08:30 - 10:00 SESSION 1 - CORONAIRE

Indications de revascularisation dans les syndromes coronaires chroniques

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DÉCLARATION DE LIENS D'INTÉRÊT AVEC LA PRÉSENTATION

Speaker's name : Cédric DELHAYE, Lille

☑ Je déclare les liens d'intérêt potentiel suivants :

Consultant / Proctoring : Abbott, Asahi, Medtronic

2 Goals of therapies in patients with Chronic coronary syndrome

1. Improve symptoms and quality of life **?**
  ➢ Measured by « soft » end-points (i.e. angina/QOL scales)

2. Improve prognosis
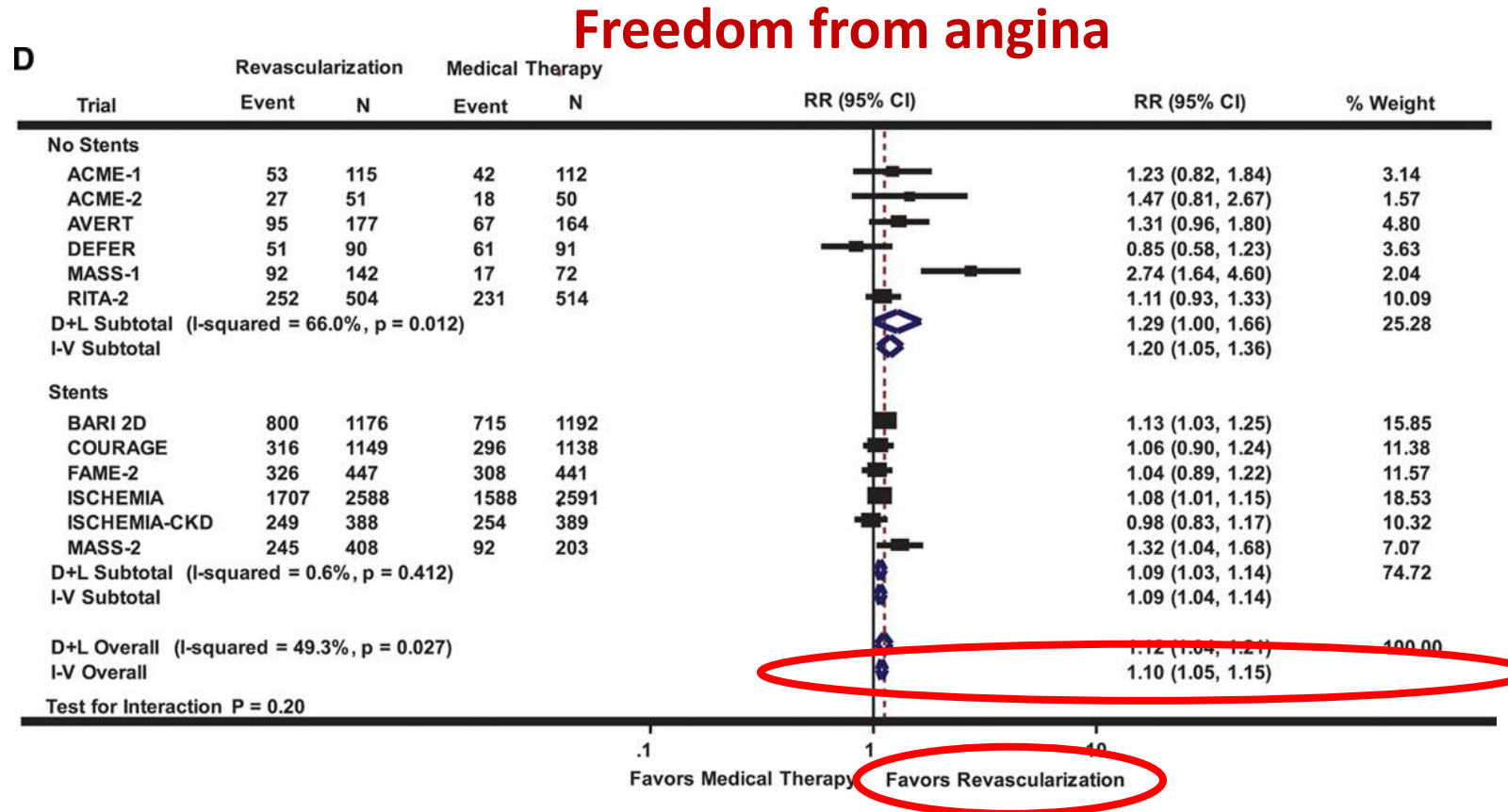 ➢ Measured by « hard » end-points (i.e. death, MI)

Meta-Analysis of 14 RCTs
Routine Revasc vs. Initial Medical Therapy in stable CAD
14 877 patients, Follow up 4.5 years

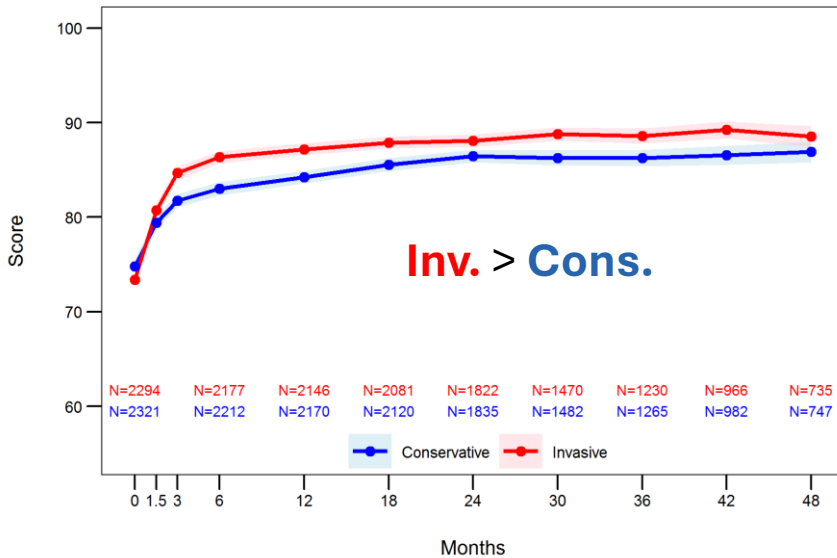**Increase in freedom from angina (RR= 1.10 [95% CI, 1.05–1.15]) with revascularization**

Freedom from angina

Trial	Revascularization		Medical Therapy		RR (95% CI)	% Weight
	Event	N	Event	N		
No Stents						
ACME-1	53	115	42	112	1.23 (0.82, 1.84)	3.14
ACME-2	27	51	18	50	1.47 (0.81, 2.67)	1.57
AVERT	95	177	67	164	1.31 (0.96, 1.80)	4.80
DEFER	51	90	61	91	0.85 (0.58, 1.23)	3.63
MASS-1	92	142	17	72	2.74 (1.64, 4.60)	2.04
RITA-2	252	504	231	514	1.11 (0.93, 1.33)	10.09
D+L Subtotal (I-squared = 66.0%, p = 0.012)					1.29 (1.00, 1.66)	25.28
I-V Subtotal					1.20 (1.05, 1.36)	
Stents						
BARI 2D	800	1176	715	1192	1.13 (1.03, 1.25)	15.85
COURAGE	316	1149	296	1138	1.06 (0.90, 1.24)	11.38
FAME-2	326	447	308	441	1.04 (0.89, 1.22)	11.57
ISCHEMIA	1707	2588	1588	2591	1.08 (1.01, 1.15)	18.53
ISCHEMIA-CKD	249	388	254	389	0.98 (0.83, 1.17)	10.32
MASS-2	245	408	92	203	1.32 (1.04, 1.68)	7.07
D+L Subtotal (I-squared = 0.6%, p = 0.412)					1.09 (1.03, 1.14)	74.72
I-V Subtotal					1.09 (1.04, 1.14)	
D+L Overall (I-squared = 49.3%, p = 0.027)					1.12 (1.04, 1.21)	100.00
I-V Overall					1.10 (1.05, 1.15)	
Test for Interaction P = 0.20						

Favors Medical Therapy   Favors Revascularization

Bangalore S et al. Circulation 2020;142(9):841-857

ISCHEMIA Trial

5 179 patients with CCS and moderate or high-risk ischemia
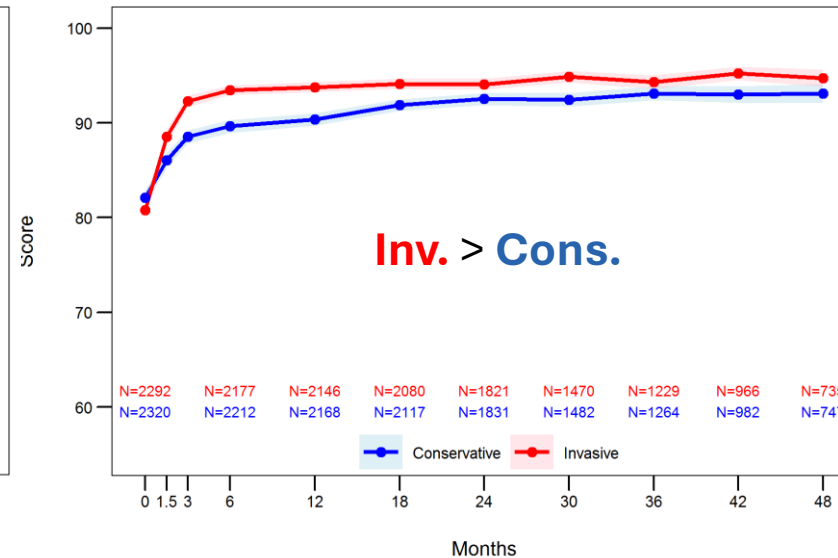### Invasive (OMT + optimal revasc) vs. Conservative strategy (OMT alone)

