Preventive PCI for Vulnerable Plaque

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Vulnerable Plaque, Past

Circadian variation and triggers of onset of acute cardiovascular disease

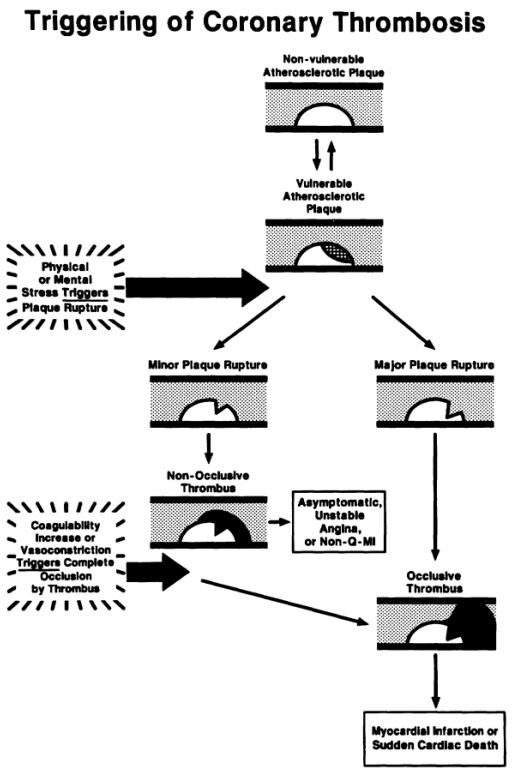

FIGURE 3. *Illustration of a hypothetical method by which daily activities may trigger coronary thrombosis. Three triggering mechanisms, 1) physical or mental stress producing hemodynamic changes leading to plaque rupture, 2) activities causing a coagulability increase, and 3) stimuli leading to vasoconstriction, have been added to the well-known scheme depicting the role of coronary thrombosis in unstable angina, myocardial infarction, and sudden cardiac death. See text for detailed discussion.*

J E Muller 1, G H Tofler, P H Stone, Circulation. 1989;79:733-743

Journal of the American College of Cardiology
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Published by Elsevier Inc.

Vol. 47, No. 8 Suppl C
ISSN 0735-1097/06/$32.00
doi:10.1016/j.jacc.2005.10.065

Pathology of the Vulnerable Plaque

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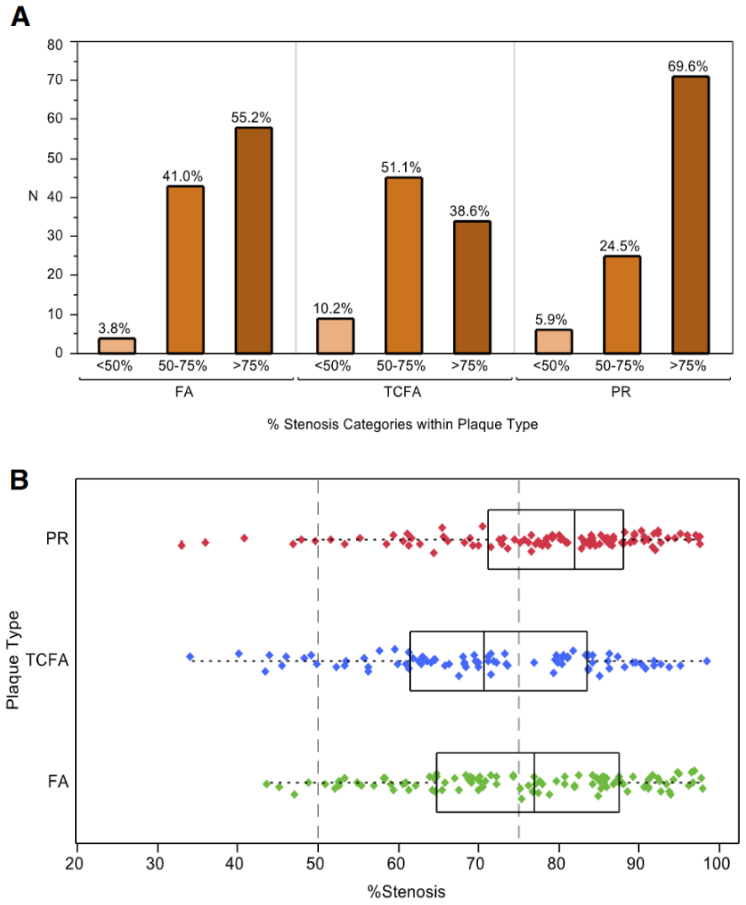
The majority of patients with acute coronary syndromes (ACS) present with unstable angina, acute myocardial infarction, and sudden coronary death. The most common cause of coronary thrombosis is plaque rupture followed by plaque erosion, whereas calcified nodule is infrequent. If advances in coronary disease are to occur, it is important to recognize the precursor lesion of ACS. Of the three types of coronary thrombosis, a precursor lesion for acute rupture has been postulated. The non-thrombosed lesion that most resembles the acute plaque rupture is the thin cap fibroatheroma (TCFA), which is characterized by a necrotic core with an overlying fibrous cap measuring <65 μm, containing rare smooth muscle cells but numerous macrophages. Thin cap fibroatheromas are most frequently observed in patients dying with acute myocardial infarction and least common in plaque erosion. They are most frequently observed in proximal coronary arteries, followed by mid and distal major coronary arteries. Vessels demonstrating TCFA do not usually show severe narrowing but show positive remodeling. In TCFAs the necrotic core length is approximately 2 to 17 mm (mean 8 mm) and the underlying cross-sectional area narrowing in over 75% of cases is <75% (diameter stenosis <50%). The area of the necrotic core in at least 75% of cases is ≤3 mm^2. These lesions have lesser degree of calcification than plaque ruptures. Thin cap fibroatheromas are common in patients with high total cholesterol (TC) and high TC/high-density lipoprotein cholesterol ratio, in women >50 years, and in those patients with elevated high levels of high sensitivity C-reactive protein. It has only recently been recognized that their identification in living patients might help reduce the incidence of sudden coronary death. (J Am Coll Cardiol 2006;47:C13–8) © 2006 by the American College of Cardiology Foundation

J Am Coll Cardiol 2006;47:C13–8

Vulnerable Plaque, More Recent

(Visually) 50-70% Diameter Stenosis



J Am Coll Cardiol 2013;61:1041–51

The PROSPECT study
prospectively confirmed that the mean angiographic diameter stenosis of the 106 lesions subsequently responsible for major adverse cardiovascular events was ***32±21%*** at baseline and ***65±16%*** at 3.4-year follow-up (p<0.001)

The mean stenosis of the progressed lesion was ***41.8±20.8%*** at the initial angiogram and ***83.9±13.9%*** at the time of the second angiogram, with a mean increase in stenosis severity of ***42.1±21.9%.***

Circulation. 2005;111:143–149

ACC.24

American College of Cardiology 73rd Annual Scientific Session
Late-Breaking Clinical Trial, April 7, 2024

PREVENT

Preventive PCI versus Medical Therapy Alone for Treatment of Vulnerable Atherosclerotic Coronary Plaques

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Disclosure

- The PREVENT trial was supported by an investigator-initiated grant from the CardioVascular Research Foundation, Abbott, Yuhan Corp, CAH-Cordis, Philips, and Infraredx, a Nipro company.
- The funders did not participate in the trial design, data analysis, or manuscript preparation.

Background

- Intracoronary imaging defined vulnerable plaque (VP) has more tendency to increase major adverse cardiac events.[4]
- Optimal medical therapy (OMT) is the standard approach to stabilise plaque vulnerability.
- The safety and effectiveness of focal preventive percutaneous coronary intervention (PCI) of non-flow limiting VP are unknown.

