Statin Use in Canadians: Trends, Determinants and Persistence

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ABSTRACT

Background: Regular statin use is an important tool in chronic disease management, lowering cholesterol levels and reducing risk of cardiovascular disease (CVD). The objectives of this study are to describe statin use in Canada by comorbidity and lifestyle risk factors, and determine persistence in statin use.

Methods: The longitudinal National Population Health Survey, 1994-2002, is a random sample of the 1994 Canadian population and five interviews were conducted at two-year intervals. A total of 8,198 respondents, aged 20 in 1994, completed all five interviews. Information collected included demographic variables, medication use, CVD lifestyle risk factors, CVD, diabetes and hypertension.

Results: Age-adjusted rates of statin use increased from 1.6% to 7.8% over the period 1994-2002. Statin use was higher with increasing age, diabetes, BMI, physician visits, and insurance for prescription medication. Although persons with CVD were more likely to take statins than those without, by 2002 still only 32.7% of heart patients were taking statins. Statin use did not increase linearly with increasing numbers of CVD risk factors or comorbidities. Of the 441 persons reporting statin use in 2000, 74.6% were still taking them in 2002. People who completed their high school education were more likely to continue taking statins than those who did not complete high school.

Conclusion: While statin use increased over time, was associated with CVD and diabetes, and to a lesser extent with increased BMI, a substantive underuse in high-risk patients remains. Helping high-risk people to increase statin use continues to be a priority for health care professionals.

MeSH terms: Statins; comorbidity; risk factors; trends; epidemiologic determinants; persistence

La traduction du résumé se trouve à la fin de l'article.

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Regular statin use is known to be effective in reducing cholesterol levels, which, in turn, reduces excess mortality associated with high LDL cholesterol,[1] decreases frequency of cardiovascular events,[2-4] and lowers mortality among seniors with newly diagnosed congestive heart failure.[5] Studies in the United States, Scotland and Scandinavia established statin therapy as a cost-effective therapy for patients at high risk of coronary artery disease with or without pre-existing diabetes or CVD.[1] Thus, cholesterol-lowering therapy is considered suitable both for primary prevention of CVD in high-risk patients and for secondary prevention after cardiovascular events have already occurred.[6-8] Although statin use has been increasing over the years, many still consider statins to be underused.[3,9-11] Our objectives then are to examine statin use in Canada by relevant risk factors and comorbidities, and to determine the extent to which persons continue taking statins for years.

METHODS

The longitudinal National Population Health Survey (NPHS) started with a randomly selected sample from the Canadian population for the 1994 cycle. Eventually, five interview cycles were accomplished at two-year intervals for the years 1994-2002. Over this time, 6.3% of the original sample died or were institutionalized, while 21.4% missed one or more of the interviews. As a result, 8,198 respondents, aged 20+ in 1994, completed all five interviews. Information obtained included demographic variables; CVD risk factors, such as height and weight, which was used to calculate body mass index (BMI); alcohol use; smoking; physical activity; and chronic diseases, including hypertension, heart diseases, diabetes.

Two questions dealt with medication use. The first was, "What is the exact name of the medication that you took [in the past two days]?"; the person was asked to spell the name as on the label of the container which was then coded using ATC coding.[12,13] A further question was asked about the use of drug groups in the last 30 days: "In the past month did you take any of the following medicine?" including heart medication, blood pressure medication, diuretics, insulin, pills to control diabetes. Heart medication, diabetes medica-

tion, and antihypertensive medication use consisted of affirmative answers to either one of these questions or both. Lipid-lowering medication (LLM) and statin use data were obtained only from exact drug use in the past two days before the interview. A question regarding insurance reimbursing prescription medication started in the 1996 cycle.

Statistical analysis used SAS version 8.2 (SAS Institute Inc., Cary, NC, USA) and consisted of frequencies and logistic regression models. Most of the results presented were weighted to represent the Canadian population. To estimate a meaningful measure of the variance, weights were scaled by dividing by sample size. Statistical significance is indicated by an asterisk. Age-standardization compensated for the aging of the population over the study period. The 1998 study population was used as standard population.

