Prevalence of persistent lipid abnormalities in statin-treated patients: Belgian results of the Dyslipidaemia International Study (DYSIS)

D. Devroey,1 R. P. Radermecker,2 B. J. Van der Schueren,3 B. Torbeyns,4 R. J. Jaken4

SUMMARY

Aim: A substantial number of cardiovascular events are not prevented by statin therapy, which is still regarded as the first-line therapy for hyperlipidaemia. Insights into the prevalence of lipid abnormalities of statin-treated patients in Belgium are lacking and may shed light on an unmet medical need for optimal use of current lipid-lowering therapies. This study aims to assess the prevalence and types of persistent lipid abnormalities in patients receiving statin therapy in a real-life primary care setting in Belgium. Methods: This cross-sectional cohort study was designed to estimate the prevalence of specific lipid abnormalities in statin-treated patients in Belgium. Total cholesterol, low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides were recorded from the patients’ medical record. Patient's total cardiovascular risk and corresponding lipid treatment goals were defined based on the recent European Society of Cardiology/European Atherosclerosis Society recommendations. Results: Overall, 56.2% of the statin-treated patients were not at goal for LDL-C. Low HDL-C (< 40 mg dl⁻¹ in men, < 45 mg dl⁻¹ in women) and elevated triglycerides (≥ 150 mg dl⁻¹) were seen in 16.3% and 29.0% of patients, respectively. Very high-risk patients were more likely to have LDL-C not at goal (71.4% of them), while 60.0% of high-risk patients and 34.1% of moderate-risk patients were not at goal for LDL-C. Of use ezetimibe (10 mg) was strongly associated with meeting LDL-C goals (OR 16.9, p < 0.0001). Conclusion: In Belgium, lipid abnormalities remained highly prevalent despite statin treatment, with more than half of all patients not reaching their LDL-C treatment goal. This finding clearly indicates that more aggressive lipid-lowering treatment is required in clinical daily practice to achieve the goals of the current guidelines.

Introduction

Cardiovascular disease (CVD) is a leading cause of mortality and will continue to be a major cause of morbidity and mortality, as the prevalence of obesity, diabetes and other risk factors continue to grow (1,2). The cardiovascular-related mortality is largely influenced by several modifiable risk factors such as smoking, sedentary lifestyle and dyslipidaemia (3–5).

Statins (HMG-CoA reductase inhibitors) have greatly advanced treatment of dyslipidaemia; for every 39 mg dl⁻¹ reduction in low-density lipoprotein cholesterol (LDL-C), the risk of major cardiovascular events is decreased by 21% (3). Therefore, statins are the first-line lipid-lowering therapy in patients at risk of CVD (6). However, a substantial number of clinical events are not prevented despite statin therapy (7–9), which may be explained by residual abnormalities in LDL-C, high-density lipoprotein cholesterol (HDL-C) and triglycerides (9,10). Despite the efficacy of current lipid-lowering therapies, several studies have questioned whether they are used in an optimal way. Various cross-sectional studies have assessed the prevalence of lipid abnormalities in different populations at risk. However, these studies have substantial differences in methodologies and definitions of target groups. Limited information is available on the prevalence of persistent dyslipidaemia in patients treated with statins in a real-life setting.
Various cross-sectional studies have assessed the prevalence of lipid abnormalities in different populations at risk (13–16). However, these studies have substantial differences in methodologies and definitions of target groups. Limited information is available on the prevalence of persistent dyslipidaemia in patients treated with statins in a real-life setting.

The objective of the Belgian part of the Dyslipidaemia International Study (DYSIS) was to assess the prevalence and types of persistent lipid abnormalities in patients receiving statin therapy in a real-life setting in Belgium, based on the most recent European Society of Cardiology and the European Atherosclerosis Society (ESC/EAS) Guidelines for the management of dyslipidaemias (6).

