

# Underutilization of Statins for Prevention of Cardiovascular Disease among Primarily African-American HIV-Infected Patients

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## Abstract

**Background:** Studies have consistently demonstrated that statin therapy reduces CHD-related mortality, but HIV-infected individuals are frequently undertreated for hyperlipidemia. Therefore, we sought to: 1. determine whether the numbers of patients recommended for statin therapy differed using the 2004 and 2013 guidelines; 2. evaluate the proportion of recommended patients who were actually receiving statins; and 3. evaluate the factors associated with statin prescription.

**Methods:** Conducted cross-sectional analysis of a retrospective cohort. 100 patients receiving care at an academic inner-city HIV clinic in 2008 were reviewed. The atherosclerotic vascular disease (ASCVD) risk score was calculated using the 2013 Pooled Cohort Equation and the 2004 and 2013 guidelines were applied to evaluate numbers of patients recommended for statin therapy. Proportions were used to report patients receiving statins among those who were recommended for treatment and several unadjusted logistic regression analyses were performed to identify factors associated with utilization of statins in recommended patients.

**Results:** 81 participants were included in the final analysis. Substantially larger numbers of HIV-infected individuals were recommended to receive statin therapy for CHD risk reduction when applying the 2013 guidelines compared to the 2004 guidelines, but less than half received statins for primary prevention as recommended. Prescription of statins was not associated with either ASCVD risk score or many traditional CHD risk factors. Diabetes mellitus was associated with increased odds of receiving statin therapy whereas hepatitis C co-infection and current smoking status were associated with decreased odds of receiving statins.

**Conclusions:** There is an increased, large and unmet need to increase statin use for prevention of CHD. Underutilization of statins was most pronounced among HIV-hepatitis C co-infected patients and HIV-infected smokers.

**Keywords:** HIV/AIDS; Atherosclerotic vascular disease and HIV; Coronary heart disease and HIV; Statins and HIV; ASCVD risk score; CHD; Statins; Coronary heart disease and Hepatitis C; Statins and Hepatitis C

## Introduction

Coronary heart disease (CHD) represents a major cause of death in HIV-infected patients [1-6]. Many factors contribute to premature CHD risk in HIV-infected individuals including traditional CHD risk factors (dyslipidemia, hypertension, diabetes), lifestyle factors (cigarette smoking and illicit substance use), and HIV-related (inflammation, hypercoagulability, immune activation, effects of antiretroviral therapy (ART) [6-12].

HIV-infected patients often have abnormal lipid metabolism, particularly hypertriglyceridemia and decreased high-density lipoprotein cholesterol (HDL-c) levels due to HIV infection itself and the use of ART, particularly protease inhibitors [13-19]. For this reason, the Infectious Disease Society of America recommends screening for dyslipidemia prior to initiating ART and three to six months after starting therapy and at least annually thereafter [20].

The 2004 National Education Program Adult Treatment Plan III (NCEP ATPIII) guidelines helped HIV clinicians determine lifestyle and pharmacological interventions based on patients' lipid profiles and their 10-year risk of developing CHD using the 2002 Framingham

risk calculation [21,22]. The main pharmacological intervention recommended to treat dyslipidemia is statins. In 2013, the ACC/AHA developed another risk score calculator that provided the composite atherosclerotic vascular disease (ASCVD) risk score using the Pooled Cohort Equation to assess patients' 10-year risk of developing CHD. They advocated using these scores to identify patients with elevated CHD risk who may benefit from moderate- or high-intensity statin therapy while de-emphasizing LDL-c cutpoints to guide statin therapy [23].

Studies have consistently demonstrated that statin therapy reduces

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CHD-related mortality, but HIV-infected individuals are frequently undertreated for hyperlipidemia and associated CHD risk factors [24-27]. However, some recent reports of decreasing CHD-associated mortality in select HIV populations have postulated that more aggressive control of CHD risk factors such as high blood pressure and abnormal lipid levels may account for the declines in some populations [28,29].

We hypothesized that more patients would be recommended for statin treatment using the 2013 ACC/AHA guidelines than with the 2004 NCEP ATP III guidelines even though this would still represent less than 50% of eligible patients using the updated guidelines. Therefore, the primary purpose of our study was to determine whether the numbers of patients recommended for statin therapy differed using the two guidelines and, secondarily, to evaluate the proportion of recommended patients who were actually receiving statins and the factors associated with statin use.

