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Variation in statin prescription among veterans with HIV and known atherosclerotic cardiovascular disease

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Abstract

Background—People with HIV have increased atherosclerotic cardiovascular disease (ASCVD) risk, worse outcomes following incident ASCVD, and experience gaps in cardiovascular care, highlighting the need to improve delivery of preventive therapies in this population.

Objective—Assess patient-level correlates and inter-facility variations in statin prescription among Veterans with HIV and known ASCVD.

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Methods—We studied Veterans with HIV and existing ASCVD, ie, coronary artery disease (CAD), ischemic cerebrovascular disease (ICVD), and peripheral arterial disease (PAD), who received care across 130 VA medical centers for the years 2018–2019. We assessed correlates of statin prescription using two-level hierarchical multivariable logistic regression. Median odds ratios (MORs) were used to quantify inter-facility variation in statin prescription.

Results—Nine thousand six hundred eight Veterans with HIV and known ASCVD (mean age 64.3 ± 8.9 years, 97% male, 48% Black) were included. Only 68% of the participants were prescribed any-statin. Substantially higher statin prescription was observed for those with diabetes (adjusted odds ratio [OR] = 2.3, 95% confidence interval [CI], 2.0–2.6), history of coronary revascularization (OR = 4.0, CI, 3.2–5.0), and receiving antiretroviral therapy (OR = 3.0, CI, 2.7–3.4). Blacks (OR = 0.7, CI, 0.6–0.9), those with non-coronary ASCVD, ie, ICVD and/or PAD only, (OR 0.53, 95% CI: 0.48–0.57), and those with history of illicit substance use (OR=0.7, CI, 0.6–0.9) were less likely to be prescribed statins. There was significant variation in statin prescription across VA facilities (10th, 90th centile: 55%, 78%), with an estimated 20% higher likelihood of difference in statin prescription practice for two clinically similar individuals treated at two comparable facilities (adjusted MOR = 1.21, CI, 1.18–1.24), and a greater variation observed for Blacks or those with non-coronary ASCVD or history of illicit drug use.

Conclusion—In an analysis of large-scale VA data, we found suboptimal statin prescription and significant interfacility variation in statin prescription among Veterans with HIV and known ASCVD, particularly among Blacks and those with a history of non-coronary ASCVD.

Condensed abstract

In a retrospective analysis of Veterans Affairs healthcare data involving 9,608 Veterans with HIV and known atherosclerotic cardiovascular disease (ASCVD) (mean age 64.3 ± 8.9 years, 97% male, 48% Black), we found suboptimal statin prescription (68%) with significant interfacility variation in statin prescription (10th, 90th centile: 55%, 78%). We estimated 20% higher likelihood of difference in statin prescription practice for two clinically similar individuals treated at two comparable facilities. Black race, history of non-coronary ASCVD, and history of substance use were associated with significantly lower likelihood of statin prescription and more variation among VA facilities in prescription practices.

Keywords

HIV; Human immunodeficiency virus; Cardiovascular disease; CVD; Statin; Health services; Health care quality

Background

With the advent and expansion of antiretroviral therapy (ART), persons living with HIV (PLWH) are living longer, but also suffering from increased morbidity and mortality from non-HIV-related conditions including atherosclerotic cardiovascular disease (ASCVD). [1,2] PLWH experience higher rates and earlier onset of ASCVD, including a 1.5- to 2-fold increased risk of acute myocardial infarction (MI) or coronary artery disease (CAD) compared to those without HIV. [2,3] Further, PLWH who experience an MI or heart failure have subsequently significantly worse clinical outcomes compared to their HIV-negative

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counterparts, [4,5] highlighting the need for focus on prevention of cardiovascular disease in PLWH.

Statin therapy is the primary pharmacotherapeutic intervention for secondary prevention of major adverse cardiovascular events in patients with ASCVD. Guidelines recommend initiation of maximally tolerated statin therapy, with the greatest risk reduction in major adverse cardiovascular events observed among patients achieving > 50% reduction in low-density cholesterol (LDL-C) levels. [6–8] Although, clinical trial data are lacking in PLWH, the benefit of statins is expected to be similar in this population. [9–11] Nonetheless, statin therapy for secondary prevention remains suboptimal for various reasons [12–14] in particular among PLWH. For instance, one prior study [15] found only 15% of post-acute coronary syndrome patients with HIV receiving high-intensity statin therapy while the corresponding value for those without HIV was 45%. Other studies have shown similar patterns of underuse in the US, both among Veteran and general HIV populations. [16,17] Understanding patterns and predictors of statin prescription among PLWH is important to help improve the delivery of this important preventive therapy for this high-risk population. However, existing data on statin use in PLWH in the general US population and Veteran population are limited because they are not up to date [16,18] or are underpowered, [19] and the variations and predictors of statin prescriptions in PLWH, in particular in those with known ASCVD, have not been well studied.

The present study aimed to assess patient-level correlates and inter-facility variations in any statin and guideline-recommended statin intensity prescription among Veterans with HIV and known ASCVD receiving HIV care within the Veterans Administration (VA) system. We hypothesized that there are significant care gaps and substantial inter-facility variations in statin prescription that can be targeted with quality improvement initiatives.

Methods

Data source and study design

This is a cross-sectional study of Veterans with HIV and an existing diagnosis of ASCVD prior to the study period who received HIV or primary care within the VA system in January 2018-December 2019 (study period). Individual patient data were obtained from the VA Corporate Data Warehouse (CDW) using the VA Informatics and Computing Infrastructure (VINCI). Facility-level data were similarly obtained from CDW, except for facility complexity which was obtained from the VA Support Services Center. [20,21] The study was approved by the Providence VA Medical Center Institutional Review Board.

