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Lipid-lowering Therapy and Goal Achievement in High-risk Patients from French General Practice

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Abbreviations: ARB = angiotensin II receptor blocker; ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CAD = coronary artery disease; CHD = coronary heart disease; CHF = coronary heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; EAS = European Atherosclerosis Society; EMR = electronic medical record; ESC = European Society of Cardiology; HAS = Haute Autorité de Santé; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering therapy; MI = myocardial infarction; NICE = National Institute for Health and Care Excellence; PAD = peripheral arterial disease; PCSK9 = proprotein convertase subtilisin/kexin type 9; TIA = transient ischemic attack.

Conflict of interest statement

JF has received grants and speaker's fees from Amgen, Merck, and Sanofi, and speaker's fees from AstraZeneca. KG was an employee of Sanofi at the time of this study. SRI is an employee of Regeneron Pharmaceuticals, Inc. DA was an employee of IQVIA at the time of this study. DLS has received modest consultant/advisory fees from Sanofi and Regeneron Pharmaceuticals, Inc.

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JF was involved with the design of the study, interpretation of data and critical review of drafts. KG was involved with the design of the study, interpretation of data, and critical review of drafts. SRI was involved with the design of the study, interpretation of data, and critical review of drafts. DA was involved with the design of the study, acquisition, analysis and interpretation of data, and critical review of drafts. DLS was involved with the design of the study, interpretation of data, and critical review of drafts. All authors provided final approval of the submitted manuscript.

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ABSTRACT

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Purpose: To summarize lipid-lowering therapy (LLT) usage patterns and achievement of guideline-identified lipid goals in a 2015 general practice cohort of French patients with atherosclerotic cardiovascular disease (ASCVD) and/or diabetes mellitus (DM).

Methods: From the IMS Health Real-World Data database, patients aged ≥ 18 years were classified hierarchically into mutually exclusive categories of ASCVD subgroups and DM. LLT use and lipid goal achievement were assessed on the date of lipid measurement. The data were compared to previously published results of LLT use and lipid goal achievement in a 2014 UK population.

Findings: Of 32,924 patients meeting the inclusion criteria, only 47.5% were prescribed a statin as of the index date. Hierarchically, the highest rates of use of any statin (73.3%) and high-intensity statin (43.3%) were among patients with recent acute coronary syndrome; rates in DM without ASCVD were 38.7% and 2.3%, respectively. Overall, achievement of low-density lipoprotein cholesterol (LDL-C) < 1.8 mmol/l (< 70 mg/dl) was only 13.9% for patients with ASCVD and 10.7% with DM. Relative to a 2014 UK population, the 2015 French cohort (data re-analyzed according to the UK statin categorization) were prescribed “high-dose statins” less frequently (31.4% vs 20.9%, and 18.7% vs 7.2%, for ASCVD and DM, respectively). Similarly, the proportion of patients with high-dose statins achieving LDL-C < 1.8 mmol/l was higher in the 2014 UK than the 2015 French population (37.3% vs 22.2%, and 36.4% vs 20.3%, for ASCVD and DM, respectively).

Implications: In a large cohort of French patients with ASCVD and/or DM, LLT usage and LDL-C goal achievement were suboptimal relative to current guidelines.

Key words: lipoprotein and hyperlipidemia, coronary artery disease, acute coronary syndrome, cardiac risk factors and prevention

Highlights

- In this study, 47.5% of French patients with ASCVD or DM received statin therapy
- Only 13.9% with ASCVD and 10.7% with DM achieved LDL-C <1.8 mmol/l
- Fewer French vs UK patients received high-dose statin and reached LDL-C <1.8 mmol/l
- Findings suggest suboptimal statin utilization and LDL-C achievement in France

Introduction

In France, cardiovascular disease is the second most common cause of mortality after cancer.¹ Across the nation, ischemic heart disease and stroke account for 12% of all deaths.² Approximately 80,000–100,000 hospitalizations annually are due to acute coronary syndromes (ACS).³

Treatment guidelines for atherogenic cholesterol, the primary modifiable risk factor for adverse atherosclerotic outcomes, include those from the European Society of Cardiology (ESC)/European Atherosclerosis Society (EAS)⁴ and the French National Authority for Health (Haute Autorité de Santé [HAS]).^{5, 6} As of 2006–2007,⁷ the vast majority of high-risk patients defined by either guideline had not achieved the recommended low-density lipoprotein cholesterol (LDL-C) goals, largely due to insufficient treatment with lipid-lowering therapy (LLT).⁸

There is a paucity of data on current atherogenic cholesterol management in patients at the highest risk of atherosclerotic events: those with established atherosclerotic cardiovascular disease (ASCVD) and/or diabetes mellitus (DM). The objective of this study was to evaluate utilization of LLT medications as well as LDL-C and non-high-density lipoprotein cholesterol (non-HDL-C) goal achievement in these patients using a 2015 real-world, generalizable French cohort.

Methods

Study population

This was a retrospective, cross-sectional, observational study using electronic medical records (EMRs) from the IMS Health Real-World Data database in France (formerly known as the Longitudinal Patient Database) that included 1.85 million patients representing approximately 2.8% of the French population, from 1200 general practitioners in 2015. These secondary data consisted of anonymized observations that had been collected through EMRs completed by French physicians during office visits. The database has been validated and is representative of the French population.⁹ In this study, a retrospective analysis was conducted utilizing a secondary database consisting of existing anonymized observations for de-identified patients, there therefore was no requirement to seek specific Ethics Committee approval.

Inclusion criteria were: ≥ 18 years of age; an LDL-C measurement within a valid range (0.0259–25.86 mmol/l [1–1000 mg/dl]) in 2015; ≥ 2 years of continuous representation in the database before the index date (defined as the last LDL-C measurement in 2015); and ≥ 1 high cardiovascular risk condition (conditions defined below). Continuous representation in the database prior to the index date was required to ensure optimal characterization of the cohort, including its demographics and clinical characteristics, as well as prior and current pharmacologic treatment.

Patients with evidence of any of the following categories of conditions during the pre-index period were identified: 1) recent ACS (myocardial infarction [MI] or unstable angina ≤ 12 months prior to the index date); 2) chronic coronary heart disease (CHD; MI or unstable or stable angina > 12 months prior to the index date

and/or history of stable angina, coronary revascularization, or another CHD diagnosis); 3) ischemic stroke/transient ischemic attack (TIA); 4) peripheral arterial disease (PAD; abdominal aortic aneurysm, carotid and intracerebral artery disease without evidence of stroke/TIA, or any revascularization or repair of these arteries); and 5) DM (type 1 or type 2). High cardiovascular risk conditions were identified using French Thesaurus codes mapped to the International Classification of Diseases, Ninth and Tenth Revisions (Supplementary Table I).

Classification was performed using two methods. The first, hierarchical classification, entailed assigning each patient to the highest mutually exclusive category for which he/she qualified (using the order above). The second, prevalent classification, entailed assigning each patient to all the categories for which he/she qualified. Thus, in hierarchical classification, each patient could only be assigned to one category but in prevalent classification, each patient could be classified into more than one category. For this manuscript, results are reported using the hierarchical classification method, while the Supplementary Material include analyses using the prevalent classification method. The first four high cardiovascular risk categories are collectively referred to as “ASCVD” in the paper.

Determination of LLT

For any medication, patients were considered to have been treated on the index date if medication supply via a written prescription was available on or within 30 days prior to the index date, regardless of the duration of the prescription. Patients not currently treated, but with evidence of a past prescription, were considered to have a history of treatment. Patients with no recorded prescription during the 2 years prior were considered to have no evidence of treatment (Supplementary Figure 1).

Statins were classified as high-intensity (atorvastatin 40 mg, 80 mg; rosuvastatin 20 mg, 40 mg; and simvastatin 80 mg) or low-to-moderate-intensity (all other statin medications and doses). For patients prescribed statins, the use of concomitant non-statin LLT was evaluated by a hierarchical classification: 1) statin plus ezetimibe; 2) statin plus a fibrate (i.e., gemfibrozil, fenofibrate, ciprofibrate, or bezafibrate); 3) statin plus the bile acid sequestrant cholestyramine; and 4) statin without any of these non-statin LLT medications (termed “statin monotherapy”). For patients prescribed only non-statin LLT, the same hierarchical classification of these medications was used.

Determination of lipid levels

LLT was evaluated on the index date to ensure that lipid measurements best reflected the impact of treatment. Relevant to the current analysis, at the time of the study, the ESC/EAS LDL-C treatment goal was <1.8 mmol/l (<70 mg/dl) or a ≥50% relative reduction for patients with ASCVD, DM type 2, and DM type 1 with target organ damage. For patients with DM not meeting the above criteria, LDL-C <2.5 mmol/l (<100 mg/dl) was the goal.⁴ The guidelines also recommended non-HDL-C as a secondary target with treatment to goals of <2.6 mmol/l (<100 mg/dl) and <3.3 mmol/l (<130 mg/dl), respectively.⁴

The HAS recommended a therapeutic LDL-C goal of approximately <2.5 mmol/l (<100 mg/dl) for those with established cardiovascular disease and DM type 2 plus other risk factors.⁵ Since administrative codes for DM do not allow for specificity of whether target organ damage was present, we analyzed achievement of both more and less stringent LDL-C and non-HDL-C goals for both ASCVD and DM.

Cross-country comparison

LLT utilization and lipid goal achievement metrics from France were compared to data from a recent analysis which included a 2014 generalizable cohort with LLT prescriptions and lipid measurements from the UK General Practice Database.¹⁰ In the UK cohort, Read codes (as opposed to French Thesaurus codes) defined the subgroups. For both countries, ASCVD subgroups were defined similarly. However, in the UK analysis, the DM subgroup selected had a somewhat higher risk based on the National Institute for Health and Care Excellence (NICE) 2014 guidelines.¹⁰ As opposed to the French analysis, in the UK analysis, DM type 2 patients had to have a QRISK[®]2 10-year risk $\geq 10\%$ and DM type 1 patients had to be age >40 years.¹⁰ To permit cross-country comparisons, the same definition of statin intensity (used by NICE in 2014) was applied for both countries. Using this definition, atorvastatin 20 mg and rosuvastatin 10 mg were reclassified from the low-to-moderate category into a “high-dose” category. We used the term “dose,” (e.g., high-dose statin) in this manuscript only when referring to cross-country comparisons. Statin dose categories for France and the UK (NICE 2014¹¹) are summarized in Supplementary Table II.

Statistical analysis

Statistical analyses were conducted with SAS[®] version 9.4 (SAS Institute, Inc, Cary, North Carolina) and were descriptive in nature. Demographics, clinical characteristics, LLT utilization, and achieved LDL-C and non-HDL-C levels were summarized via proportions and mean \pm standard deviation, as appropriate. No formal statistical tests were performed to compare the LLT utilization and lipid goal achievement between the French data and the UK cohort.

Results

The final study cohort included 32,924 patients (Supplementary Figure 2), of whom 51.5% had established ASCVD and the rest qualified due to the presence of DM. Mean age was 68.3 years, 58.9% were male, and 8.1% were smokers (Table I). Hierarchical classification yielded the following proportions in each category: recent ACS (0.9%); chronic CHD (31.0%); ischemic stroke/TIA (7.1%); PAD (12.6%); and DM (48.5%; Table I). Patient characteristics by prevalent categorizations are presented in Supplementary Table III.

The final study cohort was compared to another cohort from the same database, in which all patients met all inclusion criteria except presence of a valid LDL-C measurement in 2015. The characteristics of both cohorts were similar, suggesting that the results from the current analysis are generalizable to those without an LDL-C measurement (Supplementary Table IV). Comparison of baseline characteristics by statin treatment suggests that statin therapy was associated with higher utilization of other standard-of-care medications (Supplementary Table V).

LLT utilization

Overall, only 47.5% of patients (55.8% of ASCVD and 38.7% of DM-only patients) were prescribed a statin as of the index date. Statins were overwhelmingly used as monotherapy (Table II and Figure 1A). In the overall cohort, 16.6% of those with ASCVD and 34.3% of those with DM had no evidence of any prior LLT treatment (Figure 1B).

Overall, 4.1% of ASCVD and 5.5% of DM-only patients were prescribed a regimen consisting only of non-statin LLT (eg, ezetimibe, fibrates, cholestyramine).

In these patients, ezetimibe was prescribed in 60.0% and 44.1% of the regimens for recent ACS and chronic CHD, respectively (Table II). When non-statin LLT was considered in addition to statins, only 52.3% of the total cohort (59.9% of ASCVD and 44.2% of DM) were prescribed any LLT as of the index date. LLT utilization by prevalent categorization is presented in Supplementary Table VI and Supplementary Figure 3.

LDL-C and non-HDL-C goal achievement

Among patients with ASCVD, only 13.9% achieved the LDL-C goal of <1.8 mmol/l. By hierarchical ASCVD categories, the LDL-C <1.8 mmol/l goal was achieved by 29.0% for recent ACS, 15.7% for chronic CHD, 12.3% for ischemic stroke/TIA, and 9.5% for PAD. In the DM-only group, LDL-C goal achievement was only 10.7% and 41.1% for LDL-C <1.8 mmol/l and <2.5 mmol/l, respectively (Supplementary Figure 4).