## Methods

### Study population

We reviewed the medical records of 100 HIV-infected patients treated at the Evelyn Jordan Center (EJC), a large inner city HIV clinic associated with the University of Maryland Medical Center (UMMC). To be eligible for the study, participants had to be at least 18 years old, enrolled in and receiving HIV care at EJC on June 1, 2008, and have at least two routine HIV visits between June 1, 2008 and May 31, 2012. We selected the first 100 charts based on medical record numbers generated in chronological order to determine the feasibility of abstracting and collecting data from these medical charts for a larger retrospective cohort study. One patient had more than one medical record number resulting in 99 eligible patients remaining. Of the 99 eligible participants, 81 had data for every variable required to calculate the ASCVD risk score using the Pooled Cohort Equation [23, 30]. The calculated ASCVD risk score is analogous to the Framingham risk score in that it describes an individual's 10 year risk of developing CHD.

### Data collection

Data were collected for routine HIV visits at 3 month intervals (maximum of 4 visits per 12 month period) from June 1, 2008 to May 31, 2012 as part of the larger retrospective cohort study. A visit was defined as routine if it was a follow-up for HIV, included physical exams and addressed health maintenance issues. The presence of medical diagnoses and receipt of medications was based on documentation in the medical chart following review of the clinic and hospital medical record. The diagnosis of clinical depression was based on mental health provider notes or treatment of depression with appropriate psychiatric medication, rather than patient self-report to minimize the possibility of misdiagnosis. CHD event was defined as one of the following: history of an acute coronary syndrome (e.g. unstable angina), myocardial infarction (MI), clinical or arteriographically proven coronary artery disease (CAD) and ischemic cardiomyopathy. Cerebrovascular disease was defined as stroke or transient ischemic attack. ASCVD was defined as either CHD or cerebrovascular disease. Laboratory values and ranges were based on assays used by the UMMC reference laboratory, Labcorp. Data collected from the first 100 charts as described above were analyzed for this study.

### Statistical methods

We performed a cross-sectional analysis of 81 participants in EJC during 2008. ASCVD risk scores were calculated using the 2013 Pooled

Cohort Equation endorsed by the ACC/AHA [23]. Recommendation for statin therapy using the 2004 NCEP ATP III guidelines was based on LDL-c levels, ASCVD risk score, and other risk factors including current cigarette smoking, hypertension or on antihypertensive medication, low HDL-c (<40 mg/dL), family history of ASCVD in first degree relatives, and age (men  $\geq$  45 years; women  $\geq$  55 years) [21,22]. Patients recommended for statin therapy using the 2013 ACC/AHA guidelines were those with prior ASCVD and those without known ASCVD and one of the following: 1) ASCVD risk score  $\geq$  7.5%, 2) diabetes mellitus 40-75 years and LDL-c  $\geq$  70 mg/dl, or 3) LDL-c  $\geq$  190 mg/dl [23,30]. The proportion of patients receiving statins among those who were recommended for treatment are reported. For the secondary objective, receipt of statins was considered as a dichotomous outcome variable and several unadjusted (bivariate) logistic regression analyses were performed to identify factors associated with utilization of statins in patients recommended for statin therapy.

The analyses were performed using Stata 12.1 (StataCorp, 2011). A *p*-value <0.05 using a two tailed *z*-test for the odds ratio was considered significant.

## Results

The 81 participants were predominately men (61.7%) and African-American (95.1%) with a median age of 52 years (Table 1 and Supplemental Table 1). The most common HIV risk factor was injection drug use (IDU) (60.5%). The median CD4 cell count was 343 cells/mm<sup>3</sup>. The majority were receiving ART (87%) with mostly protease inhibitors and nucleoside reverse transcriptase inhibitors, and 55.5% were virologically suppressed. Over 70% were co-infected with hepatitis B and/or C. Almost half (45.7%) had a body mass index >25 kg/mm<sup>2</sup> and 24.7% had diabetes mellitus. One of 81 participants received lipid-lowering pharmacological intervention other than statins. Characteristics of the 18 excluded patients were not significantly different from those of included patients, and none of the excluded participants received a non-statin lipid-lowering medication (data not shown).

The median ASCVD risk scores of men and women without prior ASCVD in 2008 were 10.8 (N=45) and 4.0 (N=23), respectively. In 2012, median ASCVD risk scores of men and women were 10.7 (N=33) and 4.0 (N=15), respectively (Table 2A). In 2008, among individuals *without* prior ASCVD, two patients (2.9%) were recommended for statin therapy using the 2004 NCEP ATP III guidelines compared to 41 patients (60.3%) using the 2013 ACC/AHA guidelines. Of these recommended individuals, 12 received statins. In 2008, among individuals *with* prior ASCVD, eight patients (61.5%) were recommended for statin therapy using the 2004 guidelines compared to 13 patients (100%) using the 2013 guidelines. Of these recommended individuals, six received statins.