**Methods**

**Study design and population**

The DYSIS-Belgium study is a cross-sectional cohort study designed to estimate the prevalence of different types of lipid abnormalities in statin-treated patients in Belgium. Outpatients managed by their primary care physician (PCP) were enrolled in the study if they: (i) were on statin therapy for ≥ 3 months at the time of assessment visits; (ii) were aged ≥ 45 years; and (iii) had at least one fasting lipid parameter available in their medical chart while receiving statin therapy. Exclusion criteria included active participation in a clinical study. Each physician was allowed to include up to 12 patients. A representative sample of primary and secondary care patients were enrolled based on the setting in which patients with dyslipidaemia are usually treated. In Belgium, treatment of dyslipidaemia is being handled by essentially all general practitioners and therefore all physicians included in the study were general practitioners. The Ethical Committee of the University Hospital Brussels – Vrije Universiteit Brussel approved the protocol. All patients provided written informed consent prior to participation.

**Data collection**

All data were collected from clinical examination and medical charts from single outpatient visits between September 2011 and March 2012. Selection bias was reduced by enrolling patients from consecutive visits irrespective of the visit’s cause.

Data were submitted by paper or electronic case report forms in local language to a central database, and held and managed at the Institut für Herzinfarktforschung Ludwigshafen at the university of Heidelberg, Germany. A number of sites were visited by the study monitor for source data verification.

Patient demographic data, serum lipid parameters from the last test available within the previous 12 months for total cholesterol, LDL-C, HDL-C and triglycerides were recorded. Only results from patients who had been on statin therapy for ≥ 3 months were included in the analyses.

Specific patient-related lipid targets and the relevance of the different lipid parameters for the physicians were also recorded. The ESC/EAS recommendations were used to classify a patient’s risk and to define the LDL-C goal as well as abnormalities of HDL-C and triglycerides (6). Patients at very high risk were defined as those with pre-existing CVD, diabetes, chronic kidney disease (glomerular filtration rate < 60 mL min⁻¹ 1.73 m⁻²) and/or Systematic COrony Risk Evaluation (SCORE) ≥ 10%. LDL-C treatment goal for these patients was < 70 mg dl⁻¹ or ≥ 50% LDL-C reduction if target goal cannot be reached. High-risk patients were those with markedly elevated single risk factors such as familial dyslipidaemias and severe hypertension and/or SCORE ≥ 5% and < 10%. LDL-C treatment goal for these patients was < 100 mg dl⁻¹. Moderate-risk patients were defined as those with a SCORE between ≥ 1% and < 5%. Many middle-aged subjects belong to this risk category. Their corresponding LDL-C treatment goal was < 115 mg dl⁻¹.

Clinical variables collected were demographic and lifestyle information, anthropometric information, medical history, blood pressure and serologic data (fasting plasma glucose, haemoglobin A1c, lipids). Information collected on lipid and cardiovascular therapies included the name and daily dose of the current statin, and whether the primary reason for use was hypercholesterolaemia, as well as the name and daily dose of the statin in use at the time of the last blood test. Statin dose was categorised using a potency calculation described elsewhere (17,18). In brief, the potency of different statins was benchmarked against six simvastatin doses: 5, 10, 20, 40, 80 and 160 mg day⁻¹. Each statin dose was given a potency rating, ranging from 1 (5 mg day⁻¹) to 6 (160 mg day⁻¹). Use of other lipid-modifying therapies (cholesterol absorption inhibitor, bile acid sequesterants, fibrates, nicotinic acid) at visit and before the previous blood test was recorded. Furthermore, treatments with antihypertensives, antidiabetics or antiplatelets were also recorded.

**Statistical analysis**

Categorical variables are presented as absolute numbers and percentages. Continuous variables are reported as means with standard deviations or medians with 25th and 75th percentiles (interquartile range) as appropriate.
Multiple logistic regression analysis was performed to detect factors independently associated with LDL-C, HDL-C, and triglyceride abnormalities. Variables included in the model were: age; sex; first grade family history of premature CVD; current smoker; sedentary lifestyle; alcohol consumption > 2 units per week; body mass index (BMI) categorised as ≥ 30 kg m⁻² (obesity); waist circumference > 102 cm in men or > 88 cm in women; hypertension; diabetes mellitus; ischaemic heart disease; cerebrovascular disease; heart failure; peripheral artery disease; blood pressure ≥ 140/90 mmHg; 20–40 mg day⁻¹ vs. 10 mg day⁻¹ simvastatin equivalent; ≥ 80 mg day⁻¹ vs. 10 mg day⁻¹ simvastatin equivalent; ezetimibe; and, physician’s specialty. A stepwise backward selection (alpha = 0.05) was used to identify parameters associated with dependent variables. All statistical comparisons were two-tailed, and p < 0.05 was considered statistically significant. All analyses were performed with the Statistical Analysing System, version 9.1 (SAS Institute Inc., Cary, North Carolina). Patients who did not have the appropriate lipid parameters were not included in the analyses.

