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A Placebo-Controlled Trial of Percutaneous Coronary Intervention for Stable Angina

C.A. Rajkumar, M.J. Foley, F. Ahmed-Jushuf, A.N. Nowbar, F.A. Simader, J.R. Davies, P.D. O'Kane, P. Haworth, H. Routledge, T. Kotecha, R. Gamma, G. Clesham, R. Williams, J. Din, S.S. Nijjer, N. Curzen, N. Ruparelia, M. Sinha, J.N. Dungu, S. Ganesananthan, R. Khamis, L. Mughal, T. Kinnaird, R. Petraco, J.C. Spratt, S. Sen, J. Sehmi, D.J. Collier, A. Sohaib, T.R. Keeble, G.D. Cole, J.P. Howard, D.P. Francis, M.J. Shun-Shin, and R.K. Al-Lamee, for the ORBITA-2 Investigators*

Table 2. Eligibility criteria. Participants require all 3 to enrol.

1. Angina or angina-equivalent symptoms
2. Anatomical evidence of a severe coronary stenosis in at least 1 vessel, either: – Invasive diagnostic coronary angiography indicating ≥70% stenosis – Computerised tomography coronary angiography (CTCA) indicating severe stenosis
3. Evidence of ischaemia, on any of the following tests: – Dobutamine stress echocardiography – Stress perfusion cardiac magnetic resonance imaging (MRI) – Nuclear medicine myocardial perfusion scan – Invasive pressure wire assessment suggestive of ischaemia, as judged by the interventional cardiologist, at the time of clinical or research coronary angiography

