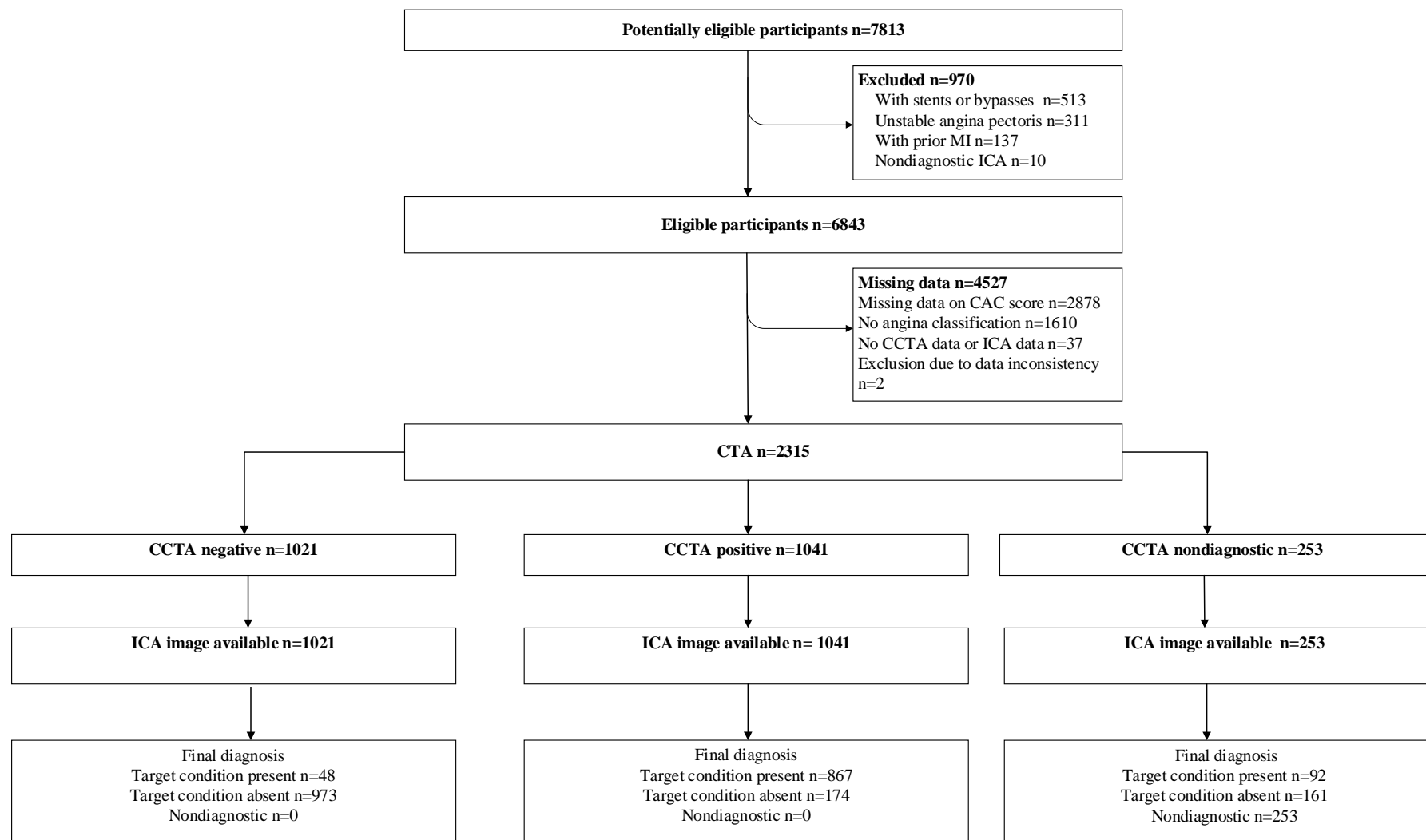


Combination of computed tomography angiography with coronary artery calcium score for improved diagnosis of coronary artery disease: a collaborative meta-analysis of stable chest pain patients referred for invasive coronary angiography

