The Association Between the Receipt of Lipid Lowering Therapy and HIV Status Among Veterans Who Met NCEP/ATP III Criteria for the Receipt of Lipid Lowering Medication

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OBJECTIVE: To examine the association between HIV infection status and the receipt of lipid lowering therapy based on National Cholesterol Education Program/Adult Treatment Panel (NCEP/ATP III) guidelines and to assess whether HIV viral load and hepatitis C (HCV) status alters that association.

PARTICIPANTS AND DESIGN: A cross-sectional analysis of survey, laboratory, and pharmacy data from 1,577 male participants (59% HIV infected) of the Veterans Aging Cohort Five-Site Study, a prospective observational cohort of U.S. veterans with and without HIV infection.

MEASUREMENTS: Receipt of lipid lowering therapy obtained from the VA pharmacy benefits management system was the main outcome.

RESULTS: The prevalence of lipid lowering therapy among HIV-infected and HIV-uninfected veterans was 15.4% vs. 37.9%, respectively, $p < 0.01$. Among veterans who met NCEP/ATP III criteria for lipid lowering therapy, HIV-infected veterans had a significantly lower prevalence for the receipt of lipid lowering therapy (adjusted odds ratio (OR)=0.43, 95% confidence interval (C.I.) 0.28–0.67) as compared with HIV-uninfected veterans. Among HIV-infected veterans, log HIV viral load (adjusted OR=0.57, 95% CI, 0.41–0.81) and HIV-HCV co-infection (adjusted OR=0.31, 95% CI=0.13–0.75) were negatively associated with receipt of lipid lowering therapy. Exposure to HAART was not associated with receipt of lipid lowering therapy.

CONCLUSIONS: Among those who met NCEP/ATP III criteria for lipid lowering therapy, HIV-infected veterans, particularly those with high HIV viral loads and HCV co-infection, were significantly less likely to receive lipid

lowering therapy. This may be a modifiable mediator of cardiovascular disease among HIV-infected individuals.

KEY WORDS: HIV; cholesterol; hepatitis C; men; veterans; cardiovascular diseases.

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INTRODUCTION

Recent studies suggest that people with HIV infection have higher rates of acute myocardial infarction and increased risk of ischemic heart disease than those who are not infected.^{1,2} Exposure to combination antiretroviral therapy (CART), particularly protease inhibitors, is associated with an increased risk of dyslipidemia^{3,4} as well as myocardial infarctions.^{5,6} Among those not infected with HIV, the National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP III) has clear guidelines for the receipt of lipid lowering therapy among high risk individuals.⁷ Among those infected with HIV, current guidelines also support the use of lipid lowering therapy.^{8,9} Implementing these recommendations, however, may be more difficult among those with HIV infection. Lipid lowering therapy can lead to elevations in liver transaminases, which may already be high among those with HIV infection due to alcohol and hepatitis C related liver disease¹⁰ and toxicity from antiretroviral therapy. However, lipid lowering therapy may be particularly important for two reasons. First, because of the increased risk of coronary heart disease (CHD, e.g., myocardial infarctions) associated with HIV,^{11–13} and second because of the possible increased risk among those with high HIV viral loads or co-infected with HCV.^{14,15}

The following are the objectives of this study: to determine whether the receipt of lipid lowering therapy is lower among men infected with HIV compared with men not infected who met NCEP/ATP III criteria for receipt of lipid lowering therapy and to determine if the receipt of lipid lowering therapy is less likely among those with elevated HIV viral load or hepatitis C infection.

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METHODS

Participants

The Veterans Aging Cohort Five-Site Study (VACS 5) is an ongoing prospective study of HIV-infected patients and similar age, race/ethnicity, and clinical site HIV-uninfected patients receiving care in general medical clinics.¹⁶ Participants were enrolled during 2001–2002 from the outpatient infectious disease (HIV infected) and General Medical (uninfected) clinics at five US Veterans Affairs (VA) Medical Centers. All consecutive HIV-infected patients in care were eligible to participate. The enrollment protocol has been summarized in detail.¹⁰ In brief, the VA has designated that HIV-infected veterans should receive primary care in the infectious disease clinic. All HIV-infected veterans being seen in these clinics were eligible. HIV negative controls were identified in the general medical clinic based upon their age, race, and site. Refusal rates were low (9%) in both clinics and this proportion did not vary by HIV status.¹⁰ The enrolled HIV-infected patients represent 49% of all HIV-infected patients seen at five Veterans Administration (VA) healthcare facilities in the United States, including: Atlanta, GA; Bronx, NY; Houston, TX; Los Angeles, CA; and, Manhattan, NY. The institutional review boards at all locations approved the study, and all participants provided written informed consent. The study is more fully described elsewhere.¹⁶

