Persistence and determinants of statin therapy among middle-aged patients for primary and secondary prevention

S. Perreault,¹ L. Blais,¹ D. Lamarre,¹ A. Dragomir,¹ D. Berbiche,¹ L. Lalonde,¹ C. Laurier,¹ F. St-Maurice² & J. Collin¹

¹Faculty of Pharmacy and ²Faculty of Medicine, University of Montreal, Montreal, Quebec, Canada

Correspondence

Sylvie Perreault, PhD, Faculty of Pharmacy, PO Box 6128, Centre-Ville Station, Montreal, Quebec, Canada H3C 3J7.

Tel: +1 514 343 6111, ext. 3149

Fax: +1 514 343 2102

E-mail: sylvie.perreault@umontreal.ca

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Aims

Statins have been shown to significantly reduce morbidity and mortality in patients with coronary artery disease (CAD), and also in patients with dyslipidaemia when statins are taken regularly. Middle-aged patients have the highest level of forecasting benefit and little is known about persistence rate of these therapies in a real-life setting. The objective was to evaluate the persistence rate of middle-aged patients initiating a statin therapy and its relation with several determinants for primary and secondary prevention.

Methods

A cohort was reconstructed using the RAMQ databases. All patients aged 50–64 years-old who received at least one statin prescription between 1 January, 1998 and 31 December, 2000 for a new intention of treatment for dyslipidaemia were included in the cohort and followed up until 30 June, 2001. The date of the first prescription of statin was defined as the index date. There were 4316 patients in the secondary prevention (CAD diagnosis) and 13 642 patients in primary prevention cohort. The cumulative persistence rate was estimated using Kaplan-Meier, and Cox regression models were used to estimate the hazard ratio of ceasing statins.

Results

We found that persistence with statins had fallen to 71% after 6 months of treatment, and had declined to 45% after 3 years in the secondary prevention cohort; the corresponding figures were 65% and 35% in the primary prevention cohort. Our results suggest that patients with dyslipidaemia in primary prevention compared with those in secondary prevention (HR: 1.18; 1.11–1.25) are less likely to be persistent. Patients with other cardiovascular risk factors such as age (HR: 0.99; 0.98–0.99), diabetes (HR: 0.84; 0.79–0.90), hypertension (HR: 0.76; 0.72–0.80) were most likely to be persistent with statins. We observed lower persistence in patients who have 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, and particularly among patients with few other cardiovascular risk factors.

Introduction

Cardiovascular disease remains the leading cause of death in North America [1]. It has been shown that the treatment of dyslipidaemia with statins significantly reduces morbidity and/or mortality among patients with coronary artery disease, and also in patients with dyslipidaemia [2–6]. According to clinical trials, statins start to demonstrate benefits on cardiovascular morbidity and mortality only after 1–2 years of use [2–6]. Findings from new trials showed that atorvastatin [7] reduced the rate of cardiovascular disease among patients with acute coronary syndrome. Heart Protection Study, a landmark study involving 20 556 patients at high risk of coronary artery disease showed that simvastatin decreased the total death rate and reduced the rate of all cardiovascular events [8]. With adjustment for lack of compliance, the actual effect may be increased by 1.5-fold [8]. Additionally, the Anglo-Scandinavian Cardiac Outcomes Trial investigators [9] compared the benefits of atorvastatin *vs.* placebo on the combined outcome of nonfatal myocardial infarction and fatal coronary artery disease among hypertensive patients with a total cholesterol level lower than 6.5 mmol l⁻¹, and provides other evidence for primary prevention with statin therapy among patients at high risk of coronary artery disease [9].

For both primary and secondary prevention, statins have to be used on a long-term basis to achieve the potential benefit. Clinical guidelines consequently highlight the need to assess and promote compliance with prescribed treatment for dyslipidaemia [10]. On the other hand, observational studies assessing persistence with statins, mainly conducted in elderly subjects, found 1-year persistence rates of 25–85% [11–14]. A recent Canadian study among elderly subjects with or without recent acute coronary syndrome has shown a persistence rate of only 40% at 2 years among patients with acute coronary syndrome, 36% for those with chronic coronary artery disease, and 26% among patients in primary prevention [15]. The long-term persistence in use of statin therapy among elderly US patients remains also low [16].