Stone GW et al. N Engl J Med 2011; 364: 226–35. Erlinge D et al. Lancet 2021; 397: 985–95.
Stone GW et al. J Am Coll Cardiol 2020; 76: 2289–301. Gaba P et al. Nat Rev Cardiol 2023; 20: 181–96.
Kedhi E et al. Eur Heart J 2021; 42: 4671–79. Mol JQ et al. JAMA Cardiol 2023; 8: 1013–21.

Objective

PREVENT

- To assess whether focal preventive PCI of non-flow-limiting, imaging defined vulnerable plaques improves clinical outcomes compared with OMT alone.

Trial Organization

PREVENT

Executive Committee Seung-Jung Park (Trial Chair), Duk-Woo Park (Co-PI), Gregg W. Stone (Co-PI) Jung-Min Ahn, Do-Yoon Kang

Additional Steering Committee Young-Keun Ahn, Won-Jang Kim, Chang-Wook Nam

Event Adjudication Committee Hanbit Park, Junghoon Lee, Ju Hyeon Kim, Jinho Lee, Hoyun Kim Yeonwoo Choi, Sangyong Jo, Kyung-Ae Kim

Data & Safety Monitoring Board June-Hong Kim, Kyoung-Ha Park, Jong-Min Song, Jon Suh Elly, Jeong-youn Bae

Participating Investigators (15 Sites in South Korea, Japan, Taiwan, and New Zealand)

Seung-Jung Park, Jung-Min Ahn, Do-Yoon Kang, Sung-Cheol Yun, Duk-Woo Park (Asan Medical Center); Young-Keun Ahn (Chonnam National University Hospital); Won-Jang Kim, Se Hun Kang (CHA Bundang Medical Center); Chang-Wook Nam (Keimyung University Dongsan Hospital); Jin-Ok Jeong, Si-Wan Choi (Chungnam National University Hospital); In-HoChae (Seoul National University Bundang Hospital); Hiroki Shiomi (Kyoto University Hospital); Hsien-Li Kao (National Taiwan University Hospital); Joo-Yong Hahn (Samsung Medical Center); Sung-Ho Her, Gyu-Seop Lee (The Catholic University of Korea, Daejeon ST. Mary's Hospital); Bong-Ki Lee (Kangwon national University Hospital); Tae Hoon Ahn, Woong Chol Kang (Gachon University Gil Medical Center); Ki-Yuk Chang (The Catholic University St. Mary's Hospital); Jei Keon Chae (Jeonbuk National Univetsity Hospital); David Smyth (Christchurch Hospital).

PREVENT Trial

PREVENT

Coronary Stenosis (>50%) with Negative FFR (≥ 0.80) and meeting two of the following (Imaging defined VP)

1. MLA ≤4.0mm^2
2. Plaque Burden >70%
3. TCFA by OCT or RF-IVUS
4. Lipid-Rich Plaque by NIRS ($_{max}LCBI_{4mm}$>315)

Preventive PCI + OMT
N=800

OMT alone
N=800

Primary endpoint : Target Vessel Failure at 2 years
(composite of death from cardiac cause, target-vessel MI, ischemic-driven target vessel revascularization, or unplanned hospitalization due to unstable or progressive angina)

Major Inclusion Criteria

PREVENT

1. Men or women at least age ≥ 18 years.
2. Patients with angiographically significant stenosis (>50%) <u>with negative FFR (>0.80) and meeting two of the following,</u>
   1) MLA < 4mm^2
   2) Plaque burden >70%
   3) TCFA detected by RF-IVUS or OCT
   4) Large lipid-rich plaque on NIRS (max$LCBI_{4mm}$ >315)
4. Eligible for PCI with Absorb BVS or EES
5. Reference vessel diameter 2.75 – 4.0 mm
6. Lesion length ≤40 mm

BVS, bioresorbable vascular scaffold; CABG, coronary artery bypass grafting; CAD, coronary artery disease; EES, everolimus-eluting stent; FFR, fractional flow reserve; maxLCBI4mm, maximal lipid core burden index in a 4 mm segment; NIRS, near-infrared spectroscopy; OCT, optical coherence tomography; RF-IVUS, radiofrequency intravascular ultrasonography; TCFA, thin-cap fibroatheroma. TCFA was defined as a ≥10% confluent necrotic core with >30° abutting the lumen in 3 consecutive frames on RF-IVUS or a lipid plaque with arc >90° and fibrous cap thickness <65 μm on OCT.

Major Exclusion Criteria

PREVENT

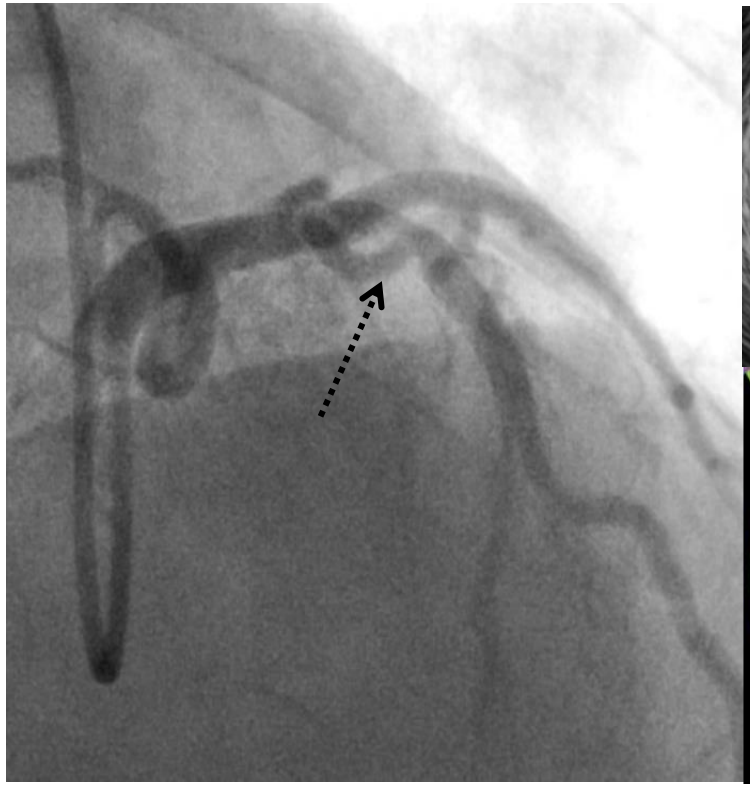
1. Patients in whom the preferred treatment is CABG.
2. Previously stented lesion
3. Bypass graft lesion
4. Patients with 3 or more target lesions
5. Patients with 2 target lesions in the same coronary artery
6. Heavily calcified or angulated lesion
7. Bifurcation lesion requiring 2-stent technique
8. Contraindication to or planned discontinuation of dual antiplatelet therapy within 1 year