Of 1,771 veteran participants in VACS5 who were eligible for the present study, 42 women were excluded due to small numbers and 152 men (9%) because complete cholesterol data within 1 year prior to their baseline survey was not available. Of note, participants who were missing cholesterol data were younger (48.6 vs. 52.2 years, $p < 0.0001$) and more likely to be black (11% vs. 6.6%, $p = 0.001$) than those with complete data. The percentage of missing cholesterol data among HIV-infected veterans and HIV-uninfected veterans was 8.9% and 8.7%, respectively. ($p = 0.9$).

At study entry, all subjects completed a self-administered questionnaire, including information on demographic characteristics,¹⁷ height and weight,¹⁷ screening for substance abuse including alcohol consumption using the Alcohol Use Disorders Identification Test (AUDIT),¹⁸ drug use,¹⁹ and current cigarette smoking, quality of life, symptoms, and prescription adherence.^{17,20,21} We also collected data on diagnoses, including treatment for alcohol disorders, and procedures using ICD-9 codes,¹⁰ prescription medications from pharmacy records, and laboratory data (e.g. serum lipids, serum transaminase levels, HIV viral load, and CD4 cell counts) from the VA electronic medical record system (questionnaires and ICD-9 coding are available at <http://www.vacohort.org>). CHD and CHD equivalents were based on National Cholesterol Education Program Adult Treatment Panel (NCEP/ATP III) Guidelines.⁷ We identified CHD using ICD-9 codes in the electronic medical record and defined it as one of the following conditions or treatment procedures prior to study entry: ischemic heart disease (ICD-9 CM 410.0 to 414.9), coronary artery bypass graft status (V45.81), or percutaneous angioplasty status (V45.82). Similarly, CHD risk equivalents were defined using ICD-9 codes: cerebrovascular disease (436–438), peripheral arterial disease (443.9), and abdominal aortic aneurysm (441.4). Diabetes mellitus was defined as having received glucose-lowering agents including insulin and/or oral hypoglycemic agents (glyburide, glipizide, chlorpromamide, metfor-

min, pioglitazone, troglitazone, and acarbose), or having a hemoglobin A1-C greater than or equal to 6.4 mg/dL, in the year prior to study entry.²²

CHD Risk Factors Based on NCEP/ATP III Guidelines⁷

We defined CHD risk factors as: (1) age over 45 years at time of study entry; (2) current cigarette smoking, defined as a yes response, “Do you now smoke cigarettes (i.e., within the last week)?” (3) hypertension as a yes response to the question, “Has a doctor ever told you that you had hypertension or high blood pressure” or ICD-9 code for hypertension; and (4) low plasma high density lipoprotein (HDL)-cholesterol level as < 40 mg/dL. Of note, we selected for analysis the highest cholesterol values on each subject retrieved from laboratory records including total cholesterol, HDL, low-density lipoprotein (LDL)-cholesterol, and serum triglycerides within the year prior to study entry. We selected values up to 1 year within study entry because cholesterol screening is only recommended every 5 years unless a high cholesterol value is identified and then it is only recommended yearly unless other circumstances are present. Thus we felt checking within 1 year of the start date of the VACS best approximated the recommendations for cholesterol screening guidelines.