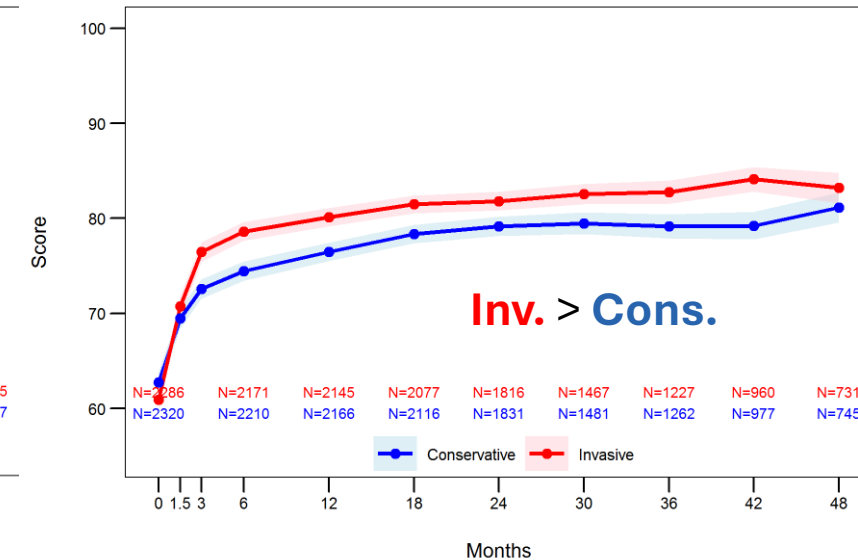## Greater improvement in angina-related health status with Invasive strategy

SAQ Summary Score

Inv. > Cons.

N=2294 N=2177 N=2146 N=2081 N=1822 N=1470 N=1230 N=966 N=735
N=2321 N=2212 N=2170 N=2120 N=1835 N=1482 N=1265 N=982 N=747

Conservative   Invasive

Physical Limitation
Angina Frequency
Quality of Life

SAQ Angina Frequency

Inv. > Cons.

N=2292 N=2177 N=2146 N=2080 N=1821 N=1470 N=1229 N=966 N=735
N=2320 N=2212 N=2168 N=2117 N=1831 N=1482 N=1264 N=982 N=747

Conservative   Invasive

SAQ Quality of Life

Inv. > Cons.

N=2286 N=2171 N=2145 N=2077 N=1816 N=1467 N=1227 N=960 N=731
N=2320 N=2210 N=2166 N=2116 N=1831 N=1481 N=1262 N=977 N=745

Conservative   Invasive

SAQ: higher scores indicating better health status

Spertus, JA. N Engl J Med 2020;382:1408-19.

Improvement in QoL is related to baseline symptoms

Probability of no angina by SAQ score in ISCHEMIA Trial

The more symptomatic (low SAQ), the more patients benefit from the invasive strategy

B Probability of Being Angina-free

Month 3   Month 12   Month 36

Probability (%)

Invasive
Conservative
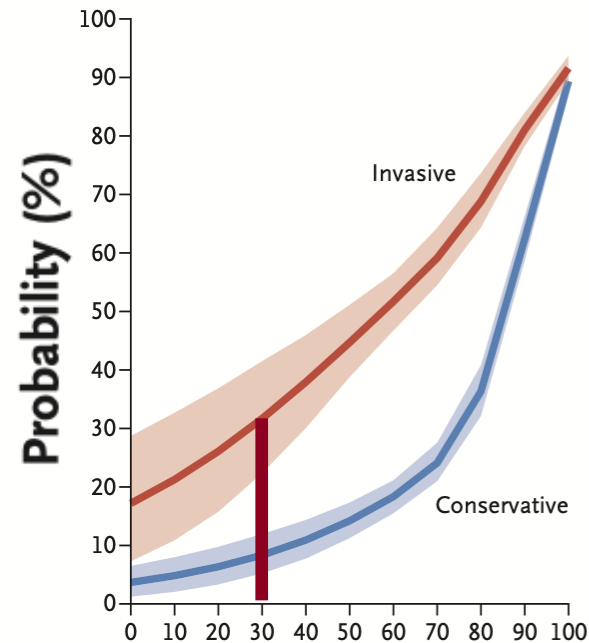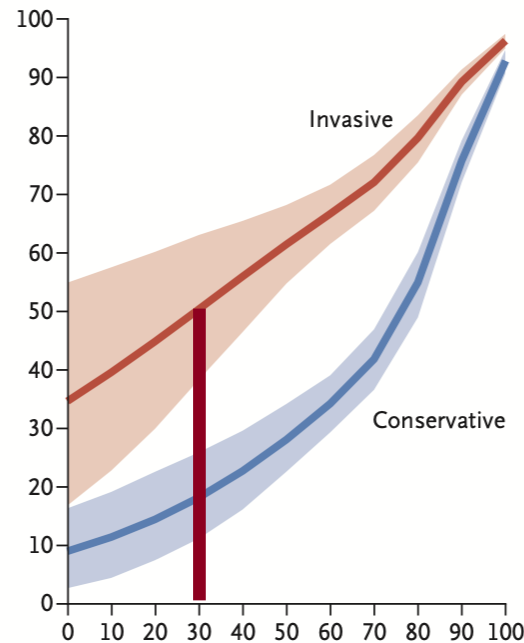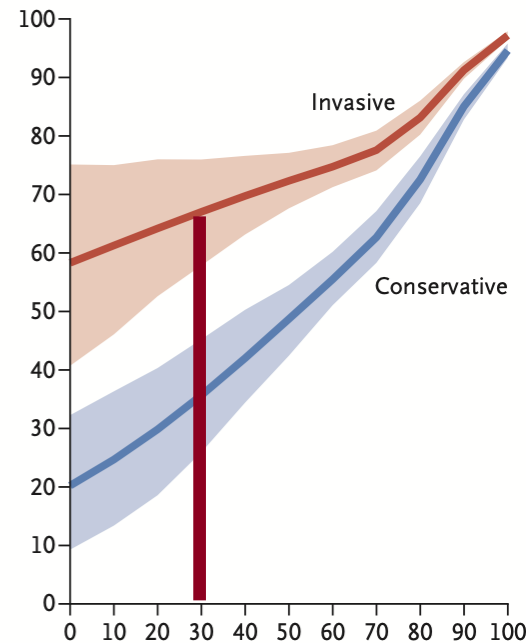
Baseline SAQ Angina Frequency Score

SAQ AF
0-30 -daily angina
31-60 -weekly angina
61-99-monthly angina
100-no angina

Spertus, JA. N Engl J Med 2020;382:1408-19.

What is the role of the placebo effect ?

ORBITA (the 1ˢᵗ sham-controlled trial of PCI)

ORBITA-2

ORBITA

PCI (n=105) vs. Sham Control (n=95) in Stable Angina (1-vessel CAD)
optimally treated medically (>85% 2 anti-anginal drugs)

Primary endpoint result
Change in total exercise time
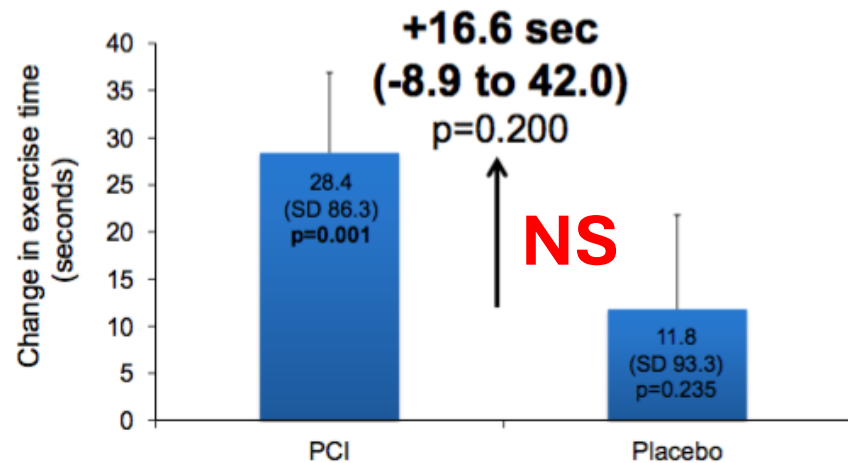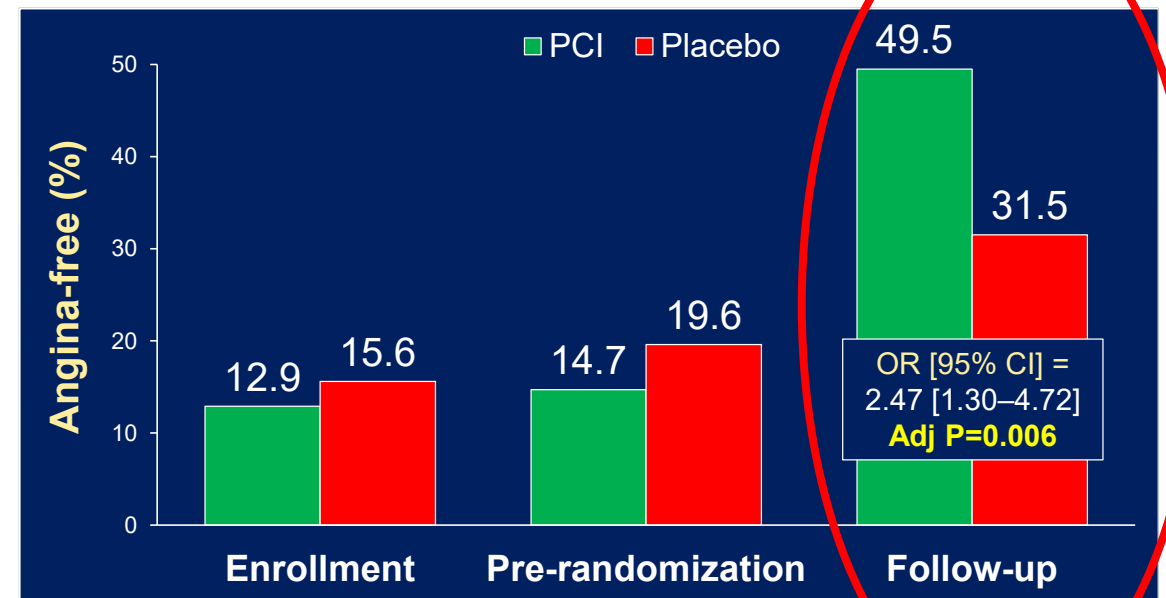
+16.6 sec
(-8.9 to 42.0)
p=0.200

