Eur J Clin Pharmacol (2005) 61: 667–674
DOI 10.1007/s00228-005-0980-z

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

**Sylvie Perreault · Lucie Blais · Alice Dragomir
Marie-Hèlène Bouchard · Lyne Lalonde
Claudine Laurier · Johanne Collin**

Persistence and determinants of statin therapy among middle-aged patients free of cardiovascular disease

Received: 20 December 2004 / Accepted: 12 May 2005 / Published online: 8 September 2005

Abstract *Aim*: Statins have been shown to significantly reduce morbidity and mortality both in patients with coronary artery disease and in those with dyslipidemia when they are taken regularly. Middle-aged patients have the highest level of forecasting benefit, and little is known about the persistence rate of these therapies in a real-life setting. *Objective*: To evaluate the persistence rate of middle-aged patients initiating statin therapy as well as its relation to patients' demographic and clinical characteristics. *Methods*: A cohort of 25,733 patients was reconstructed from prescription data recorded in the Régie de l'assurance maladie du Québec administrative database. All patients aged 50–64 years old who received at least one statin prescription between January 1, 1998 and December 31, 2000 for a new intention of treatment for dyslipidemia were included in the cohort and followed up until June 30, 2001. The date of the first prescription of statin was defined as the index date. The cumulative persistence rate was estimated using a Kaplan-Meier analysis. Cox regression models were used to estimate the rate ratio of ceasing statins after adjustment. *Results*: Mean age of patients initiating statin agents was 58 years; 39%were male, 24% received social assistance, 19% had diabetes, 30% had hypertension and 11% had a respiratory disease at cohort entry. Persistence with statin therapy fell to 67% in the first 6 months after treatment and continued to decline over the next 3 years to 39%. At 3 years, persistence varied significantly with statin agents. After controlling for individual patients' demographic and clinical characteristics, we found that patients who were prescribed fluvastatin, lovastatin and atorvastatin had a higher rate of cessation than those on simvastatin and pravastatin. The adjusted rate ratio of ceasing statin agents in patients with other risk factors of cardiovascular disease, such as diabetes (HR: 0.78; 0.75–0.82) or hypertension (HR: 0.72; 0.69–0.74), demonstrated a lower cessation rate. We observed lower persistence in patients who used the greatest number of pharmacies and prescribing physicians. *Conclusion*: This analysis indicates that barriers to persistence occur early in the therapeutic course. Overall persistence with statins is low, particularly among patients with few other cardiovascular risk factors.

S. Perreault (✉) · L. Blais · A. Dragomir · M.-H. Bouchard
L. Lalonde · C. Laurier · J. Collin
Faculty of Pharmacy, University of Montreal, P.O. Box 6128,
Centre-Ville Station, Montreal, Quebec, Canada, H3C 3J7
E-mail: sylvie.perreault@umontreal.ca
Tel.: +1-514-3436111
Fax: +1-514-3432102

Introduction

Cardiovascular disease remains the leading cause of death in North America. It has been shown that the treatment of dyslipidemia with statins significantly reduces morbidity and mortality among patients with coronary artery disease or hyperlipidemia, particularly among middle-aged patients [1–5]. Based on clinical trials, the benefits of using statins start to appear only after 1–2 years of regular use, and they need to be taken on long-term basis [1–5]. Findings from new trials in a landmark study involving 20,556 patients having a high risk of coronary artery disease showed that simvastatin decreased the death rate and reduced the rate of all cardiovascular event endpoints [6]. The Anglo-Scandinavian Cardiac Outcomes Trial investigators compared the effects of atorvastatin and a placebo on the combined outcome of non-fatal myocardial infarction and fatal coronary artery disease in hypertensive patients with a total cholesterol level of less than 6.5 mmol/l. The results of their study provide strong support for statin therapy in patients at high risk for the primary prevention [7]. Thus, for both primary and secondary prevention, statins are intended for long-term use to achieve their full benefit. Clinical guidelines consequently highlight the need to assess and promote compliance with prescribed treatment for dyslipidemia [8].