Criteria for the Receipt of Lipid Lowering Therapy

To determining which participants met criteria for lipid lowering therapy, we used the NCEP/ATP III risk factor criteria guidelines.⁷ Participants met criteria for lipid lowering therapy if they had: 1) CHD or CHD risk equivalent (i.e., cerebrovascular disease, peripheral arterial disease, abdominal aortic aneurysm, or diabetes) and LDL-cholesterol > 130 mg/dL; 2.) no CHD but 2 or more CHD risk factors and an LDL-cholesterol > 160 mg/dL, or 3) no CHD but 0 or 1 CHD risk factor and an LDL-cholesterol > 190 mg/dL.

Receipt of lipid lowering therapy was defined as receipt of one of the following cholesterol medications within one year after study entry as recorded within the VA pharmacy benefits management system: HMG CoA reductase inhibitors, (i.e. atorvastatin, lovastatin, pravastatin, and simvastatin, these were all the formulary “statin” medications available); niacin; and/or cholestyramine.

Additional Covariates

Race/ethnicity was categorized as white, black, Latino, or other based on self-report. Treatment sites were defined as the outpatient Infectious Disease (HIV-infected) and General Medical (HIV-uninfected) clinics from the five US Veterans Affairs (VA) Medical Centers. We defined hepatitis C infection (HCV) as any positive antibody test prior to survey; hepatitis B infection (HBV) as an ICD-9 code for this diagnosis; elevated liver function tests as one or more serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) values (IU/L) greater than two times the upper limit of normal in the year prior to survey; self-reported non-alcoholic substance use (e.g., cannabis, hallucinogens, opiates, cocaine); and body mass index (BMI) as self-reported weight in kilograms divided by self-reported height in meters squared. Laboratory data also

included HIV-specific measurements, including CD4 cell counts (per μL), HIV viral load (copies/mL). Pharmacy data from the VA involving combination antiretroviral therapy, defined as taking concurrently three or more antiretroviral medication, were collected for the one-year period prior to the survey.

Statistical Analysis

We compared patient characteristics and outcomes between HIV-infected and HIV-uninfected participants using t-tests and Wilcoxon signed rank tests. To assess the association between HIV status and receipt of lipid lowering therapy we used multivariable logistic regression while adjusting for potential confounders. Generalized estimating equations (GEE)²³ were used to account for patient clustering by site. Due to the expected covariance between hepatitis C infection and elevated liver function tests, we also checked a model in which all the same variables were included except hepatitis C. To ensure that prevalent CHD was not primarily responsible for differences in lipid lowering therapy by HIV status, secondary analyses were performed excluding all participants with prevalent CHD. All analyses were done using SAS v 9.1.3 (SAS, Inc., Cary, North Carolina).

RESULTS

Compared with those not infected with HIV, HIV-infected veterans were younger and more likely to be black (Table 1). Uninfected veterans were more likely to be obese than infected individuals. HIV-infected veterans were more likely to have a diagnosis of alcohol abuse or dependence, non-alcoholic substance use, hepatitis B and C infection, and elevated liver function tests.

HIV-infected veterans had a lower prevalence of CHD (5.3% vs. 17.4%) and CHD or CHD risk equivalents (39.7% vs. 46.4%, $p < 0.01$ for all, respectively) as compared with HIV-uninfected participants. While there was no significant difference in total or HDL cholesterol levels between the two groups, uninfected veterans had higher LDL cholesterol (133.5 mg/dL vs. 126.0 mg/dL) and a higher prevalence of hypertension (58.5% vs. 36.1%), while those infected with HIV had higher serum triglyceride levels (305.3 mg/dL vs. 225.8 mg/dL) and a higher prevalence of current smoking (45.1% vs. 35.0%, respectively, $p < 0.01$ for all).

The receipt of lipid lower therapy was less common among HIV-infected veterans compared to HIV-uninfected veterans (Table 2, 15.4% vs. 37.9%, respectively, $p < 0.01$). Although nearly a third of HIV-infected (27.8%) and uninfected veterans (33.6%) met criteria for receipt of lipid lowering therapy, only 39.3% of the eligible HIV-infected veterans received therapy whereas nearly two thirds (61.6%) of the uninfected veterans received lipid lowering therapy ($p < 0.01$). Moreover, of the 84.6% of HIV-infected participants not receiving lipid lowering therapy, 35.6% had CHD or a CHD risk equivalent and 61.7% had 2 or more CHD risk factors (Table 2). Among the HIV-infected veterans, the majority received either pravastatin (56.7%) or simvastatin (31.5%) whereas among the uninfected veterans 80.2% received simvastatin and 17.8% received lovastatin.

