High-intensity Statin use among Patients with Atherosclerosis in the U.S.

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Abstract

Background: Preventive therapy among patients with established atherosclerotic cardiovascular disease (ASCVD) is generally underused. Whether new guideline recommendations and a focus on implementation have improved the use of high-intensity statins is unknown.

Objectives: To evaluate the patterns and predictors of statin use among patients with ASCVD.

Methods: In this retrospective cohort study, pharmacy and medical claims data from a commercial health plan were queried for patients with established ASCVD between 31st January

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Of 601 934 pts with ASCVD on 01.31.2019, 22.5% were on high-intensity statin, 27.6% were on low- or moderate intensity statin & 49.9% were not on any statin. Concerning gaps in high-intensity statin use must be addressed among females, older pts & those with non-CAD ASCVD.

2018 and 31st January 2019. Statin use on an index date of 31st January 2019 was evaluated, as was 12-month adherence and discontinuation. Multivariable logistic regression was used to determine independent associations with varying intensity statin use.

Results: Of the 601 934 patients with established ASCVD, 41.7% were female, mean age 67.5±13.3. Overall, 22.5% of the cohort were on a high-intensity statin, 27.6% were on low- or moderate-intensity statin, and 49.9% were not on any statin. In multivariable analysis, younger patients, females and those with higher Charlson comorbidity were less likely to be prescribed any statin. Among statin users, females, older patients and those with peripheral artery disease were less likely to be on a high-intensity formulation, while a cardiology encounter in the prior year increased the odds. The majority of high-intensity stain users achieved high levels of adherence.

Conclusions: Substantial underuse of statins persists in a large, insured and contemporary cohort of patients with ASCVD from the United States. In particular, concerning gaps in appropriate statin use remain among younger patients, women and those with non-coronary ASCVD.

CONDENSED ABSTRACT

It is unknown whether new guidelines and a focus on implementation has addressed underuse of statin therapy among patients with ASCVD. Of 601 934 patients with ASCVD on the 31st January 2019, 22.5% were on high-intensity statin, 27.6% were on low- or moderate intensity statin and 49.9% were not on any statin. Younger patients, females and those with higher Charlson comorbidity were less likely to be prescribed any statin. Among statin users, females, older patients and those with PAD were less likely to be on a high-intensity formulation. Concerning gaps persist among high risk patients with ASCVD in the US.

Keywords

statins; prevention; predictors; secondary prevention; atherosclerosis

INTRODUCTION

Almost 1 in 2 Americans will develop a clinical manifestation of atherosclerotic cardiovascular disease (ASCVD) in their lifetime[1]. Once established, the risk of sustaining a subsequent ASCVD event such as a myocardial infarction, stroke, limb loss or cardiovascular death is at least 10% per year[2]. Statins can reduce the risk of ASCVD events by approximately 30%[3] with an additional 15% reduction with high-intensity compared to low or moderate-intensity regimens[4,5].

In 2013, the American College of Cardiology (ACC) and the American Heart Association (AHA) guidelines included a Class I recommendation for high-intensity statin use among patients with established ASCVD who were less than 75 years of age[6]. While the release of the guideline resulted in a demonstrable increase in the prescription of high-intensity statins, a number of studies showed the rate of use had plateaued in 2017 with approximately 30–50% of eligible patients ultimately being treated[7–13]. Since then, an update to the guidelines has broadened the high-intensity statin recommendation to class II for those over 75 years of age with ASCVD[14], with the ACC/AHA publicly calling for the need

to improve implementation of their guidelines(15). As prices have decreased with generic availability of high-intensity statins, more potential barriers to optimal statin use have been identified(16–19), and a number of initiatives, including performance and quality measures such as HEDIS (Healthcare Effectiveness Data and Information Set), have been described to improve the adoption of statins more generally(16–19). However, the impact of these developments on contemporary high-intensity statin use, particularly in the context of broader availability of non-statin alternatives such as ezetimibe and Proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors, is unknown. Since statins are inexpensive, well tolerated, and have the most robust evidence of improving clinical outcomes of all the lipid lowering therapies, continued efforts to understand and address underuse is a high priority.

In a large national commercial health plan dataset, we sought to evaluate the patterns and predictors of high-intensity statin use among patients with established ASCVD. In particular, we aimed to understand utilization patterns among key subgroups (e.g. age strata, ASCVD phenotype) as well as temporal changes in both individual statin intensity prescription and subsequent adherence.

METHODS

The New England Institutional Review Board provided an exemption from informed consent given the use of a limited, de-identified dataset. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

Data Source

Eligible patients were identified via a computerized query within the HealthCore Integrated Research Environment (HIRE); a repository of longitudinal claims which comprise medical, pharmacy and laboratory data from a large commercial health plan. The population within HIRE is geographically diverse and considered representative of the commercially insured population in the United States.

Study population

An index date of the 31st January 2019 was established with a 1-year baseline period from 31st January 2018 used to determine cohort eligibility. International Classification of Diseases, Ninth/Tenth Revisions, Clinical Modification (ICD-9/10-CM), Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) codes were used to identify patients with ASCVD. Validated code lists are available in the supplementary appendix. In brief, ASCVD was defined as those with a diagnosis or procedure code representative of coronary artery disease [CAD] (e.g. obstructive coronary atherosclerosis, prior myocardial infarction, prior percutaneous coronary intervention or coronary artery bypass grafts), peripheral arterial disease [PAD] (e.g. vascular claudication, prior percutaneous or open revascularization or amputation from poor circulation) or cerebrovascular disease (e.g. carotid atherosclerosis, ischemic stroke or prior percutaneous or open revascularization). To be included, patients were required to be 18 years of age at

the index date and to have one year of continuous medical eligibility in a health plan prior to the index date.

Follow up

Pharmacy claims were evaluated for a 12-month period of follow up from the index date of 31st January 2019.

Variables

Comorbid conditions were defined by the presence of encounters with corresponding ICD10-CM diagnosis codes in the baseline period for dyslipidemia, type 2 diabetes mellitus (T2DM), hypertension, obesity, chronic kidney disease stage 4 or 5, and depression. Charlson comorbidity score was calculated as previously described. Outpatient visits were defined by the presence of an encounter with a service location of outpatient in the baseline period with further breakdown by cardiology and primary care professional specialties. Non-statin LDL-C lowering therapy was defined as either ezetimibe and/or PCSK-9 inhibitor.