Gaps exist between recommendations and actual practice, for prevention as well as treatment. According to the literature, the rate of persistence of lipid-lowering drugs after 3 years is approximately 50% or less [9–15]. These studies were conducted mostly in elderly patients, and little is known about long-term persistence with these therapies and its determinants among middle-aged patients. The targeting of persistence-enhancing interventions that will provide the most leverage and potential benefit will require knowledge of when discontinuation is the most likely option and which patient subgroups are at the highest risk.

The aim of our study was to evaluate the persistence rate among middle-aged patients initiating a new treatment with statin agents for primary prevention and to study its relation with age, gender, other cardiovascular risk factors, co-morbidity and the use of health-care services.

Methods

Sources of data

This population-based study used the Régie de l'assurance maladie du Québec (RAMQ) databases. RAMQ is the organization administering public health-care insurance programs in the province of Quebec, Canada. RAMQ databases contain three types of files. The first type is the demographic file, which lists age, gender, postal code and year of death for all individuals registered and having a RAMQ card. The second type is the medical services file, which includes claims for all inpatient or ambulatory medical services, with such data as the nature of the medical act, date, the site where the act was provided (office, emergency, hospital) and the diagnostic code [16]. Diagnosis is coded according to ICD-9 classification, and the codes for surgical procedures are assigned according to the Canadian classification of diagnostic, therapeutic and surgical procedures [17]. These two RAMQ files pertain to residents covered by the provincial health-care insurance, which includes the whole population.

The third file is the pharmaceutical file, which contains data on all prescriptions for health-care covered drugs delivered to patients living in the community and insured by RAMQ for their medications. This file includes the name of the drug, strength, quantity, date and duration of therapy, as indicated by the pharmacist, and it pertains to residents covered by the public drug plan, namely individuals aged 65 years and older, welfare recipients and residents who do not have access to collective private drug plans. This represents about 55% of the total population of Quebec [18]. Each of the computerized files contains the individual's health insurance number, which acts as a link between files. The pharmaceutical file has been validated for research and has been used previously for pharmacoepidemiologic research studies [19, 20].

Cohort definition

An initial cohort of 65,270 patients was identified from prescription records. To be included in the cohort, subjects had to be newly treated for dyslipidemia, which was defined as having had no statin agents or other lipid-lowering drugs prescribed in the year prior to cohort entry and having had to start a new treatment for either atorvastatin, fluvastatin, lovastatin, pravastatin or simvastatin in the period from January 1, 1998 and December 31, 2000. The date of the first prescription of these agents was defined as the index date. Additional criteria for inclusion in the cohort were that subjects had to be insured by the provincial plan prior to the index date and be between 50 and 64 years of age at the time of inclusion.

Subjects had to be free of cardiovascular disease (primary prevention), as evidenced by the absence of a diagnosis or of medical procedures or drug markers for coronary artery disease in the year prior to the index date. Coronary artery disease was defined as myocardial infarction or angina (ICD-9 codes 410–414) or coronary artery bypass graft, angioplasty, stent or the use of any nitrate, including nitroglycerine; stroke (430–438); peripheral cardiac disease (440–447); congestive heart failure (428–428) or the use of these therapeutic combinations [furosemide alone or with: (1) digoxin, (2) ACE inhibitors (captopril or enalapril) or (3) β-blocker or carvedilol]; arrhythmia (427–427) or the use of drugs for cardiac arrhythmias (amiodarone, digoxin, quinidine, disopyramide, flecainamide, mexiletine, procainamide, propafenone or sotalol). The RAMQ Drug Database was also used to exclude patients who received other drugs, such as antiplatelet drugs or a low dose of acetylsalicylic acid (ASA) or anticoagulants, in the year preceding the index date.

The cohort ultimately consisted of 25,733 patients considered as being newly treated for dyslipidemia with statin agents in the period from January 1, 1998 to December 31, 2000. The date of the first prescription of these agents was defined as the index date. Subjects were followed until June 30, 2001, death, the occurrence of a diagnosis of cardiovascular disease or medical procedures or cardiac symptoms or loss of coverage under the drug plan.