Procedure

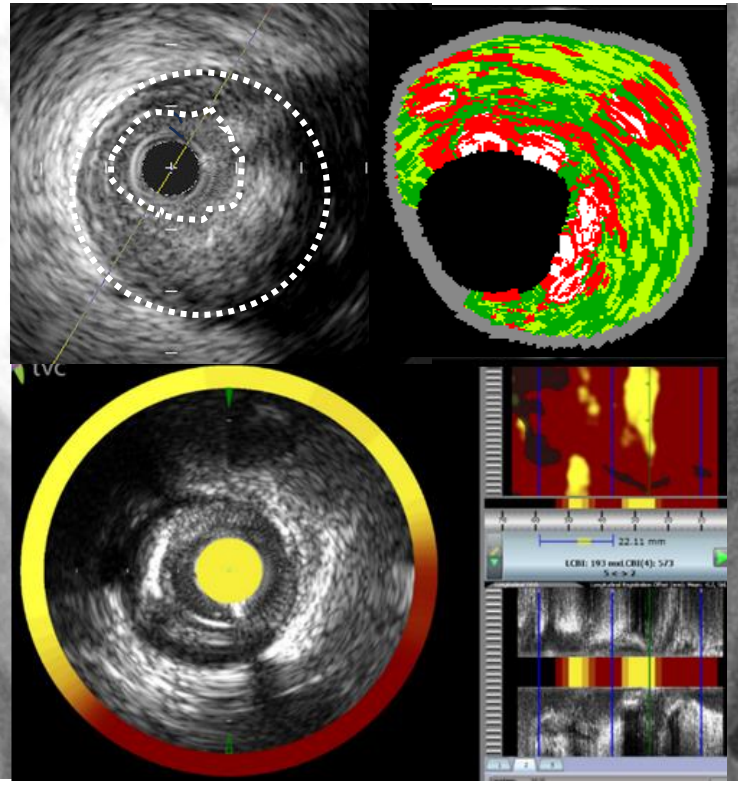
- During the initial recruitment period of the trial, PCI was performed with BVS (Absorb; Abbott). Following the withdrawal of BVS, cobalt-chromium everolimus-eluting metallic stents (Xience; Abbott) were used for the default device of PCI.
- Intravascular imaging of all target lesions was performed.
- Patients received dual antiplatelet therapy for at least 6 or 12 months after PCI according to clinical presentation and anatomical complexity.
- Clinical follow-up was done at 1, 6, 12, and 24 months and every year thereafter. Follow-up continued annually in all enrolled patients until the last enrolled patient reached 2 years after randomization.

Procedure

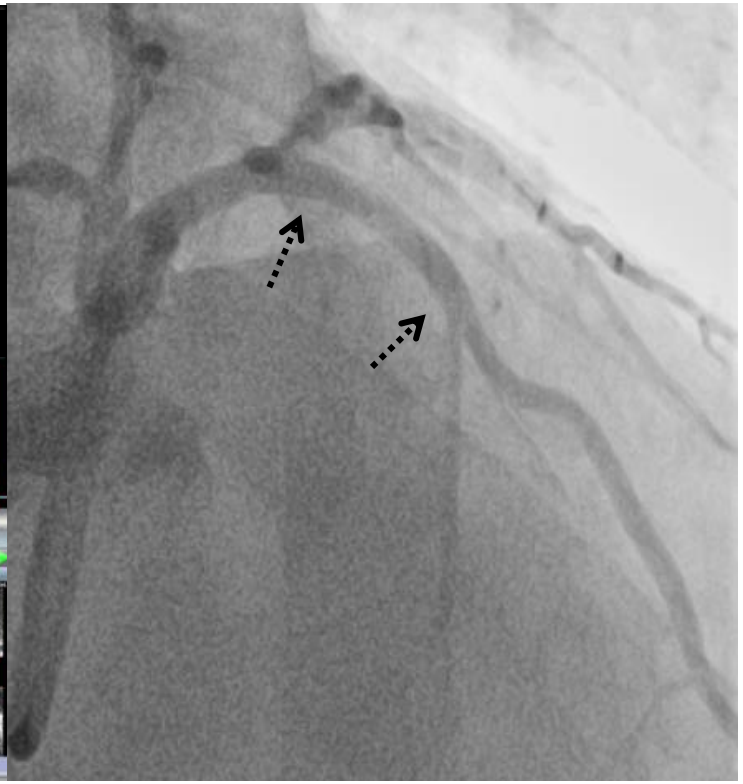
PREVENT



Diameter stenosis 70%,
FFR 0.83



MLA 2.11 mm^2
Plaque burden 79%
TCFA by RF-IVUS
$maxLCBI_{4mm}$ 573



Absorb (BVS)
3.5 mm x 18 mm

Primary Endpoint

- **Target Vessel Failure** (a composite of death from cardiac causes, target-vessel myocardial infarction, ischemia-driven target-vessel revascularization, or hospitalization for unstable or progressive angina) at 2 years after randomization

Secondary Endpoint

PREVENT

- Individual components of the primary composite outcome
- Patient-oriented composite of all-cause death, all myocardial infarctions, or any repeat revascularization
- Procedural safety outcomes
- Stroke
- Bleeding events
- Number of anti-anginal medications used at each time point

Statistical Considerations

PREVENT

Power Calculation (N = 1,600)

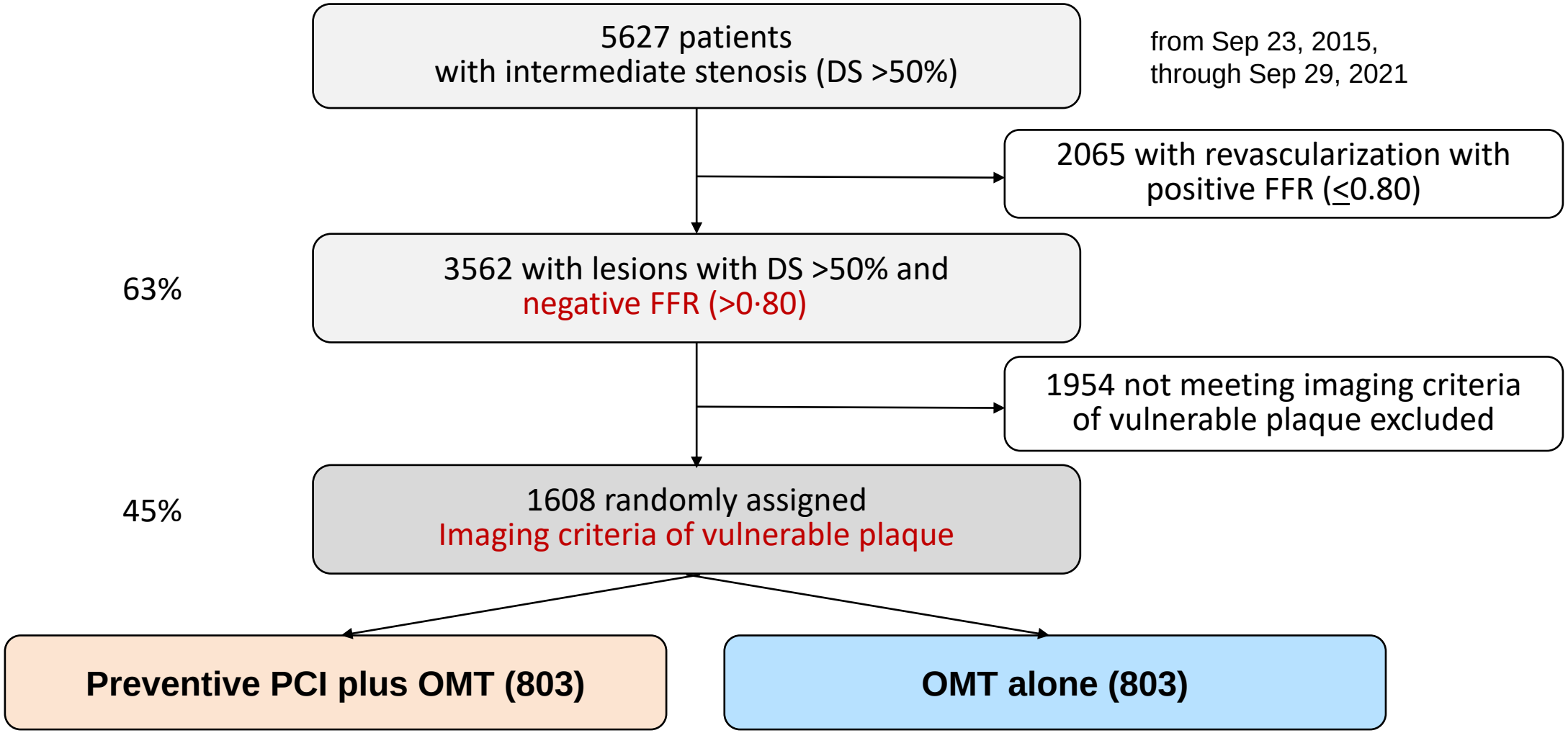
- Assuming an incidence of the primary outcome at 2-years of 8.5% for preventive PCI group and 12.0% for OMT alone group (30% relative risk reduction),
- A sample size of 1600 patients provided 80% power at a two-sided significance level of 5%, assuming a 7% loss to follow-up and crossover rate.

