DECISION-CTO

Optimal Medical Therapy With or Without Stenting For Coronary Chronic Total Occlusion

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Background

- Benefits of successful CTO-PCI include reduced angina frequency and improvements in quality of life, left ventricular ejection fraction, or survival.

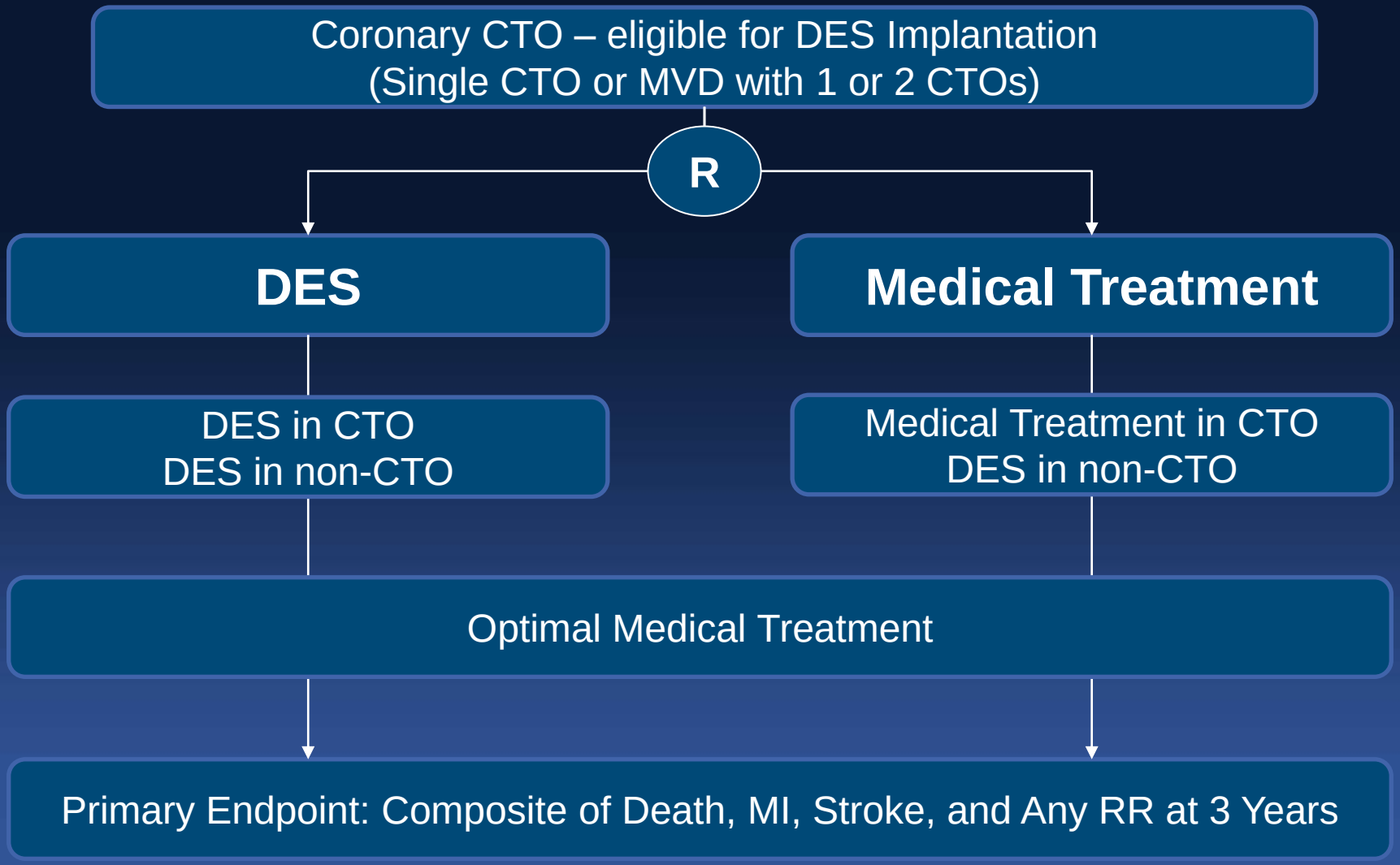
- However, CTO-PCI can lead to procedure-related complications. In addition, the evidence for CTO-PCI was obtained from observational studies, most of which compared successful and failed CTO-PCI without a control group receiving optimal medical treatment.

DECISION CTO Trial

Design

- DESIGN: a prospective, open-label, randomized trial
- OBJECTIVE: To compare the outcomes of OMT alone with PCI coupled with OMT in patients with CTO.
- PRINCIPAL INVESTIGATOR
  Seung-Jung Park, MD, PhD,
  Asan Medical Center, Seoul, Korea

DECISION CTO



Clinicaltrials.gov, Identifier: NCT01075051

Participating Centers (N=19)

Country	Site	Investigator
Korea	Asn Medical center	Seung-Jung Park
India	Ruby Hall Clinic	Shirish Hiremath
Korea	Keimyung University Dongsan Medical Center	Seung Ho Hur
Korea	Korea University Guro Hospital	Seung Un Rha
Indonesia	Medistra Hospital	Teguh Santoso
Korea	The Catholic University of Korea, Daejeon ST. Mary's Hospital	Sung-Ho Her
Korea	Chungnam National University Hospital, Daejeon	Si Wan Choi
Korea	Kangwon National University Hospital	Bong-Ki Lee
Korea	Soon Chun Hyang University Hospital Bucheon, Bucheon	Nae-Hee Lee
Korea	Kangbuk Samsung Medical Center, Seoul	Jong-Young Lee
Korea	Gangneung Asan Hospital, Gangneung	Sang-Sig Cheong,
Thailand	King Chulalongkorn Memorial Hospital	Wasan Udayachalerm
Korea	Dong-A University Hospital, Busan	Moo Hyun Kim
Korea	Chonnam National University Hospital, Gwangju	Young-Keun Ahn
Korea	Bundang Cha Medical Center, Bundang	Sang Wook Lim
Korea	Ulsan University Hospital, Ulsan	Sang-Gon Lee
Korea	Hangang Sacred Heart Hospital, Seoul	Min-Kyu Kim
Korea	Sam Anyang Hospital, Anyang	Il-Woo Suh
Taiwan	Shin Kong Hospital	Jun Jack Cheng

Major Inclusion Criteria

- Silent ischemia, stable angina, or ACS
- De novo CTO located in a proximal to mid epicardial coronary artery with a reference diameter of ≥2.5 mm
- CTO was defined as a coronary artery obstruction with TIMI flow grade 0 of at least three months' duration based on patient history.

Major Exclusion Criteria

- CTO located in
  - Distal coronary artery
  - 3 different vessel CTOs in any location
  - 2 proximal CTOs in separate coronary artery
  - left main segment
  - In-stent restenosis
  - Graft vessel
- LVEF < 30%
- Severe comorbidity

Study Procedures (1)

- Patients who were assigned to PCIs underwent CTO-PCI using DES within 30 days after randomization using standard procedures.
- In cases of failed CTO-PCI, additional attempts were allowed within 30 days after the index procedure.
- The use of specialized devices or techniques, and the choice of drug-eluting stent type were left to the operator's discretion.

Study Procedures (2)

- Revascularization for all significant non-CTO lesions within a vessel diameter of ≥2.5 mm for patients with multi-vessel coronary artery disease was recommended.
- Patients were prescribed guideline derived optimal medical treatment including aspirin, P2Y12 receptor inhibitors (>12months in case of PCI), beta-blocker, CCB, nitrate, ACEi/ARB, and statin.
- Blood pressure and diabetic control, smoking cessation, weight control, and regular exercise were recommended.