Table 1. Demographic and Clinical Characteristics by HIV Status

	HIV-infected n=926	HIV-uninfected n=651	p
Age			
Mean $\pm$ SD	49.7 $\pm$ 8.8 years	55.8 $\pm$ 9.9 years	<0.01
Median (min., max.)	49.8 (27.1, 81.1)	54.8 (23.9, 84.6)	<0.01
Race/Ethnicity (%)			
White	27.9	37.4	<0.01
Black	53.5	43.4	
Latino	11.7	11.9	
Other	6.6	7.0	
Comorbid diagnoses and conditions (%)			
Obesity (BMI $\geq$ 30)	15.7	41.4	<0.01
Alcohol abuse or dependence	23.6	17.9	<0.01
Hepatitis C infection	26.1	10.1	<0.01
Hepatitis B infection	6.3	1.0	<0.01
Elevated liver function tests*	42.7	13.1	<0.01
Non-alcoholic substance abuse	30.1	14.4	<0.01
Site (%)			
A	18.2	29.6	<0.01
B	22.8	13.0	
C	29.4	23.7	
D	13.5	15.4	
E	15.8	18.0	
Status of HIV infection			
Mean CD4 count/mm ³ (+/- 1 SD)	411.5 (270.8)		—
Log HIV RNA (copies/mL) (+/- 1 SD)	3.0 (1.3)		—
Current antiretroviral therapy use (%)	80.1		—
Combined antiretroviral therapy (CART, %)	67.5		

* Elevated liver function tests: AST or ALT > 2 times upper limit of normal

Among those veterans who met criteria for lipid lowering therapy, HIV-infected veterans and HCV infected veterans had a significantly lower prevalence for the receipt of lipid lowering therapy (odds ratio (OR)=0.43, 95% confidence interval (C.I.) 0.28–0.67 and OR=0.46, 95% CI=0.24–0.88, respectively) even after adjusting for potential confounders as compared with uninfected veterans (Table 3). Among HIV-infected veterans, log HIV viral load and HCV infection were both significantly associated with a lower prevalence for the receipt of lipid lowering therapy (OR=0.57, 95% CI=0.41–0.81 and OR=0.31, 95% CI=0.13–0.75, respectively) after adjusting for potential confounders (Table 4). Among those veterans who met criteria for lipid lowering therapy and did not have prevalent CHD, the lower odds ratio for the receipt of lipid lowering therapy among HIV-infected veterans and HIV-HCV co-infected veterans persisted (adjusted OR=0.40, 95% CI=0.19–0.86, and adjusted OR=0.38, 95% CI=0.23–0.64, respectively) as compared with uninfected veterans and those infected only with HIV.

DISCUSSION

Among a cohort of male HIV-infected and similar age, race and clinical site HIV-uninfected veterans who met NCEP/ATP III criteria for receiving lipid lowering therapy, HIV infection and

Table 2. Prevalence of CHD, CHD Risk Factors, Lipid Profiles, by HIV Infection and Receipt of Lipid Lowering Therapy Status

