Underutilization of Aspirin for Primary Prevention of Cardiovascular Disease Among HIV-Infected Patients

Greer A. Burkholder,[1] Ashutosh R. Tamhane,[2] Jorge L. Salinas,[3] Michael J. Mugavero,[1] James L. Raper,[1] Andrew O. Westfall,[2] Michael S. Saag,[1] and James H. Willig[1]

[1]Division of Infectious Diseases, [2]Department of Biostatistics, and [3]Department of Medicine, University of Alabama at Birmingham

Background. Individuals infected with human immunodeficiency virus (HIV) are at increased risk for cardiovascular disease (CVD) events compared with uninfected persons. However, little is known about HIV provider practices regarding aspirin (ASA) for primary prevention of CVD.

Methods. A cross-sectional study was conducted among patients attending the University of Alabama at Birmingham 1917 HIV Clinic during 2010 to determine the proportion receiving ASA for primary prevention of CVD and identify factors associated with ASA prescription. Ten-year risk for CVD events was calculated for men aged 45–79 and women aged 55–79. The 2009 US Preventive Services Task Force (USPSTF) guidelines were used to determine those qualifying for primary CVD prevention.

Results. Among 397 patients who qualified to receive ASA (mean age, 52.2 years, 94% male, 36% African American), only 66 (17%) were prescribed ASA. In multivariable logistic regression analysis, diabetes mellitus (odds ratio [OR], 2.60; 95% confidence interval [CI], 1.28–5.27), hyperlipidemia (OR, 3.42; 95% CI, 1.55–7.56), and current smoking (OR, 1.87; 95% CI, 1.03–3.41) were significantly associated with ASA prescription. Odds of ASA prescription more than doubled for each additional CVD-related comorbidity present among hypertension, diabetes, hyperlipidemia, and smoking (OR, 2.13, 95% CI, 1.51–2.99).

Conclusions. In this HIV-infected cohort, fewer than 1 in 5 patients in need received ASA for primary CVD prevention. Escalating likelihood of ASA prescription with increasing CVD-related comorbidity count suggests that providers may be influenced more by co-occurrence of these diagnoses than by USPSTF guidelines. In the absence of HIV-specific guidelines, interventions to improve HIV provider awareness of and adherence to existing general population guidelines on CVD risk reduction are needed.

Because of widespread availability of potent combination antiretroviral therapy (ART), the life expectancy of individuals infected with the human immunodeficiency virus (HIV) has significantly improved in developed countries [1]. As a result, more than half of HIV-infected patients in the United States are expected to be >50 years of age by 2015 [2]. Recent large cohort studies of HIV-infected patients have shown that morbidity and mortality due to non-AIDS-related events has surpassed that due to AIDS-related events in developed countries, with 6%–15% of deaths attributed to cardiovascular disease (CVD) [3–7]. HIV-infected patients appear to have an increased risk of coronary heart disease (CHD) and myocardial infarction (MI) compared with uninfected controls [8–11], and also have higher prevalence of subclinical atherosclerosis [12]. As age is an independent risk factor for CVD-related events (MI, ischemic stroke) [13, 14], we can expect temporal increases in incidence of these events as the HIV-infected population ages.

Received 15 June 2012; accepted 23 August 2012.; electronically published 31 August 2012.

Presented in part: Infectious Diseases Society of America 49th Annual Meeting, Boston, Massachusetts, 20–23 October 2011. Poster 480.

Correspondence: Greer A. Burkholder, MD, Division of Infectious Diseases, University of Alabama at Birmingham, BBRB 220D, 845 19th St S, Birmingham, AL 35294 (gburkhol@uab.edu).

Clinical Infectious Diseases 2012;55(11):1550–7

DOI: 10.1093/cid/cis752

Despite heightened awareness regarding elevated CVD risk among HIV-infected patients [15], little is known about HIV provider practices regarding the use of aspirin (ASA) for primary prevention of CVD events (ie, prevention of first MI or ischemic stroke). Owing to the absence of HIV-specific guidelines, recommendations targeted toward the general population provide the only guidance regarding HIV-infected patients qualifying for ASA for primary prevention. The 2009 United States Preventive Services Task Force (USPSTF) guidelines recommend use of ASA for primary prevention of MIs in men aged 45–79 years and ischemic strokes in women aged 55–79 years when the potential CVD benefit (events prevented) outweighs the risk of gastrointestinal hemorrhage [16]. Qualification for ASA is based on the age-stratified 10-year coronary heart disease (CHD) risk score for men (http://www.framinghamheartstudy.org/risk/coronary.html) and the 10-year stroke risk score for women (http://www.framinghamheartstudy.org/risk/stroke.html).