Outcomes of interest

The primary outcome of interest was a prescription fill for a high-intensity statin (atorvastatin 40–80mg or rosuvastatin 20–40mg) that commenced on, or covered, ± 30 days of the index date. Additional outcomes of interest were the prescription of any statin on the index date, the proportion of statin users continuing vs. discontinuing, and the proportion of days covered (PDC) by statin prescriptions over the course of a year as a measure of adherence. Continuous prescription was defined by the presence of a prescription with 0 days without treatment. The proportion of days covered (PDC) was defined as the number of days covered by a prescription divided by 365 days with high levels of adherence defined as 75% PDC. Where there were multiple values for LDL-C, the most recent value was used. Age strata were defined as 'younger' (<45 years), 'middle' (45–74 years) and 'older' (75 years) with those <75 years of age representing a key subgroup as a class I indication for high-intensity statin use.

Statistical analysis

Categorical variables are presented as frequencies and percentages and continuous variables are presented as means and standard deviations or medians and quartile 1, quartile 3, as appropriate. Univariable comparisons between mutually exclusive groups were made statistically with student's t-test or chi-square. Comparisons between non-mutually exclusive groups were made descriptively. A binomial logistic regression model was generated to identify independent predictors of a) statin use and b) high-intensity statin use, with the following clinically-relevant covariates entered into the model: age stratum, sex, ASCVD type, cardiovascular risk factors, medical comorbidities (Charlson comorbidity score of 3, CKD stage 4, depression), care patterns (LDL-C checked within 12 months and baseline non-statin LDL-C lowering therapy) and the presence of cardiology outpatient visit and primary care outpatient visit in the prior 12 months.

RESULTS

We identified 1 083 564 patients with a prior diagnosis of ASCVD and 12 months of continuous enrollment, of which 601 934 had an ASCVD diagnosis in the 12 month baseline period and were 18 years of age. The mean age was 67.5±13.3 years with 41.7% being female. Geographically 27.1% were from the Midwest, 16.7% from the Northeast, 31.2% from the South and 25.0% from the West. CAD was present in 69.2%, cerebrovascular disease in 19.5% and PAD in 35.2%. Polyvascular disease (the presence of two or more of CAD, cerebrovascular disease or PAD) was present in 19.8%.

Characteristics of statin users and non-users

Of the 601 934 patients on the index date, 22.5% were on a high-intensity statin, 27.6% were on some other statin and 49.9% were not on a statin. Cohort characteristics by statin use are presented in Table 1. Compared to those not on a statin, statin users tended to be older, more likely to be male and more likely to have CAD. In particular (Figure 2), only 43.2% of females were on a statin compared to 55.1% of males, and while similar rates of statin use were observed between the middle and older age strata (52.3% vs. 49.3%), younger patients (<45 years) were far less likely to be prescribed a statin (22.4%). Statin users had a higher proportion of ASCVD risk factors that was particularly marked for dyslipidemia and T2DM. Ezetimibe and PCSK-9 inhibitor use was higher among high intensity statin users (6.9%) compared with non-users (4.0%) and non-high statin users (4.0%). Non-users had similar attendance at primary care in the prior 12 months (81.3% vs. 80.6% [high-intensity] or 82.1% [non-high] but were less frequently seen by cardiologists compared to statin users (66.8% vs. 79.2% [high-intensity] or 71.4% [non-high]).

Characteristics of high-intensity statin users

High-intensity statin use was lowest among the poles of age; least frequent among younger patients (12.7%), followed by older patients (16.6%) followed by middle-aged (26.1%) (Figure 2). Compared with the overall cohort, users of a high-intensity statin were less likely to be female (29.2 vs. 41.7%) or have a history of PAD (26.0 vs. 35.2%) (Central Illustration). Rates of cardiovascular risk factors were higher among those using high-intensity statins although medical comorbidity burden was similar. LDL-C levels were only available in 22.8% (137174/601934) of patients. Of those, only 28.9% (39764/137174) had levels 70mg/dL with the majority of those on a high intensity statin (24786/39764).

Independent predictors of any statin use

'Middle'-aged and 'older' patients were over twice as likely as 'younger' patients to be on a statin despite having premature ASCVD (Table 2). Females were 30% less likely to be treated with a statin compared to males (OR 0.70, 95%CI 0.69–0.71). Compared with CAD, those with cerebrovascular disease were 20% less likely to receive a statin (OR 0.78, 95%CI 0.76–0.79) and those with PAD almost half as likely (OR 0.55, 95%CI 0.55–0.56). Dyslipidemia was significantly more prevalent among statin users (OR 4.23, 95%CI 4.17–4.29), as was a diagnosis of either T2DM (OR 1.47, 95%CI 1.45–1.49) or hypertension (OR 1.39, 95%CI 1.37–1.41). A high Charlson comorbidity score reduced the odds of statin

prescription (OR 0.72, 95%CI 0.71–0.73), as did the presence of depression (OR 0.93, 95%CI 0.92–0.95).

Independent predictors of high intensity statin use among statin users

While middle-aged and older patients were more likely to be on a statin overall, among statin users they were less likely to be on a high-intensity formulation compared to the younger age stratum (Table 2). In contrast to men, women were not only less likely to be on a statin overall, but were also less likely to be on a high-intensity formulation (OR 0.68, 95%CI 0.68–0.69). Patients with PAD were less than half as likely as CAD patients to be on a high-intensity statin (OR 0.43, 95%CI 0.42–0.43). The odds of high-intensity statin use were modestly increased among those with hypertension (OR 1.13, 95%CI 1.11–1.15) and T2DM (OR 1.12, 95%CI 1.10–1.14). Use of other non-statin LDL-C lowering agents increased the likelihood that a patient was also on a high intensity statin (OR 1.44, 95%CI 1.40–1.49), as did visiting a cardiologist in the prior 12 months (OR 1.21, 95%CI 1.19–1.23).

