Patterns of statin use and cholesterol goal attainment in a high-risk cardiovascular population: A retrospective study of primary care electronic medical records

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KEYWORDS: Statins; Cardiovascular risk; Primary care; LDL cholesterol; Electronic medical records

OBJECTIVE: To describe real-life patterns of statin use and cholesterol goal attainment in a retrospective cohort of patients with high cardiovascular risk.

METHODS: Retrospective cohort study of 21,636 individuals, 18.34% women, mean age 63.30 years (standard deviation 6.29). New statin users aged 35 to 74 years at high cardiovascular risk and with no previous cardiovascular disease in primary care electronic medical records (2006–2011). Patterns of statin use were based on statin type, potency, and 1-year statin switches.

OUTCOMES: Relative mean reductions over 1 year and probability of goal attainment (<3.3 mmol/L). Natural patterns of statin use were identified using multiple correspondence analysis; general linear and logistic models were used to estimate low-density lipoprotein cholesterol (LDL-C) reductions and goal attainment probability.

RESULTS: Three patterns of statin use were defined: low (3.82% of the population), moderate (71.94%), and high intensity (24.24%). After 1 year, potency decreased 42.74%, 64.16%, and 50.94%, respectively, and 37.41%, 29.47%, and 30.16% of the population stopped taking statins in low, moderate, and high patterns, respectively. Relative reductions in LDL-C: low intensity, 15.7% (95% confidence interval [CI]: 22.96 to 54.36); moderate intensity, 29.72% (95% CI: 29.12–30.32); and high intensity, 24.20% (95% CI: 8.08 to 40.32). There was a direct relationship between higher intensity patterns and greater probability of goal attainment.
Introduction

Statin effectiveness in reducing low-density lipoprotein cholesterol (LDL-C) levels is well known in high-risk populations and secondary prevention.1–2 It is estimated that 1-mmol/L reduction in LDL-C may reduce 5-year incidence of cardiovascular events and coronary revascularization by one fifth,1 and a similar effect has been observed in a comparison of intensive and less-intensive statin regimens.3–4 In addition, a study by Cholesterol Treatment Trialists’ Collaboration showed that a 1-mmol/L reduction in LDL-C safely reduces 5-year incidence of cardiovascular events and coronary revascularization in low-risk populations by 10%, regardless of age, gender, and baseline LDL-C.5

The recommended management of patients with dyslipidemia, including the patterns of statin use to achieve recommended thresholds, differs substantially between the European Society of Cardiology/European Atherosclerosis Society6 and the American College of Cardiology/American Heart Association.7 In both the cases, however, recommended patterns of statin use are based on their capacity to lower baseline LDL-C levels.

Despite these guidelines,6,7 observational studies show that the recommended goals are not being achieved in primary prevention populations, community settings,8–11 or secondary prevention.12,13 These results may be partly related to the real-life patterns of statin use.14–16 Patterns of statin use have been studied in specific populations, such as diabetics, and in secondary prevention,12,13 but real-life studies in primary prevention and other high-risk populations are scarce.17 Further description of these patterns may help to improve the management of these populations and attainment of the recommended goals.

The aim of the present study of primary care electronic medical records was to describe real-life patterns of statin use and cholesterol goal attainment in a retrospective cohort of patients with high cardiovascular risk and no history of cardiovascular disease.

Methods

Design

Retrospective cohort study.

Data source

The Information System for the Development of Research in Primary Care (SIDIAP) is a clinical database of anonymized longitudinal patient records for nearly 6 million people (80% of the Catalan population and 10.2% of the total population of Spain) registered in 274 primary care practices having a total of 3414 general practitioners (GPs).18 A subset of records from GPs who surpass predefined data quality standards19 constitutes the SIDIAPQ, which provides research-quality anonymized data on approximately 2 million patients. The information recorded includes demographic and lifestyle factors relevant to primary care settings (body mass index [BMI], smoking status, alcohol use, and so forth); clinical diagnoses, outcomes, and events (coded according to the International Classification of Diseases, 10th revision); referrals and laboratory tests; and prescribed medications actually dispensed by community pharmacies. The quality of SIDIAP data has been previously documented, and the database has been widely used to study the epidemiology of a number of health outcomes.20–23

Study population and inclusion criteria

All new statin users aged 35 to 74 years, at high cardiovascular risk and without previous history of cardiovascular disease (symptomatic peripheral arterial disease, coronary heart disease, stroke, or revascularization procedures) as recorded in SIDIAPQ between July 2006 and December 2010 were eligible for inclusion.