Because of the increasing importance of CVD risk assessment and prevention among HIV-infected patients successfully treated with ART, we conducted a cross-sectional study among patients attending a large university-based outpatient HIV clinic to assess the proportion of qualifying patients prescribed ASA for primary prevention per the USPSTF guidelines, and to examine associations of clinical, sociodemographic, and psychosocial factors with ASA prescription.

METHODS

Study Setting

The University of Alabama at Birmingham (UAB) 1917 Clinic Cohort is an ongoing prospective HIV clinical cohort protocol established in 1992 that has been well-described elsewhere (www.uab1917cliniccohort.org) [17, 18]. Our electronic database captures detailed clinical, sociodemographic, and psychosocial information on all patients receiving care at the UAB 1917 HIV/AIDS Clinic (1917 Clinic), currently including >2000 active patients. The electronic health record (EHR) and database are 100% quality controlled, with all provider notes reviewed within 72 hours of entry to ensure proper data capture regarding changes in diagnoses, allergies, and medications. In April 2008, electronic capture of patient-reported outcomes (PROs) using standardized, validated questionnaires was added to provide further systematic data capture of psychosocial variables including tobacco, alcohol, substance use, and depression [19]. HIV primary care is provided by a mix of 7 infectious diseases (ID) fellows who each have clinic once a week and 3 full-time nurse practitioners, supervised by 14 ID attending physicians. This study was approved by the UAB Institutional Review Board.

Eligibility Criteria

All HIV-infected men aged 45–79 years and HIV-infected women aged 55–79 years attending the 1917 Clinic with (1) at least 1 primary HIV provider visit between 11 December 2009 and 10 December 2010 (active patients) and (2) at least 1 primary HIV provider visit between 11 December 2008 and 10 December 2009 (established patients) were eligible for inclusion (Figure 1). New clinic patients initiating care between December 2009–2010 were excluded because the initial care of these patients typically focuses heavily on HIV and antiretroviral management. By limiting our sample to established clinic patients, we aimed to allow providers sufficient time to address non-HIV-related issues, such as ASA prescription for primary CVD prevention. Age criteria were based on the 2009 USPSTF recommendations on Aspirin for the Prevention of Cardiovascular Disease [16].

Patients with known history of CVD were excluded, as they would qualify for secondary rather than primary prevention with ASA. CVD-defining diagnoses were abdominal aortic aneurysm, acute coronary syndrome, angina pectoris,

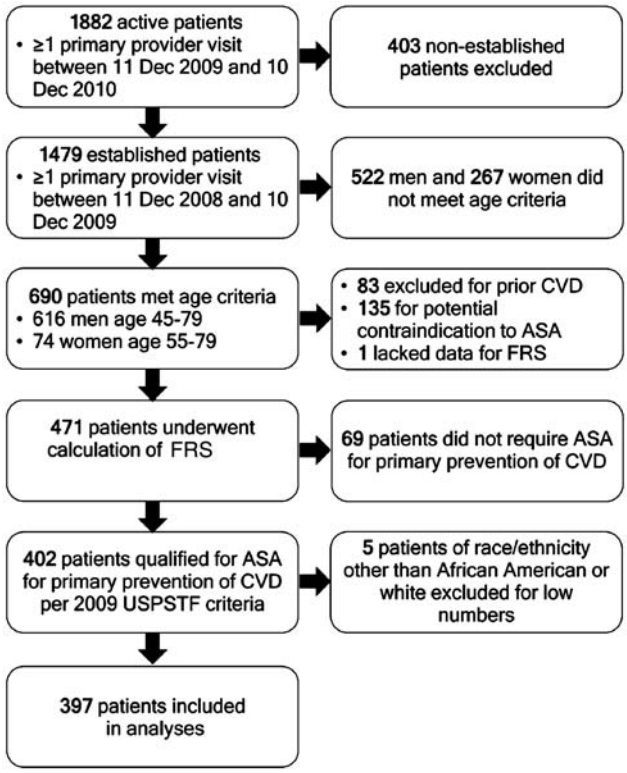

Figure 1. Flow diagram of participant selection of human immunodeficiency virus (HIV)–infected patients qualifying for primary prevention of cardiovascular disease events with aspirin at the University of Alabama at Birmingham 1917 HIV Clinic. Abbreviations: ASA, aspirin; CVD, cardiovascular disease; FRS, Framingham Risk Score; USPSTF, United States Preventive Services Task Force.