Non-HDL-C levels were available for 89.8% of patients who met the inclusion criteria for this study. The proportion of the ASCVD population achieving the non-HDL-C goal of <2.6 mmol/l was 25.6%. In the DM-only group, goal achievement was only 18.4% and 45.2% for non-HDL-C <2.6 mmol/l and <3.3 mmol/l, respectively (Supplementary Figure 5).

LDL-C and non-HDL-C goal achievement by prevalent classes is shown in Supplementary Figures 6 and 7, respectively; mean LDL-C and non-HDL-C are summarized in Supplementary Table VII.

Comparison of results with a UK population (French data re-analyzed according to the UK statin categorization)

Relative to the UK cohort,¹⁰ the French cohort was prescribed statins less frequently. By categories, statins were prescribed to 87.1% versus 73.4% of patients with recent ACS, 81.9% versus 59.5% of chronic CHD, 73.2% versus 49.7% of ischemic stroke/TIA, 72.6% versus 49.0% of PAD, and 66.1% versus 38.8% of DM patients, in the UK versus France, respectively. High-dose statins were also prescribed more frequently in the UK (Table III). By categories, high-dose statins were prescribed to 62.4% versus 51.5% of patients with recent ACS, 34.6% versus 24.7% of patients with chronic CHD, 21.5% versus 18.3% of patients with ischemic stroke/TIA, 23.2% versus 11.0% of patients with PAD, and 17.0% versus 7.2% of the DM patients, for the UK versus French population respectively (Supplementary Table VIII). While treatment with only a non-statin LLT regimen was uncommon in both countries, ezetimibe was used in these regimens more frequently in the UK: 61.6% versus 36.9% of patients in the ASCVD cohorts and 63.4% versus 14.5% of the DM patients, respectively.

Overall, compared with the 2014 UK population,¹⁰ LDL-C and non-HDL-C goal achievement were less frequent in the 2015 French population (Table IV). This overall disparity carried through to the disease categories. By hierarchical categories of ASCVD patients, LDL-C <1.8 mmol/l was achieved in the UK versus French patients in 43.8% versus 29.0% for those with recent ACS, 32.0% versus 15.7% for those with chronic CHD, 28.4% versus 12.3% for those with ischemic stroke/TIA, and 26.4% versus 9.5% for those with PAD. For DM patients, LDL-C <1.8 mmol/l was achieved in UK and French cohorts in 26.0% versus 10.7%, respectively. By hierarchical categories of ASCVD patients, non-HDL-C <2.6 mmol/l was achieved in

the UK patients versus French patients in 54.5% versus 41.6% for those with recent ACS, 43.0% versus 28.4% for those with chronic CHD, 41.5% versus 25.0% for those with ischemic stroke/TIA, and 36.9% versus 18.0% for those with PAD. For DM patients, non-HDL-C <2.6 mmol/l was achieved in 33.2% of UK and 16.3% of French cohorts.

Discussion

This study provides evidence from 2015 on LLT utilization and guideline-recommended lipid goal achievement in a generalizable French population using point-in-time assessment of LLT prescriptions and lipid measurements. It also provides data on LLT usage and lipid goal achievement for understudied populations in France, including those with ischemic stroke/TIA and PAD.

In this study, only 55.8% of patients with ASCVD and 38.7% with DM were currently prescribed a statin. Of those patients without a current LLT prescription, 41.4% with ASCVD and 61.6% with DM had no evidence of an LLT prescription within the previous 2 years. These findings highlight a significant gap between clinical practice and existing practice guidelines.⁴ In comparison to the 2006–2007 MONA LISA study,⁸ our findings demonstrate that statin utilization remains inadequate, contributing to a LDL-C <1.8 mmol/l achievement by only 13.9% of patients with ASCVD and 10.7% with DM without ASCVD.

Prior studies, many of which are less generalizable (based on database or study selection characteristics), have reported higher medication utilization than the current study. For example, 77.6% of all patients with coronary artery disease (CAD) in the French cohort of the REACH registry were treated with statins.¹² Studies from highly selected cohorts have reported even higher statin utilization, such as 92.2% for a similar population in the CORONOR study.^{12, 13} In contrast, we found that 59.9% of all patients with recent ACS and/or chronic CHD were prescribed statins, a finding that our analysis suggests is generalizable to similar populations across France.

With regard to treatment of prior ischemic stroke/TIA, a French study from 2006–2010 reported only 20.1% statin utilization in such patients but with no evidence of

CAD or PAD.¹⁴ The French cohort of the REACH registry has reported statin utilization of 58.0% in patients with cerebrovascular disease (including ischemic stroke/TIA) with or without CHD and/or PAD.¹² In comparison, for those with prior ischemic stroke/TIA, we found 49.6% statin use among patients without evidence of CAD and 52.1% use in any patient with prior stroke or TIA.

With regard to treatment of PAD, two French studies, one conducted in 2003¹⁵ and the other from 2006–2010,¹⁴ reported 53% and 33.8% statin utilization, respectively, in patients with PAD but without CAD, stroke, or TIA. The REACH registry found that 62.7% of all their PAD patients received statins.¹² Investigators in the ATTEST study found a statin prescription rate of 53% among patients with PAD alone compared with 71% for PAD with CAD or cerebrovascular disease, and 74% for CAD and/or cerebrovascular disease without PAD.¹⁵ In comparison, we found 48.9% statin use in PAD patients without CAD, stroke, or TIA, and 54.2% use in any patient with PAD.

With regard to treatment of DM without ASCVD, according to patient samples from the 2007 ENTRED¹⁶ and 2008 DIABASIS national surveys,¹⁷ statins were prescribed to 47% of French patients with type 2 DM, an appreciable increase from the 25% identified in a 2001 ENTRED sample.^{16, 17} Although the ENTRED data are generalizable, patients and providers had to agree to participate, making the data less generalizable compared with the present study. In comparison, we found 38.7% statin utilization in patients with DM types 1 and 2 but without ASCVD. Since DM type 1 was not included as an indication for statin treatment in the HAS guidelines, it is likely that this group was less well-treated than those with DM type 2.

Comparison of the French population with a similar UK population analyzed by a similar hierarchical classification methodology highlighted a substantially lower overall statin and high-dose statin use as well as lower LDL-C goal achievement in France. A recent study conducted in the Netherlands using the same methodology demonstrated similar findings with higher statin utilization rate and LDL-C goal achievement when compared with the present French population.¹⁸ It is worth noting that the Dutch analysis only included ischemic stroke, unlike the French analysis which included TIA along with ischemic stroke.

Furthermore, data from the observational Dyslipidemia International Study (DYSIS) registry are also consistent with our findings; the mean atorvastatin (or equivalent) dose in the French cohort ranged from 20 mg/day between 2008–2012 to 30 mg/day between 2013–2014, suggesting that many patients received low-to-moderate intensity therapy.¹⁹ In DYSIS, only 20.6% of French patients overall reached their LDL-C targets, compared with 40.9% in the UK; seven other European countries had similar or lower rates of goal achievement than France.²⁰

Surveys combining data from multiple European countries have reported varying use of LLTs and achievement of guidance-recommended lipid goal achievement. For example, in the EUROASPIRE III (2006–2007) survey of 8917 patients with CHD from 22 European countries, 79.8% (range 41.6%–95.4%) were reported to have been treated with LLTs, and only 45.5% (3561/6529) achieved LDL-C levels <2.5 mmol/L.²¹ In this survey, 89.1% were reported to have used statins in France and 61.7% (195/316) achieved LDL-C levels <2.5 mmol/L.²¹ In the EUROASPIRE IV (2014–2015) survey analysis of 4579 patients at high risk of cardiovascular disease, 35.6% were on LLTs, of whom 96.1% were on statins.²² Only 32.7% of those

prescribed LLTs achieved LDL-C <2.5 mmol/L.²² Of the 1158 and 2183 patients with newly diagnosed and previously known diabetes, respectively, from the EUROASPIRE IV survey, more than 80% were prescribed statins, with 18% and 28% achieving LDL-C levels <1.8 mmol/L, and 56% and 66% achieving LDL-C levels <2.5 mmol/L, respectively.²³ However, because of the difference in patient selection procedure, population size, and study design, compared with our study, it is not possible to compare the results from the surveys with our findings.

The established challenge of patient adherence to statins has been demonstrated in a French population study.²⁴ More recent challenges to appropriate usage of statins in France arose with the publication that called into question the validity of the “cholesterol hypothesis” and the evidence demonstrating the benefits of statins in preventing cardiovascular events.²⁵ Despite rapid response by a consortium of medical and patient associations,²⁶ the publication was associated with an increased probability of statin discontinuation compared to a historical reference period by about 25% in high-risk (secondary prevention) and 40% in moderate-risk (diabetic) patients; this increase in statin discontinuation was associated with a greater risk of all-cause mortality.²⁶ Complaints of muscle-related adverse effects increased dramatically. Although statin-associated muscle symptoms are a principal cause of statin non-adherence and/or discontinuation, myopathy is observed in only 0.1%–0.01% of patients taking a statin.²⁷ This is also supported by a systematic review which reported muscle symptoms as the most important adverse effect of statin treatment but re-emphasized the very low incidence of myopathy in randomized placebo-controlled clinical trials of statins.²⁸ A 2002 joint Agence Française de Sécurité Sanitaire des Produits de Santé-European Medicines Agency

study affirmed that no general musculoskeletal contraindication to statin use is warranted.²⁹

Government regulations may also play a role in suboptimal LLT utilization. In 2014, the French Ministry of Social Affairs and Health implemented a requirement for submission of forms requesting prescription of rosuvastatin or ezetimibe.³⁰ In addition, neither atorvastatin nor rosuvastatin are indicated by the HAS guidelines for secondary prevention.^{5, 6}

Beyond provider and public education on the benefits and safety of statins, performance improvement initiatives are needed to increase prescription and adherence rates. For those patients who are adherent to statins and still do not achieve lipid goals, or for those who are truly intolerant of statins even after multiple rechallenges, expanding the use of validated non-statin LLT should be considered. Ezetimibe, and the proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors evolocumab and alirocumab, have been shown in the IMPROVE-IT, FOURIER, and ODYSSEY OUTCOMES studies, respectively, to reduce cardiovascular events on top of statin therapy.³¹⁻³³

Analysis of medication adherence in the form of filled prescriptions typically has limitations in large, generalizable populations. Written prescription data overestimate patient medication adherence, as many do not fill their prescriptions or take their prescriptions as recommended. Thus, our analysis likely reflects an optimistic assessment of true medication adherence in the form of filled prescriptions in France. In addition, while our analysis suggests that patients with and without a LDL-C measurement were similar, these measurements were collected during clinical practice and thus were not prospectively specified. Lastly, our study was not

designed to explore the causes for the observed sub-optimal use of statins in the French population compared with other European countries such as the UK.

In conclusion, this study demonstrates suboptimal statin utilization among patients with established ASCVD and/or DM in a generalizable 2015 French population. Achievement of LDL-C and non-HDL-C goals as recommended by the 2011 ESC/EAS guidelines were also suboptimal. The analysis also provides novel evidence about the treatment of previously understudied subgroups of high-risk patients. The gap between existing treatment and the guideline recommendations can best be decreased through a multicomponent strategy.

Conflict of interest statement

JF has received grants and speaker's fees from Amgen, Merck, and Sanofi, and speaker's fees from AstraZeneca. KG was an employee of Sanofi at the time of this study. SRI is an employee of Regeneron Pharmaceuticals, Inc. DA was an employee of IQVIA at the time of this study. DLS has received modest consultant/advisory fees from Sanofi and Regeneron Pharmaceuticals, Inc.

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JF was involved with the design of the study, interpretation of data and critical review of drafts. KG was involved with the design of the study, interpretation of data, and critical review of drafts. SRI was involved with the design of the study, interpretation of data, and critical review of drafts. DA was involved with the design of the study, acquisition, analysis and interpretation of data, and critical review of drafts. DLS was involved with the design of the study, interpretation of data, and critical review of drafts. All authors provided final approval of the submitted manuscript.

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Table I. Patient characteristics for the overall study cohort and hierarchical disease categories.

