

Retrospective cohort study of statin prescribing for primary prevention among people living with HIV

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Abstract

Objective: To compare statin prescribing rates between intermediate-risk people living with human immunodeficiency virus (HIV; PLWH) and intermediate-risk patients without a diagnosis of HIV for primary prevention of atherosclerotic cardiovascular disease (ASCVD).

Methods: Retrospective cohort study. Electronic health record data were used to identify a cohort of PLWH aged 40–75 years with a calculated 10-year ASCVD risk between 7.5%–19.9% as determined by the Pooled Cohort Equation (PCE). A matched cohort of primary prevention non-HIV patients was identified. The primary outcome was the proportion of PLWH who were prescribed statin therapy compared to patients who were not living with HIV and were prescribed statin therapy

Results: 81 patients meeting study criteria in the PLWH cohort were matched to 81 non-HIV patients. The proportion of patients prescribed statins was 33.0% and 30.9% in the PLWH and non-HIV cohorts, respectively ($p = 0.74$).

Conclusion and relevance: This study evaluated statin prescribing in PLWH for primary prevention of ASCVD as described in the 2018 AHA/ACC/Multisociety guideline. Rates of statin prescribing were similar, yet overall low, among intermediate-risk primary prevention PLWH compared to those not diagnosed with HIV.

Keywords

human immunodeficiency virus, Statins, dyslipidemia, hypercholesterolemia, preventative medicine

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Introduction

Human immunodeficiency virus (HIV) is considered a chronic inflammatory disease.¹ People living with HIV (PLWH) are at a 1.5- to 2-fold higher risk of atherosclerotic cardiovascular disease (ASCVD) than patients without the immune deficiency.^{2,3} Even when controlling for age and co-morbidities, multiple epidemiological studies have demonstrated higher rates of ASCVD among PLWH, suggesting an underlying mechanism of the disease that increases ASCVD risk.^{3–5} With advances in antiretroviral therapy (ART), increased access to care, and longer lifespan of PLWH, chronic diseases such as ASCVD and type 2 diabetes contribute to more deaths in PLWH than acquired immune deficiency syndrome (AIDS)-related complications.^{2,6} Traditional risk factors for ASCVD such as

hypertension (HTN), hypercholesterolemia, type 2 diabetes, and smoking have higher rates of occurrence in PLWH.²

Given the benefits of statins for non-HIV infected individuals and the established increase in ASCVD in

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PLWH, the 2018 American Heart Association (AHA)/American College of Cardiology (ACC)/Multisociety cholesterol guideline identifies HIV and other chronic inflammatory disorders (e.g., rheumatoid arthritis) as risk-enhancing factor(s) to consider in the discussion of statin initiation therapy for primary prevention of ASCVD when the individual's 10-year ASCVD risk is 7.5% to 19.9% (intermediate risk).⁷ Previous cholesterol guidelines did not provide extensive detail regarding the management of ASCVD in this at-risk patient population.^{6–9} This gap in comprehensive guidance on the management of ASCVD in this population led to the creation of the 2019 AHA Scientific Statement on the management of cardiovascular disease in PLWH, which includes the 2018 AHA/ACC/Multisociety guideline recommendations.⁶

Few studies have examined statin eligibility and prescribing rates among PLWH with additional indications for statin therapy as defined in multiple cholesterol guidelines (e.g., primary prevention, diabetes, secondary prevention, and severe hypercholesterolemia). Within these cohort studies of PLWH, rates of eligible patients receiving statins ranged from 42% to 73%.^{10–13} Our study compared statin prescribing rates at Denver Health between intermediate-risk PLWH and intermediate-risk patients without a diagnosis of HIV.

Methods

Study design and patient population

This 1:1 retrospective cohort study included one cohort of PLWH and one cohort of patients without a diagnosis of HIV. A cross-sectional data pull was performed on January 27, 2020. The data pull included all data elements collected dating back 18 months and the most recent value was used if multiple values documented over this 18 month period. All patients received their health care within the Denver Health system. Pertinent to this study, HIV ART is provided within both specialty and primary care clinics. This study was approved by the Denver Health Sponsored Programs and Research Office and the Colorado Multiple Institutional Review Board.

Outcomes

The primary outcome of this study was to evaluate the proportion of intermediate-risk PLWH who were prescribed statin therapy compared to intermediate-risk patients without a diagnosis of HIV and were prescribed statin therapy for primary prevention of ASCVD.

