Cardiovascular disease risk prediction in the HIV Outpatient Study

Supplemental Online Materials

***eTable 1**. Algorithm for coding outcomes for cardiovascular disease risk prediction equations based on diagnoses and treatments/procedures in HIV Outpatient Study (HOPS) participants.*

Equation	Outcome Description	Diagnoses	Treatments / Procedures
Framingham general cardiovascular risk score	Composite CHD (coronary death, MI, coronary insufficiency, angina), cerebrovascular events (stroke, TIA), PAD, heart failure	Coronary death, CAD, MI, Angina, Stroke, TIA, PAD, Intermittent claudication, Heart failure	None
ACC/AHA Pooled Cohort equations	Hard ASCVD (nonfatal MI, fatal or nonfatal stroke, CHD death)	MI, CAD, Stroke	None
Data Collection on Adverse Effects of Antiretroviral Drugs (D:A:D) Study equation	Composite CVD (Fatal or nonfatal MI including sudden death, stroke, invasive coronary artery procedures, death from other CHD)	MI, CAD, Stroke, Sudden death, Unknown cause of death (a HOPS death that was not witnessed but had no identified underlying cause)	Coronary artery bypass surgery, angioplasty, heart stenting
Systematic COronary Risk Evaluation (SCORE) equation	CHD death, fatal stroke	<u>Outcomes:</u> Fatal MI, stroke, PAD or CAD <u>Risk factors:</u> Angina, Aneurysm, Atherosclerosis, Heart failure, Hypertension, PVD, TIA, CKD	Angioplasty, coronary artery ultrasound

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CAD, coronary artery disease; CHD Coronary Heart Disease, CKD, chronic kidney disease; CVD, cardiovascular disease; MI, myocardial infarction; PAD, peripheral arterial disease; PVD, Peripheral vascular disease; TIA, transient ischemic attack. CKD was defined as a glomerular filtration rate (GFR) measured by MDRD calculated in QA processing from creatinine labs and put in LXCGFR: consecutive GFRs < 60 over a period of at least 3 months or urine microalbumin spot >30 µg/mL: consecutive measurements > 30 over a period of at least 3 months.

eTable 2. *Concordance in risk score classification by the four selected cardiovascular disease risk prediction equations in HIV Outpatient Study (HOPS) participants.*

	10-year Cardiovascular Disease Risk Estimation			
HOPS Participants	**Framingham general cardiovascular risk score**	**ACC/AHA Pooled Cohort equations**	**SCORE (high-risk) equation**	**D:A:D equation**
Any length of follow-up (n = 2,392)				
Highest risk stratum, n (%)	491 (21.5)	553 (24.2)	556 (24.4)	549 (24.0)
Kappa coefficient[a]	Reference	0.92	0.92	0.93
Pearson χ^2	--	4.77	5.24	4.19
χ^2 *P*-value[b]	--	0.03	0.02	0.04
≥ 10 years of follow-up (n = 725)				
Highest risk stratum, n (%)	168 (24.3)	184 (26.6)	193 (27.9)	185 (26.7)
Kappa coefficient[a]	Reference	0.94	0.91	0.94
Pearson χ^2	--	0.98	2.34	1.10
χ^2 *P*-value[b]	--	0.32	0.13	0.29

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; D:A:D, Data Collection on Adverse Effects of Antiretroviral Drugs Study; Systematic COronary Risk Evaluation (SCORE) equation; IQR, interquartile range;.

a. A Kappa coefficient of 1.0 indicates perfect agreement between the Framingham general cardiovascular risk score and other equations. A Kappa coefficient >0.90 indicates excellent agreement.

b. A χ^2 *P*-value <0.05 indicates significant difference in the proportion of participants classified in the highest risk stratum between the Framingham general cardiovascular risk score and other equations.

eTable 3. *Sensitivity analysis comparing model fit for for 5-year CVD risk estimation by the ACC/AHA Pooled Cohort and D:A:D equations among HIV Outpatient Study (HOPS) participants.*