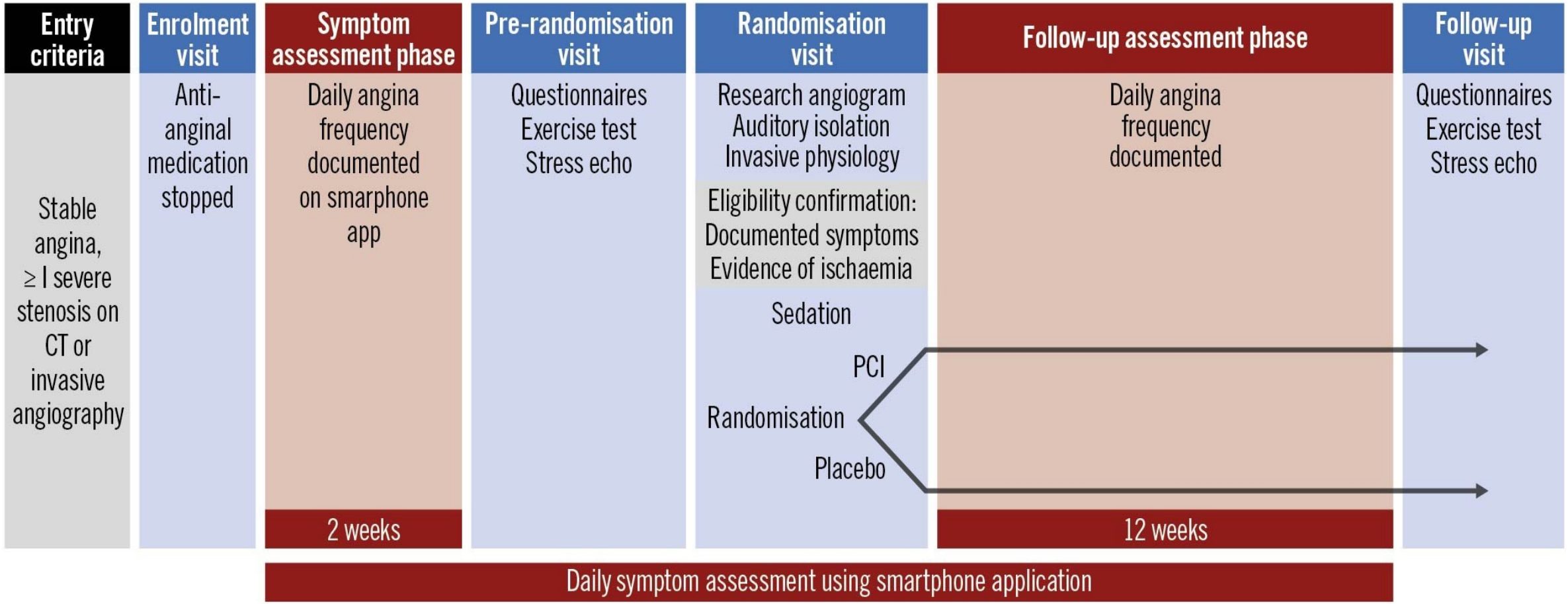

Entry criteria
Stable angina, ≥ I severe stenosis on CT or invasive angiography
Enrolment visit
Anti-anginal medication stopped
Symptom assessment phase
Daily angina frequency documented on smarphone app
2 weeks
Pre-randomisation visit
Questionnaires
Exercise test
Stress echo
Randomisation visit
Research angiogram
Auditory isolation
Invasive physiology
Eligibility confirmation:
Documented symptoms
Evidence of ischaemia
Sedation
PCI
Randomisation
Placebo
Follow-up assessment phase
Daily angina frequency documented
12 weeks
Follow-up visit
Questionnaires
Exercise test
Stress echo
Daily symptom assessment using smartphone application

Table 1. Demographic and Baseline Clinical Characteristics.*

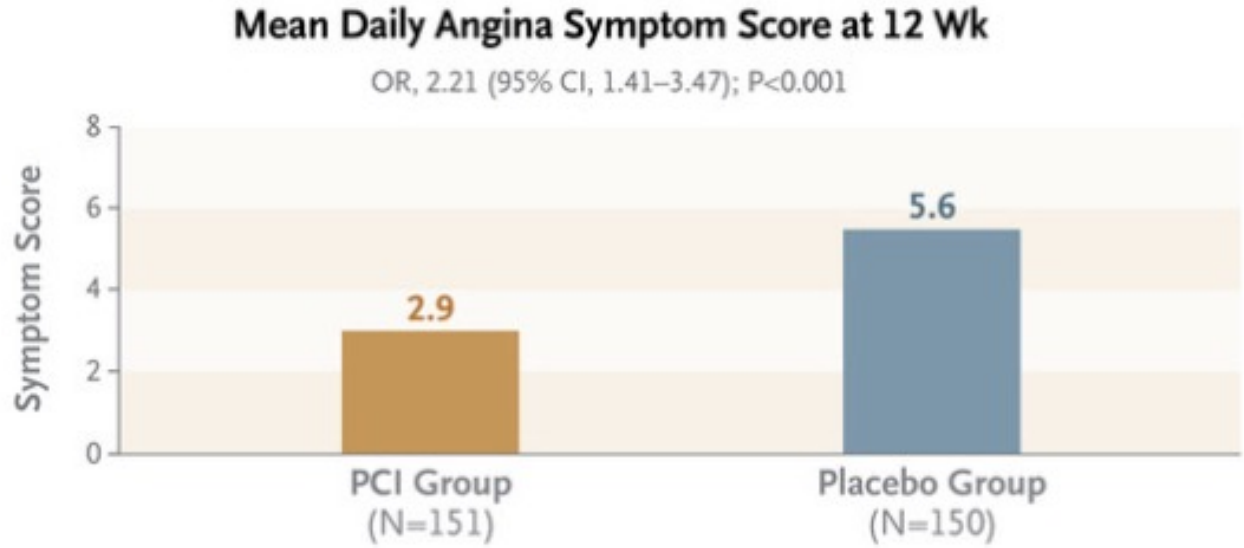
Characteristic	PCI (N=151)	Placebo (N=150)	Overall (N=301)
Age — yr	65±9	64±9	64±9
Male sex — no. (%)	120 (79)	118 (79)	238 (79)
Hypertension — no. (%)	97 (64)	92 (61)	189 (63)
Diabetes — no. (%)			
Non–insulin-dependent	40 (26)	24 (16)	64 (21)
Insulin-dependent	9 (6)	11 (7)	20 (7)
Hyperlipidemia — no. (%)	113 (75)	104 (69)	217 (72)
Smoking status — no. (%)			
Never smoked	65 (43)	50 (33)	115 (38)
Previous smoker	67 (44)	84 (56)	151 (50)
Current smoker	19 (13)	16 (11)	35 (12)
Left ventricular systolic function — no. (%)†			
Normal	144 (95)	146 (97)	290 (96)
Mild impairment	6 (4)	3 (2)	9 (3)
Moderate impairment	1 (1)	1 (1)	2 (1)
CCS class — no. (%)‡			
I	10 (7)	1 (1)	11 (4)
II	87 (58)	87 (58)	174 (58)
III	54 (36)	62 (41)	116 (39)
Median time since diagnosis of angina (IQR) — mo	8 (4–14)	8 (5–14)	8 (5–14)