Three secondary outcomes performed prospectively defined subgroup analyses. The first compared the

intensity (low, moderate, or high) of the prescribed statins among the two cohorts. The second included a comparison of patients' total number of non-HIV risk factors as identified by the 2018 AHA/ACC/Multisociety guideline (Table 1). Lastly, statin adherence, characterized as a proportion of days covered (PDC) $\geq 80\%$, was assessed using refill history among patients who filled their statin prescription within the Denver Health system.

Inclusion/exclusion criteria

Primary prevention patients were identified as candidates for statin therapy based on 2018 AHA/ACC/Multisociety cholesterol guideline recommendations. Inclusion criteria consisted of individuals receiving primary care within the Denver Health system aged 40–75 years, without a history of clinical ASCVD (carotid intervention, cerebrovascular disease, coronary artery bypass grafting, coronary occlusion, coronary rupture, coronary thrombus, ischemic heart disease, myocardial infarction, percutaneous coronary intervention, peripheral artery disease, stable angina, stroke, transient ischemic attack, unstable angina) and a 10-year ASCVD risk of 7.5%–19.9% according to the Pooled Cohort Equation (PCE).^{7,14} Patients were excluded if they had a history of diabetes, alanine aminotransferase (ALT) greater than three times the upper limit of normal, current treatment for a hepatitis C infection, a hepatitis C viral load greater than zero IU/mL, a low density lipoprotein cholesterol (LDL-C) < 70 mg/dL, currently pregnant or breastfeeding, or if their 10-year ASCVD risk score was outside the range of 7.5%–19.9%.

Patients with a diagnosis of HIV were included in the PLWH cohort. Patients without a diagnosis of HIV were identified for inclusion into the control cohort and matched 1:1 with PLWH based on age and gender.

Statistical analysis

Baseline demographics were compared using unpaired t-tests for continuous data and chi-squared tests for categorical data. An a priori level of significance was defined as a p-value < 0.05 . Laboratory, medication, and demographic information were determined by the most recent information available within the electronic health record prior to the reference date of January 27, 2020. The most recent non-lipid laboratory values and vital signs documented within the past two years were used for analysis. The most recent lipid panel available since 2014 was used.

The primary outcome of the proportion of patients with an active statin order at the reference date was analyzed with a Chi-square test. Secondary outcomes

Table 1. Risk enhancing factors.

Risk-enhancing factor	2018 AHA/ACC/Multisociety Guideline Definition	Study definition
Family history of premature ASCVD	Males < 55 years old Females < 65 years old	Not assessed
Primary hypercholesterolemia	LDL-C 160–189 mg/dL Non-HDL-C 190–219 mg/dL	LDL-C 160–189 mg/dL Non-HDL-C 190–219 mg/dL
Metabolic Syndrome	≥3 of the following: Increased waist circumference Elevated TG >150 mg/dL BP ≥130/85 mm Hg or treatment Elevated glucose ≥100 mg/dL Low-HDL-C Men <40 mg/dL, Women <50 mg/dL	≥3 of the following: BMI ≥25 kg/m ² TG >150 mg/dL BP ≥130/85 mm Hg or treatment Blood glucose ≥100 mg/dL Low-HDL-C Men <40 mg/dL, Women <50 mg/dL
Chronic Kidney Disease	eGFR 15–59 mL/min per 1.73 m ² with or without albuminuria; not treated with dialysis or kidney transplantation	eGFR 15–59 mL/min per 1.73 m ²
Chronic Inflammatory Conditions	Psoriasis Rheumatoid arthritis Lupus HIV/AIDS	Psoriasis Rheumatoid arthritis Lupus Inflammatory Bowel Disease
History of premature menopause and history of pregnancy-associated conditions that increase later ASCVD	Menopause before 40 years old Pre-eclampsia	Menopause before 40 years old Pre-eclampsia
High-Risk Ethnicities	South Asian	Not assessed
Lipid/Biomarkers	TG ≥175 mg/dL on 3 occasions hsCRP ≥2 mg/dL Lipoprotein (a) ≥50 mg/dL Apolipoprotein (B) ≥130 mg/dL Ankle-brachial index <0.9	TG ≥175 mg/dL Not assessed Not assessed Not assessed Not assessed