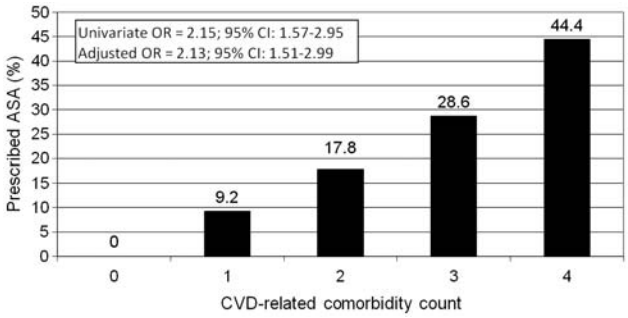

Figure 2. Increasing odds of aspirin (ASA) prescription with increasing cardiovascular disease (CVD)–related comorbidity count[a] in human immunodeficiency virus (HIV)–infected patients (N = 397) at the University of Alabama at Birmingham 1917 HIV Clinic meeting 2009 United States Preventive Services Task Force criteria [16] for ASA for primary prevention of CVD events. Abbreviations: ASA, aspirin; CI, confidence interval; CVD, cardiovascular disease; OR, odds ratio. [a]Includes diabetes mellitus, hypertension, hyperlipidemia, and current smoking.

angioplasty, arterial disease, carotid endarterectomy, carotid artery stenosis, cerebrovascular accident or disease, claudication, coronary artery bypass graft, coronary artery disease, heart disease not otherwise specified, ischemic heart disease, myocardial infarction, femoral artery bypass, percutaneous transluminal coronary angioplasty, peripheral vascular disease, stroke, transient ischemic attack, and unstable angina.

Patients with a potential contraindication to ASA were also excluded. These contraindications included any history of upper or lower gastrointestinal bleeding, gastric or duodenal ulcer, intracranial bleeding, bleeding diathesis, or discontinuation of any nonsteroidal anti-inflammatory drug (NSAID) including ASA for allergy, adverse event, or side effects. Other contraindications were diagnoses indicating upper gastrointestinal pain on a patient's active problem list; current treatment with antiplatelet agents or NSAIDs other than ASA, or with an anticoagulant; or most recent platelet measurement of $<60 \times 10^3/\mu L$.

Sources of Data

Sociodemographic information, co-occurring medical diagnoses, medications, vital signs, and clinically relevant laboratory results were obtained by query (MS SQL) of the UAB 1917 Clinic Cohort electronic database. Data regarding psychosocial variables was obtained from PROs. Patients complete computerized, standardized questionnaires approximately every 6 months to assess alcohol use (Alcohol Use Disorders Identification Test–Consumption [AUDIT-C]), substance use (Alcohol, Smoking, and Substance Involvement Screening Test [ASSIST]), and depression (Patient Health Questionnaire–9 [PHQ-9]) [19]. Tobacco use was drawn from both the PRO tobacco use questionnaire and EHR active problem list. Information on smoking was required to compute CVD risk scores, and in patients lacking a PRO tobacco use questionnaire, EHR tobacco use data were utilized. Each patient's index visit was defined as the most recent nonurgent primary HIV provider visit on or prior to the electronic data extraction date (10 December 2010).

Calculation of CVD Risk

Scores for men were calculated using the Framingham Risk Score (FRS) for 10-year risk of CHD [20]. Factors used in this algorithm included age at the index visit; systolic and diastolic blood pressure as single, nonstandardized measures obtained by electronic sphygmomanometer at the index visit; most recent random total cholesterol and high-density lipoprotein cholesterol values within 12 months of the index visit; and diabetes mellitus (DM) and smoking status. Fasting status for cholesterol measurements was not routinely available. DM was defined as any history of a DM diagnosis or diabetes-related complication, or presence of a medication used to treat DM on a patient's active medication list. Current tobacco use was defined as current cigarette smoking of any amount on most recent PRO tobacco use questionnaire, or if no PRO was available within 12 months of the index visit, a diagnosis indicating tobacco use on the patient's active problem list in the EHR.

Scores for women were calculated using the Framingham 10-year Stroke Risk Score [21]. Factors used in this algorithm included age, systolic blood pressure, and DM and smoking status with ascertainment as indicated above for men. The score also incorporated current antihypertensive medication use, and any history of atrial fibrillation or left ventricular hypertrophy. Routine electrocardiography and echocardiography were not available. Prior history of CVD is a component of the stroke risk score, but patients with known or suspected CVD were excluded from our study as our focus was on primary prevention.

Qualification for ASA for primary prevention of MI in men and ischemic stroke in women was determined using age-stratified 10-year risk scores according to the 2009 USPSTF recommendations [16].

Primary Outcome

The primary outcome was ASA prescription, defined as the presence of oral ASA or combination medication containing ASA at any dose on the active medication list for patients qualifying for primary prevention of CVD on the date of the index visit. UAB 1917 Clinic providers are trained to enter all medications taken by a patient on this list, regardless of whether they are prescribed by our clinic, or obtained from an outside provider or over the counter.