Pre-Specified Statistical Analysis

- Primary intention-to-treat analysis
- Time-to-first-event estimate with Kaplan–Meier methodology
- Cox proportional hazard models to estimate the treatment effects
- Sensitivity analyses in the per-protocol and as-treated populations
- Absolute differences and 95% confidence intervals calculated at 2 years (primary outcome), 4 years (median follow-up), and 7 years (maximum follow-up)
- An interaction term between randomized groups and key subgroups for primary outcome.

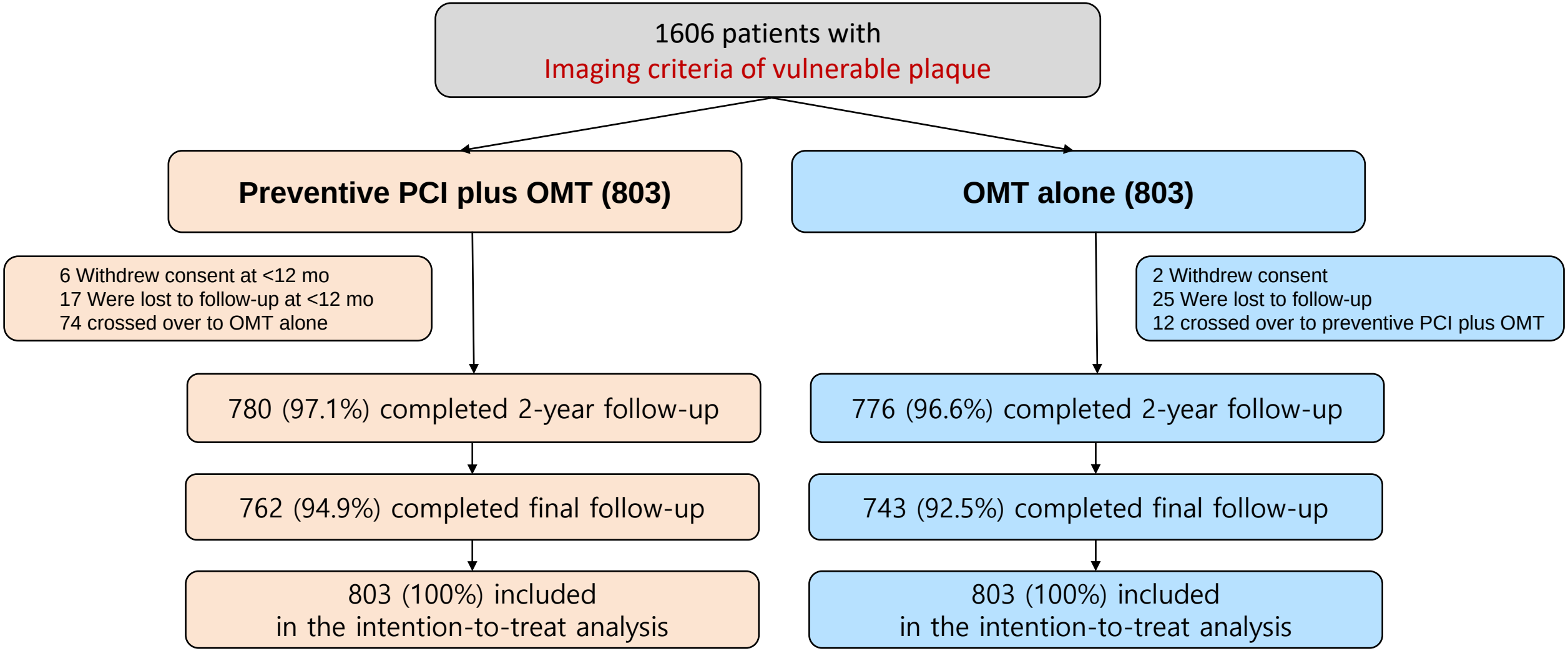
Patient Flow and Follow Up

PREVENT



Patient Flow and Follow Up

PREVENT



Baseline Characteristics

PREVENT

	Preventive PCI plus OMT (N=803)	OMT alone (N=803)
Age — years	64 (58 – 71)	65 (59 – 71)
Female sex	197 (25%)	232 (29%)
Body-mass index — kg/m^2	24.6 (22.9 – 26.5)	24.7 (22.9 – 26.4)
Diabetes mellitus — no. (%)	244 (30%)	246 (31%)
Hypertension — no. (%)	519 (65%)	536 (67%)
Dyslipidemia — no. (%)	721 (90%)	709 (88%)
Current smoking — no. (%)	136 (17%)	139 (17%)
Previous PCI — no. (%)	109 (14%)	85 (11%)
History of cerebrovascular disease — no. (%)	52 (6%)	50 (6%)
Left ventricular ejection fraction [%], (N=843)†	63 (60 – 66)	63 (60 – 66)
Clinical presentation — no. (%)		
Stable angina or silent ischemia	670 (83%)	677 (84%)
Unstable angina	106 (13%)	91 (11%)
Non-ST elevation myocardial infarction	18 (2%)	28 (3%)
ST-elevation myocardial infarction	9 (1%)	7 (1%)

Data are median (inter-quartile range), or n (%). †Preventive percutaneous coronary intervention group n=485; optimal medical therapy group n=358.

Anatomic Characteristics

PREVENT

	Preventive PCI plus OMT (N=831)	OMT alone (N=841)
Qualifying criteria for target lesions†	N=831	N=841
MLA <4.0 mm^2 by gray-scale IVUS or OCT	809 / 831 (97%)	817 / 841 (97%)
Plaque burden >70% by gray-scale IVUS	792 / 815 (97%)	805 / 831 (97%)
Large lipid-rich plaque by NIRS ($maxLCBI_{4mm}$>315)	99 / 348 (28%)	94 / 369 (26%)
TCFA defined by OCT or radiofrequency IVUS	39 / 571 (7%)	40 / 679 (6%)
Target lesion location		
Left anterior descending artery	416 (50%)	400 (48%)
Left circumflex artery	170 (20%)	147 (17%)
Right coronary artery	245 (29%)	294 (35%)
Median FFR values of target lesions	0.87 (0.83 – 0.90)	0.86 (0.83 – 0.90)
QCA of target lesions		
Diameter stenosis — %	56.6 (9.2)	52.6 (9.8)
Minimal lumen diameter — mm	1.3 (0.3)	1.5 (0.4)
Reference vessel diameter — mm	3.1 (0.4)	3.1 (0.5)
Lesion length — mm	23.6 (8.5)	19.3 (8.3)

Core Lab-Imaging Analysis

PREVENT

	Preventive PCI plus OMT (N=831)	OMT alone (N=841)
IVUS measurements	N = 811	N = 830
Lesion length — mm	23.7 (8.7)	22.6 (9.1)
Minimal lumen area — mm^2	2.78 (0.87)	2.83 (0.87)
Minimal lumen area ≤4.0 mm^2	784 / 811 (97%)	801/830 (97%)
Plaque burden — %	75.9 (6.9)	76.4 (4.4)
Plaque burden >70%	718 / 809 (89%)	753 / 829 (91%)
NIRS measurements	N = 348	N = 369
Plaque-level max$LCBI_{4mm}$ > 315	144 (41%)	138 (37%)
RF-IVUS measurements	N = 456	N = 575
TCFA defined by RF-IVUS	57 / 465 (13%)	73 / 575 (13%)
OCT measurements	N = 63	N = 21
TCFA defined by OCT	11 / 63 (18%)	7 / 21 (33%)
No· of high-risk plaque features†		
Lesions with ≥2 of 4 high-risk features	736 (89%)	760 (90%)
Lesions with ≥3 of 4 high-risk features	163 (20%)	177 (21%)
Lesions with 4 of 4 high-risk features	12 (1%)	13 (2%)

