SUPPLEMENTAL MATERIAL

Supplemental Methods: Calculation of 5-Year Cardiovascular Risk Functions

A. Framingham 5-Year ASCVD Risk

The following describes how to calculate 5-year ASCVD risk from the Framingham ASCVD risk function. In the formulas below, the following are the variables used:

Age = Age in years;
TC = Total Cholesterol in mg/dl;
HDL = HDL Cholesterol in mg/dl;
SBP = Systolic Blood Pressure in mmHg;
"Hypertension Rx" = 1 if the subject is on antihypertensive medication, 0 otherwise;
"No Hypertension Rx" =1 if the subject is *not* on antihypertensive medication, 0 otherwise;
"Current Smoker" = 1 if subject is a current smoker, 0 otherwise;
"Prevalent Diabetes" = 1 if subject has prevalent diabetes, 0 otherwise.

Note further that, in the equations below, ln(x) = "natural logarithm of x" and "exp (x)" = e^x where e = 2.7182818.

Men:

Calculate: L = 3.06117*ln(Age) + 1.12370*ln(TC) – 0.93263*ln(HDL) + 1.99881*ln(SBP)*(Hypertension Rx) + 1.93303*ln(SBP)*(No Hypertension Rx) + 0.65451*Current Smoker + 0.57367*Prevalent Diabetes

Risk = $0.514*(1 - 0.95087^{\exp(L - 23.9802)})$

In the above equation: (a) 0.95087 is an estimate of the 5-year ASCVD risk at the average value of the covariates in the Framingham sample used to develop the model; (b) 23.9802 is calculated on the Framingham sample used to develop the model by first multiplying the mean of each risk factor by its corresponding coefficient above and then summing up these products; and (c) 0.514 is the adjustment factor required to apply the above Framingham function, originally developed for general CVD, to ASCVD; it is the ratio of the ASCVD rate to general CVD rate in the Framingham sample used to develop the function . The user may replace these values with the corresponding values from the user's population if available and desired.

B. Framingham 5-Year CHD Risk

The following describes how to calculate 5-year CHD risk from the Framingham CHD risk function. In the formulas below, the following are the variable used:

Age = Age in years;

Let SBP = Systolic Blood Pressure in mmHg; let DBP = Diastolic Blood Pressure in mmHg. Set "Optimal BP" to 1 if SBP<120 and DBP<80, otherwise set "Optimal BP" to = 0 and set "Normal BP" to 1 if SBP<130 and DBP<85, otherwise set "Normal BP" to 0 and set "High Normal BP" to 1 SBP<140 and DBP<90, otherwise set "High Normal BP" to 0 and set "Stage I

HTN" to 1 SBP<160 and DBP<100, otherwise set "Stage I HTN" to 0 and set "Stage II-IV HTN" to 1 if SBP ≥ 160 *or* DBP ≥ 100, 0 otherwise.

For men, let TC = total cholesterol in mg/dl:
"TC<160" = 1 if TC<160, 0 otherwise
"160≤TC≤199" = 1 if 160≤TC≤199, 0 otherwise
"200≤TC≤239" = 1 if 200≤TC≤239, 0 otherwise
"240≤TC≤279" = 1 if 240≤TC≤279, 0 otherwise
"TC≥280" = 1 if TC≥280, 0 otherwise

For women, let TC = total cholesterol in mg/dl:
"TC<160" = 1 if TC<160, 0 otherwise
"160≤TC≤199" = 1 if 160≤TC≤199, 0 otherwise
"TC≥200" = 1 if TC≥200, 0 otherwise

Let HDL = HDL Cholesterol in mg/dl:
"HDL<35" = 1 if HDL<35
"35≤HDL≤44" = 1 if 35≤HDL≤44, 0 otherwise
"45≤HDL≤49" = 1 if 45≤HDL≤49, 0 otherwise
"50≤HDL≤59" = 1 if 50≤HDL≤59, 0 otherwise
"HDL≥60" = 1 if HDL≥60, 0 otherwise

"Current Smoker" = 1 if subject is a current smoker, 0 otherwise;
"Prevalent Diabetes" = 1 if subject has prevalent diabetes, 0 otherwise.

Note further that, in the equations below, "exp (x)" = e^x where e = 2.7182818.

