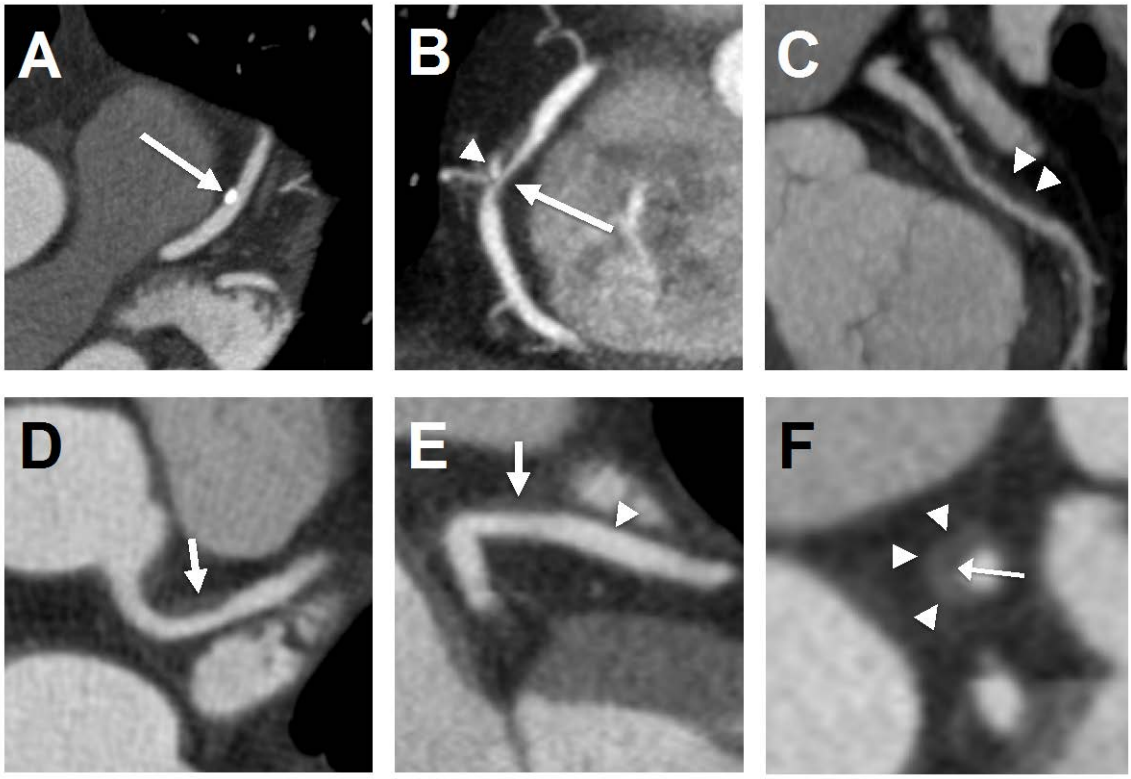
Supplementary Online Content

Ferencik M, Mayrhofer T, Bittner DO, et al. Use of high-risk coronary atherosclerotic plaque detection for risk stratification of patients with stable chest pain: a secondary analysis of the PROMISE randomized clinical trial. *JAMA Cardiol*. Published online January 10, 2018. doi:10.1001/jamacardio.2017.4973.

This supplementary material has been provided by the authors to give readers additional information about their work.