Drug exposure and assessment of persistence

The drug database was searched for any statin agents dispensed to eligible subjects during the study period. In order to reconstruct the drug regimens, we developed a computer program that used data on the dispensing date, amount dispensed and duration of treatment. We identified patients who had begun a treatment with a single statin agent (monotherapy) and stratified them according to statin agent used: atorvastatin, fluvastatin, lovastatin, pravastatin or simvastatin.

The primary outcome of persistence was defined as having any statin prescription dispensed at least every 60 days after the end date of a previous prescription for statin as a class. We chose this 60-day grace period because the current package size and refill practice in Canada are 30-day pack size refill every month. This allowed the assessment of persistence to a therapy with any statin agent. For instance, a subject switching from one statin to another without interruption was considered to be persistent with non-exclusive use. We examined the effect of this 60-day grace period by measuring the impact on the persistence estimate using 45 days or 120 days for the grace period.

We also estimated the assessment of persistence with a given statin (exclusive use); in this case, a subject was considered to be non-persistent if he/she had not acquired a prescription for this statin within 60 days of the end of the prescription duration. We measured the proportion of continuation of the initial therapy prescribed, the proportion of at least one switch but still persistent or those who stopped therapy entirely during the first year following the initiation.

Determinants

The variables considered as potential determinants of treatment non-persistence included age, gender, social assistance status, site of residency, specific co-morbidities (diabetes mellitus, hypertension and respiratory disease), use of antidepressive or anxiolytic agents [21, 22], number of different classes of drugs, number of total doses of medication per day and utilization of health-care services [22]. Age (in years), gender (male or female), social assistance (yes or no) and site of residency (rural or urban) were identified at the index date from data in the beneficiary's file.

Co-morbidities were defined as follows: diabetes by ICD-9 code 250 or by the use of insulin or hypoglycemic agents; hypertension by essential hypertension ICD-9 code 401 or by the use of thiazides, angiotensin-converting enzyme inhibitors without furosemide, calcium channel blockers or β-blockers without any other markers of coronary heart disease; respiratory disease by the use of at least two prescriptions of inhaled β-agonists or any pharmacologic agents used for respiratory disease; depression and anxiety by the use of antidepressive or anxiolytic agents [23]. These were assessed in the year prior to the index date and during the follow-up period.

The mean number of different types of classes of drugs per month (defined by the American Hospital Formulary classes) and the mean number of daily doses of medication were assessed using the prescription data files in the year preceding the index date and during the follow-up period. Health-care service utilization was measured by computing the number of prescribing physicians, of dispensing pharmacies consulted, of medical visits, and of hospitalizations during the year preceding the index date and the follow-up period.

Statistical analysis

The cumulative persistence rate was estimated using the Kaplan-Meier analysis [24]. Cox regression models with time-dependent covariables (co-morbidities and health-care services) were constructed to estimate the rate ratio of non-persistence to statin agents for a maximum follow-up period of 3 years. All models were adjusted for potential determinants described previously.

The analyses of the exclusive use for a statin agent were measured as the proportion of subjects who continued the initial therapy prescribed, the proportion of those who had at least one switch but were still persistent and the proportion of those who stopped therapy entirely during the first year following the initiation. All subjects included in the exclusive use analysis of a statin

