



Original Article

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Statin Initiation: Guideline Concordance and Characteristics of New Users in Quebec, Canada

Sarasa M.A. Johnson^{1,2}, Manon Choinière^{1,3}, Michèle Bally¹, Marie-Pierre Dubé^{3,4}, Jean-Claude Tardif⁴, Daniel Gaudet^{5,6}, Jean Bergeron⁷, Hélène Lanctôt¹, Jacques Lelorier^{1,2,3,*}

¹Centre de Recherche du Centre Hospitalier de l'Université de Montréal (CRCHUM), Montreal, Canada

²Canadian Network of Observational Drug Effect Studies, Montreal, Canada

³Department of Medicine, Faculty of Medicine, Université de Montréal, Montreal, Canada

⁴Montreal Heart Institute, Université de Montréal, Montreal, Canada

⁵Clinical Lipidology Unit, Université de Montréal Community Genomic Medicine Center, Chicoutimi, Quebec, Canada

⁶Department of Medicine, Université de Montréal and ECOGENE-21, Chicoutimi, Quebec, Canada

⁷Centre de Recherche du CHU de Québec – Université Laval, Quebec, Canada

Corresponding author: Jacques Lelorier, MD, PhD, FRCP(C), FISPE, Centre de Recherche du Centre Hospitalier de l'Université de Montréal, Office S03.2918, 850, rue Saint-Denis, Montréal (Québec) H2X 0A9, Canada. Tel: 514-890-8000, ext. 12918. Email: jacques.le.lorier@umontreal.ca

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ABSTRACT

Statins are widely prescribed for the prevention of cardiovascular (CV) events. Our objective was to describe the characteristics of patients newly prescribed a statin by general practitioners and assess the concordance of prescribing with national guidelines. Patients who were 18 years or older, French-speaking, available for the 2-year study duration, and had no history of statin use were recruited. Biological parameters were measured, and medical history, sociodemographic characteristics, and health behaviours were recorded using structured questionnaires. Patients' eligibility for a statin was assessed using the Canadian Cardiovascular

Society's dyslipidemia guidelines. Of the 1631 new statin-users enrolled, 47.6% were women. The mean age for all patients was 57.4 years. According to the Canadian guidelines, 50.6% of patients were considered at high risk for a CV event or had a statin-indicated condition. Moderate and low-risk patients represented 26.7 and 22.7% of patients, respectively.

Keywords: *guideline adherence; HMG-CoA reductase inhibitors; prospective cohort; statins*

INTRODUCTION

Cardiovascular (CV) diseases are responsible for almost one-third of Canadian deaths.¹ A decrease in mortality from recurrent events has been observed and is attributed to better control of CV risk factors such as smoking, cholesterol, and hypertension.² In 2016, the Canadian Cardiovascular Society (CCS) updated its guidelines and published detailed flow charts to guide physicians on the selection of patients who should be screened and eventually treated for their dyslipidemia.³ These last recommendations broadened the scope of who is recommended for screening, including lowering the recommended age for women to begin screening from ≥ 50 years to ≥ 40 years; on par with men. For the first time, the updated guidelines also explicitly distinguished between individuals regarded as at high risk of a CV event (Framingham Risk Score (FRS) $\geq 20\%$) and those with a "statin-indicated" condition.

Despite the presence of multiple guidelines and recommendations, there remains concern that statins are not being prescribed to those who could benefit most.^{4,5} It is therefore imperative to gain a better understanding of who is being initiated on statin therapy. Previous observational studies have attempted to describe new statin user populations and assess guideline concordance using large administrative health databases or surveys.⁴⁻⁸ However, few were able to determine if patients were truly first-time statin users, and often lacked information on important CV risk factors like family history, lifestyle behaviours, and patients' perspectives on the importance of lowering their blood cholesterol levels.

Given the preponderant role of statin therapy, in the prevention of atherosclerosis, and the fact that these drugs are mostly prescribed by general practitioners, we considered it of interest to constitute a prospective cohort of patients newly started on these drugs in Quebec, Canada – the OBServationSTATin cohort (OBSTAT). The objective of this study was to describe the characteristics of patients receiving a statin prescription for the first time and to assess the appropriateness of statin initiation using both historical and current Canadian guidelines.

METHODS

Study population

From 2008 to 2011, we approached physicians practicing within 2 h driving-time of Montreal, Quebec City, or Chicoutimi in Quebec, Canada. Most of these physicians had either participated in a previous study or were part of the large clinical research network of the University of Montreal.⁹ Physicians were asked to propose participation in our study to every patient they were initiating on statin therapy for the first time in the patient's life. Cardiologists associated with the Montreal Heart Institute and pharmacists who filled the initial statin prescription were also invited to participate.