NS

PCI: 28.4 (SD 86.3) p=0.001
Placebo: 11.8 (SD 93.3) p=0.235

Angina-Free Status

PCI   Placebo

Enrollment: 12.9 / 15.6
Pre-randomization: 14.7 / 19.6
Follow-up: 49.5 / 31.5

OR [95% CI] = 2.47 [1.30–4.72]
Adj P=0.006

Al-Lamee R et al. Circulation. 2018;138:1780–1792

Al-Lamee R et al. Lancet 2018; 391: 31–40

ORBITA

PCI (n=105) vs. Sham Control (n=95) in Stable Angina (1-vessel CAD)
optimally treated medically (>85% 2 anti-anginal drugs)

PCI objectively reduced ischemia
(dobutamine stress echocardiography)

The higher the ischemia, the more effective PCI will be
(lower angina frequency score & freedom from angina)

Secondary endpoint results

Blinded evaluation of ischaemia reduction

Peak stress wall motion index score	PCI n = 80	Placebo n = 57
Pre-randomization	1.11 (0.18)	1.11 (0.18)
Follow-up	1.03 (0.06)	1.13 (0.19)
Δ (Pre-randomization to follow-up)	-0.08 (0.17) **p<0.0001**	0.02 (0.16) p=0.433
Difference in Δ between arms	-0.09 (-0.15 to -0.04) **p=0.0011**	

Al-Lamee R et al.
Circulation. 2018;138:1780–1792

$p_{interaction} = 0.031$

$p_{interaction} = 0.116$

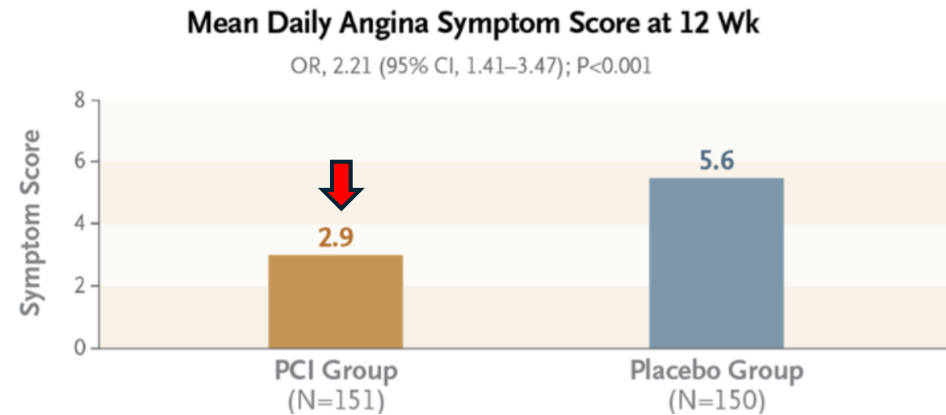Al-Lamee R et al. Circulation. 2019;140:1971–1980

ORBITA-2

PCI (n=151) vs Sham control (n=150) in stable angina with evidence of ischemia
AND little or no antianginal medications
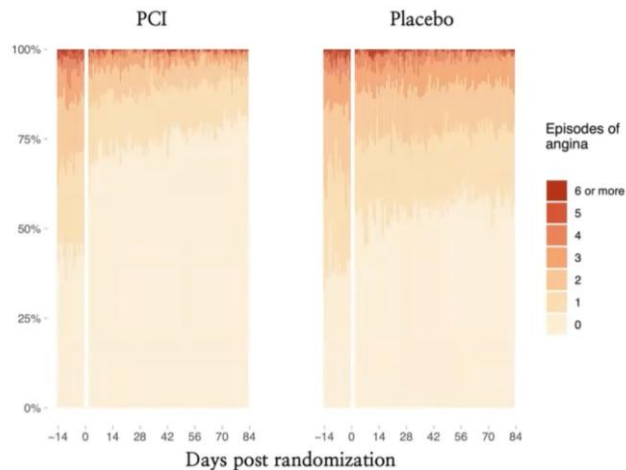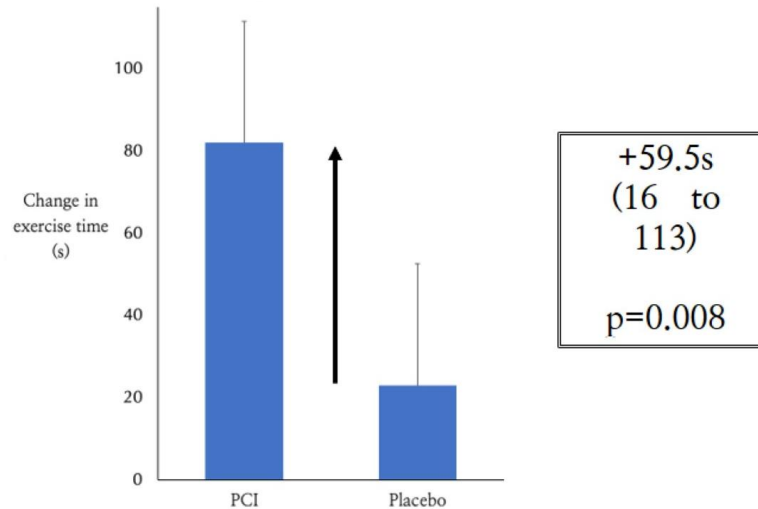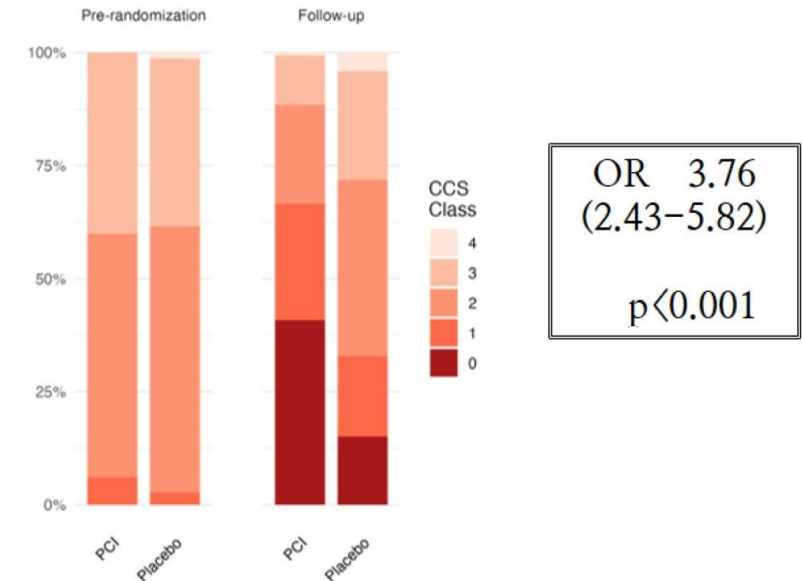
Primary endpoint – angina symptom score

PCI   Placebo

Adverse events
Angina, requiring antianginals

Angina, but no antianginals

Angina free, no antianginals

Days post-randomization
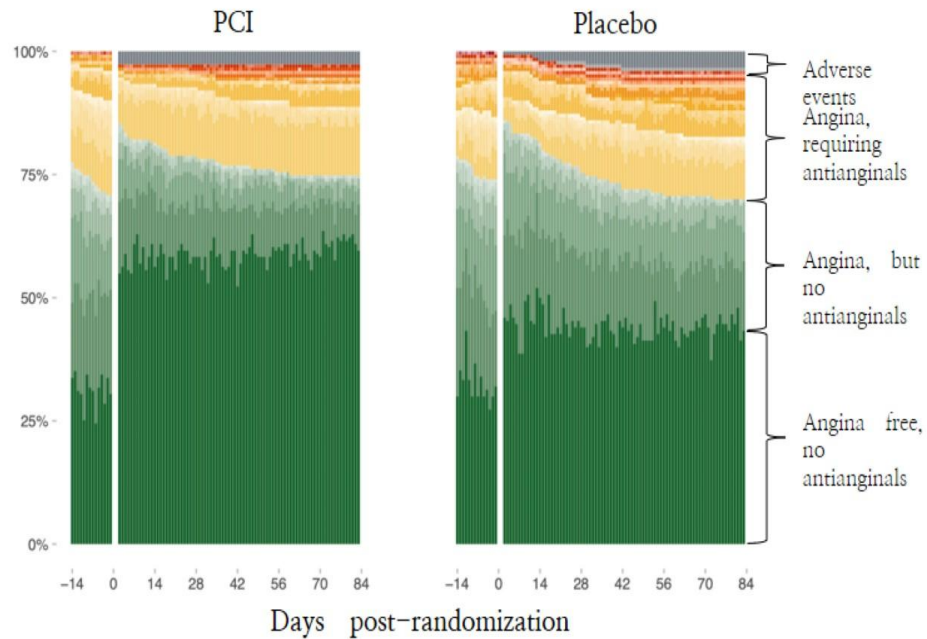
ORBITA₂

PCI improved angina symptom score

Mean Daily Angina Symptom Score at 12 Wk
OR, 2.21 (95% CI, 1.41–3.47); P<0.001

2.9 — PCI Group (N=151)
5.6 — Placebo Group (N=150)

Symptom Score

Higher scores indicating lower angina health status

Rajkumar CA et al. N Engl J Med 2023;389:2319-30.