Electronic Supplementary Material

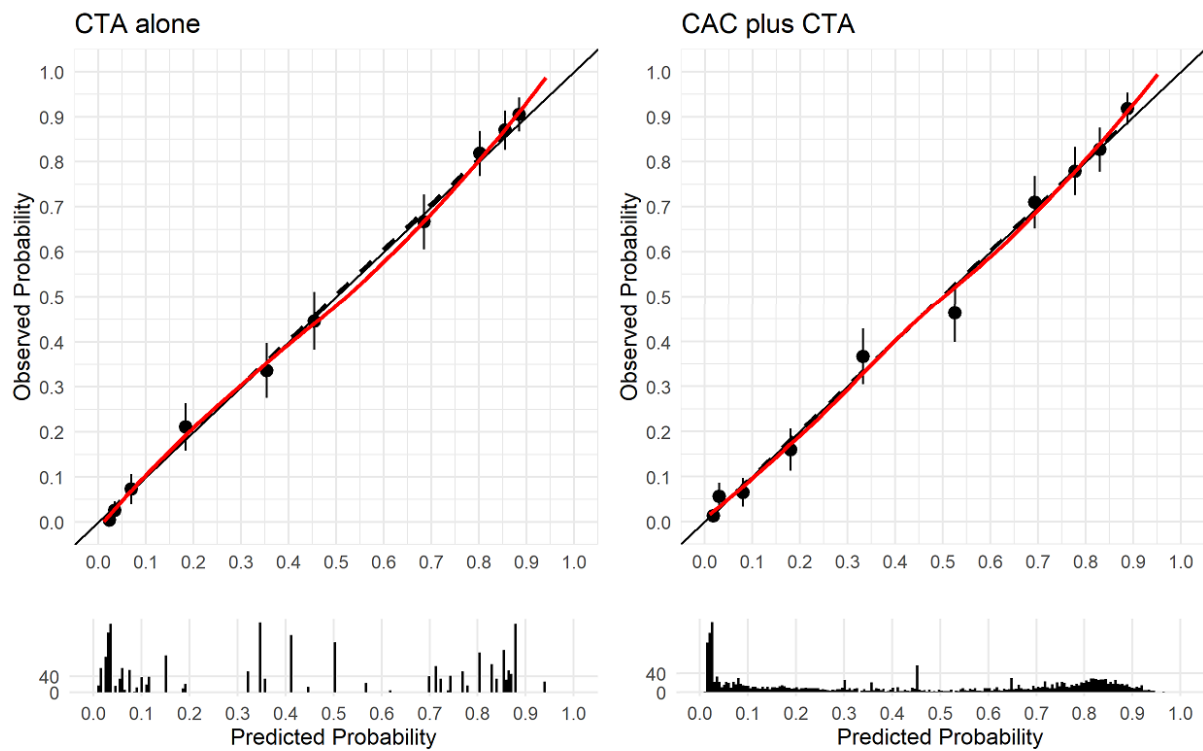
APPENDIX RESULTS

Appendix Figure 1: Flowchart

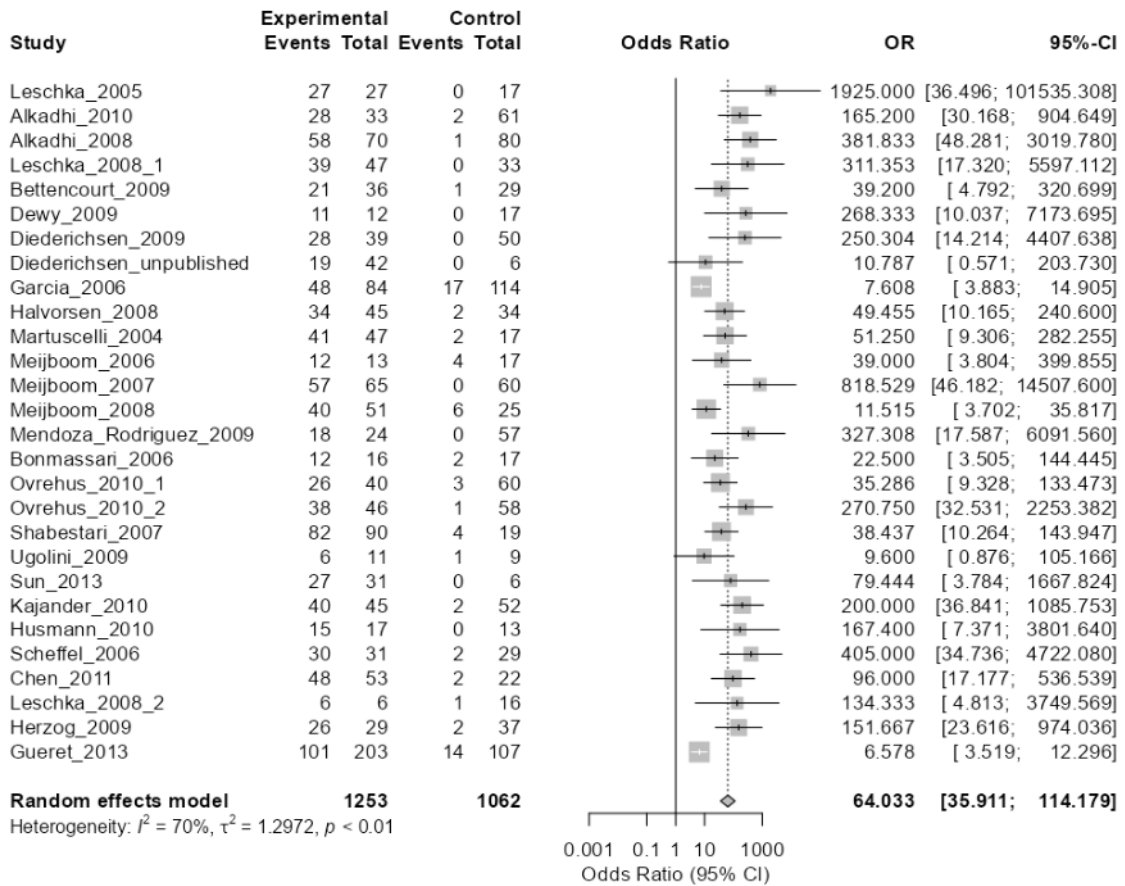


Overall, 2315 patients with complete data on age, gender, chest pain type, and CAC score from 29 