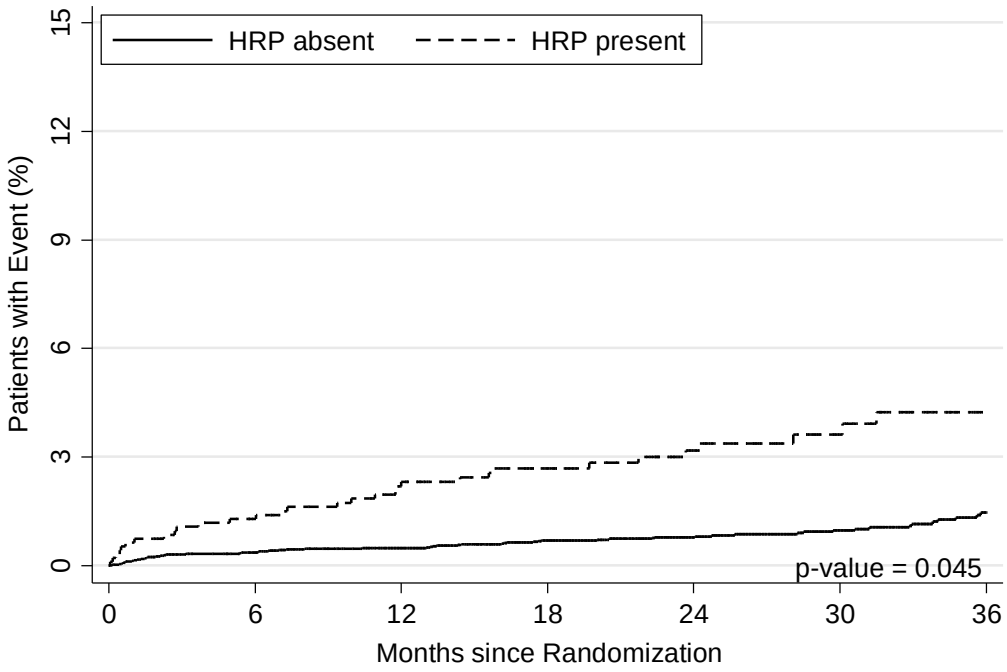
eFigure 1. Evaluation of Coronary CTA Datasets for the Detection of Coronary Plaque, Stenosis, and High-risk Plaque Features.

Coronary CTA images were evaluated in axial and multiplanar reformatted images. **Panel A** Any structure with a density of ≥130 HU that could be visualized separately from the contrast-enhanced coronary lumen, could be assigned to the coronary artery wall, and could be identified in at least two independent planes was defined as calcified plaque (arrow). The image shows calcified plaque in the proximal left anterior descending coronary artery and the degree of stenosis was graded as 1-29%. **Panel B** If both calcified (arrowhead) and non-calcified plaque components were present, the plaque was classified as partially calcified. The partially calcified plaque in the mid right coronary artery was causing 70-99% stenosis (arrow). **Panel C** Non-calcified coronary plaque was defined as any discernible structure that could be assigned to the coronary artery wall, had a CT number below the contrast-enhanced coronary lumen, but above the surrounding connective tissue, and could be identified in at least two independent planes. The example shows non-calcified plaque (arrowheads) in the left circumflex coronary artery with 30-49% stenosis. This example also shows a high-risk plaque feature of low CT attenuation. If low CT attenuation was visually noted in non-calcified plaque, readers placed three random region-of-interest measurements (approximately 0.5-1.0 mm^2) in the non-calcified low CT attenuation portion of the plaque. Low CT attenuation plaque was defined as the mean CT number within these three regions of interest <30 HU. **Panel D** Large non-calcified plaque (arrow) in the proximal left anterior descending coronary artery with positive remodeling. **Panel E** Positive remodeling was assessed visually in multiplanar reformatted images reconstructed in long axis and short axis view of the vessel. Additional manual measurements of outer vessel diameter were performed at readers' discretion and threshold of 1.1 (ratio of outer vessel diameter at the plaque site – arrow – divided by outer vessel diameter at reference site – arrowhead) was used to define positive remodeling. **Panel F** The napkin ring sign was defined as a ring-like peripheral higher attenuation (arrowhead) with central low CT attenuation non-calcified portion of the coronary plaque (arrow) in the cross-sectional view of the vessel