Procedural Characteristics

PREVENT

	Preventive PCI plus OMT (N=803)	OMT alone (N=803)
PCI of target lesion, per patient, any†	729 / 803 (91%)	12 / 803 (1%)
Drug-eluting stent implantation	491 / 729 (67%)	7 / 12 (58%)
Bioabsorbable scaffold implantation	237 / 729 (33%)	5 / 12 (42%)
Number of stents or scaffolds implanted	1 (1 – 1)	0 (0 – 0)
Stent or scaffold diameter — mm	3.5 (3.0 – 3.5)	3.25 (3.0 – 3.5)
Total stent or scaffold length — mm	23 (18 – 28)	23 (18 – 28)
Intravascular imaging used to optimize stent or scaffold implantation	729 / 729 (100%)	12 / 12 (100%)
PCI of non-target lesions, per patient, any	290 / 803 (36%)	286 / 803 (36%)
Number of lesions treated	0 (0 – 1)	0 (0 – 1)
Number of stents implanted	0 (0 – 1)	0 (0 – 1)
Stent diameter — mm	3.25 (3.0 – 3.5)	3.25 (3.0 – 3.5)
Total stent length — mm	38 (23 – 51)	38 (28 – 51)

Data are median (inter-quartile range), or n (%). †One patient underwent balloon angioplasty only.

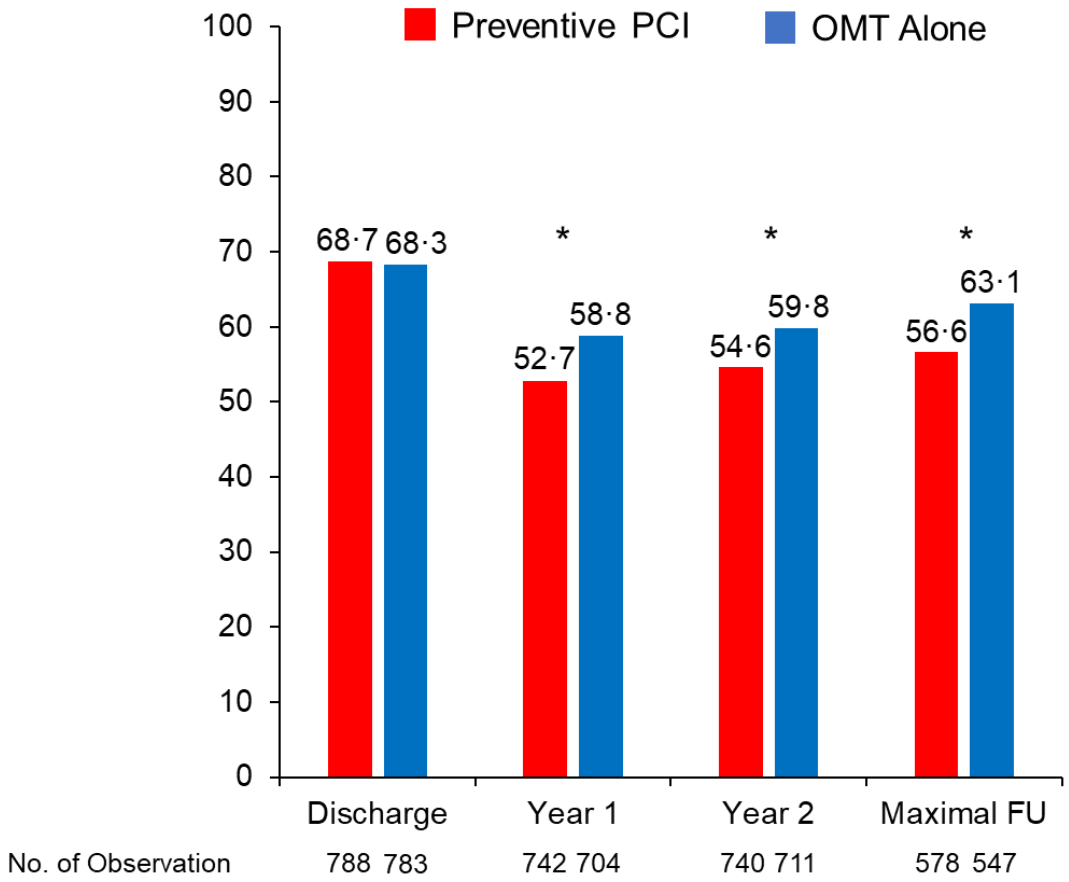
Procedural Safety Outcomes : As-treated population

PREVENT

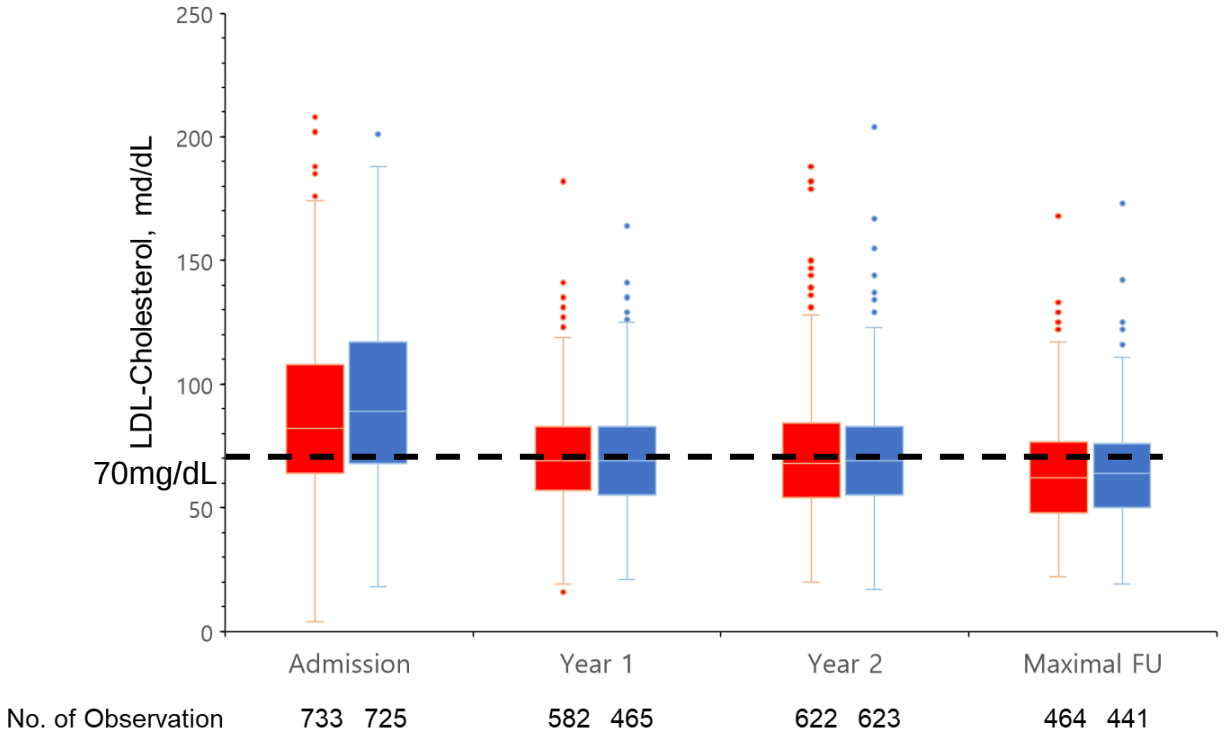
	Preventive PCI (N=741)	OMT alone (N=865)
Patients without non-target vessel PCI	N=461	N=569
Total PCI time — min	29 (18 – 45)	0
Total amount of contrast media used — mL	150 (120 – 200)	0
Patients with non-target vessel PCI	N=280	N=296
Total PCI time — min	57 (40 – 73)	46 (25 – 65)
Total amount of contrast media used — mL	250 (200 – 300)	200 (150 – 250)
Preventive PCI-related acute adverse events no. (%)		
Acute stent or scaffold thrombosis	1 (<1%)	0
Distal dissection of at least type B	1 (<1%)	0
Side branch occlusion	2 (<1%)	0
Distal embolization	1 (<1%)	0
Coronary perforation	0	0

Data are median (inter-quartile range), or n (%).