In 2012, among individuals *without* prior ASCVD, one patient (2.1%) was recommended for statin therapy using the 2004 guidelines compared to 27 patients (56.3%) using the 2013 guidelines. Of these recommended individuals, nine received statins. In 2012, among individuals *with* prior ASCVD, none were recommended for statin therapy using the 2004 guidelines compared to three patients (60%) using the 2013 guidelines. Of these three individuals, two received statins (Table 2A).

There were substantial differences in the proportion of patients recommended for statin therapy who were actually receiving statins when comparing the 2004 NCEP ATP III and the 2013 ACC/AHA guidelines (Table 2B). For primary prevention in 2008, statins were

Variable	Men (n=50)	Women (n=31)	Total (n=81)
	% (n)	% (n)	% (n)
<b>Socio-demographic Indicators</b>			
Sex	61.7 (50)	38.3 (31)	100 (81)
Age in years (median)	54	50	52
Race			
Black/African American	94.0 (47)	96.8 (30)	95.1 (77)
<b>Behavioral indicators</b>			
Cigarette Smoker	56.0 (28)	54.8 (17)	55.6 (45)
Alcohol Use	26.0 (13)	22.6 (7)	24.7 (20)
Illicit drug use	6.0 (3)	22.6 (7)	12.4 (10)
Mode of transmission			
IDU	68.0 (34)	48.4 (15)	60.5 (49)
Heterosexual	20.0 (10)	51.6 (16)	32.1 (26)
MSM	12.0 (6)	-	7.4 (6)
<b>Clinical Indicators</b>			
ARVs			
PIs	53.7 (22)	44.0 (11)	50.0 (33)
NNRTIs	36.6 (15)	52.0 (13)	42.4 (28)
NRTIs only	17.1 (7)	8.0 (2)	13.6 (9)
Median CD4 cell count (cells/mm <sup>3</sup> )	392	123	343
Undetectable viral load (copies/ml)	60.0 (30)	48.4 (15)	55.6 (45)
GFR >=59	84.0 (42)	80.7 (25)	82.7 (67)
Diabetes mellitus	22 (11)	29.0 (9)	24.7 (20)
Hepatitis C	82.0 (41)	58.1 (18)	72.8 (59)
Prior CHD event	6.0 (3)	6.5 (2)	6.2 (5)
Prior Cerebrovascular Disease	4.0 (2)	19.4 (6)	9.9 (8)
Prior non-ASCVD CVD event	12.0 (6)	3.2 (1)	8.6 (7)
Family history of CVD	66.0 (33)	77.4 (24)	70.4 (57)
Antihypertensive Use	48.0 (24)	45.2 (14)	46.9 (38)
Systolic blood pressure (median)	132	129	130
Total cholesterol (median)	161	156	157
HDL (median)	41	44	41
LDL (median)	84	91	87
Triglycerides (median)	138	116	120

**Notes:** MSM= men who have sex with men, IDU= injection drug use, PI= protease inhibitor, NNRTI= non-nucleoside reverse transcriptase inhibitor, NRTI= nucleoside reverse transcriptase inhibitor, CHD= coronary heart disease, ASCVD= atherosclerotic vascular disease, CVD= cardiovascular disease, GFR=Glomerular filtration rate, HDL=high-density lipoprotein, LDL=low-density lipoprotein Table 1: Characteristics of HIV- Infected Participants at the Evelyn Jordan Center of the University of Maryland Medical Center

**Table 1:** Characteristics of HIV- Infected Participants at the Evelyn Jordan Center of the University of Maryland Medical Center

overprescribed in 10 out of 12 patients using the 2004 guidelines and under prescribed using the 2013 guidelines as only 12 of 41 patients received treatment. Similarly, for primary prevention in 2012 only one patient was recommended but nine received statins using the 2004 guidelines compared to nine of 27 recommended patients received treatment using the 2013 guidelines. For secondary prevention in 2008, six of eight recommended patients received statins using the 2004 guidelines compared to six of 13 recommended patients using the 2013 guidelines. For secondary prevention in 2012, two of three recommended patients received statins using the 2013 guidelines. There were no patients recommended for statins using the 2004 guidelines.