Patterns of high-intensity statin use among patients < 75 years of age

In the key subgroup of patients < 75 years old, high-intensity statin users were less commonly women (26.2 vs. 38.9%), more likely to have obesity (22.5 vs. 11.6%) less often had PAD (23.0 vs. 35.5%) or cerebrovascular disease (16.5 vs. 27.2%) and generally had lower medical comorbidity burden (Charlson score   3, 19.8 vs. 38.5%; CKD   4, 31.8 vs. 5.2%) compared with those   75 years old (Supplementary Table 1). Those < 75 years old on high-intensity statins attended fewer outpatient appointments (median 21 vs. 30) reflected in lower proportions having seen a cardiologist in the last 12 months (78.3 vs. 82.1%) and a primary care physician over the same period (79.7 vs. 83.4%).

Proportion of days covered by high-intensity statins

Over 80% of high-intensity statin users at index were able to achieve high levels of adherence (Table 3). Compared with the low adherence group (<50% PDC), the high adherence group had a greater proportion of older patients (24.3 vs. 18.4%) and a lower proportion of younger patients (1.9 vs. 3.9%). Among the least adherent group (PDC <50%), there was a higher prevalence of CKD (8.7 vs. 6.7%) and depression (18.0 vs. 15.0%) compared with the most adherent group.

Trajectory of statin use

Compared to the index date, there was essentially no difference in the final proportions of patients on high-intensity statin, non-high-intensity statin or no statin therapy at 12 months (Figure 3). In total only 19.1% of patients underwent some form of change in statin therapy however almost half of these (9.2%) were related to down-titration or discontinuation. Of the patients on no statin at index, 83.6% (n=253 459) were still not on any statin at follow up with the vast majority (81.3%, n=246 253) receiving no prescription for any statin over a 12 month period. Of the remaining 16.4% (n=49 607) on no statin at index, 9.2% (n=27 767) ended up on a non-high intensity statin and 7.2% (n=21 840) were on a high-intensity statin at follow-up.

Of the patients on non-high-intensity statin at index, 81.7% (n=133 043) remained on a similar formulation at follow up with only 326 of those patients undergoing some form of unsuccessful up-titration in between. At 12 months, only 3.8% (n=6 305) of the non-high intensity group at index were commenced and remained on high-intensity statin at follow up while 15.2% (n=24 740) were no longer receiving a prescription for any statin.

Of the patients on high-intensity statin at index, 83.7% (n=113 876) remained on a high-intensity statin at follow-up with 202 patients undergoing some period of down-titration in the interim. At 12 months, 1.7% (n=2 358) were on a non-high-intensity statin at 12 months while 14.6% (n=19 878) were on no statin at all, of whom 276 were transiently on a non-high-intensity statin.

Continuation and discontinuation of high-intensity statin

Individuals in the oldest stratum tended to be more likely to discontinue their high-intensity statin, as did women (Table 4). Patients with PAD more commonly discontinued their high-intensity statin while the reverse was true for those with T2DM. Those discontinuing high-intensity statins in follow up had a higher burden of medical comorbidities.

DISCUSSION

This multicenter analysis of over 600 000 patients with established ASCVD represents one of the largest contemporary analyses of statin prescribing habits in the United States. The study has a number of important findings. First, despite having established ASCVD, barely half of our population were on a statin and less than a quarter overall were on a high-intensity formulation. Second, younger patients and females were less likely to receive any form of statin therapy. Third, among statin users, women and those with non-CAD ASCVD were less likely to be on a high-intensity formulation whereas those seeing a cardiologist were more likely. Finally, multiple opportunities for care improvement exist; among the no-statin cohort almost two-thirds had seen a cardiologist in the prior 12 months, and among those with the lowest levels of adherence, over 80% had seen their PCP or cardiologist in the prior 12 months.

Our finding that only 50.1% of patients were using a statin is lower than other comparable studies which have reported usage rates between 60 and 70% among patients with established ASCVD. The reasons underlying the lower usage rates observed here are likely multifactorial, but most probably relate to three key differences. First, most other studies reporting statin use among ASCVD patients have evaluated prescription fill rates within 30 days of an index event whereas our cohort deliberately included patients with any qualifying ASCVD encounter in the prior 12 months. Not only is prescription highest around an acute event, but discontinuation increases over time (20); thus, our estimates are likely to be a more representative snapshot of a general ASCVD population rather than an incident ASCVD cohort. Second, some studies have relied on self-reported medication use which would over-estimate 'use' when compared to prescription fill(12). Thirdly, our use of a 30-day prescription window from a single index date is a relatively strict definition of use and when relaxed to 'any use' over 365 days, approaches a more comparable 66%. However, notwithstanding differences in study population or outcome measure, our data add

to the compelling narrative that statin use remains suboptimal. Low rates of statin use have been repeatedly shown to associate with higher mortality(21), even after adjustment for the presence of any healthy adherer effect(11). Most importantly, the randomized trial evidence showing reductions in death and major vascular events makes understanding and addressing underuse a public health priority.

Despite guideline recommendations, less than half of our statin users and only 22.5% overall were on a high-intensity formulation. These figures suggest that despite early uptake in high-intensity statin use following the 2013 guidelines, there has been limited progress over the last 2–3 years. This is of particular concern as our cohort ought to reflect a comparably well-treated population with high rates of adherence and excellent access to care evidenced by over two-thirds having seen a cardiologist and over three-quarters having seen a PCP within the prior 12 months. The finding that only 19% of this cohort underwent some form of statin-related medication change over a 12 month period is consistent with data from the GOULD registry which showed that only 17.1% of patients with ASCVD underwent intensification of lipid lowering therapy in a 2 year period(22). The lack of medication changes together with evidence that over 70% of this cohort's LDL-C were not to target supports the presence of significant clinician inertia (23). Some of the contributing factors may include a lack of knowledge of guidelines and the role of high-intensity statins(17), discordance between guideline knowledge and physician prescribing habits(24), a lack of confidence navigating perceived statin-intolerance(25) as well as contrarian beliefs about the role of statins(26). Given prior studies have previously documented evidence of widespread practice and provider-level variation in the use of high-intensity statins(27,28), multifaceted interventions harnessing educational outreach as well as audit-and-feedback are likely to be needed to overcome patient, clinician and system-level barriers. The development of novel models of care elevating the role of nurses and pharmacists in multidisciplinary care(29) as well as the potential for harnessing remote and digital management platforms(30), in addition to interventions aimed at patients (31) offers hope, although data supporting their capacity for dissemination at scale is awaited.