ORBITA-2

PCI (n=151) vs Sham control (n=150) in stable angina with evidence of ischemia
AND little or no antianginal medications

Rajkumar CA et al. N Engl J Med 2023;389:2319-30.

2024 ESC Guidelines for the management of chronic coronary syndromes

Developed by the task force for the management of chronic coronary syndromes of the European Society of Cardiology (ESC)

Endorsed by the European Association for Cardio-Thoracic Surgery (EACTS)

Revascularization to improve symptoms

In CCS patients with **persistent angina or anginal equivalent, despite guideline-directed medical treatment**, myocardial revascularization of functionally significant obstructive CAD is recommended to improve symptoms.	I	A

Vrints C et al. European Heart Journal (2024) **45**, 3415–3537

2 Goals of therapies in patients with Chronic coronary syndrome

1. Improve symptoms and quality of life
➢ Measured by « soft » end-points (i.e. angina/QOL scales)

2. Improve prognosis
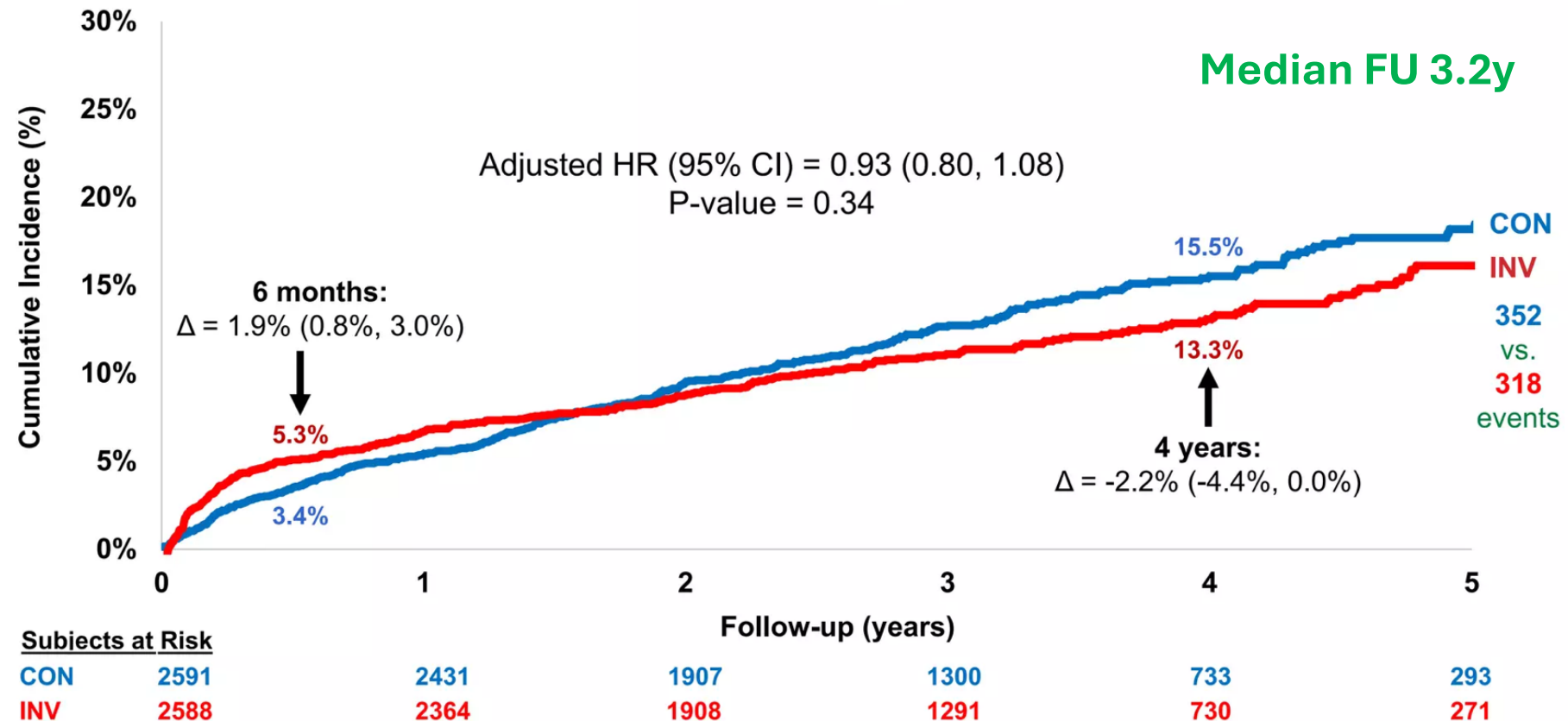➢ Measured by « hard » end-points (i.e. death, MI)

?

ISCHEMIA Trial

5 179 patients (38 countries) with CCS and moderate or high-risk ischemia
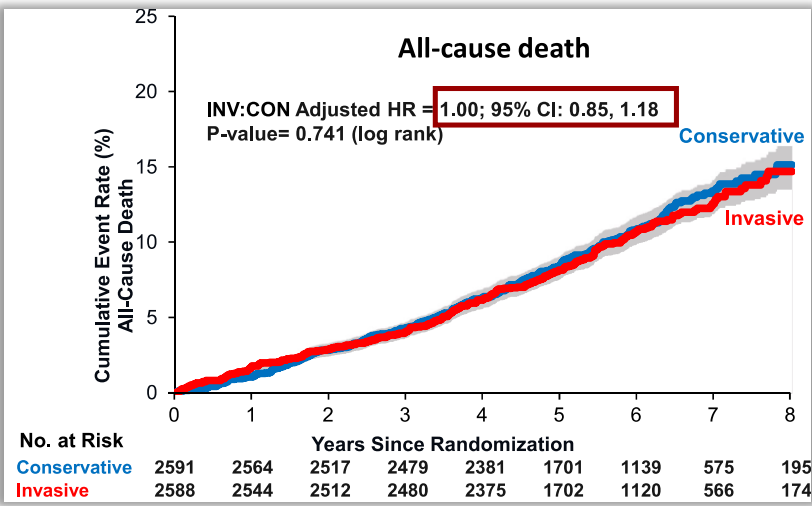### Invasive (OMT + optimal revasc) vs. Conservative strategy (OMT alone)

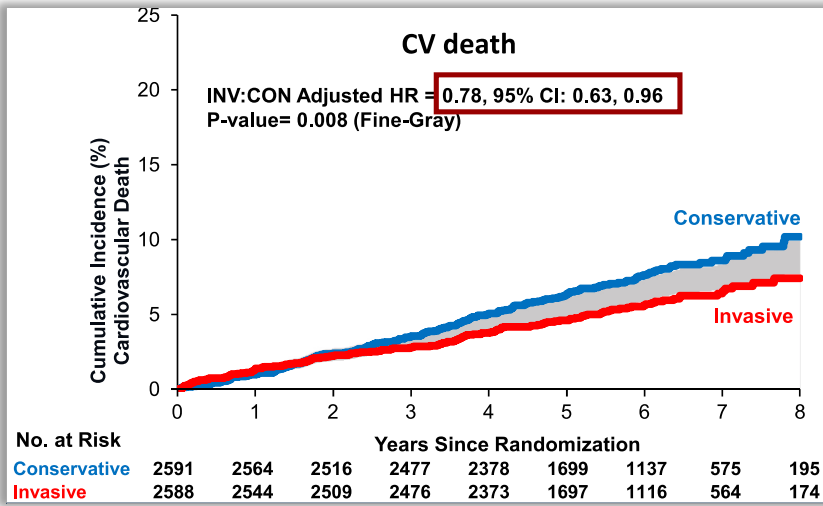Primary endpoint: CV death, MI or hospitalization for arrest, HF or UA

Maron et al. N Engl J Med 2020;382:1395-407

ISCHEMIA-EXTEND: Invasive vs. Conservative strategy
Follow-up 5.7y

**No Benefit on long-term mortality but reduction in CV Death**

All-cause death

INV:CON Adjusted HR = 1.00; 95% CI: 0.85, 1.18
P-value= 0.741 (log rank)

Conservative
Invasive

Cumulative Event Rate (%) All-Cause Death

Years Since Randomization

No. at Risk									
Conservative	2591	2564	2517	2479	2381	1701	1139	575	195
Invasive	2588	2544	2512	2480	2375	1702	1120	566	174

CV death

INV:CON Adjusted HR = 0.78, 95% CI: 0.63, 0.96
P-value= 0.008 (Fine-Gray)

Conservative
Invasive

Cumulative Incidence (%) Cardiovascular Death

Years Since Randomization

No. at Risk									
Conservative	2591	2564	2516	2477	2378	1699	1137	575	195
Invasive	2588	2544	2509	2476	2373	1697	1116	564	174

Non-CV death

INV:CON Adjusted HR = 1.44, 95% CI: 1.08, 1.91
P-value= 0.016 (Fine-Gray)

Invasive
Conservative

Cumulative Incidence (%) Non-Cardiovascular Death

Years Since Randomization

No. at Risk									
Conservative	2591	2564	2516	2477	2378	1699	1137	575	195
Invasive	2588	2544	2509	2476	2373	1697	1116	564	174

