Supplemental Figures

Figure 1. Hazard Ratios for Cholesterol Efflux Capacity Adjusted for Coronary Calcium and Family History
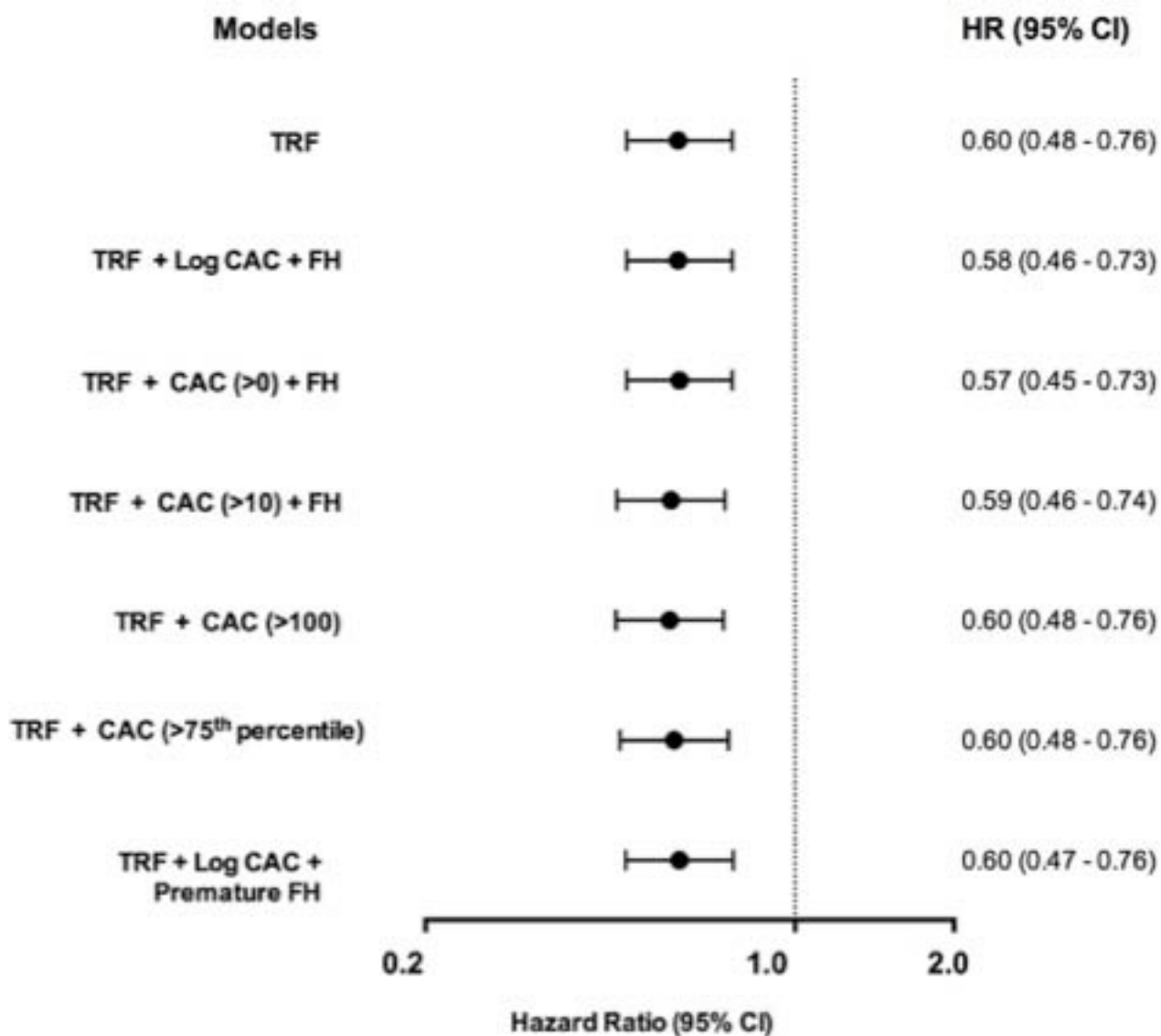
Hazard ratios for 1 standard deviation increase in cholesterol efflux derived from Cox proportional hazards models for incident ASCVD and adjusted for traditional risk factors, including age, sex, race, diabetes, systolic blood pressure, smoking, body mass index, total cholesterol level, HDL-C, anti-hypertensive medi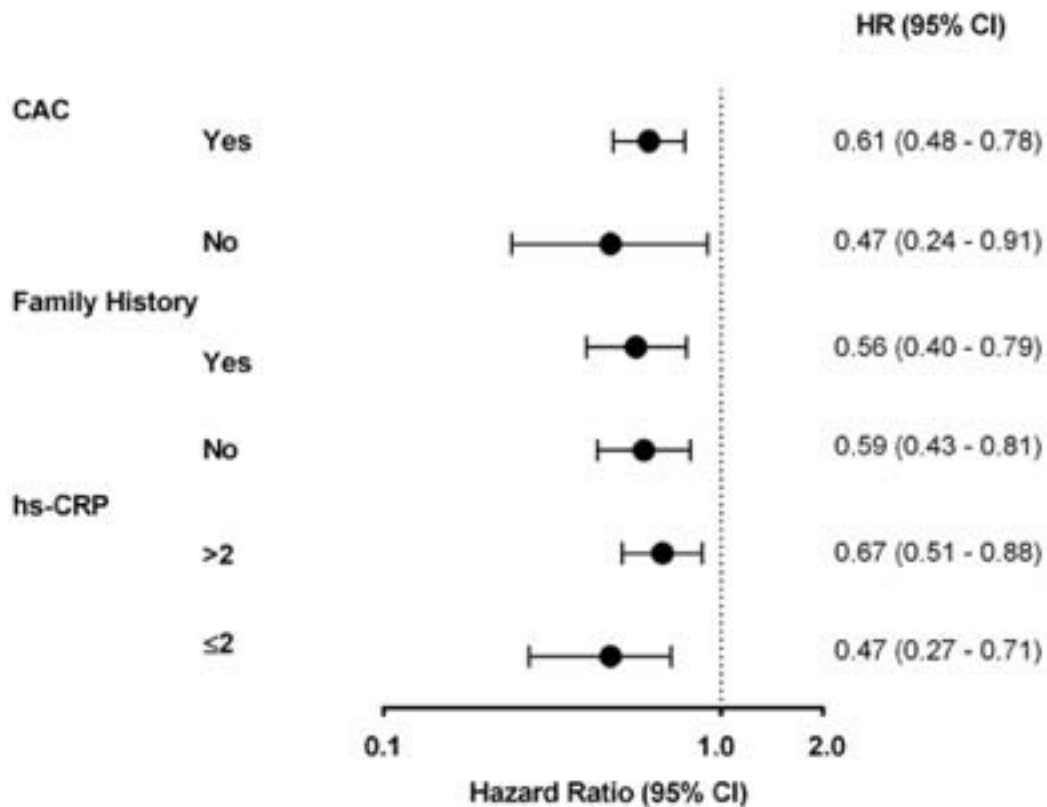cation, and statin medication. **TRF:** Traditional risk factors; **CAC:** Coronary artery calcium; **FH:** Family history of myocardial infarction.