	5 year CVD Risk Estimation			
	ACC/AHA Pooled Cohort equations[a]	2010 D:A:D equation[b]	**2016 Updated D:A:D equation-Full model[c]**	**2016 Updated D:A:D equation-Reduced model[d]**
All HOPS Participants (n = 2,283)				
Median risk score (IQR)	1.4 (0.5-3.0)	1.9 (0.9-3.8)	1.8 (0.9-3.7)	1.7 (0.8-3.3)
Expected/observed events	58/93	73/141	68/141	62/141
Ratio expected/observed[e]	0.62	0.52	0.48	0.44
Hosmer-Lemeshow χ^2	29.16	23.96	33.33	36.15
Hosmer-Lemeshow *P*-value[f]	< 0.001	<0.01	< 0.001	< 0.001
C-statistic[g]	0.69	0.69	0.71	0.72
HOPS Participants with ≥10 years of follow-up (n = 692)				
Median risk score (IQR)	1.5 (0.5-3.3)	2.2 (1.1-4.1)	2.1 (1.0-3.8)	1.8 (0.9-3.3)
Expected/observed events	18/32	23/33	21/33	18/33
Ratio expected/observed[e]	0.56	0.70	0.64	0.55
Hosmer-Lemeshow χ^2	10.78	10.93	19.09	12.72
Hosmer-Lemeshow *P*-value[f]	0.21	0.21	0.014	0.12
C-statistic[g]	0.67	0.66	0.68	0.71

Abbreviations: CVD, cardiovascular disease; IQR, interquartile range; SBP, systolic blood pressure. Study specific outcomes are as follows: Data Collection on Adverse Effects of Antiretroviral Drugs (D:A:D) study equation - Fatal or non-fatal myocardial infarction (MI, including sudden death), coronary heart disease (CHD), stroke, transient ischemic attack, death from other cardiovascular disease; American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort equations -MI, fatal or non-fatal stroke, and CHD death.

a. Predicted ASCVD risk = $1 - S_0(t)^{e^{\wedge}(\text{individual score} - \text{Mean score})}$

b. The 2010 D:A:D model includes: years of exposure to indinavir and lopinavir/r, current exposure to abacavir, sex, age, family history of CVD, current or former cigarette smoking, diabetes, total cholesterol, HDL cholesterol, and systolic blood pressure, Friis-Moller N, et al. Predicting the risk of cardiovascular disease in HIV-infected patients: the data collection on adverse effects of anti-HIV drugs study. *Euro J Cardiovasc Prev Rehab* **2010**; 17(5): 491-501.

c. The 2016 D:A:D full model includes: Ln age, sex, diabetes, family history of CVD, current or former smoking, Ln cholesterol, Ln HDL, Ln SBP, Ln2 CD4 count, current exposure to abacavir, years of exposure to PI,and years of exposure to NRTI. Friis-Moller N, et al. An updated prediction model of the global risk of cardiovascular disease in HIV-positive persons: The Data-collection on Adverse Effects of Anti-HIV Drugs (D:A:D) study. *Euro J Prev Cardiol* **2016**; 23(2): 214-223.

d. The 2016 D:A:D reduced model includes: Ln age, sex, diabetes, family history of CVD, current or former smoking, Ln cholesterol, Ln HDL, Ln SBP, and Ln2 CD4 count. Friis-Moller N, et al. An updated prediction model of the global risk of cardiovascular disease in HIV-positive persons: The Data-collection on Adverse Effects of Anti-HIV Drugs (D:A:D) study. *Euro J Prev Cardiol* **2016**; 23(2): 214-223.

e. A ratio of expected /observed events of 1.0 indicates that the number of expected events equals the number of observed events. More cases are observed than expected if the ratio expected/observed is less than 1.0; i.e. a ratio of 0.6 is 40% less than 1.0 and would indicate a decrease or underestimation of 40%.

f. A Hosmer-Lemeshow χ^2 p-value <0.05 indicating lack of goodness of fit.

g. *C*-statistic thresholds to determine discriminative ability of our models: 0.50 to 0.59, poor; 0.60 to 0.69, moderate; 0.70 to 0.79, good; ≥0.80, very good or excellent.

eTable 4. *Sensitivity analysis comparing model fit for five- and 10-year ASCVD risk estimation among HIV Outpatient Study (HOPS) participants aged 40-79 years using the ACC/AHA Pooled Cohort equations.*

	ACC/AHA Pooled Cohort equations	
	5-year ASCVD Risk Estimation[a]	10-year ASCVD Risk Estimation
All HOPS participants (n = 1,369)		
Median risk score (IQR)	2.3 (1.1-4.2)	5.5 (2.7-10.0)
Expected/observed events	49/80	111/130
Ratio expected/observed[b]	0.61	0.85
Hosmer-Lemeshow χ^2	8.03	6.08
Hosmer-Lemeshow *P*-value[c]	0.43	0.64
C-statistic[d]	0.62	0.63
HOPS participants with ≥10 years of follow-up (n = 447)		
Median risk score (IQR)	2.2 (1.1-4.2)	5.3 (2.8-9.7)
Expected/observed events	15/29	35/57
Ratio expected/observed[b]	0.52	0.61
Hosmer-Lemeshow χ^2	4.93	7.91
Hosmer-Lemeshow *P*-value[c]	0.76	0.44
C-statistic[d]	0.58	0.60