Independent Variables

Independent variables included sociodemographic factors (age, sex, race, and insurance status at index visit); most recent $CD4^+$ cell count and plasma HIV-1 RNA within 12 months prior to the index visit; Framingham Risk Score; CVD risk factors including hypertension (HTN), DM, hyperlipidemia, and current cigarette smoking; CVD-related comorbidity count; body mass index (BMI); current depression; and at-risk alcohol use or substance use. HTN was defined as history of HTN diagnosis or the presence of a medication used to treat HTN on a patient's active medication list. Hyperlipidemia was defined as history of dyslipidemia, familial dysbetalipoproteinemia, hypercholesterolemia, hyperlipidemia, or hypertriglyceridemia, or the presence of a lipid-lowering drug on a patient's active medication list. CVD-related comorbidity count was determined by a patient's total number of diagnoses among DM, HTN, hyperlipidemia, and current smoking, with a range of 0–4.

Statistical Analysis

Continuous variables are reported as mean (SD), and categorical variables are reported as frequencies and percentages. Univariate and multivariable analyses were conducted using logistic regression models producing crude and adjusted odds ratios (ORs) and corresponding 95% confidence intervals (CIs), respectively. Clinically relevant variables determined a priori and included in multivariable analysis regardless of univariate *P* values and parameter estimates were age (years), sex, race/ethnicity, $CD4^+$ cell count (<200 cells/μL, 200–350 cells/μL, >350 cells/μL), BMI (obese [BMI ≥30 kg/m^2] vs non-obese [BMI <30 kg/m^2]), DM, HTN, hyperlipidemia, current cigarette smoking, and length of time in care (years). Multicollinearity was assessed using variance inflation factors and model fit using the Hosmer-Lemeshow goodness-of-fit test. Predictive value of multivariable models was assessed using C-statistics. Statistical significance was set at a 2-sided .05 level. Analyses were performed using SAS statistical software (Cary, North Carolina), version 9.2.

RESULTS

Framingham risk scores were calculated for 471 established patients meeting eligibility criteria. Of these, 402 (85%) met USPSTF criteria to receive ASA for primary prevention of CVD. Only 5 qualifying patients were of race/ethnicity other than African-American or white; they were excluded owing to low numbers. The remaining 397 patients qualifying for ASA were included in the analyses.

Among the 397 qualifying study participants, the mean age (±SD) was 52.2 ± 5.9 years, 36% of the patients were African American, and 94% were male (Table 1). HIV risk group was men who have sex with men in 66%, heterosexual transmission in 23%, and intravenous drug use in 11%. The majority of patients were insured (46% private insurance, 38% public insurance, 16% uninsured). Most patients (96%) were taking antiretroviral drugs, HIV RNA was suppressed (<50 copies/mL) in 60%, and $CD4^+$ cell count was >350 cells/μL in 70%.

Only 66 patients (17%) were prescribed ASA for primary CVD prevention. Notably, half of the 397 patients qualifying for ASA had intermediate to high risk for CVD-related events (10-year risk ≥10%); 39% were current smokers; 16% had DM, 62% HTN, 63% hyperlipidemia, and 20% were obese (BMI ≥30). Of the higher risk patients (10-year risk ≥10%), only 22% were prescribed ASA. No significant clustering of ASA prescription by individual primary HIV provider was observed.

Factors Associated With ASA Prescription

In univariate analysis, HTN, DM, hyperlipidemia, higher CVD-related comorbidity count, higher 10-year risk for CVD events, and longer time in care were significantly associated with increased odds of ASA prescription, whereas CD4 count <200 cells/μL was associated with decreased odds of ASA prescription. Most recent HIV RNA was not significantly associated with ASA prescription. (Table 2) In multivariable logistic regression analysis, factors significantly associated with ASA prescription included DM (OR, 2.60 [95% CI, 1.28–5.27]), hyperlipidemia (OR, 3.42 [95% CI, 1.55–7.56]), and current smoking (OR, 1.87 [95% CI, 1.03–3.41]), while adjusted for age, sex, race/ethnicity, CD4 count, BMI, HTN, and length of time in care. FRS and CVD-related comorbidity count were not included in this model because of collinearity with multiple included variables. In a separate multivariable model (not shown), 10-year CVD risk per FRS was included in place of characteristics impacting the score (age, sex, DM, HTN, hyperlipidemia, and current smoking). For every 5% increase in 10-year CVD risk per FRS, odds of ASA prescription increased by 35% (OR, 1.35 [95% CI, 1.12–1.62]), after adjusting for race/ethnicity, CD4 count, BMI, and length of time in care. An additional multivariable analysis was performed with CVD-related comorbidity count replacing individual comorbidities (data not shown). After adjusting for sex, race/ethnicity, CD4 count, BMI, and length of time in care, odds of ASA prescription more than doubled for each increase in comorbidity count (OR, 2.13 [95% CI, 1.51–2.99]; Figure 2).