To be eligible for participation in this study, patients had to be older than 18 years of age, able to understand French, and available for the 2-year study duration. We excluded patients who had taken a statin in the past or who were already participating in a study of lipid-modifying therapy.

Procedure and measures

A signed consent form was obtained from all referrers. The patients they referred also signed forms agreeing to receive a call from our team. Patients were advised to delay the initiation of the statin until after they had been contacted by our research nurse (<7 days). Then the nurse explained the nature of the study and verified their eligibility. If the patient agreed, then an initial appointment was set up in her office or the patient's home.

During the initial visit, the research nurse invited the patient to sign a second, more detailed informed consent form. A blood sample was taken and biological parameters such as waist circumference were measured. An interview (of 30–45 min) was conducted and a corresponding questionnaire was filled out. Data were collected for the following variables: demographic information, personal and familial medical histories, current and past medication use, and history of medication side effects. Details on the context of the statin prescription were also obtained including if the previous action was taken to reduce cholesterol.

The appropriateness of statin initiation was assessed using the 2009 and 2016 Canadian Guidelines for the Management of Dyslipidemia and Prevention of Cardiovascular Disease.^{2,3} At the time of data collection, only the 2009 CCS guidelines were available; the 2016 CCS guidelines were published after data collection was completed. Therefore, we assessed the appropriateness of statin initiation using both the current and then prevailing guidelines.^{2,3}

Statistical analysis

Descriptive statistics were used to summarize the characteristics of patients in the cohort and to categorize their CV risk. All data analysis was conducted using SAS V9.4 software.

The study was initially approved by the ethics committee of the Montreal Heart Institute on September 28, 2007 (project #07-970). Ethical approval was subsequently received from the review boards of all participating institutions.

RESULTS

We contacted 666 health practitioners (nurses, pharmacists, and physicians), of which 639 accepted our invitation to participate in this study. Through these health practitioners, 2180 patients were referred and 1631 eligible new statin-users were enrolled. The majority of participants were referred from clinicians in the city of Montreal and surrounding areas (65.1%), with 32.0% recruited from Chicoutimi, and the remaining 2.9% from Quebec City. The majority of patients initiated on a statin were first prescribed rosuvastatin (66.7%) or atorvastatin (31.3%). Patients were much more likely to be started on a high dose versus a low dose of statins (65.2% vs 34.8%, respectively). Table 1 displays the source of patient referrals and the specialty of the statin-prescribing physician. As expected from our source populations, general practitioners constituted

TABLE 1. The Specialty of Referrers and Statin Prescribers (n = 1631).

Specialty	N	%
Referrers*		
Generalist	1111	69.1
Specialist	51	3.2
Pharmacist	445	27.3
Nurse	24	1.5
Prescribers†		
Generalist	1544	94.7
Specialists		
Biochemistry	2	0.1
Cardiology	22	1.3
Endocrinology	14	0.9
Internal medicine	30	1.8
Nephrology	1	0.1
Neurology	8	0.5
Rheumatology	10	0.6

*Referrers indicate the type of health practitioner who referred the patient to our study.

†Prescribers are the physicians who initiated the patient on statin therapy.

the majority of statin prescribers (94.7%), with a minority of patients prescribed statins by specialists including cardiologists (1.3%) and internists (1.8%).

Characteristics of patients at the time of statin initiation are presented in Table 2. Of those enrolled, 47.6% were women and the mean age for all patients was 57.4 years. A total of 29.9% of new statin-users had an FRS greater than 20%.

Table 3 shows patients' risk levels according to the 2016 CCS guidelines, and how prevalent criteria

TABLE 2. Characteristics of Patients at Baseline (n = 1631).

Characteristic	% or mean (SD)
Age	57.4 (10.8)
Female	47.6
<i>Biological parameters</i>	
Total cholesterol (mmol/L)	5.9 (1.0)
LDL-cholesterol (mmol/L)	3.7 (0.9)
HDL-cholesterol (mmol/L)	1.3 (0.4)
Total cholesterol/HDL ratio	5.0 (1.7)
HbA1c (%)	5.8 (0.8)
<i>BMI</i>	
Underweight: BMI < 18.5	0.5
Normal: BMI = 18.5–24.9	25.2
Pre-obese: BMI = 25.0–29.9	44.0
Obese: BMI ≥ 30.0	30.4
Central obesity*	57.8
<i>Medical history</i>	
Current smoker	21.2
Hypertension	42.8
Diabetes	12.8
History of stroke	2.8
Congestive heart failure	0.5
History of myocardial infarction	0.9
Peripheral vascular disease	2.7
CABG or PTCA	0.7
Valvular disease	1.0
Angina	2.4