Results

Patients and treatment
In total, 941 patients were recruited by 121 general practitioners (GP) around Belgium (distribution of GP’s across Belgium was 57.7% in Flanders, 35.0% in Wallonia and 7.3% in Brussels). Patient characteristics are presented in Table 1. Mean age of all patients was 67.4 ± 9.9 years. Sixty-one per cent of the patients were at very high risk of cardiovascular complications, 37.6% had pre-existing CVD, 54.0% had metabolic syndrome and 31.0% were diabetic.

The most frequently used statin was simvastatin (44.8%), followed by atorvastatin (25.8%) and rosuvastatin (21.0%). Notably, only 11.6% of patients received additional lipid therapies to statins. Ezetimibe (10 mg) was used by 7.2% of all patients; 3.3% received it as a combination tablet with statin while 3.9% was using ezetimibe and a statin as two separate tablets (data not shown).

Most of the patients were using lower dose statin potencies (potency 1–4, equivalent to simvastatin 5–40 mg day⁻¹) compared with higher dose statin

| Table 1 Patient characteristics, risk categories and lipid parameters |
|---------------------------------------------------------------|
| All patients (N = 941) | Men (N = 557) | Women (N = 379) |
|------------------------|--------------|-----------------|
| Age (years) [mean ± SD] | 67.4 ± 9.9   | 66.5 ± 10.2     | 68.7 ± 9.4  |
| Caucasian (%)          | 99.5         | 99.8            | 99.1       |
| Family Hx of premature CHD (%) | 32.8 | 34.2 | 30.2 |
| Current smokers (%)    | 11.8         | 14.6            | 7.9        |
| Hypertension (%)       | 70.3         | 70.0            | 70.6       |
| Systolic BP (mmHg) [mean ± SD] | 131.9 ± 13.6 | 131.8 ± 13.3 | 132.7 ± 14.2 |
| Diastolic BP (mmHg) [mean ± SD] | 78.0 ± 7.9   | 78.4 ± 7.8      | 77.5 ± 7.9 |
| Waist circumference (cm) [mean ± SD] | 99.7 ± 14.4 | 103.7 ± 13.3 | 93.8 ± 14.0 |
| BMI (kg m⁻²) [mean ± SD] | 28.2 ± 5.0  | 28.4 ± 4.5      | 28.0 ± 5.7 |
| BMI>30 kg m⁻² (%)       | 28.9         | 28.4            | 30.1       |
| CVD (%)                | 37.6         | 45.0            | 26.7       |
| Diabetes mellitus (%)  | 31.0         | 34.9            | 25.1       |
| Metabolic syndrome (IDF) (%) | 54.0 | 56.6 | 50.5 |
| **ESC risk level (2011)** |
| Very high-risk patient (%) | 61.0 | 69.1 | 48.7 |
| High-risk patient (%)   | 9.3          | 8.3             | 10.8       |
| Moderate-risk patient (%) | 20.0 | 14.7 | 28.0 |
| Low-risk patient (%)    | 9.8          | 7.9             | 12.4       |
| LDL-C (mg dl⁻¹) [mean ± SD] | 99.4 ± 32.1 | 96.0 ± 30.3 | 104.1 ± 32.8 |
| HDL-C (mg dl⁻¹) [mean ± SD] | 56.3 ± 17.4 | 52.4 ± 16.2 | 62.1 ± 17.4 |
| Total cholesterol (mg dl⁻¹) [mean ± SD] | 181.5 ± 36.6 | 175.2 ± 33.9 | 190.4 ± 37.4 |
| Triglycerides (mg dl⁻¹) [median (IQR)] | 117.0 (86.0–161.0) | 119.5 (88.0–165.5) | 113.5 (85.0–154.0) |
| Fasting plasma glucose (mg dl⁻¹) [median (IQR)] | 100.0 (90.0–116.0) | 102.5 (92.0–120.0) | 96.0 (88.0–108.0) |
| HbA1c [%] in diabetics [median (IQR)] | 6.7 (6.2–7.3) | 6.7 (6.2–7.4) | 6.7 (6.2–7.3) |