Primary End Point

At 3 year, a composite of

- Death from any cause
- Myocardial infarction
  - Periprocedural MI: CK-MB > 5 times UNL
  - Spontaneous MI: any cardiac enzyme elevation
- Stroke
- Any repeat revascularization

Original Power Calculation

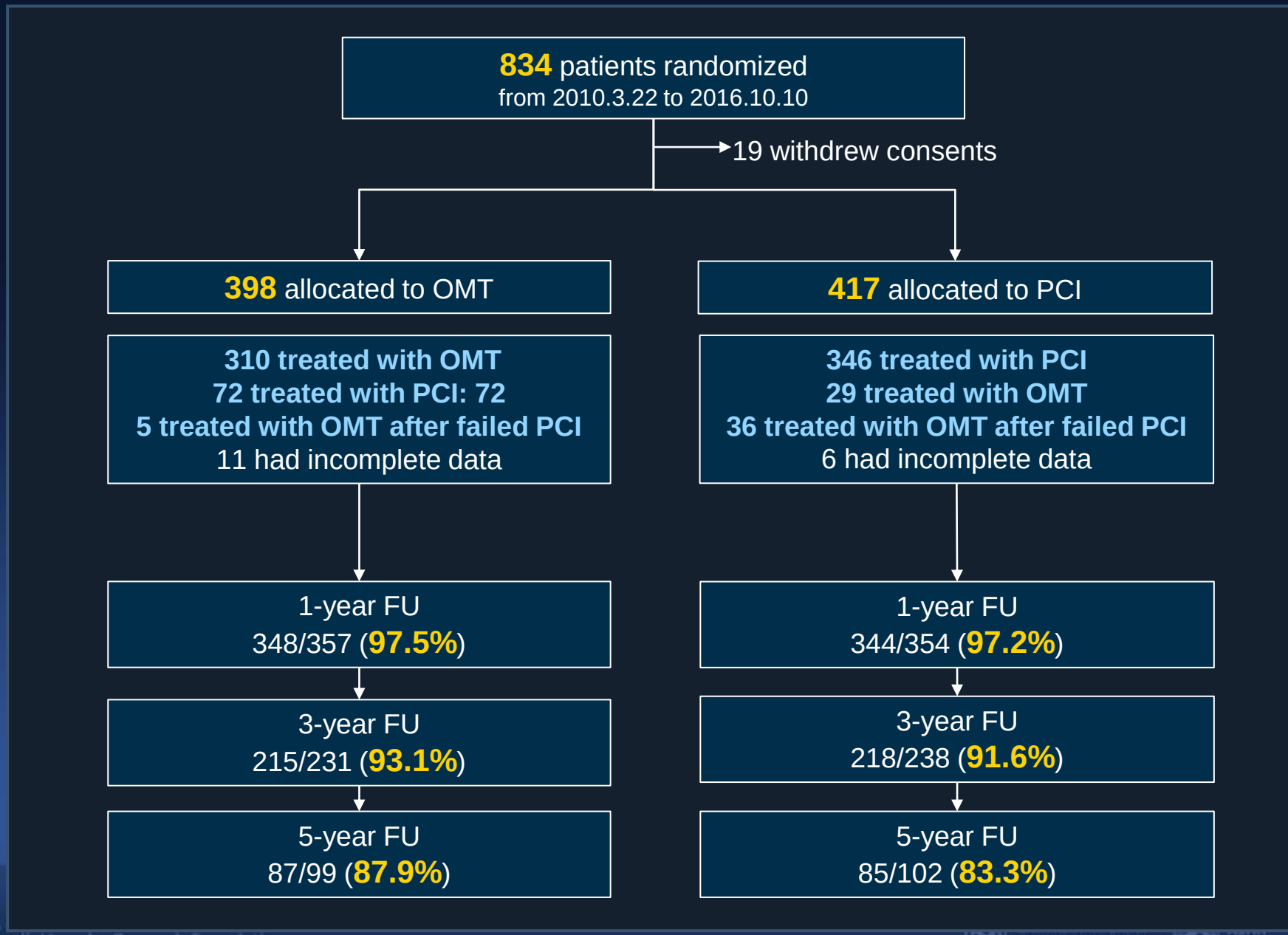
Non-inferiority Design for Primary Endpoint

- Assumed primary event rate: 17% at 3 years
- A noninferiority margin : event rate ratio 0.7
- A one-sided type I error rate : 0.025
- Power : 80%
- Dropout rate: 5%
- Assumed sample size: 1,284 patients

Premature Termination of Trial

- Because enrollment was slower than anticipated, enrollment was stopped in September 2016 as recommended by the data and safety monitoring board by which time 834 patients had been enrolled.
- The sponsor and study leadership were unaware of study results at the time of this decision.

Study Flow


834 patients randomized
from 2010.3.22 to 2016.10.10
19 withdrew consents
398 allocated to OMT
417 allocated to PCI
310 treated with OMT
72 treated with PCI: 72
5 treated with OMT after failed PCI
11 had incomplete data
346 treated with PCI
29 treated with OMT
36 treated with OMT after failed PCI
6 had incomplete data
1-year FU
348/357 (97.5%)
1-year FU
344/354 (97.2%)
3-year FU
215/231 (93.1%)
3-year FU
218/238 (91.6%)
5-year FU
87/99 (87.9%)
5-year FU
85/102 (83.3%)

Reasons for Crossover

OMT to PCI (N=77)	Number of Patients
Doctors' preference (PI feels PCI is beneficial for patient)	
For symptom control	25
Decreased LV systolic function	5
Positive noninvasive stress test	10
Multiple risk factors	12
For improvement of vital status	1
Patients' preference (patient strongly wants PCI)	24
PCI to OMT (N=65)	
Failed PCI	36
Doctors' preference (PI feels OMT is beneficial for patient)	
Controlled or improved symptom	12
Negative noninvasive stress test	3
High probability of failure	2
High risk of procedure	2
Patients' preference	10

Statistical Analysis

- All analyses were performed according to the intention-to-treat principle. Further sensitivity analyses were performed in the per-protocol and as-treated population.
- Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazard models, with robust standard errors that accounted for clustering effect of stratified randomization.
- Noninferiority test using the Z-test with 95% CI of difference in the 3-year event rate.
- Survival curves were estimated using Cox model and the Kaplan-Meier method
- For quality of life analysis, we assumed the missing values were missing at random, and compared mean values of two groups using Student's t-test at specific time points.
- All P-values and CIs were two-sided. SAS software version 9.3 was used for all statistical analyses.

Baseline Characteristics

ITT Population

	OMT (N=398)	PCI (N=417)	P value
Age (years)	62.9±9.9	62.2±10.2	0.35
Male sex	315 (81.4%)	342 (83.2%)	0.50
BMI, kg/m^2	25.4±3.3	25.6±3.6	0.66
Hypertension	235 (60.7%)	261 (63.5%)	0.50
Diabetes mellitus	133 (34.4%)	132 (32.1%)	
Hypercholesterolemia	215 (55.6%)	248 (60.3%)	0.17
Current smoker	102 (26.4%)	125 (30.4%)	0.20
Previous PCI	74 (19.1%)	62 (15.1%)	0.13
Previous MI	34 (8.8%)	45 (10.9%)	0.31
Previous CABG	5 (1.3%)	4 (1.0%)	0.75
Chronic renal failure	5 (1.3%)	6 (1.5%)	0.84
LVEF, %	57.2±9.4%	57.2±9.8%	0.95

Baseline Characteristics

ITT Population

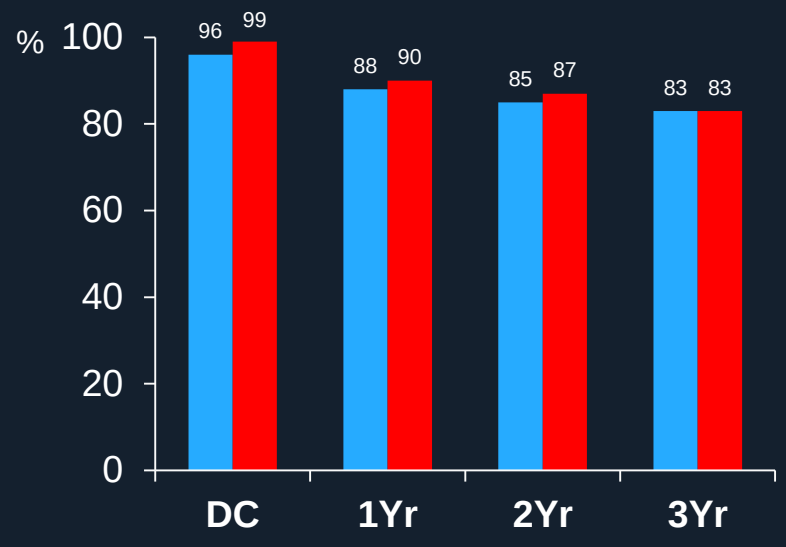
	OMT (N=398)	PCI (N=417)	P value
Clinical presentation			0.58
Stable angina	290 (74.9%)	297 (72.3%)	
Unstable angina	75 (19.4%)	84 (20.4%)	
AMI	22 (5.7%)	30 (7.3%)	
Location of CTO			0.71
LAD	161 (41.6%)	183 (44.5%)	
LCX	42 (10.9%)	40 (10.2%)	
RCA	184 (47.5%)	186 (45.3%)	
Multivessel disease	286 (73.9%)	301 (73.3%)	0.76
SYNTAX score	21.0±9.5	21.2±9.1	0.79
J-CTO score	2.3±1.2	2.2±1.2	0.23
PCI at any lesion	215 (54.0%)	374 (89.7%)	<0.001
Among PCI patients (CTO or non-CTO)			
Number of total stents	2.0±1.4	2.4±1.3	<0.001
Total stent length, mm	53.6±39.4	71.2±40.5	<0.001