ACC: American College of Cardiology; AHA: American Heart Association; ASCVD: atherosclerotic cardiovascular disease; BMI: body mass index; BP: blood pressure; eGFR: estimated glomerular filtration rate; HDL-C: high density lipoprotein cholesterol; hsCRP: high sensitivity c-reactive protein; LDL-C: low density lipoprotein cholesterol; non-HDL: non-high density lipoprotein cholesterol; TG: triglycerides.

were evaluated using a similar statistical analysis to the primary outcome for categorical data. Comparison of statin intensity, categorized as low, moderate, or high based on the specific statin and dose of the active order, utilized a 3×2 Chi-square test. Total non-HIV risk-enhancing factors were tallied for each patient with an active statin order and a 5×2 Chi-square test was performed. Lastly, the proportion of patients considered adherent to statin therapy with a PDC ≥80% was analyzed using a Chi-square test for those with statin fill history available.¹⁵

Results

Baseline demographics

A total of 440 PLWH aged 40–75 years without a history of ASCVD were identified. After excluding patients based on the defined exclusion criteria, 81 patients were included in the final PLWH cohort (Figure 1). Accordingly, 81 patients without a

diagnosis of HIV who met the study criteria were matched based on age and gender to form the control cohort.

A comparison of baseline characteristics is presented in Table 2. Patients in the PLWH cohort were more likely to have lower systolic blood pressure, lower body mass index (BMI), presence of other inflammatory diseases, and an estimated glomerular filtration rate (eGFR) of 15–59 mL/min/1.73 m². Differences in primary insurance coverage were also observed, with the majority (58%) of the non-HIV cohort having Medicaid compared to only 33% of the PLWH cohort. All other baseline demographic characteristics were similar among both cohorts. Of note, some patients did not have a recent eGFR and/or BMI documented in the EHR.

Primary outcome: Statin prescribing

Among PLWH, 27 of the 81 patients (33.0%) had an active order for statin therapy while 25 of the 81

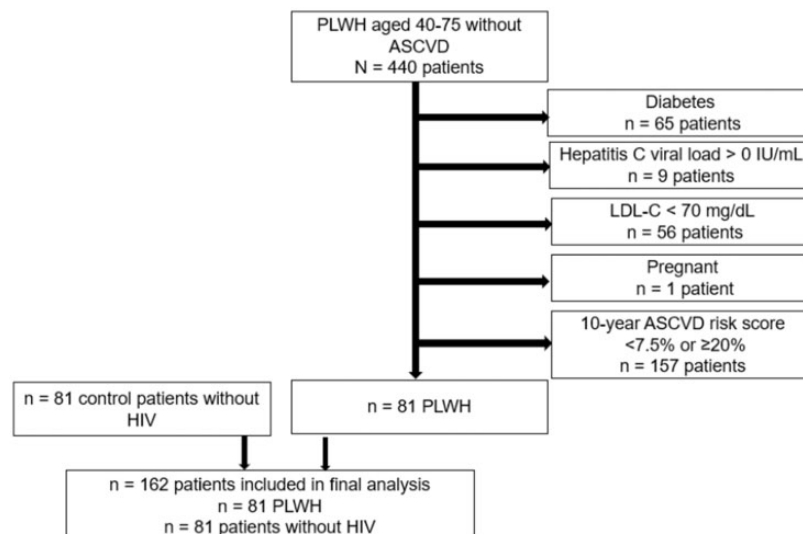


Figure 1. Cohort inclusion and exclusion criteria.

Table 2. Baseline demographics.

