Supplemental Online Content

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

eTable 1. Baseline Characteristics in Minimal-Risk vs Elevated-Risk Participants in the PRECISE Trial

Variable	Minimal-Risk Participants (N = 422)	Elevated-Risk Participants (N = 1681)
Age*, mean (SD), y	45.6 (8.6)	61.7 (9.8)
Sex*		
Male	118/422 (28.0%)	938/1681 (55.8%)
Female	304/422 (72.0%)	743/1681 (44.2%)
White/Non-Hispanic*	313/422 (74.2%)	1454/1681 (86.5%)
Body mass index, mean (SD), kg/m^2	30.0 (7.5)	30.0 (6.1)
Cardiovascular risk factor history		
Diabetes mellitus*	37/422 (8.8%)	336/1681 (20.0%)
Dyslipidemia*	139/422 (32.9%)	1210/1681 (72.0%)
Family history of premature (age <55 y)* coronary artery disease	146/422 (34.6%)	653/1681 (38.8%)
Hypertension*	126/422 (29.9%)	1122/1681 (66.7%)
Current/former smoker*	147/422 (34.8%)	951/1681 (56.6%)
Risk scores		
PROMISE Minimal Risk Score		
Mean (SD)	0.633 (0.128)	0.203 (0.123)
Median (Q1, Q3)	0.609 (0.526, 0.721)	0.182 (0.099, 0.296)
Diamond–Forrester pretest probability score, mean (SD)	32.1 (22.6)	61.3 (23.1)
Euro 2019 pretest probability score, mean (SD)	7.3 (3.8)	20.6 (11.5)
PCE 10-Year risk score, mean (SD)	2.44 (2.22)	14.15 (11.58)
Primary symptom		
Chest pain/pressure/tightness - substernal or left anterior	338/422 (80.1%)	1222/1681 (72.7%)
Chest pain/pressure/tightness - other location	40/422 (9.5%)	146/1681 (8.7%)
Arm or shoulder pain	5/422 (1.2%)	20/1681 (1.2%)
Back pain	1/422 (0.2%)	2/1681 (0.1%)
Dizziness/lightheaded	2/422 (0.5%)	8/1681 (0.5%)
Epigastric pain/abdominal pain	5/422 (1.2%)	17/1681 (1.0%)
Palpitations	14/422 (3.3%)	28/1681 (1.7%)
Shortness of breath/dyspnea	17/422 (4.0%)	195/1681 (11.6%)
Symptoms related to physical/mental stress *		
Yes, occurs with mild exertion/mild stress	75/422 (17.8%)	462/1681 (27.5%)
Yes, occurs with moderate exertion/moderate stress	88/422 (20.9%)	480/1681 (28.6%)

Variable	Minimal-Risk Participants (N = 422)	Elevated-Risk Participants (N = 1681)
Yes, occurs with strenuous exertion/severe stress	15/422 (3.6%)	60/1681 (3.6%)
No, unrelated to exertion or stress	223/422 (52.8%)	620/1681 (36.9%)
Unknown	21/422 (5.0%)	59/1681 (3.5%)
Site characterization of the primary symptom		
Typical angina	67/422 (15.9%)	439/1681 (26.1%)
Atypical	288/422 (68.2%)	909/1681 (54.1%)
Non-cardiac Pain	8/422 (1.9%)	13/1681 (0.8%)
Dyspnea	20/422 (4.7%)	143/1681 (8.5%)
Unable to characterize	39/422 (9.2%)	177/1681 (10.5%)
Systolic blood pressure, mean (SD), mmHg	126.4 (14.3)	134.1 (17.5)
Diastolic blood pressure, mean (SD), mmHg	78.4 (10.4)	79.8 (10.2)

Abbreviation: PCE: Pooled Cohort Equations. *indicates characteristics included in the PROMISE Minimal Risk Score.

Data shown are n/N (%) except where indicated

eTable 2: Medication Use at Each Visit, Stratified by Baseline Use

Variable	Minimal-Risk Deferred Testing Arm (N = 214)	Minimal-Risk Usual Testing Arm (N = 208)	CMH P-Value
Beta blocker usage at baseline	30/214 (14.0%)	23/208 (11.1%)	
Beta blocker usage at 45 days	30/195 (15.4%)	26/188 (13.8%)	0.63
Beta blocker usage at 6 months	28/164 (17.1%)	20/165 (12.1%)	0.47
Beta blocker usage at 12 months	23/160 (14.4%)	18/158 (11.4%)	0.36
Calcium channel blocker usage at baseline	17/214 (7.9%)	9/208 (4.3%)	
Calcium channel blocker usage at 45 days	15/195 (7.7%)	10/188 (5.3%)	0.77
Calcium channel blocker usage at 6 months	11/164 (6.7%)	10/165 (6.1%)	0.92
Calcium channel blocker usage at 12 months	11/160 (6.9%)	10/158 (6.3%)	0.77
Short-acting nitrates usage at baseline	11/214 (5.1%)	5/208 (2.4%)	
Short-acting nitrates usage at 45 days	10/195 (5.1%)	6/188 (3.2%)	0.69
Short-acting nitrates usage at 6 months	7/164 (4.3%)	3/165 (1.8%)	0.67
Short-acting nitrates usage at 12 months	7/164 (4.3%)	3/165 (1.8%)	0.58
Long-acting nitrates usage at baseline	3/214 (1.4%)	2/208 (1.0%)	
Long-acting nitrates usage at 45 days	4/195 (2.1%)	4/188 (2.1%)	0.54
Long-acting nitrates usage at 6 months	0/164 (0.0%)	2/165 (1.2%)	0.22
Long-acting nitrates usage at months	0/160 (0.0%)	2/158 (1.3%)	0.22
Antiplatelet usage at baseline	24/214 (11.2%)	23/208 (11.1%)	
Antiplatelet usage at 45 days	26/195 (13.3%)	19/188 (10.1%)	0.387
Antiplatelet usage at 6 months	20/164 (12.2%)	15/165 (9.1%)	0.191
Antiplatelet usage at 12 months	19/160 (11.9%)	10/158 (6.3%)	0.060
Lipid-lowering med usage at baseline	33/214 (15.4%)	23/208 (11.1%)	
Lipid-lowering med usage at 45 days	33/195 (16.9%)	24/188 (12.8%)	0.601
Lipid-lowering med usage at 6 months	27/164 (16.5%)	15/165 (9.1%)	0.105
Lipid-lowering med usage at 12 months	26/160 (16.3%)	17/158 (10.8%)	0.558
Anti-hypertensive usage at baseline	73/214 (34.1%)	55/208 (26.4%)	
Anti-hypertensive usage at 45 days	64/195 (32.8%)	52/188 (27.7%)	0.784
Anti-hypertensive usage at 6 months	51/164 (31.1%)	44/165 (26.7%)	0.715
Anti-hypertensive usage at 12 months	48/160 (30.0%)	43/158 (27.2%)	0.527