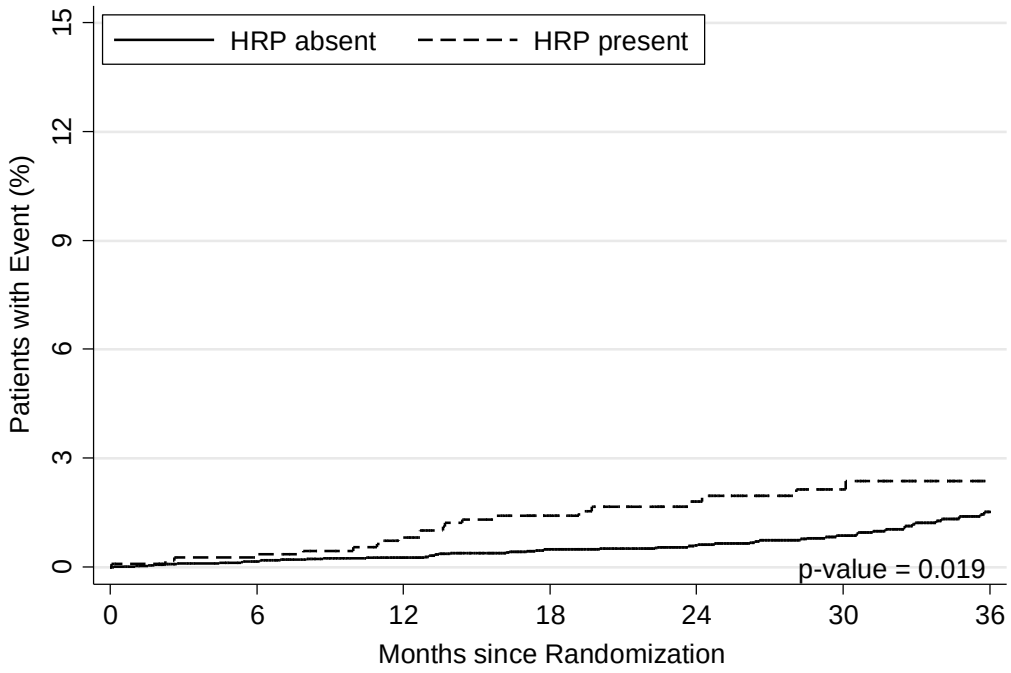
eFigure 2. Kaplan–Meier Estimates of the Composite Secondary End Point of Cardiovascular Death, Myocardial Infarction, or Hospitalization for Unstable Angina and Tertiary End Point of Death, or Myocardial Infarction as a Function of Time After Randomization.

A. The figure shows Kaplan-Meier estimates for the composite secondary end point of cardiovascular death, myocardial infarction, or hospitalization for unstable angina stratified by the presence of high-risk plaque (HRP) and adjusted for ≥70% stenosis in any coronary artery or ≥50% in the left main coronary artery and ASCVD risk score.



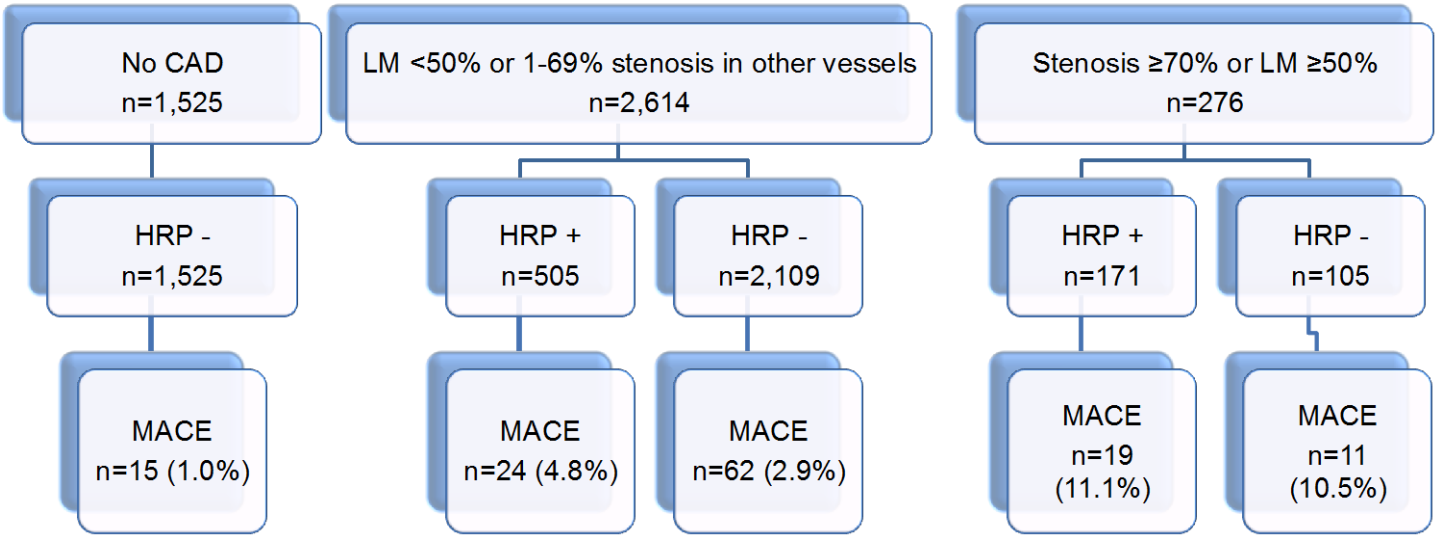
Number at risk							
HRP present	676	640	602	494	368	242	119
HRP absent	3739	3586	3359	2735	2062	1333	704