All-cause Death = **↓ CV Death** **↑ Non-CV Death**

Chaitman BR et al. Circulation. 2021;143:790–804

15

ISCHEMIA-EXTEND: Invasive vs. Conservative strategy
Follow-up 5.7y

Reduction in CV Death with Invasive Approach
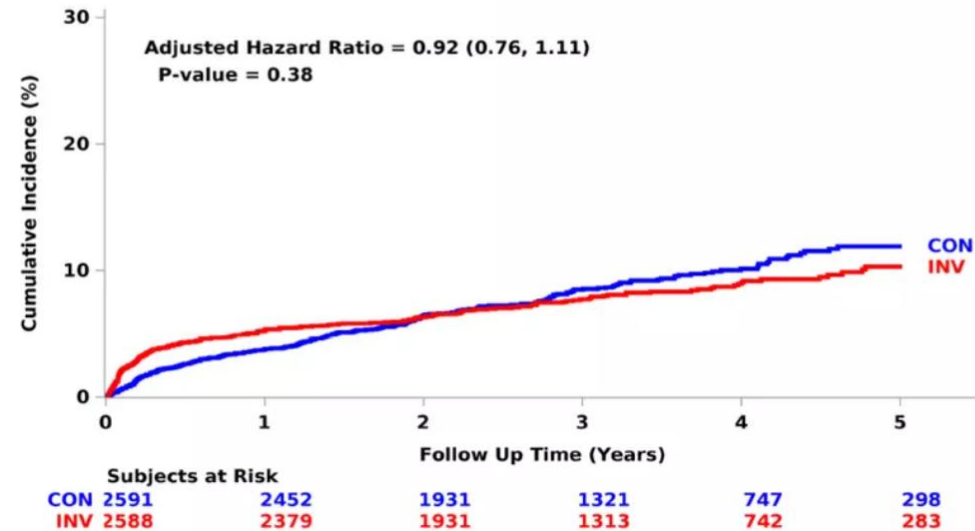### Most marked in pts with multivessel CAD

Hochman J et al. Circulation. 2023;147:8–19.
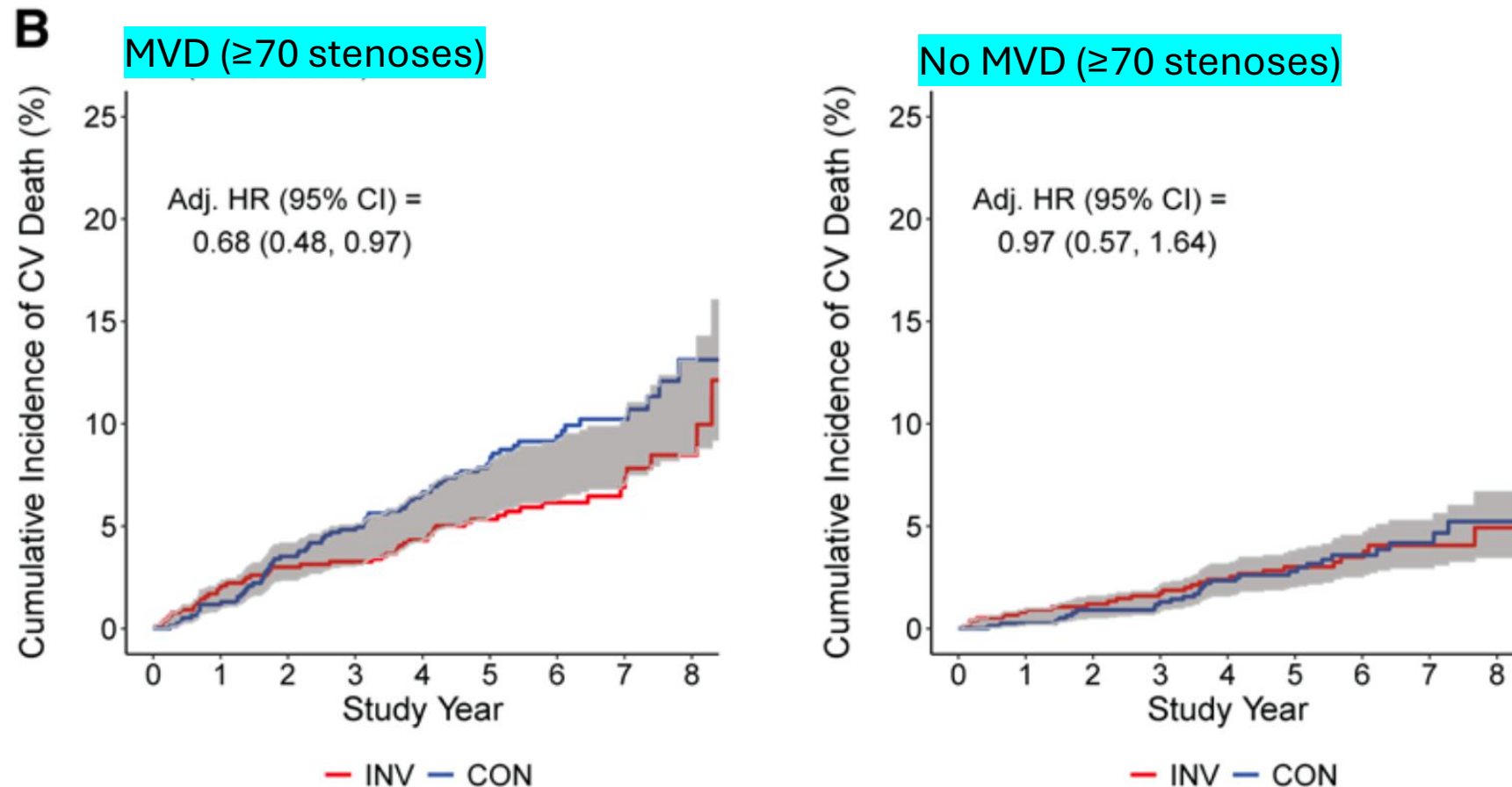
ISCHEMIA Trial: Invasive vs. Conservative strategy

No benefit on All-MI But Reduction in Spontaneous MI

All-MI ═   ⬆ **Procedural MI**   ⬇ **Spontaneous MI**
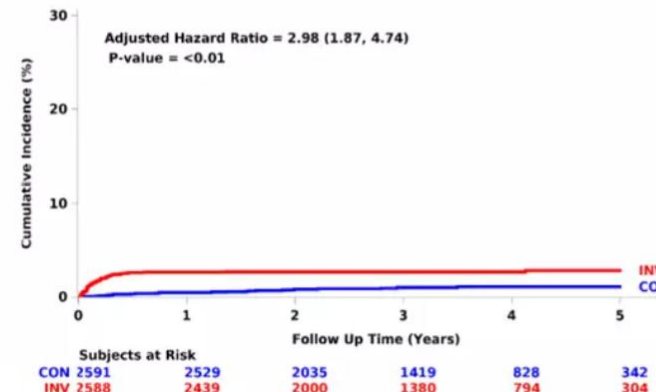
Maron et al. N Engl J Med 2020;382:1395-407
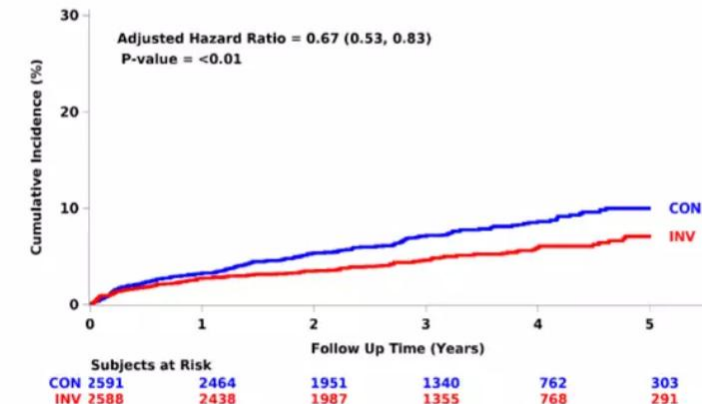
ISCHEMIA Trial: Invasive vs. Conservative strategy

Prognostic impact of Procedural MI vs. Spontaneous MI

Prognosis (Death & CV death) of MI types

A — Prognosis of MI Types in ISCHEMIA Primary MI Definition

No significat prognostic impact
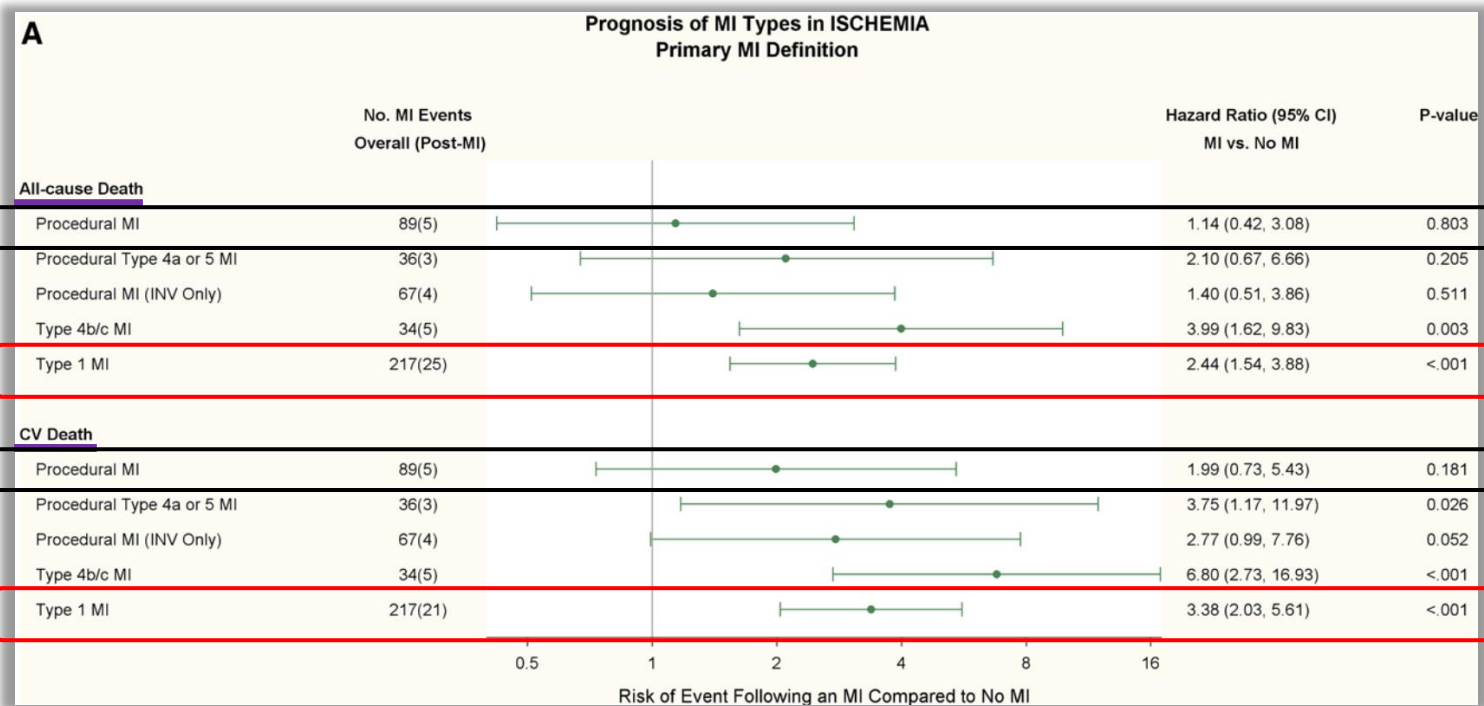
Prognostic impact +++