Proportion of High-intensity Statin or Moderate-intensity Statin plus Ezetimibe Therapy

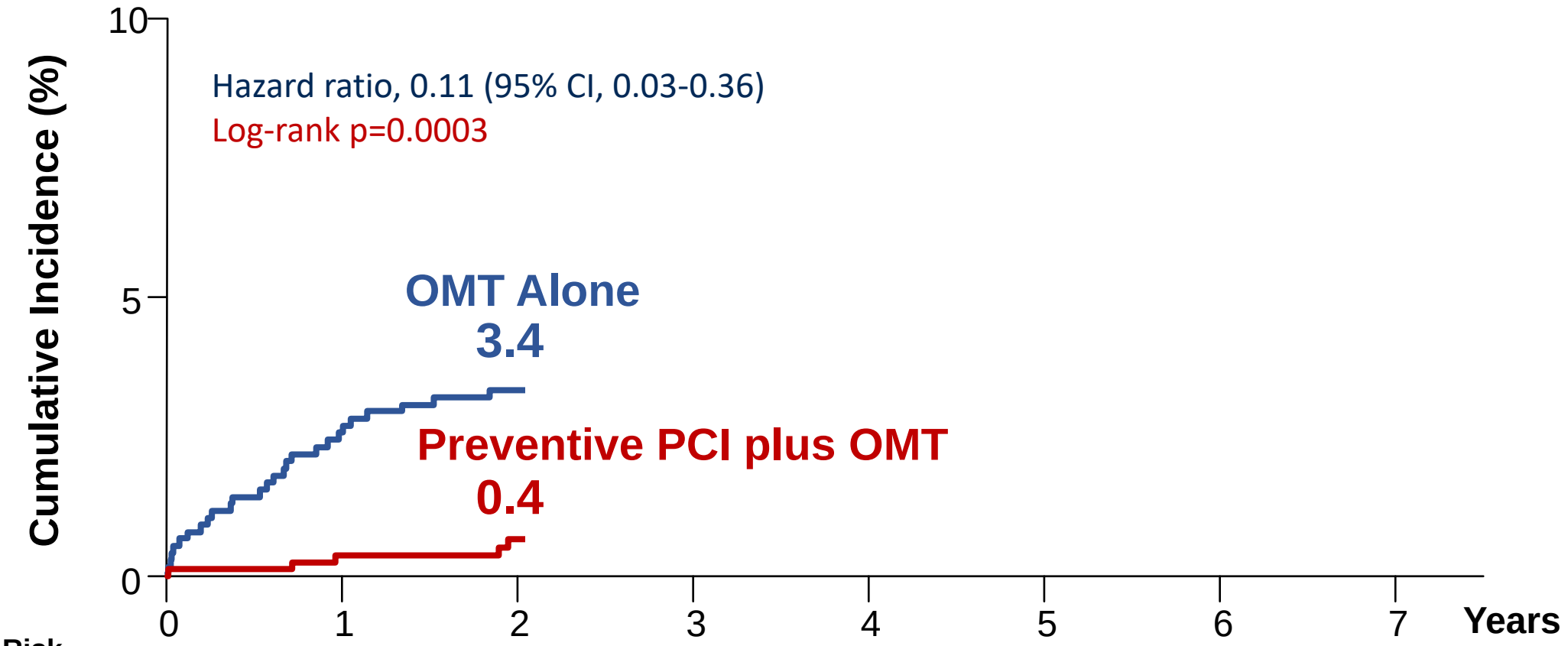


LDL at Follow-up: 64 mg/dL



Primary Composite Outcome:
Target Vessel Failure at 2 Year F/U

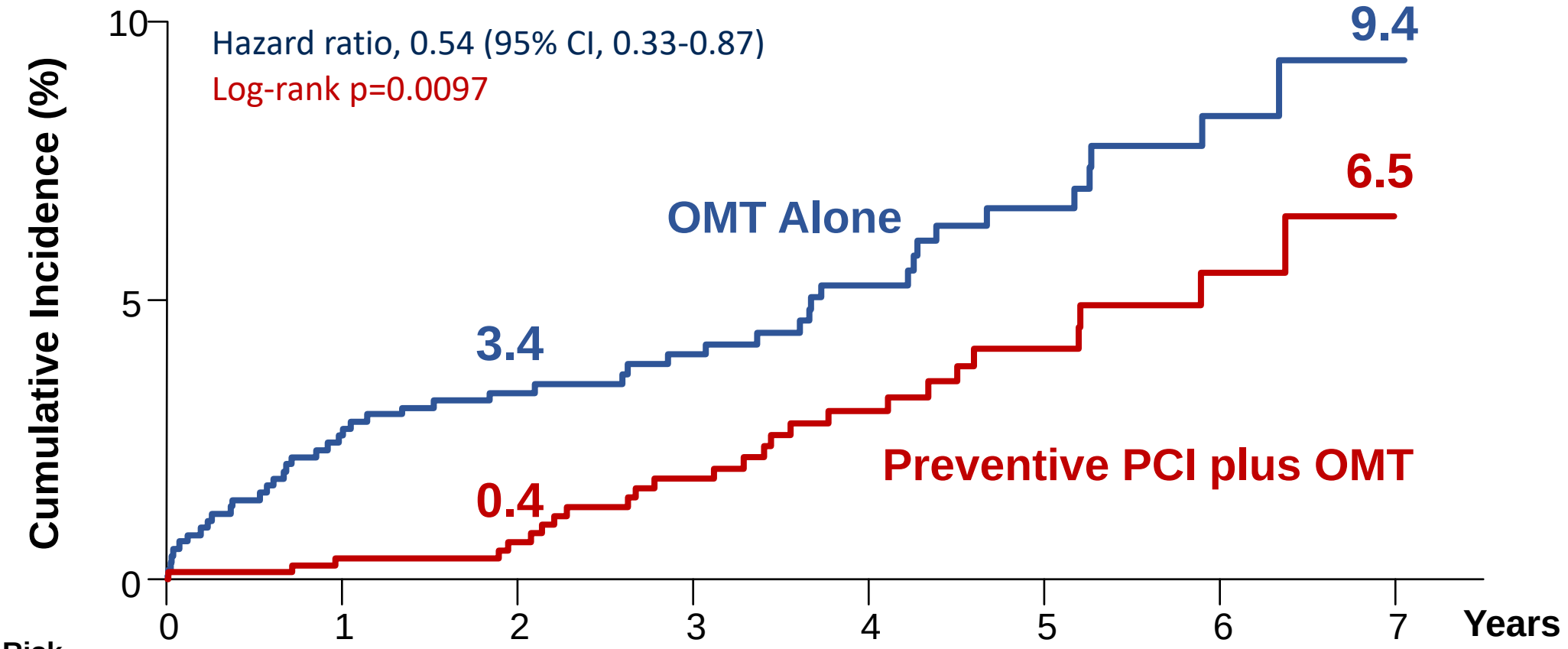
PREVENT



No. at Risk								
OMT Alone	803	765	710	544	432	308	198	61
Preventive PCI Plus OMT	803	792	745	570	450	320	198	77