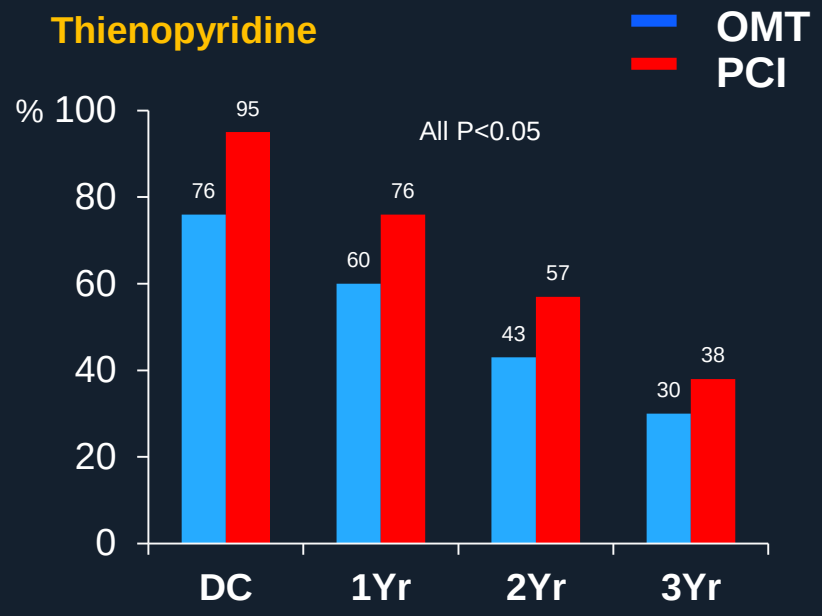
CTO PCI Characteristics

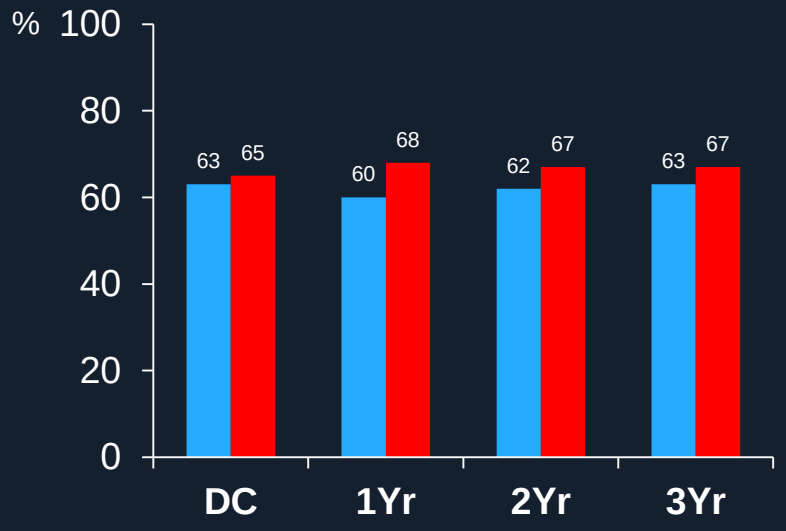
Attempted PCI	N=459
CTO PCI success	418 (91.1%)
Retrograde approach	113 (24.6%)
Lesion passaged wire	
Low penetration force wire	117/418 (28.0%)
Intermediate to high penetration force wire	301/418 (72.0%)
CTO technique	
Single wire technique only	309/418 (73.9%)
Parallel wire technique	72/418 (17.2%)
IVUS-guided wiring	25/418 (6.0%)
CART technique	55/418 (13.2%)
Additional back-up support	
Corsair	91/418 (21.8%)
Microcatheter other than Corsair	230/418 (55.0%)
Over-the-wire balloon	6/418 (1.4%)