Study population

Veterans with HIV diagnoses were identified using relevant International Classification of Diseases, Ninth Revision (ICD-9) and International Classification of Diseases, 10th Revision (ICD-10) codes for asymptomatic or symptomatic HIV infection and AIDS recorded during or any time prior to the study period, using a previously validated approach. [22,23] Veterans had to receive care in at least one outpatient primary care clinic or infectious disease/HIV clinic visit during the year 2018–2019 to be included. ASCVD was defined by the

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presence of at least one inpatient or outpatient ICD code or current procedural terminology (CPT) code (primary or secondary) for either coronary artery disease (CAD), coronary artery revascularization procedures (ie, coronary artery bypass grafting, percutaneous coronary intervention), peripheral arterial disease (PAD), peripheral artery revascularization procedures, ischemic cerebrovascular disease (ICVD), or cerebrovascular procedures any time prior to the study period based previously used algorithms. [14,24] (ICD code and procedure code available from authors).

Outcome-Statin prescription

We included two outcomes of interest: (1) any statin prescription, and (2) guideline recommended statin intensity prescription. Information on statin prescription dispensed at VA pharmacies was obtained from the VA Pharmacy Benefits Management dataset. For the small minority of Veterans who filled their statin in non-VA pharmacies (2.5% of veterans with HIV and ASCVD), we used data from non-VA medication tables. Any statin prescription was defined as having at least one statin prescription (of any intensity) filled from a VA pharmacy during the study period *December 2018 to January* 2019 or having a statin prescription recorded under non-VA medication records for Veterans receiving medications from outside pharmacies. “Guideline recommended statin intensity prescription” is a subset of the “any statin prescription” and was defined as high-intensity statin prescription for patients ≤75 and at least moderate-intensity statin for patients >75 years of age, as per the 2018 ACC/AHA cholesterol guideline.6 High-intensity statin therapy included 40 to 80 mg of atorvastatin daily or 20 to 40 mg of rosuvastatin daily. Moderate-intensity statin therapy included 10 to 20 mg of atorvastatin, 5 to 10 mg of rosuvastatin, 20 to 40 mg of simvastatin 40 to 80 mg of pravastatin, 40 mg of lovastatin, 2 to 4 mg of pitavastatin, 80 mg of fluvastatin XL, or 40 mg of fluvastatin twice daily. For individuals who had multiple statin dispenses from VA pharmacy with different doses, we took the highest dose dispensed for the purpose of determining the statin intensity.

Covariates

Data on relevant covariates included demographic variables (eg, age, sex, race), behavioral factors (smoking, alcohol abuse, illicit drug use), and medical comorbidities (eg, diabetes, hypertension, chronic kidney disease). The presence of comorbidity was defined by the presence of at least one inpatient or outpatient ICD code for the respective diagnoses recorded at any time during or prior to the study period. Overall multimorbidity was assessed using the Elixhauser comorbidity index.[23] Smoking status was obtained from health factor data based on screening questionnaires administered in VA clinics and was dichotomized as current/former smoker vs never smoker. Where available we obtained the following HIV-specific variables: viral load, CD4 T-cell count, and whether the patient was prescribed an antiretroviral regimen with one or more antiretroviral medications during the study period. For viral load and CD4 T-cell count, the most recent value available between the years 2017–2019 was used. CD4 count was dichotomized as <200 vs ≥200 cells/μL. Viral load was dichotomized as undetectable (or <75 copies/mL) vs detectable (≥75 copies/mL). In addition to the Veteran-specific characteristics described above, data on VA facility-level characteristics that could potentially impact variation in statin prescription were obtained, including facility size, geographic region, complexity, and rurality.[12,13,20,21] VA

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facility size was included as a three-level variable after categorizing the facilities into small, medium, and large facilities based on the number of HIV patients they follow in their clinics.

Statistical analyses

The primary comparison was between Veterans with HIV and known ASCVD who did or did not receive statin prescriptions (ie, “no statin” vs “any statin” prescription). Secondary analyses compared “no statin” vs “guideline-recommended intensity statin” prescription. Categorical variables were presented as numbers and percentages, and continuous variables were presented as median and interquartile ranges. The proportion of participants in each statin category (ie, “no statin”, “any statin”, “guideline-recommended intensity statin”) was assessed overall and within clinically relevant subgroups, such as males and females, age ≤ vs > 75 years, diabetes status, smoking status, and by categories of CD4 count (<200 vs ≥200 cells/μL) and viral load (<75 vs ≥75 copies/mL). Predictors of statin prescription were assessed in two-level hierarchical multivariate logistic regression models, with “any statin” or “guideline-recommended intensity statin” prescription as an outcome, by including individual-level variables (ie, demographics, behavioral, type of ASCVD, and comorbidity variables), and facility-level characteristics (ie, VA facility size, region, complexity, and rurality) as fixed-effects in the model, while the individual VA facilities were included as random effects to account for clustering of patients within each VA facility. To compare statin prescriptions between individuals with CAD vs with other types of ASCVD, we combined ICVD, PAD, and CAD into one variable known as “ASCVD type” with 3 categories, ie, (1) ASCVD type: all CAD, (2) ASCVD type: ICVD only, (3) ASCVD type: PAD +/−ICVD. Inter-facility variation in statin prescription (“any statin” and “guideline-recommended intensity statin”) was similarly calculated in two-level multivariable hierarchical logistic regression models. The VA facility random-effects parameters from the hierarchical models were used to calculate the median odds ratios (MORs).[25] Ninety-five percent confidence intervals for the MORs were generated through bootstrapping in 1,000 replicates, using the quantile methods. The MOR allows control for differences in individuals and facilities, so that patients with similar characteristics across similar facilities are compared to each other. It allows comparison of statin prescription pattern between two VA facilities while accounting for differences in patient characteristics such as age, sex, race, other demographic factors, type of ASCVD and illness burden, as well as facility characteristics such as facility size, region, or complexity. Therefore, the MOR quantifies the likelihood of difference in statin prescription practice between two similar VA facilities for patient with similar baseline characteristics. For example, an MOR of 1.3 for statin therapy reflects 30% likelihood that two facilities would differ in statin prescription practice to similar types of Veterans with HIV and known ASCVD.[14,25] Missing values in CD4 count < count vs ≥200 cells/μL and viral load < vs ≥75 copies/mL binary indicators were imputed using multiple imputation techniques, using Multivariate Imputation by Chained Equations (MICE) implemented in R, before these variables were included in the regression models.