RESULTS

LLM use increased from 1.9% of Canadians in 1994 to 8.3% in 2002. This increase was entirely due to increasing statin use, while use of other LLM was low and decreased (Table I). While larger proportions of the elderly and the overweight took statins, no such increase was seen for smokers and the physically inactive (Table II). CVD, diabetic and hypertensive patients showed the greatest increases in statin use over the years. Among the provinces, Quebec showed greater and earlier statin use, followed by Ontario, while BC and Prairie residents showed the least statin use. The likelihood of statin use increased with age, number of general practitioner visits, and availability of insurance for prescription medication (Table III). Overweight and obese Canadians were more likely to be prescribed statins than those of 'normal' weight, however overweight (BMI 25-29.9 kg/m^2) respondents increased statin use earlier than the obese (BMI 30+ kg/m^2). The greatest predictors of statin use were age and existing heart disease in the earlier cycles, and age, heart disease and antihypertensive medication use in more recent years.

The interrelation between risk factors and comorbidity is shown only for the year 2002 (Table IV) but was similar to earlier cycles. Although persons with comorbidity were more likely to take statins than those without, no consistent linear relationship of statin use with comorbidity and/or CVD risk factors was seen. About 75% of statin users continue taking statin for at least two years once started (Table V).

TABLE I

Age-standardized Percentages of Canadian Population Using LLM by Cycle, Weighted for the Canadian Population

(Overall N=8198)	1994	1996	1998	2000	2002
All LLM	1.9	3.2	4.4	5.7	8.3
Statins	1.6	2.7	3.8	5.2	7.8
Other	1.3	0.5	0.6	0.5	0.5

LLM: lipid-lowering medication

TABLE II

Age-standardized Percentages of the Canadian Population Using Statins by Cycle, Weighted for the Canadian Population

		Percentage of Population Using Statins				
		1994	1996	1998	2000	2002
		%	%	%	%	%
(Overall N=8198)		1.6	2.7	3.8	5.2	7.8
Age (years)	<60	0.9	1.6	2.1	2.6	3.9
	≥60	3.4	5.8	8.4	12.3	18.4
Sex	Male	1.6	2.7	4.1	5.2	8.2
	Female	1.6	2.7	3.6	5.2	7.3
Education	<HS	1.4	2.9	4.2	6.5	7.4
	≥HS	1.7	2.8	3.9	4.9	8.3
BMI (kg/m^2)	<25.0	1.5	2.1	3.3	3.8	5.3
	25.0-29.9	1.7	3.7	4.5	6.2	9.0
	≥30.0	0.7	2.3	3.7	6.9	10.5
Alcohol use*	None/moderate	1.5	2.9	4.1	5.1	8.0
	Excess	1.7	2.8	3.7	6.0	7.8
Physical activity	More active	1.8	3.0	3.8	5.3	7.9
	Inactive	1.3	2.5	3.9	5.3	7.7
Current smoking status	None	1.5	2.8	3.9	5.3	7.7
	Smoker	1.7	2.3	3.5	4.1	7.5
GP visits	None	0.2	0.4	2.1	2.5	5.1
	1-3	1.5	2.7	3.1	4.0	6.5
	>3	2.6	4.3	6.0	8.0	10.6
Self-reported heart disease	No	1.1	2.1	2.9	4.1	6.1
	Yes	10.6	20.2	20.9	28.5	32.7
Heart medication	No	1.2	2.1	2.8	3.5	5.7
	Yes	7.8	16.6	21.7	33.3	32.8
Self-reported diabetes	No	1.6	2.6	3.7	4.7	6.8
	Yes	1.2	4.8	7.8	13.0	22.7
Diabetes medication	No	1.6	2.6	3.7	5.0	7.1
	Yes	2.7	6.1	10.5	11.8	31.5
Self-reported hypertension	No	1.3	2.1	3.1	3.8	5.5
	Yes	2.9	7.6	9.2	10.8	17.1
Antihypertensive medication	No	1.3	1.9	2.8	2.8	4.8
	Yes	3.4	10.6	12.2	14.7	24.7
Insurance for prescription	No	–	2.2	3.0	4.1	5.0
	Yes	–	3.1	4.1	5.6	8.4
Regions of Canada	Prairies	1.4	1.6	2.2	2.9	4.6
	BC	1.3	1.9	3.3	4.0	5.7
	Atlantic	0.7	2.0	3.8	5.2	6.8
	Ontario	1.4	2.9	3.8	6.0	9.0
	Quebec	2.4	3.9	5.3	6.1	9.4