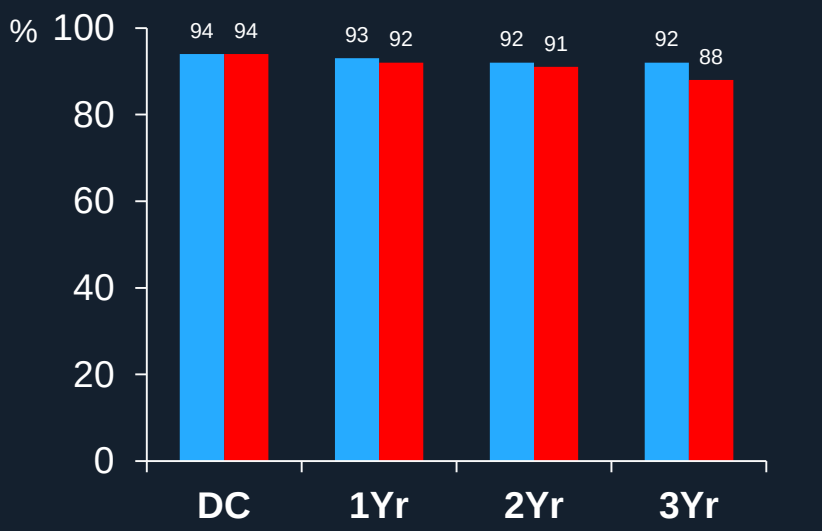
Medication at Follow-Up

ITT Population





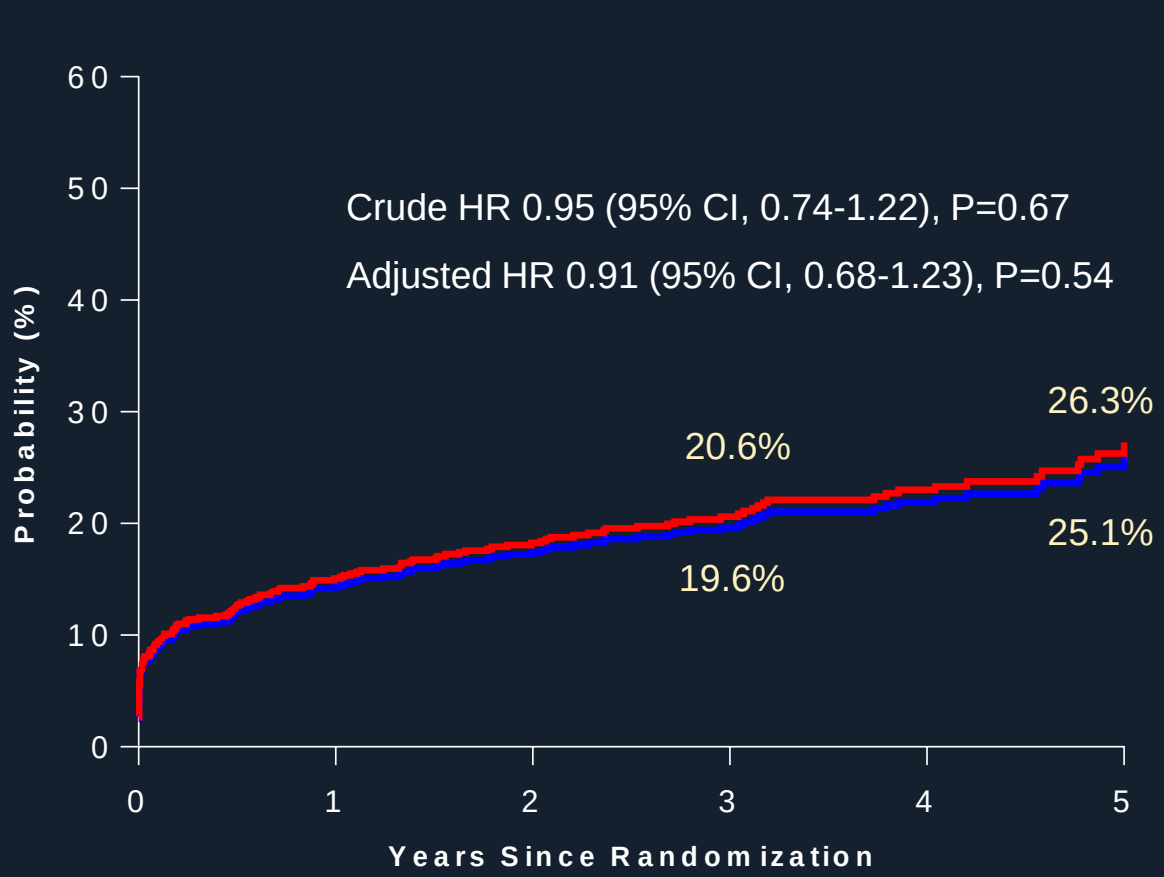




ITT Population

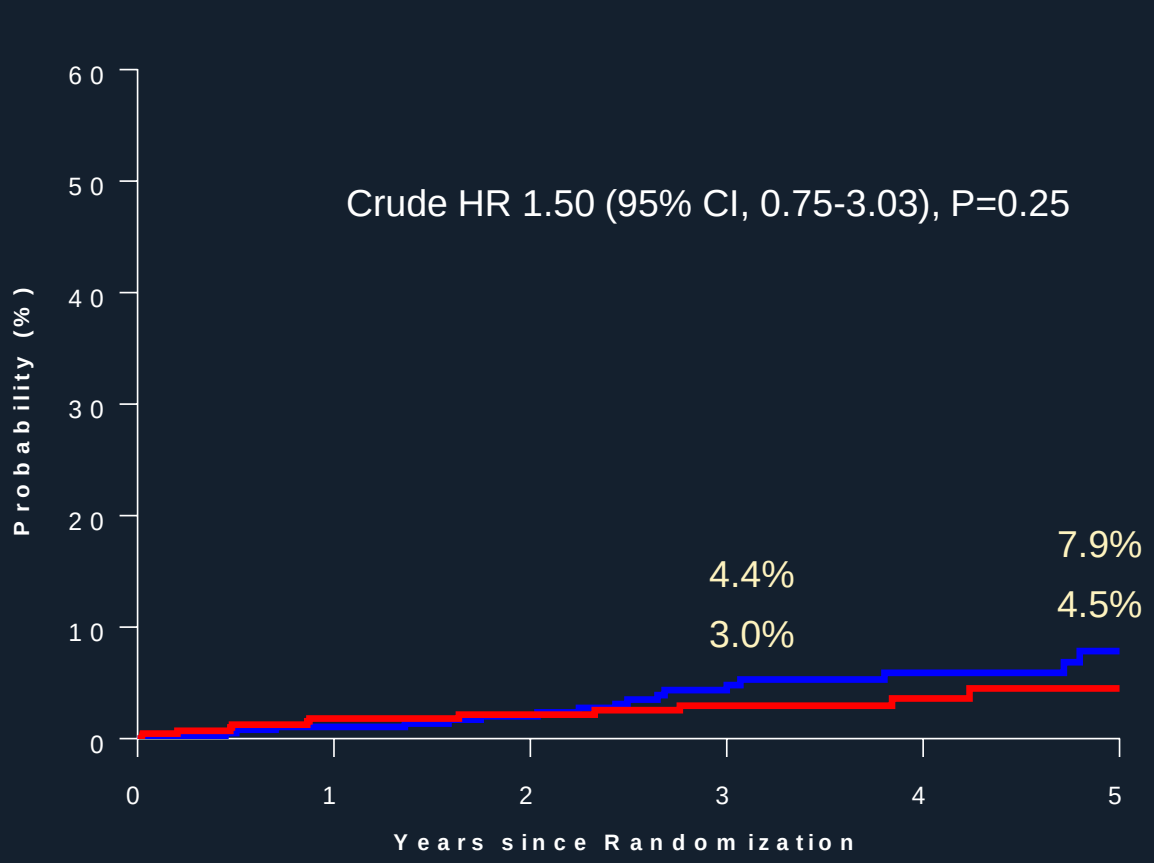
Primary End Point

(Death, MI, Stroke, Any Repeat Revascularization)



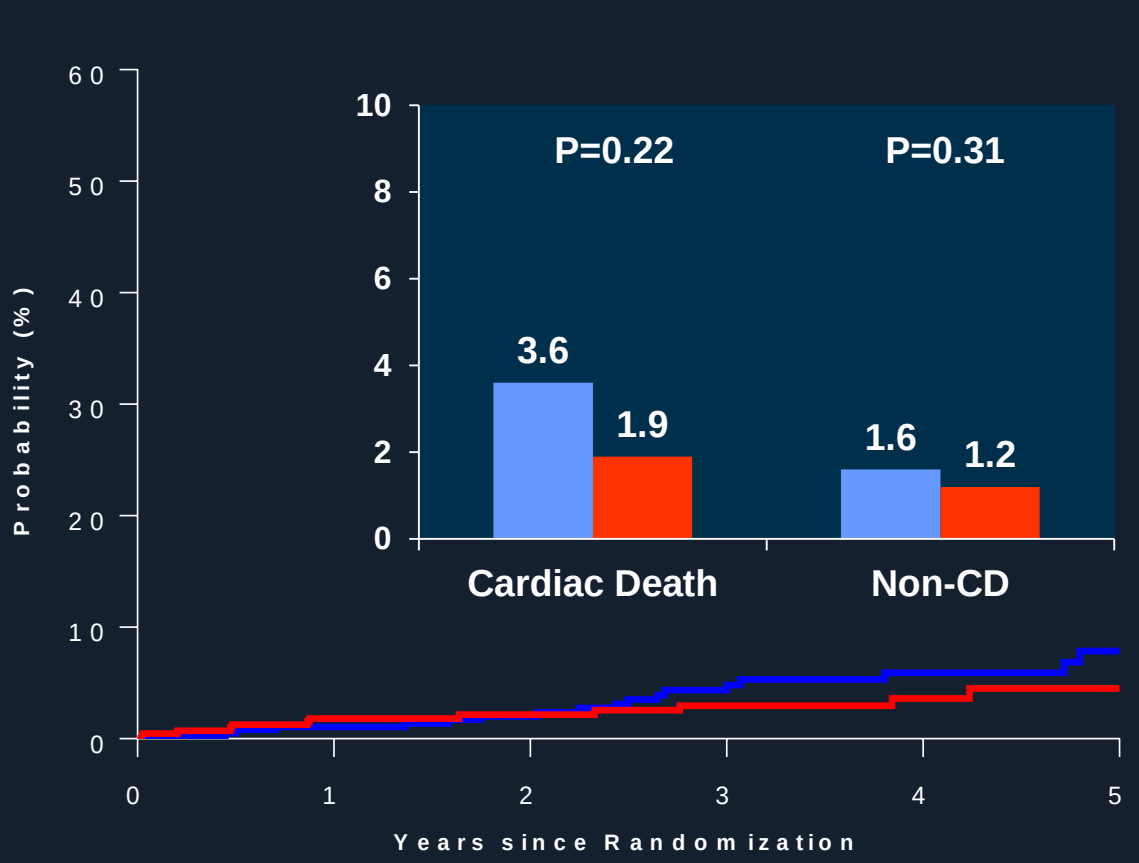
No. at Risk						
OMT	398	305	246	178	129	72
PCI	417	293	241	175	117	65