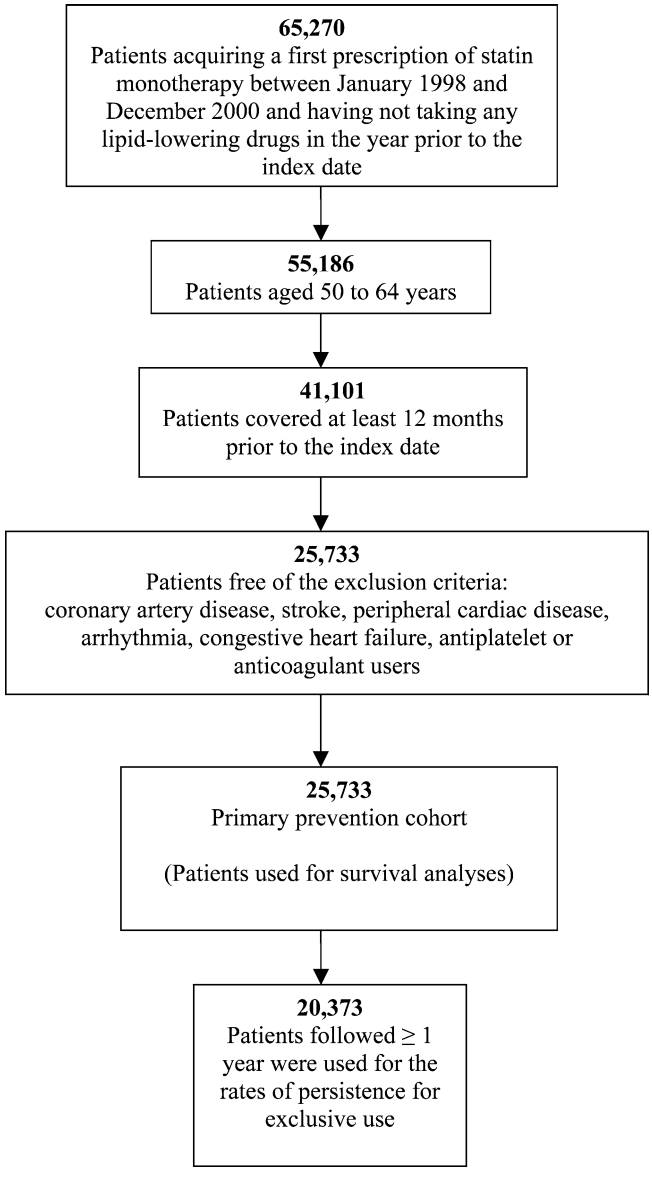

Fig. 1 Flow chart of inclusion and exclusion criteria that were applied to the population-based study

agent had to have at least a 1-year period of follow-up. A chi-square test was used to estimate the difference in proportion compared with pravastatin and simvastatin.

Residuals from regression models were assessed for multicollinearity or deviance [25, 26]. The analyses were performed on SAS software, version 12; SAS Institute, Cary, N.C.), and $p < 0.05$ was the level of significance.

Ethical considerations

No patient or physician identifiers were provided to the researchers; only scrambled identifiers were used throughout the study. The study was approved by the University of Montreal's Research and Ethics Committee.

Results

Characteristic demographic

As shown in Fig. 1, after applying the inclusion and exclusion criteria, we identified a total of 25,733 subjects as being newly treated with statin agents in the form of a single therapy of atorvastatin, fluvastatin, lovastatin, pravastatin or simvastatin. Characteristics of these newly treated patients for primary prevention are shown in Table 1. At cohort entry, mean age was 58 years, 39% were male, 24% were receiving social assistance and 26% were living in a rural environment. The corresponding values for the excluded patients were: mean age 58 years, 46% male, 28% receiving social assistance and 26% living in a rural environment. The reason for censoring during follow-up were most likely associated with the end of follow-up (72%), development of exclusion criteria (25%) and loss of coverage under drug plan (3%).

The clinical characteristics of patients who initiated a new statin treatment for primary prevention were as follows: 19% had diabetes, 30% had hypertension, 11% had respiratory disease, 10% were users of antidepressive agents and 28% were using anxiolytic agents. In the year prior to index date, patients had used an average of 1.5 medications per month and had used the services of an average of 1.4 pharmacies. Among the patients, 20% had had at least three different medications; 25% had had at least three prescribing physicians; 25% had had at least two dispensing pharmacies in the year preceding the index date.

Atorvastatin was used most often (49%) as the first statin agent, followed by pravastatin (24%), simvastatin (19%), fluvastatin (6%) and lovastatin (2%) (Table 1).

Measurement of persistence

As shown in Fig. 2, the persistence of use of statin agents decreased in the first 6 months following initiation of treatment: 67% were persistent at 6 months and persistence continued to decline over the next 3 years to reach 39%. Persistence during the 1-year follow-up period varied according to the statin used to initiate the treatment: 57% of those who had initiated with simvastatin or atorvastatin remained persistent; for pravastatin, 56%; for fluvastatin, 54%; for lovastatin, 50%. Persistence of statin use during the 3-year follow-up period was 40% for those who had started with simvastatin, 39% for pravastatin and atorvastatin, 34% for fluvastatin and 32% for lovastatin.