Analyses were performed using SAS 9.4 (SAS Institute Inc., Cary, North Carolina, USA) and R 4.0.2 software. We calculated point estimates and 95% confidence intervals (95%

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CIs) for relative risk comparisons. A two-sided *P*-value < .05 was considered statistically significant.

Results

Patient population

Among 33,510 Veterans who received HIV-related care within the VA from 2018–2019, 9,608 had known ASCVD (including 6,274 with CAD, 3,421 with PAD, and 3,297 with ICVD). Of the 9608 Veterans with HIV and ASCVD 7938 (82.6%) received care in infectious disease clinic, while the rest were seen at primary care clinics. Overall 4% of the patients had one visit, 2.1% had 2 visits, 2.7% had 3 visits and 91.1% had 4 or more visits with an infectious disease or primary care at the VA during the study period. The mean age was 64.3 ± 8.9 years with mostly male (9,345 [97%]) and predominantly Black (4,613 [48%]) or white (4,431 [46%]) participants. Hypertension was present in 6,074 (63%), diabetes was present in 2,608 (27%), and chronic kidney disease (CKD) was present in 3,355 (36%). Most patients (85%) were on ART, with 2,169 (27%) of those patients on active regimens that included protease inhibitors (PIs). CD4 counts were available for 80% of the entire study population with 94% of the available population having a CD4 count ≥200 cells/μL. HIV viral load data were available for 74% of the study population with 71% of the available population having a viral load of <75 copies/mL. The patients who did not have viral load data available and those who were not virally suppressed had fewer physician visits and were less likely to be on ART.

Statin prescription

Table I and Supplement Table I show patient characteristics of the study population by statin prescription. Overall, 68% were prescribed statins with 45% of the entire population prescribed statins at recommended doses. Prescription rates were lower among females and Blacks as compared to males and White patients, respectively. Similarly, prescription rates were higher for patients with higher CD4 counts, lower viral loads, and current ART regimens. Higher statin prescription rates were also seen among patients with a history of diabetes, hypertension, CKD, heart failure, and CAD. Prescription of guideline recommended intensity statins followed similar patterns with the exception that patients >75 years old (vs those ≤75 years), who were prescribed guideline recommended intensity statin more frequently (Table I, Supplement Table I).

Multivariate predictors of statin prescription

Figure 1A displays adjusted odds ratios for any statin prescription according to relevant patient characteristics. Patients were less likely to be prescribed statins if they were older than 75 years (OR 0.81, 95% CI: 0.69–0.95) or Black (OR 0.70, 95% CI: 0.63–0.78). When comparing Veterans with non-coronary ASCVD (ie, those with ICVD and/or PAD but not CAD) vs those with CAD, those with non-coronary ASCVD were less likely to be prescribed statins (OR 0.53, 95% CI: 0.48–0.57). Patients were significantly more likely to receive statins if they had a history of diabetes (OR 2.27, 95% CI: 1.99–2.57), or hypertension (OR 2.28, 95% CI: 2.06–2.54). Those on ART (OR 2.95, 95% CI: 2.58–3.37) and with CD4 counts ≥200 cells/μL (OR 1.73, 95% CI: 1.45–2.08) were also more likely to

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be prescribed statins (Figure 1A). A similar pattern was seen with recommended intensity statin prescriptions, except for age where the association reversed, with veterans older than 75 years is more likely to be prescribed guideline-recommended intensity statins (OR 1.84, 95% CI: 1.59–2.13) (Figure 1B). Patients with PI prescriptions (OR 0.57, CI: 0.51–0.64) were less likely to be prescribed guideline-recommended intensity statins (Figure 1B).

Study level characteristics were generally not statistically significantly associated with statin prescription, except for medium complexity facilities and Pacific region facilities which had lower prescription rates for guideline-recommended intensity statins (Supplement Table II).

Inter-facility variation in statin prescriptions

Inter-VA facility variation in any (Table II) and guideline-recommended intensity (Table III) statin prescriptions were assessed using median facility prescription, 10th and 90th percentiles, and MORs, overall and within clinically relevant subgroups. Median interquartile range values of statin prescriptions (any and recommended intensity) are shown in Supplementary Table III. In Figure 2 the proportion of participants with any statin prescription is shown across the VA facilities (waterfall plot, Figure 2A) and by state (heat map, Figure 2B). Further, the proportion of Veterans with any statin prescription is shown by Veteran Integrated Service Network (VISN) and VA region in Supplement Table IV. Overall, the median statin prescription rate was 67% across all VA facilities (10th-90th percentile: 55%–78%) (Table II). The adjusted MOR for any statin prescription was 1.21 (1.18–1.24), indicating a 21% difference in statin prescription patterns between comparable facilities for individuals with comparable characteristics. The inter-facility variation was different by levels of certain individual characteristics (Table II). The median (10th–90th percentile) of any statin prescription rate for Black and White participants was 64 (42–100) and 69 (55–83), respectively. Adjusted MORs were 1.32 for blacks vs 1.14 for whites, indicating greater variation in addition to lower statin prescription practice among facilities for black patients. Similarly, more inter-facility variation in any statin prescription was noted for Veterans who were >75 years old, and those with a history of non-coronary ASCVD, history of depression, alcohol abuse, or substance abuse (Table II). Findings were broadly comparable for guideline-recommended intensity statin prescription (Table III). Supplement Tables V and VI show inter-facility variation in statin prescriptions (any and recommended intensity) by facility-level characteristics.

Discussion

In an analysis of a VA dataset composed of 9,608 Veterans with HIV and preexisting ASCVD who received care at 130 VA facilities across the US in the years 2018/19, we found suboptimal statin prescription (68% for any and 45% for guideline-recommended intensity statin prescription) based on patient characteristics alone. We identified several important patient-level correlates of statin prescriptions. Particularly Black participants, those with history of non-coronary ASCVD, and those with history of substance use were less likely to be prescribed statins. On the other hand, patients with a history of diabetes, and prior coronary revascularization procedures had substantially higher statin prescription rates after accounting for comorbidity and facility level covariates. Those

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receiving ART, CD4 count ≥200 cells/μL or suppressed viral load were more likely to be treated with statins. Significant variation in statin prescription rate was noted across VA facilities that was not explained by several patient- and facility-level characteristics with an average 21% difference in statin prescription practice for two similar individuals followed at two comparable facilities. We found comparable results for prescription of guideline-recommended intensity statins.