Death from any cause



No. at Risk						
OMT	398	344	285	207	140	81
PCI	417	337	285	202	142	74

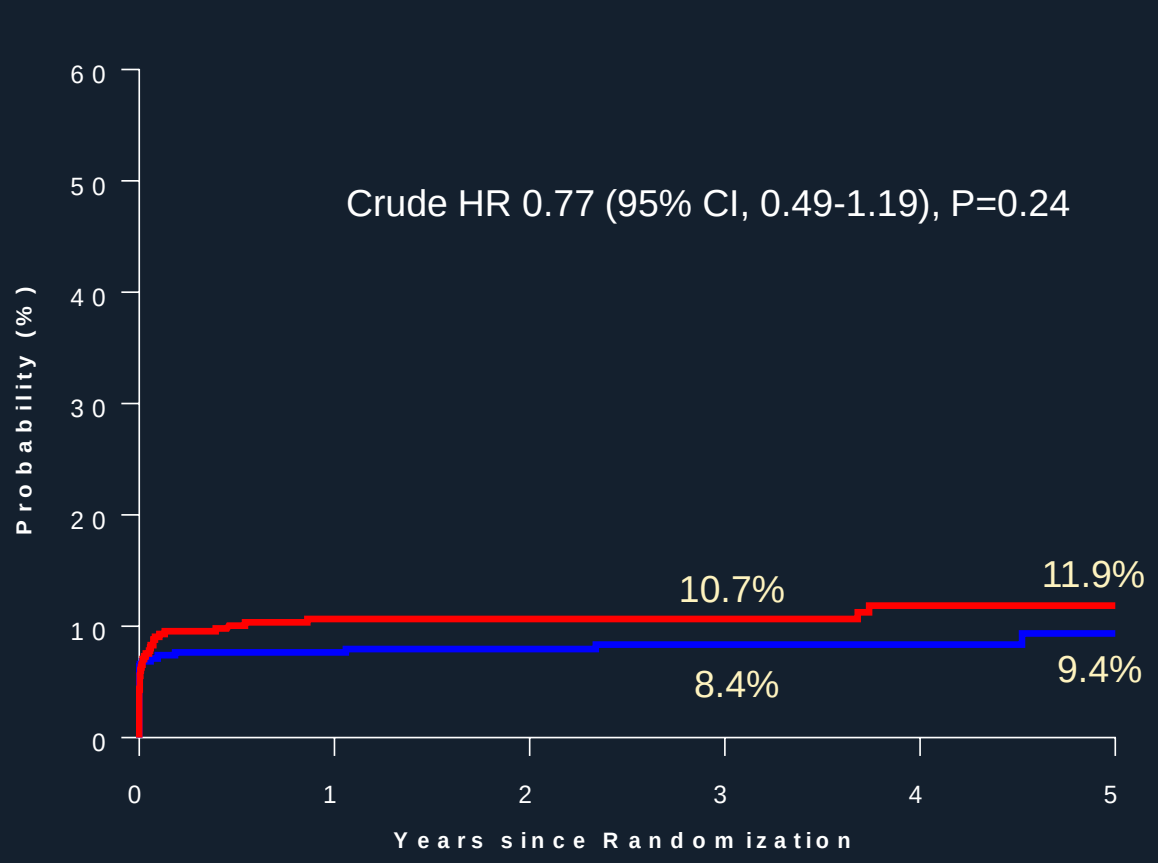
Death from any cause



No. at Risk						
OMT	398	344	285	207	140	81
PCI	417	337	285	202	142	74

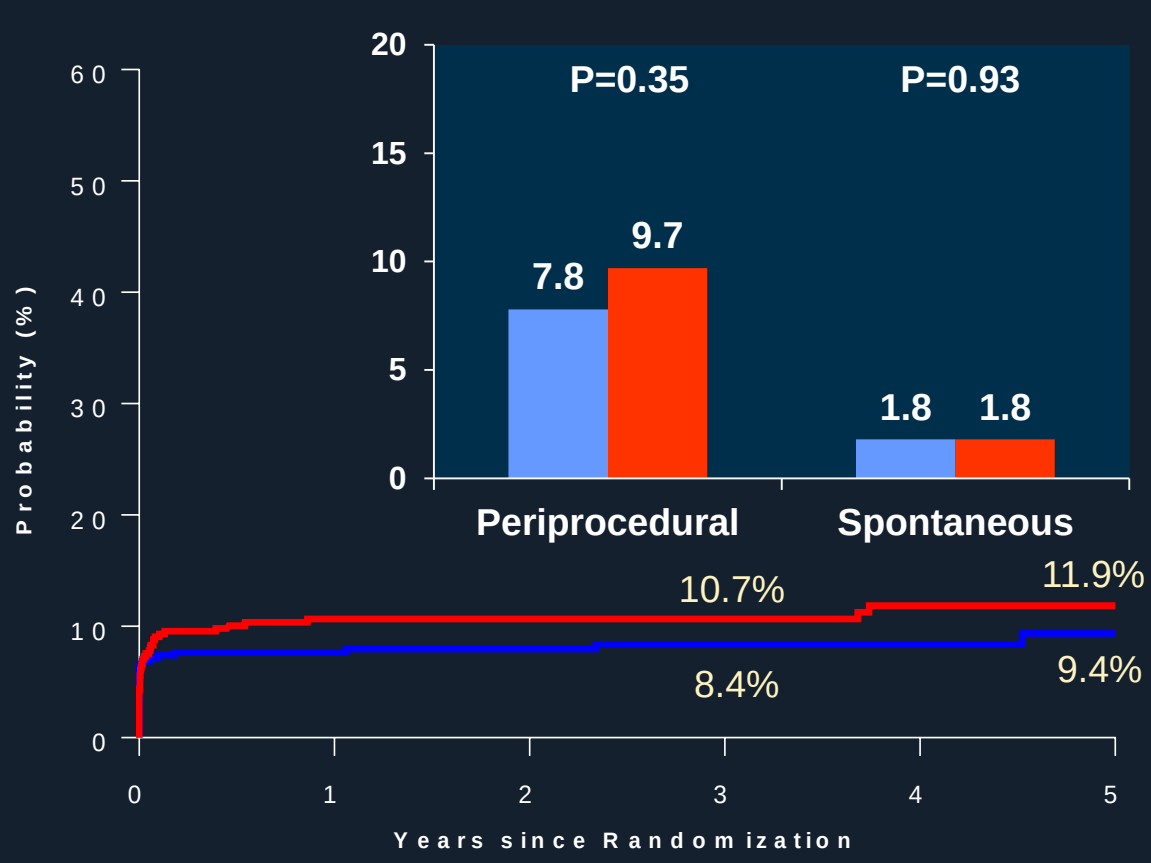
ITT Population

Myocardial Infarction



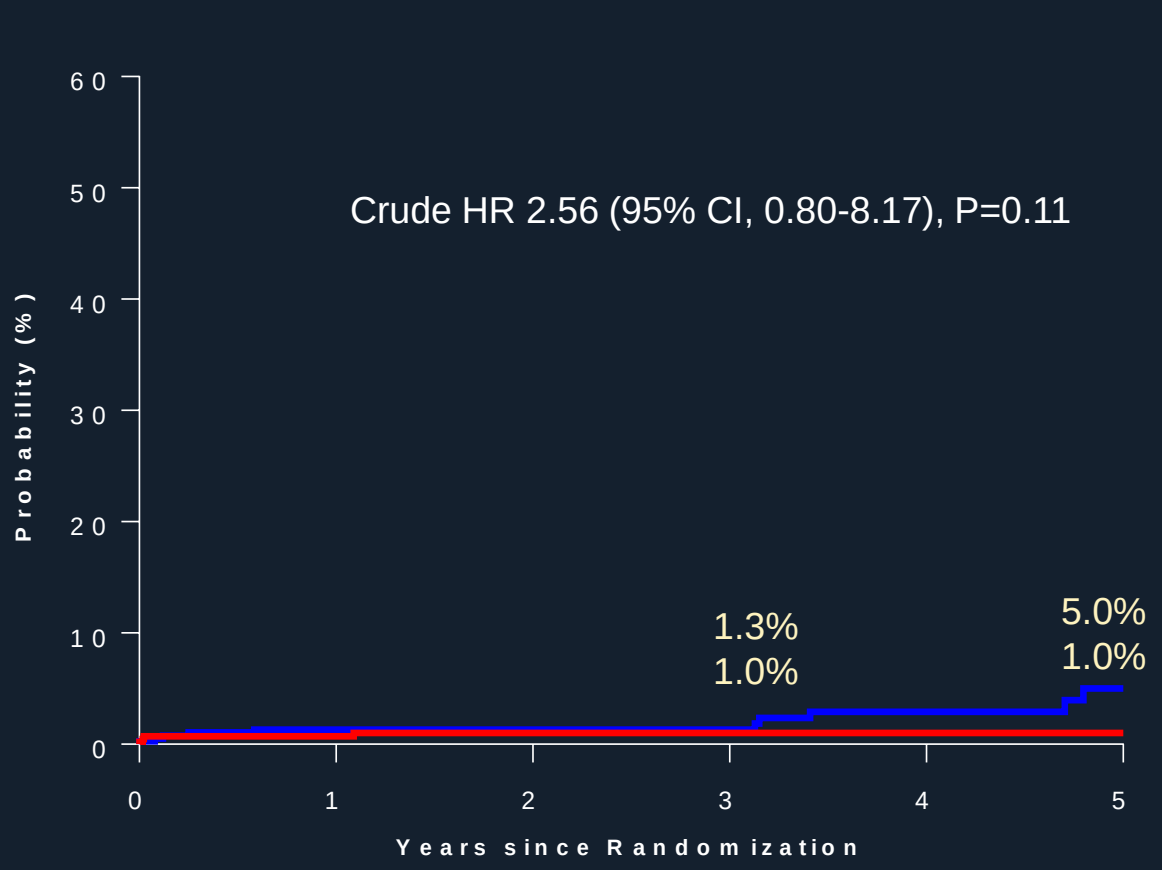
No. at Risk						
OMT	398	317	260	189	129	73
PCI	417	300	255	181	125	64