In a sensitivity analysis, persistence was defined as acquiring a statin agent within 45–120 days of the end date of a previous prescription. Results revealed similar patterns of progressive discontinuation of statin agents over time. For instance, at 6 months and 3 years following the index date and using the definition of persistence based on 45 instead of 60 days, we found similar persistence rates: for example, 64 versus 67% at 6 months and 36 versus 39% at 3 years; the corresponding values when the definition of persistence was based on 120 days were 74 versus 67% (6 months) and 46 versus 39% (3 years).

As shown in Table 2 (considering exclusive use of a statin agent), the initial choice of statin agent seems to predict the different switching proportions to a new agent at 1-year of follow-up, particularly for fluvastatin, for which the rate of switching was 8%, compared to pravastatin (5%) and simvastatin (3%). This difference in switching rate between simvastatin and pravastatin was statistically significant ($p < 0.05$). Initial statin choice influenced the proportion of discontinuation; for lovas-

Table 1 Characteristics of patients initiating new statin treatments in the Quebec RAMQ database in 1998–2000

	Total population in Quebec in 2001 (50–64 years)[a]	Total cohort population	Excluded patients	Total primary prevention cohort	Patients followed for more than 1 year
Number of patients	1,299,765	41,101	15,368	25,733	20,353
Mean age (±SD)[b]	56.2 ± 1.2	58.1 ± 4.6	58.1 ± 4.6	57.9 ± 4.6	57.9 ± 4.6
Male[b]	49%	46%	46%	39%	38%
Social assistance status[b]	10%	29%	28%	24%	24%
Rural environment (yes/no)[b]	35%	27%	26%	26%	26%