	Total cohort N = 32,924	Recent ACS n = 293	Chronic CHD n = 10,213	Ischemic stroke/TIA n = 2324	PAD n = 413	DM n = 15,962
Demographics						
Age, mean (SD)	68.3 (12.2)	64.2 (14.1)	71.0 (11.7)	69.7 (13.0)	71.0 (11.4)	65.8 (11.9)
Male, %	58.9	73.7	69.4	52.3	62.3	52.0
Cardiovascular risk conditions, %						
Recent ACS	0.9	100	N/A	N/A	N/A	N/A
Chronic CHD	31.8	87.4	100	N/A	N/A	N/A
Ischemic stroke/TIA	8.4	3.8	4.2	100	N/A	N/A
PAD	18.4	10.2	16.2	10.8	100	N/A
DM	63.9	17.7	32.0	23.9	29.2	100
Behaviors and comorbidities of interest, %						
Current smokers	8.1	14.3	8.4	6.9	14.1	6.4
Hypertension	67.6	45.1	64.3	67.3	72.0	69.2
History of CHF ^a	3.6	2.7	6.8	2.4	2.8	2.0
CKD	1.9	1.4	2.4	2.2	2.8	1.3
Stage V ^b	0.2	0	0.2	0.1	0.2	0.1
Dementia ^a	0.5	0.3	0.5	1.1	0.5	0.4
COPD ^a	10.1	9.6	12.8	8.4	16.9	6.9
Diagnosis associated with musculoskeletal pain	87.4	86.7	88.9	86.4	89.6	86.0
Moderate/severe liver disease ^a	0.3	0	0.1	0.1	0.3	0.4
Concomitant medications, %						

Beta-blockers	44.9	77.8	71.1	34.3	31.9	32.3
ACEIs/ARBs	65.8	74.4	72.8	64.7	63.5	61.9
Clopidogrel	19.3	20.8	38.3	21.3	33.1	3.3

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; N/A = not applicable; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

^aBased on Quan-Charlson comorbidity scale components.

^bStage V includes end-stage renal disease and dialysis.

Table II. LLT use in the overall study cohort and hierarchical disease categories.

%	Total cohort N = 32,924	Recent ACS n = 293	Chronic CHD n = 10,213	Ischemic stroke/TIA n = 2324	PAD n = 4132	DM n = 15,962
High-intensity statin	6.9	43.3	13.3	10.4	4.5	2.3
Monotherapy	92.2	98.4	91.0	95.0	92.4	92.4
Plus ezetimibe	7.4	1.6	8.7	5.0	6.5	6.8
Plus fibrate	0.3	0	0.2	0	0.5	0.5
Plus other non-statin LLT	0.1	0	0.1	0	0.5	0.3
Low-to-moderate-intensity statin	40.6	30.0	46.2	39.2	44.4	36.4
Monotherapy	89.3	95.5	84.4	93.3	91.5	91.7
Plus ezetimibe	10.1	4.5	15.0	6.4	7.8	7.4
Plus fibrate	0.1	0	0.1	0.2	0.1	0.2
Plus other non-statin LLT	0.6	0	0.5	0.1	0.6	0.7
Non-statin LLT only	4.8	1.7	3.8	3.7	5.1	5.5
Ezetimibe	24.4	60.0	44.1	22.4	28.9	14.5
Fibrate	74.6	40.0	53.8	75.3	70.1	85.1
Other non-statin LLT	1.0	0	2.0	2.4	0.9	0.5
Evidence of prior LLT	22.5	14.7	23.9	22.5	23.6	21.4
High-intensity statin	29.0	58.1	42.8	35.6	26.1	20.9
Low-to-moderate-intensity statin	57.9	41.9	50.8	56.2	65.6	65.9
Non-statin LLT	9.5	0	6.4	8.2	8.3	13.2
No evidence of prior LLT	25.2	10.2	12.7	24.2	22.4	34.3

ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Numbers in the gray bars denote absolute percentages. They add up to 100% when added vertically for each column. Numbers in the white bars are relative percentages of the absolute percentages in the gray bars. Subcategories in the white bars are hierarchical. ASCVD subgroups represent hierarchical categorization.

Table III. Comparison of LLT utilization between the UK¹⁰ and French study populations.

% %	ASCVD		DM	
	UK (n = 91,479)	France (n = 16,962)	UK ^a (n = 56,962)	France (n = 15,962)
High-dose statin	31.4	20.9	18.7	7.2
Monotherapy	92.2	93.9	92.0	95.9
Plus ezetimibe	4.1	5.9	2.6	3.4
Moderate-dose statin	42.1	23.9	42.6	20.6
Monotherapy	98.2	80.1	98.2	86.7
Plus ezetimibe	1.0	19.0	0.8	12.0
Low-dose statin	5.6	11.0	4.8	11.0
Monotherapy	96.3	95.6	96.1	98.6
Plus ezetimibe	2.8	4.2	0.9	1.2
Non-statin only	1.9	4.1	1.7	5.5
Ezetimibe	61.6	36.9	63.4	14.5
No evidence of prior LLT	6.5	16.6	22.1	34.3

ASCVD = atherosclerotic cardiovascular disease; DM = diabetes mellitus; LLT = lipid-lowering therapy.

Data are percentages. French data re-analyzed according to the UK statin dose definition.

^aUK data reanalyzed to only include DM type 1 and 2 patients for the purpose of comparison with the French study population.

Table IV. Achievement of LDL-C and non-HDL-C goals – comparison between French and UK¹⁰ populations.

%	ASCVD		DM	
	UK (n = 91,479)	France (n = 16,962)	UK ^a (n=56,962)	France (n=15,962)
LDL-C <1.8 mmol/l				
High-dose statin	37.3	22.2	36.8	20.3
Moderate-dose statin	37.8	19.1	41.0	19.9
Low-dose statin	22.9	8.9	26.4	9.4
Non-statin LLT	6.4	5.3	6.1	4.5
LDL-C <2.5 mmol/l				
High-dose statin	78.9	70.9	74.2	61.2
Moderate-dose statin	81.9	65.7	79.0	63.6
Low-dose statin	68.3	44.3	65.7	44.4
Non-statin LLT	32.3	27.6	31.0	29.0
Non-HDL-C <2.6 mmol/l^b				
High-dose statin	47.9	42.9	41.5	29.2
Moderate-dose statin	52.1	37.7	49.4	33.6
Low-dose statin	36.8	19.4	35.8	16.8
Non-statin LLT	12.1	10.0	9.5	9.1
Non-HDL-C <3.3 mmol/l^b				
High-dose statin	79.5	74.5	72.3	62.3
Moderate-dose statin	84.4	71.5	79.3	66.2
Low-dose statin	73.7	53.2	66.8	47.5
Non-statin LLT	40.0	35.5	35.1	33.0

ASCVD = atherosclerotic cardiovascular disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering therapy; non-HDL-C = non-high-density lipoprotein cholesterol.

French data re-analyzed according to the UK statin dose definition.

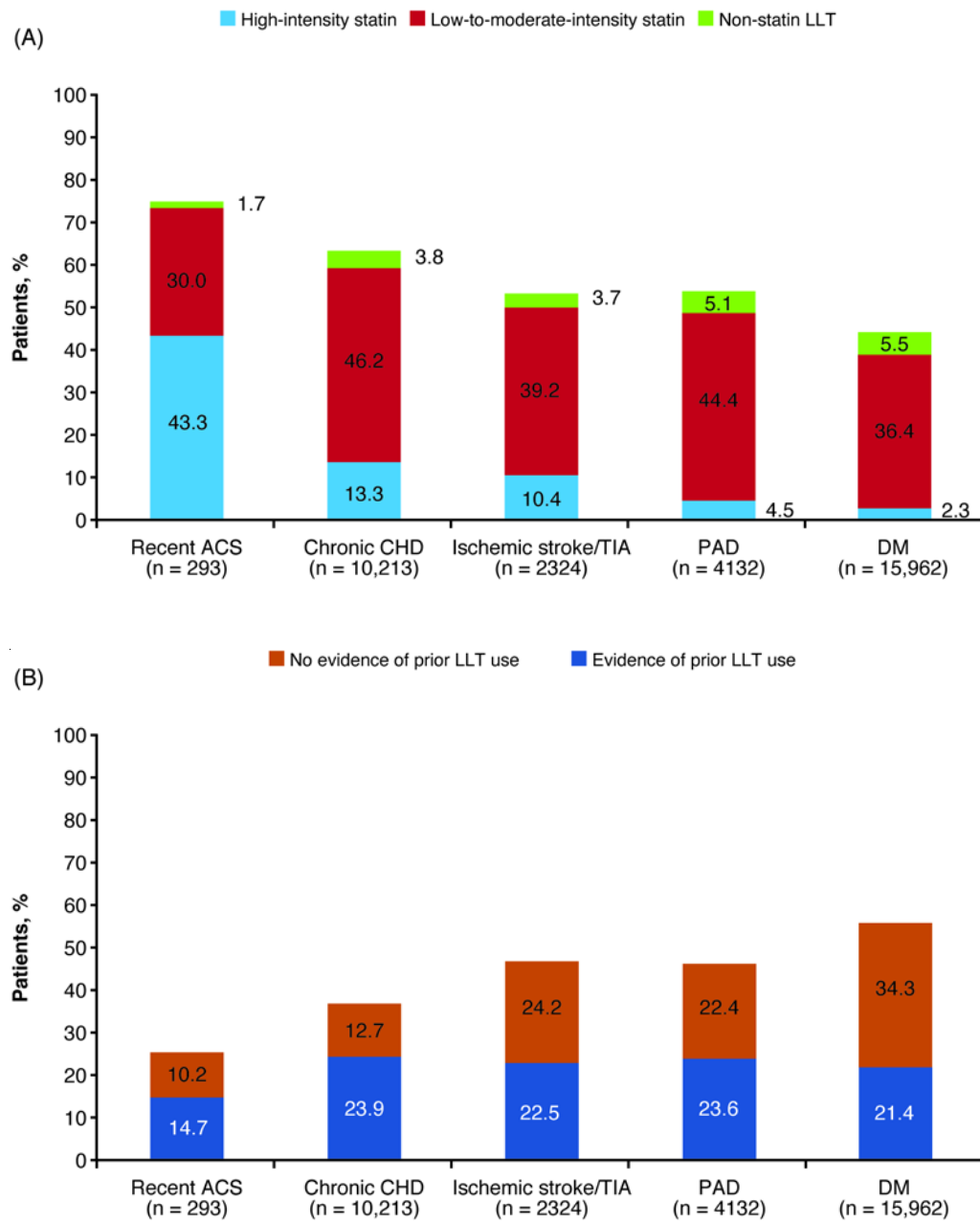
^aUK data reanalyzed to only include DM type 1 and 2 patients for the purpose of comparison with the French study population.

^bNon-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data.

Figure captions

Figure 1. Absolute proportions of LLT treatment by hierarchical disease categories in (A) treated and (B) non-treated patients. ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Figure 1.



Supplementary Material

Supplementary Table I. French Thesaurus codes for disease categorization.

Cardiovascular risk level	Disease category	Brief code description	Code	Description
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128101	Recurrent MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128092	MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128095	Complicated MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128683	Q-wave MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128685	Non-Q-wave MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128748	Q-wave MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128750	Non-Q-wave MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128883	Anterior MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128884	Inferior MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	128885	Lateral MI
01 - Recent ACS 02 - CHD	01 - MI	Acute MI	143638	MI
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	128077	New-onset angina pectoris
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	128080	Unstable angina pectoris
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	128083	Vasospastic angina pectoris
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	128110	UNSTABLE ANGINA PECTORIS (ANGINA STATUS) **DELETED**
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	143723	Angina decubitus
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	143724	Unstable angina pectoris
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	128110	UNSTABLE ANGINA PECTORIS (ANGINA STATUS) **DELETED**
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	144977	Overlapping angina attacks
01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	144979	Syncopal angina pain

01 - Recent ACS 02 - CHD	02 - Angina	Unstable angina	128784	Angina at rest
01 - Recent ACS 02 - CHD	03 - Other ACS	Other ACS	277193	ACS
01 - Recent ACS 02 - CHD	03 - Other ACS	Other ACS	128878	ACS
01 - Recent ACS 02 - CHD	03 - Other ACS	Other ACS	128879	ACS with elevated enzyme levels
01 - Recent ACS 02 - CHD	03 - Other ACS	Other ACS	128880	ACS with normal enzyme levels
01 - Recent ACS 02 - CHD	03 - Other ACS	Other ACS	128156	Dressler syndrome
01 - Recent ACS 02 - CHD	03 - Other ACS	Other ACS	128153	Acute pericarditis of MI
02 - CHD	02 - Angina	Stable angina	219794	Effort angina
02 - CHD	02 - Angina	Stable angina	264549	Effort angina
02 - CHD	02 - Angina	Stable angina	143722	Effort angina
02 - CHD	02 - Angina	Stable angina	128065	Effort angina
02 - CHD	02 - Angina	Stable angina	128068	Spontaneous angina
02 - CHD	02 - Angina	Stable angina	128071	Complicated angina of multiple origin
02 - CHD	02 - Angina	Stable angina	128074	Stable angina
02 - CHD	02 - Angina	Stable angina	128459	Angina with normal coronary arteries
02 - CHD	02 - Angina	Stable angina	128597	Prinzmetal angina
02 - CHD	02 - Angina	Stable angina	128838	Angina
02 - CHD	02 - Angina	Stable angina	143151	Abdominal angina
02 - CHD	02 - Angina	Stable angina	143632	ANGINA, CORONARY INSUFFICIENCY **DELETED
02 - CHD	02 - Angina	Stable angina	143677	Angina
02 - CHD	02 - Angina	Stable angina	128459	Angina with normal coronary arteries
02 - CHD	02 - Angina	Stable angina	128653	Coronary insufficiency
02 - CHD	02 - Angina	Stable angina	128673	Syndrome X (coronary insufficiency)
02 - CHD	02 - Angina	Stable angina	150652	Angina pain
02 - CHD	02 - Angina	Stable angina	151262	Angina pain
02 - CHD	02 - Angina	Stable angina	143632	ANGINA, CORONARY INSUFFICIENCY **DELETED**
02 - CHD	02 - Angina	Stable angina	184202	Angina pain
02 - CHD	02 - Angina	Stable angina	275961	Angina pectoris
02 - CHD	02 - Angina	Stable angina	139971	Angina pain