Myocardial Infarction



No. at Risk						
OMT	398	317	260	189	129	73
PCI	417	300	255	181	125	64

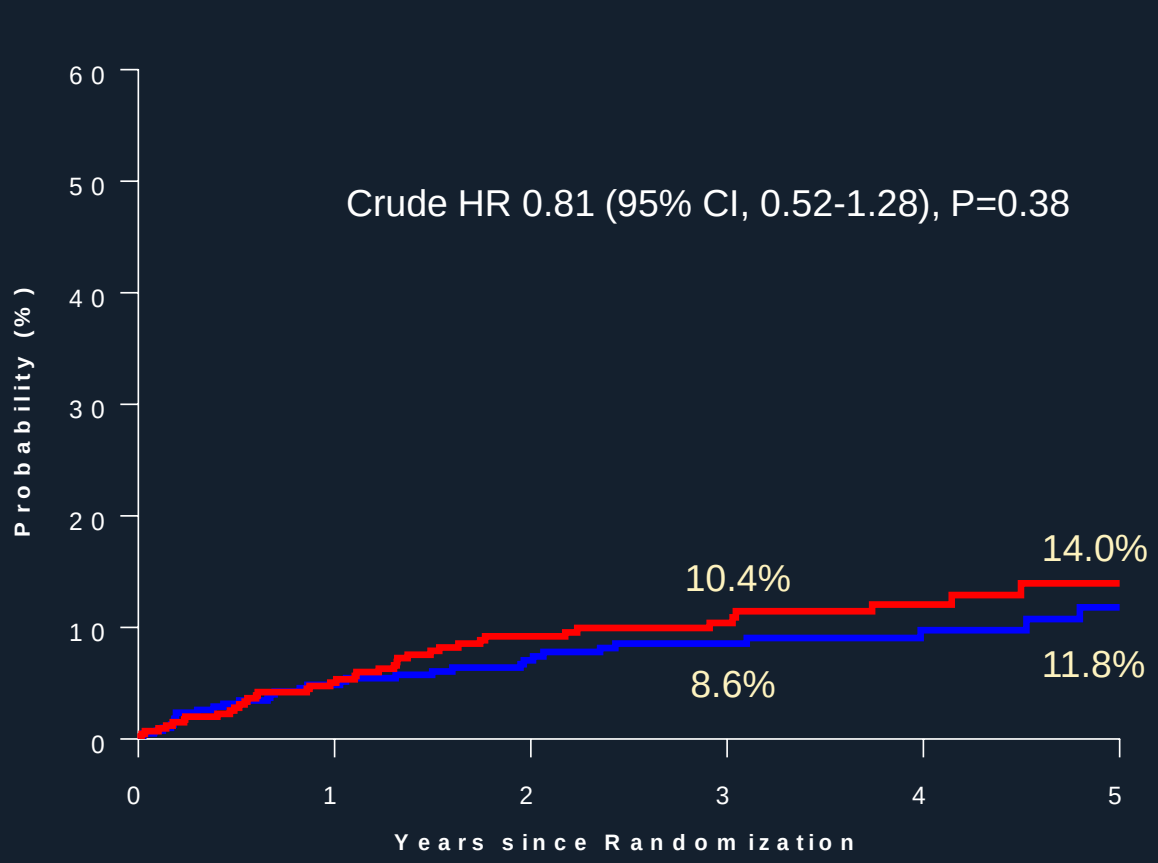
Stroke



No. at Risk

OMT	398	339	280	203	137	77
PCI	417	337	284	201	142	74

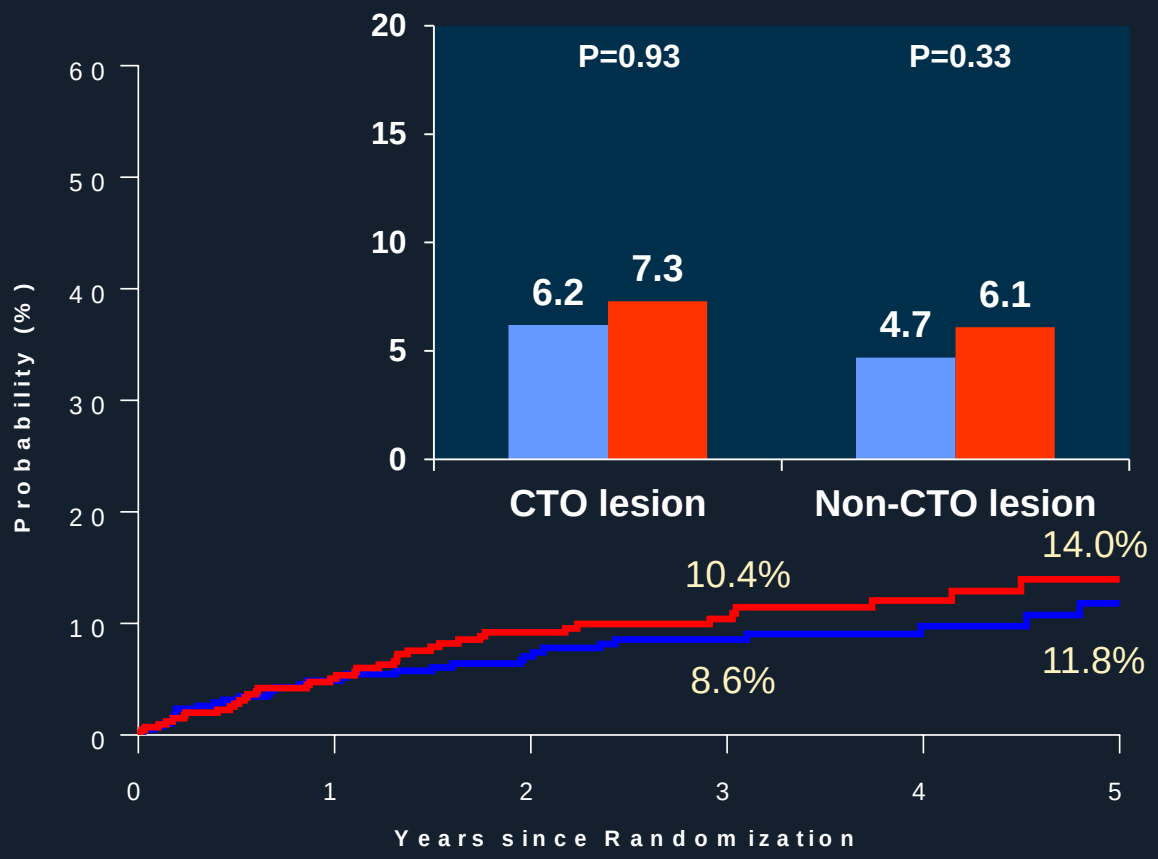
Repeat Revascularization



No. at Risk

OMT	398	330	270	292	129	74
PCI	417	321	259	181	129	65

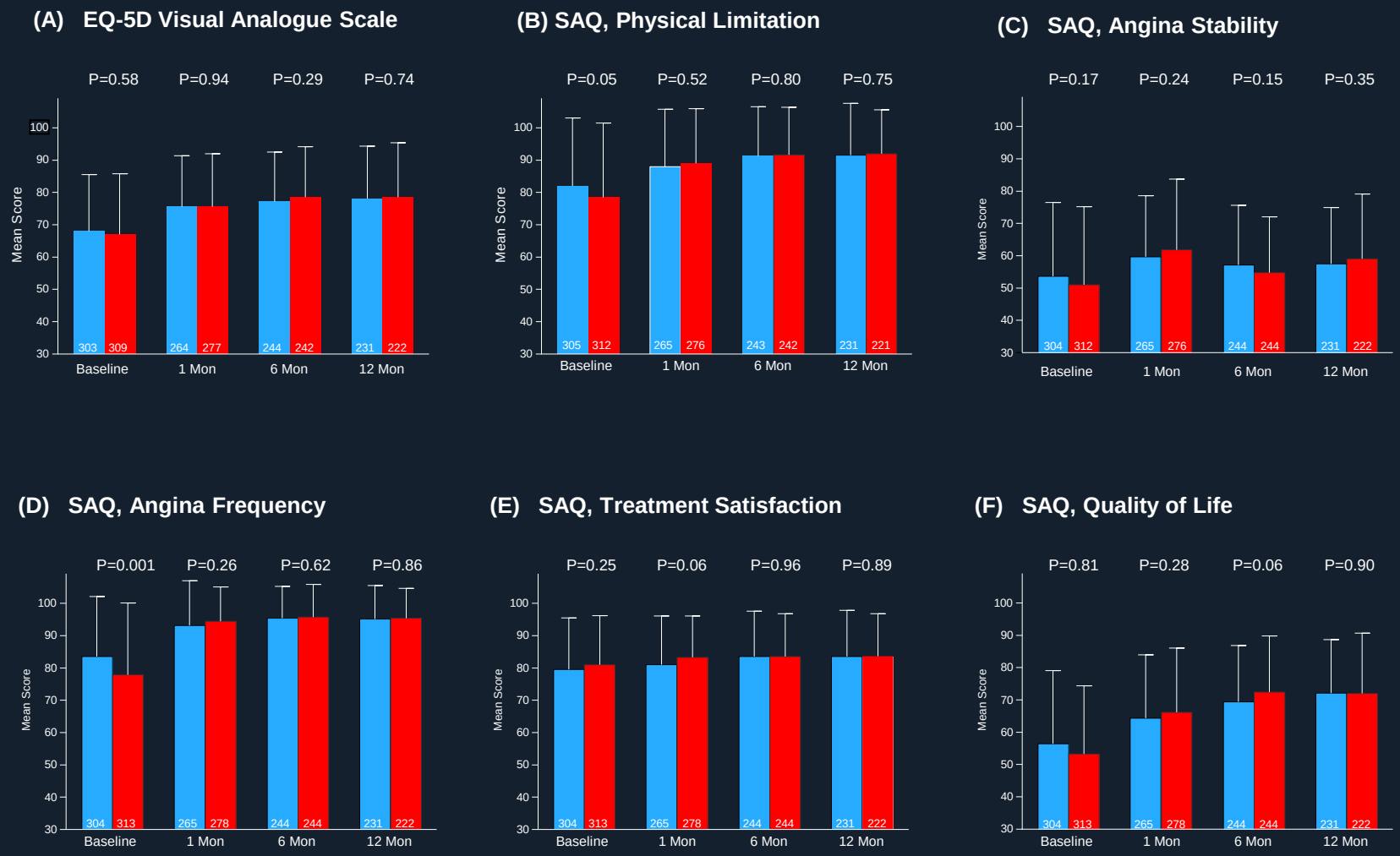
Repeat Revascularization



No. at Risk						
OMT	398	330	270	292	129	74
PCI	417	321	259	181	129	65

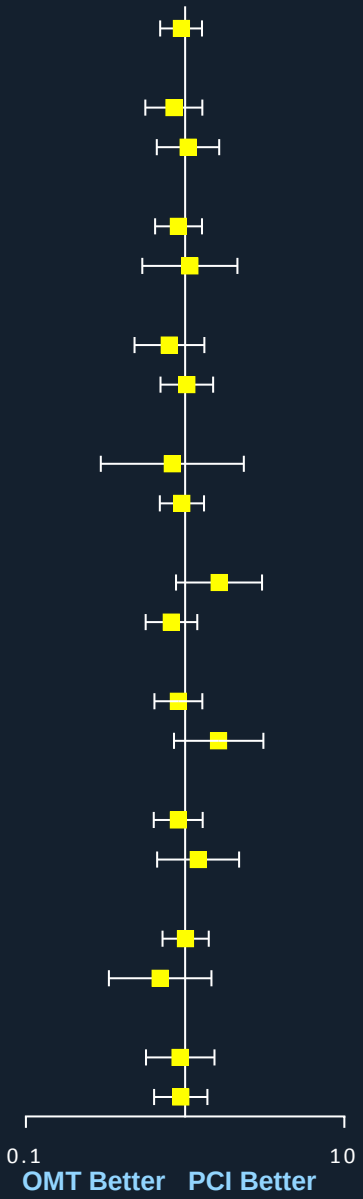
Quality of Life Measures Over Time

ITT Population



Subgroup Analysis

Subgroup	OMT	PCI	Hazard ratio (95% CI)	p value for Interaction
	no. of patients with event/total no. (%)			
Overall	81/387 (20.9)	86/411 (20.9)	0.95 (0.70−1.28)	
Age				0.51
≥ 65 y	43/172 (25.0)	48/174 (27.6)	0.85 (0.56−1.29)	
< 65 y	38/215 (17.7)	38/237 (16.0)	1.05 (0.67−1.64)	
Sex				0.65
Male	63/315 (20.0)	71/342 (20.8)	0.91 (0.65−1.28)	