* Excess alcohol use defined for males as ≥14 drinks per week, for females as ≥9 drinks per week

DISCUSSION

Statins are the most commonly used LLM in Canada, and were responsible for the increases in LLM use, as also found in other Canadian studies.[14] Increases in statin use were also found in the US, although one US study found that statin use levelled after 2000.[11] Over the years, individual statins waxed and waned, with atorvastatin (Lipitor) dominating the Canadian market by 2002.[14] The highest statin utilization was by known cardiovascular patients, followed by those with diabetes and hypertension patients. Statin therapy is known to cause a significant reduction in cardiovascular death and disability and has been shown to be highly cost effective for persons at high risk.[1] While there were increases in statin therapy in recent years, still less than half of the patients with cardiovascular disease or diabetes are using statins, despite guidelines recommending the therapy for them all.[15,16] Increased use of statins in these

TABLE III

Determinants of Statin Use by Cycle: Logistic Regression Models Adjusted for Age and Sex, Weighted for the Canadian Population

		Statin Use				
		1994	1996	1998	2000	2002
(Overall N=8198)		OR	OR	OR	OR	OR
Age (years)	<40	1.0	1.0	1.0	1.0	1.0
	40-59	12.3*	3.8*	4.2*	4.8*	5.6*
	≥60	31.3*	11.2*	12.0*	16.2*	16.5*
Sex	Female/male	1.1	1.0	0.9	1.0	0.8
Education	≥HS vs. <HS	1.2	0.9	0.9	0.7	1.2
BMI (kg/m^2)	<25.0	1.0	1.0	1.0	1.0	1.0
	25.0-29.9	1.4	2.2*	1.6*	2.0*	2.0*
	≥30.0	0.6	1.3	1.5	2.2*	2.6*
Alcohol use†	Excess vs. mod.	1.0	1.0	0.9	1.1	0.9
Physical activity	Less/more active	0.7	0.9	1.1	0.9	0.9
Current smoking	Yes/no	1.3	0.9	1.0	0.9	1.0
GP visits in past 12 months	≥3 vs. <3	2.6*	2.2*	2.4*	2.4*	1.9*
Self-reported heart disease	Yes/no	7.7*	7.5*	7.0*	6.2*	6.0*
Heart medication	Yes/no	5.4*	6.2*	7.2*	8.4*	6.1*
Self-reported diabetes	Yes/no	0.5	1.8	2.0	2.8*	3.3*
Diabetes medication	Yes/no	1.4	2.4	2.1	2.8*	3.3*
Self-reported hypertension	Yes/no	2.1	3.3*	2.8*	3.3*	3.5*
Antihypertensive medication	Yes/no	2.8*	4.9*	5.8*	6.7*	6.7*
Insurance for prescriptions	Yes/no	–	1.5	1.4	1.3	1.8*
Regions of Canada	Prairies	1.0	1.0	1.0	1.0	1.0
	BC	1.1	1.4	1.6	1.5	1.3
	Atlantic	0.6	1.5	2.1	2.1	1.6
	Ontario	1.1	2.3	2.1	2.4*	2.2*
	Quebec	1.6	3.0*	3.2*	2.6*	2.3*

* Statistically significant at p<0.05
† Excess alcohol use defined for males as ≥14 vs. <14 drinks/week, for females as ≥9 vs. <9 drinks/wk

TABLE IV

Percentage Statin Use in 2002 By Risk Factors and Comorbidity, Weighted for the Canadian Population

Comorbidity*	Number of Risk Factors†				
(N=8198)	0	1	2	≥3	All
	%	%	%	%	%
None	1.4	3.9	3.4	3.9	3.4
One	12.4	34.3	41.7	22.8	32.4
Two	15.4	18.4	14.9	11.9	15.6
Three	1.8	24.1	16.0	20.1	18.5

* Comorbidity includes CVD (heart diseases and strokes), diabetes, hypertension
† Risk factors include any of: current smoker, excess alcohol use (i.e., for males ≥14 drinks per week, for females ≥9 drinks per week), physically inactive, BMI>25.

cases would further reduce cardiovascular death and disability in high-risk Canadians.