[a]Source: Institut de la statistique du Québec
[b]At the index date

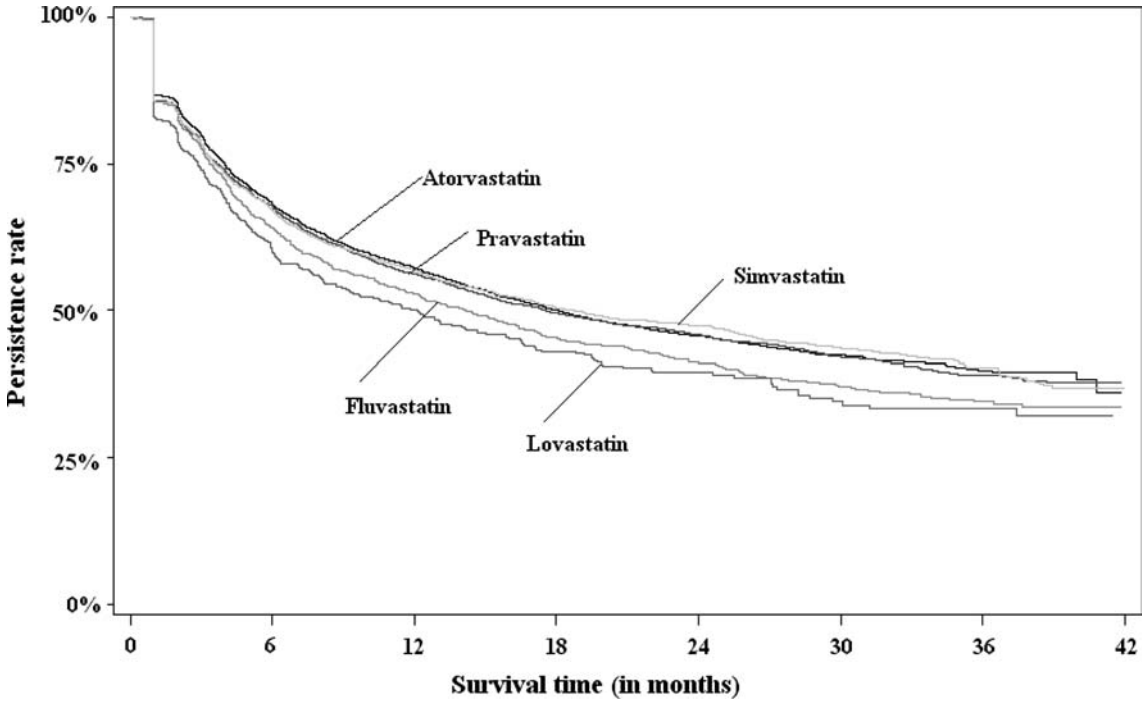

Fig. 2 Cumulative rate of persistence with first intention of statin treatments

tatin, this was 55%; for fluvastatin, 53%; for atorvastatin, 51%; this in comparison to pravastatin (49%) and simvastatin (49%).

Therapeutic class and persistence

During the 3 years of follow-up, after controlling for individual patients' socio-demographic, clinical characteristics and health-care utilization (Table 4), we found that patients who were prescribed atorvastatin as a first agent, fluvastatin or lovastatin were more likely to discontinue their treatment than patients who were prescribed pravastatin or simvastatin (Table 3); the corresponding hazard ratios (HR) 1.08 (range: 1.03–1.14), 1.18 (1.05–1.32) and 1.13 (1.05–1.22), respectively. Similar values were also observed with simvastatin, but not for atorvastatin where the level of significance was not achieved (HR: 1.05; 1.00–1.11).

Relationship between patient characteristics and persistence

As shown in Table 4, the adjusted rate ratios of ceasing statin agents were non-significant for age (HR: 1.00; 0.99–1.00) and social assistance status (HR: 1.04; 0.99–1.08), indicating that increasing age or welfare-recipient status did not decrease the rate ratio of cessation. Gender and rural environment did affect the rate ratio of cessation: being male (HR: 0.93; 0.90–0.97) or living in a rural environment (HR: 0.89; 0.85–0.93) was associated with a lower rate of cessation. Subjects with other cardiovascular risk factors, such as diabetes (HR: 0.78; 0.75–0.82) or hypertension (HR: 0.72; 0.69–0.74) or having other co-morbidities, such as respiratory disease (HR: 0.67; 0.63–0.71), being an anxiolytic user (HR: 0.87; 0.82–0.93) or taking antidepressive agents (HR: 0.87; 0.83–0.91), decreased the rate ratio of ceasing statin therapy.

Table 2 Rates of persistence for exclusive use of statin agents among primary prevention cohort at 1-year period of follow-up

Statin agents	Mean dose used (median dose) (mg)	Continuation of initial drug (%)	Switched to at least another drug class (%)	Discontinued therapy (%)
All ($n = 25{,}733$)		43	5	52
Pravastatin ($n = 6{,}111$)	20 (20)	46	5**	49
Simvastatin ($n = 4{,}877$)	15 (10)	48	3	49
Atorvastatin ($n = 12{,}609$)	13 (10)	47*	1**	51*
Fluvastatin ($n = 1{,}554$)	27 (20)	40*	8*	53*
Lovastatin ($n = 582$)	21 (20)	40*	5	55*

*Compared to pravastatin and simvastatin, $p < 0.05$;
**Compared to simvastatin, $p < 0.05$

Table 3 Rate ratio of ceasing statin treatment based on statin agents as first intention, at 3 years of follow-up

Statin agents as first intention	Adjusted rate ratio[a] (95% confidence interval)	
Pravastatin	Reference	0.97 (0.92–1.03)
Simvastatin	1.03 (0.98–1.09)	Reference
Atorvastatin	1.08 (1.03–1.14)	1.05 (1.00–1.11)
Fluvastatin	1.18 (1.05–1.32)	1.15 (1.02–1.29)
Lovastatin	1.13 (1.05–1.22)	1.10 (1.02–1.19)

[a]Adjusted for patients' socio-demographic, clinical characteristics and health care utilization (see Table 4)

Table 4 Rate ratio of ceasing statin treatment based on patients' socio-demographic, clinical characteristics and health care utilization, at 3 years of follow-up