TABLE 2. Characteristics of Patients at Baseline (n = 1631).(Continued)

Characteristic	% or mean (SD)
Family history of CV risk [†]	91.1
Family history of CV disease [†]	47.2
<i>Framingham Risk Score</i>	
FRS > 20%	29.9
FRS = 10–20%	40.6
FRS < 10%	29.5
Number of drugs per day	3.5 (2.9)
<i>Context of statin initiation</i>	
Taken prior actions to reduce cholesterol	49.5
Understood their treatment	91.5
Perceived cholesterol reduction as important	98.3
Informed about potential adverse effects of statins by MD	56.9
<i>Sociodemographic characteristics</i>	
Education (years)	12.8 (3.6)
White ethnicity	97.9
Urbanity	86.6
Living at home	98.1
Living alone	17.8
Married/Free union	73.4
Employed/Student	54.5
Private insurance coverage [‡]	58.7
<i>Family income category</i>	
<\$30,000	15.2
\$30,000 – \$59,999	25.5
\$60,000 – \$99,999	23.0
>\$100,000	17.4
Did not want to answer	19.0

BMI: body mass index; CABG: coronary artery bypass graft; CV: cardiovascular; FRS: Framingham Risk Score; HDL: high-density lipoprotein; LDL: low-density lipoprotein; PTCA: percutaneous transluminal coronary angioplasty.

*Women: waist circumference ≥ 88 cm; men: waist circumference ≥ 102 cm.

[†]First degree relatives.

[‡]The remaining 41.3% were covered by the provincial health insurance plan.

TABLE 3. Cardiovascular Risk Level Categorization of Patients and Prevalence of Criteria Using the 2016 CCS Guidelines (n = 1631).

Criteria*	Sub-criteria	n [†]	% of n in that risk level
Statin-indicated condition – n = 374 (22.9%)			
Clinical atherosclerosis		136	36.4
Diabetes‡	Age ≥40 years	181	48.4
	Age ≥30 years and type 1 and duration ≥15 years	0	0.0
LDL-C ≥5 mmol/L		87	23.3
High risk – n = 451 (27.7%)			
FRS ≥20%		451	100.0
Intermediate risk – n = 435 (26.7%)			
LDL-C ≥ 3.5 mmol/L		268	61.6
Non-HDL-C ≥ 4.3 mmol/L		304	69.9
Male 50+	Low HDL (<1 mmol/L)	26	6.0
	High waist circumference (>102 cm)	48	11.0
	Smoker	39	9.0
	Hypertension	45	10.3
Female 60+	Low HDL (<1 mmol/L)	10	2.3
	High waist circumference (>88 cm)	109	25.1
	Smoker	80	18.4
	Hypertension	88	20.2
FRS 10 < 20%		131	30.1
Low risk – n = 371 (22.7%)			
FRS <10%		371	100.0

CCS: Canadian Cardiovascular Society; FRS: Framingham Risk Score; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

*We did not have data on the following criteria: abdominal aortic aneurysm, chronic kidney disease, Apo B > 1.2 g/L.

†People can be counted more than once if they meet multiple criteria but are included only in one risk level.

‡We did not have data on the sub-criteria: microvascular disease.

were in each group. Based on these guidelines, 27.7% of patients were considered to be at high risk for a CV event and 22.9% had a statin-indicated condition. Table 4 presents the risk categorization of patients using both the 2009 and 2016 CCS guidelines. Results were similar using both sets of guidelines, with 75.6 and 77.3% of patients considered eligible for statin therapy based on the 2009 and 2016 guidelines, respectively.

DISCUSSION

Statins are the most prescribed class of medications in Canada.¹⁰ Therefore, understanding who is receiving treatment and how concordant prescribing practices are with guideline recommendations is an important public health issue. We found that the majority of patients started on statin therapy in the OBSTAT cohort had been initiated on treatment for primary prevention (77%). The remainder of

TABLE 4. Cardiovascular Risk Level Categorization Based on then Prevailing and Current Canadian Dyslipidemia Guidelines (n = 1631).

Risk level	CCS 2009 n (%)	CCS 2016 n (%)
High risk or statin-indicated condition <i>Recommendation: Include statins in lipid management</i>	755 (46.4)	825 (50.6)
Intermediate risk <i>Recommendation: Include statins in lipid management</i>	476 (29.2)	435 (26.7)
Low risk <i>Recommendation: Do not include statins in lipid management</i>	400 (24.5)	371 (22.7)

CCS: Canadian Cardiovascular Society.

patients had been started on treatment for secondary prevention (8%) or other statin-indicated conditions (15%). Our results show that based on both the 2009 and 2016 CCS guidelines,^{2,3} more than three-quarters of patients initiated on a statin were considered to be at moderate or high risk of having a CV event, or had a statin-indicated condition, suggesting that statin initiation was reasonably appropriate in this population.