B. The figure shows Kaplan-Meier estimates for the composite tertiary end point of death, or myocardial infarction stratified by the presence of high-risk plaque (HRP) and adjusted for ≥70% stenosis in any coronary artery or ≥50% in the left main coronary artery and ASCVD risk score.



Number at risk							
HRP present	676	664	633	521	397	258	133
HRP absent	3739	3663	3473	2832	2169	1403	770

eFigure 3. Major Adverse Cardiovascular Event Incidence Proportion (Death, Non-Fatal Myocardial Infarction, or Hospitalization for Unstable Angina) Stratified by the Degree Of Stenosis and Presence of High-Risk Plaque.
Abbreviations: CAD, coronary artery disease; HRP, high-risk plaque; LM, left main coronary artery; MACE, major adverse cardiovascular event.



eTable 1. Results of univariable and multivariable Cox proportional hazard analysis demonstrating the predictive value of high-risk plaque for the outcome of major adverse cardiovascular events (death, non-fatal myocardial infarction, or hospitalization for unstable angina pectoris).

	Prevalence – n/N (%)	Incidence proportion – n/N (%)	Incidence proportion for non-positive group – n/N (%)	Unadjusted HR (95% CI)	Adjusted HR (95% CI) for significant stenosis	Adjusted HR (95% CI) for significant stenosis and ASCVD risk score
Any high-risk plaque	676/4415 (15.3)	43/676 (6.3)	88/3739 (2.4)	2.73 (1.89–3.93)	1.82 (1.19–2.76)	1.72 (1.13–2.62)
Both positive remodeling and low CT attenuation present	179/4415 (4.1)	14/179 (7.8)	117/4236 (2.8)	2.85 (1.64–4.97)	1.47 (0.80–2.69)	1.56 (0.85–2.84)
At least one of positive remodeling and low CT attenuation present	671/4415 (15.2)	43/671 (6.4)	88/3744 (2.6)	2.75 (1.91–3.96)	1.84 (1.21–2.79)	1.74 (1.14–2.65)
Two high-risk plaque features present	258/4415 (5.8)	22/258 (8.5)	109/4157 (2.6)	3.26 (2.06–5.15)	1.73 (1.02–2.95)	1.71 (1.00–2.92)
Three high-risk plaque features present	85/4415 (1.9)	7/85 (8.2)	124/4330 (2.9)	2.73 (1.27–5.84)	1.33 (0.60–2.96)	1.37 (0.62–3.05)

eTable 2. Results of univariable and multivariable Cox proportional hazard analysis demonstrating the predictive value of the presence of any coronary plaque, high-risk plaque, and significant coronary stenosis for the outcome of major adverse cardiovascular events (death, non-fatal myocardial infarction, or hospitalization for unstable angina pectoris).