Female	18/72 (25.0)	15/69 (21.7)	1.07 (0.54−2.13)	
Diabetes				0.45
Yes	29/133 (21.8)	32/132 (24.2)	0.80 (0.48−1.32)	
No	52/254 (20.5)	54/279 (19.4)	1.03 (0.70−1.50)	
Previous myocardial infarction				0.77
Yes	6/34 (17.6)	9/45 (20.0)	0.83 (0.30−2.34)	
No	75/353 (21.2)	77/366 (21.0)	0.96 (0.70−1.32)	
Acute coronary syndrome				0.18
Yes	29/97 (29.9)	26/113 (23.0)	1.64 (0.88−3.05)	
No	52/290 (17.9)	60/298 (20.1)	0.82 (0.57−1.19)	
Typical chest pain				0.56
Yes	65/278 (23.4)	64/311 (20.6)	0.91 (0.64−1.29)	
No	16/109 (14.7)	22/100 (22.0)	1.63 (0.85−3.11)	
Ejection fraction				0.44
≥ 50%	60/321 (18.7)	63/332 (19.0)	0.91 (0.64−1.30)	
< 50%	21/66 (31.8)	23/79 (29.1)	1.21 (0.67−2.19)	
Multi-vessel disease				0.39
Yes	69/286 (24.1)	69/301 (22.9)	1.01 (0.72−1.41)	
No	12/101 (11.9)	17/110 (15.5)	0.70 (0.33−1.47)	
CTO located in the left anterior descending artery				0.98
Yes	29/161 (18.0)	34/183 (18.6)	0.93 (0.57−1.53)	
No	52/226 (23.0)	52/228 (22.8)	0.94 (0.64−1.38)	