Our findings demonstrate suboptimal statin prescription for PLWH with existing ASCVD at VA facilities, and highlight specific subgroups including Black patients, patients with history of non-coronary ASCVD, and those with history of substance use that may require special focus for prevention by clinicians. The current study extends findings from prior reports[26] to PLWH. It provides updated data on underutilization of statins in PLWH[16,18] focusing on those with ASCVD and identifies additional predictors that may be relevant for targeting this population to improve statin prescription. To our knowledge, this is the first study to examine correlates and inter-facility variations in statin prescription rates among PLWH and pre-existing ASCVD. In keeping with prior studies, we found lower prescription among females,[19,27] but the study power was limited due to the small number of female participants.

While guideline recommendation is for all patients with known ASCVD to be on statins, patients may not tolerate statins for various reasons, including adverse drug reactions or advanced liver disease. Taking an example from a large recent secondary ASCVD prevention trial[28] where patients are motivated and closely followed with likely maximal statin treatment rate, we may expect the highest possible statin prescription rate for secondary prevention to be around 95%. The current finding of 68% for any statin prescription among Veterans with HIV and ASCVD, therefore, highlights the gap in statin prescription from what would be ideally expected for this population. On the other hand, prior data in non-Veteran non-HIV US population experiencing first ASCVD event showed 60% of statin use in 2016,[29] suggesting the presence of comparable or possibly worse gaps in non-VA (non-HIV) populations. The significant variation between facilities in terms of statin prescriptions in the present study indicates potential opportunities for improvement at facilities with lower statin use, perhaps through adaption of best practices identified at higher-performing centers.

PLWH experience higher rates of major cardiovascular events, even after adjusting for traditional CVD risk factors, often experiencing such events several years earlier than those without HIV.[4,5,22] Various lines of research evidence also suggests that HIV-associated inflammatory and immune processes likely contribute significantly to the development and progression of atherosclerosis, independent of CD4 counts or viral levels.[4,7,8] Besides lowering LDL-C levels, statins appear to play a role in down-regulating inflammatory and immune activated pathways decreasing the development of unstable coronary plaque in PLWH who have upregulated immune systems, emphasizing the need to ensure statin treatment for PLWH with existing ASCVD or those at increased risk of ASCVD.[11,30]

Implementing ASCVD prevention strategies can be challenging in PLWH. Gaps in care of PLWH have been documented for acute MI and other cardiovascular conditions.[2–5,22,23]

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Indeed, several factors may interfere with optimal prescription of, and adherence to statin therapy. Balancing competing care priorities may complicate efforts to simultaneously achieve adherence to multiple medications.[12,31] Clinicians treating PLWH may focus primarily on HIV control and may not have sufficient time to address CVD. Similarly, patients, especially those without prior clinical ASCVD events who were diagnosed through non-invasive cardiovascular testing, may possibly prioritize HIV care over CVD care. In addition, long-term adherence to cardiovascular medications can be challenging, as PLWH may typically experience treatment side effects and complications (eg, muscle ache with statins) while the health benefits (eg, reductions in risk of recurrent MI) may not be immediately apparent to the patient.[12,31]

Physician concerns about drug interactions is a related factor that can influence statin prescription, especially at recommended intensity. This is particularly important in individuals taking PIs or cobicistat “boosted” ART regimens, which have significant interactions with statins.[32,33] Consistent with this, we found a lower prescription of recommended intensity statin among those taking PI-based regimens in our study. Similarly, we observed more variability in statin prescriptions for those taking PIs across VA facilities which may reflect the challenge of dosing statins in this group. Similarly, our finding of the lower prescription rate of recommended intensity statins in the VA Pacific regions may be related to more frequent statin dose adjustments to account for drug interactions, by physicians in this region who presumably have more extensive experience with HIV management.

By investigating the correlates of statin prescription among PLWH with existing ASCVD, this study can help focus the clinicians’ efforts on those groups of patients that need the most attention. In addition, the demonstration of significant inter-facility variation in statin prescriptions in the present study suggests that organizational leadership and policymakers can consider ways of adapting practices and strategies from higher-performing centers to lower-performing ones through implementation of programs for quality improvement. Several (non-VA) studies using various implementation strategies to improve CVD care for PLWH, including evidence-based statin therapy, are currently underway.[34] For example, the EXTRA-CVD study focuses on improving hypertension and cholesterol management in the HIV specialty clinic context through a nurse-led intervention.[34] Such strategies, if proven to be effective in PLWH, may also be applicable in the VA system. Other approaches that may be worthwhile to study include incorporation of a clinical pharmacist in the HIV care team, which may help to improve statin prescriptions by ensuring guideline recommendations are followed and concerns for drug interactions and side effects are addressed.[35]

The strengths of the study include, (1) use of a VA-wide large-scale data to address the question of statin treatment in secondary prevention of ASCVD in HIV; (2) investigation of wide range of comorbidities and correlates of statin prescription, and accounting for them in assessing inter-facility variation in statin prescription; (3) a focus in implementation, seeking to maximize the impact of a well-established therapy to improve ASCVD outcomes in PLWH; and (4) a wide range of findings that complement and are supported by current literature on the topic of secondary prevention of ASCVD in PLWH. Additionally, the findings showed internal validity across a wide range of analyses and statistical adjustments.