Primary Composite Outcome:
Target Vessel Failure at 7 Year F/U

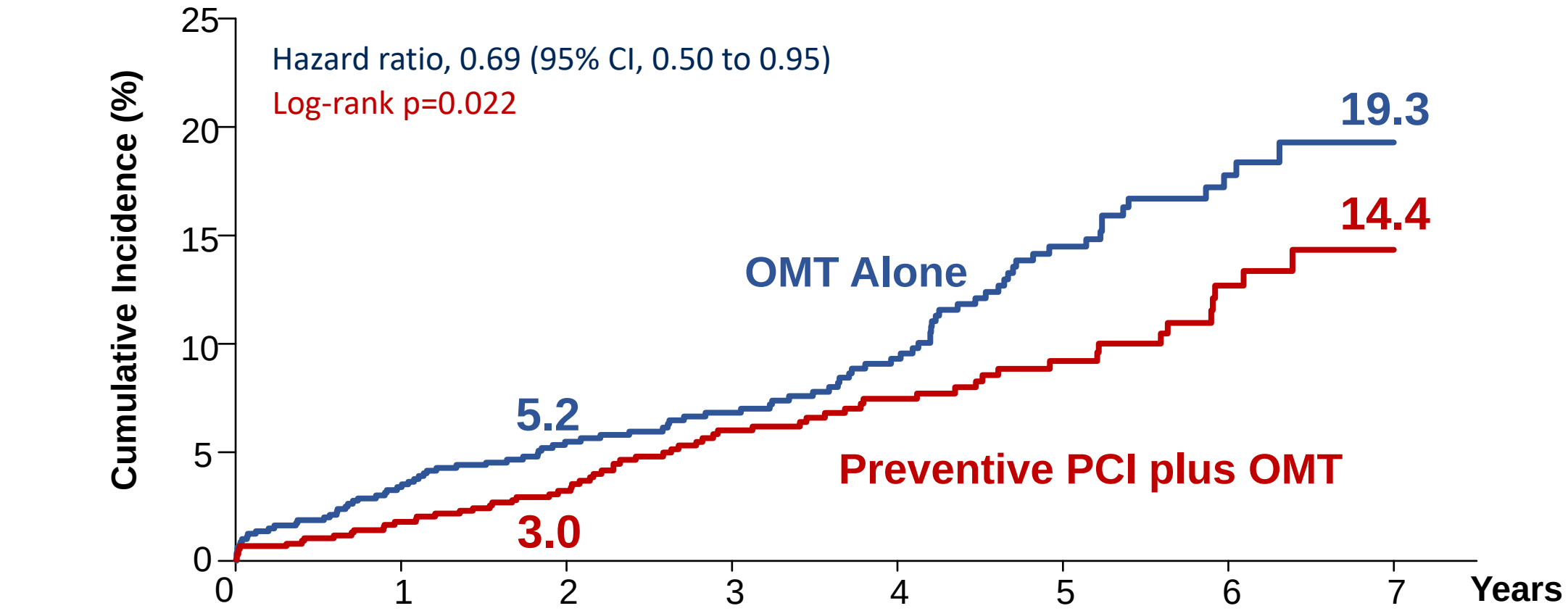
PREVENT



No. at Risk								
OMT Alone	803	765	710	544	432	308	198	61
Preventive PCI Plus OMT	803	792	745	570	450	320	198	77

Patient-Oriented Composite Outcome:
Death from Any cause, Any MI, or Any RR

PREVENT



No. at Risk							
OMT Alone	803	761	700	536	424	297	190	58
Preventive PCI Plus OMT	803	781	728	551	431	302	187	72

Individual Components of the Primary Composite Outcome

PREVENT

Endpoints	Preventive PCI plus OMT (N=803)	OMT alone (N=803)	Difference in event rates (95% CI)	Hazard ratio (95% CI)
Primary composite outcome				**0·54 (0·33 to 0·87)**
At 2 years‡	3 (0·4%)	27 (3·4%)	-3·0 (-4·4 to -1·8)	**0·11 (0·03 to 0·36)**
At 4 years	17 (2·8%)	37 (5·4%)	-2·6 (-4·7 to -0·4)	
At 7 years	26 (6·5%)	47 (9·4%)	-2·9 (-7·3 to 1·5)	
Death from cardiac causes				0·87 (0·31 to 2·39)
At 2 years	1 (0·1%)	6 (0·8%)	-0·6 (-1·3 to 0·02)	
At 4 years	5 (0·8%)	7 (0·9%)	-0·1 (-1·1 to 0·9)	
At 7 years	7 (1·4%)	8 (1·3%)	0·1 (-1·4 to 1·5)	
Target-vessel related MI				0·62 (0·20 to 1·90)
At 2 years	1 (0·1%)	6 (0·8%)	-0·6 (-1·3 to 0·02)	
At 4 years	4 (0·6%)	7 (10%)	-0·3 (-1·3 to 0·6)	
At 7 years	5 (1·0%)	8 (1·4%)	-0·3 (-1·7 to 1·1)	

Event rates (%) shown are Kaplan–Meier estimates in the intention-to-treat population.

Individual Components of the Primary Composite Outcome

PREVENT

Endpoints	Preventive PCI plus OMT (N=803)	OMT alone (N=803)	Difference in event rates (95% CI)	Hazard ratio (95% CI)
Ischemia-driven target-vessel revascularization				**0·44 (0·25 to 0·77)**
At 2 years	1 (0·1%)	19 (2·4%)	-2·3 (-3·4 to -1·2)	
At 4 years	10 (1·7%)	29 (4·4%)	-2·7 (-4·6 to -0·8)	
At 7 years	17 (4·9%)	38 (8·0%)	-3·2 (-7·4 to 1·1)	
Hospitalization for unstable or progressive angina				**0·19 (0·06 to 0·54)**
At 2 years	1 (0·1%)	12 (1·5%)	-1·4 (-2·3 to -0·5)	
At 4 years	4 (0·7%)	16 (2·4%)	-1·7 (-3·0 to -0·4)	
At 7 years	4 (0·7%)	21 (4·9%)	-4·2 (-7·17 to -1·4)	

Secondary Endpoint Outcomes

PREVENT

Endpoints	Preventive PCI plus OMT (N=803)	OMT alone (N=803)	Difference in event rates (95% CI)	Hazard ratio (95% CI)
Death from any cause				0·61 (0·35 to 1·06)
At 2 years	4 (0·5%)	10 (1·3%)	-0·8 (-1·7 to 0·2)	
At 4 years	11 (1·8%)	17 (2·6%)	-0·8 (-2·4 to 0·8)	
At 7 years	20 (5·2%)	32 (7·4%)	-2·3 (-6·0 to 1·5)	
Non-target-vessel myocardial infarction				0·91 (0·39 to 2·15)
At 2 years	8 (1.0%)	12 (1·5%)	0·1 (-0·8 to 1·1)	
At 4 years	10 (1.3%)	8 (1.1%)	0·3 (-0·9 to 1·4)	
At 7 years	10 (1.3%)	11 (2.2%)	-0·9 (-2·6 to 0·8)	
Non-target-vessel revascularization				0·88 (0·51 to 1·52)
At 2 years	13 (1·6%)	13 (1·7%)	-2·2 (-4·1 to -0·2)	
At 4 years	22 (3·1%)	19 (2·7%)	-1·8 (-4·7 to 1·2)	
At 7 years	24 (4·8%)	27 (5·6%)	-4·9 (-10·8 to 1·1)	