CHD, coronary heart disease; BP, blood pressure; BMI, Body mass index; CVD, cardiovascular disease; DM, diabetes mellitus; IDF, International Diabetes Federation; Very high risk = pre-existing CVD, diabetes, chronic kidney disease (glomerular filtration rate < 60 ml min⁻¹ 1.73 m⁻²) and/or SCORE ≥ 10%. High risk = markedly elevated single risk factors and/or SCORE ≥ 5% and < 10. Moderate risk = SCORE between ≥ 1% and < 5%. Low risk = SCORE < 1%.
potencies (potency 5–6, equivalent to simvastatin 80–160 mg day\(^{-1}\)) (Figure 1). More specifically, in non-very high risk patients, the most often used statin dose potency was 3 (44.4%), while very high-risk patients were mostly treated with statin dose potency 4 (49.9%) (Figure 1).

### Lipid parameters and CVD risk

The mean LDL-C in all patients was 99.4 ± 32.1 mg dl\(^{-1}\). More than half of all patients (56.2%) had LDL-C not at goal according to the 2011 ESC/EAS guidelines. Complete results of serum lipids are given in Table 2. Low HDL-C (< 40 mg dl\(^{-1}\) in men and < 45 mg dl\(^{-1}\) in women) and elevated triglycerides (> 150 mg dl\(^{-1}\)) were seen in 16.3% and 29.0% of patients, respectively. More patients at very high risk had LDL-C not at goal (71.4% of them), while 60.0% of high-risk patients and 34.1% of moderate-risk patients were not at goal for LDL-C.

A high percentage of both diabetic patients (73.8%) and patients with previous CVD (71.2%) analysed separately had LDL-C not at goal (≥ 70 mg dl\(^{-1}\)). A large proportion of patients with a SCORE of more than 10% (without patients with prior CVD and diabetes) were not at goal for LDL-C (88.2%) (Table 3).

Examination of the distribution of serum lipid abnormalities revealed that abnormally high LDL-C was the most frequent lipid anomaly, either alone (34.3%) or in combination with elevated triglycerides (17.8%), low HDL-C (9.6%) or both (5.5%; Figure 2A). Elevated fasting triglycerides were most frequent with elevated LDL-C, while low HDL-C was seen most often with the combination of elevated LDL-C and elevated triglycerides.

More specifically in very high-risk patients, only 16.4% displayed no lipid abnormalities, while 42.7% had only abnormal LDL-C (Figure 2B). In non-very high risk patients, almost half of these patients

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**Figure 1** Statin dose potency according to patients' risk status. *Statin dose potency 1 is equivalent to Simvastatin 5 mg day\(^{-1}\), potency 2 is equivalent to Simvastatin 10 mg day\(^{-1}\), potency 3 is equivalent to Simvastatin 20 mg day\(^{-1}\), potency 4 is equivalent to Simvastatin 40 mg day\(^{-1}\), potency 5 is equivalent to Simvastatin 80 mg day\(^{-1}\) and potency 6 is equivalent to Simvastatin 80 mg day\(^{-1}\).