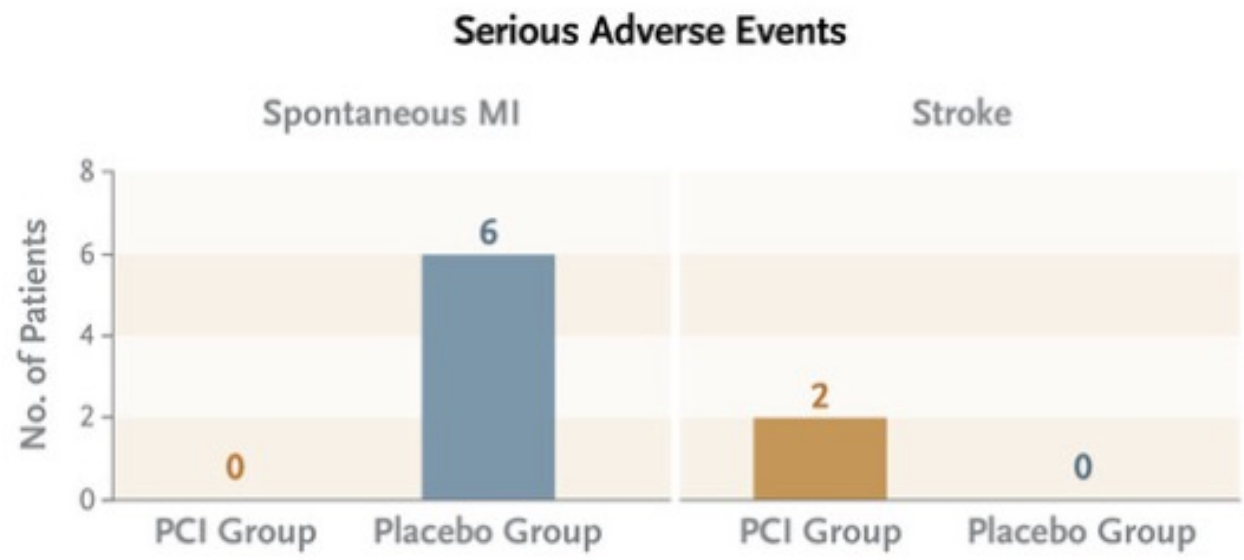
Table 2. Procedural Characteristics.