DISCUSSION

Our study found that ASA was markedly underprescribed among HIV-infected patients at risk for CVD events. Less than 20% of patients meeting the 2009 USPSTF criteria for ASA for primary prevention of CVD events were prescribed ASA. Even when the focus was narrowed to patients at intermediate to

Table 1. Characteristics of HIV-Infected Patients (N = 397) at the University of Alabama at Birmingham 1917 Clinic Meeting 2009 United States Preventive Services Task Force Criteria [16] for Aspirin for Primary Prevention of Cardiovascular Disease Events

Characteristic	ASA Prescribed (n = 66) No. (%)[a]	ASA Not Prescribed (n = 331) No. (%)[a]	Total (N = 397) No. (%)[a]
Age, years, mean ± SD	53.4 ± 6.0	52.0 ± 5.9	52.2 ± 5.9
Male sex	60 (91)	312 (94)	372 (94)
Race			
White	48 (73)	206 (62)	254 (64)
African-American	18 (27)	125 (38)	143 (36)
HIV risk factor[b]			
IVDU	4 (6)	41 (12)	45 (11)
MSM	43 (65)	218 (66)	261 (66)
Heterosexual	19 (29)	71 (22)	90 (23)
Insured (private/public)	55 (83)	279 (84)	334 (84)
$CD4^+$ count (cells/μL)			
<200	2 (3)	39 (12)	41 (10)
200–350	12 (18)	65 (20)	77 (19)
>350	52 (79)	227 (69)	279 (70)
Plasma HIV-1 RNA <50 copies/mL	36 (55)	202 (61)	238 (60)
On antiretroviral therapy	62 (94)	320 (97)	382 (96)
Obesity (BMI ≥30 kg/m^2)	14 (22)	66 (20)	80 (20)
10-year risk for CVD event[c] ≥10%	43 (65)	157 (47)	200 (50)
Median (IQR) 10-year risk for CVD event, percentage	13 (7–16)	8 (7–13)	10 (7–13)
Hypertension	48 (73)	197 (60)	245 (62)
Diabetes mellitus	21 (32)	41 (12)	62 (16)
Hyperlipidemia	55 (83)	194 (59)	249 (63)
Current smoker	29 (44)	127 (39)	156 (39)
Current substance use[b]	1(2)	26 (9)	27 (8)
At-risk alcohol use[b]	7 (11)	42 (14)	49 (13)
Current depression[b]	9 (14)	44 (14)	53 (14)
Length of time in care, years, mean ± SD	8.4 ± 3.8	7.1 ± 3.8	7.3 ± 3.8
Median No. of visits in prior 12 months (IQR)[d]	2 (2–3)	2 (2–3)	2 (2–3)
Hepatitis C	8 (12)	48 (15)	56 (14)

Abbreviations: ASA, aspirin; BMI, body mass index; CVD, cardiovascular disease; HIV, human immunodeficiency virus; IQR, interquartile range; IVDU, intravenous drug user; MSM, men who have sex with men; SD, standard deviation.

[a] Column percentages.

[b] Missing data: HIV risk factor, 1; BMI, 3; alcohol use (AUDIT-C), 32; substance use (ASSIST), 35; depression score (PHQ-9), 27.

[c] Based on Framingham Risk Score for Coronary Heart Disease in men and Framingham Stroke Risk Score in women.

[d] Nonurgent visits with a HIV primary provider.

high risk for events (10-year risk ≥10%), which constituted 50% of the study sample, only 22% were on ASA.

We evaluated clinical, sociodemographic, and psychosocial characteristics associated with ASA prescription in HIV-infected patients, which have not been addressed in the extant literature. As expected, traditional CVD risk factors (DM, hyperlipidemia, and current smoking) were associated with increased odds of ASA prescription. An interesting observation was the escalating likelihood of ASA prescription with increasing CVD-related comorbidity count. This suggests that provider ASA prescribing patterns may be influenced more by co-occurrence of these diagnoses rather than by FRS and USPSTF guidelines, given that all 397 patients qualified for ASA based on these guidelines yet <20% were receiving it.

A 2005 national survey of primary care physicians, cardiologists, and obstetrician/gynecologists found that physician perception of CVD risk predicted recommendations regarding preventive measures including ASA use, but frequently differed from calculated risk using the FRS [22]. Provider dependence on clinical assessment alone in the absence of a CVD risk score carries the dual hazard of failure to prescribe ASA for patients in whom it is indicated, and unnecessary

Table 2. Factors Associated With Aspirin Prescription Among HIV-Infected Patients at the University of Alabama at Birmingham 1917 Clinic Meeting 2009 United States Preventive Services Task Force Criteria [16] for Aspirin for Primary Prevention of Cardiovascular Disease Events