02 - CHD	02 - Angina	Stable angina	144858	Angina pain
02 - CHD	02 - Angina	Stable angina	143725	Prinzmetal angina
02 - CHD	02 - Angina	Stable angina	150607	Effort angina
02 - CHD	02 - Angina	Stable angina	204160	Effort angina
02 - CHD	02 - Angina	Stable angina	277164	Coronary spasm
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128089	Coronary atherosclerosis
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	277168	Three-vessel coronary stenosis
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	180366	Coronary insufficiency
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	270115	Stenosis of a coronary artery
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	275982	Three-vessel coronary disease
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	143678	Coronary insufficiency
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128762	CHD
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128881	CHD
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	270052	Coronary artery dilatation with active stent
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128578	Coronary artery dilatation without stent
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128581	Coronary artery dilatation with stent
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	143434	Coronary artery dilatation without stent
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	143435	Coronary artery dilatation with stent
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128575	Post-MI repair of ventricular ectasia
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	143684	Chronic ischemic heart disease
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128107	Silent ischemia
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128496	Mitral insufficiency due to ischemic heart disease
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128679	Chronic ischemic heart disease
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128730	Ischemic mitral insufficiency

02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128768	Ischemic cardiomyopathy
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128098	Sequelae of MI
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	179983	Cardiac monitoring
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128462	Post-MI monitoring
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128104	Cardiac readaptation
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	143631	Coronary angioplasty
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	277190	Post-coronary angioplasty monitoring
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	277178	Coronary disease follow-up
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128371	Coronary bypass
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	128465	Coronary artery bypass grafting monitoring
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	143646	Coronary bypass
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	151044	Coronary artery bypass grafting monitoring
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	263433	Coronary artery bypass grafting monitoring
02 - CHD	06 - CHD Diagnosis	Other chronic ischemic heart disease	270166	Coronary artery bypass grafting monitoring
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133505	Cerebral ischemic accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140329	Cerebral ischemic accident due to another etiology
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140330	Cerebral ischemic accident of undetermined etiology
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	143292	Cerebral ischemic accident of the anterior cerebral artery
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	143293	Cerebral ischemic accident of the posterior cerebral artery
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	128170	Progressive carotid vascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	128173	Carotid vascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134444	Cerebral infarction due to thrombosis of the precerebral arteries
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134446	Cerebral infarction due to embolism of the precerebral arteries

03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134448	Cerebral infarction due to occlusion or stenosis of the precerebral arteries
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	144224	Ischemic cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133512	Recurrent cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133516	Arteriopathic cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133522	Vascular accident affecting the middle cerebral artery
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133524	Vascular accident affecting the anterior cerebral artery
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134450	Cerebral infarction due to thrombosis of the cerebral arteries
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134452	Cerebral infarction due to embolism of the cerebral arteries
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134454	Cerebral infarction due to occlusion or stenosis of the cerebral arteries
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140320	Cerebral ischemic accident of the sylvian fissure
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140321	Cerebral ischemic accident of the superficial artery of the sylvian fissure
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140322	Cerebral ischemic accident of the deep artery of the sylvian fissure
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140324	Cerebral ischemic accident due to cardiac embolism
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140325	Cerebral ischemic accident due to arterial embolism
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140327	Cerebral ischemic accident due to stenosis, atherothrombosis
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	140327	Cerebral ischemic accident due to stenosis, atherothrombosis
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133501	Cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	133503	Evolving cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	144150	Cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	208582	Cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	276482	Cerebrovascular accident
03 - Ischemic stroke	04 - Stroke	Ischemic stroke	134460	Cerebral infarction
04 - PAD	05 - PAD	PVD	134470	Occlusion and stenosis of precerebral arteries, multiple and bilateral
04 - PAD	05 - PAD	PVD	134472	Occlusion and stenosis of another precerebral artery

04 - PAD	05 - PAD	PVD	134474	Occlusion and stenosis of a precerebral artery
04 - PAD	05 - PAD	PVD	134476	Occlusion and stenosis of the middle cerebral artery
04 - PAD	05 - PAD	PVD	134478	Occlusion and stenosis of the anterior cerebral artery
04 - PAD	05 - PAD	PVD	134480	Occlusion and stenosis of the posterior cerebral artery
04 - PAD	05 - PAD	PVD	134482	Occlusion and stenosis of cerebellar arteries
04 - PAD	05 - PAD	PVD	134484	Occlusion and stenosis of cerebral arteries, multiple and bilateral
04 - PAD	05 - PAD	PVD	134486	Occlusion and stenosis of another cerebral artery
04 - PAD	05 - PAD	PVD	134488	Occlusion and stenosis of a cerebral artery
04 - PAD	05 - PAD	PVD	134470	Occlusion and stenosis of precerebral arteries, multiple and bilateral
04 - PAD	05 - PAD	PVD	134472	Occlusion and stenosis of another precerebral artery
04 - PAD	05 - PAD	PVD	134474	Occlusion and stenosis of a precerebral artery
04 - PAD	05 - PAD	PVD	276434	Carotid artery thrombosis
04 - PAD	05 - PAD	PVD	277167	Bilateral carotid stenosis
04 - PAD	05 - PAD	PVD	128726	Atheroma of the carotid artery
04 - PAD	05 - PAD	PVD	269964	Carotid endarterectomy
04 - PAD	05 - PAD	PVD	277167	Bilateral carotid stenosis
04 - PAD	05 - PAD	PVD	128736	Carotid thromboendarterectomy
04 - PAD	05 - PAD	PVD	128789	Carotid atherosclerosis
04 - PAD	05 - PAD	PVD	128833	Unblocking of the carotid artery
04 - PAD	05 - PAD	PVD	133762	Unblocking of the carotid artery
04 - PAD	05 - PAD	PVD	134468	Occlusion and stenosis of the carotid artery
04 - PAD	05 - PAD	PVD	134468	Occlusion and stenosis of the carotid artery
04 - PAD	05 - PAD	PVD	143502	Angioplasty of a carotid artery
04 - PAD	05 - PAD	PVD	143655	Carotid stenosis
04 - PAD	05 - PAD	PVD	269925	Arterial thrombosis of the lower extremity
04 - PAD	05 - PAD	PVD	128834	Acute ischemia of the lower

				extremity
04 - PAD	05 - PAD	PVD	128887	Acute ischemia of the upper extremity
04 - PAD	05 - PAD	PVD	128832	Arterial embolism of a lower extremity
04 - PAD	05 - PAD	PVD	136255	Arterial embolism of the lower extremities
04 - PAD	05 - PAD	PVD	153616	Distal arterial embolism
04 - PAD	05 - PAD	PVD	277259	Arterial dilatation of the lower extremity with stent
04 - PAD	05 - PAD	PVD	128377	Angioplasty
04 - PAD	05 - PAD	PVD	128828	Angioplasty of the peripheral arteries
04 - PAD	05 - PAD	PVD	143315	Angioplasty
04 - PAD	05 - PAD	PVD	143503	Angioplasty of a peripheral artery
04 - PAD	05 - PAD	PVD	143504	Angioplasty of a renal artery
04 - PAD	05 - PAD	PVD	276652	Iliac angioplasty
04 - PAD	05 - PAD	PVD	275998	Bypass
04 - PAD	05 - PAD	PVD	277172	Arterial stent
04 - PAD	05 - PAD	PVD	143504	Angioplasty of a renal artery
04 - PAD	05 - PAD	PVD	277171	Renal artery stent
04 - PAD	05 - PAD	PVD	276109	Arterial stent
04 - PAD	05 - PAD	PVD	276357	Arterial restenosis
04 - PAD	05 - PAD	PVD	277172	Arterial stent
04 - PAD	05 - PAD	PVD	143328	Endarterectomy
04 - PAD	05 - PAD	PVD	128380	Arteriectomy
04 - PAD	05 - PAD	PVD	128383	Thrombo-endarterectomy
04 - PAD	05 - PAD	PVD	128395	Arterial prosthesis
04 - PAD	05 - PAD	PVD	143314	Aneurysmectomy
04 - PAD	05 - PAD	PVD	277170	Intra-stent stenosis
04 - PAD	05 - PAD	PVD	277173	Iliac stent
04 - PAD	05 - PAD	PVD	277259	Arterial dilatation of the lower extremity with stent
04 - PAD	05 - PAD	PVD	269694	Surgically repaired aortic aneurysm
04 - PAD	05 - PAD	PVD	269878	Aneurysm of the splenic artery
04 - PAD	05 - PAD	PVD	128760	Abdominal aortic aneurysm

04 - PAD	05 - PAD	PVD	128474	Monitoring of a surgically repaired aneurysm
04 - PAD	05 - PAD	PVD	128187	Aneurysm of the subrenal aorta
04 - PAD	05 - PAD	PVD	128193	Rupture of an abdominal aortic aneurysm
04 - PAD	05 - PAD	PVD	128813	PAD
04 - PAD	05 - PAD	PVD	128584	Lower extremity arteritis - stage I
04 - PAD	05 - PAD	PVD	128587	Lower extremity arteritis - stage II
04 - PAD	05 - PAD	PVD	128590	Lower extremity arteritis - stage III
04 - PAD	05 - PAD	PVD	128593	Lower extremity arteritis - stage IV
04 - PAD	05 - PAD	PVD	128716	PAD
04 - PAD	05 - PAD	PVD	128781	Peripheral arteriopathy
04 - PAD	05 - PAD	PVD	138336	Claudication
04 - PAD	05 - PAD	PVD	145382	Limb claudication
04 - PAD	05 - PAD	PVD	145383	Calf claudication
04 - PAD	05 - PAD	PVD	145384	Thigh claudication
04 - PAD	05 - PAD	PVD	150493	Intermittent claudication
04 - PAD	05 - PAD	PVD	151200	Intermittent claudication
04 - PAD	05 - PAD	PVD	181327	Claudication
04 - PAD	05 - PAD	PVD	143633	Lower extremity arteritis
04 - PAD	05 - PAD	PVD	143713	PAD
04 - PAD	05 - PAD	PVD	275517	Lower extremity arteritis follow-up
04 - PAD	05 - PAD	PVD	128193	Rupture of an abdominal aortic aneurysm
04 - PAD	05 - PAD	PVD	128176	LOWER EXTREMITY ARTERITIS STAGES I AND II **DELETE**
04 - PAD	05 - PAD	PVD	128177	LOWER EXTREMITY ARTERITIS STAGES III AND IV **DELETE**
04 - PAD	05 - PAD	PVD	128841	Arterial ulcer
05 - DM	07 - DM	DM	132993	Type I DM (insulin-dependent)
05 - DM	07 - DM	DM	132996	Type II DM (noninsulin-dependent)
05 - DM	07 - DM	DM	132999	Asymptomatic DM
05 - DM	07 - DM	DM	133161	Insulin-requiring DM
05 - DM	07 - DM	DM	143870	Type 1 DM
05 - DM	07 - DM	DM	143871	Type 2 DM

05 - DM	07 - DM	DM	143908	DM
05 - DM	07 - DM	DM	143951	Insulin-requiring DM
05 - DM	07 - DM	DM	146119	DM
05 - DM	07 - DM	DM	146998	DM
05 - DM	07 - DM	DM	181265	Type 1 DM - nonidentified
05 - DM	07 - DM	DM	275765	Type 2 DM - nonidentified
05 - DM	07 - DM	DM	277325	Insulin-treated type 2 DM
05 - DM	07 - DM	DM	152520	Monitoring of DM
05 - DM	07 - DM	DM	152763	DM check-up
05 - DM	07 - DM	DM	152766	Education of the diabetic patient
05 - DM	07 - DM	DM	276069	Diabetic dermatitis
05 - DM	07 - DM	DM	276057	Decompensated diabetic ketoacidosis
05 - DM	07 - DM	DM	143943	Type 1 DM with multiple complications
05 - DM	07 - DM	DM	143944	Type 1 DM complicated by nephropathy
05 - DM	07 - DM	DM	143945	Type 1 DM complicated by neuropathy
05 - DM	07 - DM	DM	143946	Type 1 DM complicated by retinopathy
05 - DM	07 - DM	DM	143947	Type 2 DM with multiple complications
05 - DM	07 - DM	DM	143948	Type 2 DM complicated by nephropathy
05 - DM	07 - DM	DM	143949	Type 2 DM complicated by neuropathy
05 - DM	07 - DM	DM	143950	Type 2 DM complicated by retinopathy
05 - DM	07 - DM	DM	133005	Chronic complications of diabetes
05 - DM	07 - DM	DM	139484	Glomerulonephritis related to DM
05 - DM	07 - DM	DM	276074	Decompensated DM
05 - DM	07 - DM	DM	129212	Diabetic malum perforans
05 - DM	07 - DM	DM	133105	Coma in the diabetic patient
05 - DM	07 - DM	DM	133196	Diabetic ketoacidosis
05 - DM	07 - DM	DM	133651	Diabetic neuropathy
05 - DM	07 - DM	DM	134661	Diabetic mononeuritis
05 - DM	07 - DM	DM	134711	Diabetic polyneuritis

05 - DM	07 - DM	DM	135471	Diabetic cataract
05 - DM	07 - DM	DM	135479	Diabetic retinopathy
05 - DM	07 - DM	DM	138194	Diabetic arthropathy
05 - DM	07 - DM	DM	139870	Diabetic nephropathy
05 - DM	07 - DM	DM	140129	Confusional state due to diabetic ketoacidosis
05 - DM	07 - DM	DM	141591	Diabetic arthropathy
05 - DM	07 - DM	DM	143197	Diabetic gastroparesis
05 - DM	07 - DM	DM	144219	Diabetic mononeuritis
05 - DM	07 - DM	DM	144223	Diabetic polyneuritis
05 - DM	07 - DM	DM	144245	Diabetic neuropathy
05 - DM	07 - DM	DM	144444	Diabetic retinopathy
05 - DM	07 - DM	DM	133011	Diabetic coma
05 - DM	07 - DM	DM	139913	Incipient nephropathy (DM)

ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; MI = myocardial infarction; PVD = peripheral vascular disease.