Coronary heart disease risk was calculated using the Framingham function adapted and validated in the Spanish population by the Registre Gironí study24 and the systematic coronary risk evaluation function.25 High cardiovascular risk was defined as Registre Gironí 10-year risk $\geq 10\%$ or systematic coronary risk evaluation function $\geq 5\%$.

Study entry and follow-up

Study period was from July 2006 through December 2011, with enrollment from July 2006 to December 2010. Patients were censored at the date of death, transfer from SIDIAPQ, or the end of the study period (31 December 2011).

Statin exposure

To prevent survivor bias and covariate measurement bias, a “new users design” was selected over “all statin users”. New users were defined as receiving statins for the
first time or after a hiatus of at least 6 months. The date of this new statin prescription was considered the index date.

Statin exposure was calculated according to the definition of 1-year adherence, or Medical Possession Ratio (MPR): the number of days of statin supplied during 12 consecutive months, divided by 365 days.

Outcomes

Patterns of statin use were based on the following variables:

- Statin type: simvastatin, pravastatin, lovastatin, fluvastatin, rosuvastatin, or atorvastatin.
- Statin potency, classified by LDL-C reduction.26,27
  - Low (<30% reduction): 20 to 40-mg fluvastatin, 10 to 20-mg lovastatin, 10-mg pravastatin, or 5-mg simvastatin.
  - Moderate (30%–40% reduction): 10 to 20-mg atorvastatin, 80-mg fluvastatin, 40-mg lovastatin, 20 to 40–80-mg pravastatin, or 10 to 20-mg simvastatin.
  - High (40%–50% reduction): 40-mg atorvastatin, 40 to 80-mg simvastatin, or 5-mg rosuvastatin.
  - Very high (>50% reduction): 80-mg atorvastatin or 10 to 20–40-mg rosuvastatin.
- Statin switches: combination of any change in statin type or potency change at 1 year after treatment initiation. Accordingly, the following scenarios were defined:
  - No statin change and no potency change
  - No statin change and increased potency
  - No statin change and decreased potency
  - Statin change and no potency change
  - Statin change and increased potency
  - Statin change and decreased potency
  - Stopped taking statin: no statin invoicing in the 6 months months beyond the end of study follow-up.

LDL cholesterol goal attainment

Attainment was assessed by relative mean reductions during 1-year follow-up and the probability of goal attainment (yes/no). Data are presented for the probability of LDL-C goal attainment at values <3.36 mmol/L and <2.59 mmol/L. The study analyzed a goal of LDL-C < 3.36 mmol/L in accordance with the local guidelines that were in place during the study period (2006–2011). The current recommended goal for control of dyslipidemia in the high-risk primary prevention populations with low incidence of cardiovascular events is LDL-C < 2.59 mmol/L.28

Covariates

Anonymized baseline patient characteristics were obtained from SIDIAPQ: age, gender, systolic blood pressure and diastolic blood pressure, BMI, vascular risk factors (obesity, diabetes mellitus, hypertension, dyslipidemia, smoking, high-risk alcohol intake), and total cholesterol, LDL-C, high-density lipoprotein cholesterol (HDL-C), triglycerides, and glucose levels.

Statistical analysis

Categorical variables are presented as percentages and continuous variables as mean (standard deviation [SD]) or median [first–third quartiles], as appropriate. We used 10 multiple imputations by chained equations29 to replace baseline and 1-year missing values for total cholesterol, LDL-C, triglycerides, glucose, systolic blood pressure, diastolic blood pressure, and BMI. The specific characteristics of the study population (high-risk patients) made the missing-at-random assumption plausible. In addition to incorporating the missing-at-random assumption, we conducted a sensitivity analysis, comparing case-complete results with the multiple imputation process. Only individuals being part of all imputations were included in the analysis.