Characteristic	PCI (N=151)	Placebo (N=150)	Overall (N=301)
No. of vessels with disease — no. (%)*			
1 vessel	122 (81)	120 (80)	242 (80)
2 vessels	25 (17)	27 (18)	52 (17)
3 vessels	4 (3)	3 (2)	7 (2)
Vessels leading to patient randomization†			
No. of vessels	193	190	383
Left anterior descending coronary artery — no. (%)	108 (56)	103 (54)	211 (55)
Circumflex coronary artery — no. (%)	16 (8)	17 (9)	33 (9)
Right coronary artery — no. (%)	42 (22)	43 (23)	85 (22)
Branch vessels — no. (%)	27 (14)	27 (14)	54 (14)
Serial stenoses — no. (%)	29 (19)	20 (13)	49 (16)
Percent diameter stenosis‡			
Mean	61±18	62±17	61±18
Median (IQR)	60 (48–74)	63 (50–74)	61 (49–74)
Area of stenosis‡			
Percentage	80±15	82±15	81±15
Median (IQR) — %	83 (73–92)	85 (75–93)	84 (74–92)
Fractional flow reserve			
Mean	0.60±0.16	0.62±0.16	0.61±0.16
Median (IQR)	0.61 (0.47–0.74)	0.65 (0.51–0.75)	0.63 (0.49–0.75)
No. of vessels assessed — no./total no. of target vessels	178/193	171/190	349/383
Instantaneous free-wave ratio§			
Mean	0.68±0.22	0.71±0.23	0.70±0.22
Median (IQR)	0.76 (0.50–0.86)	0.81 (0.58–0.89)	0.78 (0.55–0.87)
No. of vessels assessed — no./total no. of target vessels	178/193	174/190	352/383
Interventions			
Median no. of stents implanted (IQR)	2 (1–2)	—	—
Median total length of stent implanted (IQR) — mm	42 (23–64)	—	—
Median diameter of stent implanted (IQR) — mm	3.0 (2.5–3.5)	—	—
No. of stents in which postdilation was performed — no./total no. (%)	242/284 (85)	—	—
Intravascular imaging performed — no. (%)	104 (69)	—	—
Type of drug-eluting stent¶			
Everolimus-eluting — no. (%)	171 (60)	—	—
Zotarolimus-eluting — no. (%)	83 (29)	—	—
Other drug-eluting stent — no. (%)	29 (10)	—	—

Table 3. Primary and Secondary End Points.*

End Point	PCI (N=151)		Placebo (N=150)		Odds Ratio or Difference (95% CI)†
	value	*no. of patients with data*	*value*	*no. of patients with data*	
Primary end point: angina symptom score — mean score‡	2.9	151	5.6	150	2.21 (1.41 to 3.47)§
Mean daily angina episodes — no.	0.3	151	0.7	150	3.44 (2.00 to 5.91)
Mean daily antianginal medication use — units¶	0.2	151	0.3	150	1.21 (0.70 to 2.10)
Secondary end points					
Mean treadmill exercise time — sec	700.9	123	641.4	112	59.5 (16.0 to 103.0)
CCS class — mean	0.9	147	1.7	146	3.76 (2.43 to 5.82)
End points assessed with the use of the SAQ‖					
Frequency of angina	80.6	146	66.2	145	14.4 (9.5 to 19.4)
Physical limitation	82.7	139	73.9	144	8.8 (4.7 to 12.9)
Angina stability	61.8	145	55.3	145	6.5 (0.5 to 12.5)
Quality of life	62.8	145	51.6	145	11.2 (6.2 to 16.1)
Freedom from angina	40	146	15	145	3.69 (2.10 to 6.46)
EQ-5D-5L descriptive system — mean score**	0.82	145	0.73	144	0.09 (0.05 to 0.13)
EQ-VAS — mean score**	73.1	146	66.9	143	6.2 (2.4 to 10.0)
Stress echocardiography score — mean score††	0.79	119	1.95	111	−1.17 (−1.56 to −0.78)


Mean Daily Angina Symptom Score at 12 Wk
OR, 2.21 (95% CI, 1.41–3.47); P<0.001
Symptom Score
8
6
4
2
0
2.9
5.6
PCI Group
(N=151)
Placebo Group
(N=150)


Serious Adverse Events
Spontaneous MI
Stroke
No. of Patients
8
6
4
2
0
0
6
2
0
PCI Group
Placebo Group
PCI Group
Placebo Group