Supplementary Table II. Statin dose categories for France and UK cross-country comparisons.

Statin intensity	France	UK (NICE 2014 [1])
High	Atorvastatin 40, 60, and 80 mg	Atorvastatin 20, 40, 60, and 80 mg
	Rosuvastatin 20 and 40 mg	Rosuvastatin 10, 20, and 40 mg
	Simvastatin 80 mg	Simvastatin 80 mg
Moderate/low	Atorvastatin 10, 20, and 30 mg	N/A
	Rosuvastatin 5 and 10 mg	
	Simvastatin 10, 20, and 40 mg	
	Pravastatin 10, 20, and 40 mg	
	Fluvastatin 20, 40, and 80 mg	
Medium	N/A	Atorvastatin 10 mg
		Rosuvastatin 5 mg
		Simvastatin 20 and 40 mg
		Fluvastatin 80 mg
Low	N/A	Simvastatin 10 mg
		Pravastatin 10, 20, and 40 mg
		Fluvastatin 20 and 40 mg

N/A = not applicable.

1. National Institute for Health and Care Excellence. Cardiovascular disease: risk assessment and reduction, including lipid modification. 2014. Available at <http://www.nice.org.uk/guidance/cg181>.

Supplementary Table III. Patient characteristics for the overall study cohort and prevalent disease categories.

	Total cohort N = 32,924	Recent ACS n =293	Chronic CHD n = 10,469	Ischemic stroke/TIA n = 2763	PAD n = 6068	DM n = 21,040
Demographics						
Age, mean (SD)	68.3 (12.2)	64.2 (14.1)	70.9 (11.8)	70.5 (12.7)	71.9 (11.1)	67.1 (11.8)
Male, %	58.9	73.7	69.5	55.2	67.6	56.3
Cardiovascular risk conditions, %						
Recent ACS	0.9	100	2.4	0.4	0.5	0
Chronic CHD	31.8	87.4	100	15.8	27.7	0
Ischemic stroke/TIA	8.4	3.8	4.2	100	6.0	3.4
PAD	18.4	10.2	16.1	13.1	100	9.2
DM	63.9	17.7	31.6	26.2	32.0	100
Behaviors and comorbidities of interest, %						
Current smokers, %	8.1	14.3	8.5	7.6	14.1	7.2
Hypertension	67.6	45.1	63.8	68.9	72.5	71.2
History of CHF ^a	3.6	2.7	6.7	3.7	4.5	3.2
CKD	1.9	1.4	2.4	2.6	3.6	1.9
Stage V ^b	0.2	0	0.2	0.2	0.2	0.2
Dementia ^a	0.5	0.3	0.5	1.1	0.6	0.4
COPD ^a	10.1	9.6	12.8	9.6	18.5	8.7
Diagnosis associated with musculoskeletal pain	87.4	86.7	88.9	86.9	90.1	86.8
Moderate/severe liver disease ^a	0.3	0	0.1	0.1	0.3	0.4

Concomitant medications, %						
Beta-blockers	44.9	77.8	71.4	41.1	44.6	40.0
ACEIs/ARBs	65.8	74.4	72.9	67.6	68.9	66.7
Clopidogrel	19.3	20.8	37.8	27.0	41.0	12.0

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; N/A = not applicable; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

^aBased on Quan-Charlson comorbidity scale components.

^bStage V includes end-stage renal disease and dialysis.

Supplementary Table IV. Comparison of baseline characteristics for those with and without a LDL-C measurement in 2015 using hierarchical classification.

	Combined ASCVD and/or DM		ASCVD		DM	
	With LDL-C measurement (n = 32,924)	Without LDL-C measurement (n = 100,254)	With LDL-C measurement (n = 16,962)	Without LDL-C measurement (n = 52,574)	With LDL-C measurement (n = 15,962)	Without LDL-C measurement (n = 47,680)
Demographics						
Age, mean (SD)	68.3 (12.2)	66.7 (14.7)	70.7 (11.9)	69.0 (14.9)	65.8 (11.9)	64.2 (14.1)
Male, %	58.9	56.4	65.4	62.0	52.0	50.3
Cardiovascular risk conditions, %						
Recent ACS	0.9	0.9	1.7	1.7	0	0
Chronic CHD	31.8	32.5	61.7	61.6	0	0
Ischemic stroke/TIA	8.4	8.9	16.3	16.0	0	0
PAD	18.4	16.6	35.8	32.9	0	0
DM	63.9	59.5	29.9	22.8	100	100
Comorbidities of interest, %						
Hypertension	67.6	60.9	66.2	59.9	69.2	62.2

History of CHF ^a	3.6	3.8	5.2	5.5	2.0	2.0
CKD	1.9	1.9	2.4	2.5	1.3	1.4
Stage V ^b	0.2	0.3	0.2	0.4	0.1	0.2
Dementia ^a	0.5	0.7	0.6	0.8	0.4	0.5
COPD ^a	10.1	9.6	13.2	12.3	6.9	6.7
Diagnosis associated with musculoskeletal pain	87.4	81.9	88.7	83.4	86.0	80.2
Moderate/severe liver disease ^a	0.3	0.2	0.2	0.2	0.4	0.3

Concomitant medications, %

Beta-blockers	44.9	41.0	56.7	51.6	32.3	29.1
ACEIs/ARBs	65.8	59.2	69.4	61.9	61.9	56.2
Clopidogrel	19.3	17.8	34.4	30.9	3.3	3.5

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; ASCVD = atherosclerotic cardiovascular disease; CHD, coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

^aBased on Quan-Charlson comorbidity scale components.

^bStage V includes end-stage renal disease and dialysis.

The final study cohort was compared to another cohort from the same database who met the all the inclusion criteria, except presence of a valid LDL-C measurement in 2015 to ensure the generalizability of the study population. Compared with the population without a valid LDL-C measurement, those for whom a LDL-C measurement was available were 1.5 years older and 2% more males. Although differences were statistically significant due to large numbers, most were small and not of clinical importance. Patients prescribed beta-blockers, ACE inhibitors, ARBs, and clopidogrel were more likely to have had an LDL-C measurement.

Supplementary Table V. Comparison of baseline characteristics according to statin therapy.

	ASCVD				DM			
	High-intensity statin	Low-to-moderate-intensity statin	Any current statin	No current statin	High-intensity statin	Low-to-moderate-intensity statin	Any current statin	No current statin
Demographics								
Age, mean (SD)	68.9 (11.3)	71.8 (10.6)	70.7 (10.9)	70.7 (13.0)	66.5 (10.3)	67.3 (10.6)	67.1 (10.6)	65.0 (12.7)
Male, %	74.7	67.4	70.1	59.5	57.0	53.0	53.8	50.9
Cardiovascular risk conditions, %								
Recent ACS	4.3	1.1	2.3	1.0	–	–	–	–
Chronic CHD	75.0	61.0	66.3	56.0	–	–	–	–
Ischemic stroke/TIA	15.7	14.9	15.2	17.7	–	–	–	–
PAD	27.3	39.2	34.7	37.1	–	–	–	–
DM	31.3	33.7	32.8	26.3	100	100	100	100
Comorbidities of interest, %								
Hypertension	63.4	71.0	68.2	63.8	77.2	77.8	77.7	63.7
History of CHF ^a	5.5	5.0	5.2	5.1	2.6	2.2	2.2	1.9

CKD	1.9	2.6	2.4	2.5	1.8	1.2	1.3	1.2
Stage IV-V ^b	0.1	0.1	0.1	0.3	0.1	0.1	0.1	0.1
Dementia ^a	0.3	0.6	0.5	0.7	0.3	0.3	0.3	0.4
COPD ^a	12.7	14.3	13.7	12.5	8.9	7.5	7.8	6.3
Diagnosis associated with musculoskeletal pain	87.4	90.7	89.5	87.7	86.6	88.1	87.8	84.9
Moderate/severe liver disease ^a	0.1	0.2	0.2	0.2	0.2	0.2	0.2	0.5

Concomitant medications, %

Beta-blockers	73.8	59.7	65.0	46.1	40.3	36.2	37	29.4
ACEIs/ARBs	81.0	74.0	76.7	60.3	73.8	72.6	72.9	55.0
Clopidogrel	45.9	39.1	41.6	25.2	7.5	4.4	5.0	2.3

ACEI = angiotensin-converting enzyme inhibitor; ACS = acute coronary syndrome; ARB = angiotensin II receptor blocker; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; CHF = congestive heart failure; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

^aBased on Quan-Charlson comorbidity scale components.

^bStage V includes end-stage renal disease and dialysis.

Supplementary Table VI. Use of LLT in overall cohort and by prevalent disease categories.

	Total cohort N = 32,924	Recent ACS n = 293	Chronic CHD n = 10,469	Ischemic stroke/TIA n = 2763	PAD n = 6068	DM n = 21,040
High-intensity statin	6.9	43.3	14.1	11.3	7.6	4.5
Monotherapy	92.2	98.4	91.6	95.2	90.4	92.8
Plus ezetimibe	7.4	1.6	8.1	4.8	8.7	6.5
Plus fibrate	0.3	0	0.2	0	0.4	0.4
Plus other non-statin LLT	0.1	0	0.1	0	0.4	0.2
Low-to-moderate-intensity statin	40.6	30.0	45.8	40.8	46.6	39.6
Monotherapy	89.3	95.5	84.6	92.2	88.5	90.6
Plus ezetimibe	10.1	4.5	14.8	7.5	10.8	8.5
Plus fibrate	0.1	0	0.1	0.2	0.1	0.2
Plus other non-statin LLT	0.6	0	0.5	0.1	0.6	0.7
Non-statin LLT only	4.8	1.7	3.8	3.5	4.5	5.2
Ezetimibe	24.4	60.0	44.3	22.7	31.8	18.4
Fibrate	74.6	40.0	53.7	75.3	66.4	80.7
Other non-statin LLT	1.0	0	2.0	2.1	1.8	0.9
Evidence of prior LLT	22.5	14.7	23.7	22.6	24.4	22.1
High-intensity statin	29.0	58.1	43.1	37.4	32.7	25.5
Low-to-moderate-intensity statin	57.9	41.9	50.6	54.0	60.6	64.2
Non-statin LLT	9.5	0	6.3	8.6	6.7	11.3
No evidence of prior LLT	25.2	10.2	12.6	21.8	16.9	28.6

ACS = acute coronary syndrome; ASCVD = atherosclerotic cardiovascular disease; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Numbers in the gray bars denote absolute percentages. They add up to 100% when added vertically for each column. Numbers in the white bars are relative percentages of the absolute percentages in the gray bars. Subcategories in the white bars are hierarchical. ASCVD subgroups represent prevalent categorization.

Supplementary Table VII. Mean LDL-C and non-HDL-C levels and threshold achievement in hierarchical disease categories.