Characteristic	PLWH (n = 81)	Non-HIV (n = 81)	p-Value
Age, mean (SD)	57.0 (6.0)	57.0 (6.0)	1.00
40–49	10 (12.3%)	10 (12.3%)	
50–59	43 (53.1%)	43 (53.1%)	
60–69	25 (30.9%)	25 (30.9%)	
70–75	3 (3.7%)	3 (3.7%)	
Female n (%)	9 (11.1)	9 (11.1%)	1.00
Race n (%)			0.76
White	39 (48.1%)	41 (50.6%)	
Black	21 (25.9%)	23 (28.4%)	
Other	21 (25.9%)	17 (21.0%)	
Smoker, n (%)	40 (49.4%)	41 (50.6%)	0.88
Anti-hypertensive, n (%)	42 (51.9%)	42 (51.9%)	1.00
Systolic BP, mean (SD)	128.6 (10.1)	132.6 (12.5)	0.03
Total cholesterol, mean (SD)	194.6 (32.9)	194.3 (30.7)	0.95
HDL-C, mean (SD)	45.7 (13.9)	48.9 (13.0)	0.13
LDL-C, mean (SD)	114.2 (25.7)	110.2 (26.1)	0.32
Risk Score, mean (SD)	11.3% (3.1%)	11.6% (3.1%)	0.54
7.5%–9.9%	34 (42.0%)	26 (32.1%)	
10%–14.9%	34 (42.0%)	43 (53.1%)	
15%–19.0%	13 (16.0%)	12 (14.8%)	
BMI, n (SD)	26.5 (4.7)	29.9 (5.9)	<0.001
Primary payer, n (%)			<0.001
Medicaid	27 (33.3%)	47 (58.0%)	
Commercial	30 (24.7%)	6 (7.4%)	
Medicare	20 (24.7%)	16 (19.8%)	
Self Pay	3 (3.7%)	4 (4.9%)	
Financial assistance	1 (1.2%)	8 (9.9%)	
Triglycerides, mean (SD)	183.1 (112.4)	183.0 (95.1)	1.00
Inflammatory diseases, n (%)	13 (16.0%)	4 (4.9%)	0.02
Lupus	0 (0.0%)	0 (0.0%)	
Psoriasis	3 (3.7%)	1 (1.2%)	
Rheumatoid arthritis	2 (2.5%)	2 (2.5%)	

(continued)

Table 2. Continued.

Characteristic	PLWH (n = 81)	Non-HIV (n = 81)	p-Value
Inflammatory bowel	8 (9.9%)	4 (4.9%)	
eGFR 15–59, n (%)	10 (12.3%)	3 (3.7%)	0.04
No eGFR	9 (11.1%)	22 (27.2%)	
Early menopause, n (%)	0 (0.0%)	0 (0.0%)	1.00
Pre-eclampsia, n (%)	0 (0.0%)	0 (0.0%)	1.00
Metabolic syndrome, n (%)	36 (44.4%)	42 (51.9%)	0.35
Hypercholesterolemia, n (%)	9 (11.1%)	6 (7.4%)	0.42

Age (years), BMI: body mass index (kg/m^2); BP: blood pressure (mm Hg); Early menopause: ≤ 40 years old; eGFR: estimated glomerular filtration rate ($\text{mL}/\text{min}/1.73 \text{ m}^2$); HDL-C: high density lipoprotein cholesterol (mg/dL); Hypercholesterolemia: LDL-C 160–189 mg/dL or non-HDL-C 190–219 mg/dL; LDL-C: low density lipoprotein cholesterol (mg/dL); Risk Score: 10-year ASCVD risk-score from the Pooled Cohort Equation (%); SD: standard deviation; Total Cholesterol (mg/dL); Triglycerides (mg/dL).

Table 3. Statin prescribing.

	PLWH (n = 81)	Non-HIV (n = 81)	p-Value
Active statin order, n (%)	27 (33.0%)	25 (30.9%)	0.74
Statin intensity, n (%)	PLWH (n = 27)	Non-HIV (n = 25)	p-Value
High	8 (29.7%)	9 (36.0%)	0.58
Moderate*	18 (66.7%)	16 (64.0%)	
Low	1 (3.7%)	0 (0.0%)	
Non-statin (not included)	3	1	
Statin adherence, n (%)			0.01
PDC $\geq 80\%$	15 (55.6%)	3 (12.0%)	
PDC $< 80\%$	3 (11.1%)	6 (24.0%)	
No dispensing at Denver Health	9 (33.3%)	16 (64.0%)	

Non-statins: fibrates and fish oil; PDC: proportion of days covered.

*Two patients prescribed a moderate-intensity statin were also prescribed a non-statin lipid-lowering therapy.

patients (30.9%) within the non-HIV cohort did (Table 3). This difference between cohorts was not statistically significant ($p = 0.74$).

Secondary outcome: Statin intensity and dosing

A description of the intensity of the prescribed statins is included in Table 3. Patients prescribed a combination of a statin and a non-statin medication were categorized based on the statin. The prescribed statin intensity was similar between cohorts ($p = 0.58$). Two-thirds of patients in both cohorts received moderate intensity statin therapy and one-third received high intensity statin therapy. There was no difference in statin intensity prescribed relative to ASCVD risk score. The predominate statins prescribed across both cohorts were atorvastatin and rosuvastatin (50% and 34.6%, respectively). Atorvastatin was more commonly prescribed in the non-HIV cohort (68%) whereas rosuvastatin was more commonly prescribed in the PLWH cohort (48%). Patients prescribed other lipid-lowering therapies, such as fenofibrate or over-the-counter fish oil,

without statin therapy were not included in the subgroup analysis.