The survey data used in this study have both strengths and limitations. NPHS strengths include its representativeness of the Canadian population, allowing conclusions to be drawn on behalf of the Canadian population. Considerable information is available on lifestyle risk factors, comorbidity and medication use, while repeated interviews on the same people allowed for the detection of changes. The NPHS also has limitations. The attrition was 21% over the five cycles, which appears sizable but works out to only about 6% per cycle. It is possible that loss to follow-up may have been selective for some attributes. Whether such selection would be more for a sample of the Canadian population than for the rest of the population is debatable. Further limitations were that chronic illnesses and drug use were self-reported, and that no information was available on the severity of the comorbid conditions. Of particular concern was the lack of measured cholesterol level, which is an important indication for statin use. However, while originally statins were thought to be effective only for patients with elevated cholesterol levels, statins are now indicated in nearly all patients with heart disease and diabetes.[17] Thus, risk factors and CVD comorbidity should be becoming more important as indications for statin use.

Persons with CVD risk factors such as increased age, excess weight and comorbidities were more likely to take statins than those without. Surprisingly, statin use for obese individuals increased at a slower rate than that for overweight people. This lack of an earlier increase for the obese has also been found elsewhere,[18] even though there seems to be no rational explanation for this finding. Even now, one would expect more than 10% of the obese to be taking statins because of their greatly increased risk for heart disease, diabetes and hypertension. The presence of CVD lifestyle risk factors, e.g., smoking, lack of physical activity, were not found to show an association with statin use in the present study and elsewhere.[19-22] Apparently, physicians are not using a quantitative cardiovascular risk assessment when prescribing statin therapy.[6,16] New Zealand scientists advocate treating people with antihypertensives and LLM based on their absolute cardiovascular risk profile.[23,24] This approach is also advocated in the Canadian lipid guidelines,[6] and implies more aggressive treatment for smokers, similar to persons with diabetes, or hypertension. It is becoming more accepted that people with heart disease and cholesterol level in the normal range will also benefit from taking statins.[17,25] While diabetics show an increase in statin use, their increase is lower than that of heart patients and hypertensives, in spite of the finding that persons with diabetes, even without CVD, have been shown to benefit as much from statin use as people with CVD but without diabetes.[26,27]

Once started, it is important to continue statin use as the benefits are related to consistent long-term reduction in LDL cholesterol.[15,28] Generally, a year after starting statin therapy, two thirds of people were still taking statins,[29-31] although some studies found lower proportions.[32] Persistence in statin use in the present study appears quite high at 74.6% after two years. This may be explained by the fact that even in the first interview, most respondents had been taking statins for months, and non-compliant patients were likely removed earlier. About 10% of first-time statin users are known not to refill their prescriptions after the first one.[29,33-35] A study using a survival curve found that after three years, the curve became nearly horizontal – there were few further non-compliant patients. In the present study, persistence in use was higher for people with high school education and for those with heart

disease. Increased use for high-risk people was also observed by other studies.[34,35] The finding that diabetics were not more persistent in statin use than non-diabetics is unfortunate since diabetics are at high risk of CVD problems. This lack of persistence could conceivably be related to the many medications many diabetics are already prescribed. Abughosh et al. found statin discontinuation rates to be higher for those with only partial drug coverage as compared to those with full coverage.[31] Our study also found a 5.7% increase in persistence with insurance coverage but this difference was not statistically significant. The difference between the studies may be at least partially due to differences in types of insurance coverage, since in Canada all seniors are covered for many prescription drugs. Statins, on the whole, are well tolerated,[36] and the increasing use and the high persistence rates attest to that. The high persistence rate might suggest that underuse in high-risk patients is related more to underprescribing by physicians than to underadherence by patients.