Natural patterns of statin use based on statin type, potency, and 1-year change were identified using multiple correspondence analysis (MCA), which allows representation in N-multidimensional space of relationships between a set of categorical variables that would otherwise be difficult to observe in contingency tables30 and to show groups of individuals with the same characteristics. From the multidimensional space created, individuals were classified in patterns according to proximity criteria by means of the k-means algorithm, using 1000 different seeds and 40 iterations.31

Relative mean reductions in LDL-C were calculated, and logistic models were used to estimate the probability of goal attainment by patterns of statin use identified by MCA.

Two analyses were performed: a first analysis including all individuals regardless of adherence, which reflects real life, and a second analysis including only individuals with high adherence (MPR ≥ 70%), to test sensitivity. Logistic models were further adjusted for gender, age, diabetes, hypertension, smoking, and total-cholesterol and glucose levels.

Results

Between 2006 and 2010, 21,636 individuals fulfilled all inclusion criteria. Only 159 participants were lost to follow-up, all of them due to transfer out of the SIDIAPQ database.

The missing data for incomplete variables and a comparison of complete-case data set and the completed (imputed) data set are shown in Supplementary Tables S1–S7.

Baseline characteristics

Women constituted 18.34% of the sample. Mean age and median cardiovascular risk were 63.30 (SD 6.29) and 11.75 [1st 9.76–3rd 14.90] years, respectively. Diabetes was present in 56% of participants, hypertension in nearly 68%, smoking in 52%, and dyslipidemia in 71%. Total-cholesterol and LDL-C goal attainment were achieved by 10.78% and 18.95% of participants, respectively (Table 1).
The proportion of patients with MPR > 70% was 51.81% (n = 11,209); mean MPR was 68.77% (SD 15.55). These patients showed a slightly worse cardiovascular risk profile than that of the total sample (see Supplementary Table S8).

**Statin patterns**

**Multiple correspondence analysis**

Statin use patterns were identified from a 5-dimensional space MCA, which accounted for 48.43% of the total variance. (See Supplementary Table S9.)

**Patterns of statin use**

Three patterns of statin use were defined by MCA, on the basis of homogeneous clinical constructs sharing the same characteristics and representativeness (ie, sample size, as summarized in Table 2).

**Low-intensity pattern (3.82% of the population)**

Individuals taking lovastatin (51.82%), pravastatin (37.89%), or fluvastatin (10.29%), primarily, with either no statin change/potency decrease (42.74%) or stopped taking statin (37.41%).

**Moderate-intensity pattern (71.94% of the population)**

Individuals taking simvastatin (92.08%), primarily, with either no statin change/potency decrease (64.16%) or stopped taking statin (29.47). The most frequently prescribed pattern was simvastatin at moderate doses (10–20 mg).

**High-intensity pattern (24.24% of the population)**

Individuals taking atorvastatin (56.51%) or simvastatin (38.02%), primarily, with either no statin change/potency decrease (50.94%), stopped taking statin (30.16%), or had a statin change/potency decrease (16.93%).

Baseline characteristics were similar between statin use patterns, except for a larger proportion of women and diabetics in the high-intensity pattern and a smaller proportion of hypertension in the low-intensity pattern. Dyslipidemia was more frequent in the moderate- and high-intensity patterns. (Table 3)

Patterns and baseline characteristics of individuals with MPR > 70 are shown in Supplementary Tables S10–S11.

**LDL-cholesterol reduction and goal attainment**

Regarding LDL-C profile, mean baseline levels (mmol/L) were somewhat lower in the low-intensity pattern total population (3.93 [SD 1.00]), compared with moderate- and high-intensity patterns 4.22 (SD 0.96) and 4.17 (SD 1.19), respectively; likewise, patients with a low-intensity pattern and MPR > 70% had lower LDL-C levels. After 1 year of follow-up, mean LDL-C levels (mmol/L) ranged from 3.18 (SD 1.06) to 2.96 (SD 1.18) in the total population and from 3.05 (SD 1.03) to 2.73 (SD 1.09) in the population with MPR > 70% (Table 4).