In particular, the low rates of discontinuation suggest the need for a renewed focus on shifting the perceptions of those who have already discontinued, largely on the account of intolerance, and to begin the lengthy process of rechallenge(32). A number of studies have shown patients previously considered intolerant are able to resume statin use(25,33–35). While optimism surrounds the emergence of a number of non-statin alternatives for lipid lowering(36), these agents remain costly and ought to be added to baseline statin therapy as most were studied. Thus in order to achieve patient-level treatment goals and cost-effective lipid-lowering, greater use of high-intensity statins has both individual and population-level implications.

Our study included over 20 000 patients less than 45 years of age which represents one of the largest cohorts to evaluate statin prescribing in those with very premature ASCVD. Our concerning finding that only 22.4% of 'younger' patients were using a statin likely reflects a knowledge gap around premature ASCVD contributing to underuse at both the patient and clinician level. It is clear that 'younger' patients are less likely to use statins despite established and premature ASCVD. At the patient level there may be a

mismatch between actual and perceived future risk of a recurrent event – either overly optimistic or fatalistic - which could lead to suboptimal behavioral choices including statin discontinuation and non-adherence(18,37–40). Further, given the inverse association between age and online information seeking(41,42), younger patients may be more likely to acquire the prevailing belief from the media that statins are harmful and thus may be more likely to refuse treatment or discontinue(43). At the clinician level, a lower burden of traditional risk factors(44,45) may lead to the misconception that the need for secondary preventive therapies is negated or mitigated. This phenomenon is likely especially pertinent among individuals further out from their index event.

This data adds to the growing body of literature shining light on treatment disparity by sex. Women in our cohort were not only undertreated with statins, but even those using a statin were significantly less likely to be receiving a high intensity formulation and had higher rates of discontinuation. While variation in ASCVD risk factor profile, greater medical comorbidity burden or older age are frequently cited as reasons for less aggressive secondary preventive care among women, after adjustment for these factors women remained half as likely to be on a high intensity statin compared to men. Our study also confirmed greater rates of high-intensity statin discontinuation among women(13). With no evidence of heterogeneity in efficacy by gender(46), ongoing work must not only address misperceptions and barriers to the prescription of high-intensity statins in women(47), but also further understand (and address) differences in tolerability which may relate to sex-based variation in statin metabolism(48).

Our study confirms that patients with PAD continue to represent a neglected ASCVD subgroup with respect to statin use. PAD has long been recognized as a high risk ASCVD manifestation for both cardiovascular and non-cardiovascular mortality, and yet relative under-treatment has been documented for over 20 years(49) with fewer than 20% receiving a statin as recently as 2013(7). In more contemporary data from 2017, Colantonio et al. evaluated a harmonized Medicare and MarketScan cohort of over 900 000 US patients with established ASCVD and found between 33.9 and 56.0% of patients with PAD were on some dose and formulation of statin with between 15.6 and 29.1% of those reporting high intensity use(50). This is remarkably consistent with our own finding that 44.5% of PAD patients received a statin, of which only 37.5% received a high-intensity formulation, reaffirming not only the persistent gap in PAD care but also a lack of progress. For a disease affecting >200 million worldwide that carries a high risk of mortality and morbidity, and for which statins have proven efficacy, (and high intensity statins incremental benefit(51)), the lack of guideline(14,52) adoption is of ongoing concern.

There are limitations to our study. Administrative claims data are subject to misclassification; we attempted to mitigate this through the use of validated code lists. Coding for myalgia and muscle aches is generally poor in administrative claims data and thus parsing out statin intolerance as a contributor to statin non-prescription was not possible. Additionally there may be use of statins that is not captured through billing, with relatively inexpensive prescriptions being paid with cash. This is unlikely a major factor in the era of electronic prescriptions. Our study evaluated prescription dispensing and thus the impact of primary non-adherence to a written prescription cannot be determined. The study

included only privately insured participants, and thus does not include uninsured patients. However as one of the larger insurers with approximately 37 million fully insured members, Anthem/ HealthCore represents a large portion of U.S. healthcare recipients. Furthermore the described gaps are likely to be even larger in uninsured populations.

CONCLUSION

Our study of over 600 000 patients from the United States with established atherosclerotic cardiovascular disease reveals substantial underuse of statins and their high intensity formulations that is likely a major contributor to preventable death and disability. In particular, gaps in the care of younger patients, women, and those with non-coronary ASCVD show no signs of improving when compared to prior literature. Multifaceted intervention must be refined and implemented to address barriers to guideline-recommended care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ACKNOWLEDGEMENTS

ABBREVIATIONS

ASCVD	atherosclerotic cardiovascular disease
CAD	coronary artery disease
CKD	chronic kidney disease
HEDIS	Healthcare Effectiveness Data and Information Set
LDL-C	low-density lipoprotein cholesterol
PAD	peripheral artery disease
PCP	primary care physician
PCSK-9	Proprotein convertase subtilisin/kexin type 9
PDC	proportion of days covered
T2DM	Type 2 diabetes mellitus

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CLINICAL PERSPECTIVES

Competency in Systems-Based Practice:

Statin medications, particularly high-intensity formulations, are underutilized among patients with established atherosclerosis in the U.S. Younger patients, women, and those with comorbidities are less likely to take statin therapy, while statin users who are older, female, or have peripheral artery disease are less likely to receive high-intensity formulations.