Abbreviation: CMH: Cochran–Mantel–Haenszel.

eTable 3: Participants Identified as Minimal Risk by the PROMISE Minimal Risk Score with Significant or Severe Initial Test Findings

Randomization Arm	Test Results	Clinical History
Positive Initial Test Followed by ICA and Revascularization		
Deferred Testing	CCTA ICA	39yoF HTN, HLD presented with CP. CCTA with multi-vessel disease (severe RCA, moderate prox LAD, significant mid LAD, mild in LCX). ICA with 3VD. Referred for CABG
Usual Testing	Nuclear Stress ICA	55yoF HLD, presented with CP found to have large reversible defect in LAD distribution. ICA with severe stenosis in proximal LAD and LCX. Referred for PCI to both vessels.
Positive Initial Test Without Follow-up Testing		
Deferred Testing	CCTA	49yoF HTN, HLD presented with CP. CCTA with CAC 207, mild stenosis in RCA and LAD, with positive FFR_{CT} in a diagonal, LAD distal and RCA branch vessels. No further testing.
Usual Testing	Nuclear Stress	49yoF presented with CP, ischemia in apical lateral wall. No further testing.
Usual Testing	Stress TTE	42yoF HTN, presented with CP found to have resting EF 40% on TTE and walls did not augment. No further testing.
"False Positive" Initial Test		
Usual Testing	Nuclear ICA	53yoF, nuclear stress with anterior ischemia. ICA normal coronaries
Usual Testing	Exercise ECG Stress TTE	53yoF HTN, HLD presented with dyspnea, stress ECG w/hypertensive response to exercise and positive ST changes. Stress echo normal.
Usual Testing	Nuclear ICA	28yoM presented with CP, nuclear stress with inferior/posterior ischemia. ICA normal coronaries
Usual Testing	Stress MRI CCTA	51yoF HLD, HTN, presented with CP, MRI anterior stress perfusion defect.

		CCTA < 25% stenosis in RCA, otherwise normal coronaries
Usual Testing	Stress Echo CCTA	46yoF presented with CP, stress TTE with septal/anterior/apical ischemia. CCTA normal coronaries
Usual Testing	Exercise ECG ICA	55yoF h/o presented with dyspnea, stress ECG positive. ICA with < 50% in LAD otherwise normal
Usual Testing	Nuclear Stress CCTA	40yoM presented with CP, nuclear w/ischemia in septal/anterior/apical walls. CCTA normal coronaries
Usual Testing	Nuclear Stress ICA	55yoF HLD, HTN, presented with CP, nuclear with septal/anterior/apical ischemia. ICA normal coronaries.
Usual Testing	Nuclear Stress ICA	50yoF evaluated with nuclear stress which showed artifact vs inferior ischemia, ICA with normal coronaries and normal coronary flow reserve in RCA

Abbreviations: CABG: coronary artery bypass grafting; CAC: coronary artery calcium score; CCTA: coronary computed tomographic angiography; CP: chest pain; ECG: electrocardiogram; FFR: fractional flow reserve: HLD: hyperlipidemia; HTN: hypertension; ICA: invasive coronary angiography; LAD: left anterior descending; LCX: left circumflex; MRI: magnetic resonance imaging; PCI: percutaneous coronary intervention; RCA: right coronary artery; TTE: transthoracic echocardiography; 3VD: 3-vessel disease.

False positive defined as initial testing showing significant or severe abnormal findings with subsequent test showing normal or only mildly abnormal findings.

eFigure 1: Kaplan–Meier Estimates of the Composite Primary Endpoint as a Function of Time after Randomization

Shown are unadjusted Kaplan–Meier estimates of the primary composite endpoint (death from any cause, nonfatal MI, invasive catheterization without significant CAD). In an unadjusted Cox model of time to the composite primary endpoint, the HR (95% CI) for the precision arm deferred testing group compared to the usual testing group was 0.15 (0.03, 0.66), p=0.012. The inset shows the same data on an enlarged y-axis.