Relative mean reductions in LDL-C at 1 year were: low intensity, 15.70% (95% confidence interval [CI]: 22.96 to 54.36); moderate intensity, 29.72% (95% CI: 29.12–30.32); and high intensity, 24.20% (95% CI: 28.08 to 40.32). For patients with MPR > 70%, the 1-year LDL-C relative reductions were greater: low intensity 23.26% (95% CI: 232.04 to 78.57); moderate intensity, 34.53% (95% CI: 33.34–35.72); and high intensity, 34.06% (95% CI: 13.62–54.51).

Figure 1 shows the probability of LDL-C goal attainment (Fig. 1A: <3.36 mmol/L and Fig. 1B: <2.59 mmol/L) according to patterns of statin use and MPR. Patients in the low-intensity pattern were less likely to achieve the goal than were patients in the moderate-intensity pattern. The probability of goal attainment was higher in patients with MPR > 70% than in the total population, except for patients in the low-intensity pattern. However, patients in the high-intensity pattern were more likely to achieve goal attainment than all others, regardless of MPR (Fig. 1A and 1B). (See complete models in Supplementary Tables S7 and S12.)
Discussion

The present study showed 3 clinically relevant patterns of statin use, based on statin type, potency, and 1-year change, observed in a high-risk cardiovascular population without previous cardiovascular events. Correspondence analysis enabled the identification of natural patterns of statin use by type, potency, and changes to treatment made in a real-life scenario. Three clinical patterns were defined according to their capacity to achieve LDL-C reduction. Most of this high-risk population was started on moderate simvastatin therapy, which is in accordance with current guidelines and previous observational studies.

The most frequent pattern of statin use was simvastatin in moderate doses. The second most frequent was atorvastatin or simvastatin in high or moderate potency, and the third was lovastatin or pravastatin in low potency. The statin type and potency characteristics of the low-intensity pattern clearly differed from the other 2 patterns; therefore, it is not surprising that few differences were observed between the moderate- and high-intensity patterns. Furthermore, the criteria for prescribing one pattern or another did not seem to be related either to baseline LDL-C levels or to cardiovascular risk profile; goal attainment at 1 year was also similar between all the patterns. At 1-year follow-up, approximately half of the population remained with the same statin but at lower potency, and one-third had stopped taking statins, regardless of the intensity pattern. Statin change was uncommon, and the population in the moderate- and high-intensity patterns was more likely to achieve goal attainment than those in the low-intensity pattern.

We found that 16% to 26% of patients initiating statin therapy were already at goal. This might reflect uncertainty about patient management due to differences in cardiovascular risk definition and goal attainment of the different guidelines available at the time. Furthermore, moderate- and high-intensity patterns showed similar baseline LDL-C levels, and it seems that the high-intensity pattern was not initially prescribed. Patients in both the moderate- and high-intensity groups had baseline LDL-C levels of about 4.2 mmol/L, so that starting with moderate statin therapy to achieve an expected reduction of approximately 1.5 mmol/L (35%) could reach treatment goals in most cases in both groups. Nonetheless, strategies to enhance the alignment between initial pattern prescribed and LDL-C level or cardiovascular risk should be implemented to improve the percentage of individuals reaching therapeutic goals.

Likewise, some patients in the low-intensity group with a baseline LDL-C level of about 4 mmol/L achieved their goal attainment by starting with low-potency statins. However, a non-negligible proportion (31.62%) of individuals in low-intensity patterns with higher than 4.4 mmol/L LDL-C would likely need a higher intensity of treatment to achieve the minimum goal (3.36 mmol/L). Furthermore, only 58%, 63%, and 66% of patients were at goal in low-, moderate-, and high-intensity patterns, respectively, after 1 year of treatment. These percentages of goal attainment were in accordance with previous studies, which reported successes ranging from 20% to 60%, depending on statin type and regardless of cardiovascular risk. Thus, the patterns observed in real life did not achieve the expected