No significant prognostic impact

Prognostic impact +++

	No. MI Events Overall (Post-MI)	Hazard Ratio (95% CI) MI vs. No MI	P-value
All-cause Death			
Procedural MI	89(5)	1.14 (0.42, 3.08)	0.803
Procedural Type 4a or 5 MI	36(3)	2.10 (0.67, 6.66)	0.205
Procedural MI (INV Only)	67(4)	1.40 (0.51, 3.86)	0.511
Type 4b/c MI	34(5)	3.99 (1.62, 9.83)	0.003
Type 1 MI	217(25)	2.44 (1.54, 3.88)	<.001
CV Death			
Procedural MI	89(5)	1.99 (0.73, 5.43)	0.181
Procedural Type 4a or 5 MI	36(3)	3.75 (1.17, 11.97)	0.026
Procedural MI (INV Only)	67(4)	2.77 (0.99, 7.76)	0.052
Type 4b/c MI	34(5)	6.80 (2.73, 16.93)	<.001
Type 1 MI	217(21)	3.38 (2.03, 5.61)	<.001

Risk of Event Following an MI Compared to No MI

Chaitman BR et al. Circulation. 2021;143:790–804

ISCHEMIA Trial: Invasive vs. Conservative strategy

Reduction in CV Death/MI with invasive Rx for severe CAD pts

3 Vessels ≥ 70% or 2 Vessels ≥ 70% w/prox LAD

CV Death or MI — Duke Score 6, N=659, 3V ≥70% or 2V ≥70% w/prox LAD
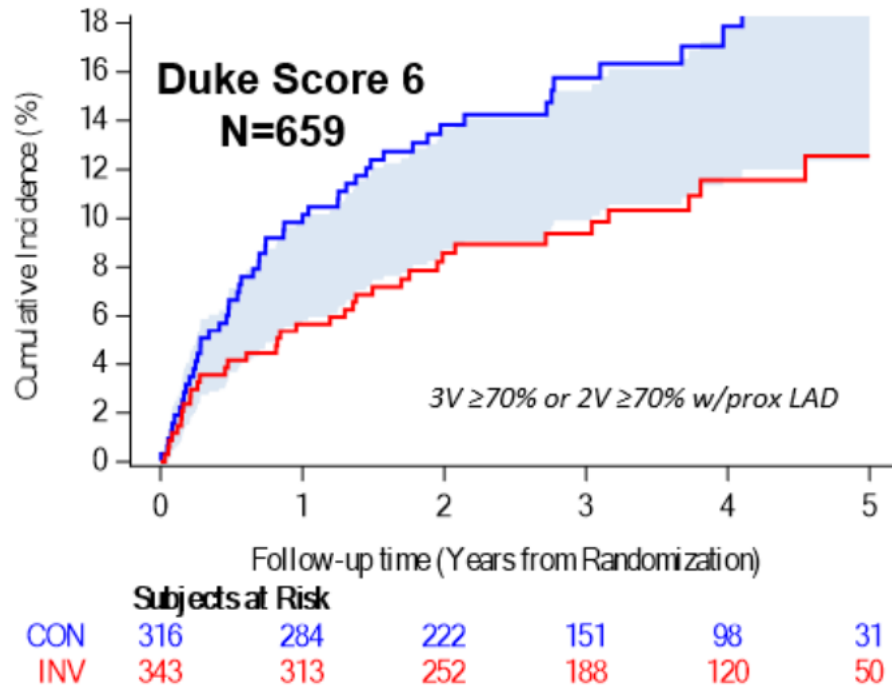
	Events, n		4-y event rate, %			Interaction P value
	Invasive strategy	Conservative strategy	Invasive strategy	Conservative strategy	Difference (95% CI), %	
Cardiovascular death or myocardial infarction						0.33
1-Vessel CAD ≥50%	3	4	3.3 (0.9 to 8.6)	8.7 (2.5 to 19.9)	−5.4 (−14.9 to 4.2)	
1-Vessel CAD ≥70% or 2-vessel ≥50%	26	25	8.8 (5.7 to 12.8)	8.7 (5.6 to 12.5)	0.2 (−4.7 to 5.1)	
2-Vessel CAD ≥70% or 3-vessel ≥50% or 70% proximal LAD	38	48	10.2 (7.2 to 13.9)	12.8 (9.5 to 16.7)	−2.6 (−7.5 to 2.3)	
3-Vessel CAD ≥70% or 2-vessel ≥70% including proximal LAD	34	50	11.6 (8.1 to 15.7)	17.9 (13.4 to 22.8)	−6.3 (−12.4 to −0.2)	

Reynolds H. et al, Circulation 2021;144:1024-1031

Largest Meta-analysis of Elective Revasc in Stable CAD

25 trials, 19 806 pts rand to PCI/CABG vs. Medical Treatment, mean 5.7y FU
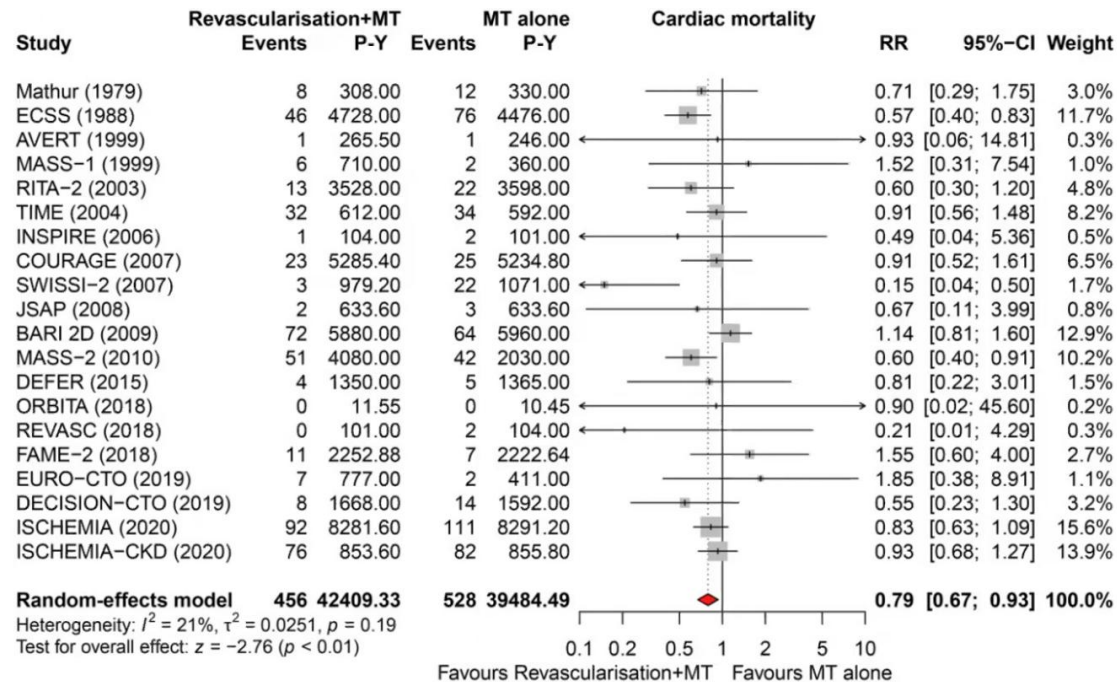
Cardiac Death reduced 21% (95% CI 7-33)
≃**0.3% / year**
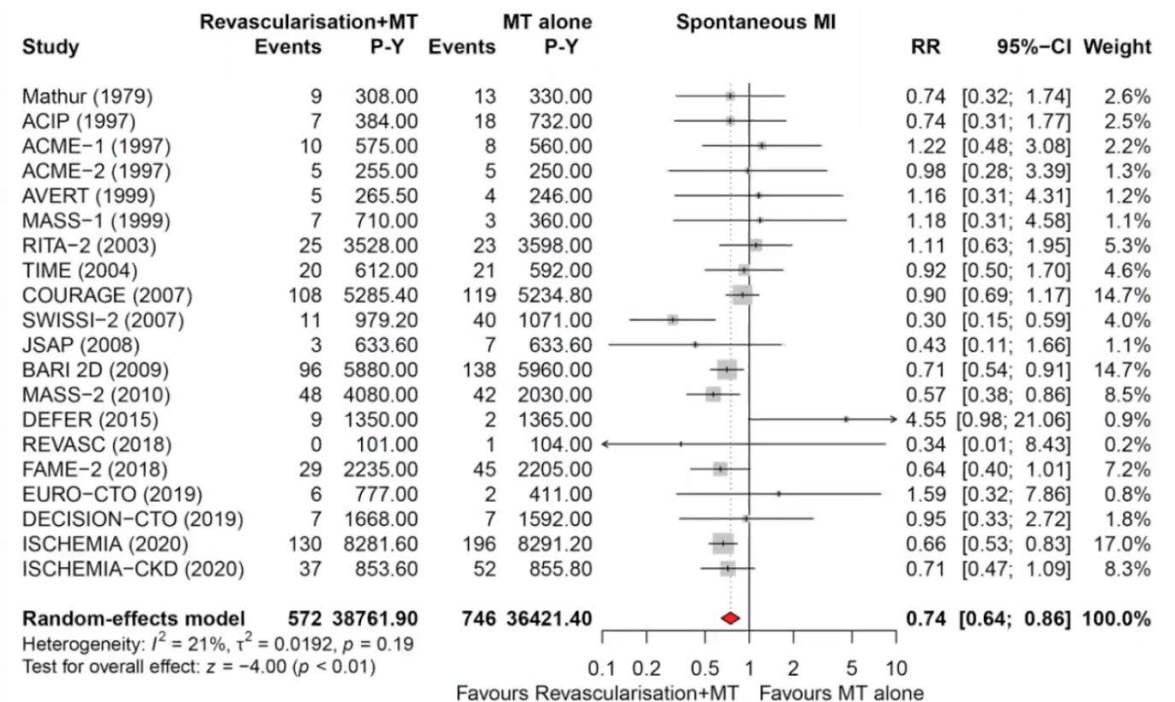
Spontaneous MI reduced 26% (95% CI 14-36)
≃**0.5% / year**