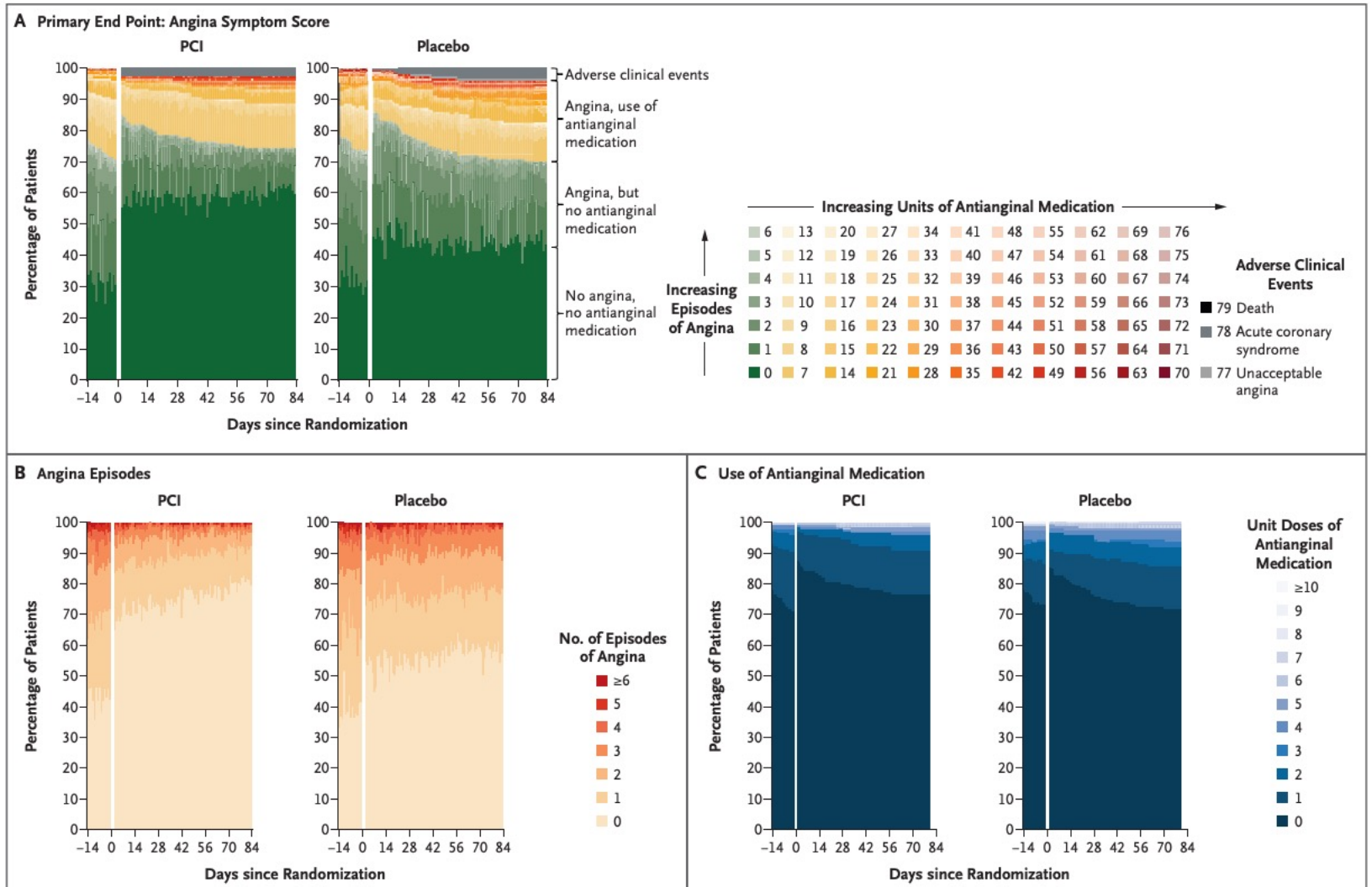
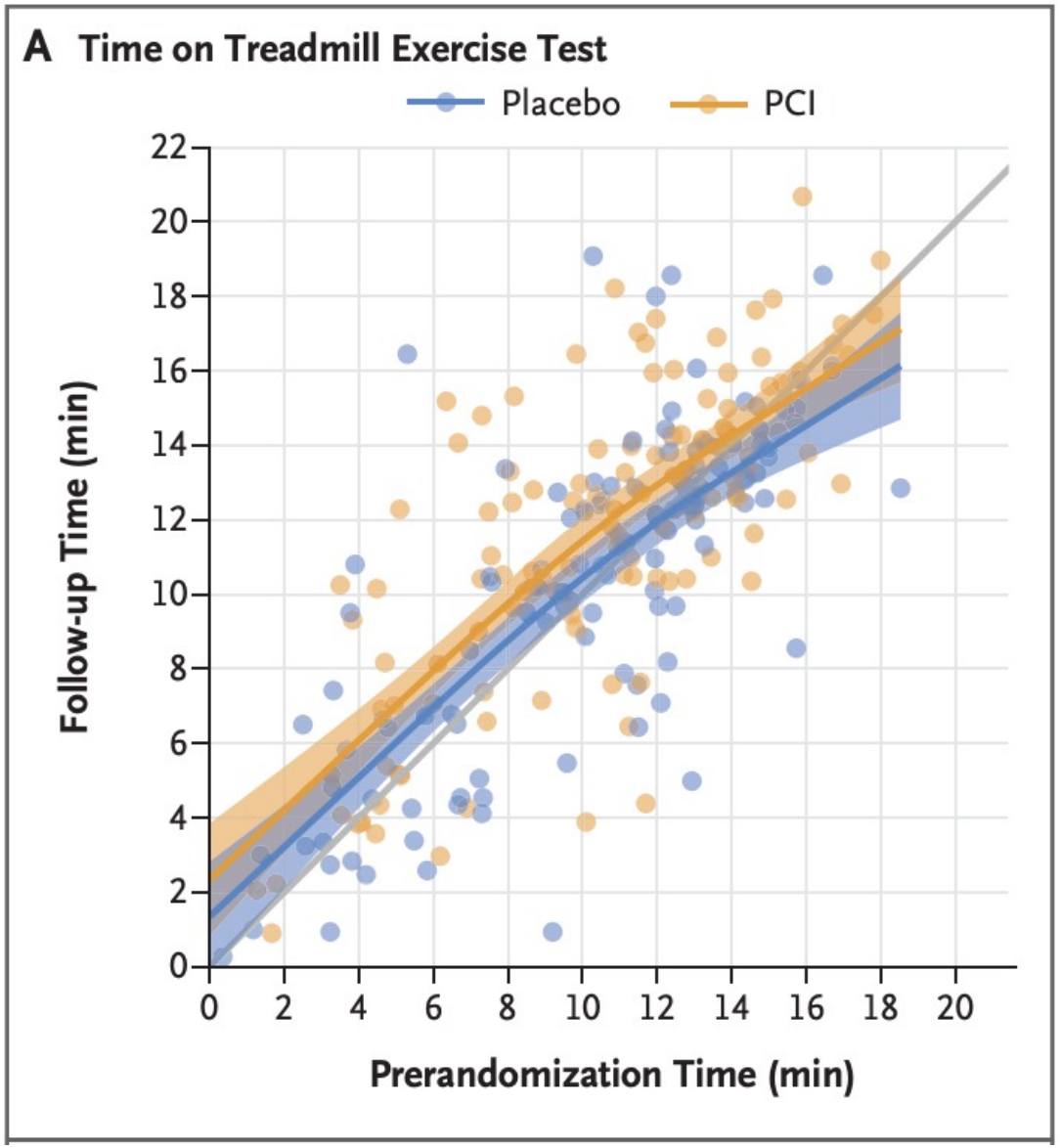