Translational Outlook:

Auditing, feedback and benchmarking of high-intensity statin therapy (rather than simply the use of any statin drug) may be needed promote more frequent use.
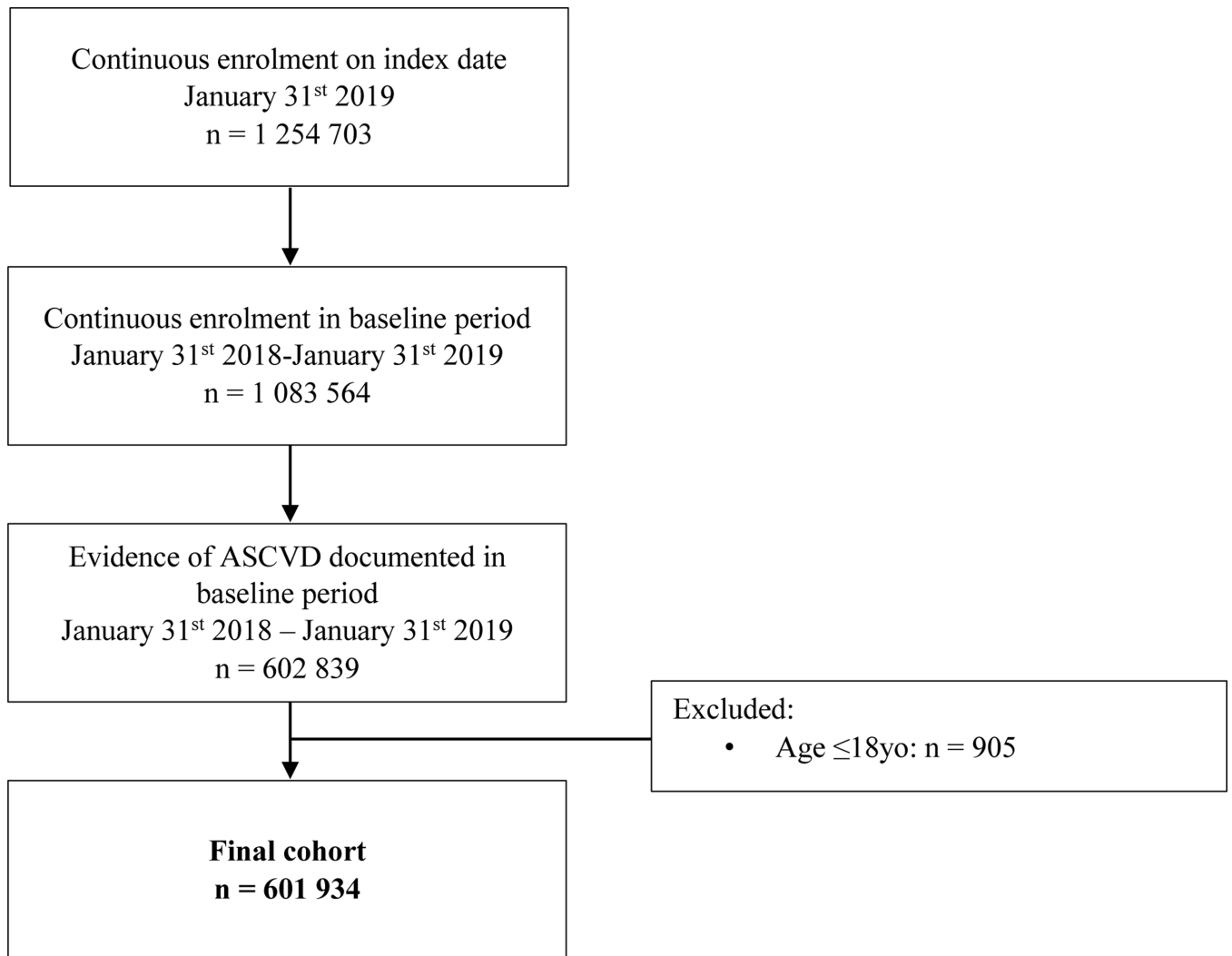
Figure 1. CONSORT Diagram.
Progressive identification of eligible participants based on inclusion criteria to generate final analytic cohort of 601 934.
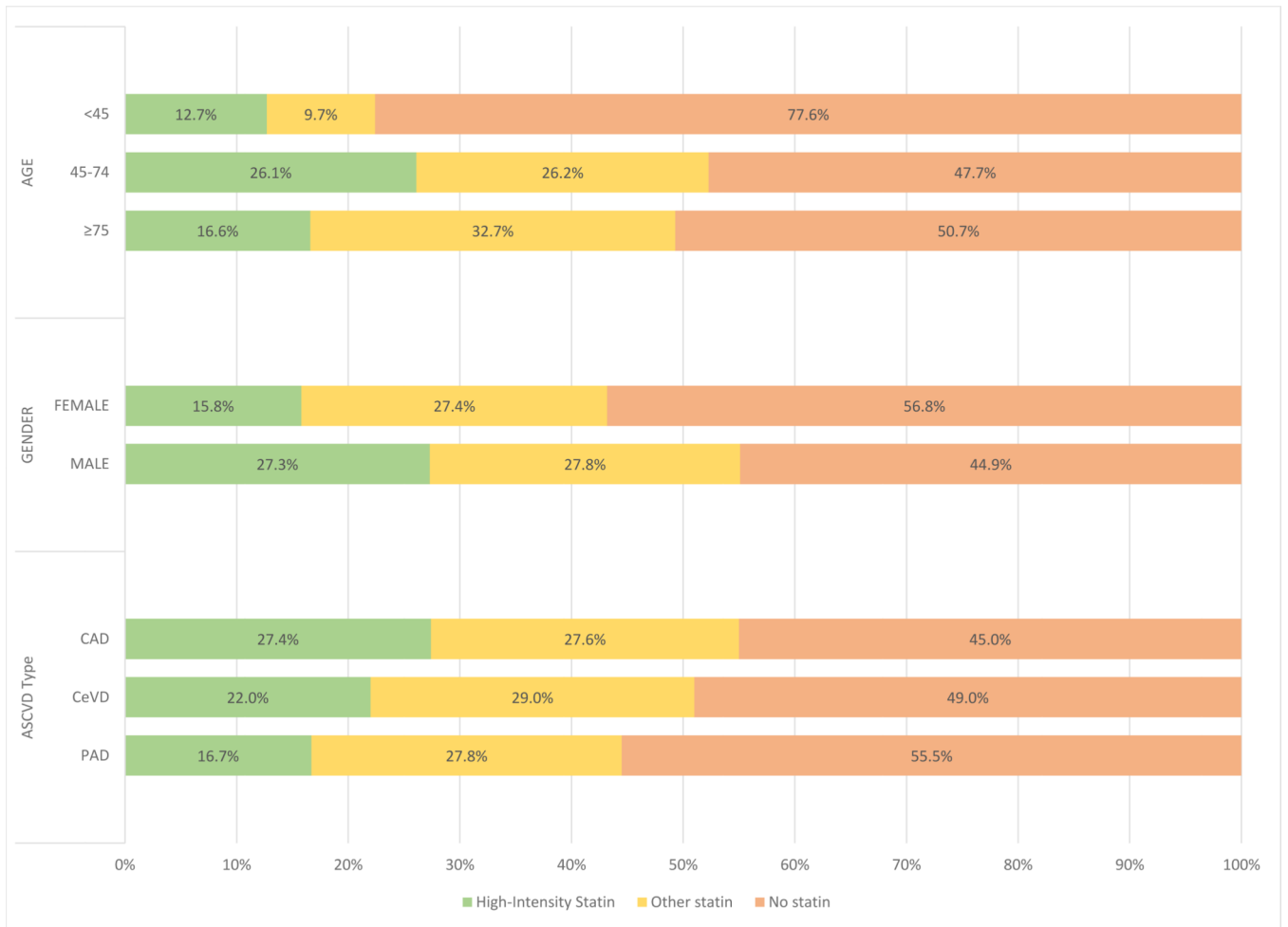
Figure 2. Statin use among key subgroups.