Figure 2. Hazard Ratios for Cholesterol Efflux Capacity Among Participants with Prevalent Coronary Calcium, Family History, or Elevated Hs-CRP

Hazard ratios for 1 standard deviation increase in cholesterol efflux derived from Cox proportional hazards models for incident ASCVD and adjusted for traditional risk factors, including age, sex, race, diabetes, systolic blood pressure, smoking, body mass index, total cholesterol level, HDL-C, anti-hypertensive medication, and statin medication. Models stratified by presence or absence of coronary calcium, family history, or elevated hs-CRP. **CAC:** Coronary artery calcium; **hs-CRP:** High sensitivity C-reactive protein.

Models		HR (95% CI)
TRF		0.60 (0.48 - 0.76)
TRF + Log CAC + FH		0.58 (0.46 - 0.73)
TRF + CAC (>0) + FH		0.57 (0.45 - 0.73)
TRF + CAC (>10) + FH		0.59 (0.46 - 0.74)
TRF + CAC (>100)		0.60 (0.48 - 0.76)
TRF + CAC (>75th percentile)		0.60 (0.48 - 0.76)
TRF + Log CAC + Premature FH		0.60 (0.47 - 0.76)

Hazard Ratio (95% CI)

		HR (95% CI)
CAC		
	Yes	0.61 (0.48 - 0.78)
	No	0.47 (0.24 - 0.91)
Family History		
	Yes	0.56 (0.40 - 0.79)
	No	0.59 (0.43 - 0.81)
hs-CRP		
	>2	0.67 (0.51 - 0.88)
	≤2	0.47 (0.27 - 0.71)

Hazard Ratio (95% CI)

Supplemental Table 1. Net Reclassification of Events and Non-Events with Adding Continuous Cholesterol Efflux to Risk Factors for Incident ASCVD

Model		Reclassified Up, %	Reclassified Down, %	NRI
	Event	65.3	34.4	*0.31*
TRF+CAC+Efflux	*Nonevent*	39.7	60.3	*0.21*
	Total			*0.52 (0.26 – 0.66)*
	Event	65.4	34.4	*0.31*
TRF+FH+Efflux	*Nonevent*	38.4	61.6	*0.23*
	Total			*0.54 (0.30 – 0.71)*
	Event	63.3	36.5	*0.27*
TRF+Hs-CRP+Efflux	*Nonevent*	40.3	59.7	*0.20*
	Total			*0.46 (0.23 – 0.63)*