**Table 2** Proportion of patients whose lipid levels were not at goal or abnormal (%)

|                         | All patients (N = 872) | Very high risk* (N = 531) | High risk (N = 85) | Moderate risk (N = 176) | Low risk (N = 80) |
|-------------------------|------------------------|---------------------------|-------------------|------------------------|------------------|
| LDL-C not at goal [%]†  | 56.2                   | 71.4                      | 60.0              | 34.1                   | 0.0              |
| Low HDL-C               |                         |                           |                   |                        |                  |
| (< 40 [men]/45 [women] mg dl\(^{-1}\)) [%] | 16.3                   | 21.1                      | 4.7               | 10.2                   | 10.0             |
| Elevated TG             |                         |                           |                   |                        |                  |
| (> 150 mg dl\(^{-1}\)) [%] | 29.0                   | 31.3                      | 31.8              | 25.6                   | 18.8             |

*Very High risk = CVD, Diabetes, and/or SCORE risk ≥10% (Chronic Kidney disease was not documented in DYSIS).
†LDL ≥ 115 mg dl\(^{-1}\) in patients with SCORE risk 1–4%, LDL ≥ 100 mg dl\(^{-1}\) in patients with SCORE risk 5–9%, LDL ≥ 70 mg dl\(^{-1}\) in patients with CVD, DM, and/or SCORE risk ≥ 10%.
(48.7%) had no lipid abnormalities but 21.1% of them had LDL-C abnormalities (Figure 2C).

**Multiple logistic regression analysis**

Age ≥ 70 years, alcohol consumption of > 2 units per week, diabetes, ischaemic heart disease and blood pressure ≥ 140/90 mmHg were all positively associated with LDL-C abnormalities (Table 4). No use of ezetimibe was very strongly, positively associated with LDL-C abnormalities (OR 16.9, p < 0.0001).

Only ischaemic heart disease and diabetes were positively associated with low HDL-C. Current

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**Table 3** Proportion of specific patients within the very high risk category whose lipid levels were not at goal or abnormal (%)

| Condition | CVD + DM (N = 121) | CVD (w/o DM) (N = 208) | DM (w/o CVD) (N = 149) | SCORE > 10% (N = 51) |
|-----------|-------------------|------------------------|------------------------|-----------------------|
| LDL-C > 70 mg dl⁻¹ and LDL-reduction < 50% [%] | 61.2 | 71.2 | 73.8 | 88.2 |
| Low HDL-C (< 40 [men] / 45 [women] mg dl⁻¹) [%] | 27.3 | 17.8 | 26.2 | 3.9 |
| Elevated TG (> 150 mg dl⁻¹) [%] | 36.4 | 30.8 | 34.2 | 13.7 |

**Figure 2** Distribution of single and multiple combined lipid abnormalities. (A) all patients, (B) very high-risk patients (CVD, Diabetes and/or SCORE ≥ 10%), and (C) non-very high risk patients (SCORE < 10%). ESC, European Society of Cardiology; CVD, cardiovascular disease.
smoking, sedentary lifestyle, large waist circumference and hypertension were positively associated with elevated triglycerides. On the contrary, age ≥ 70 years was strongly and negatively associated with elevated triglycerides (Table 4).

Diabetes was the only factor positively associated with LDL-C not at goal in combination with low HDL-C and elevated triglycerides (OR 4.83, p < 0.0001).

**Discussion**

In this Belgian observational study, we investigated serum lipid goal achievement in statin-treated patients stratified by their cardiovascular risk according to the recent ESC/EAS guidelines (6). Here, we have shown that only about 30% of all patients in this study had no residual lipid abnormalities. Given that the patients in this study were receiving statin therapy, it was disappointing that LDL-C still remained elevated in more than half of the patients. Moreover, a large number of patients had abnormal HDL-C and/or triglycerides, either alone or in combination with other lipid parameters.

A number of cross-sectional epidemiologic studies have also investigated the prevalence of lipid abnormalities and statin use (12,15,16,19–24). These studies, however, were limited to specific populations, focused on specific lipid parameters such as LDL-C or HDL-C, or had mixed patients with different lipid-lowering therapies. With the current observational study, we analysed the prevalence of residual dyslipidaemia in statin-treated patients in both primary and secondary prevention in Belgium. To our knowledge, this is the first such study in Belgium focused solely on statin users in a real-life setting.