Table 2 Patterns of statin use resulting from the k-means algorithm

<table>
<thead>
<tr>
<th>Pattern variables</th>
<th>Low intensity = 826 (3.82%)</th>
<th>Moderate intensity = 15,565 (71.94%)</th>
<th>High intensity = 5245 (24.24%)</th>
<th>Total = 21,636</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of statin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simvastatin</td>
<td>0</td>
<td>92.08</td>
<td>38.02</td>
<td>75.46</td>
</tr>
<tr>
<td>Lovastatin</td>
<td>51.82</td>
<td>0</td>
<td>0</td>
<td>1.98</td>
</tr>
<tr>
<td>Pravastatin</td>
<td>37.89</td>
<td>5.71</td>
<td>1.64</td>
<td>5.95</td>
</tr>
<tr>
<td>Fluvastatin</td>
<td>10.29</td>
<td>2.20</td>
<td>1.05</td>
<td>2.23</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>0</td>
<td>0</td>
<td>56.51</td>
<td>13.70</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td>0</td>
<td>0</td>
<td>2.78</td>
<td>0.67</td>
</tr>
<tr>
<td>Potency</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>92.01</td>
<td>0</td>
<td>0</td>
<td>3.51</td>
</tr>
<tr>
<td>Moderate</td>
<td>7.99</td>
<td>99.88</td>
<td>22.65</td>
<td>77.65</td>
</tr>
<tr>
<td>High</td>
<td>0</td>
<td>0.12</td>
<td>74.64</td>
<td>18.18</td>
</tr>
<tr>
<td>Very high</td>
<td>0</td>
<td>0</td>
<td>2.71</td>
<td>0.66</td>
</tr>
<tr>
<td>1-y change</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No statin/no potency</td>
<td>3.75</td>
<td>3.31</td>
<td>1.58</td>
<td>2.91</td>
</tr>
<tr>
<td>No statin/1 potency</td>
<td>0</td>
<td>0</td>
<td>0.04</td>
<td>0.01</td>
</tr>
<tr>
<td>No statin/2 potency</td>
<td>42.74</td>
<td>64.16</td>
<td>50.94</td>
<td>60.14</td>
</tr>
<tr>
<td>Statin/no potency</td>
<td>9.81</td>
<td>2.81</td>
<td>0.31</td>
<td>2.47</td>
</tr>
<tr>
<td>Statin/1 potency</td>
<td>5.33</td>
<td>0.26</td>
<td>0.04</td>
<td>0.40</td>
</tr>
<tr>
<td>Statin/2 potency</td>
<td>0.97</td>
<td>0</td>
<td>16.93</td>
<td>4.14</td>
</tr>
<tr>
<td>Stopped taking statin</td>
<td>37.41</td>
<td>29.47</td>
<td>30.16</td>
<td>29.94</td>
</tr>
</tbody>
</table>

Numbers are column percentages.
reductions. Poor adherence has been pointed out in these studies as the main explanatory factor for goal attainment failure although some authors have suggested that genetics34,35 and lifestyle factors36 may play a role. In our study, one-third of patients had stopped taking statins at 1 year of treatment, which might also explain the lack of any major differences in goal attainment observed between patterns of statin use.

Other authors have suggested that poor adherence to treatment might be explained by variables related to physicians, behaviors, beliefs, unmeasured or perceived adverse effects, age, gender, presence of comorbidities, and costs.12,37,38,39 Importantly, patients with poor adherence are more likely to have a higher incidence of cardiovascular and cerebrovascular events and all-cause mortality than adherent patients.14–16,40 In addition, recent results showed that treatment adherence plays an important role in the cost-effectiveness of statin treatment in primary prevention,41 such that one of the first-line strategies to improve statin effectiveness recommended in primary care is to implement interventions focused on improving adherence that take into consideration patient, GP, and health system characteristics.42 Our results on goal attainment when only adherent (MPR.70%) patients were considered reinforced this recommendation.