Men:

Calculate: L = 0.05327*Age + 0.09478*Optimal BP + 0.00*Normal BP + 0.42251*High Normal BP + 0.65945*Stage I HTN + 0.89640*Stage II-IV HTN - 0.37808*(TC<160) + 0.00*(160≤TC≤199) + 0.56956*(200≤TC≤239) + 0.74378(240 ≤TC≤279) + 0.82841*(TC≥280) + 0.60738*(HDL<35) + 0.36842*(35≤HDL≤44) + 0.00*(45≤HDL≤49) + 0.00*(50≤HDL≤59) - 0.46075*(HDL≥60) + 0.52517*Prevalent Diabetes + 0.72774*Current Smoker.

Risk = $1 - 0.97565^{\exp(L - 3.823)}$

In the above equation: (a) 0.97565 is an estimate of the 5-year CHD risk at the average value of the covariates in the Framingham sample used to develop the model; (b) 3.823 is calculated on the Framingham sample used to develop the model by first multiplying the mean of each risk factor by its corresponding coefficient above and then summing up these products. The user may replace these values with the corresponding values from the user's population if available and desired.

C. ACC/AHA 5-Year ASCVD Risk

The following describes how to calculate 5-year ASCVD risk from the ACC/AHA ASCVD risk function. In the formulas below, the following are the variables used:

Age = Age in years;

TC = Total Cholesterol in mg/dl;
HDL = HDL Cholesterol in mg/dl;
SBP = Systolic Blood Pressure in mmHg;
“Hypertension Rx” = 1 if the subject is on antihypertensive medication, 0 otherwise;
“No Hypertension Rx” =1 if the subject is not on antihypertensive medication, 0 otherwise;
“Current Smoker” = 1 if subject is a current smoker, 0 otherwise;
“Prevalent Diabetes” = 1 if subject has prevalent diabetes, 0 otherwise.

Note further that, in the equations below, ln(x) = “natural logarithm of x” and “exp (x)” = e^x where e = 2.7182818.

Men:

Calculate: L = 12.344*ln(Age) + 11.853*ln(HDL) - 2.664*ln(Age)*ln(TC) - 7.990*ln(HDL) + 1.769*ln(Age)*ln(HDL) + 1.797*ln(SBP)*(Hypertension Rx) + 1.764* ln(SBP)*(No Hypertension Rx) + 7.837*Current Smoker - 1.795*ln(Age)*Current Smoker + 0.658*Prevalent Diabetes

Risk = $1 – 0.962539^{\exp(L – 61.18)}$

In the above equation: (a) 0.962539 is an estimate of the 5-year ASCVD risk at the average value of the covariates in the ACC/AHA sample used to develop the model; (b) 61.18 is calculated on the ACC/AHA sample used to develop the model by first multiplying the mean of each risk factor by its corresponding coefficient above and then summing up these products. The user may replace these values with the corresponding values from the user’s population if available and desired.

Supplemental Tables

Supplemental Table 1. Predicted and observed risk for HIV-infected men (median 5-year predicted or observed risk and quartiles).

	Framingham CHD	ACC/AHA ASCVD	Framingham ASCVD
Predicted risk scores based on established functions	2.0% (1.2%, 3.7%)	2.9% (1.6%, 5.7%)	2.8% (1.6%, 5.0%)
Observed risk	5.2% (3.9%, 6.8%)	9.2% (7.4%, 11.4%)	8.4% (6.7%, 10.5%)
Predicted risk scores based on "HIV function"	3.7% (2.1%, 6.8%)	7.8% (5.3%, 11.6%)	6.8% (4.3%, 10.6%)

CHD indicates coronary heart disease; ACC, American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease. "HIV function" indicates Cox models developed from the HIV cohort.