Several parameters were shown to be clearly associated with high LDL-C. For example, ischaemic heart disease and diabetes were associated with LDL-C not at goal. This illustrates that especially these very high-risk patients need better or more powerful treatment to obtain their corresponding target levels. On the contrary, add-on therapy with ezetimibe treatment was very strongly associated with low LDL-C.

Serum lipid goal achievement in patients included in this study was based on the most recent ESC/EAS guidelines for the management of dyslipidaemias (6). These guidelines were published around June 2011, while this study started recruiting patients in October 2011. The implementation of recently published guidelines may take some time to be implemented into clinical practice. This observation can be reinforced by the fact that following analysis of the

### Table 4 Multivariate analysis for predictors of therapeutic goal achievement

|                  | LDL-C not at goal* (70/100/115 mg dl⁻¹) OR (95% CI) p-value* | Low HDL-C* (< 40 (m)/45 (w) mg dl⁻¹) OR (95% CI) p-value* | Elevated TG* (> 150 mg dl⁻¹) OR (95% CI) p-value* | LDL-C not at goal and low HDL-C and elevated TG* OR (95% CI) p-value* |
|------------------|---------------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------|---------------------------------------------------------------|
| Age ≥ 70 years   | 2.090 (1.47–2.98) < 0.0001                                    | n.s.                                                     | 0.506 (0.35–0.74) 0.0004                         | n.s.                                                         |
| Current smoker   | n.s.                                                          | n.s.                                                     | 1.045 (1.05–2.96) 0.0335                          | n.s.                                                         |
| Sedentary lifestyle| n.s.                                                        | n.s.                                                     | 1.458 (1.01–2.1) 0.0437                           | n.s.                                                         |
| Alcohol consumption > 2 units per week | n.s.                                                        | 1.035 (1.03–2.07)                                    | n.s.                                                     | n.s.                                                         |
| Waist circumference > 102 (m)/88 cm (w) | n.s.                                                        | n.s.                                                     | n.s.                                                     | n.s.                                                         |
| Hypertension     | n.s.                                                          | n.s.                                                     | n.s.                                                     | n.s.                                                         |
| Diabetes mellitus| 1.467 (1.00–2.15) 0.0496                                    | 3.077 (1.99–4.76) < 0.0001                             | n.s.                                                     | n.s.                                                         |
| Ischaemic heart disease | 2.026 (1.35–3.05) 0.0007                                    | 1.637 (1.04–2.59) 0.0352                             | n.s.                                                     | n.s.                                                         |
| BP >140/90 mmHg (systolic/diastolic) | 1.680 (1.16–2.43) 0.0061                                    | n.s.                                                     | n.s.                                                     | n.s.                                                         |
| No ezetimibe     | 16.9 (6.25–50) < 0.0001                                      | n.s.                                                     | n.s.                                                     | n.s.                                                         |

*Models contained the following variables: age, sex, 1st grade family history of premature CVD, current smoker, sedentary lifestyle, alcohol consumption > 2 units per week, BMI ≥ 30 kg m⁻² (obesity), waist circumference > 102 cm in men/88 cm in women, hypertension, diabetes mellitus, ischaemic heart disease, cerebrovascular disease, heart failure, peripheral artery disease, BP > 140/90 mmHg (systolic/diastolic), 20–40 vs. 10 mg day⁻¹ simvastatin equivalent, ≥ 80 vs. 10 mg day⁻¹ simvastatin equivalent; Ezetimibe, Backward selection (alpha = 0.05) was done. m, men; w, women; BP, blood pressure; Card, cardiologist; Endo, endocrinologist; Dia, diabetologist; Int, internist; Oth, other specialty; n.s., not significant (p > 0.05); OR, odds ratio; CI, confidence interval. Factors with odds ratios (OR) > 1 indicate significant positive association with the lipid anomaly at the top of each column. Factors with OR < 1 indicate significant negative association with the corresponding lipid anomaly. Non-significant associations are represented by n.s.
current dataset based on the previous ESC guidelines of 2007, still nearly 40% of all patients had LDL-C above their corresponding target (data not shown).

Thus, with this study we have shown that real-life daily practice is not yet in keeping with what is recommended in the guidelines. This, again, highlights the importance of implementation programs because it has been shown that disease outcome may be favourably influenced by the thorough application of clinical recommendations (6).