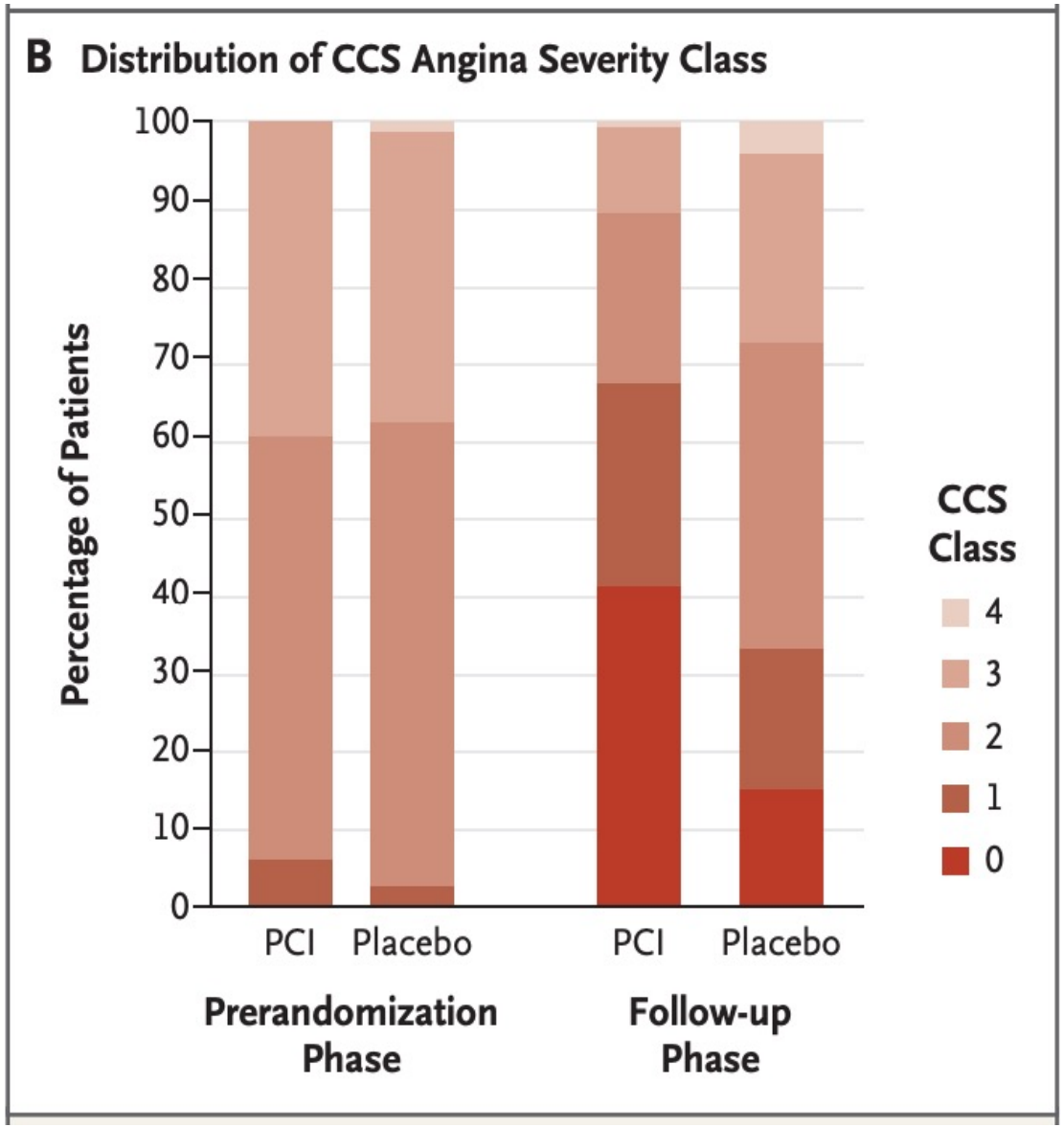