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; AUC, area under the curve; IQR, interquartile range.

a. Predicted ASCVD risk = $1 - S_0(t)^{e\text{^}(\text{individual score} - \text{Mean score})}$ [23]

b. A ratio of expected /observed events of 1.0 indicates that the number of expected events equals the number of observed events. More cases are observed than expected if the ratio expected/observed is less than 1.0; i.e. a ratio of 0.6 is 40% less than 1.0 and would indicate a decrease or underestimation of 40%.

c. A Hosmer-Lemeshow χ^2 p-value <0.05 indicates indicating lack of goodness of fit.

d. *C*-statistic thresholds to determine discriminative ability of our models: 0.50 to 0.59, poor; 0.60 to 0.69, moderate; 0.70 to 0.79, good; ≥0.80, very good or excellent.

eTable 5. *Sensitivity analysis comparing model fit for 5- and 10-year ASCVD risk estimation among HIV Outpatient Study (HOPS) participants aged 40-79 years, without diabetes, with an LDL cholesterol level ≤190 mg/dL, and who were not taking statins at baseline or follow-up.*

	ACC/AHA Pooled Cohort equations	
	5-year ASCVD Risk Estimation[a]	10-year ASCVD Risk Estimation
All HOPS participants (n = 253)		
Median risk score (IQR)	2.8 (1.4-4.8)	6.7 (3.3-11.1)
Expected/observed events	10/32	23/50
Ratio expected/observed[b]	0.31	0.46
Hosmer-Lemeshow χ^2	4.70	3.87
Hosmer-Lemeshow *P*-value[c]	0.79	0.87
C-statistic[d]	0.61	0.62
HOPS participants with ≥10 years of follow-up (n = 127)		
Median risk score (IQR)	2.6 (1.3-4.8)	6.0 (3.2-11.2)
Expected/observed events	5/16	11/27
Ratio expected/observed[b]	0.31	0.41
Hosmer-Lemeshow χ^2	8.45	13.8
Hosmer-Lemeshow *P*-value[c]	0.39	0.09
C-statistic[d]	0.61	0.57

Abbreviations: ACC/AHA, American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; IQR, interquartile range; LDL, low-density lipoprotein.

a. Predicted ASCVD risk = $1 - S_0(t)^{e^{\wedge}(\text{individual score} - \text{Mean score})}$ [23]

b. A ratio of expected /observed events of 1.0 indicates that the number of expected events equals the number of observed events. More cases are observed than expected if the ratio expected/observed is less than 1.0; i.e. a ratio of 0.6 is 40% less than 1.0 and would indicate a decrease or underestimation of 40%.

c. A Hosmer-Lemeshow χ^2 p-value <0.05 indicates poor model calibration.

d. *C*-statistic thresholds to determine discriminative ability of our models: 0.50 to 0.59, poor; 0.60 to 0.69, moderate; 0.70 to 0.79, good; ≥0.80, very good or excellent.

eTable 6. *Sensitivity analysis comparing 10-year CVD event estimates and model fit using the Systematic COronary Risk Evaluation (SCORE) equations for high- and low risk populations among HIV Outpatient Study participants.*

	10-year CVD Risk Estimation	
	SCORE Low-Risk Equation	SCORE High-Risk Equation
All HOPS Participants (n = 2,283)		
Median risk score (IQR)	0.7 (0.1-0.8)	0.5 (0.1-1.4)
Expected/observed events	17/18	31/18
Ratio expected/observed[a]	0.94	1.72
Hosmer-Lemeshow χ^2	12.55	7.46
Hosmer-Lemeshow *P*-value[b]	0.13	0.49
C-statistic[c]	0.55	0.59
HOPS Participants with ≥10 years of follow-up (n = 692)		
Median risk score (IQR)	0.3 (0.1-0.8)	0.5 (0.2-1.5)
Expected/observed events	5/0	10/0
Ratio expected/observed[a]	n/r	n/r
Hosmer-Lemeshow χ^2	n/r	n/r
Hosmer-Lemeshow *P*-value[b]	n/r	n/r
C-statistic[c]	n/r	n/r

Abbreviations: IQR, Interquartile range.