Patients presented by baseline statin use (high-intensity = green; other statin = yellow, and no statin = orange) within key subgroups of age, gender and ASCVD phenotype.

CAD - coronary artery disease; CeVD – cerebrovascular disease; PAD – peripheral artery disease;
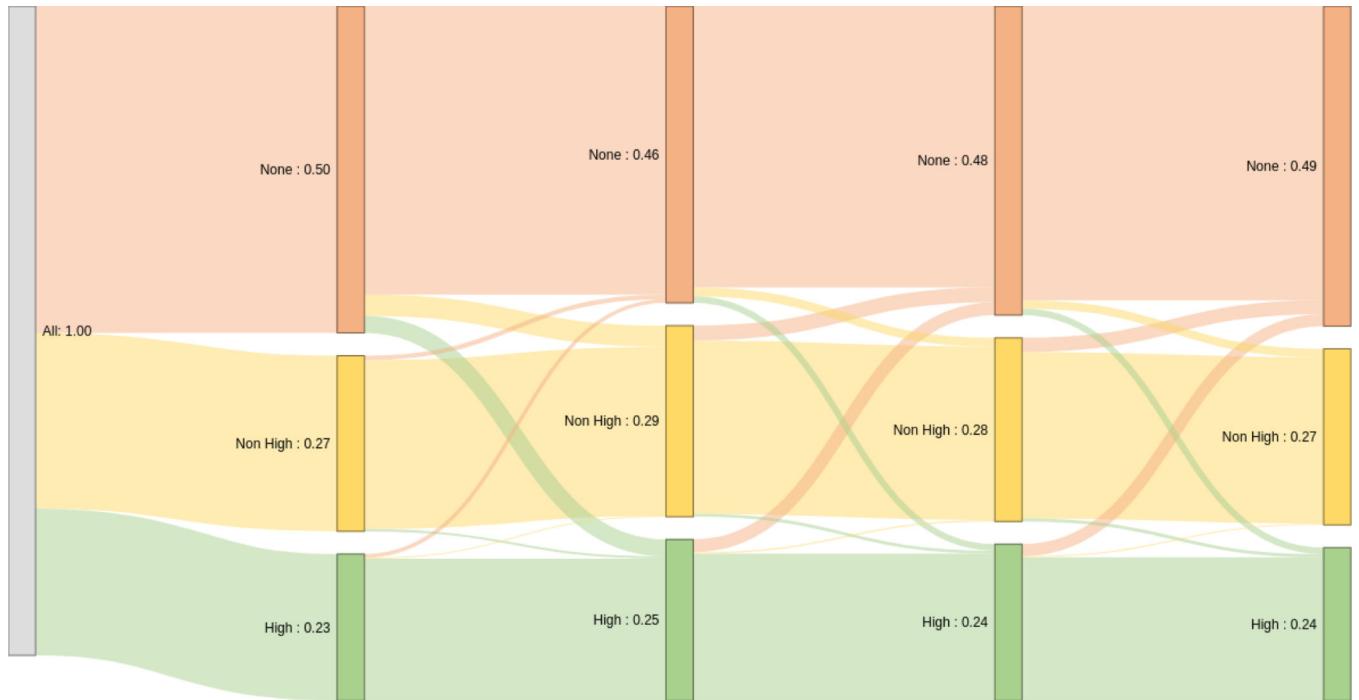
Figure 3. Sankey diagram illustrating the dynamics of statin use in follow-up.
The proportion of patients receiving high-intensity statins are shaded green, those receiving non-high-intensity statins in yellow and no statin in orange. The black numbers represent the shaded proportion as a percentage of the overall population. The vertical lines represent 3-month intervals.
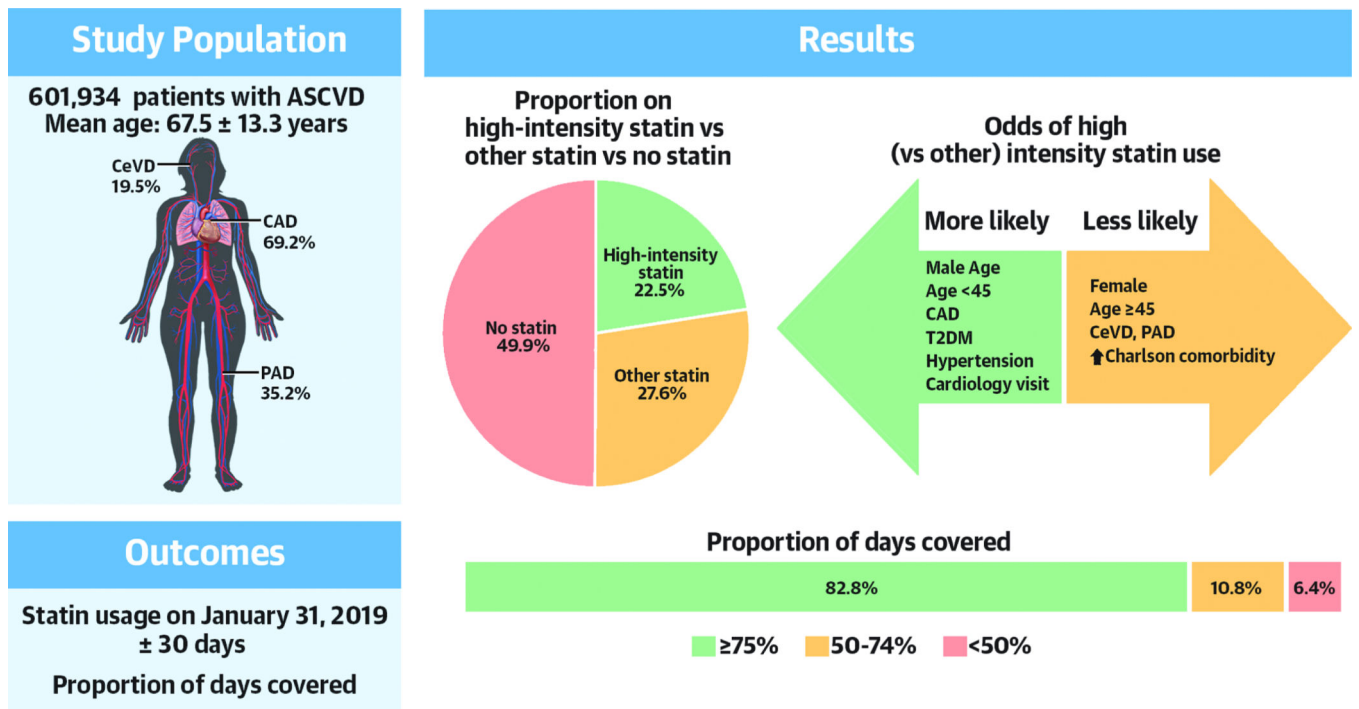
Central illustration. Statin use in 601934 ASCVD patients on 31st January 2019.
Proportion on high-intensity statin vs. other statin vs. no statin. Odds of high (vs. other)
intensity statin use. Proportion of days covered among users of high-intensity statins.