Group	Prevalence – n/N (%)	Incidence proportion – n/N (%)	HR (95% CI)	HR (95% CI) adjusted for ASCVD risk score
No Plaque	1525/4,415 (34.5)	15/1525 (1.0)	Base	Base
HRP(–) & SS(–)	2109/4415 (47.8)	62/2,109 (2.9)	3.04 (1.73–5.34)	2.64 (1.49–4.69)
HRP(–) & SS(+)	105/4415 (2.4)	11/105 (10.5)	11.75 (5.40–25.58)	9.31 (4.21–20.61)
HRP(+) & SS(–)	505/4415 (11.4)	24/505 (4.8)	4.84 (2.54–9.23)	4.31 (2.25–8.26)
HRP(+) & SS(+)	171/4415 (3.9)	19/171 (11.1)	12.24 (6.22–24.10)	8.68 (4.25–17.73)

HRP(+) = High Risk Plaque present; HRP(–) = High Risk Plaque absent
SS(+) = Stenosis ≥70% in any coronary artery or ≥50% in the left main coronary artery; SS(–) = otherwise.

eTable 3. Results of univariable and multivariable Cox proportional hazard analysis demonstrating the predictive value of high-risk plaque for the outcome of major adverse cardiovascular events (death, non-fatal myocardial infarction, or hospitalization for unstable angina pectoris) in patient subgroups.

Subgroup	Prevalence – n/N (%)	Incidence proportion – n/N (%)	Incidence proportion for non-positive group – n/N (%)	HR (95% CI)	HR (95% CI) adjusted for significant stenosis and ASCVD risk score
Overall	676/4,415 (15.3)	43/676 (6.3)	88/3739 (2.4)	2.73 (1.89–3.93)	1.72 (1.13–2.62)
Sex					
Women	248/2,283 (10.9)	14/248 (5.7)	40/2,035 (2.0)	2.89 (1.58–5.33)	2.41 (1.25–4.64)
Men	428/2,132 (20.1)	29/428 (6.8)	48/1,704 (2.8)	2.43 (1.53–3.85)	1.40 (0.81–2.39)
Age					
< median age	303/2,207 (13.7)	23/303 (7.6)	29/1,904 (1.5)	5.07 (2.93–8.76)	2.33 (1.20–4.51)
≥ median age	373/2,208 (16.9)	20/373 (5.4)	59/1,835 (3.2)	1.68 (1.01–2.79)	1.36 (0.77–2.39)
BMI					
< median BMI	375/2,188 (17.1)	26/375 (6.9)	47/1,813 (2.6)	2.71 (1.68–4.38)	1.95 (1.13–3.35)
≥ median BMI	297/2,188 (13.6)	16/297 (5.4)	41/1,891 (2.2)	2.49 (1.40–4.43)	1.31 (0.66–2.57)
Diabetes mellitus					
No diabetes	530/3,507 (15.1)	34/530 (6.4)	68/2,977 (2.3)	2.83 (1.88–4.27)	1.68 (1.04–2.70)
Diabetes	146/908 (16.1)	9/146 (6.2)	20/762 (2.6)	2.41 (1.10–5.30)	1.69 (0.67–4.23)
Smoking					
No smoking	256/2,158 (11.9)	13/256 (5.1)	34/1,902 (1.8)	2.75 (1.45–5.22)	1.51 (0.71–3.22)
Smoking	420/2,256 (18.6)	30/420 (7.1)	54/1,836 (2.9)	2.51 (1.61–3.93)	1.76 (1.06–2.93)
Race					
Non-Hispanic white	527/3,401 (15.5)	34/527 (6.5)	70/2,874 (2.4)	2.65 (1.76–3.99)	1.70 (1.07–2.70)
Other race/ethnicity	139/969 (14.3)	8/139 (5.8)	18/830 (2.2)	2.70 (1.17–6.21)	1.78 (0.66–4.81)