Lipid-lowering therapies
The average statin dose potency was 3–4 (simvastatin equivalent 20–40 mg day\(^{-1}\)). The large number of statin-treated patients with residual dyslipidaemia may suggest the need for increasing (i) the use of higher doses of statins or (ii) the use of combination therapy. Earlier statin trials have concluded that the proportional reduction in risk is mainly achieved by the absolute reduction in LDL-C, and that more intensive LDL-reduction yields further reductions in risk (3,25). Currently, both the use of higher doses of statins or combination therapy are well-validated strategies to further reduce LDL.

Multivariate analysis did not indicate higher statin dose to be associated with target achievement for LDL-C. Moreover, it is well-known that high dose statins are associated with an increased risk of myopathy (26). More importantly, a recent meta-analysis of data from 5 statin trials has shown that intensive-dose statin therapy was associated with an increased risk of new-onset diabetes compared with moderate-dose therapy (27).

In this study, use of alternative therapies combined with statins was low. Despite the small number of patients treated with ezetimibe (\(n = 68\)), multivariate analysis indicated that treatment with ezetimibe (10 mg) was strongly associated with LDL-C goal achievement. However, the question remains whether an additional LDL-C lowering using ezetimibe also results in a reduction of cardiovascular events (28,29), which might also partly explain the low number of patients on ezetimibe in this study. The results of the ongoing IMProved Reduction of Outcomes: Vytorin Efficacy International Trial (IMPROVE-IT) comparing ezetimibe plus simvastatin with simvastatin monotherapy with regard to CVD outcomes after acute coronary syndromes should further elucidate the effect of ezetimibe on CVD events (30).

Lipid levels and cardiovascular risk
Almost three-quarters of all patients included by the 121 primary care physicians had residual lipid abnormalities despite statin therapy, and more than half had elevated LDL-C, either as a single anomaly or in combination with either low HDL-C and/or elevated triglycerides.

The analysis of the statin dose potencies according to the patients’ risk status showed that very high-risk patients were using more potent statins when compared with non-very high risk statins. Despite their more intense treatment, a large number of them were not at goal for their LDL-C. More specifically, of all diabetic patients in this study, nearly 74% of them had LDL-C \(\geq 70\) mg d\(^{-1}\). This finding was also reinforced by the fact that the presence of diabetes was strongly associated with abnormal LDL-C in the association analysis. Moreover, diabetes was the only factor independently associated with LDL-C not at goal in combination with low HDL-C and elevated triglycerides. This confirms the mixed type of dyslipidaemia often seen in this specific population.

Limitations
Some limitations of our study should be mentioned. Firstly, this was a cross-sectional, observational study without any long-term outcome evaluations. Secondly, data analyses were based on patients’ medical records. No blood sample collection or central evaluation of the lipid parameters at the time of visit was performed so measurement of lipid parameters may not be standardised. This, however, truly reflected the clinical practice. Primary care physicians willing to participate in this study were recruited, which may result in better outcomes as these physicians were more motivated to treat their dyslipidaemia patients. Finally, our study did not collect data on the full patient lifestyle, including nutritional habits, in-depth genetic predisposition to CVD (although family history was assessed), or treatment compliance. These variables also have some impact on the patients’ lipid levels, so there is potential for residual confounding because of these unmeasured or mis-measured variables.

Conclusions
In this Belgian observational study, lipid abnormalities were highly prevalent in statin-treated patients, with only about 30% of patients having no residual lipid abnormalities. More than half of all patients had LDL-C not at goal, either as the only lipid abnormality or combined with either abnormal HDL-C or triglycerides or both. Most of the patients in this study were very high-risk patients. Within this patient risk group, more than 70% had abnormal LDL-C despite the fact that they were receiving higher statin doses compared with non-very high risk patients. This finding clearly indicates that more
aggressive lipid-lowering treatment is required in clinical daily practice to achieve the goals of the current guidelines.

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Author contributions

All authors contributed to the data analysis/interpretation, drafting, critical revision and approval of this trial.

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