Table 1

Cohort Characteristics by Statin Use

	Overall (N = 601,934 [100%])	High-Intensity Statin (n = 135,569 [22.5%])	Other Statin (n = 166,231 [27.6%])	No Statin (n = 300,134 [49.9%])	*P* Value
Age, y	67.5 ± 13.3	65.9 ± 11.1	70.0 ± 11.9	66.9 ± 14.7	<0.0001
<45 (younger)	23,801 (4.0)	3,017 (2.2)	2,313 (1.4)	18,471 (6.1)	<0.0001
45–74 (middle)	383,630 (63.7)	100,247 (73.9)	100,365 (60.4)	183,018 (61.0)	<0.0001
75 (older)	194,503 (32.3)	32,305 (23.8)	63,553 (38.2)	98,645 (32.9)	<0.0001
Sex					<0.0001
Female	250,875 (41.7)	39,576 (29.2)	68,778 (41.4)	142,521 (47.5)	
Male	351,059 (58.3)	95,993 (70.8)	97,453 (58.6)	157,613 (52.5)	
Cardiovascular history					
CAD	416,349 (69.2)	114,115 (84.2)	115,218 (69.3)	187,016 (62.3)	<0.0001
CeVD	117,202 (19.5)	25,843 (19.1)	34,046 (20.5)	57,313 (19.1)	<0.0001
PAD	211,616 (35.2)	35,269 (26.0)	58,811 (35.4)	117,536 (39.2)	<0.0001
ASCVD risk factors					
Dyslipidemia	474,823 (78.9)	123,762 (91.3)	150,393 (90.5)	200,668 (66.9)	<0.0001
T2DM	219,188 (36.4)	55,717 (41.1)	68,047 (40.9)	95,424 (31.8)	<0.0001
Hypertension	493,050 (81.9)	118,245 (87.2)	144,239 (86.8)	230,566 (76.8)	<0.0001
Obesity	109,334 (18.2)	27,009 (19.9)	29,782 (17.9)	52,543 (17.5)	<0.0001
Medical comorbidities					
Charlson comorbidity score 3	157,451 (26.2)	32,879 (24.3)	44,205 (26.6)	80,367 (26.8)	<0.0001
CKD stage 4	16,392 (2.7)	3,545 (2.6)	4,663 (2.8)	8,184 (2.7)	0.006
Depression	101,990 (16.9)	21,218 (15.6)	26,223 (15.8)	54,549 (18.2)	<0.0001
Care patterns					
LDL-C checked last 12 months	153,305 (25.5)	38,395 (28.3)	44,262 (26.6)	70,648 (23.5)	<0.0001
Ezetimibe/PCSK-9 inhibitor	27,855 (4.6)	9,408 (6.9)	6,597 (4.0)	11,850 (4.0)	<0.0001
Outpatient visits	25 (13–44)	23 (12–42)	26 (14–45)	25 (13–45)	<0.0001
Cardiology visit	426,788 (70.9)	107,360 (79.2)	118,717 (71.4)	200,711 (66.8)	<0.0001
PCP visit	489,589 (81.3)	109,261 (80.6)	136,477 (82.1)	243,851 (81.3)	<0.0001

Values are mean ± SD, n (%), or median IQR.

ASCVD = atherosclerotic cardiovascular disease; CAD = coronary arterydisease; CKD = chronic kidneydisease; LDL-C = low-density lipoprotein cholesterol; PAD = peripheral artery disease; PCP = primary care physician; PCSK-9 = proprotein convertase subtilisin/kexin type 9; PDC = proportion of days covered; T2DM = type 2 diabetes mellitus.

Table 2.