Based on a Cardiovascular Life Expectancy Model to estimate the benefits of risk factor modification in the primary and secondary prevention of cardiovascular disease, forecasting benefits of treating hyperlipidaemia have shown that high-risk individuals had more benefits than lower-risk individuals, younger individuals more than elderly, and men more than women [17, 18]. Middle-aged patients have the highest level of forecasting benefit, and little is known about long-term persistence rate of these therapies in a real-life setting, as well as its

determinants. In order to target persistence enhancing interventions, we require the knowledge of the time during therapy when discontinuation is most likely, and which patient subgroups are at highest risk. The aim of our study was to evaluate the persistence rate of middle-aged patients newly treated with statin, and to study its relation with age, gender, cardiovascular risk factors and use of health care services for primary and secondary prevention.

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 programmes in the province of Quebec, Canada. RAMQ databases contain three types of files. First, the demographic file lists age, gender, postal code and year of death for all individuals registered and having a RAMQ card. Second, the medical services file includes claims for all inpatient or ambulatory medical services with data such as, the nature of the medical act, date, the site where the act was provided (office, emergency, hospital) and the diagnostic code [19]. Diagnosis is coded according to ICD-9 classification and the code for surgical procedures are assigned according to the Canadian classification of diagnostic, therapeutic and surgical procedures [20]. Third, the pharmaceutical file contains data on all prescriptions for 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. The RAMQ databases pertain to residents covered by the provincial health care insurance which included the whole population; and by the public drug plan, which represents about 55% of the total population of Quebec [21]. Each of the computerized files contains the individual's health insurance number, which acts as a link between them. The pharmaceutical file has been validated for research and have been previously used for pharmacoepidemiological research studies [22, 23].

Cohort definition

The cohort of 35 412 patients was identified from prescription records. To be included in the cohort, subjects had initiated a new intention of treatment for dyslipidaemia, defined as having had no statin agents or other lipid-lowering drugs prescribed in the year preceding the index date (the date of the first prescription) and should have started a new treatment for either atorvastatin, fluvastatin, lovastatin, pravastatin or simvastatin in

the period from 1 January, 1998 to 31 December, 2000. The date of the first prescription of these agents was defined as the index date. Furthermore, patients had to be insured in the provincial plan for 12 months in the year prior to the index date, and aged between 50 and 64 years of age at the index date.

The study assessed persistence in two separate patient cohorts: (1) secondary prevention cohort: patients with coronary artery disease defined as those with a diagnosis of myocardial infarction or angina (ICD-9 codes 410–414), coronary artery bypass graft or angioplasty or the use of nitrates including nitroglycerine (as confirmed in the prescription claim database) within the year before the index date; and (2) primary prevention cohort: subjects with no indication of a cardiovascular disease as evidenced by the absence of a diagnosis or drug markers in the year prior to index date for: myocardial infarction or angina (ICD-9 codes 410–414), coronary artery bypass graft, angioplasty 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 (a) digoxin (b) ACE inhibitors (captopril or enalapril) or (c) beta-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 ASA (acetylsalicylic acid) or anticoagulants in the year preceding the index date.

The two final cohorts consisted of 4316 individuals for the secondary prevention cohort, and 13 642 patients for the primary prevention cohort. Subjects were followed until 30 June, 2001, or until they died, had the occurrence of diagnosis of cardiovascular disease, emigrated from the province, or lost of coverage under the RAMQ insurance 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 a statin. This allowed the assessment of persistence with a therapy with any statin agent. For instance, a subject switching from one statin to another statin without interruption is being considered as persistent with nonexclusive use. We also estimated the assessment of persistence with a given statin (exclusive use); in this case a subject was considered nonpersistent if he had not renewed his statin prescription in the 60-day period following the end of the prescription duration. We examined the effect of this grace period by measuring the impact on the persistence estimate, using 45 days or 120 days for the grace period.

Determinants

The variables considered as potential determinants of treatment cessation included: age, gender, social assistance status, site of residency, chronic disease score, comorbidities such as, diabetes mellitus, hypertension, respiratory disease, use of hormone replacement therapy (HRT), antidepressive or anxiolytic agents [24, 25] number of different pharmacological agents, and number of daily doses of medication and utilization of health care services [15, 16]. 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.