Hosmer-Lemshow χ^2 and p-value are not reported (n/r) among participants with ≥10 years of follow-up due to a low number of observed events.

a. A ratio of expected /observed events of 1.0 indicates that the number of expected events equals the number of observed events. More cases are observed than expected if the ratio expected/observed is less than 1.0; i.e. a ratio of 0.6 is 40% less than 1.0 and would indicate a decrease or underestimation of 40%.

b. A Hosmer-Lemeshow χ^2 p-value <0.05 indicates poor model calibration.

c. *C*-statistic thresholds to determine discriminative ability of our models: 0.50 to 0.59, poor; 0.60 to 0.69, moderate; 0.70 to 0.79, good; ≥0.80, very good or excellent.

eTables 7 and 8. Comparison of participants included and excluded in the current analysis.

A total of 2540 subjects were excluded for missing total or HDL cholesterol or blood pressure measurements used to calculate CVD risk. We have compared the characteristics of included and excluded participants in order to understand if there were differences between the groups that could have biased the sample or compromised the generalizability of the report. Excluded participants differed from included participants in several ways (eTable 7). Compared to included participants, a greater proportion of excluded participants were enrolled in HOPS earlier (81.4% of excluded vs 75.1% of included participants enrolled prior to 2005), were slightly younger at their baseline visit (median age 40.5 years for excluded vs 42.2 years for included participants), were male (81.4% vs 75.9% for excluded vs included participants, respectively), and had private health insurance (58.0% vs 53.4% for excluded vs included participants, respectively).

Although years since HIV diagnosis was similar among the two groups, excluded participants had higher Nadir and baseline CD4+ T-cell counts compared to participants who were included in the analysis and a lower proportion had prior AIDS defining illnesses. Antiretroviral therapy use at baseline and cumulative years of antiretroviral therapy use among users was also lower among those excluded. A lower proportion of excluded participants were overweight or obese, had diabetes, hypertension, or hyperlipidemia, and statin and aspirin use were lower compared to participants who were included in the analysis. However it is important to keep in mind that those proportions are based only upon excluded participants for whom those measurements are available in HOPS medical records. Many excluded participants are missing various pieces of clinical data. Excluded participants had significantly fewer years of follow up (3.7 vs 6.5 years for excluded vs included participants respectively), significantly lower incidence of CVD events, and significantly higher incidence of non-CVD events (eTable 8).

eTable 7: Comparison of characteristics of HIV Outpatient Study (HOPS) excluded from analysis due to missing measurements versus included patients.

	Median (IQR) or Proportion		
Participant characteristics[a]	Excluded HOPS participants (N = 2,540)	Included HOPS participants (N = 2,283)	P-value
Year of HOPS entry, n (%)			< 0.001
1998 or earlier	812 (32.0)	809 (35.4)	
1999-2005	1,255 (49.4)	906 (39.7)	
2006-2010	473 (18.6)	568 (24.9)	
Age, median (IQR) years	40.5 (35.0-46.7)	42.2 (36.4-48.4)	< 0.001
Male sex, n (%)	2,067 (81.4)	1,732 (75.9)	< 0.001
Race and ethnicity, n (%)			< 0.001
White, non-Hispanic	1,370 (53.9)	1,144 (50.1)	
Black, non-Hispanic	783 (30.8)	775 (34.0)	
Hispanic	272 (10.7)	295 (12.9)	
Other	115 (4.5)	69 (3.0)	
Insurance, n (%)			0.001
Private	1,474 (58.0)	1,219 (53.4)	
Public, other	1,066 (42.0)	1,064 (46.6)	
History of injection drug use, n (%)	205 (8.1)	222 (9.7)	
Smoking[c], n (%)	1,020 (40.2)	952 (41.7)	0.32
Alcohol use, n (%)			< 0.001
>14 drinks/week	110 (4.3)	104 (4.6)	
7-14 drinks/week	183 (7.2)	141 (6.2)	
< 7 drinks/week	968 (38.1)	797 (34.9)	
None (“never” or “previously”)	683 (26.9)	858 (37.6)	
Missing information	596 (23.5)	383 (16.8)	
Body mass index (BMI), n (%)			< 0.001
Overweight or obese (BMI ≥ 25 kg/m^2)	1,086 (42.8)	1,141 (50.0)	
Normal weight or underweight (< 25 kg/m^2)	1,212 (47.7)	1,058 (46.3)	
Missing information	242 (9.5)	84 (3.7)	
Diabetes mellitus[d], n (%)	222 (8.7)	378 (16.6)	< 0.001
Hypertension[e], n (%)	690 (27.2)	1,091 (47.8)	< 0.001
Systolic blood pressure, median (IQR), mmHg	120 (110-130), n=1398	120 (112-130)	0.82
Diastolic blood pressure, median (IQR), mmHg	80 (70-84), n=1397	80 (70-84)	0.32
Hypercholesterolemia[f], n (%)	309 (12.2), n=2326	386 (16.9)	< 0.001
Total cholesterol, median (IQR) mg/dL	181 (153-212), n=2318	185 (155-221)	< 0.001
LDL cholesterol, median (IQR) mg/dL	100 (80-126), n=2151	104 (79-131)	0.041
HDL cholesterol, median (IQR) mg/dL	41 (34-51), n=2175	40 (33-51)	0.35
Non-HDL cholesterol, median mg/dL	137 (110-168), n=2173	139 (112-176)	0.001
Triglycerides, median mg/dL	144 (95-234), n=2275	153 (100-256)	0.001
Statin use[g], n (%)	162 (6.4)	303 (13.3)	< 0.001
Aspirin use[g], n (%)	91 (3.6)	109 (4.8)	0.046
Family history of cardiovascular disease[h], n (%)	19 (0.8)	25 (1.1)	0.27