	Adjusted rate ratio[a] (95% confidence interval)
Socio-demographic characteristics	
Age (continuous)[b]	1.00 (0.99–1.00)
Sex (male vs. female)[b]	0.93 (0.90–0.97)
Social assistance status (yes/no)[b]	1.04 (0.99–1.08)
Rural environment (yes/no)[b]	0.89 (0.85–0.93)
Clinical characteristics	
Diabetes mellitus[c,d] (yes/no)	0.78 (0.75–0.82)
Hypertension[c,d] (yes/no)	0.72 (0.69–0.74)
Respiratory disease[c,d] (yes/no)	0.67 (0.63–0.71)
Antidepressive agents[c,d] (yes/no)	0.87 (0.82–0.93)
Anxiolytic agent[c,d] (yes/no)	0.87 (0.83–0.91)
Health-care utilization	
Mean number of different classes of drugs/month[c] (≥3)	0.40 (0.38–0.43)
Mean number of total oral doses of drugs/day[c] (continuous)	1.17 (1.14–1.19)
Mean number of dispensing pharmacies[c] (≥2)	1.63 (1.55–1.72)
Mean number of prescribing physicians[c] (≥3)	1.63 (1.55–1.72)
Mean number of medical visits/month[c] (continuous)	1.35 (1.30–1.40)
Hospitalization[e] (yes/no)	0.70 (0.66–0.74)

[a]The crude rate ratios have similar values
[b]Taken at the index date
[c]Taken in the year prior the index date and during follow-up
[d]Receiving pharmacologic treatment or ICD-9 code diagnosis
[e]Admission in the year preceding the index date and during the follow-up

Patients who had a larger number of different classes of drugs prescribed (HR: 0.40; 0.38–0.43) were related to a lower rate of cessation, but the total number of doses per day (HR: 1.17; 1.14–1.19) was associated with a higher cessation rate. A significant relationship was found between the use of health-care resources and statin cessation rate. Patients showed an increased rate ratio of cessation of 63% when they had ≥2 pharmacies or an increased ratio of cessation of 63% when they consulted with ≥3 prescribing physicians. The fact of having more medical visits significantly increased the rate of cessation by 35%, while being hospitalized had a significant positive impact on statin cessation rate (HR: 0.70; 0.66–0.74) (Table 4).

Discussion

Despite abundant evidence of the capacity of statin therapy to reduce cardiovascular morbidity and/or mortality, our results indicate that their actual use in typical populations of middle-aged patients is likely to substantially undercut their potential. An understanding of the impact of predictors of long-term persistence with statins has implications for the approach to managing individual patients.

We found that persistence with statin therapy had fallen to 67% after the first 6 months of treatment, and after 3 years, had declined to 39%. The rate of persistence is low over time. Persistence at 3 years varied according to the statin agent used initially, with pravastatin and simvastatin presenting higher rates of persistence. Our results suggest that newly treated middle-aged patients with dyslipidemia with other cardiovascular risk factors, such as diabetes or hypertension, were the most likely to be persistent to statin therapy. The predictors of suboptimal persistence identified here provide additional information supporting earlier results in which we observed lower persistence in patients who used the greatest number of pharmacists, prescribing physicians or health-care services.

The efficacy of HMG-CoA reductase inhibitors in modifying lipid levels and reducing the risk of coronary artery disease has been well established among patients in both primary or secondary prevention, showing a decrease in cardiovascular morbidity and/or mortality, particularly among patients at high risk of cardiovascular disease and/or those with coronary artery disease [1–8]. Clinical trials evaluating the efficacy of statins in primary prevention trials showed 5-year persistence rates ranging from 70 to 85% [4, 6, 7]. Earlier observational studies assessing persistence of statins have been

mainly in periods excluding the new products and were evaluated mainly among elderly patients [9–12]. They do not separate the results into primary and secondary prevention, except in one study that was conducted in the elderly. These studies found 1-year persistence rates of 25–85% for patients initiated on lipid-lowering drugs [9–12]. Recent studies among elderly subjects with or without acute coronary syndrome showed a low rate of compliance to statin agents [13], with persistence declining substantially over time [14]; the rate of persistence of statin agents at 2 years was only 26% for primary prevention [13]. Our results are in agreement with those among patients older than 65 years without cardiovascular disease [13]. Gaps exist between recommendations and actual practice for prevention as well as treatment.