Comorbidities were defined as follows: diabetes by ICD-9 code 250 or by the use of insulin or hypoglycaemic 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 beta-blockers without any other markers of coronary heart disease; HRT by the use of drug markers; respiratory disease by the use of at least two prescriptions of inhaled beta-agonists or any pharmacological agents used for respiratory disease; and use of antidepressive or anxiolytic agents [24, 25] during the year preceding the index date and during the follow-up period.

The mean number of different types of drugs per month 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. The health care services utilization was measured by computing the number of prescribing physicians, of dispensing pharmacies consulted, and medical visits in the year preceding the index date and during the follow-up period. The fact of being hospitalized recorded in the year preceding the cohort entry.

Statistical analysis

The cumulative persistence rate was estimated using Kaplan–Meier failure time analysis [26]. The log-rank analysis yielded the average rate ratio (with the proportional reduction in this ratio expressed as percentage), and the test of statistical significance (two-sided *P*-value). Cox regression models with time-dependent covariables were constructed by standard statistical tests on proportionality to estimate the hazard ratio of nonpersistence with statin agents. All models were adjusted for potential determinants described previously. Residuals from regression models were assessed for violations of the assumptions of normality, multicollinearity, or deviance [27, 28]. Demographic and clinical data were compared among primary and secondary prevention populations with the Chi-square test and *t*-test, for categorical and continuous variables, respectively. The analyses were performed on Statistical Analysis System Software version 8 (SAS Institute, Cary, North Carolina), and the level of significance was $P < 0.05$.

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

Population characteristics

As shown in Figure 1, after applying the inclusion and exclusion criteria, a total of 4316 patients for the secondary prevention cohort and 13 642 patients for the primary prevention cohort were identified as being newly treated with statin agents in the form of a single therapy of atorvastatin, fluvastatin, lovastatin, pravastatin or simvastatin. Baseline characteristics of both cohorts in the year preceding the index date are shown in Table 1. Compared with patients of the primary prevention cohort, patients in the secondary prevention cohort were more likely to be men and have been hospitalized. They have visited more physicians and have slightly more comorbidities.

Among patients for secondary prevention cohort newly treated with a single statin, pravastatin was used most often for the initial prescription (42%) followed by simvastatin (36%). A total of 6% of patients received an initial prescription of fluvastatin, 13% received atorvastatin and 3% lovastatin. These estimates were 39, 31, 10, 16, and 4%, for the primary prevention cohort, respectively.

Figure 1

Flow chart of inclusion and exclusion criteria

Patterns of use

As shown in Figure 2, the persistence with statin agents decreased in the first 6 months following initiation of treatment in the secondary prevention cohort: 71% were persistent at 6 months and the rate continued to decline over the next 3 years (45%). Patients in the secondary prevention cohort had higher rates of persistence at all times compared with those in the primary prevention cohort, e.g. 65 and 35% at 6 months and 3 years, respectively ($P < 0.0001$). The abrupt decrease of persistence rate in the first month for the primary prevention cohort was attributed to only one prescription fulfilled in 87% of cases, and for the secondary prevention cohort, 52% of these cases were attributed to only one prescription fulfilled and 34% had developed an exclusion criteria. Demographic and clinical data of the patients removed earlier were quite similar to those observed in the total population of primary and secondary prevention cohorts.

Sensitivity analysis of the definition of persistence was also performed using a grace period of 45 or 120 days; the results revealed similar patterns of

Table 1

Characteristics of middle-aged patients initiating a new statin treatment in Quebec RAMQ Database in 1998–2001