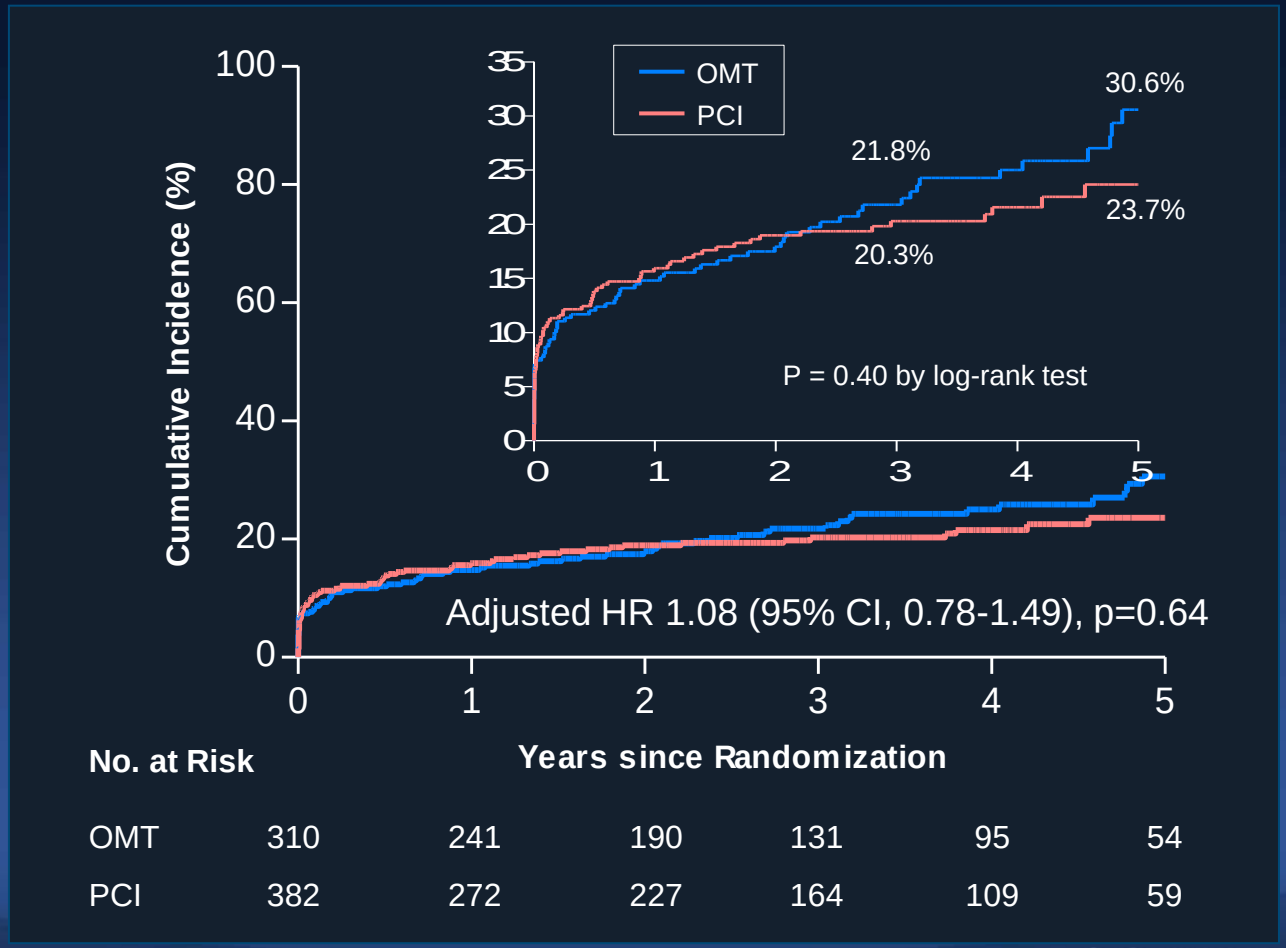
Per Protocol Analysis

OMT vs. PCI attempt

Primary Outcome

(Death, MI, Stroke, Any Repeat Revascularization)

Per Protocol Population



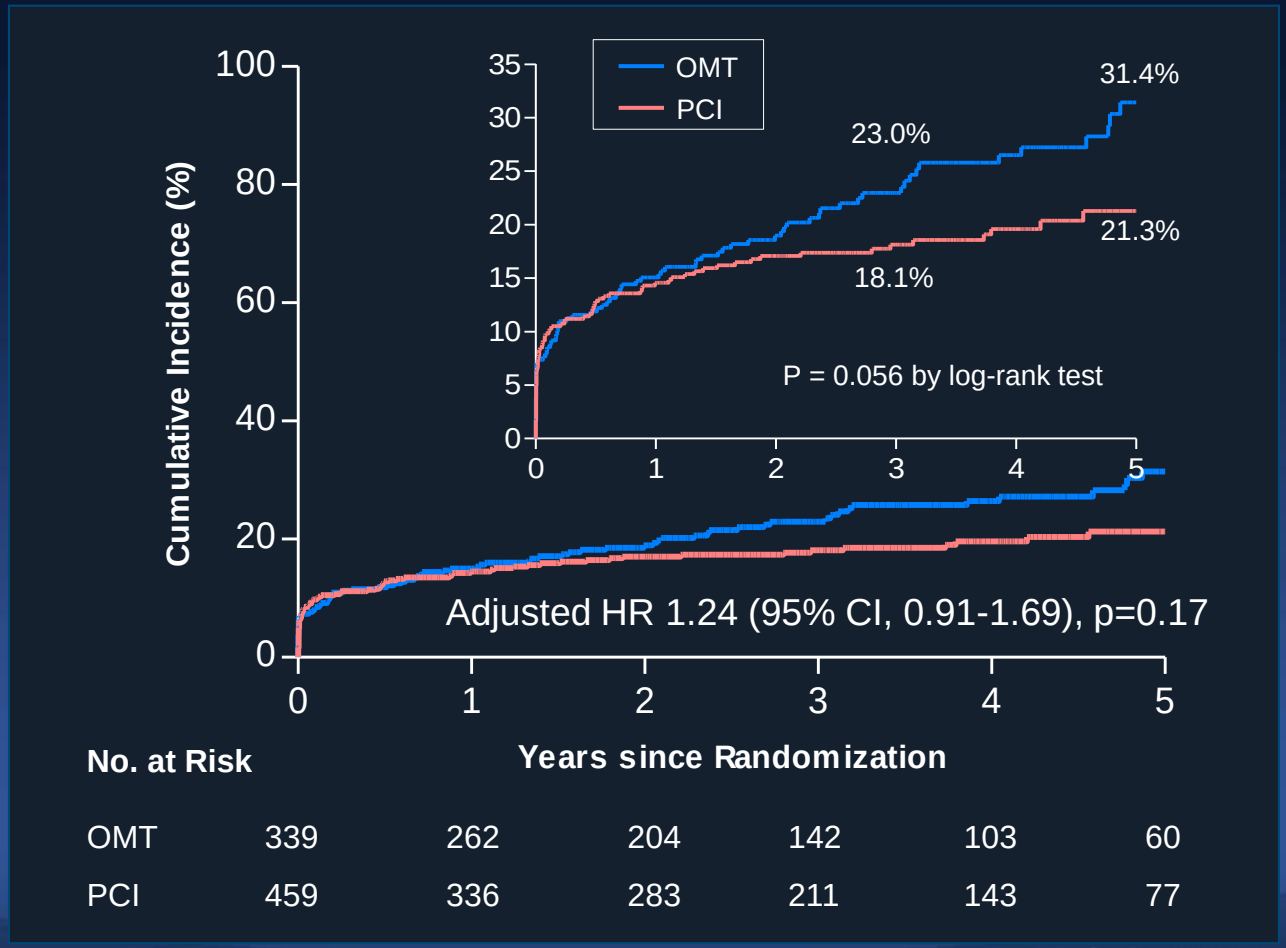
As Treated Analysis

OMT vs. PCI attempt

Primary Outcome

(Death, MI, Stroke, Any Repeat Revascularization)

As Treated Population



Conclusion

- The DECISION-CTO trial is the first randomized clinical trial to compare the strategy of OMT alone with that of PCI in patients with coronary CTO.
- Our results showed that OMT as an initial strategy was statistically not different compared to PCI in terms of the composite of death, MI, stroke, or any revascularization at 3 years.
- The measures of health-related quality of life in the OMT and the PCI groups were comparable throughout the follow-up period

Conclusion

- However, despite statistical no difference, we did not provide firm conclusion for role of OMT in the CTO patients due to early termination and lower enrolment than anticipated.
- There is a signal for role of OMT, but further randomized clinical trials are necessary.