	HIV-infected		HIV-uninfected	
	Currently receiving lipid lower therapy N=143	Not currently receiving lipid lowering therapy N=783	Currently receiving lipid lower therapy N=247	Not currently receiving lipid lowering therapy N=404
CHD and CHD risk equivalents (%)				
Coronary artery disease	16.8	3.2	30.8	9.2
Cerebrovascular disease	4.2	1.5	2.8	1.7
Diabetes mellitus	51.0	33.1	56.3	26.5
Peripheral vascular disease	3.5	1.5	6.1	2.7
Abdominal aortic aneurysm	0.7	—	0.4	—
CHD or CHD risk equivalent*	62.2	35.6	69.2	32.4
CHD risk factor (%)				
Age over 45 years	86.7	68.3	93.2	84.4
Cigarette smoking, current	37.1	46.6	33.1	36.1
Hypertension	53.8	32.8	72.9	49.8
Low HDL cholesterol	25.9	37.9	30.0	35.1
LDL is greater than target value	70.6	19.9	54.7	20.8
Lipid profile (mmol/L, mean $\pm$ SD)				
Total cholesterol	14.8 $\pm$ 2.9	11.0 $\pm$ 2.7	12.4 $\pm$ 2.3	11.1 $\pm$ 2.2
LDL-cholesterol	9.1 $\pm$ 2.4	6.6 $\pm$ 2.2	8.0 $\pm$ 2.0	7.1 $\pm$ 2.0
HDL-cholesterol	2.7 $\pm$ 0.8	2.5 $\pm$ 0.8	2.6 $\pm$ 0.6	2.6 $\pm$ 0.7
Triglycerides	26.4 $\pm$ 17.0	15.2 $\pm$ 12.3	14.5 $\pm$ 8.8	11.3 $\pm$ 9.8
Number of CHD risk factors (%)				
0	2.7	10.2	1.6	5.7
1	23.7	28.1	13.0	27.0
2	41.9	36.5	46.2	37.1
3	26.6	21.6	30.4	24.3
4	4.9	3.6	8.9	5.9

* (Coronary heart disease (CHD) or CHD risk equivalent was defined as coronary heart disease, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, cerebrovascular disease, peripheral artery disease, abdominal aortic aneurysm, or diabetes)

HCV infection were significantly associated with a lower receipt of lipid lowering therapy even after adjusting for multiple potential confounders. Among HIV-infected veterans, a high HIV viral load and HCV were also associated with a lower

receipt of lipid lowering therapy after adjusting for confounders. The association between HIV, HIV-HCV co-infection and receipt of lipid lowering therapy persisted even when participants with CHD were excluded from the analyses.

Table 3. The Association between the Receipt of Lipid Lowering Therapy and HIV Status Among VACS Participants

Characteristics	Percentage receiving lipid lower therapy (%)	Unadjusted odds ratio (95% C.I.) for receipt of lipid lowering therapy N=476	Adjusted odds ratio (95% C.I.) for receipt of lipid lowering therapy* N=476
HIV infection (yes)	39.3	0.40 (0.28–0.58)	0.43 (0.28–0.67)
HIV infection (no)	61.6	1 (referent)	1 (referent)
Age (continuous in yrs)	49.6	1.05 (1.02–1.07)	1.03 (1.01–1.06)
Ethnicity			
White	54.1	1 (referent)	1 (referent)
Black	48.9	0.81 (0.54–1.22)	1.07 (0.68–1.67)
Hispanic	46.4	0.73 (0.40–1.35)	1.09 (0.54–2.23)
Other	38.2	0.52 (0.25–1.12)	0.57 (0.23–1.38)
Obesity (BMI $\geq$ 30)	53.3	1.26 (0.86–1.83)	0.94 (0.62–1.43)
Alcohol abuse or dependence	44.8	0.79 (0.50–1.23)	0.90 (0.49–1.67)
Hepatitis C infection	29.5	0.38 (0.21–0.68)	0.46 (0.24–0.88)
Hepatitis B infection	50.0	1.02 (0.25–4.12)	1.25 (0.3–5.3)
Elevated liver function tests	45.2	0.79 (0.52–1.19)	1.28 (0.79–2.06)
Substance abuse, not including alcohol or cigarette smoking	39.6	0.61 (0.38–0.96)	0.86 (0.45–1.63)
CHD risk group (compared with low risk 0–1 risk factor)	34.2	1 (referent)	1 (referent)
High (CHD or CHD risk equivalent)	54.4	2.29 (1.13–4.63)	1.76 (0.81–3.86)
Intermediate (No CHD, >2 risk factors)	40.0	1.28 (0.59–2.78)	0.94 (0.41–2.19)
Treatment site (compared to E) †	51.6	1 (referent)	1 (referent)
A	57.6	1.28 (0.59–2.78)	1.32 (0.70–2.51)
B	41.2	0.66 (0.37–1.16)	0.60 (0.31–1.15)
C	46.3	0.81 (0.47–1.40)	0.74 (0.41–1.34)
D	52.4	1.04 (0.58–1.87)	1.09 (0.57–2.07)