On the other hand, patients in low-intensity patterns should be shifted to moderate patterns, as the probability of goal attainment is higher. Likewise, high-potency statins or

### Table 3 Baseline characteristics by statin use patterns

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Low</th>
<th>Moderate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>17.68</td>
<td>17.71</td>
<td>20.34</td>
</tr>
<tr>
<td>Obesity</td>
<td>45.40</td>
<td>42.04</td>
<td>45.34</td>
</tr>
<tr>
<td>Current smokers</td>
<td>49.27</td>
<td>52.57</td>
<td>51.52</td>
</tr>
<tr>
<td>High-risk alcohol intake</td>
<td>11.5</td>
<td>12.96</td>
<td>12.74</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>64.04</td>
<td>71.34</td>
<td>71.99</td>
</tr>
<tr>
<td>Hypertension</td>
<td>74.82</td>
<td>67.2</td>
<td>70.56</td>
</tr>
<tr>
<td>Diabetes</td>
<td>55.21</td>
<td>54.55</td>
<td>60.44</td>
</tr>
<tr>
<td>Age</td>
<td>64.83 (5.82)</td>
<td>63.35 (6.26)</td>
<td>62.90 (6.41)</td>
</tr>
<tr>
<td>BMI*</td>
<td>29.94 (4.65)</td>
<td>29.79 (4.80)</td>
<td>30.28 (5.04)</td>
</tr>
<tr>
<td>SBP*</td>
<td>144.02 (17.72)</td>
<td>143.71 (16.71)</td>
<td>144.26 (17.42)</td>
</tr>
<tr>
<td>DBP*</td>
<td>81.74 (11.44)</td>
<td>81.90 (10.50)</td>
<td>82.22 (10.89)</td>
</tr>
<tr>
<td>Triglycerides, mmol/L*</td>
<td>1.82 (1.32–2.60)</td>
<td>1.40 (1.03–1.97)</td>
<td>1.46 (1.08–2.00)</td>
</tr>
<tr>
<td>Glucose, mmol/L*</td>
<td>7.46 (2.94)</td>
<td>6.13 (2.18)</td>
<td>6.80 (2.58)</td>
</tr>
</tbody>
</table>

BMI, body mass index; CV, cardiovascular; DBP, diastolic blood pressure; SBP, systolic blood pressure.

Numbers are row percentages unless otherwise stated.

*Continuous variables are described as mean (standard deviation) or median (first quartile–third quartile).

### Table 4 Baseline, 1-year total cholesterol and low-density lipoprotein cholesterol (LDL-C) levels, and percentage of goal attainment in the total population and in patients with MPR > 70%

<table>
<thead>
<tr>
<th>Lipid profiles</th>
<th>Total population</th>
<th>MPR &gt; 70%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Total-C, mmol/L</td>
<td>6.10 (1.09)</td>
<td>6.46 (1.04)</td>
</tr>
<tr>
<td>Low &lt; 5.17 mmol/L</td>
<td>18.92</td>
<td>9.93</td>
</tr>
<tr>
<td>1-y Total-C&lt;sup&gt;+&lt;/sup&gt;</td>
<td>5.26 (1.06)</td>
<td>5.16 (1.09)</td>
</tr>
<tr>
<td>Low &lt; 5.17 mmol/L</td>
<td>48.69</td>
<td>54.13</td>
</tr>
<tr>
<td>HDL-C, mmol/L&lt;sup&gt;+&lt;/sup&gt;</td>
<td>1.24 (0.31)</td>
<td>1.30 (0.36)</td>
</tr>
<tr>
<td>Low &lt; 4.22 mmol/L</td>
<td>3.93 (1.00)</td>
<td>4.22 (0.96)</td>
</tr>
<tr>
<td>LDL-C &lt; 3.36 mmol/L</td>
<td>26.5</td>
<td>16.92</td>
</tr>
<tr>
<td>LDL-C &lt; 2.59 mmol/L</td>
<td>7.78</td>
<td>3.98</td>
</tr>
<tr>
<td>1-y LDL-C&lt;sup&gt;+&lt;/sup&gt;</td>
<td>3.18 (1.06)</td>
<td>3.08 (1.09)</td>
</tr>
<tr>
<td>LDL-C &lt; 3.36 mmol/L</td>
<td>57.95</td>
<td>63.16</td>
</tr>
<tr>
<td>LDL-C &lt; 2.59 mmol/L</td>
<td>28.12</td>
<td>33.46</td>
</tr>
</tbody>
</table>

HDL-C, high-density lipoprotein cholesterol; MPR, Medical Possession Ratio; Total-C, total cholesterol.