It is hard to gauge what proportion of the population should be taking statins. Using existing guidelines in the 1990s, it was found that 2-8% of the population would benefit depending on which guidelines were used.[37] More recently, the prevailing opinion on statin use has become less conservative, now even including high-risk persons with normal cholesterol levels.[7,17] Statin use has been suggested as an indicator of good medical care after an acute myocardial infarction (AMI).[38] However, not all persons with known hyperlipidemia are taking statins. A Canadian study found that while 5% of the elderly population (60+) had hyperlipidemia, less than 60% of these were taking statins.[39] Thus, in spite of guidelines, high-risk individuals remain untreated in Canada[40] and elsewhere. In the US, a study indicated that no more than 50% of people with hyperlipidemia received LLM.[41] In our study, cholesterol level was not available, but only a minority of those with heart disease and diabetes were treated, which highlighted the significant underuse of statins in Canada. Besides, even of those receiving statins, not all were likely to have achieved recommended cholesterol levels.[20] The various divergences from recommended statin usage identified in this study indicate a clear need for education programs for both the public and for health care professionals, to ensure that those at high risk of cardiovascular death and disability receive this cost-effective therapy to reduce their risk.

TABLE V

Persistence in Statin Use: Of Cycle 2000 Statin Takers, % Still Taking Statins in 2002

(N=441)		Persistence %	p
Overall		74.6	
Age (years)	<60	69.9	0.12
	≥60	76.7	
Sex	Male	73.5	0.66
	Female	75.4	
Education	<HS	69.9	0.03*
	HS+	79.2	
BMI (kg/m^2)	<25	70.9	0.19
	25-30	74.7	
	>30	78.6	
Smoking	No	76.0	0.08
	Yes	65.6	
GP visits	<3	71.3	0.98
	≥3	71.4	
Heart disease	No	72.7	0.20
	Yes	77.4	
Heart medication	No	70.7	0.02*
	Yes	80.3	
Diabetes	No	75.0	0.75
	Yes	73.1	
Diabetes medication	No	74.5	0.88
	Yes	75.4	
Hypertension	No	71.9	0.20
	Yes	77.0	
Antihypertensives	No	71.4	0.17
	Yes	77.1	
Insurance for Rx	No	70.1	0.28
	Yes	75.7	

* statistically significant at $p<0.05$.

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RÉSUMÉ

Contexte : La prise régulière de statine est un outil important dans le traitement des maladies chroniques et la réduction de la cholestérolémie et des risques de maladie cardiovasculaire (MCV). Nous avons voulu décrire l'utilisation des statines au Canada en fonction de deux facteurs (la comorbidité et le risque lié aux habitudes de vie) et déterminer la persistance dans la prise de statine.

Méthode : Cinq entretiens ont été menés tous les deux ans dans le cadre de l'Enquête nationale sur la santé de la population (1994–2002), une enquête longitudinale auprès d'un échantillon aléatoire de la population canadienne. En tout, 8 198 répondants âgés de 20 ans en 1994 se sont prêtés aux cinq entretiens. Les données recueillies englobaient des variables démographiques, la consommation de médicaments, les facteurs de risque de MCV liés aux habitudes de vie, les MCV, le diabète et l'hypertension artérielle.

Résultats : Les taux de prise de statine rajustés selon l'âge ont grimpé de 1,6 % à 7,8 % entre 1994 et 2002. La prise de statine s'élevait avec l'âge, le diabète, l'indice de masse corporelle (IMC), les visites chez le médecin et le fait d'avoir une assurance-médicaments. Les personnes ayant une MCV étaient plus susceptibles de prendre des statines que les personnes qui n'en avaient pas, mais en 2002, les cardiaques qui prenaient des statines n'étaient encore que 32,7 %. La prise de statine n'a pas augmenté de façon linéaire avec les facteurs de risque de MCV ou les comorbidités. Sur les 441 personnes qui prenaient des statines en 2000, 74,6 % en prenaient encore en 2002. Les diplômés du secondaire étaient plus susceptibles d'avoir continué à prendre des statines que les non-diplômés.

Conclusion : La prise de statine a augmenté au fil du temps, et elle était associée à l'augmentation des MCV, du diabète et, dans une moindre mesure, de l'IMC, mais les patients à risque élevé sous-utilisaient encore beaucoup ce médicament. Aider les personnes à risque élevé à accroître leur prise de statine demeure donc une priorité pour les professionnels de la santé.