Characteristic	Unadjusted OR (95% CI) for ASA Prescription[a]	*P* Value	Adjusted OR (95% CI) for ASA Prescription[a,b]	*P* Value
Age (per 10 years)	1.44 (.94–2.19)	.09	1.25 (.75–2.09)	.40
Male sex	0.61 (.23–1.59)	.31	0.58 (.18–1.86)	.36
Race/ethnicity				
White	1.0	…	1.0	…
African American	0.62 (.34–1.11)	.11	0.55 (.27–1.11)	.10
CD4 count (cells/μL)				
>350	1.0	…	1.0	…
200–350	0.81 (.41–1.60)	.54	0.79 (.37–1.66)	.53
<200	**0.22 (.05–.96)**	**.04**	0.34 (.08–1.51)	.16
Obesity (BMI ≥30 kg/m^2)[c]	1.12 (.58–2.15)	.73	0.94 (.45–1.95)	.86
Hypertension	**1.81 (1.01–3.25)**	**.046**	1.39 (.72–2.71)	.33
Diabetes mellitus	**3.30 (1.79–6.09)**	**<.001**	**2.60 (1.28–5.27)**	**.01**
Hyperlipidemia	**3.53 (1.78–6.99)**	**<.001**	**3.42 (1.55–7.56)**	**.002**
Current smoking	1.26 (.74–2.15)	.40	**1.87 (1.03–3.41)**	**.04**
Length of time in care (per year)	**1.10 (1.02–1.18)**	**.02**	1.03 (.95–1.12)	.46
Plasma HIV-1 RNA <50 copies/mL	0.77 (.45–1.31)	.33	…	…
10-year risk for CVD event (per 5% increase)[d,e]	**1.35 (1.13–1.62)**	**.001**	…	…
CVD-related comorbidity count (per increase of 1)[e,f]	**2.15 (1.57–2.95)**	**<.001**	…	…

Bold typeface indicates statistical significance at .05 level.

Abbreviations: ASA, aspirin; BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HIV, human immunodeficiency virus; OR, odds ratio.

[a] Logistic regression.

[b] Clinically relevant factors included in the model (N = 394). Variance inflation factor for all the included factors <3; Hosmer-Lemeshow goodness-of-fit test, *P* = .93; C-statistic = 0.749.

[c] BMI data were missing for n = 3.

[d] Based on Framingham Risk Score for Coronary Heart Disease in men and Framingham Stroke Risk Score in women.

[e] Used in separate analyses not shown on table; discussed in text.

[f] No. of conditions present among diabetes mellitus, hypertension, hyperlipidemia, and current smoking.

prescription of ASA in low-risk patients for whom risk of gastrointestinal bleeding outweighs potential CVD benefit.

The low rate of ASA prescription observed in our study is consistent with findings from the only 2 similar published studies regarding use of antiplatelet therapy for prevention of CVD-related events in HIV-infected patients. One was conducted at Hospital Gandia in Spain, where among 120 consecutive HIV-infected patients, 30.8% qualified for primary prevention of CVD with ASA by the 2009 USPSTF guidelines but only 2 were taking ASA [23]. Another study in Germany found that of HIV-infected patients with 10-year Framingham risk 10%–20%, only 2.4% were receiving antiplatelet therapy, and of those with 10-year risk >20%, only 31.9% were receiving antiplatelet therapy (the authors did not distinguish between antiplatelet therapy for primary and secondary prevention) [24]. These 2 studies point to underprescribing of ASA in settings different than ours, highlighting a widespread need for greater attention among HIV providers on the role of ASA in CVD risk reduction.

Studies in the general population report racial disparities in ASA use, with whites more likely to use ASA for primary prevention of CVD-related events than African-Americans [25–27]. However, we noted no difference in ASA prescription between whites and African-Americans. We expected to see lower likelihood of ASA prescription in patients with more advanced HIV ($CD4^+$ cell count <200 cells/μL), presuming providers would be more focused on HIV management than on general health maintenance issues like CVD risk reduction. Although $CD4^+$ cell count <200 cells/μL was significantly associated with lower odds of ASA prescription in univariate analysis, this association was not present in our multivariable model, potentially due to sample size. The absence of clustering of ASA prescribing by individual provider in our study suggests underutilization of ASA is a systemic problem, rather than a matter of deficiencies in the practice of select providers. The reasons behind low utilization of ASA for primary prevention of CVD by HIV providers is likely multifactorial. HIV providers may be unfamiliar with general population

guidelines and recommendations. Of note, there is an absence of guidance in the HIV-specific literature [15, 28]. The relative impact of lack of clarity on the part of HIV providers regarding their role as primary care physicians, difficulty balancing the demands of caring for complex patients with myriad medical and social problems, patient-provider encounter time constraints, or some combination of these factors will require further study.