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Limitations

Some limitations of the present study also merit consideration. First, while the study demonstrated the gap in statin prescription for Veterans with HIV and pre-existing ASCVD, which was based on filled prescription data for patients receiving treatment at VA pharmacies and based on physicians' documentation of statins on electronic health records for those receiving treatment from outside pharmacies, we recognize that statin prescriptions (or filling) do not automatically translate to actual statin treatment. Based on findings from one study that revealed 75% of respondents failed to fill their statin prescription and often cited fear of side effects and inadequate health literacy as reasons for non-adherence.[14] Since our study did not attempt to investigate adherence to medication regimens, it is important to consider this caveat when interpreting the results. The actual gap in statin treatment could be higher than implied in this study. Second, while we used the general clinical guidelines to define recommendations for the intensity of statin, this did not consider drug-drug interactions that are common with ART or other restrictive factors such as statin allergy or intolerance. Indeed, the definition of "guideline-recommended statin intensity" in HIV may be difficult to define and dependent on the setting (eg, type of ART regimen and the use of other interacting drugs such as antifungals). Third, in comparing between-facility variation in statin prescriptions, despite adjusting for sociodemographic factors, comorbidities, and including a number facility-level characteristics in hierarchical models, we may not have accounted for all the factors that may contribute to between-facility differences in prescription patterns. That the associations were broadly consistent between adjusted and unadjusted models indicates that our findings on inter-facility variations are likely to represent true between-facility differences and opportunities for improvement. Information on additional facility-level factors, such as type and number of HIV providers in the HIV clinics, location of cardiovascular preventive care for HIV patients (eg, HIV clinic or primary care clinic), and types of specialty services that are collocated with the HIV clinics could have helped to shed light into some of the organizational factors that may influence statin prescription for this population. Fourth, the generalizability of the study may be limited because it was based on a predominantly male US Veteran population. However, the findings of suboptimal statin prescription, predictors of statin prescriptions, and interfacility variations have consistencies with existing literature on cardiovascular care in HIV and likely have relevance beyond the Veteran population. Finally, we did not have Medicare/Medicaid data available for these analyses, which may limit some of the available data such as information on a statin (if filled at an outside pharmacy and this was not documented in the patient electronic medical record by VA provider) or viral load (if test performed at an outside laboratory, in which case the scanned copies of the laboratory record will not be available in the VA electronic database for analyses).

Clinical perspective

In a retrospective analysis of VA data, we found suboptimal prescriptions of statins for secondary prevention of ASCVD in PLWH. We also identified several important patient-level correlates of statin prescriptions. Black participants, those with a history of non-coronary ASCVD, and those with a history of substance use were less likely to be prescribed statins. Understanding the care gaps and predictors of statin use in secondary prevention of

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ASCVD in PLWH can provide practitioners with more insight into which patients from their panels may be at risk of being undertreated.

Translational outlook

This study will contribute to the growing body of evidence that helps to identify and address patient-level, prescriber-level, and system-level factors contributing to the suboptimal treatment of ASCVD risk among specific patient populations. Further studies, including non-Veteran populations and larger proportions of females, additionally looking at data on medication adherence and other preventive measures (eg, hypertension treatment), as well as incident clinical outcomes, will help to address these gaps in cardiovascular care. Ultimately, such endeavors will enable the increased uptake of evidence-based interventions to ensure HIV patients do not fall through the cracks in missing preventative therapies that have the potential to curb morbidity and mortality.

Conclusions

In an analysis of large-scale VA data, we found suboptimal statin prescription and significant interfacility variation in statin prescription among Veterans with HIV and known ASCVD, particularly those who are Black, and those with history of non-coronary ASCVD, or history of illicit drug use. By identifying these care gaps and their correlates, we aim to provide practitioners and policy-makers with more insight on how to improve cardiovascular care for PLWH.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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The authors are solely responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Abbreviations:

ART	Antiretroviral therapy cardiovascular disease
CAD	coronary artery disease
CDW	Corporate Data Warehouse
CKD	chronic kidney disease
CI	Confidence Interval

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CPT	Current procedural terminology
HIV	Human immunodeficiency virus
ICD-9	International Classification of Diseases, Ninth Revision
ICD-10	International Classification of Diseases, Tenth Revision
ICVD	Ischemic cerebrovascular disease
LDL-C	low-density cholesterol
MOR	Median odds ratio
OR	Odds ratio
PAD	Peripheral arterial disease
PLWH	persons living with HIV
PI	Protease inhibitors
VA	Veterans Affairs
VINCI	VA Informatics and Computing Infrastructure

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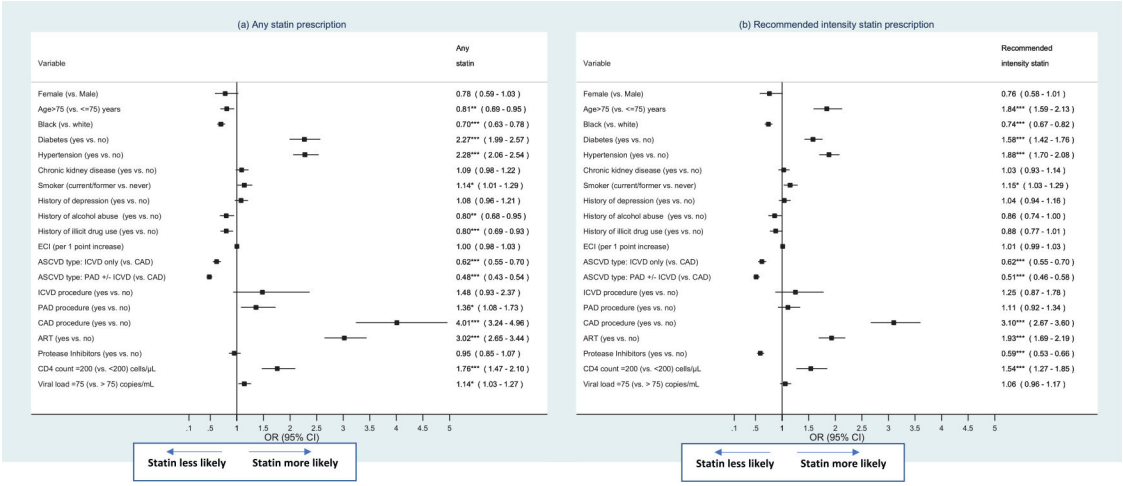

Figure 1.