Secondary outcome: Risk-enhancing factors

No statistically significant differences were observed among the total number of non-HIV risk-enhancing factors between cohorts ($p = 0.36$; Table 4). The only statistically significant difference relative to non-HIV risk-enhancing factors among patients prescribed statins occurred among those with an eGFR of 15–59 mL/min/1.73 m^2 . In the PLWH cohort, 5 of the 27 (18.5%) had an eGFR of 15–59 mL/min/1.73 m^2 versus none of the 25 (0.0%) among the non-HIV cohort. While the PLWH cohort did have more patients with an eGFR of 15–59 mL/min/1.73 m^2 ($p = 0.02$), 7 of the 25 patients (28.0%) in the non-HIV cohort did not have eGFR data available.

Secondary outcome: Statin adherence

Fifteen of the 27 (55.6%) patients with an active statin prescription in the PLWH cohort had a PDC $\geq 80\%$

Table 4. Risk-enhancing factors among patients prescribed statins.

	PLWH (n = 27)	Non-HIV (n = 25)	p-Value
Total Risk-Enhancing Factors, n (%)			0.36
0	4 (14.8%)	7 (28.0%)	
1	12 (44.4%)	7 (28.0%)	
2	6 (22.2%)	9 (36.0%)	
3	4 (14.8%)	2 (8.0%)	
4	1 (3.7%)	0 (0.0%)	
Specific risk-enhancing factors, n (%)			
Triglycerides \geq 175 mg/dL	16 (59.3%)	11 (44.0%)	0.60
Primary hypercholesterolemia	4 (14.8%)	3 (12.0%)	0.77
Metabolic syndrome	10 (37.0%)	15 (60.0%)	0.10
eGFR 15-59 mL/min/1.73m ²	5 (18.5%)	0 (0.0%)	0.02

Hypercholesterolemia: LDL-C 160-189 mg/dL or non-HDL-C 190-219 mg/dL; Metabolic syndrome: \geq 3 of the following (blood glucose \geq 100 mg/dL, blood pressure \geq 130/85 mm Hg or treatment, Body Mass Index \geq 25 kg/m², high density lipoprotein cholesterol [men $<$ 40 mg/dL, women $<$ 50 mg/dL], triglycerides $>$ 150 mg/dL).

compared to only 3 of the 25 (12.0%) of patients in the non-HIV cohort ($p=0.01$). Nine of the 27 patients (33.3%) in the PLWH cohort and 16 of the 25 patients (64.0%) in the non-HIV cohort did not fill their statin prescription at a Denver Health pharmacy and, rendering them unavailable for subgroup analysis.

Discussion

Rates of statin prescribing for intermediate-risk primary prevention patients without diabetes were similar between PLWH and those patients without a diagnosis of HIV. However, overall rates of statin prescribing were low in both cohorts. Among patients who were prescribed statin therapy, statin intensity and total number of risk-enhancing factors were similar between patients with and without HIV. Most patients were prescribed moderate-intensity statin therapy (59.3% in the PLWH cohort and 69.0% in the control cohort) which aligns with the 2018 AHA/ACC/Multisociety cholesterol guideline recommendation for statin intensity for this intermediate-risk level. This study was not designed to evaluate the association between ART regimens and statin therapy or statin intensity. Statins are metabolized via cytochrome P450 enzymes while certain concurrent ART therapies, such as protease inhibitors, may alter the function of these enzymes and cause drug-drug interactions.¹⁶ Statins such as atorvastatin or pitavastatin with lower risk for protease inhibitor drug-drug interactions may be used by providers to help mitigate these risks.^{16,17} As noted in the results section, atorvastatin was the most commonly prescribed statin across both cohorts. Additionally, statins such as rosuvastatin may require lower doses to reduce the incidence of reactions.^{16,17} Rosuvastatin was the most commonly prescribed statin in the PLWH cohort and was most commonly

prescribed at the 5 mg dose, which aligns with use of lower doses to avoid potential drug interactions.