When only an exclusive use was considered(Table 2), we observed higher proportions of persistence for treatment with pravastatin and simvastatin. Simvastatin and pravastatin were the statin agents with the strongest clinical evidence supporting their use at the time of this study period [1–3, 5]. We could also argue that the perceptions of the physician influenced the rate of persistence, but we could not exclude the possibility of a lack of efficacy, adverse drug effect or the expenditures to the patients. For instance, according to the mean dose used during the first year of follow-up, we can expect a LDL cholesterol reduction $\leq 25\%$ for fluvastatin or lovastatin, but for pravastatin, simvastatin and atorvastatin, we can expect a LDL cholesterol reduction $\geq 30\%$ [27, 28]. Moreover, since the incidence of myopathy associated with statin therapy is dose-related [29], the mean dose of atorvastatin used during the first year may have induced a higher incidence rate of adverse effects as compared with pravastatin and simvastatin. All of these statements are speculative, and can not be deduced from the data from this study.

In the case of cardiovascular illnesses, non-compliance could have a significant impact on anticipated benefits and actual effectiveness, since a minimum exposure of 1–2 years is required before a significant impact on risk levels is seen [1–8]. Drug use that proves to be efficacious in randomized clinical trials may therefore be completely ineffective in a real-life application. In fact, some pharmacoeconomic studies using modeling and efficacy based on data from clinical trials have not reported satisfactory cost-effectiveness ratios, particularly for the primary prevention in low-risk patients [30, 31].

This finding reflects the need for physicians and pharmacists to identify those dyslipidemic individuals who may benefit from targeted patient counseling. In addition, more innovative studies are required to follow up on prescriptions for medications, such as continuous electronic monitoring of compliance as a disease management strategy [32]. A realistic new chronic-disease model of disease management involving the implementation of such programs as patient–professional partnerships, multidisciplinary teams, self-management education, clinical information systems, decision support and clinical indicators needs to be developed.

We have identified several limitations to this study. *First*, there was a lack of clinical data (e.g., lipid values) on each patient. *Second*, there was no control for the discontinuation by the prescriber for clinical reasons, such as adverse drug reaction or lack of efficacy. *Third*, we used several markers in an attempt to exclude patients with some of these other conditions, but the conditions may have been miscoded. *Four*, we were not able to control for the potential misclassification of drug use without a prescription (physician samples) or any change in lifestyle. *Five*, the evaluation of drug use was based on dispensation instead of drug administration, which may have led to a non-differential information bias. *Six*, we excluded patients who received a low dose of ASA (acetylsalicylic acid) but the exclusion procedure may be biased by OTC sales.

The ulitilization of administrative databases to measure drug exposure presents many advantages over other means of data collection, such as interviews or self-administered questionnaires [33–37]. *First*, administrative databases avoid the problem of recall bias, which is known to be a major source of bias in research. *Second*, it is usually difficult for patients to report the medications they are taking when details, such as the exact name, dose and quantity, are required. *Third*, the use of computerized databases allows the researcher to capture drug history over a long period of time.

We conclude that in current practice, barriers to persistence occur early during the course of statin therapy and that the rate of persistence is low among patients in primary prevention. Because long-term persistence to statin therapy is essential for clinical benefits, we suggest that if policy makers are to succeed at promoting optimal drug utilization based on evidence-based statin therapy, new educational strategies must be developed. At this point in time, the critical issue is the education of physicians and patients with respect to the advantages of persisting in the treatment. This issue has enormous clinical, public health and economic implications.

Acknowledgements This work was supported by the Social Sciences and Humanities Research Council of Canada (CRSH). Sylvie Perreault PhD and Lyne Lalonde are research scholars receiving financial support from the Fonds de la recherche en santé du Québec. Lucie Blais and Johanne Collin are research scholars receiving financial support from the Canadian Institutes of Health Research and CRSH, respectively.

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