	Total cohort N = 32,924	Recent ACS n = 293	Chronic CHD n = 10,213	Ischemic stroke/TIA n = 2324	PAD n = 4132	DM n = 15,962
LDL-C						
Mean (\pm SD), mmol/l	2.7 (1.0)	2.2 (0.9)	2.5 (1.0)	2.7 (1.0)	2.8 (1.0)	2.8 (1.0)
<1.8 mmol/l, %	12.3	29.0	15.7	12.3	9.5	10.7
1.8–<2.5 mmol/l, %	33.6	41.6	39.5	35.2	29.8	30.5
2.5–<3.4 mmol/l, %	33.8	20.5	28.7	32.1	36.6	36.8
3.4–<4.1 mmol/l, %	13.9	4.8	10.9	13.3	16.6	15.4
\geq 4.1 mmol/l, %	6.3	4.1	5.1	7.1	7.5	6.7
Non-HDL-C^a						
Mean (\pm SD), mmol/l	3.4 (1.1)	2.8 (1.0)	3.2 (1.0)	3.3 (1.1)	3.5 (1.1)	3.5 (1.0)
<2.6 mmol/l, %	21.1	41.6	28.4	25.0	18.0	16.3
2.6–<3.3 mmol/l, %	25	25.6	27.6	24.2	23.8	23.6
3.3–<4.1 mmol/l, %	23.3	14.7	19.6	22.4	25.0	25.5
4.1–<4.9 mmol/l, %	13	5.8	10.1	12.3	14.3	14.8
\geq 4.9 mmol/l, %	7.5	3.8	6.1	7.1	9.1	8.0

ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; non-HDL-C = non-high-density lipoprotein cholesterol; PAD = peripheral arterial disease; SD = standard deviation; TIA = transient ischemic attack.

^aNon-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data.

Supplementary Table VIII. Comparison of LLT between French and UK [1] study populations by hierarchical disease categories.

	Recent ACS		Chronic CHD		Ischemic stroke/TIA		PAD		DM	
	UK (n = 3386)	France (n = 293)	UK (n = 63,387)	France (n = 10,213)	UK (n = 2614)	France (n = 2324)	UK (n = 12,854)	France (n = 4132)	UK ^a (n = 56,962)	France (n = 15,962)
High-dose statin	62.4	51.5	34.6	24.7	21.5	18.3	23.2	11.0	18.7	7.2
Monotherapy	93.3	98.7	91.8	92.9	93.2	96.5	92.3	95.4	92.0	95.9
Plus ezetimibe	1.0	1.3	4.8	6.9	2.9	3.5	3.4	4.0	2.6	3.4
Moderate-dose statin	22.6	15.4	41.4	24.2	46.2	21.9	44.3	24.9	42.6	20.6
Monotherapy	98.6	91.1	97.9	75.4	98.7	89.6	98.6	86.2	98.2	86.7
Plus ezetimibe	0.6	8.9	1.2	23.7	0.7	10.0	0.6	12.7	0.8	12.0
Low-dose statin	2.1	6.5	5.9	10.6	5.5	9.5	5.1	13.1	4.8	11.0
Monotherapy	93.8	100	95.9	93.5	97.4	97.7	97.1	98.7	96.1	98.6
Plus ezetimibe	6.3	0	3.2	6.3	1.7	1.8	2.3	1.3	0.9	1.2
Non-statin only	0.9	1.7	2.0	3.8	1.7	3.7	1.9	5.1	1.7	5.5
Ezetimibe, monotherapy	70.4	60.0	61.3	44.1	65.5	22.4	55.6	28.9	63.4	14.5
No evidence of prior LLT	5.6	10.2	4.1	12.7	10.5	24.2	12.0	22.4	22.1	34.3

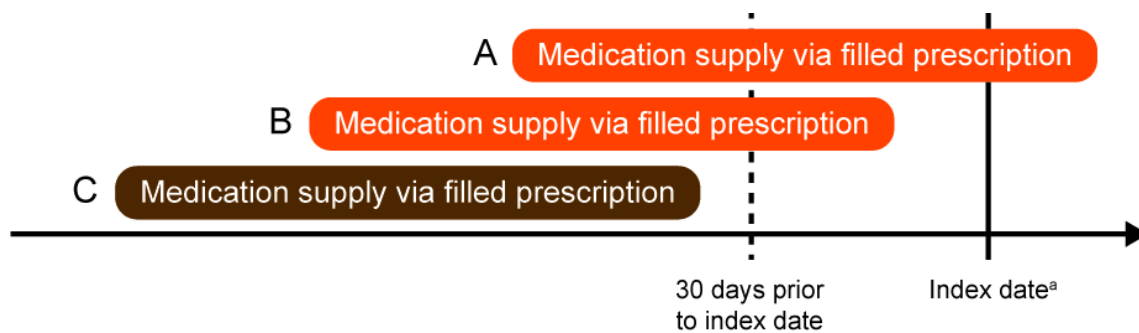
ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Data are percentages. French data re-analyzed according to the UK statin dose definition.

^aUK data reanalyzed to only include DM type 1 and 2 patients for the purpose of comparison with the French study population [1].

1. Steen DL, Khan I, Ansell D, et al. Retrospective examination of lipid-lowering treatment patterns in a real-world high-risk cohort in the UK in 2014: Comparison with the National Institute for Health and Care Excellence (NICE) 2014 lipid modification guidelines. *BMJ Open* 7 (2017) e013255.

Supplementary Figure 1. Determination of treatment status as of the index date.



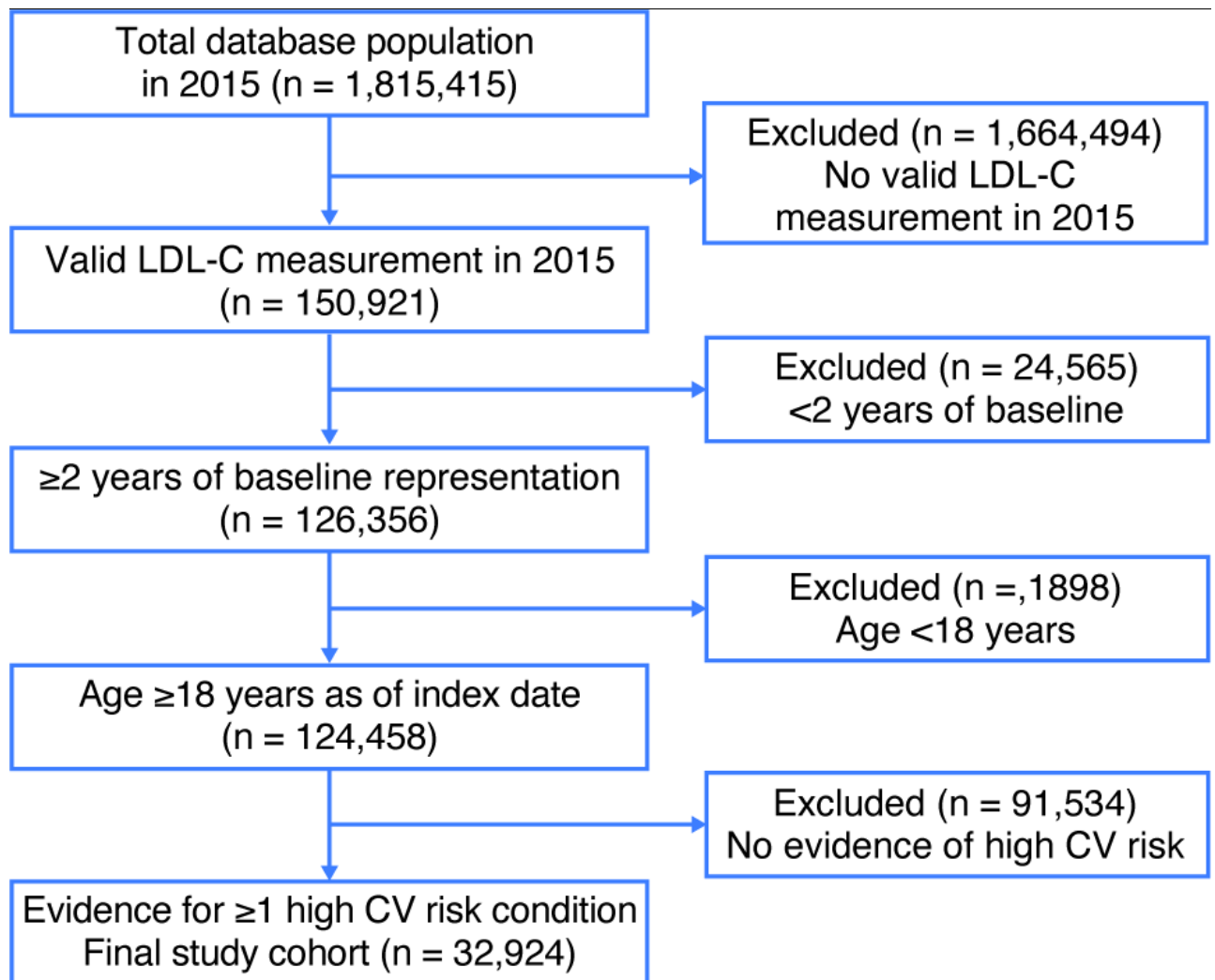
LDL-C = low-density lipoprotein cholesterol; LLT = lipid-lowering therapy.

^a Defined as the last LDL-C measurement in 2015.

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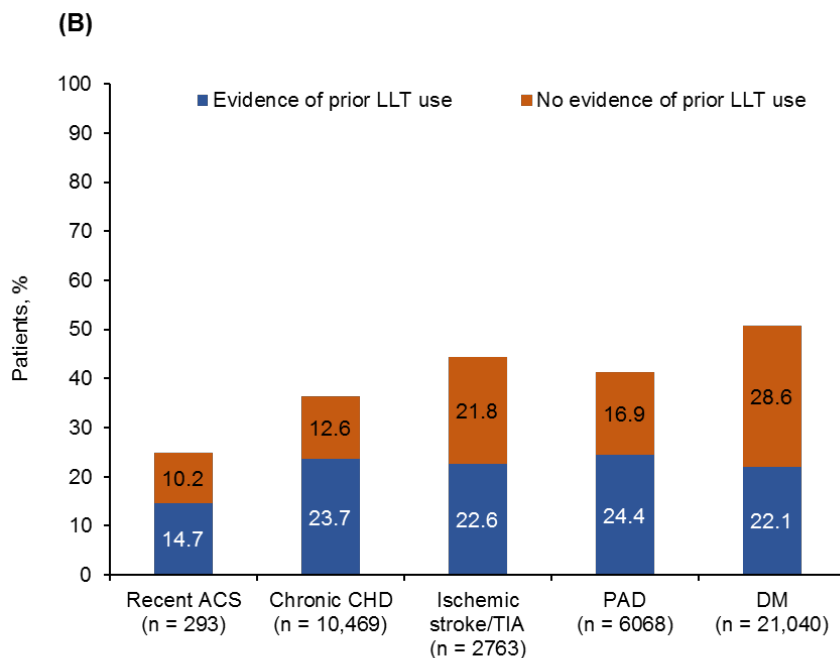
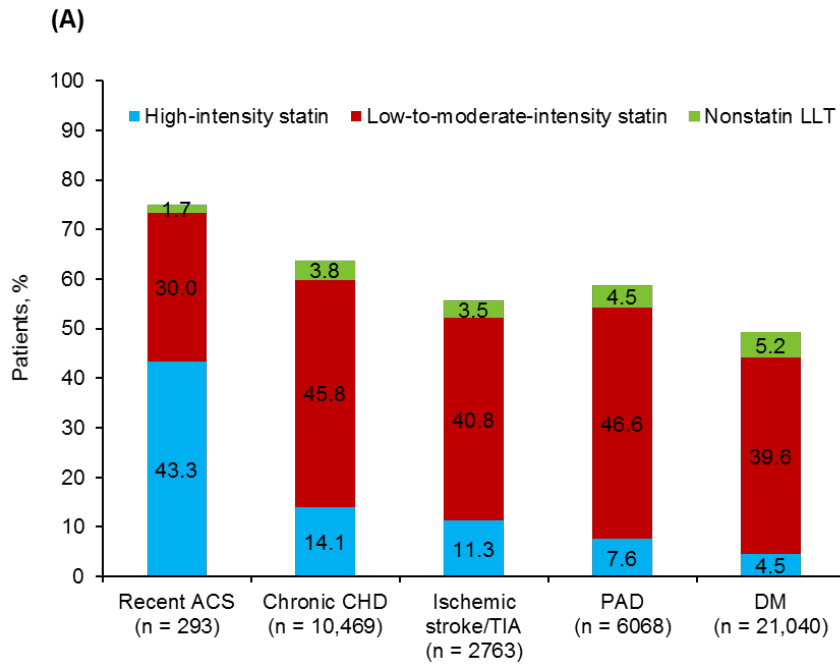
Orange bars (A and B) denote scenarios whereby a patient is deemed to be currently treated with LLT as of the index date, since there is (A) evidence of medication supply (established via recorded prescription) on, or (B) within 30 days of index date. The brown bar (C) denotes a scenario whereby the patient is not being deemed as currently treated as of the index date, since there is no evidence of medication supply within 30 days before the index date.

Supplementary Figure 2. Cohort selection.