Diabetes mellitus (OR=4.73, 95% CI=1.53, 14.63;  $p=0.007$ ) was the only factor significantly associated with increased odds of statin use

whereas current smoking status (OR=0.21, 95% CI=0.07, 0.67;  $p=0.008$ ) and hepatitis C (OR=0.13, 95% CI=0.04, 0.42;  $p<0.001$ ) were significantly associated with decreased odds of statin use (Table 3). Gender, race, the ASCVD risk score, other traditional CHD risk factors, and the HIV-related parameters were not associated with statin use.

	Median (n) ACC/AHA 2013 ASCVD Risk Score <sup>a</sup>		Recommended for Statin Therapy NCEP ATP III 2004 Guidelines <sup>b</sup>		Recommended for Statin Therapy ACC/AHA 2013 Guidelines <sup>c</sup>		Receiving Statin Therapy	
	Male	Female	Male	Female	Male	Female	Male	Female
No prior ASCVD in 2008	10.8 (45)	4.0 (23)	1	1	34	7	8	4
Known ASCVD in 2008	27.3 (5)	12.7 (8)	4	4	5	8	2	4
Patients in 2012 who had no prior ASCVD and at least one visit in 2012	10.7 (33)	4.0 (15)	1	0	24	3	6	3
Known ASCVD in 2012	17.7 (3)	6.7 (2)	0	0	1	2	1	1

ASCVD= atherosclerotic vascular disease; ACC/AHA= American College of Cardiology/American Heart Association; NCEP= National Cholesterol Education Program; ATP= Adult Treatment Panel; <sup>a</sup>: <http://tools.cardiosource.org/ASCVD-Risk-Estimator/>; <sup>b</sup>: National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 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) final report. Circulation 2002; 106(25):3143-3421; <sup>c</sup>: Stone NJ, Robinson J, 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 2013.

**Table 2A:** Median Framingham Risk Score, Recommended and Statin Use in HIV-Infected Participants at the Evelyn Jordan Center of the University of Maryland Medical Center.

	Receiving Statin Therapy	Percentage of Recommended Patients Receiving Statins (n recommended)	
		2004 NCEP ATP III Guidelines <sup>a</sup>	2013 ACC/AHA Guidelines <sup>b</sup>
Primary Prevention 2008	12	600% (2)	29% (41)
Secondary Prevention 2008	6	75% (8)	46% (13)
Primary Prevention 2012	9	900% (1)	33% (27)
Secondary Prevention 2012	2	NA (0)	67% (3)

NCEP= National Cholesterol Education Program; ATP= Adult Treatment Panel; ACC/AHA= American College of Cardiology/American Heart Association; NA= not applicable; <sup>a</sup>: National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). 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) final report.; <sup>b</sup>: 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.

**Table 2B:** Statin Recommended and Actual Usage in HIV-Infected Participants at the Evelyn Jordan Center of the University of Maryland Medical Center

	Receipt of Statin Therapy		p-value
	N	Odds Ratio (95% CI)	
<b>Socio-demographic Indicators</b>			
Age in years	81	1.07 (0.98, 1.17)	0.137
Males	50	0.72 (0.25, 2.08)	0.542
Race			
Caucasian	4 <sup>a</sup>	-	-
African-American	77	-	-
Employment			
Yes	17	0.67 (0.17, 2.69)	0.576
No (RC)	58	1.00	-
<b>Behavioral indicators</b>			
Current smoking	45	<b>0.21</b> (0.07, 0.67)	<b>0.008</b>
Current Alcohol Use	20	1.13 (0.34, 3.69)	0.842
Current Illicit drug use	10	0.84 (0.16, 4.38)	0.840
<b>Clinical Indicators</b>			
Time since HIV diagnosis			
5-10 years (RC)	11	1.00	-
11-20 years	32	1.26 (0.22, 7.22)	0.795
>20 years	38	1.40 (0.25, 7.68)	0.701
Receiving ART	62	2.96 (0.61, 14.23)	0.176
Receiving PIs	33	0.51 (0.16, 1.62)	0.255
Most recent CD4 cell count (cells/mm <sup>3</sup> )			
<200 (RC)	11	1.00	-
≥200	68	3.08 (0.37, 25.91)	0.301
Undetectable viral load (copies/ml)			
Yes	45	1.56 (0.51, 4.75)	0.430
No (RC)	35	1.00	-
BMI (kg/m <sup>2</sup> )			
<30.0 (RC)	65	1.00	-
≥30.0	14	2.22 (0.64, 7.76)	0.211
GFR (ml/min/1.73m <sup>2</sup> )			
≥59 (RC)	67	1.00	-
<59	14	0.95 (0.23, 3.83)	0.937
Diabetes Mellitus	20	<b>4.73</b> (1.53, 14.63)	<b>0.007</b>
Hepatitis C co-infection	59	<b>0.13</b> (0.04, 0.42)	<b>&lt;0.001</b>
Cancer*	14	0.53 (0.11, 2.63)	0.438
Prior non-ASCVD CVD	7	0.56 (0.06, 4.97)	0.602
Family history of CVD	57	0.77 (0.23, 2.26)	0.667
Total Cholesterol (mg/dl)			
≤200 (RC)	63	1.00	-
>200	18	3.01 (0.95, 9.50)	0.06
LDL (mg/dl)			
<160 (RC)	76	1.00	-
160 or more	2	3.47 (0.21, 58.45)	0.388
Triglycerides (mg/dl)			
<200 (RC)	63	1.00	-
200 or more	17	2.32 (0.71, 7.52)	0.161
ASCVD Risk Score			
Elevated Risk	45	0.99 (0.29, 3.41)	0.993
Low Risk (RC)	28	1.00	-