All-cause mortality [0.94 (0.87–1.01), P=0.11], any MI (P=0.14)
did not differ significantly between strategies.

Navarese EP et al. European Heart Journal (2021) 42, 4638–4651

The Ischemia Trial

2 major Exclusion Criteria:

- LVEF <35%

- ≥ 50% LM ds.

Benefit of revascularization in patients with ICM & LVEF ≤ 35%

STITCH
RCT: CABG+OMT vs. OMT alone

REVIVED
RCT: PCI+OMT vs. OMT alone
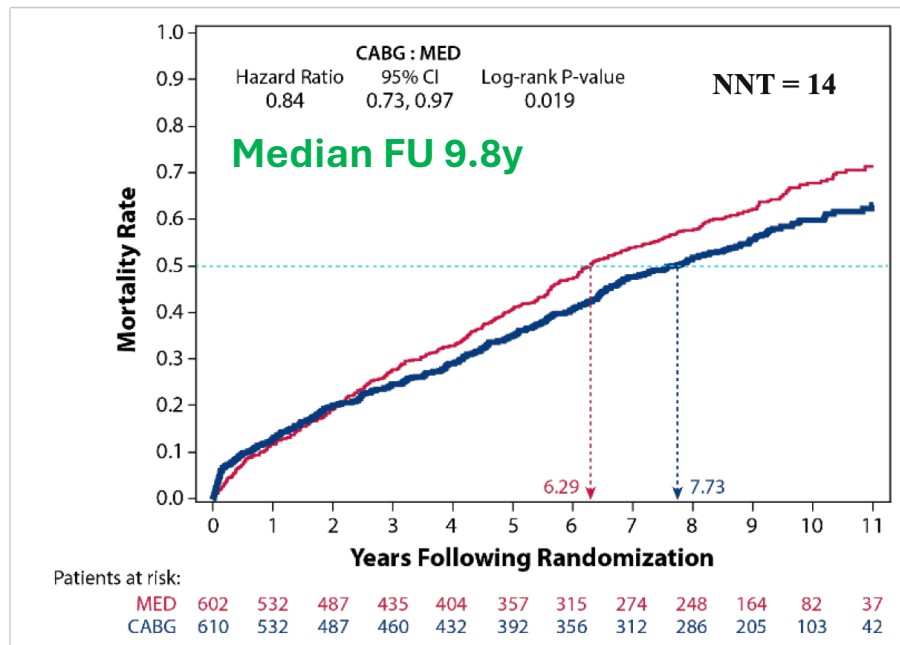
Velazquez E et al. N Engl J Med 2016;374:1511-20.
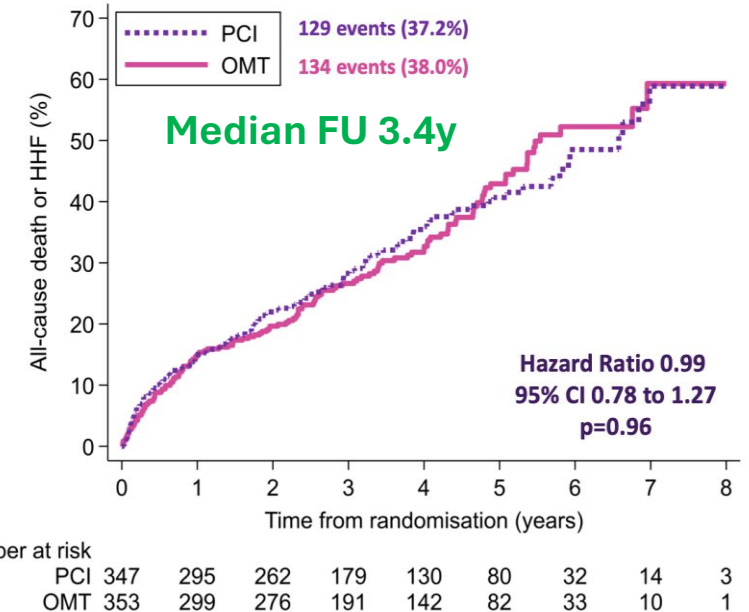
Perera D et al. N Engl J Med 2022;387:1351-60.

2024 ESC Recommandations for Revascularization in patients with Chronic Coronary Syndrome with LVEF > 35%

Vrints C et al. European Heart Journal (2024) **45**, 3415–3537.
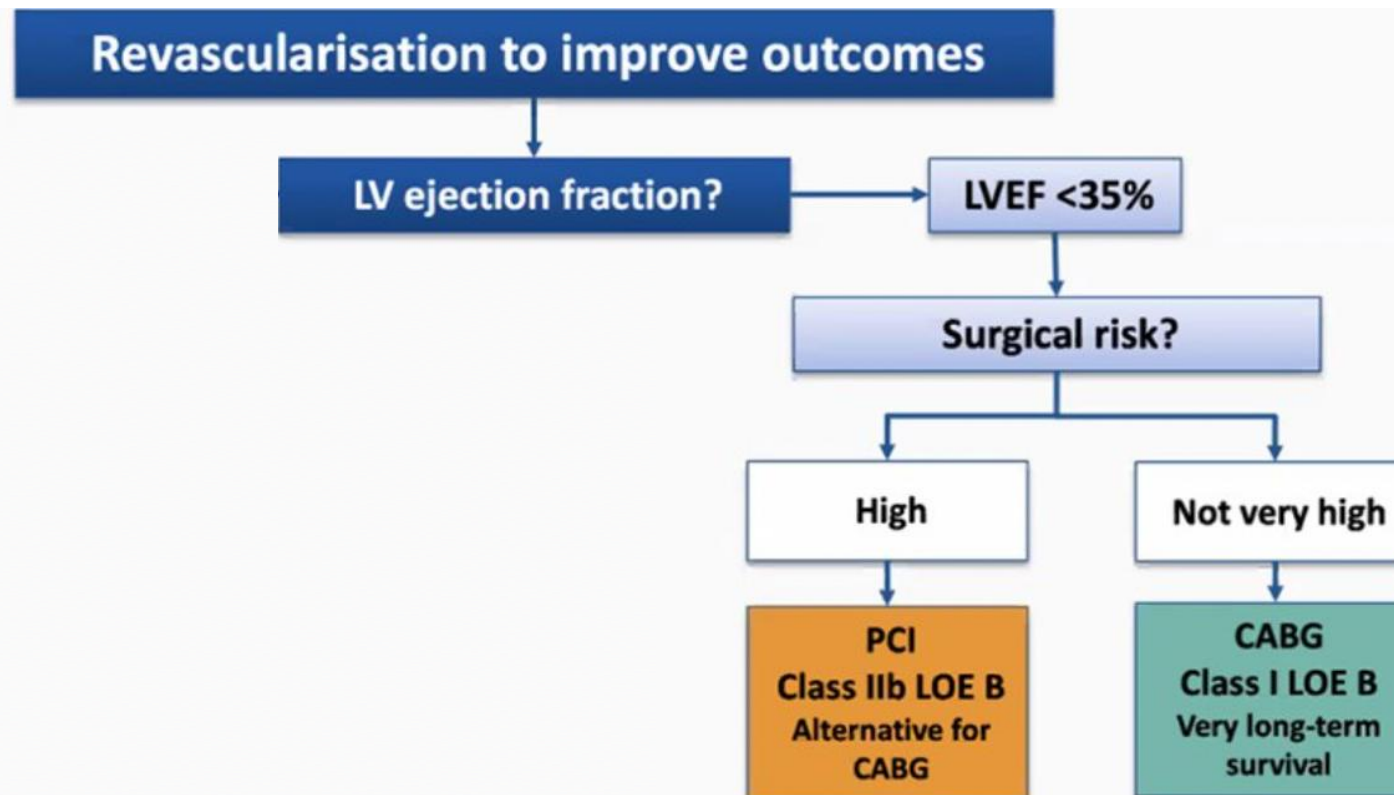
2024 ESC Recommandations for Revascularization in patients with Chronic Coronary Syndrome with LVEF < 35%

LVEF < 35%		
Choice between revascularization or MT alone, after careful evaluation by the **Heart Team**	I	C

Coronary anatomy
Correlation between CAD & LV dysfunction
Comorbidities/life expectancy
Individual risk-to-beneft ratio
Patient perspectives

Revascularisation to improve outcomes

LV ejection fraction? → LVEF <35%

Surgical risk?