Multivariable odds ratios of A, any statin and B, recommended intensity statin prescription among Veterans with HIV and known ASCVD for several individual characteristics (9,680 patients across 130 facilities). ∗∗∗ $P < .005$, ∗∗ $P < .01$, ∗ $P < .05$. The black boxes represent odds ratios, the horizontal bars represent 95% confidence intervals [a]All the variables in the table were included as fixed effects in the multivariate hierarchical model, except for prior ICVD, PAD and CAD procedures which were not included in the main model as they are subsets of history of ICVD, PAD and CAD, respectively. ASCVD was included as ICVD, PAD, and CAD (three variables) in the main model. The odds ratios of ASCVD types were determined in a secondary model that combined ICVD, PAD and CAD into one variable (ASCVD type) with 3 categories - ASCVD type: all CAD, ASCVD type: ICVD only, ASCVD type: PAD +/−ICVD. Similarly, Odds ratios for prior ICVD, PAD and CAD procedures were estimated in a secondary model adjusting for history of prior procedure instead of history of ICVD, PAD and CAD. Four facility level characteristics (facility size, complexity, rurality, and VA region) were also included as fixed effect. VA facility was included as random effects. Illicit drug use includes opioids, sedatives, cannabis, hallucinogens, cocaine, amphetamine drug use. ART, antiretroviral therapy; ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; ECI, Elixhauser comorbidity index; ICVD, ischemic cerebrovascular disease; PAD, peripheral artery disease.

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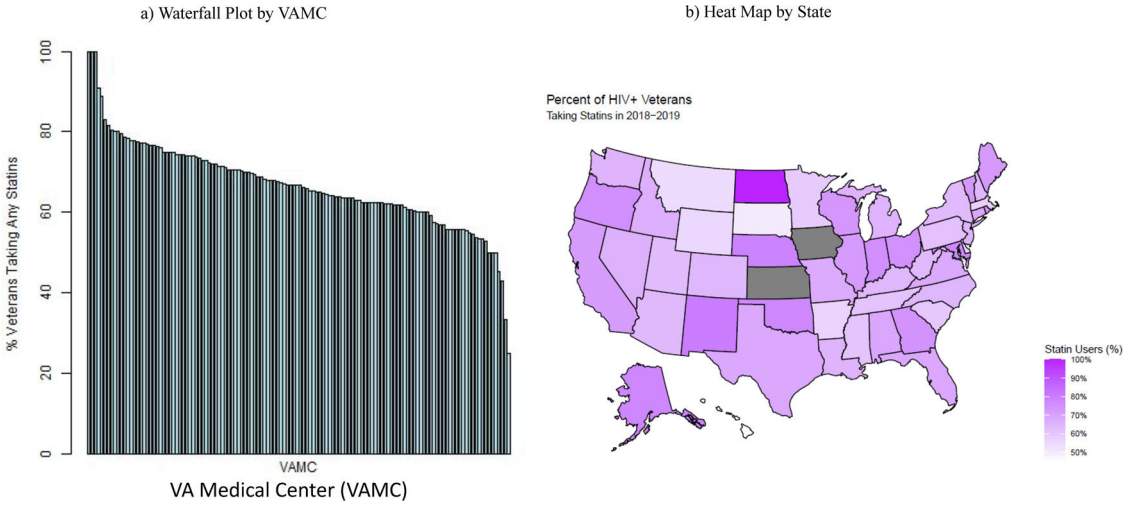

Figure 2.

Percentage of Veterans with HIV and known ASCVD with any statin prescription, A, waterfall plot by VA facility, and B, heat map by US states In Figure 2A, each bar graph represents the percentage of station prescription in each facility. In Figure 2B the various shades represent percentage of Veterans with statin prescription by state. ASCVD, atherosclerotic cardiovascular disease; VAMC, VA Medical Center.

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Table I.

Characteristics of the study population comprising 9,608 veterans with HIV and ASCVD

Patient characteristics	*N* Available	Statin prescription		
		Any statin(*n* = 6522)	Recommended intensity statin (*n* = 4311)	No statin(*n* = 3086)
Overall	9608	6522 (67.9%)	4311 (44.9%)	3086 (32.1%)
Age, mean (SD)	9608	64.9 (8.1)	65.4 (8.5)	62.9 (10.2)
Age ≤ 75 Y	8661	5887 (68.0%)	3751 (43.3%)	2774 (32.0%)
Male Sex	9345	6372 (68.2%)	4221 (45.2%)	2973 (31.8%)
Race - White	4431	3147 (71.0%)	2123 (47.9%)	1284 (29.0%)
Race - Black	4613	2986 (64.7%)	1936 (42.0%)	1627 (35.3%)
History of diabetes mellitus	2630	2161 (82.2%)	1500 (57.0%)	469 (17.8%)
History of hypertension	6074	4589 (75.2%)	3144 (51.8%)	1485 (24.5%)
History of CHF	1383	1078 (78.0%)	779 (56.3%)	305 (22.1%)
History of CKD	3355	2431 (72.5%)	1638 (48.8%)	924 (27.5%)
History of smoking *	2357	1646 (69.8%)	1118 (47.4%)	711 (30.2%)
Alcohol use	1242	768 (61.84%)	505 (40.7%)	474 (38.2%)
Illicit drug use †	1719	1071 (62.3%)	699 (40.7%)	648 (37.7%)
History of depression	2932	2036 (69.4%)	1350 (46.0%)	896 (30.6%)
PTSD	3133	2087 (66.61%)	1360 (43.41%)	1046 (33.39%)
Psychotic disorders	1420	963 (67.82%)	616 (43.38%)	457 (32.18%)
ECI, mean (SD)	9608	5.30 (3.09)	5.42 (3.2)	4.44 (3.2)
History of ICVD	3297	2262 (68.6%)	1522 (46.2%)	1035 (31.4%)
History of PAD	3421	2327 (68.0%)	1555 (45.5%)	1094 (32.0%)
History of CAD	6274	4574 (72.9%)	3146 (50.1%)	1700 (27.1%)
Prior ICVD procedure	158	132 (83.5%)	94 (59.5%)	26 (16.5%)
Prior PAD procedure	744	624 (83.9%)	453 (60.9%)	120 (16.15%)
Prior CAD procedure	1203	1086 (90.3%)	850 (70.7%)	117 (9.7%)
Antiretroviral therapy	8154	5830 (71.5%)	3792 (46.5%)	2324 (28.5%)
Protease inhibitors	2169	1518 (70.0%)	809 (37.3%)	651 (30.0%)
CD4 ≥ 200 cells/μL	7213	5204 (72.2%)	3399 (47.1%)	2009 (27.9%)