We also found that almost all patients said they understood their treatment, and perceived cholesterol reduction as important. However, only around half of the patients said they had previously taken actions to lower their cholesterol, including most of those at low risk. This is problematic considering that both the 2009 and 2016 guidelines recommend modifications to health behaviours as the only course of action for those at low risk. Additionally, the 2009 CCS guidelines, which were available to clinicians at the time, suggest that lifestyle changes be attempted before statin therapy for individuals considered at intermediate risk.^{2,3}

Although the majority of statin initiations in our study were in line with guideline recommendations, it is also important to address that more than 20% of patients considered to be at low risk

of a CV event were inappropriately started on statin therapy. The general trend of statins being overused amongst those at low risk is an ongoing concern in Canada and is common in other countries as well.^{4,11,12} This observation could be due to a general increase in optimism for the potential clinical benefit of statins over time. However, a survey of Canadian primary care physicians suggests that gaps in knowledge regarding traditional and emerging CV risk assessment tools could also play a significant role.¹³

In comparison to a previous Canadian study of guideline concordance, we found a smaller proportion of statin users considered to be at high risk of a CV event.⁹ However, our findings show slightly higher levels of guideline-concordant prescribing compared to UK studies that looked at the appropriateness of statin prescribing during the same time frame.^{4,5} A concurrent US study showed an even higher proportion of patients appropriately initiated on a statin, with only 20% of patients not being considered eligible based on the predominant American guidelines.⁶ However, a direct comparison of the appropriateness of prescribing is challenging, considering variations in source population across studies; especially, with the prevalence of existing CV disease.

Another important consideration in comparing guideline adherence is the variation in criteria themselves. When comparing concordance with the 2009 and 2016 CCS guidelines, we found that slightly more patients were considered to be at high risk or have a statin-indicated condition based on the newer guidelines.^{2,3} In addition, studies that have directly compared the most recent CCS guidelines to other major international guidelines, found that the Canadian guidelines tend to categorize more patients as high risk and eligible for statin therapy.^{7,14}

Strengths and limitations

Our study has several strengths; the first being the wide scope of the questionnaire which collected

diverse health information pertinent to statin initiation that is not usually available in these types of studies. The second is the high response rate from practitioners who were approached to participate in this study. High response rates from patients eligible for entry to the study were also observed, as well as excellent compliance from patients with a lengthy questionnaire, blood sampling, and biological measurements.

However, the study has several limitations. Firstly, data collection for this study was completed in 2011, and prescribing practices in Quebec may have changed since this time; though this is unlikely. Secondly, the data we collected did not include some of the new criteria contained in the 2016 CCS guidelines to determine statin eligibility including Apo B, history of abdominal aortic aneurysm, history of chronic kidney disease, and some sub-criteria for those with diabetes. This may have affected our final risk categorization, most likely resulting in an underestimation of individuals considered to have a statin-indicated condition. Thirdly, as the physicians approached to participate in this study were identified through their participation in a previous research study, they are not necessarily representative of all general practitioners in Quebec. Additionally, our cohort consisted almost entirely of white patients, and therefore more research is needed on the appropriateness of statin prescribing in ethnic minorities; especially, given the elevated CV risk in some of these groups.¹⁵ However, the fact that we followed patients living in both urban and rural settings and have a wide range of family incomes represented, suggests that the cohort is relatively generalizable. Finally, though previous Canadian studies have reported on the underuse of statins amongst high-risk individuals,^{11,12} our study design only enabled us to capture data on statin overuse, and not statin underuse in this population.

Recommendations

As the vast majority of patients in our study were prescribed a statin by a general practitioner,

increasing awareness about the risk-reduction potential of statins in high-risk patients and lack of benefit of statins amongst low-risk individuals could help ensure more targeted prescribing. This, along with the promotion of risk calculations, such as the FRS or Cardiovascular Life Expectancy Model would help practitioners to distinguish low-risk patients; and therefore, could aid in reducing the overuse of statins in this group.

CONCLUSIONS

By prospectively following new statin patients and collecting information, not usually available in these types of studies, our study was able to provide insight into the characteristics of patients being initiated on statin treatment in a Canadian context. Our assessment also showed that statin initiation was relatively concordant with national guidelines; however, the overprescribing of statins to those at low risk of CV events remains a concern. Future research should be done to explore the reasons behind this continued overprescription of statins, and to evaluate strategies for improving targeted prescribing.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare in relation to this article.

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