	Primary prevention cohort	Secondary prevention cohort	P-value
Number of patients	13 642	4316	
Mean age ($\pm$ SD) *	57.7 $\pm$ 4.0	57.8 $\pm$ 4.0	0.03
Male*	38%	62%	<0.0001
Social assistance status*	24%	29%	<0.0001
Rural environment (yes/no)*	27%	31%	<0.0001
Diabetes mellitus†‡	17%	18%	0.53
Hypertension†‡	43%	41%	0.03
HRT women†‡	25%	17%	<0.0001
Respiratory disease†‡	10%	14%	<0.0001
Antidepressive agents†‡ (yes/no)	10%	10%	0.55
Anxiolytic agent†‡ (yes/no)	28%	32%	<0.0001
Mean number of different classes of drugs month ⁻¹ ‡ ($\pm$ SD)	1.5 $\pm$ 1.5	1.9 $\pm$ 1.8	<0.0001
Mean number of total oral doses of drugs day ⁻¹ ‡ ($\pm$ SD)	1.6 $\pm$ 1.3	1.8 $\pm$ 1.5	<0.0001
Mean number of different pharmacies‡ ($\pm$ SD)	1.4 $\pm$ 1.0	1.4 $\pm$ 1.0	0.0002
Mean number of medical visits‡ ($\pm$ SD)	7.2 $\pm$ 6.5	8.6 $\pm$ 8.8	<0.0001
Mean number of prescribing physicians‡ ($\pm$ SD)	2.1 $\pm$ 1.7	2.6 $\pm$ 2.2	<0.0001
Hospitalization‡ (yes/no)	15%	44%	<0.0001

*At the index date; †ICD-9 code or receiving pharmacological treatment; ‡In the year prior to the index date.

Figure 2

Cumulative rate of persistence with statin treatments for primary prevention cohort and coronary artery disease cohort

progressive discontinuation of statins over time. At 3 years following the index date, using the definition of persistence based on 45 or 120 days of grace period, persistence rates for the secondary prevention cohort were 42 and 52% (compared with 45%), respectively; and for the primary prevention cohort were 31 and 42% (compared with 35%), respectively.

Persistence after 6 months varied according to the statin agent (Table 2). Considering an exclusive use of a given statin agent, the persistence rates were 76% with pravastatin, 77% with simvastatin, but relatively worse persistence was observed with atorvastatin (69%), fluvastatin (63%) and lovastatin (67%) for the secondary prevention cohort; the corresponding figures were at 69% for pravastatin, 70% for simvastatin, and significantly lower persistence with atorvastatin (58%), fluvastatin (65%) and lovastatin (64%) in the primary prevention cohort.

Predictors of hazard ratio of ceasing statin treatments

As shown in Table 3, after accounting for possible confounders, relative to patients in the secondary prevention cohort, drug cessation was more likely among patients receiving statin prescriptions in the primary prevention cohort (HR: 1.18; 1.11–1.25). The adjusted hazard ratios of ceasing statin agents were significant for age (HR: 0.99; 0.98–0.99), meaning that being older significantly decreased the hazard ratio of cessation. Subjects having other cardiovascular risk factors, such as being male (HR: 0.85; 0.81–0.90), diabetes (HR: 0.84; 0.79–0.90) and hypertension (HR: 0.76; 0.72–0.80), and for women, using HRT (HR: 0.86; 0.81–0.91) (at the time

Table 2

Rates of persistence for exclusive use among secondary prevention cohort and primary prevention cohort

	Secondary prevention cohort		Primary prevention cohort	
	Mean dose used	Rate of persistence (%)	Mean dose used	Rate of persistence (%)
Atorvastatin	16 mg	69*	15 mg	58*
Fluvastatin	27 mg	63*	28 mg	65*
Lovastatin	23 mg	67*	21 mg	64*
Pravastatin	22 mg	76	20 mg	69
Simvastatin	17 mg	77	15 mg	70

P-value <0.05 (reference = simvastatin).