Numbers are percentages unless otherwise stated.

*Continuous variables are described as mean (standard deviation).
more intensive treatment with ezetimibe or other lipid-lowering drugs should be recommended to patients who require a larger LDL-C reduction to reach therapeutic targets, patients with good treatment adherence who do not achieve the goal with a moderate pattern of therapy or patients at very high risk.13,17

**Strengths and limitations**

The access to high-quality, internally validated electronic medical records provided a large sample size, warranted high external validity,43 and reflected real-life clinical conditions. Clinical trials usually include a very definite type of individual with specific characteristics, while at the same time excluding specific populations such as diabetics, women, or the very elderly.44,45

In clinical trials, effectiveness is also related to very strict control of treatment adherence and persistence.46 Observational studies also can be used for monitoring long-term adherence.47 Whenever high persistence is taken into account, observational studies provide results similar to clinical trials on overall mortality and non-fatal cardiovascular reduction.48,14 These very specific patterns of use in clinical trials do not accurately represent real-life clinical conditions.14–16

Low data quality could result in misclassification. In this study, both the presence of cardiovascular risk factors and outcomes were previously validated.20 Moreover, data on statin exposure were obtained from the official records of community pharmacies that invoice the National Health Service.

To avoid selection bias, where the population with missing data somehow differs from those with complete data, we imputed the missing values for continuous variables instead of excluding records with missing data. In our study, the characteristics of the complete-case analysis did not differ from imputed data.

In addition to these strengths, we acknowledge several study limitations. First, individuals were categorized by patterns according to a proximity criterion using the k-means algorithm in the correspondence analysis; therefore, groups could differ slightly depending on the initial seeds. Nonetheless, the patterns remained unchanged after using multiple seeds and iterations. Second, we could not measure some potential confounders such as physical activity and diet and could not evaluate the reasons for the GP’s therapeutic choices. Third, MPR was assessed on a monthly basis, so, we could not accurately estimate adherence. Fourth, non–HDL-C and apolipoprotein B together with LDL-C have been shown to be adequate target for risk reduction. However, non–HDL-C and apolipoprotein B are not available in SIDIAP as they are not routinely collected in laboratory tests. Fifth, the low percentage of women is a shortcoming. However, the proportion of women in primary prevention of the study may be representative of our general population considering that the percentage of women at high risk (>10%) is very low in our context.24

Finally, the study focused only on patterns of statin use; consequently, goal attainment in patients with combined treatments was not analyzed.

In conclusion, 3 real-life patterns of statin use were identified according to statin type, potency, and 1-year change in a high-risk population from a community setting. The prescription patterns were not related to baseline LDL levels. Lipid management strategies in primary care should be focused on enhancing the alignment between initial pattern prescribed and LDL-C level or cardiovascular risk and improving treatment adherence, including a consideration of the characteristics of the patients, GPs and health systems involved. Finally, patients started at low-potency statins should be switched to a moderate potency because the probability of goal attainment is higher. Likewise, more intensive therapies and increased dose should be considered.

**Figure 1**  Probability of low-density lipoprotein cholesterol (LDL-C) goal attainment (A: LDL-C < 3.36 mmol/L and B: LDL-C < 2.59 mmol/L) according to patterns of statin use and MPR. MPR, Medical Possession Ratio; OR, odds ratio.
in patients who require a larger LDL-C reduction to reach therapeutic targets, patients with good treatment adherence who do not achieve the goal with a moderate pattern of therapy, or patients at very high risk.

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Maria García-Gil and Rafel Ramos declare having done design and statistical consultancy for Amgen and Ferrer, unrelated to the present study.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jacl.2015.10.007.

References