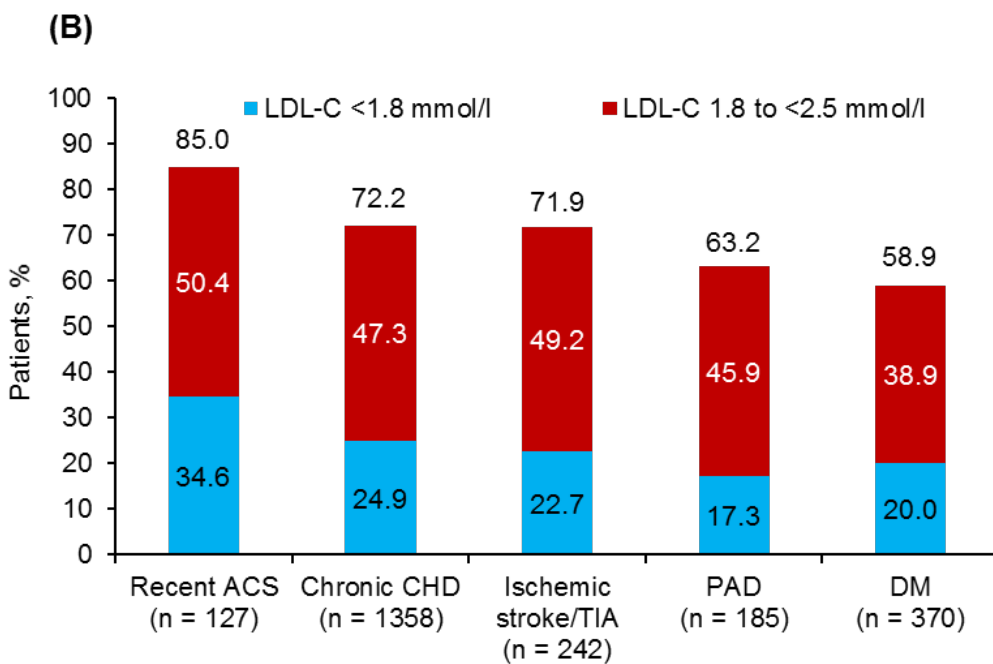
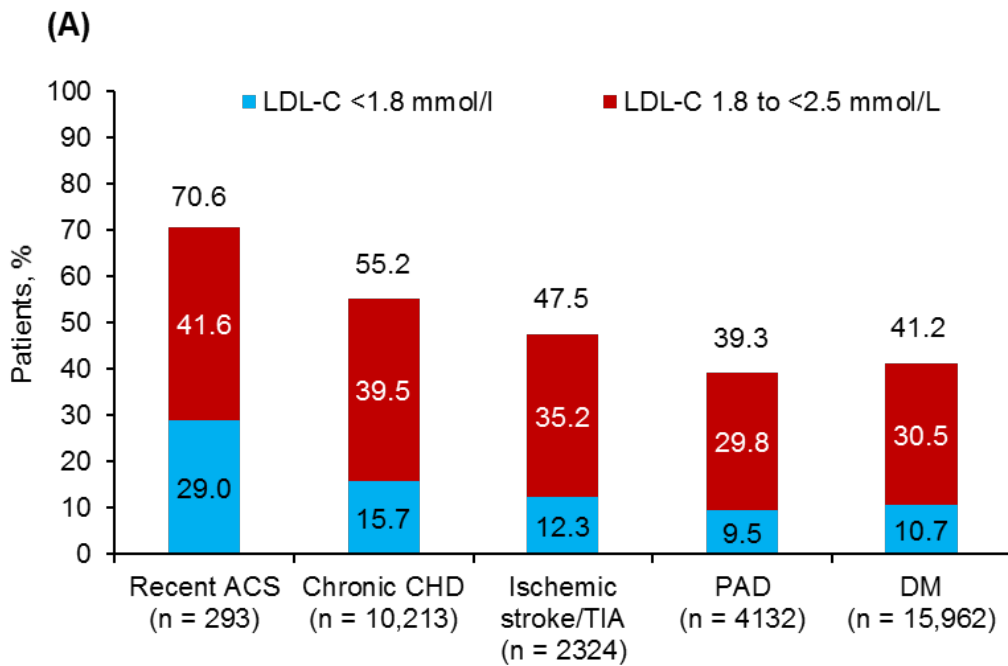
CV = cardiovascular; LDL-C = low-density lipoprotein cholesterol.

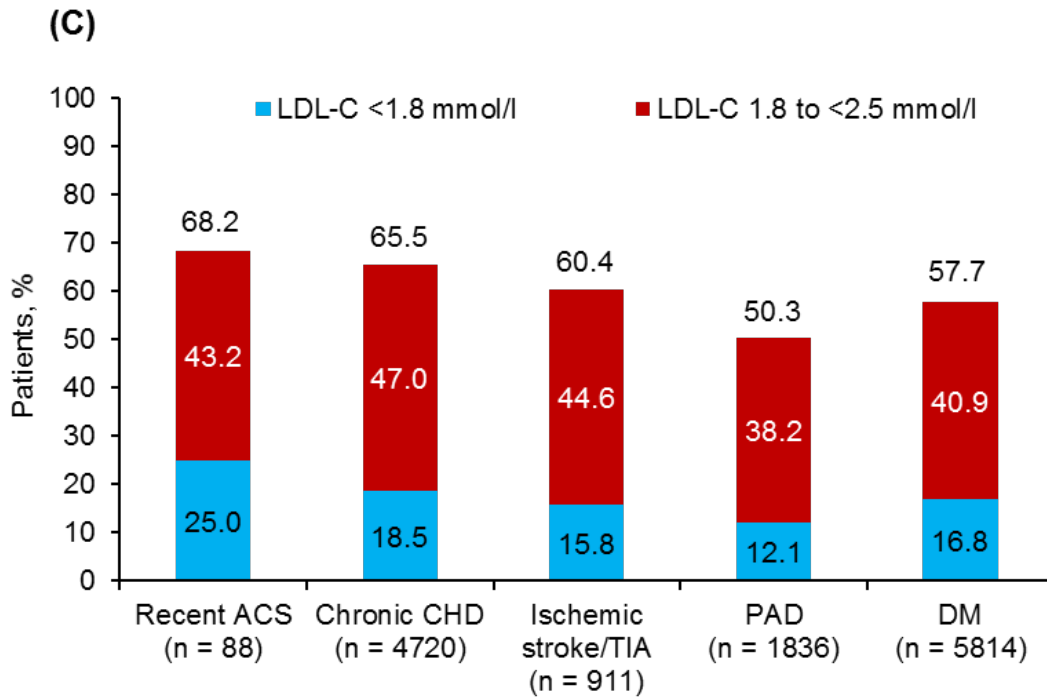
Supplementary Figure 3. Absolute proportions of (A) patients currently treated and (B) not currently treated, by prevalent disease categories.



ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LLT = lipid-lowering therapy; PAD = peripheral arterial disease; TIA = transient ischemic attack.

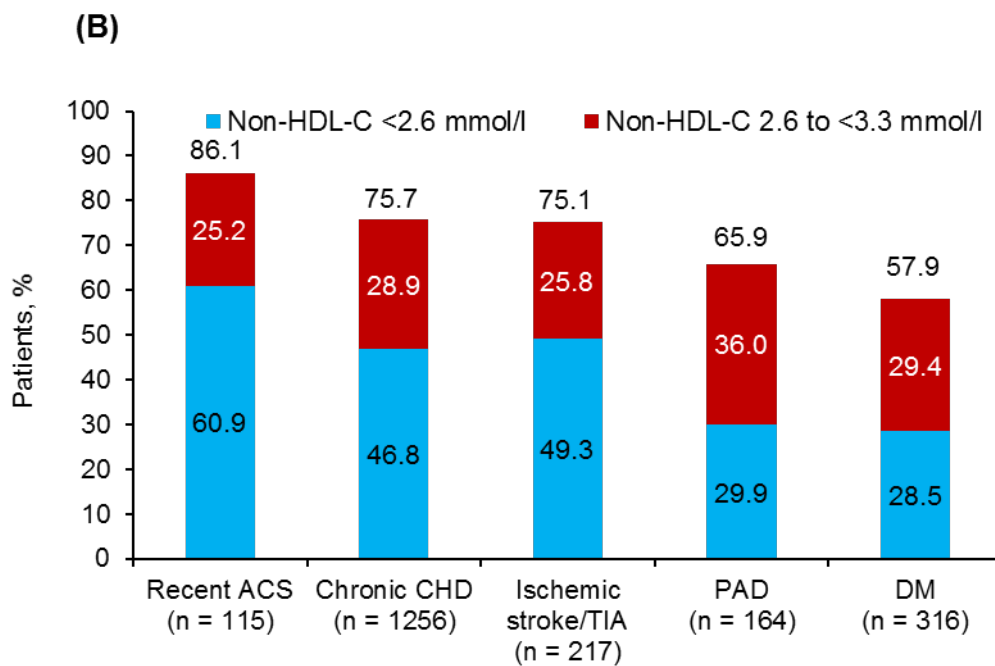
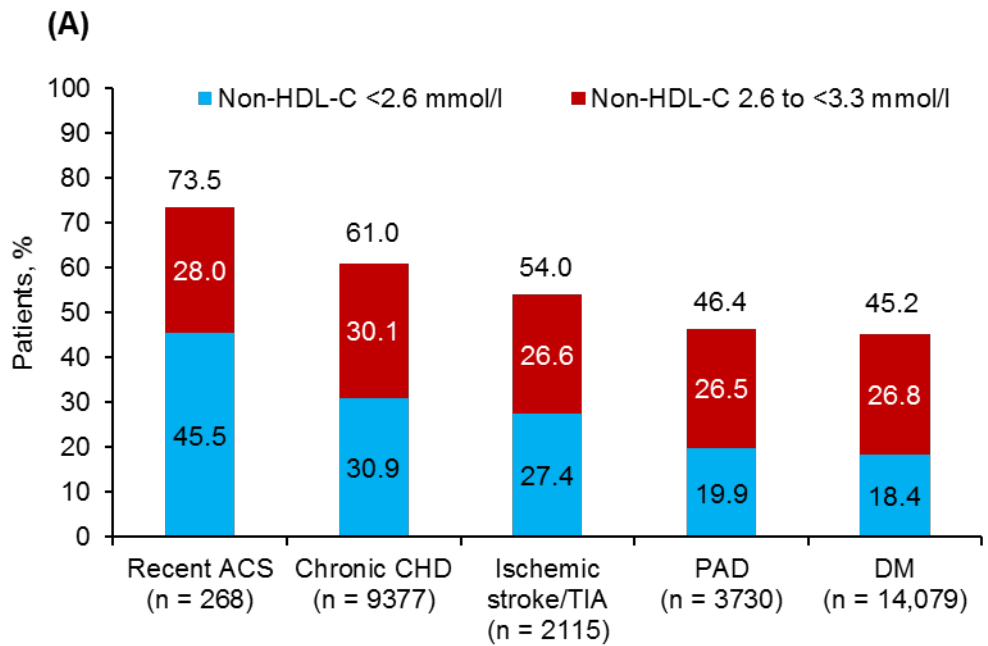
Supplementary Figure 4. Subgroup analyses of LDL-C goal achievement by hierarchical disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.

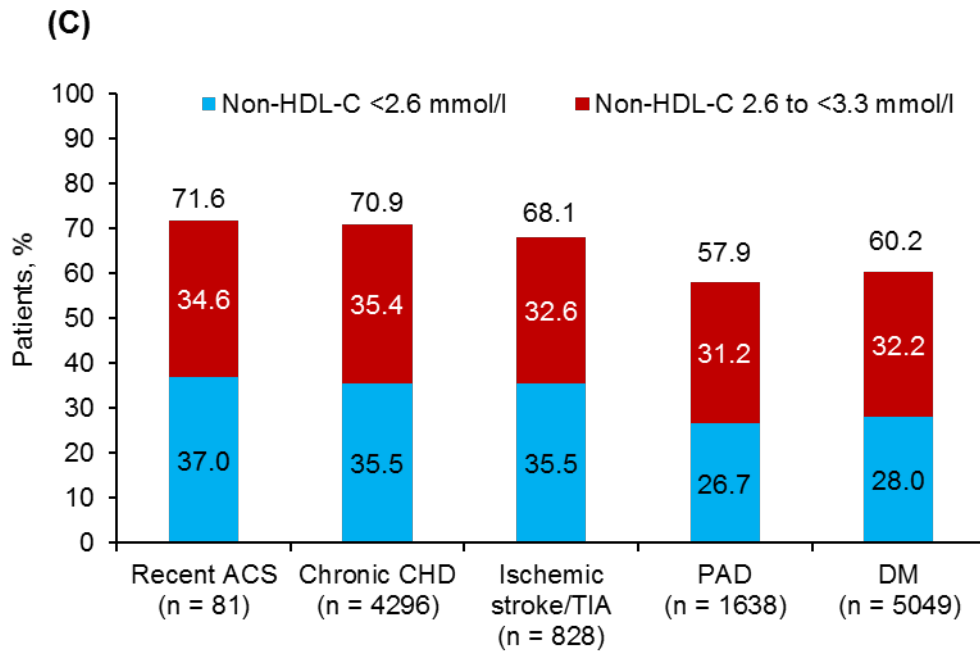




ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack.