*Analyses adjust for all covariates simultaneously in the model for all participants who met criteria for lipid lowering therapy (n=476)

†Generalized estimating equation (GEE) analysis clustered on site of care

Table 4. The Association between the Receipt of Lipid Lowering Therapy and Hepatitis C Status Among HIV-infected VACS Participants

Characteristics	Percentage receiving lipid lower therapy	Unadjusted odds ratio (95% C.I.) for receipt of lipid lowering therapy N=257	Adjusted odds ratio (95% C.I.) for receipt of lipid lowering therapy* N=257
HCV infection (yes)	24.5	0.42 (0.21–0.88)	0.31 (0.13–0.75)
HCV infection (no)	42.8	1 (referent)	1 (referent)
Age (continuous in yrs)	39.3	1.06 (1.02–1.09)	1.07 (1.03–1.11)
Ethnicity			
White	39.5	1 (referent)	1 (referent)
Black	38.0	0.94 (0.53–1.66)	1.58 (0.82–3.03)
Hispanic	41.4	1.08 (0.46–2.56)	2.19 (0.68–7.04)
Other	44.4	1.23 (0.44–3.43)	1.95 (0.66–5.74)
Obesity (BMI ≥ 30)	32.1	0.67 (0.36–1.26)	0.56 (0.26–1.22)
Alcohol abuse or dependence	34.7	0.78 (0.41–1.50)	1.27 (0.52–3.08)
Hepatitis B infection	50.0	1.56 (0.31–7.89)	1.60 (0.38–6.69)
Elevated liver function tests	42.3	1.22 (0.27–1.90)	1.76 (0.93–3.33)
Substance abuse, not including alcohol or cigarette smoking	31.7	0.65 (0.35–1.20)	0.87 (0.36–2.09)
CHD risk group (compared with low risk 0–1 risk factor)	38.5	1 (referent)	1 (referent)
High (CHD or CHD risk equivalent)	42.0	1.16 (0.50–2.70)	0.99 (0.39–2.49)
Intermediate (No CHD, >2 risk factors)	30.9	0.72 (0.27–1.90)	0.60 (0.21–1.70)
Treatment site (compared to E) †	33.3	1 (referent)	1 (referent)
A	47.4	1.8 (0.82–3.93)	2.28 (0.90–5.74)
B	36.4	1.14 (0.49–2.66)	0.74 (0.27–2.01)
C	29.1	0.82 (0.36–1.87)	0.66 (0.25–1.69)
D	50.0	2 (0.90–4.47)	1.96 (0.78–4.90)
Serum CD4 levels in cells/mm ³ (continuous)	39.3	1 (1.00–1.00)	1 (1.00–1.00)
Log viral load units (continuous)	39.3	0.66 (0.51–0.86)	0.57 (0.41–0.81)
Using combined antiretroviral therapy	39.4	1.03 (0.54–1.95)	0.79 (0.34–1.82)

*Analyses adjust for all covariates simultaneously in the model for all participants who met criteria for lipid lowering therapy (n=476)

†Generalized estimating equation (GEE) analysis clustered on site of care

While primary²⁴ and secondary prevention trials²⁵ report a reduction in cardiovascular risk among those treated with lipid lowering therapy who are not infected with HIV, no such data exist among those infected with HIV. Nevertheless, current guidelines recommend the use of lipid lowering therapy because of the dyslipidemia associated with combination antiretroviral therapy.^{26,27} As presented elsewhere,²⁸ our study concluded that the receipt of lipid lowering therapy was low among those infected with HIV, including those with and without prevalent CHD.