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Patient characteristics	*N* Available	Statin prescription		
		Any statin(*n* = 6522)	**Recommended intensity statin (*n* = 4311)**	**No statin(*n* = 3086)**
Viral load < 75 copies/mL	5053	3685 (72.9%)	2389 (47.3%)	1368 (27.1%)

ASCVD included ICVD, PAD, and CAD. Note recommended-dose statin is a subset of any-dose statin. The sum of any-dose statin and no statin make 100%. ART, antiretroviral therapy; ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CHF, congestive heart failure; CKD, chronic kidney disease; ECI, Elixhauser comorbidity index; ICVD, ischemic cerebrovascular disease; PAD, peripheral artery disease; PTSD, post traumatic stress disorder.

*Current or former.

†Illicit drug use including opioids, sedatives, cannabis, hallucinogens, cocaine, amphetamine use or prescription drug abuse.

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Table II.

Variation in any statin prescription across VA medical centers, overall and within subgroups

Variable	*N* patients	*N* Facilities	Median (10th, 90th percentile)	Unadjusted MOR (95% CI)	Adjusted MOR (95% CI)
Overall	9608	130	66.7 (55.2, 77.9)	1.25 (1.22–1.29)	1.21 (1.18–1.24)
Male	9345	130	66.7 (54.7, 78.2)	1.25 (1.22–1.29)	1.24 (1.21–1.28)
Age ≤ 75 Y	8661	130	66.7 (51.7, 78.6)	1.28 (1.24–1.32)	1.27 (1.23–1.3)
Age > 75 Y	947	112	66.7 (47.4, 100)	1.14 (1.12–1.16)	1 (1–1)
White	4431	130	69.2 (55,82.6)	1.16 (1.13–1.18)	1.14 (1.12–1.16)
Black	4613	120	63.6 (41.5, 100)	1.34 (1.29–1.39)	1.32 (1.27–1.37)
History of diabetes (yes)	4260	125	75 (60.3, 86.8)	1.28 (1.24–1.33)	1.3 (1.26–1.35)
History of diabetes (no)	5348	130	61.2 (47.7, 80.1)	1.27 (1.23–1.31)	1.28 (1.24–1.31)
History of hypertension (yes)	6074	129	75.8 (60, 90.1)	1.26 (1.22–1.3)	1.23 (1.2–1.27)
History of hypertension (no)	3534	129	55 (33.3–67.7)	1.3 (1.26–1.34)	1.28 (1.24–1.32)
History of CKD (yes)	3355	126	71 (50, 93)	1.27 (1.23–1.32)	1.29 (1.25–1.33)
History of CKD (no)	6253	130	63.1 (51.8, 78.7)	1.23 (1.2–1.26)	1.22 (1.2–1.26)
History of Depression (yes)	2932	128	69 (48.9, 95.6)	1.4 (1.34–1.46)	1.39 (1.34–1.46)
History of Depression (no)	6676	130	66.5 (50, 80)	1.22 (1.19–1.25)	1.2 (1.17–1.23)
History of smoking (yes)	2357	127	70 (33.3, 100)	1.42 (1.36–1.48)	1.31 (1.26–1.35)
History of smoking (no)	7251	130	66.7 (54.5, 79.7)	1.24 (1.21–1.28)	1.23 (1.2–1.26)
History of Alcohol abuse (yes)	1242	118	61.5 (25, 100)	1.51 (1.43–1.6)	1.53 (1.45–1.62)
History of Alcohol abuse (no)	8366	130	66.7 (57, 78.8)	1.23 (1.2–1.26)	1.22 (1.19–1.25)
History of illicit drug use (yes)	1719	123	61.3 (33.3, 100)	1.39 (1.33–1.45)	1.36 (1.31–1.42)
History of illicit drug use (no)	7889	130	67.1 (55.8, 79.9)	1.23 (1.2–1.26)	1.23 (1.19–1.26)
History of ICVD (yes)	3267	125	69.2 (50, 87)	1.41 (1.36–1.47)	1.38 (1.33–1.44)
History of ICVD (no)	6341	129	66.7 (52.6, 81.2)	1.24 (1.2–1.27)	1.24 (1.21–1.28)
History of PAD (yes)	3118	126	64.3 (50, 81.5)	1.29 (1.25–1.34)	1.33 (1.28–1.38)
History of PAD (no)	6490	130	68 (51.4, 81.8)	1.28 (1.24–1.32)	1.25 (1.22–1.29)
History of CAD (yes)	6267	129	72.7 (59.1, 84.8)	1.18 (1.15–1.2)	1.15 (1.13–1.17)
History of CAD (no)	3341	125	54.3 (33.3, 75)	1.36 (1.31–1.42)	1.38 (1.32–1.44)
ART (yes)	8154	130	70.8 (56, 83.4)	1.28 (1.24–1.31)	1.28 (1.25–1.33)
ART (no)	1454	122	50 (20.7, 79.5)	1.08 (1.07–1.09)	1 (1–1)

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Variable	*N* patients	*N* Facilities	Median (10th, 90th percentile)	Unadjusted MOR (95% CI)	Adjusted MOR (95% CI)
Protease Inhibitors (yes)	2169	124	71.2 (50, 100)	1.26 (1.22–1.3)	1.2 (1.17–1.23)
Protease Inhibitors (no)	7439	130	66.7 (50, 77.4)	1.24 (1.21–1.28)	1.23 (1.2–1.26)
CD4 count < 200 cells/μL	647	106	50 (0, 100)	1.24 (1.2–1.28)	1 (1–1)
CD4 count ≥ 200 cells/μL	8961	130	67.4 (55.6, 79)	1.24 (1.21–1.28)	1.24 (1.21–1.27)
Viral load ≤ 75 copies/mL	6649	130	68.3 (56, 80.7)	1.25 (1.22–1.28)	1.23 (1.2–1.26)
Viral load > 75 copies/mL	2959	124	60 (39.6, 92.5)	1.29 (1.25–1.34)	1.28 (1.24–1.32)

Note – subgroups with less than 500 patients were excluded because the data were insufficient for these analyses.