Table 3

Hazard ratio of ceasing statin treatments

	Hazard ratio (95% confidence interval)	
	Crude	Adjusted
Cardiovascular disease status		
Secondary prevention	Reference	Reference
Primary prevention	1.30 (1.23–1.38)	1.18 (1.11–1.25)
Age (continuous)*	0.98 (0.98–0.99)	0.99 (0.98–0.99)
Male (yes/no)*	1.01 (0.97–1.05)	0.85 (0.81–0.90)
Social assistance status (yes/no)*	0.92 (0.87–0.96)	1.01 (0.96–1.07)
Rural environment (yes/no)*	0.86 (0.82–0.90)	0.89 (0.85–0.94)
Diabetes mellitus†‡ (yes/no)	0.76 (0.72–0.81)	0.84 (0.79–0.90)
Hypertension†‡ (yes/no)	0.63 (0.61–0.66)	0.76 (0.72–0.80)
HRT women†‡ (yes/no)	0.81 (0.77–0.87)	0.86 (0.81–0.91)
Respiratory disease†‡ (yes/no)	0.68 (0.64–0.72)	0.66 (0.62–0.71)
Antidepressive agents†‡ (yes/no)	0.78 (0.73–0.83)	0.89 (0.83–0.96)
Anxiolytic agent†‡ (yes/no)	0.79 (0.75–0.82)	0.88 (0.84–0.93)
Number of different classes of drugs month ⁻¹ ‡ (=3)	0.42 (0.36–0.50)	0.45 (0.42–0.48)
Mean number of total oral doses of drugs day ⁻¹ ‡ (continuous)	1.11 (1.08–1.39)	1.18 (1.15–1.20)
Number of dispensing pharmacies‡ (≥2)	2.08 (1.96–2.22)	1.76 (1.65–1.89)
Number of prescribing physicians‡ (≥3)	1.59 (1.51–1.68)	1.77 (1.66–1.89)
Mean number of medical visits month ⁻¹ ‡ (continuous)	1.02 (0.98–1.06)	1.06 (1.01–1.11)
Hospitalization§ (yes/no)	0.85 (0.81–0.90)	0.88 (0.83–0.93)

*At the index date; †ICD-9 or receiving pharmacological treatment; ‡In the year prior to the index date and during the follow-up; §In the year preceding the index date.

of the study period) decreased the hazard ratio of ceasing statin therapy.

Again, the fact of having a respiratory disease (HR: 0.66; 0.62–0.71), being users of antidepressive agents (HR: 0.89; 0.83–0.96) or anxiolytic agents (HR: 0.88; 0.84–0.93), and living in a rural environment (HR: 0.89; 0.85–0.94) were also less likely to cease their statin

agents. And, subjects receiving social assistance (HR: 1.01; 0.96–1.07) was not associated with a better or lower cessation rate.

A greater number of different classes of drugs taken (≥3) (HR: 0.45; 0.42–0.48) was associated with a lower rate of cessation. The total number of daily doses (HR: 1.18; 1.15–1.20) significantly increases the rate of

cessation. A significant relationship was found between the use of health care resources and cessation in statin agents. For instance, patients showed an increased hazard ratio of cessation when they had two or more pharmacies (HR: 1.76; 1.65–1.89) or consulted with three or more prescribing physicians (HR: 1.77; 1.66–1.89). The fact of having more medical visits after the index date (HR: 1.06; 1.01–1.11) significantly increased the rate of cessation. But the fact of being hospitalized had a significant positive impact on statin cessation rate (HR: 0.88; 0.83–0.93).

Discussion

Considering that at least 1–2 years of treatment are necessary to reduce cardiovascular morbidity and/or mortality, the observed low persistence with treatment is likely to attenuate treatment effectiveness. An understanding of predictors of long-term persistence with statins has implications for the approach to the management of individual patient.

We found that persistence with statin therapy in the secondary prevention cohort had fallen to 71 and 45% at 6 months and 3 years, respectively. In the primary prevention cohort, persistence with statin therapy had fallen to 65% after the first 6 months of treatment, and after 3 years, had declined to 35%. The rates of persistence are low over time. Our study identifies patient characteristics that can be used to predict poor persistence. Our results suggest that newly treated middle-aged patients with dyslipidaemia concurrent with coronary artery disease, and those with other cardiovascular risk factors such as age, male, diabetes, hypertension were the most likely to persist with statin therapy. The predictors of suboptimal persistence identified here add information to previous work in which we observed lower persistence in patients who had the greatest number of pharmacies and prescribing physicians, and greater use of health care services.