The lower rates of lipid lowering therapy observed among HIV-infected veterans, particularly those with higher viral loads or hepatitis C, may have important implications on the risk of future cardiovascular events. Recent studies involving both HIV-infected and uninfected controls^{1,2} as well as previous studies from a large health maintenance organization²⁹ suggest that the rates of incident cardiovascular disease events are higher among HIV-infected people as compared with HIV-uninfected people. Whether the increased cardiovascular risk is a function of dyslipidemia associated with antiretroviral therapy is not entirely clear, but the increased risk of cardiovascular disease appears to occur following the initiation of antiretroviral therapy.^{2,5} Based on results from the SMART study, a non suppressed HIV viral load appears to be an independent predictor of increased CHD risk.³⁰ Similarly, among those who are co-infected with HCV, several studies suggest that HCV may be associated with an increased risk of subclinical^{31,32} or clinical atherosclerosis³³ and HIV-HCV co-infection may be associated with an increased risk of cardiovascular disease.¹⁴ Whether less aggressive lipid management contributes to the increased risk of CHD among HIV-infected

people, particularly those with higher viral loads or co-infection with hepatitis C, is not known.

The disparity in receipt of lipid lowering therapy between HIV-infected and similar uninfected veterans suggests that prescribing of lipid lowering therapy may play an important role in CVD risk among those infected with HIV. These data do not provide a clear rationale for this disparity. Possible explanations include a 'learning curve' in terms of implementing cholesterol treatment guidelines among those infected with HIV combined with the high prevalence of liver disease (i.e., hepatitis C) among those infected with HIV. In this study, clinics associated with lower receipts of lipid lowering therapy also had the highest prevalence of hepatitis C. The potential drug-drug interactions between antiretroviral therapy (ART) and lipid lowering medications may also be partially responsible. In the present study, ART was associated with a lower, but not significant, reduction in the receipt of lipid lowering therapy. Alternatively, HIV providers may be aware of the guidelines for management of dyslipidemia but have adopted the accepted 'switch the offending drug' as initial management of dyslipidemia.

The present study has several limitations that warrant comment. First, since our population consisted entirely of male veterans, our results may not be generalizable to women or people outside the Veterans Administration Healthcare System (VAHS). Second, there is the possibility of non-differential misclassification due to participants receiving lipid lowering therapy outside of the VAHS, however, as medications are free or at minimal charge for veterans who are actively receiving care within VAHS clinics, we expect this misclassification to be small. Third, because the NCEP/ATP III guidelines

focus on LDL cholesterol, we did not include data on gemfibrozil or other medications used in the treatment of hypertriglyceridemia, a common consequence of some antiretroviral therapy. Fourth, the use of ICD-9 codes, which have been validated by others,¹⁰ may have resulted in some misclassification, however, we do not expect this misclassification to be differential. Fifth, as we only had HCV antibody testing, and not viral RNA, we could not account for those individuals who might have had their HCV spontaneously resolve.³⁴ Sixth, there is always the possibility of misclassification of HIV status (i.e., HIV-uninfected participants were actually HIV-infected). However, the likelihood is that this misclassification would only have strengthened the present associations. Other results are possible although not likely. Seventh, as these data were collected in 2001–2002, it is possible that the use of lipid lowering therapy by providers has increased in response to the emergence of CHD in the HIV population. However, the impediments to lipid lowering therapy in the HIV population (e.g., liver disease, HCV, alcohol use) still presently exist. Eighth, we selected the highest cholesterol value when assessing the receipt of lipid lowering therapy. It is possible that some participants may not have been fasting for those levels, but we do not expect this potential misclassification to be differential. Ninth, as a secondary data analysis, we did not have information on the providers' assessment of the risks and benefits to the patients associated with lipid lowering agents. Lastly, we cannot comment on whether the rates of lipid lowering therapy observed among the HIV-infected veterans are similar to other HIV-infected people who received their care outside the Veterans Affairs Health Care system. However, prior studies have reported that the rates for the receipt of cholesterol screening³⁵ and the level (i.e., quality) of care for hyperlipidemia³⁶ among people receiving their care at Veteran Affairs Medical Centers was higher as compared with nationally representative samples of people receiving care outside the Veteran Affairs Health Care system. Thus we expect our estimated rates to be at least as high as those observed outside the VA system.

In conclusion, we observed that the receipt of lipid lowering therapy among veterans infected with HIV, especially those with high HIV viral loads or co-infected with HCV, was significantly lower as compared with veterans without HIV. This finding, if confirmed in other studies, suggests an important modifiable risk factor for CHD among those with HIV and/or HCV infection.

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