CI, confidence interval; MOR, median odds ratio.

Other legend as per Table I.

MORs, calculated from VA facility random-effects parameters in the hierarchical models, serve as index of between-facility variability in statin prescription pattern for it serves as metrics that quantifies the degree of variation in practice between two given VHA facilities. For example, an MOR of 1.3 for statin therapy reflects 30% likelihood that two similar facilities would differ in prescribing statin to similar patients with HIV. Confidence intervals were calculated using the bootstrapping (1000 replicates, quantile method).

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Table III.

Variations in recommended intensity statin prescriptions across VA medical centers, overall and within subgroups

Variable	*N* patients	*N* Facilities	Median (10th, 90th percentile)	Unadjusted MOR (95% CI)	Adjusted MOR (95% CI)
Overall	9608	130	45.3 (28.5–60.1)	1.28 (1.24–1.32)	1.24 (1.21–1.27)
Male	9345	130	45.6 (29.2–58.6)	1.29 (1.25–1.33)	1.31 (1.27–1.35)
Age ≤ 75 Y	8661	130	42.9 (23.8–60)	1.33 (1.29–1.37)	1.35 (1.3–1.39)
Age > 75 Y	947	112	60.8 (33.8–100)	1 (1–1)	1 (1–1)
White	4431	130	48.1 (32.7–64.7)	1.28 (1.24–1.32)	1.3 (1.26–1.34)
Black	4613	120	40.1 (0–60.1)	1.3 (1.25–1.34)	1.26 (1.22–1.29)
History of diabetes (yes)	4260	125	50 (30.3–66.7)	1.3 (1.26–1.35)	1.3 (1.25–1.34)
History of diabetes (no)	5348	130	39.2 (26.8–62.5)	1.24 (1.21–1.27)	1.3 (1.26–1.34)
History of hypertension (yes)	6074	129	50.6 (33.3–69.2)	1.29 (1.25–1.33)	1.3 (1.26–1.35)
History of hypertension (no)	3534	129	32.1 (16.7–50)	1.21 (1.18–1.25)	1.23 (1.2–1.26)
History of CKD (yes)	3355	126	47.7 (16.7–69.2)	1.29 (1.25–1.34)	1.28 (1.24–1.32)
History of CKD (no)	6253	130	43 (28.6–60)	1.27 (1.24–1.31)	1.33 (1.29–1.38)
History of Depression (yes)	2932	128	46.1 (21.8–71.5)	1.35 (1.3–1.4)	1.33 (1.28–1.38)
History of Depression (no)	6676	130	44 (27.2–60)	1.25 (1.22–1.29)	1.29 (1.25–1.33)
History of smoking (yes)	2357	127	50 (0–70.2)	1.44 (1.37–1.51)	1.46 (1.39–1.53)
History of smoking (no)	7251	130	42.9 (28.6–57.9)	1.25 (1.21–1.28)	1.28 (1.24–1.32)
History of Alcohol abuse (yes)	1242	118	39 (0–69.2)	1.43 (1.37–1.5)	1.41 (1.34–1.48)
History of Alcohol abuse (no)	8366	130	44.6 (32.9–57.9)	1.26 (1.23–1.3)	1.3 (1.26–1.34)
History of illicit drug use (yes)	1719	123	37.5 (0–67.7)	1.36 (1.3–1.42)	1.33 (1.28–1.38)
History of illicit drug use (no)	7889	130	45.7 (29.9–60.1)	1.28 (1.24–1.32)	1.31 (1.27–1.35)
History of ICVD (yes)	3267	125	45.5 (17.3–66.7)	1.28 (1.24–1.32)	1.3 (1.25–1.34)
History of ICVD (no)	6341	129	45.2 (28.4–60.8)	1.27 (1.23–1.31)	1.3 (1.26–1.34)
History of PAD (yes)	3118	126	42.9 (21.4–65.5)	1.34 (1.29–1.4)	1.37 (1.32–1.42)
History of PAD (no)	6490	130	44.9 (29–62.6)	1.28 (1.24–1.32)	1.29 (1.25–1.33)
History of CAD (yes)	6267	129	50 (34.5–66.7)	1.29 (1.25–1.33)	1.3 (1.26–1.34)
History of CAD (no)	3341	125	33.3 (4–50)	1.3 (1.26–1.34)	1.33 (1.28–1.38)
ART (yes)	8154	130	46.6 (28.5–66.7)	1.31 (1.27–1.36)	1.34 (1.3–1.39)
ART (no)	1454	122	35.5 (0–57)	1.03 (1.03–1.04)	1 (1–1)

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Variable	*N* patients	*N* Facilities	Median (10th, 90th percentile)	Unadjusted MOR (95% CI)	Adjusted MOR (95% CI)
Protease Inhibitors (yes)	2169	124	36 (11.7–69)	1.41 (1.35–1.47)	1.43 (1.37–1.51)
Protease Inhibitors (no)	7439	130	45.9 (29.5–60.6)	1.22 (1.19–1.25)	1.24 (1.21–1.28)
CD4 count < 200 cells/μL	647	106	25 (0–73.2)	1.4 (1.33–1.46)	1.38 (1.32–1.45)
CD4 count ≥ 200 cells/μL	8961	130	45.5 (29.5–60)	1.27 (1.23–1.3)	1.3 (1.26–1.34)
Viral load ≤ 75 copies/mL	6649	130	46.2 (30–62.7)	1.3 (1.26–1.34)	1.34 (1.3–1.39)
Viral load > 75 copies/mL	2959	124	40 (16.1–63.6)	1.2 (1.17–1.23)	1.2 (1.17–1.23)

Legend as per Table II.