High → PCI Class IIb LOE B Alternative for CABG

Not very high → CABG Class I LOE B Very long-term survival

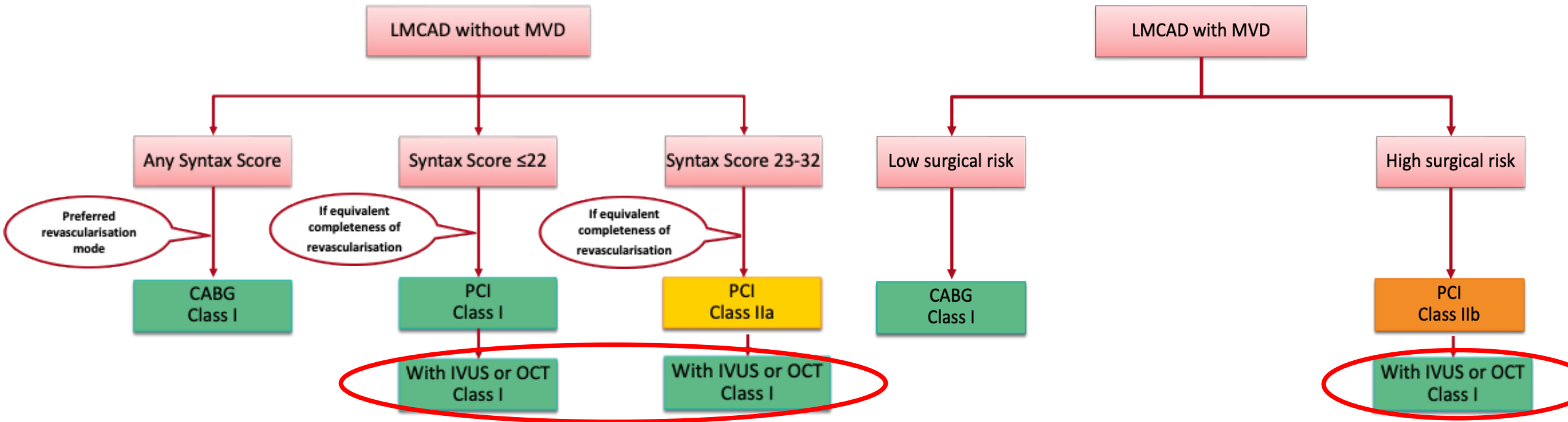Vrints C et al. European Heart Journal (2024) **45**, 3415–3537.

Mehilli J. ESC 2024

Revascularization modalities according to anatomic complexity of CAD:

PCI or CABG ?

# 2024 ESC Recommandations for Revascularization in patients with Single or double-vessel CAD

Single- or double-vessel disease involving the proximal LAD		
In CCS patients with significant single- or double-vessel disease involving the proximal LAD and insufficient response to guideline-directed medical therapy, CABG or PCI is recommended over medical therapy alone to improve symptoms and outcomes.[52,321,719,791,792]	I	A
In CCS patients with complex significant single- or double-vessel disease involving the proximal LAD, less amenable to PCI, and insufficient response to guideline-directed medical therapy, CABG is recommended to improve symptoms and reduce revascularization rates.[877–879]	I	B
Single- or double-vessel disease not involving the proximal LAD		
In symptomatic CCS patients with significant single- or double-vessel disease not involving the proximal LAD and with insufficient response to guideline-directed medical therapy, PCI is recommended to improve symptoms.[50,321,732]	I	B
In symptomatic CCS patients with significant single- or double-vessel disease not involving the proximal LAD and with insufficient response to guideline-directed medical therapy, not amenable to revascularization by PCI, CABG may be considered to improve symptoms.	IIb	C

Vrints C et al. European Heart Journal (2024) **45**, 3415–3537.

Revascularization in CCS for Unprotected Left Main

Recommendations	Class	Level
Left main disease		
In CCS patients at low surgical risk with significant left main coronary stenosis, CABG:		
• is recommended over medical therapy alone to improve survival;	I	A
• is recommended as the overall preferred revascularization mode over PCI, given the lower risk of spontaneous myocardial infarction and repeat revascularization.	I	A
In CCS patients with significant left main coronary stenosis of low complexity (SYNTAX score ≤22), in whom PCI can provide equivalent completeness of revascularization to that of CABG, PCI is recommended as an alternative to CABG, given its lower invasiveness and non-inferior survival.	I	A
In CCS patients with significant left main coronary stenosis of intermediate complexity (SYNTAX score 23–32), in whom PCI can provide equivalent completeness of revascularization to that of CABG, PCI should be considered, given its lower invasiveness and non-inferior survival.	IIa	A
Left main with multivessel disease		
In CCS patients at low surgical risk with suitable anatomy, CABG is recommended over medical therapy alone to improve survival.	I	A
In CCS patients at high surgical risk, PCI may be considered over medical therapy alone.	IIb	B

Revascularization in CCS for Multivessel CAD
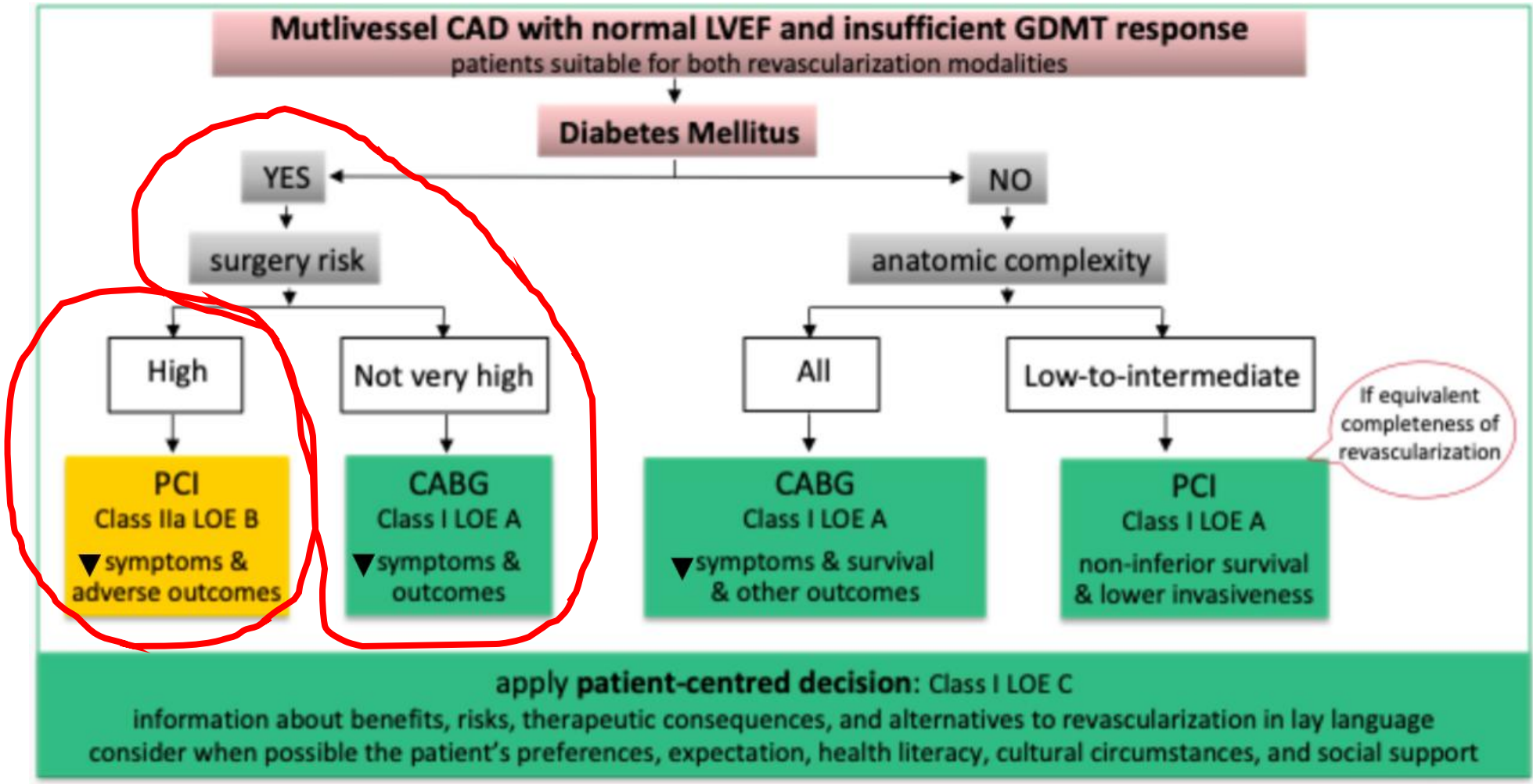
Chronic Coronary Syndrome: What place for revascularization ?

Conclusions

<u>Symptoms & QOL:</u>

✓ **Revascularization improves symptoms and QoL in patients with stable angina medically treated.**

✓ **The more symptomatic (and ischemic) the patients are, the greater the benefit of revascularization.**

✓ **PCI has been shown to be an effective antianginal treatment as first line therapy in sham-RCT.**

<u>Prognosis:</u>

✓ **Revascularization do not have impact on survival but may decrease the risk of cardiac death and spontaneous MI at long-term at the cost of an increased risk of periprocedural MI.**

✓ **Decision between CABG and PCI depends on the patient's profile, complexity of coronary anatomy, procedural factors, LVEF, the patient's preference, and outcome expectations.**

Thank you

cedric.delhaye@chu-lille.fr