Clinical trials evaluating the efficacy of statins in secondary prevention trials had 5-year persistence rates at 81 and 94% [2–4]; and among primary prevention trials, a 5-year persistence rates was at 70% [5, 6]. Observational studies assessing persistence with statins have been mainly done in periods which excluded the new products, and were evaluated among elderly subjects and mainly with lovastatin therapy [11–14]. They did not separate into primary and secondary prevention, except for one study which was conducted in elderly subjects. The results of these studies found 1-year persistence rates of only 25–85% for patients who started a therapy with lipid-lowering drugs [11–14]. Recent studies among elderly subjects with or without acute

coronary syndrome show a low rate of compliance [16], and the persistence declines substantially over time [15]. The rates of persistence at 2 years were only 40% for patients with acute coronary syndrome, 36% for patients with chronic coronary artery disease, and at 26% for primary prevention [15].

Our results differ from those of Andrade *et al.* [11] who found a 1-year persistence rate of 85% among patients taking lovastatin, but are in agreement with those found among patients older than 65 years with and without cardiovascular disease [15]. Gaps exist between recommendations and actual practice, for prevention as well as treatment.

Considering only an exclusive use, we observed higher rate of persistence for treatment with pravastatin and simvastatin for the primary and secondary prevention. Simvastatin and pravastatin are the statin agents with the strongest clinical evidence supporting their use at the time of study period [2–4,6]. However, we could not exclude, particularly among patients for secondary prevention cohort, that the statin prescription may be from hospital department, and this fact may be a contributing factor to higher persistence. We could also argue that the perception of the doctor influences the rate of persistence but we could not exclude the possibility of a lack of efficacy or adverse drug effect. For instance, as shown in Table 2, the mean dose used of fluvastatin or lovastatin (expected LDL cholesterol reduction $\geq 25\%$) may have conducive to a lack of efficacy compared with those used for pravastatin and simvastatin (expected LDL cholesterol reduction $\geq 30\%$) [29]. Moreover, since the incidence of myopathy associated with statin therapy is dose-related [30] the mean dose used of atorvastatin may have induced an higher incidence rate of adverse effects compared with those used for pravastatin and simvastatin.

The efficacy of statin therapy in reducing the risk of coronary artery disease, particularly among middle-aged patients, has been well established among patients whether in primary or secondary prevention [2–9], showing a decrease of cardiovascular morbidity and/or mortality, particularly with high-risk and/or coronary artery disease patients if taken on regular basis [2–9]. Recent evidence demonstrated the early benefits of statin therapy and the potential harm of sudden cessation of statin agents after an acute myocardial infarction [31–34]. This fact emphasizes the importance of compliance with statin therapy.

Nonpersistence with dyslipidaemic agents is not an isolated problem because we observed this phenomenon for the treatment of many other chronic diseases. For instance, the persistence at 12 months after an initial

statin prescription for the primary and secondary cohorts (53% and 62%) was about the same as the rate we found for antihypertensive agents (65%) [35] but lower than medication for cardiac heart failure (70%) [36].

We have identified several limitations of this study. First, the lack of information on clinical data on each patient, such as lipid values. Second, the lack of information on 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 other medical conditions, but the conditions may have been miscoded. Fourth, we were not able to control for the potential misclassification of drug use without a prescription (physician samples) or any change in lifestyle. Fifth, the evaluation of drug use is based on dispensation instead of drug administration and may lead to a nondifferential information bias.

Using administrative databases to measure drug exposure presents many advantages over other means of data collection, such as interview or self-administered questionnaires. First, using administrative databases we avoid recall bias which is known as 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 [37–41]. Third, the use of computerized databases allows us to capture drug history over a long period of time.

This finding reflects the need for patients, physicians and pharmacists to identify those dyslipidaemic individuals who may benefit from targeted patient counseling and drug monitoring. More studies of innovative approaches to follow prescriptions of chronic diseases are needed [42]. A realistic new chronic disease model of disease management involving implementation of programme including patient-professional partnership, multidisciplinary team, self-management education, clinical information systems, decision support and clinical indicators needs to be developed. A new chronic disease model needs also to promote studies of indicator performance and cost-effectiveness analyses [43–48].

We conclude that in current practice, barriers to persistence occur early in the course of statin therapy, and the rate of persistence is low among patients in both primary and secondary prevention. Because long-term persistence with statin therapy is essential for clinical benefits, we suggest that educational strategies must be developed if policy makers are to succeed at promoting optimal drug utilization based on evidence-based statin

treatments. The critical issue is the education of physicians and patients concerning persistence with treatment. This issue has enormous clinical, public health, and economic implications.

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