Years since HIV diagnosis, median (IQR)	6.0 (1.4-11.0)	6.1 (1.7-11.4)	0.21
Prior AIDS-defining illness, n (%)	531 (20.9)	773 (33.9)	< 0.001
Nadir CD4+ cell count, median (IQR) cells/mm^3	285 (132-445), n=2414	211 (68-370)	< 0.001
Baseline CD4+ cell count, median (IQR) cells/mm^3	431 (252-636), n=2414	396 (229-600)	< 0.001
Viral load, median (IQR) copies/mL	654 (25-21,282), n=2527	490 (25-21,600)	0.59
Antiretroviral therapy use at baseline[g], n (%)	1,971 (77.6)	2,055 (90.0)	< 0.001
Combination antiretroviral therapy[i]	1,897 (74.7)	1,984 (86.9)	< 0.001
Nucleoside reverse transcriptase inhibitors	1,945 (76.6)	2,025 (88.7)	< 0.001
Abacavir	658 (25.9)	620 (27.2)	0.34
Didanosine	405 (15.9)	388 (17.0)	0.35
Non-nucleoside reverse transcriptase inhibitors	1,137 (44.8)	1,072 (47.0)	0.13
Efavirenz	765 (30.1)	731 (32.0)	0.16
Boosted protease inhibitors	700 (27.6)	853 (37.4)	< 0.001
Indinavir[j]	217 (8.5)	321 (14.1)	< 0.001
Lopinavir	448 (17.6)	527 (23.1)	< 0.001
Cumulative years of antiretroviral therapy use among users[j], median (IQR)	3.7 (1.6-5.8)	4.4 (2.1-6.5)	< 0.001
Combination antiretroviral therapy	2.9 (1.4-4.7)	3.7 (1.8-5.0)	< 0.001
Nucleoside reverse transcriptase inhibitors	3.7 (1.6-5.8)	4.4 (2.1-6.4)	< 0.001
Abacavir	1.3 (0.4-2.6)	1.1 (0.5-2.3)	0.33
Didanosine	1.3 (0.5-2.9)	1.4 (0.6-3.0)	0.23
Non-nucleoside reverse transcriptase inhibitors	1.7 (0.8-2.9)	1.6 (0.7-3.0)	0.70
Efavirenz	1.4 (0.5-2.6)	1.2 (0.4-2.5)	0.18
Boosted protease inhibitors	0.8 (0.3-1.4)	0.9 (0.4-1.5)	0.031
Indinavir	1.9 (0.8-3.8)	2.2 (1.0-4.0)	0.14
Lopinavir	0.6 (0.2-1.1)	0.7 (0.4-1.3)	0.021

Abbreviations: IQR, interquartile range; HDL, high-density lipoprotein.

a. Baseline date is the later of first HOPS visit or January 1, 2002. Baseline window of observation is from 365 days before through 275 days after baseline date.

b. Since the later of first HOPS visit or January 1, 2002.

c. Tobacco smoking (smoking) was ascertained per medical record at entry into the HOPS and by medical record and supplemental patient survey during HOPS observation.