studies were included from the CoMe-CCT dataset (7813 patients from 76 studies)

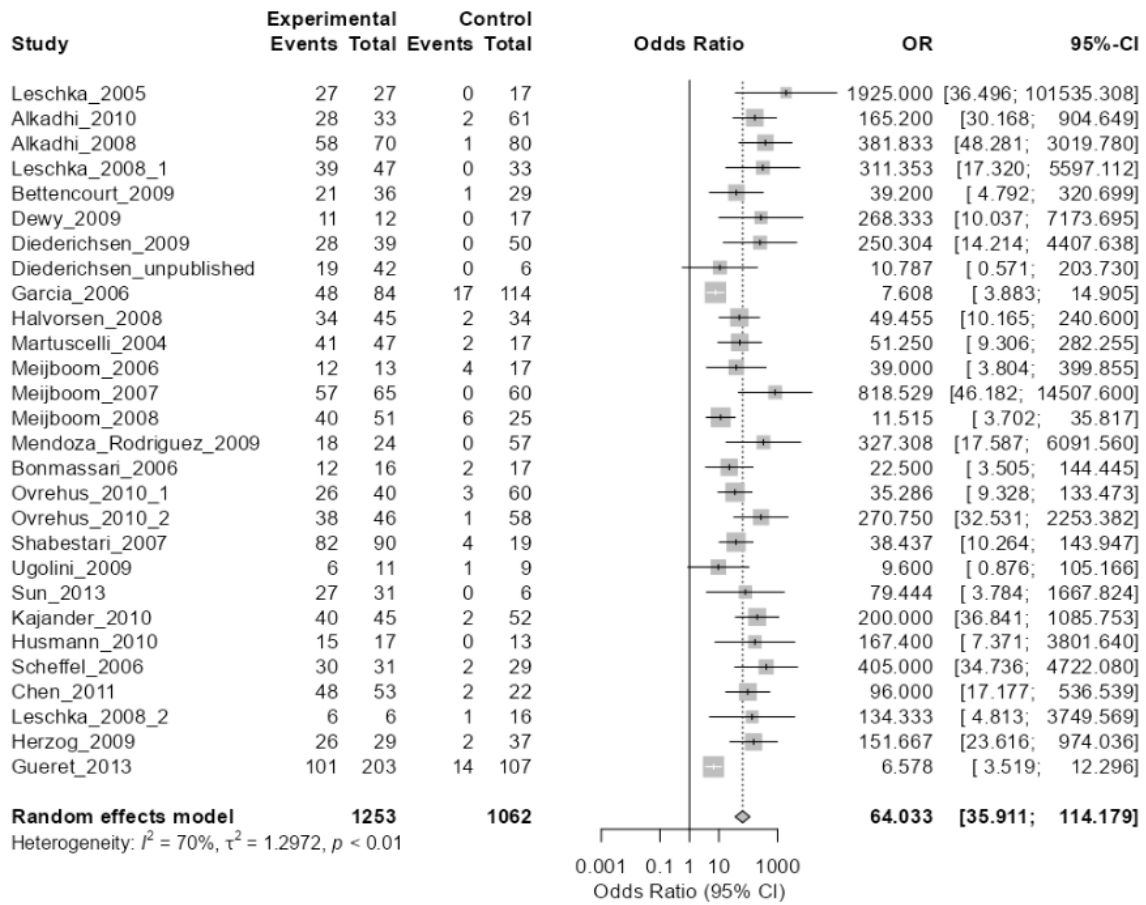
Appendix Figure 2: Calibration plot of the CAC-plus-CTA model and CTA-alone model



Appendix Figure 3: Forest plot of the CTA-alone model.