**Notes:** ART= antiretroviral therapy consisting of at least 3 antiretroviral medications; PI= protease inhibitor, BMI= body mass index, ASCVD= atherosclerotic vascular disease, CVD= cardiovascular disease, GFR=Glomerular filtration rate, LDL=low-density lipoprotein

\*= history of cancer or active cancer diagnosis

RC is reference category

<sup>a</sup> there are no cases of statin therapy receipt among Caucasian.

**Table 3:** Factors Associated with Statin Therapy among HIV-Infected Participants at the Evelyn Jordan Center of the University of Maryland Medical Center

## Discussion

In this study, we found that substantially larger numbers of HIV-infected individuals were recommended to receive statin therapy for CHD risk reduction when applying the 2013 ACC/AHA guidelines for treatment of cholesterol compared to the 2004 NCEP ATP III guidelines. We also found that prescription of statins was not associated with either ASCVD risk score or many traditional CHD risk factors, and that diabetes mellitus was associated with increased odds of receiving statin therapy whereas hepatitis C co-infection and current smoking status were associated with decreased odds of receiving statins. Finally, HIV-infected patients in this predominantly African American clinic with a large percentage of women and IDUs received statins for primary prevention less than half as often as recommended by current guidelines.

Pencina et al. demonstrated that greater numbers of patients in the general population would be recommended for statin therapy using the updated guidelines compared to the older guidelines, but a comparison of guidelines for statin initiation has been limited in the HIV population [31]. In our study, we found a marked difference in numbers of patients recommended for statin therapy for primary prevention: 2.9% using 2004 NCEP ATP III guidelines compared to 60.3% of our patients when using the 2013 ACC/AHA guidelines. This difference was much higher than that reported by Zanni et al. who reported that 8% of their 108 HIV-infected patients were recommended for statin therapy for primary prevention by the 2004 guidelines compared to 21% of patients when using the 2013 guidelines [32]. These differences in numbers of patients recommended for statins in the two studies may be partly due to differences in study population and design.

We also found that while more individuals than recommended were receiving statins for primary prevention using the 2004 NCEP ATP III guidelines only 29% and 33% recommended individuals were receiving them when the 2013 ACC/AHA guidelines were applied in 2008 and 2012, respectively. This comparison highlights the significantly larger numbers of HIV-infected patients who could benefit from more intensive CHD risk reduction measures using 2013 guidelines, which is significant given the excess, premature burden of CHD observed in HIV-infected individuals. It also suggests that provider perception may play a large role in statin prescription when considering the discrepancy between recommendation for statin therapy and actual use since patients were both over utilizing and underutilizing statins when applying different guidelines.

None of the reported studies to date have identified an association between hepatitis C co-infection and decreased statin use. The association of hepatitis C and statin use is important in light of our earlier study which demonstrated that chronic hepatitis C infection was associated with higher CHD risk [unpublished data]. A recent data analysis from the Multicenter AIDS Cohort Study (MACS) showed elevated transaminase levels were associated with not achieving LDL-c targets suggesting a reluctance of providers to initiate statins which are potentially hepatotoxic [33]. This may explain the underutilization of statins among HIV-hepatitis C co-infected patients.