A majority of PLWH prescribed a statin who fill their prescription within the Denver Health system were adherent as indicated by a PDC \geq 80%. This was significantly higher than the non-HIV cohort; however, only 9 of the 25 patients (36%) without a diagnosis of HIV filled their statin prescription within the Denver Health system. PLWH are encouraged to fill their medications at a Denver Health pharmacy to ensure patients receive education, adherence support, and evaluation for drug interaction. Fill histories from pharmacies outside of the health system were unavailable. Adherence to ART among PLWH varies significantly based on factors such as chronic disease burden, medication cost, and stigma of the disease; however, this may also be due to the \geq 95% PDC threshold required for optimal HIV viral load suppression.¹⁸⁻²¹ PLWH with adequate adherence to chronic medications for non-HIV conditions, such as HTN or behavioral health indications, with a similar PDC threshold of \geq 80% used in our study has shown to be as high as 82.7%.²¹ Successful strategies used to improve ART adherence in PLWH, such as case management and patient counseling, may present as viable options to incorporate other chronic medications such as statins.¹⁸

Previous studies evaluating statin prescribing rates for various indications in PLWH reported ranges from 42%-72%.¹⁰⁻¹³ One cohort study of more than 3,000 PLWH in Washington, D.C. found that 52% of patients were eligible for statin therapy for primary or secondary prevention according to at least one cholesterol guideline.¹⁰ Among this group, 49%-73% of eligible patients were prescribed statins depending on the cholesterol guideline utilized.¹⁰ Additionally, Mosepele et al. compared the 2013 ACC/AHA and

ATP III cholesterol guidelines in a cohort of 1,394 PLWH and found that 42.8% of patients had guideline indications for statin therapy and 66.4% of these patients received a statin prescription.¹¹ The 33% statin prescribing rate within our analysis is much lower than previously described. Compared to other studies, our study included a smaller sample size and was conducted within a single health system. The smaller sample size in this study also may have been due to our strict inclusion and exclusion criteria that aligned with the 2018 AHA/ACC/Multisociety cholesterol guideline definition of intermediate-risk.⁷ Additionally, previous studies cited herein only included analyses prior to the publication of the 2018 AHA/ACC/Multisociety cholesterol guideline. These studies included patient populations with all statin indications beyond just primary prevention, such as clinical ASCVD, diabetes, and severe hypercholesterolemia.^{10–13} By limiting the inclusion and exclusion criteria, our study uniquely evaluated the role of HIV as a risk-enhancing factor use of statin therapy in intermediate-risk patients.

This study has a few limitations. First, some of the data, specifically eGFR and BMI, were incomplete within the EHR. The cohort of PLWH with available eGFR data possessed statistically significantly higher rates of having an eGFR of 15–59 mL/min/1.73 m²; however, it is noteworthy that only 11.1% of the PLWH cohort did not have a reportable eGFR compared to the 27.2% of the non-HIV group. Second, the use of surrogate markers of secondary outcomes, such as BMI to replace waist circumference, were required to create sufficient data to identify risk-enhancing factors such as metabolic syndrome. Collecting and documenting waist circumference within the EHR is not a routine practice; therefore, BMI was the only consistently available measurement to identify metabolic syndrome. Lastly, laboratory values used to calculate the 10-year ASCVD risk score may have been influenced by statin therapy and thus may have altered the inclusion and exclusion of patients within each cohort. For example, some patients who were excluded secondary to an LDL-C of <70 mg/dL may have been taking a statin that reduced their LDL-C below 70 mg/dL. Despite these limitations, this study yields beneficial information to help guide future practice.

The 2018 AHA/ACC/Multisociety cholesterol guideline includes HIV as one of many factors to favor initiation of statin therapy in intermediate-risk patients. Beyond lipid-lowering benefits, statin therapy is hypothesized to modulate the inflammatory effects of ASCVD.^{2,7,22} In PLWH, treatment with rosuvastatin results in significant reductions in inflammatory markers (e.g., soluble CD14), lymphocytes, and monocyte activation in patients treated with ART.^{22,23}

A moderate-intensity statin is recommended under this circumstance as a Class IIa recommendation with a B level of evidence supported by observational data cohorts that displayed either an increased ASCVD risk or observed stain benefit in PLWH.⁷