Results from this single-center study in the southeastern United States may not be generalizable to other geographical regions or HIV clinical settings. The proportion of women was modest (6%), limiting our ability to draw broad inferences about this segment of the HIV-infected population. Due to the observational design, we can identify associations but cannot determine causality, and there may be unmeasured confounders for which we have not accounted. As this study is cross-sectional, we do not take account of the potential variability of the FRS over time, and we also note the FRS has not been validated in an HIV-infected population and may underpredict CVD risk in patients on ART [29]. However, in the absence of a more precise, validated HIV-specific scoring system, it is appropriate to use the FRS [15, 30].

We used a single, nonstandardized blood pressure measurement in our risk calculations, and fasting lipids were not routinely available. However, the purpose of this study was to evaluate provider practices regarding ASA prescription. We feel our methods are reflective of how our providers would likely calculate CVD risk scores in practice. In addition, there is literature suggesting that fasting lipids may not be necessary for CVD risk prediction [31]. Data on comorbidities and ASA prescription were extracted from the EHR, and underreporting by providers may have affected our estimates, although we note that our system of 100% quality assurance reduced this potential limitation and bias.

We observed significant underutilization of ASA in the prevention of first CVD-related events among HIV-infected persons engaged in medical care. HIV-specific guidelines regarding the use of ASA are needed. In the short term, interventions to improve HIV provider knowledge of and adherence to existing recommendations governing CVD prevention and management for the general population would be beneficial. The development and implementation of computerized decision support systems to enhance provider awareness of patients who would benefit from ASA for primary prevention of CVD-related events would likely advance adherence to this important prevention strategy.

Notes

Acknowledgments. Special thanks to Suneetha Thogaripolly for data retrieval, and to Kenneth Saag, MD, MSc, Monika M. Safford, MD, Todd M. Brown, MD, C. Suzanne Baker, RN, MPH, Ryan Outman, MS, and the UAB Center for Outcomes and Effectiveness Research and Education. We thank the UAB 1917 Clinic Cohort staff and management for their assistance with this project.

Financial support. This work was supported by the UAB Center for AIDS Research (P30-AI27767), the CFAR Network of Integrated Clinical Systems (1R24 AI067039-1), the Mary Fisher CARE Fund, and a Bristol Myers-Squibb Virology Research Fellows training grant (to G. A. B.). M. J. M. is supported by the National Institute of Mental Health (grant number K23MH082641). G. A. B. is supported in part by the Agency for Healthcare Research and Quality (grant number 5T32HS013852).

Potential conflicts of interest. G. A. B. has received research support from the Bristol-Myers Squibb Virology Fellows Research Training Program for the 2010–2012 academic years. M. J. M. has received consulting fees (advisory board) from Merck Foundation, Bristol-Myers Squibb, and Gilead Sciences, and grant support to UAB from Tibotec Therapeutics, Pfizer, Bristol-Myers Squibb, and Definicare. A. O. W. has consulted for Definicare. M. S. S. has received grant support and/or has consulted for Ardea Biosciences, Avexa, Boehringer Ingelheim Pharmaceuticals, Bristol-Myers Squibb, Gilead Sciences, GlaxoSmithKline, Merck & Co, Pfizer, Tibotec Therapeutics, Vertex Pharmaceuticals, and ViiV Healthcare, and has equity ownership in Definicare. J. H. W. has received research support from Bristol-Myers Squibb, Pfizer, Tibotec Therapeutics, and Definicare, and has consulted for Bristol-Myers Squibb and Gilead Sciences. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

References

1. Mocroft A, Ledergerber B, Katlama C, et al. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. Lancet **2003**; 362:22–9.
2. Effros RB, Fletcher CV, Gebo K, et al. Workshop on HIV infection and aging: what is known and further research directions. Clin Infect Dis **2008**; 47:542–53.
3. Marin B, Thiébault R, Buchar HC, et al. Non-AIDS defining deaths and immunodeficiency in the era of combination antiretroviral therapy. AIDS **2009**; 23:1743–53.
4. Neuhaus J, Angus B, Kowalska JD, et al. Risk of all-cause mortality associated with non-fatal AIDS and serious non-AIDS events among adults infected with HIV. AIDS **2010**; 24:697–706.
5. The Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996–2006: collaborative analysis of 13 HIV cohort studies. Clin Infect Dis **2010**; 50:1387–96.
6. The Data Collection on Adverse Events of Anti-HIV Drugs (D:A:D) Study Group. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D study. AIDS **2010**; 24:1537–48.
7. Hasse B, Ledergerber B, Furrer H, et al. Morbidity and aging in HIV-infected persons: the Swiss HIV Cohort Study. Clin Infect Dis **2011**; 53:1130–9.
8. Obel N, Thomsen HF, Kronberg G, et al. Ischemic heart disease in HIV-infected and HIV-uninfected individuals: a population based cohort study. Clin Infect Dis **2007**; 44:1625–31.
9. Klein D, Hurley LB, Quesenberry CP Jr, Sidney S. Do protease inhibitors increase the risk of coronary heart disease in patients with HIV-1 infection? J Acquir Immune Defic Syndr **2002**; 30:471–7.
10. Durand M, Sheehy O, Baril J-G, Lelorier J, Trembley CL. Association between HIV infection, antiretroviral therapy and risk of acute myocardial infarction: a cohort and nested case-control study using Québec's public health insurance database. J Acquir Immune Defic Syndr **2011**; 57:241–53.
11. Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients

with human immunodeficiency virus disease. J Clin Endocrinol Metab **2007**; 92:2506–12.
12. Lo J, Abbara S, Shturman L, et al. Increased prevalence of subclinical coronary atherosclerosis detected by computed tomography angiography in HIV-infected men. AIDS **2010**; 24:243–53.
13. Grundy SM, Pasternak R, Greenland P, Smith S, Fuster V. Assessment of cardiovascular risk by use of multiple-risk-factor assessment equations: a statement for healthcare professionals from the American Heart Association and the American College of Cardiology. Circulation **1999**; 100:1481–92.
14. Sacco RL, Benjamin EJ, Broderick JP, et al. Risk factors. Stroke **1997**; 28:1507–17.
15. Grinspoon SK, Grunfeld C, Kotler DP, et al. State of the science conference: initiative to decrease cardiovascular risk and increase quality of care for patients living with HIV/AIDS. Circulation **2008**; 118:198–210.
16. US Preventive Services Task Force. Aspirin for the prevention of cardiovascular disease: U.S. Preventive Services Task Force Recommendation Statement. Ann Intern Med **2009**; 150:396–404.
17. Chen RY, Accortt NA, Westfall AO, et al. Distribution of health care expenditures for HIV-infected patients. Clin Infect Dis **2006**; 42:1003–10.
18. Willig JH, Aban I, Nevin CR, et al. Darunavir outcomes study: comparative effectiveness of virologic suppression, regimen durability, and discontinuation reasons for three-class experienced patients at 48 weeks. AIDS Res Hum Retroviruses **2010**; 26:1279–85.
19. Kozak MS, Mugavero M, Ye J, et al. Patient reported outcomes in routine care: advancing data capture for HIV cohort research. Clin Infect Dis **2012**; 54:141–7.
20. Wilson PWF, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB. Prediction of coronary heart disease using risk factor categories. Circulation **1998**; 97:1837–47.
21. D'Agostino RB, Wolf PA, Belanger AJ, Kannel WB. Stroke risk profile: adjustment for antihypertensive medication. The Framingham Study. Stroke **1994**; 25:40–3.
22. Mosca L, Linfante AH, Benjamin EJ, et al. National study of physician awareness and adherence to cardiovascular disease prevention guidelines. Circulation **2005**; 111:499–510.
23. Tornero C, Ventura A, Mafe M. Aspirin is indicated for primary prevention of cardiovascular disease in HIV-infected patients. J Acquir Immune Defic Syndr **2010**; 54:560.
24. Reinsch N, Neuhaus K, Esser S, Potthoff A, Hower M, Mostardt S. Are HIV patients undertreated? Cardiovascular risk factors in HIV: results of the HIV-HEART Study. Eur J Cardiovasc Prev Rehabil **2012**; 19:267–74.
25. Glasser SP, Cushman M, Prineas R, et al. Does differential prophylactic aspirin use contribute to racial and geographic disparities in stroke and coronary heart disease (CHD)? Prev Med **2008**; 47:161–6.
26. Sanchez DR, Diez Roux AV, Michos ED, et al. Comparison of the racial/ethnic prevalence of regular aspirin use for the primary prevention of coronary heart disease from the Multi-Ethnic Study of Atherosclerosis. Am J Cardiol **2011**; 107:41–6.
27. Rodondi N, Vittinghoff E, Cornuz J, et al. Aspirin use for the primary prevention of coronary heart disease in older adults. Am J Med **2005**; 118:1288.e1–9.
28. Aberg JA, Kaplan JE, Libman H, et al. Primary care guidelines for the management of persons infected with human immunodeficiency virus: 2009 update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis **2009**; 49:651–81.
29. Law MG, Friis-Møller N, El-Sadr WM, et al. The use of the Framingham equation to predict myocardial infarctions in HIV-infected patients: comparison with observed events in the D:A:D study. HIV Med **2006**; 7:218–30.
30. Friis-Møller N, Thiébaut R, Reiss P, et al. Predicting the risk of cardiovascular disease in HIV-infected patients: the Data Collection on Adverse Effects of Anti-HIV Drugs Study. Eur J Cardiovasc Prev Rehabil **2010**; 17:491–501.
31. Langsted A, Freiberg JJ, Nordestgaard BG. Fasting and nonfasting lipid levels: influence of normal food intake on lipids, lipoproteins, apolipoproteins, and cardiovascular risk prediction. Circulation **2008**; 118:2047–56.