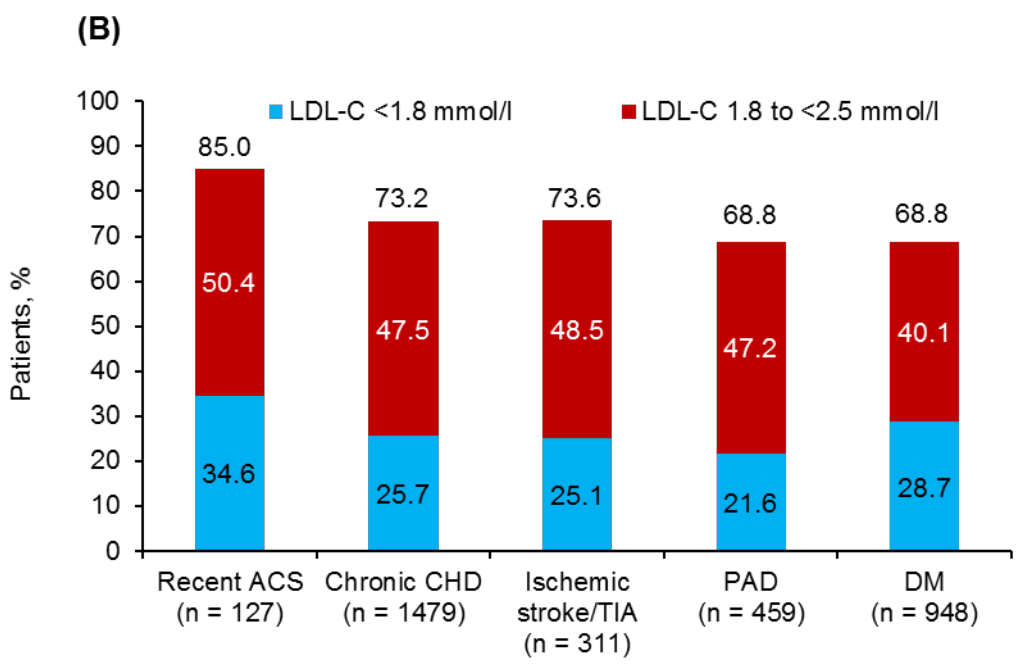
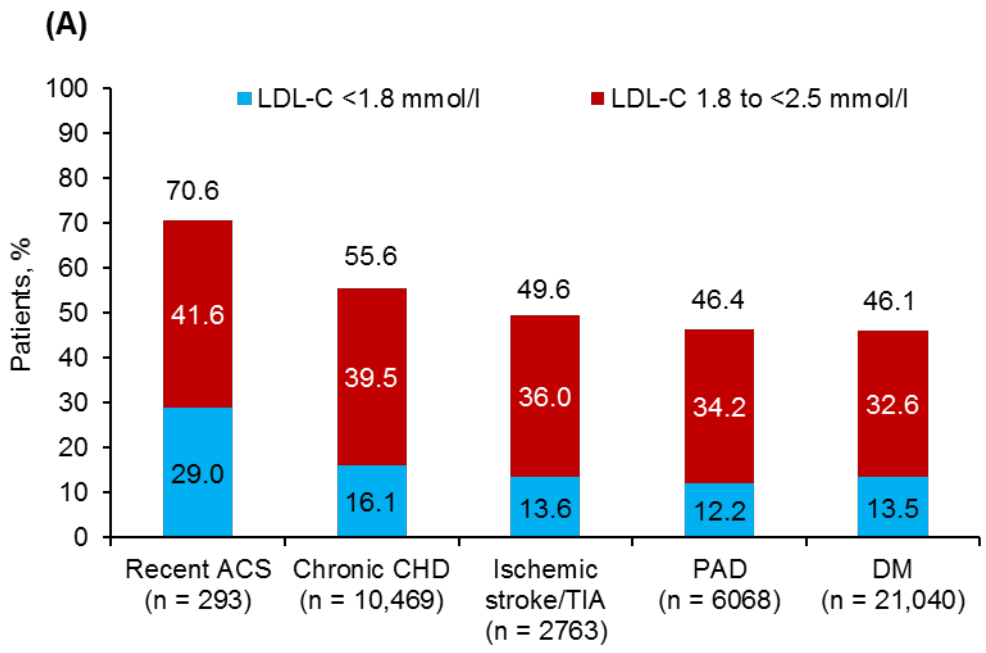
Supplementary Figure 5. Subgroup analyses of non-HDL-C goal achievement by hierarchical disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.



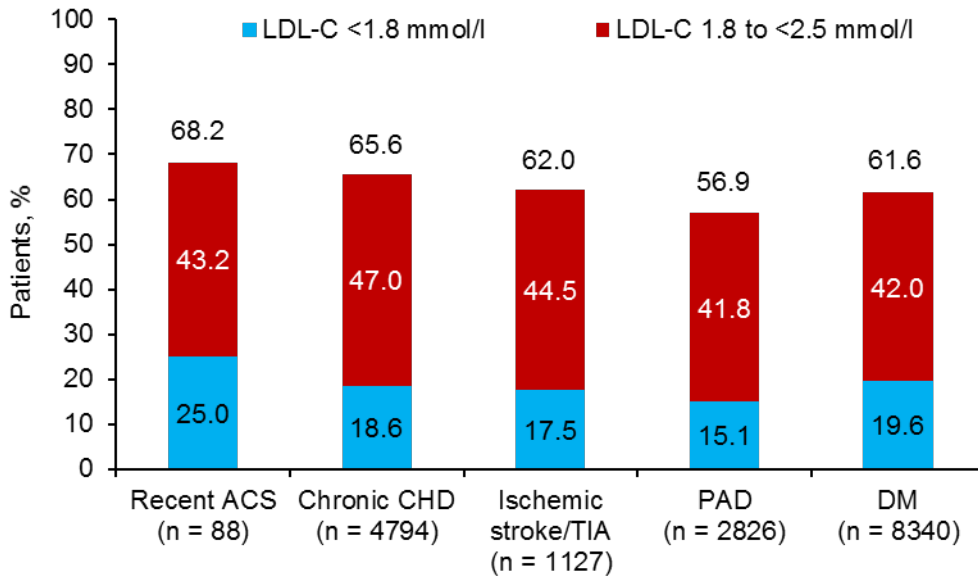


Non-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data. ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; non-HDL-C = non-high-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack.

Supplementary Figure 6. Subgroups of LDL-C goal achievement by prevalent disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.

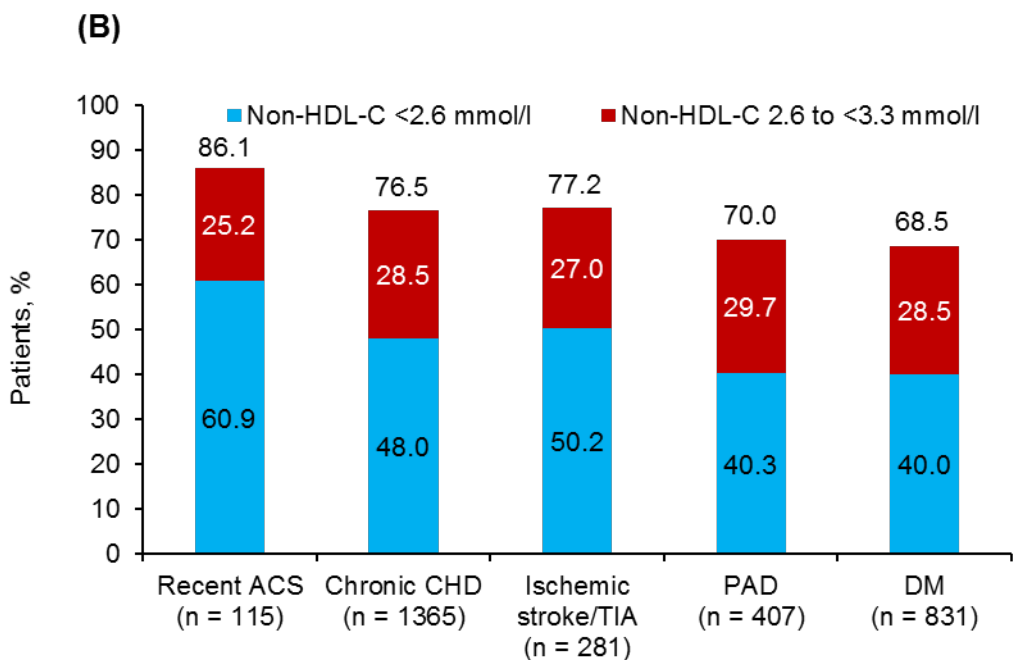
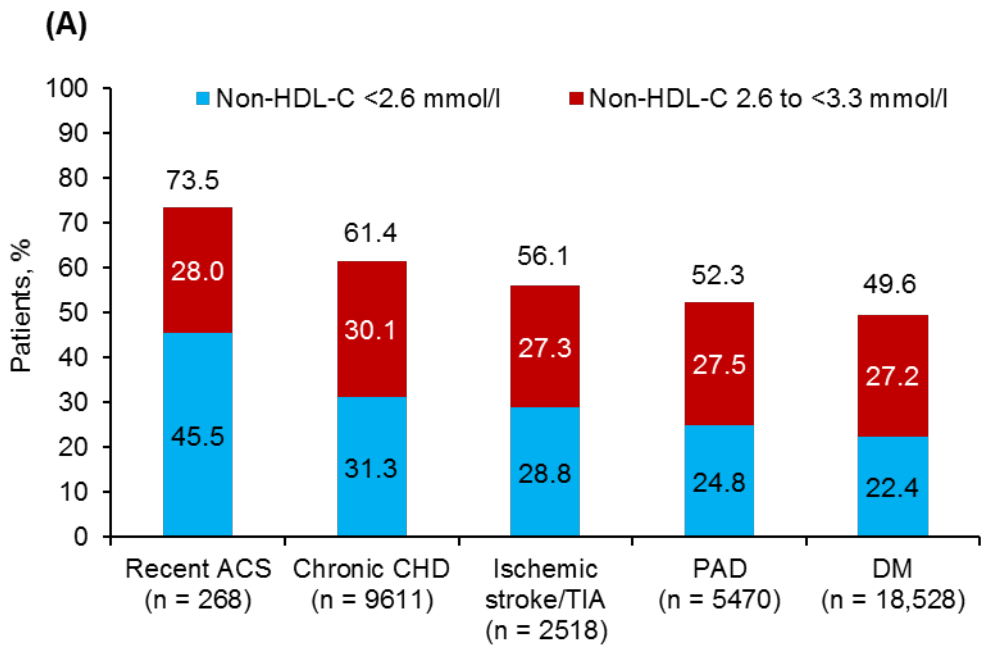


(C)

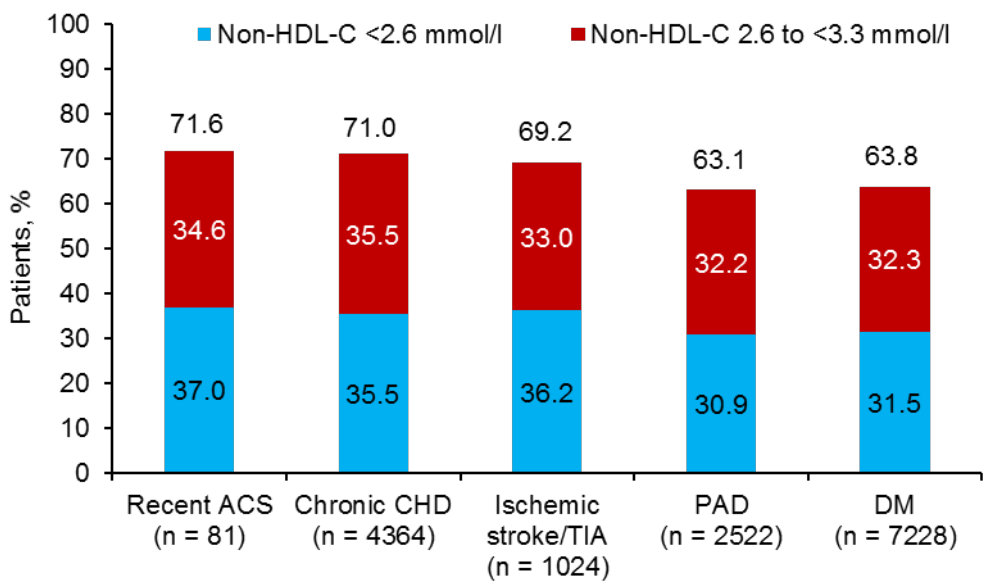


ACS = acute coronary syndrome; CHD = coronary heart disease; DM =, diabetes mellitus; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack

Supplementary Figure 7. Subgroups of non-HDL-C goal achievement by prevalent disease classification for patients (A) combined: treated and not treated, (B) treated with high-intensity statin, and (C) treated with low-to-moderate intensity statin.



(C)



Non-HDL-C measurements were missing for 1472 and 1883 of the ASCVD and DM French population, respectively. Overall, 10.2% were missing non-HDL-C data. ACS = acute coronary syndrome; CHD = coronary heart disease; DM = diabetes mellitus; non-HDL-C = non-high-density lipoprotein cholesterol; PAD = peripheral arterial disease; TIA = transient ischemic attack.