Independent predictors of a) any statin use and b) high-intensity statin use

	Any statin vs. no statin			High intensity vs. other statin		
	OR	95% CI	p value	OR	95% CI	p value
Age						
<45 (younger)	Ref			Ref		
45–74 (middle)	2.66	2.58 – 2.75	<0.0001	0.83	0.79 – 0.87	<0.0001
75 (older)	2.09	2.02 – 2.15	<0.0001	0.44	0.42 – 0.46	<0.0001
Sex						
Male	Ref			Ref		
Female	0.70	0.69 – 0.71	<0.0001	0.68	0.68 – 0.69	<0.0001
Cardiovascular history						
CAD	Ref			Ref		
CeVD	0.78	0.76 – 0.79	<0.0001	0.65	0.63 – 0.66	<0.0001
PAD	0.55	0.55 – 0.56	<0.0001	0.43	0.42 – 0.43	<0.0001
ASCVD Risk factors						
Dyslipidemia	4.23	4.17 – 4.29	<0.0001	1.03	1.01 – 1.05	0.013
T2DM	1.47	1.45 – 1.49	<0.0001	1.12	1.10 – 1.14	<0.0001
Hypertension	1.39	1.37 – 1.41	<0.0001	1.13	1.11 – 1.15	<0.0001
Obesity	0.99	0.98 – 1.01	0.20	1.00	0.98 – 1.02	0.96
Medical comorbidities						
Charlson comorbidity 3	0.72	0.71 – 0.73	<0.0001	0.95	0.93 – 0.97	<0.0001
CKD Stage 4	1.03	1.02 – 1.05	0.0006	1.04	1.02 – 1.06	<0.0001
Depression	0.93	0.92 – 0.95	<0.0001	1.10	1.08 – 1.12	<0.0001
Care patterns:						
LDL-C checked last 12months	1.09	1.08 – 1.11	<0.0001	0.91	0.90 – 0.93	<0.0001
Ezetimibe/PCSK-9i	0.89	0.87 – 0.92	<0.0001	1.44	1.40 – 1.49	<0.0001
Outpatient visits						
Cardiology visit PCP visit	1.06	1.04 – 1.07	<0.0001	1.21	1.19 – 1.23	<0.0001
PCP visit	0.91	0.89 – 0.92	<0.001	0.97	0.96 – 0.99	0.0016

Table 3.

High-intensity statin users by proportion of days covered.

	Proportion of days covered		
	<50%	**50–74%**	**75%**
	n = 8 051 (6.4%)	**n = 13 673 (10.8%) n**	**n = 104 679 (82.8%)**
Age, mean±SD	63.4±11.2	64.3±11.3	66.2±11.0
<45 (younger)	315 (3.9)	428 (3.1)	2 029 (1.9)
45–74 (middle)	6 254 (77.7)	10 487 (76.7)	77 196 (73.7)
75 (older)	1 482 (18.4)	2 758 (20.2)	25 454 (24.3)
Sex			
Female	2 575 (32.0)	4 204 (30.8)	29 694 (28.4)
Male	5 476 (68.0)	9 469 (69.3)	74 985 (71.6)
Cardiovascular history			
CAD	6 507 (80.8)	11 311 (82.7)	88 878 (84.9)
CeVD	1 543 (19.2)	2 583 (18.9)	19 648 (18.8)
PAD	2 208 (27.4)	3 725 (27.2)	26 501 (25.3)
ASCVD Risk factors			
Dyslipidemia	7 276 (90.4)	12 553 (91.8)	95 694 (91.4)
T2DM	3 302 (41.0)	5 868 (42.9)	42 615 (40.7)
Hypertension	6 915 (85.9)	11 899 (87.0)	91 362 (87.3)
Obesity	1 683 (20.9)	2 852 (20.9)	20 676 (19.8)
Medical comorbidities			
Charlson comorbidity 3	2 058 (25.6)	3 382 (24.7)	24 472 (23.4)
CKD Stage 4	701 (8.7)	1 023 (7.5)	6 961 (6.7)
Depression	1 445 (18.0)	2 349 (17.2)	15 691 (15.0)
Care patterns:			
LDL-C checked last 12months	2 461 (30.6)	4 245 (31.1)	29 164 (27.9)
Baseline non-statin LLT	511 (6.4)	1 007 (7.4)	7 340 (7.0)
Outpatient visits, median [Q1-Q3]	22 [11–42]	23 [12–41]	23 [12–41]
Cardiology visit	6 322 (78.5)	10 607 (77.6)	83 151 (79.4)
PCP visit	6 540 (81.2)	11 020 (80.6)	84 041 (80.3)

CAD - coronary artery disease; CeVD – cerebrovascular disease; CKD – chronic kidney disease; LDL-C – low-density lipoprotein cholesterol; PAD – peripheral artery disease; PCP – primary care physician;

Table 4.

Persistence of high-intensity statin use in follow-up.

	High intensity statin use	
	Continued **n = 126 403 (93.3)**	**Discontinued** **n = 9 166 (6.7)**
Age, mean±SD	65.8±11.1	67.4±11.8
<45 (younger)	2 772 (2.2)	245 (2.7)
45–74 (middle)	93 937 (74.3)	6 310 (68.8)
75 (older)	29 694 (23.5)	2 611 (28.5)
Sex		
Female	36 473 (28.9)	3 103 (33.9)
Male	89 930 (71.2)	6 063 (66.2)
Cardiovascular history		
CAD	106 696 (84.4)	7 419 (80.9)
CeVD	23 774 (18.8)	2 069 (22.6)
PAD	32 434 (25.7)	2 835 (30.9)
ASCVD Risk factors		
Dyslipidemia	115 523 (91.4)	8 239 (89.9)
T2DM	51 785 (50.0)	3 932 (42.9)
Hypertension	110 176 (87.2)	8 069 (88.0)
Obesity	25 211 (19.9)	1 798 (19.6)
Medical comorbidities		
Charlson comorbidity 3	29 912 (23.7)	2 967 (32.4)
CKD Stage 4	8 685 (6.9)	1 067 (11.6)
Depression	19 485 (15.4)	1 733 (18.9)
Care patterns:		
LDL-C checked last 12months	35 870 (28.4)	2 525 (27.6)
Baseline non-statin LLT	8 858 (7.0)	550 (6.0)
Outpatient visits, median [Q1-Q3]	23 [12–41]	27 [14–50]
Cardiology visit	100 080 (79.2)	7 280 (79.4)
PCP visit	101 601 (80.4)	7 660 (83.6)