Current smoking was also observed to be associated with decreased odds of statin use but this was not noted in the Data Collection on Adverse Events in Anti-HIV Drugs Study (D.A.D.) analysis from 1999-2006 of predominantly Caucasian men with comparatively much less IDU. The differences in findings may be due to differences in patient and provider study populations [34]. In the HIV Outpatient Study (HOPS) and MACS analyses, however, current smoking was associated

with lesser achievement of target LDL-c goals which may be explained by lower LDL-c targets due to presence of this risk factor that require more aggressive lipid-lowering therapy [26,33]. These observations are important because of the higher prevalence and risk of MI attributed to smoking in the HIV population compared to the general population [8].

We found that diabetes mellitus was associated with increased odds of patients receiving statins. Similar associations were also observed in the D.A.D. cohort analysis [34]. However, the D.A.D analysis found that family history of CVD, elevated total cholesterol and hypertriglyceridemia were also associated with statin use, and this was not demonstrated in our study perhaps due to differences in study population, time periods investigated, or sample sizes and consequent power to detect these associations. Lichenstein et al. found that race and gender were associated with achievement of lipid targets in an analysis from the HOPS, but they did not identify factors associated with prescription of pharmacological treatment and the HOPS represented substantially more Caucasians, men, and much less IDU than our study population [26].

Finally, we found that the majority of HIV-infected individuals who met criteria for statin therapy using current guidelines were not receiving it. This finding was consistent with the suboptimal use of statins observed in the D.A.D. cohort and in the HIV-HEART study, but different than in the HOPS in which 81-87% of those with elevated LDL-c or non-HDL-c recommended for therapy were receiving treatment [25,26,34]. However, therapy in the HOPS data was defined much more broadly than in the current study and included prescription of one of numerous different lipid-lowering agents (statins, ezetimibe, bile acid sequestrants, nicotinic acid) and documentation of exercise.

The underutilization of statins was not only observed in primary prevention of CHD but also in secondary prevention of CHD in our study and in the D.A.D. cohort analysis. Though the D.A.D analysis showed that statin use had modestly increased over calendar time, peaking around 2001, our study did not reveal a similar increase of statin use over time. This lack of increase in statin use in our study may be due to the predominantly minority study population with majority IDU, relatively lower resources, poorer access, and less sustained engagement in care, which highlights the need of HIV providers caring for underserved populations to be more proactive and vigilant in prescribing statins for CHD risk reduction.

There are important strengths to our study. This is one of only two studies to our knowledge comparing the differences in numbers of HIV-infected patients recommended for statin therapy when applying the NCEP ATP III 2004 versus the 2013 ACC/AHA guidelines. Second, our finding that HIV-hepatitis C coinfecting individuals received even greater suboptimal statin use than HIV- monoinfected individuals is an important addition to the literature. Finally, our study population consists of demographic risk groups that are often underrepresented in larger HIV cohorts and is one of the few evaluating prescription of statins that included large percentage of women. This is important given the observed differential CHD rates in HIV-infected women compared to men in reports from Boston and France as well as in our earlier study [2,4] [unpublished data].

There are important limitations to our study. First, the small sample size may have limited our ability to detect other significant associations with initiation of statins. We are reassured that other studies, including an abstract from the 2015 Conference on Retroviruses and Opportunistic Infections of the Veterans Affairs Clinical Case Registry

of 13,293 HIV-infected males, evaluating the impact of the 2013 ACC/AHA among HIV-infected patients have also reported increased numbers of HIV-infected recommended to be receiving statins [32]. Second, the cross-sectional nature of the study did not allow us to identify change of CHD risk factors associated with change of statin use over time nor allow us to report on statin initiation rather than statin utilization. However, both of these are appropriately being addressed in the longitudinal phase of our study. Third, the retrospective design did not allow capture of all data relevant to CV risk such as anthropometric measures and accurate assessment of lipodystrophy that may influence provider perception of CHD risk and prescription of statins. Lastly, we were not able to document individual provider use accurately and account for provider bias in our analysis.

In conclusion, our study demonstrated an increased, large and unmet need to increase statin use for prevention of CHD. Underutilization of statins based on the updated 2013 ACC/AHA guidelines was most pronounced among HIV-hepatitis C co-infected patients and HIV-infected smokers. Prescription of statins was not associated with objective, standardized CVD risk assessment tools but only with presence of a selected co-morbidity which suggests that HIV provider perception of individual patient need for statins likely plays a large role in practice behavior. Further studies evaluating utilization of statins are needed to inform and improve HIV provider knowledge of and adherence to current guidelines for prevention and management of CHD. HIV-specific guidelines regarding statin use are urgently needed.

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