Following the publication of the 2018 AHA/ACC/Multisociety cholesterol guideline, new data supporting the use of statins and other lipid-lowering therapy among PLWH has been published and additional trials are underway. Registry data of PLWH within the U.S. Veterans Affairs system notes a 52% mortality reduction among PLWH with consistent statin use.²⁴ Additionally, lack of randomized, controlled trials within this patient population led to the currently ongoing trial of pitavastatin, known as the REPRIEVE (Randomized Trial to Prevent Vascular Events in HIV) trial.²⁵ The REPRIEVE trial will be the first to specifically evaluate major adverse cardiovascular events (MACE) in over 7,500 primary prevention PLWH initiated on a moderate-intensity statin or placebo.²⁵ If REPRIEVE demonstrates that pitavastatin reduces MACE in PLWH, it could further justify statin therapy as a standard of care in PLWH with ASCVD risk factors.

System-wide prospective interventions by clinical pharmacists have been shown to increase guideline-directed statin therapy for indications such as diabetes and ASCVD.^{25–29} These approaches are Class I recommendations in the 2018 AHA/ACC/Multisociety cholesterol guideline for implementation of evidence-based statin therapy.⁷ A similar combination of approaches including chart review, reporting systems, and prospective recommendations and/or direct prescribing by a clinical pharmacist or health promotion team has the potential to be utilized in the PLWH population. Educational opportunities such as continuing medical education presentations to address concerns about pill burden or ART-statin drug-drug interactions or EHR notifications of items like “best practice alerts” might increase statin prescribing in primary prevention PLWH.

Conclusion and relevance

This study evaluated rates of statin prescribing in PLWH for primary prevention of ASCVD as described in the 2018 AHA/ACC/Multisociety cholesterol guideline. Rates of statin prescribing were similar, yet overall low, among intermediate-risk primary prevention PLWH compared to similar patients who were not diagnosed with HIV. Future clinical and educational interventions, as well as potential results from ongoing clinical trials, may help close this gap in this at-risk patient population.

DECLARATIONS

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Declaration of conflicting interests

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Ethical approval

This study was approved by the Denver Health Sponsored Programs and Research Office and the Colorado Multiple Institutional Review Board.

Guarantor

Joel Marrs.

Contributorship

JM and JN conceived the study and its design. JN performed data collection. JM and JN performed statistical analysis. JM, JN, JS, RH, and SA wrote the manuscript. JM, JN, JS, RH, and SA performed grammatical editing. JM and JN performed formatting. JM and JN take responsibility for the article as a whole.

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References

- Deeks SG, Tracy R and Douek DC. Systemic effects of inflammation on health during chronic HIV infection. *Immunity* 2013; 39: 633–645.
- Nou E, Lo J, Hadigan C, et al. Pathophysiology and management of cardiovascular disease in patients with HIV. *Lancet Diabetes Endocrinol* 2016; 4: 598–610.
- Triant VA, Lee H, Hadigan C, et al. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab* 2007; 92: 2506–2512.
- Currier JS, Taylor A, Boyd F, et al. Coronary heart disease in HIV-infected individuals. *J Acquir Immune Defic Syndr* 2003; 33: 506–512.
- Freiberg MS, Chang CC, Kuller LH, et al. HIV infection and the risk of acute myocardial infarction. *JAMA Intern Med* 2013; 173: 614–622.
- Feinstein MJ, Hsue PY, Benjamin LA, et al.; on behalf of the American Heart Association Prevention Science Committee of the Council on Epidemiology and Prevention and Council on Cardiovascular and Stroke Nursing; Council on Clinical Cardiology; and Stroke Council. Characteristics, prevention, and management of cardiovascular disease in people living with HIV: a scientific statement from the American Heart Association. *Circulation* 2019; 140: e98–e124.
- Grundy SM, Stone NJ, Bailey AL, et al. 2018 ACC/AHA/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019; 73: 3168–3209.
- Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. Executive summary of the third report of the national cholesterol education program (NCEP) Expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA* 2001; 285: 2486–2497.
- Dubé MP, Stein JH, Aberg JA, et al. Guidelines for the evaluation and management of dyslipidemia in human immunodeficiency virus (HIV)-infected adults receiving antiretroviral therapy: recommendations of the HIV Medical Association of the Infectious Disease Society of America and the adult AIDS Clinical Trials Group. *Clin Infect Dis* 2003; 37: 613–627.
- Levy ME, et al. Evaluation of statin eligibility, prescribing practices, and therapeutic responses using ATP III, ACC/AHA, and NLA dyslipidemia treatment guidelines in a large urban cohort of HIV-Infected outpatients. *AIDS Patient Care STDs* 2018; 32: 58–431.
- Mosepele M, Regan S, Massaro J, et al. Impact of the American College of Cardiology/American Heart Association cholesterol guidelines on statin eligibility among human immunodeficiency virus-Infected individuals. *Open Forum Infect Dis* 2018; 5: 1–7.
- Schafer J, Patel R, Hastain N, et al. Patients living with HIV infection are less likely to receive the correct intensity of statin therapy for cardiovascular disease risk reduction. In: *IDWeek* 2019, 2–6 October 2019, Washington, DC.
- Riesterberg RA, Furman A, Cowen A, et al. Differences in statin utilization and lipid lowering by race, ethnicity, and HIV status in a real-world cohort of persons with human immunodeficiency virus and uninfected persons. *Am Heart J* 2019; 209: 79–87.
- Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014; 63: 2889–2934.