Figure 1. Angina Symptom Score and Its Components.

Panel A shows the individual patient data composition of the primary end point, angina symptom score, according to trial group. The method for derivation of the score is depicted to the right of the individual patient data, and the overall calculated scores are shown next to the colored boxes. Panel B shows the individual patient data for daily angina episodes, irrespective of the number of units of antianginal medication that were prescribed. Panel C shows the number of units of antianginal medications that were prescribed for each patient on each day of the trial. PCI denotes percutaneous coronary intervention.





Panel A shows the treadmill exercise time at the 12-week follow-up according to the prerandomization exercise time. The shaded areas indicate 95% confidence intervals. Panel B shows the distribution of the physicianassessed Canadian Cardiovascular Society (CCS) angina severity class during the prerandomization and followup phases. The CCS class ranges from 0 to IV, with class 0 indicating no angina and class IV indicating angina at rest. The widths of the confidence intervals have not been adjusted for multiplicity; therefore, they should not be used to make definitive conclusions regarding the effects of PCI.

CONCLUSIONS

Among patients with stable angina who were receiving little or no antianginal medication and who had objective evidence of ischemia, PCI resulted in a better health status with respect to angina than a placebo procedure at 12 weeks.

LIMITATIONS AND REMAINING QUESTIONS

- The duration of follow-up was only 12 weeks.
- The withdrawal of patients' antianginal medication may have led to behavioral changes that could have affected outcomes.
- The smartphone application that patients used to report symptoms was available in English only; translation was provided as necessary.