Category-less NRI (95%CI) calculated for the addition of continuous efflux to base models: 1) TRF + CAC>0; 2) TRF + FH; 3) TRF + hs-CRP≥2 mg/L. Reclassification separated by those with incident ASCVD and those without incident ASCVD during follow up. NRI = Net Reclassification Index; TRF = Traditional Risk Factors; CAC = Coronary Artery

Calcium; FH = Family History; hs-CRP = high-sensitivity C-reactive protein

Supplemental Table 2. Reclassification with Addition of Cholesterol Efflux to Coronary Calcium > 0

TRF	TRF+Efflux				Total	↑ Risk	↓ Risk	NRI
+Events	<5%	5-7.5	7.5-20	≥ 20%				
<5%	13	8	0	0	21			
5-7.5	6	2	7	0	15			
7.5-20	0	2	23	10	35			
≥ 20%	0	0	6	35	41			
Total	19	12	36	45	112	24	14	9.8%

-Events	<5%	5-7.5	7.5-20	≥ 20%				
<5%	1208	70	0	0	1278			
5-7.5	88	35	56	0	179			
7.5-20	1	80	208	36	325			
≥ 20%	0	0	17	61	78			
Total	1297	185	281	97	1860	162	186	1.3%

Total NRI	0.11 (95%CI 0.006-0.22)

Net Reclassification Index (NRI) calculated with the addition of cholesterol efflux > median added to traditional risk factors

(TRF: age, sex, race, diabetes, systolic blood pressure, smoking, body mass index, total cholesterol, HDL-C, anti-

hypertensive medication status, statin use) + CAC>0. Risk categories of <5%, 5-7.5%, 7.5-20%, and ≥ 20% used for

groups with events and non-events separately. 95% CI for NRI calculated using boot-strapping.

Supplemental Table 3. Reclassification with Addition of Cholesterol Efflux to Family History

+Events	TRF+Efflux				Total	↑ Risk	↓ Risk	NRI
TRF	<5%	5-7.5	7.5-20	≥ 20%				
<5%	20	5	0	0	25			
5-7.5	1	3	5	0	9			
7.5-20	0	6	23	8	37			
≥ 20%	0	0	3	38	41			
Total	21	14	31	46	112	18	10	7.1%

-Events	<5%	5-7.5	7.5-20	≥ 20%				
<5%	1205	85	1	0	1291			
5-7.5	89	43	50	0	182			
7.5-20	0	75	201	32	308			
≥ 20%	0	0	21	58	79			
Total	1294	203	273	90	1860	168	185	0.9%

Total	
	0.08 (95%CI -0.01-0.18)
NRI	

Net Reclassification Index (NRI) calculated with the addition of cholesterol efflux > median added to traditional risk factors

(TRF: age, sex, race, diabetes, systolic blood pressure, smoking, body mass index, total cholesterol, HDL-C, anti-

hypertensive medication status, statin use) + family history (FH). Risk categories of <5%, 5-7.5%, 7.5-20%, and ≥ 20%

used for groups with events and non-events separately. 95% CI for NRI calculated using boot-strapping.

Supplemental Table 4. Reclassification with Addition of Cholesterol Efflux to Elevated hs-CRP ≥ 2 g/L

+Events	TRF+Efflux				Total	↑ Risk	↓ Risk	NRI
TRF	<5%	5-7.5	7.5-20	≥ 20%				
<5%	20	4	0	0	24			
5-7.5	2	2	8	0	12			
7.5-20	1	3	25	8	37			
≥ 20%	0	0	1	37	38			
Total	23	9	34	45	111	20	7	11.7%

-Events	<5%	5-7.5	7.5-20	≥ 20%				
<5%	1203	78	0	0	1281			
5-7.5	90	40	56	0	186			
7.5-20	0	75	206	27	308			
≥ 20%	0	0	17	58	75			
Total	1293	193	279	85	1850	161	182	1.1%

Total	
NRI	0.13 (95%CI 0.03-0.22)

Net Reclassification Index (NRI) calculated with the addition of cholesterol efflux > median added to traditional risk factors

(TRF: age, sex, race, diabetes, systolic blood pressure, smoking, body mass index, total cholesterol, HDL-C, anti-

hypertensive medication status, statin use) + hs-CRP ≥ 2 g/L. Risk categories of <5%, 5-7.5%, 7.5-20%, and ≥ 20% used

for groups with events and non-events separately. 95% CI for NRI calculated using boot-strapping.