Secondary Endpoint Outcomes

PREVENT

Endpoints	Preventive PCI plus OMT (N=803)	OMT alone (N=803)	Difference in event rates (95% CI)	Hazard ratio (95% CI)
Definite stent or scaffold thrombosis				0·66 (0·11 to 3·95)
At 2 years	1 (0.1%)	3 (0·4%)	-0·3 (-0·8 to 0·3)	
At 4 years	2 (0·3%)	3 (0·4%)	0·2 (-1·1 to 1·5)	
At 7 years	2 (0.3%)	3 (0·4%)	-0·4 (-2·3 to 1·5)	
Stroke				0·99 (0·43 to 2·29)
At 2 years	5 (0·6%)	6 (0.8%)	-0·1 (-1·0 to 0·7)	
At 4 years	10 (1.5%)	9 (1.3%)	0·3 (-0·9 to 1·4)	
At 7 years	11 (1.8%)	11 (2.2%)	-0·9 (-2·6 to 0·8)	
Bleeding events (Major)				0·90 (0·38 to 2·11)
At 2 years	5 (0·6%)	4 (0.5%)	-0·8 (-1· 8 to 0·2)	
At 4 years	8 (1·4%)	6 (0.9%)	-0·3 (-1·4 to 0·9)	
At 7 years	10 (1.9%)	6 (0.9%)	0·4 (-1·1 to 1·8)	

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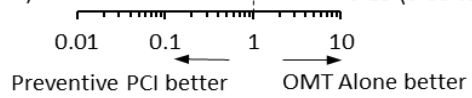
Subgroup Analyses of the Primary Outcome at 2-year Follow-up

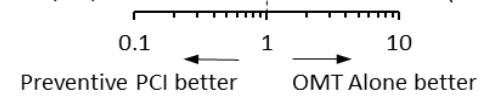
Subgroup	Preventive PCI	OMT Alone	Hazard Ratios (95% CI)	P-for-Interaction
	No. of events/no. of patients (Cumulative 2-Yr incidence, %)			
Age				0·435
< 65 years	1/408 (0·3)	15/394 (3·9)	0·06 (0·01 to 0·47)	
≥ 65 years	2·395 (0·5)	12/409 (3·0)	0·17 (0·04 to 0·76)	
Sex				0·974
Male	2/606 (0·3)	17/571 (3·0)	0·11 (0·03 to 0·47)	
Female	1/197 (0·5)	10/232 (4·4)	0·11 (0·02 to 0·89)	
Diabetes mellitus				0·989
Yes	0/244 (0)	9/246 (3·7)	NC	
No	3/559 (1·2)	18/557 (3·3)	0·16 (0·05 to 0·56)	
Acute coronary syndrome				0·989
Yes	0/133 (0)	8/126 (6·7)	NC	
No	3/670 (0·5)	19/677 (2·8)	0·16 (0·05 to 0·53)	
PCI of non-target vessel				0·988
Yes	0/290 (0)	13/286 (4·6)	NC	
No	3/513 (0·6)	14/517 (2·8)	0·21 (0·06 to 0·74)	
Median diameter stenosis by QCA				0·180
≥ 55%	1/491 (0·2)	14/316 (4·5)	0·04 (0·01 to 0·34)	
< 55%	2/308 (0·7)	13/484 (2·7)	0·24 (0·05 to 1·07)	
Median fractional flow reserve value				0·920
≤ 0·86	3/412 (0·7)	14/395 (3·6)	0·20 (0·06 to 0·71)	
> 0·86	0/389 (0)	13/405 (3·3)	NC	
Intracoronary imaging screening tools				NA
Gray-scale IVUS only	3/303 (1·0)	6/261 (2·3)	0·41 (0·10 to 1·66)	
RF-IVUS	0/506 (0)	18/635 (2·9)	NC	
NIRS-IVUS	1/333 (0·3)	12/346 (3·5)	0·09 (0·01 to 0·66)	
OCT	1/67 (1·5)	1/20 (5·0)	0·30 (0·02 to 4·76)	
Preventive PCI modalities				0·772
BVS era	1/265 (0·4)	12/281 (4·3)	0·09 (0·01 to 0·67)	
CoCr-EES era	2/538 (0·4)	15/522 (2·9)	0·13 (0·03 to 0·55)	



PREVENT

Subgroup Analyses of the Primary Outcome at 7-year Follow-up

Subgroup	Preventive PCI	OMT Alone	Hazard Ratios (95% CI)	P-for-Interaction
	No. of events/no. of patients (%)			
Age				0·619
< 65 years	13/408 (3·2)	25/394 (6·4)	0·48 (0·25 to 0·94)	
≥ 65 years	13/395 (3·3)	22/409 (5·4)	0·61 (0·31 to 1·20)	
Sex				0·996
Male	19/606 (3·1)	32/571 (5·6)	0·54 (0·31 to 0·96)	
Female	7/197 (3·6)	15/232 (6·5)	0·53 (0·22 to 1·31)	
Diabetes mellitus				0·696
Yes	8/244 (3·3)	13/246 (5·3)	0·62 (0·26 to 1·50)	
No	18/559 (3·2)	34/557 (6·1)	0·51 (0·29 to 0·89)	
Acute coronary syndrome				0·380
Yes	4/133 (3·0)	11/126 (8·7)	0·33 (0·11 to 1·05)	
No	22/670 (3·3)	36/677 (5·3)	0·60 (0·35 to 1·01)	
PCI of non-target vessel				**0·007**
Yes	5/290 (1·7)	24/286 (8·4)	0·19 (0·07 to 0·51)	
No	21/513 (4·1)	23/517 (4·4)	0·91 (0·50 to 1·64)	
Median diameter stenosis by QCA				**0·014**
≥ 55%	11/491 (2·2)	23/316 (7·3)	0·28 (0·14 to 0·58)	
< 55%	15/308 (4·9)	24/484 (5·0)	0·95 (0·50 to 1·81)	
Median fractional flow reserve value				0·771
≤ 0·86	16/412 (3·9)	25/395 (6·3)	0·59 (0·32 to 1·11)	
> 0·86	10/389 (2·6)	22/405 (5·4)	0·46 (0·22 to 0·97)	
Intracoronary imaging screening tools				NA
Gray-scale IVUS only	10/306 (3·3)	14/261 (5·4)	0·50 (0·22 to 1·12)	
RF-IVUS	15/506 (3·0)	31/635 (4·9)	0·55 (0·29 to 1·01)	
NIRS-IVUS	15/333 (4·5)	24/346 (6·9)	0·63 (0·33 to 1·20)	
OCT	5/67 (7·5)	3/20 (15·0)	0·41 (0·10 to 1·71)	
Preventive PCI modalities				**0·018**
BVS era	19/265 (7·2)	22/281 (7·8)	0·89 (0·48 to 1·65)	
CoCr-EES era	7/538 (1·3)	25/522 (4·8)	0·25 (0·11 to 0·59)	



Study Limitations

PREVENT

- The study was open-label, introducing the risks of placebo effects and ascertainment bias.
- The observed rates of the primary outcome were substantially lower than expected in both groups.
- The selection of imaging modality to assess plaque vulnerability was left to operator discretion.
- 9% in the preventive PCI group and 1% in the OMT alone group crossed over.
- The study did not collect data to examine the cost-effectiveness of a preventive PCI strategy.
- DAPT use was greater in the preventive PCI group.

Summary of Key Findings

PREVENT

- The PREVENT trial is the first large-scale, randomized controlled study comparing preventive PCI plus OMT versus OMT alone for the treatment of non-flow-limiting imaging defined vulnerable plaques.
- In the PREVENT trial, preventive PCI reduced the composite risk of death from cardiac causes, target-vessel MI, ischemia-driven TVR, or hospitalization for unstable or progressive angina at 2 years.
- Preventive PCI also reduced the composite patient-oriented outcome of risk of all-cause death, any MI, or any repeat revascularization.
- This benefit was sustained throughout the 7-year follow-up period.

Conclusions

PREVENT

- In the PREVENT trial, preventive PCI plus OMT resulted in a lower incidence of major adverse cardiac events compared with OMT alone in patients with non-flow-limiting vulnerable plaques

- Our key findings might provide novel insights on the role of preventive PCI on non-flow-limiting high-risk vulnerable plaques in the future.