d. Two fasting glucose levels > 125 mg/dL or two non-fasting glucose levels > 200 mg/dL within a six month period, taking insulin or other antidiabetic medications for at least 30 days, having a HbA1c result > 7 but not during pregnancy, or having a diagnosis of diabetes.

e. Blood pressure ≥ 140 mm Hg systolic or ≥ 90 mm Hg diastolic or current use of blood pressure medications.

f. Total cholesterol ≥ 240 mg/dL or LDL ≥ 160 mg/dL.

g. Any use during baseline window, defined above.

h. If information was unavailable, the participant was coded as having no family history of cardiovascular disease.

i. Combination antiretroviral therapy was defined as the following regimens: (1) any combination of 3 antiretrovirals (ARVs) that included a protease inhibitor (PI); non-nucleoside reverse transcriptase inhibitor (NNRTI); a fusion, entry or integrase inhibitor; or a CCR5 antagonist; (2) any combination of 3 nucleoside reverse transcriptase inhibitors (NRTIs) that included abacavir (ABC) or tenofovir (TDF), with the exception of the following combinations: ABC+TDF+lamivudine and didanosine + TDF + lamivudine; (3) 2 full-dose PIs; (4) a ritonavir-boosted PI combined with either an NNRTI or fusion inhibitor; (5) an integrase inhibitor combined with either a PI, an NNRTI, an entry inhibitor or a CCR5 antagonist [21].

j. From start of antiretroviral use to baseline date.

eTable 8: Follow-up information and incident cardiovascular disease events of HIV Outpatient Study (HOPS) excluded from analysis due to missing measurements versus included patients, January 2002 – September 2013.

	Median (IQR) or Proportion		
Participant characteristics[a]	Excluded HOPS participants (N = 2,540)	Included HOPS participants (N = 2,283)	P-value
Person years of follow up	10,638	15,056	
Years follow-up, median (interquartile range)	3.7 (1.7-6.1)	6.5 (3.3-10.4)	< 0.001
Statin use during follow-up[b], n (%)	437 (17.2)	666 (29.2)	< 0.001
Aspirin use during follow-up[c], n (%)	230 (9.1)	331 (14.5)	< 0.001
Patients with Incident cardiovascular disease, n (%)	131 (5.2)	195 (8.5)	< 0.001
Non-fatal cardiovascular disease events/procedures, n (% of incident CVD patients)			
Angina	31 (23.7)	28 (14.4)	0.046
Angioplasty	6 (4.6)	11 (5.6)	0.87
Cerebrovascular accident (stroke)	20 (15.3)	28 (14.4)	0.95
Coronary artery bypass graft	4 (3.1)	7 (3.6)	1.00
Coronary artery disease	54 (41.2)	94 (48.2)	0.26
Coronary stent (diagnosis or treatment)	2 (1.5)	6 (3.1)	0.48
Heart Failure	25 (19.1)	10 (5.1)	< 0.001
Myocardial infarction	27 (20.6)	34 (17.4)	0.56
Peripheral vascular disease	12 (9.2)	22 (11.3)	0.67
Transient ischemic attack	10 (7.6)	17 (8.7)	0.89
Fatal cardiovascular disease[d] event, n (%)	26 (1.0)	18 (0.8)	0.48
Non-cardiovascular disease cause of death, n (%)	178 (7.0)	89 (3.9)	< 0.001

a. Since the later of first HOPS visit or January 1, 2002.

b. Defined as prescription or reported use of statins for at least 30 days since baseline

c. Defined as: prescribed or reported use of any dose of aspirin daily for at least six months during follow-up.

d. Included: fatal myocardial infarction (MI), fatal stroke, fatal peripheral vascular disease (PVD), and fatal coronary artery disease (CAD).

Note: Study specific outcomes are as follows: Framingham general cardiovascular risk score - Composite CHD (coronary death, MI, coronary insufficiency, angina), cerebrovascular events (stroke, TIA), PAD, heart failure; American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort equations - MI, stroke, coronary artery disease (CAD); Systematic COronary Risk Evaluation (SCORE) – fatal MI, stroke, peripheral vascular disease, CAD; Data Collection on Adverse Effects of Antiretroviral Drugs (D:A:D) Study equation - fatal or non-fatal MI (including sudden death), CAD, stroke, death from other CHD. A total of 195 persons experienced an incident cardiovascular disease (CVD) event that was included in at least one of the CVD risk prediction equations. The number of events exceeds the number of individuals because outcomes differed by study equation. For patients who experienced multiple CVD events, the first event was defined as the incident event for the risk equation.