Appendix Figure 4: Forest plot of the CAC-plus-CTA model.



Appendix Table 1. Internal validation for CAC-plus-CTA model and CTA-alone model					
Performance Measure	Original Model	Bootstrap Sample	Original Sample	Optimism	Bootstrap corrected
CTA-alone model					
AUC ^a	80.2%	80.4%	80.4%	0.0000	80.2%
Brier Score ^b	0.149	0.149	0.149	0.0002	0.149
Scaled Brier Score ^c	0.4	0.4	0.4	0.00	0.4
Discrimination Slope ^d	0.400	0.397	0.396	0.000	0.399
Calibration Slope ^e	0.994	0.982	0.994	-0.0117	1.006
CAC-plus-CTA model					
AUC ^a	87.2%	87.2%	87.1%	-0.00002	87.2%
Brier Score ^b	0.132	0.132	0.132	0.000	0.132
Scaled Brier Score ^c	0.47	0.47	0.47	0.0001	0.47
Discrimination Slope ^d	0.455	0.454	0.455	-0.0013	0.456
Calibration Slope ^e	0.984	0.971	0.985	-0.0136	0.998
^a AUC: area under the receiver-operating-characteristic curve as a concordance statistics ^b Brier score: measuring the accuracy of probabilistic predictions by quantifying the prediction error. A perfect model has a zero Brier score ^c Scaled Brier score: is scaled by its maximum score and accounts for the outcome (CAD) prevalence. A perfect model has a score of 1 ^d Discrimination slope: is the difference in mean of predicted probabilities between disease (CAD) and no disease (no CAD) ^e Calibration slope: measures the agreement between the actual outcome and predicted probabilities.					

Appendix Table 2. Diagnostic Performance of CAC-plus-CTA and CTA-alone model			
	CAC plus CTA	CTA alone	p-value*
	<i>n/total n (% [95% CI*])</i>	<i>n/total n (% [95% CI*])</i>	
Diagnostic accuracy	1895 / 2315 (81.9% [81.7-82.0])	1840 / 2315 (79.5% [79.4-79.7])	<0.0001
Sensitivity	846/1007 (83.9% [81.6-86.2])	867 / 1007 (86.1% [84.0-88.2])	<0.021
Specificity	1050 / 1308 (80.3% [78.1-82.4])	973/1308 (74.4% [72.0-86.8])	<0.0001
Positive predictive value	846 / 1103 (76.6% [74.1-79.1])	867/1202 (72.1% [69.6-74.7])	<0.0001
Negative predictive value	1050/ 1212 (86.6% [84.7-88.5])	973/1113 (87.4% [85.5-89.4])	0.257

Appendix Table 3. Estimates of the mixed-effect logistic regression model of CTA-alone and CAC-plus-CTA models (n=2315)

	Estimate (S.E.)	p value	Odds Ratio (95% CI)
CTA-alone model			
CTA	2.91 (0.116)	< 0.001	18.3 (14.63 to 23.03)
Model constant	-1.897 (0.124)	—	—
Random intercept (τ^2)^b	0.167(0.411)		
BIC	2256.9		
logLik	-1116.8		
CAC-plus-CTA model			
Log CAC score ^c	0.362 (0.026)	< 0.001	1.44 (1.37 to 1.51)
CTA	2.67 (0.123)	< 0.001	14.51 (11.42 to 18.54)
Model constant	-3.257 (0.183)	—	—
Random intercept (τ^2)^b	0.272 (0.522)		
BIC	2028.4		
logLik	-998.7		
BIC: Bayesian information criterion			
^a Typical angina is defined as: retrosternal chest discomfort, precipitation by exertion, and prompt relief (within 30 s-10 min) by rest or nitroglycerin. Patients in whom two, one, or none of these three criteria were found were classified as having atypical angina, nonanginal chest discomfort, and other chest discomfort, respectively.			
^b Variance component estimate (τ^2) for random intercept			
^c Log CAC score was used to overcome its nonnormality.			
CAC cut-off value = $e^{(\beta_{CTA}/\beta_{\log CAC})} = 1715$			

Appendix Table 4. Likelihood ratio test comparing the CTA-alone and CAC-plus-CTA models (n=2315)

	BIC	logLik	Deviance	X ²	p value
CTA alone	2256.9	-1116.8	2233.7		
CAC plus CTA	2028.4	-998.7	1997.4	236.25	<0.001