Supplemental Table 2. Baseline characteristics of HIV-infected women age 30-74

	All (N=431)	No CHD Event (N=416)	CHD Event (N=15)
Age (yrs) - mean+/-SD	49.3±9.2 (431)	49.2±9.2 (416)	50.1±9.5 (15)
Age (yrs) - (min, max)	(30.1,73.3)	(30.1,73.3)	(30.6,68.1)
Race/ethnicity - % (n)			
White	32.5 (140/431)	32.5 (135/416)	33.3 (5/15)
Black	44.5 (192/431)	44.0 (183/416)	60.0 (9/15)
Hispanic	16.2 (70/431)	16.6 (69/416)	6.7 (1/15)
Other/Unknown	6.7 (29/431)	7.0 (29/416)	0.0 (0/15)
Total cholesterol (mg/dL) - mean+/-SD	178.3±42.7 (431)	179.4±42.2 (416)	149.9±47.0 (15)
Total cholesterol (mg/dL) categories - % (n)			
< 160	29.9 (129/431)	29.1 (121/416)	53.3 (8/15)
160-199	40.6 (175/431)	40.9 (170/416)	33.3 (5/15)
200-239	21.6 (93/431)	21.9 (91/416)	13.3 (2/15)
240-279	6.7 (29/431)	7.0 (29/416)	0.0 (0/15)
>= 280	1.2 (5/431)	1.2 (5/416)	0.0 (0/15)
HDL cholesterol (mg/dL) - mean+/-SD	49.8±16.7 (431)	50.2±16.5 (416)	38.9±17.6 (15)
HDL cholesterol (mg/dL) categories - % (n)			
< 35	16.9 (73/431)	15.6 (65/416)	53.3 (8/15)
35-44	23.2 (100/431)	23.3 (97/416)	20.0 (3/15)
45-49	14.4 (62/431)	14.7 (61/416)	6.7 (1/15)
50-59	18.6 (80/431)	19.0 (79/416)	6.7 (1/15)
>= 60	26.9 (116/431)	27.4 (114/416)	13.3 (2/15)
Systolic blood pressure – mean+/-SD	120.1±17.1 (431)	120.2±17.0 (416)	118.4±18.1 (15)
Treated systolic blood pressure - mean+/-SD (n)	127.1±18.8 (128)	127.3±18.8 (121)	122.7±19.0 (7)
Untreated systolic blood pressure - mean+/-SD (n)	117.2±15.4 (303)	117.3±15.4 (295)	114.6±17.6 (8)
Blood pressure categories - % (n)			
Optimal (SBP<120, DBP<80)	45.2 (195/431)	45.2 (188/416)	46.7 (7/15)
Normal (SBP<130, DBP<85)	24.4 (105/431)	24.0 (100/416)	33.3 (5/15)
High Normal (SBP<140, DBP<90)	11.1 (48/431)	11.3 (47/416)	6.7 (1/15)
Stage I HTN (SBP<160, DBP<100)	13.9 (60/431)	14.2 (59/416)	6.7 (1/15)
Stage II-IV HTN (SBP>=160, DBP>=100)	5.3 (23/431)	5.3 (22/416)	6.7 (1/15)
Antihypertensive medication - % (n)	29.7 (128/431)	29.1 (121/416)	46.7 (7/15)
Smoking - % (n)	38.1 (164/431)	36.8 (153/416)	73.3 (11/15)
Diabetes - % (n)	16.7 (72/431)	16.6 (69/416)	20.0 (3/15)
CD4 count - median (Q1, Q3)	465 (299,665)	468 (299,666)	351 (276,571)
CD4 count < 200 cells/mm^3 - % (n/N)	15.0% (59/393)	14.7 (56/380)	23.1 (3/13)
HIV viral load < 400 copies/mL - % (n/N)	67.0% (239/357)	67.8 (234/345)	41.7 (5/12)
Log HIV viral load - median (Q1, Q3)	3.9 (3.4,4.4)	3.9 (3.3,4.4)	4.0 (3.6,4.7)
ART use - % (n)	94.2 (406/431)	94.5 (393/416)	86.7 (13/15)
Duration follow-up (yrs) - median (Q1, Q3)	4.7 (3.4,5.0)	4.8 (3.5,5.0)	2.8 (1.6,3.8)
5-year hard CHD rate - % (n)	3.5 (15)	-	-

	All (N=431)	No CHD Event (N=416)	CHD Event (N=15)
5-year hard CHD incidence rate (per 1000 PY)	8.7	-	-
5-year ASCVD rate - % (n)	6.3 (27)	-	-
5-year ASCVD incidence rate (per 1000 PY)	15.8	-	-

SD indicates standard deviation; mg, milligrams; dL, deciliter; HDL, high-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; HTN, hypertension; Q1, quarter 1; Q3, quarter 3; ART, antiretroviral therapy; CHD, coronary heart disease; PY, person years; ASCVD, atherosclerotic cardiovascular disease.
HIV viral load is represented as the median log viral load among individuals with detectable viral loads. Hard CHD is defined as MI or coronary death. ASCVD is defined as MI, stroke, or coronary death.