15. National Center for Chronic Disease Prevention and Health Promotion. Calculating proportion of days covered (PDC) for antihypertensive and antidiabetic medications: an evaluation guide for grantees, www.cdc.gov/dhbsp/docs/med-adherence-evaluation-tool.pdf (accessed 30 June 2020).
16. Rosenson RS, Colantonio LD, Burkholder GA, et al. Trends in utilization of statin therapy and contraindicated statin use in HIV-infected adults treated with antiretroviral therapy from 2007 through 2015. *J Am Heart Assoc* 2018; 7: e010345.
17. Chastain DB, Stover KR and Riche DM. Evidence-based review of statin use in patients with HIV on antiretroviral therapy. *J Clin Transl Endocrinol* 2017; 8: 6–14.
18. Holtzman CW, Brady KA and Yehia BR. Retention in care and medication adherence: current challenges to antiretroviral therapy success. *Drugs* 2015; 75: 445–454.
19. Iacob SA, Iacob DG and Jugulete G. Improving the adherence to antiretroviral therapy, a difficult but essential task for a successful HIV treatment-clinical points of view and practical considerations. *Front Pharmacol* 2017; 8: 831.
20. Beer L, Tie Y, Weiser J, et al. Nonadherence to any prescribed medication due to costs among adults with HIV infection – United States, 2016–2017. *MMWR Morb Mortal Wkly Rep* 2019; 68: 1129–1133.
21. Langness J, Cook PF, Gill J, et al. Comparison of adherence rates for antiretroviral, blood pressure, or mental health medications for HIV-positive patients at an academic medical center outpatient pharmacy. *J Manag Care Spec Pharm* 2014; 20: 809–814.
22. Moore RD, Bartlett JG and Gallant JE. Association between use of HMG CoA reductase inhibitors and mortality in HIV-infected patients. *PLoS One* 2011; 6: e21843.
23. Funderburg NT, Jiang Y, Debanne SM, et al. Rosuvastatin reduces vascular inflammation and T-cell and monocyte activation in HIV-infected subjects on antiretroviral therapy. *J Acquir Immune Defic Syndr* 2015; 68: 396–404.
24. Drechsler H, Ayers C, Cutrell J, et al. Consistent use of lipid lowering therapy in HIV infection is associated with low mortality. *BMC Infect Dis* 2021; 21: 150.
25. Grimspoon Sk, et al. Rationale and design of the randomized trial to prevent vascular events in HIV (REPRIEVE). *Am Heart J* 2019; 212: 23–35.
26. Renner HM, Hollar A, Stolpe SF, et al. Pharmacist-to-prescriber intervention to close therapeutic gaps for statin use in patients with diabetes: a randomized controlled trial. *J Am Pharm Assoc (2003)* 2017; 57: S236–S242.e1.
27. Haby HE, Alm RA, Corona AR and Hall AC. Population health model for pharmacist assessment and independent prescribing of statins in an ambulatory care setting. *J Am Pharm Assoc (2003)* 2020; 60: 130–137.
28. Anderson SJ, Marrs JC, Chachas CR, et al. Evaluation of a pharmacist-led intervention to improve statin use in persons with diabetes. *J Manag Care Spec Pharm* 2020; 26: 910–917.
29. Troksa KT, Billups SJ, Claus L, et al. Effectiveness of a pharmacist-led population health approach to implementing statin therapy in primary prevention patients with type 2 diabetes mellitus. *J Am Coll Clin Pharm* 2020; 3: 723–728.