution

<sup>†</sup> using modified Framingham Risk Score

<sup>‡</sup> under 2012 Canadian Cardiovascular Society guidelines

**Source:** 2007 to 2009 and 2009 to 2011 Canadian Health Measures Survey, combined.

**Table B**

**Adjustment factors used to convert cholesterol values to pre-treatment levels**

Statin	Total cholesterol		Triglycerides	
	LDL	HDL	LDL	HDL
Atorvastatin (all doses)	+2.0	+1.8	-0.1	+0.3
Fluvastatin (all doses)	+1.6	+1.6	-0.1	+0.2
Lovastatin (all doses)	+1.2	+1.5	-0.1	+0.3
Pravastatin (all doses)	+1.3	+1.2	-0.1	+0.2
Rosuvastatin (all doses)	+2.2	+2.2	-0.1	+0.4
Simvastatin (all doses)	+1.6	+1.4	-0.1	+0.4

**Notes:** For respondents taking statin medications, total cholesterol, LDL and HDL cholesterol, and triglyceride levels were adjusted to pre-treatment levels based on the results of a meta-analysis<sup>29</sup> that collated the effects of various statins on blood lipids. For instance, for respondents taking Atorvastatin (any dose), 2 units were added to their total cholesterol.