Supplemental Table 3. Discrimination of the Framingham CHD, ACC/AHA, and Framingham ASCVD functions in race-stratified analyses among men

	Framingham CHD		ACC/AHA		Framingham ASCVD	
	***c* statistic**	**95% CI**	***c* statistic**	**95% CI**	***c* statistic**	**95% CI**
Black	0.68	0.54, 0.82	0.73	0.62, 0.85	0.75	0.63, 0.87
White	0.72	0.64, 0.79	0.67	0.60, 0.74	0.67	0.60, 0.74
Non-black	0.68	0.6, 0.76	0.65	0.58, 0.72	0.66	0.59, 0.72

CHD indicates coronary heart disease; ACC, American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CI, confidence interval.

Supplemental Table 4. Calibration of the Framingham hard CHD, ACC/AHA, and Framingham ASCVD functions in race-stratified analyses among men

	Framingham CHD			ACC/AHA			Framingham ASCVD		
	χ^2 statistic	p value	DF	χ^2 statistic	p value	DF	χ^2 statistic	p value	DF
Black	0.8393	0.3596	1	1.1834	0.2767	1	3.3584	0.0669	1
White	5.5775	0.0615	2	14.9367	0.0106	5	14.454	0.0250	6
Non-black	10.7725	0.0292	4	22.141	0.0024	7	22.9163	0.0008	6

CHD indicates coronary heart disease; ACC, American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease.

Supplemental Table 5. Coefficients for coronary heart disease risk factors among men and women combined

Framingham CHD	
Risk Factor	**HIV Function (95% CI)**
Age	0.04 (0.01, 0.07)
Blood Pressure	
Optimal (SBP<120, DBP<80)	-0.215 (-0.857, 0.427)
Normal (SBP<130, DBP<85)	Reference
High Normal (SBP<140, DBP<90)	-0.108 (-0.859, 0.644)
Stage I HTN (SBP<160, DBP<100)	-0.425 (-1.225, 0.375)
Stage II-IV HTN (SBP≥160, DBP≥100)	0.302 (-0.697, 1.3)
Total Cholesterol	
< 160	0.585 (-0.031, 1.2)
160-199	Reference
200-239	0.14 (-0.626, 0.905)
240-279	0.543 (-0.47, 1.555)
>= 280	1.343 (-0.146, 2.833)
HDL	
<35	0.379 (-0.364, 1.121)
35-44	-0.31 (-1.075, 0.455)
45-49	Reference
50-59	-0.645 (-1.6, 0.311)
>= 60	-1.048 (-2.213, 0.117)
Diabetes	0.603 (0.011, 1.194)
Smoking	0.988 (0.462, 1.513)
Sex	0.156 (-0.443, 0.755)
ACC/AHA ASCVD	
Risk Factor	**HIV Function (95% CI)**
Ln Age	-4.942 (-33.51, 23.625)
Ln Total Cholesterol	2.067 (-22.726, 26.86)
Ln Total Cholesterol x Sex	-1.649 (-3.155, -0.143)
Ln HDL Cholesterol	-10.829 (-28.18, 6.521)
Ln Treated SBP	0.25 (-1.303, 1.803)
Ln Untreated SBP	0.199 (-1.367, 1.766)
Smoking	-1.226 (-12.427, 9.976)
Diabetes	0.336 (-0.141, 0.812)
Ln Age x Ln Total Cholesterol	-0.407 (-6.595, 5.781)
Ln Age x Ln HDL Cholesterol	2.512 (-1.825, 6.85)
Ln Age x Smoking	0.451 (-2.341, 3.243)
Sex	8.495 (0.826, 16.163)
Framingham ASCVD	
Risk Factor	**HIV Function (95% CI)**
Ln Age	2.937 (1.42, 4.453)
Ln Age x Sex	-2.231 (-4.789, 0.328)
Ln Total Cholesterol	0.514 (-0.428, 1.455)
Ln Total Cholesterol x Sex	-1.875 (-3.328, -0.423)
Ln HDL Cholesterol	-0.806 (-1.387, -0.226)
Ln Treated SBP	0.607 (-0.922, 2.135)
Ln Untreated SBP	0.529 (-1.014, 2.073)
Smoking	0.558 (0.169, 0.947)

Diabetes	0.266 (-0.211, 0.744)
Sex	18.579 (6.066, 31.093)