

28th
TCTAP

MAY 6-9, 2023
GRAND WALKERHILL SEOUL,
KOREA

Left Main and Multivessel Disease – Practice Changes after ISCHEMIA

Fahim H. Jafary, M.D., F.A.C.C., F.S.C.A.I.

Diplomate, American Board of Medicine – Cardiovascular Diseases & Interventional Cardiology

Diplomate, Certification Boards of Nuclear Cardiology & Cardiovascular CT

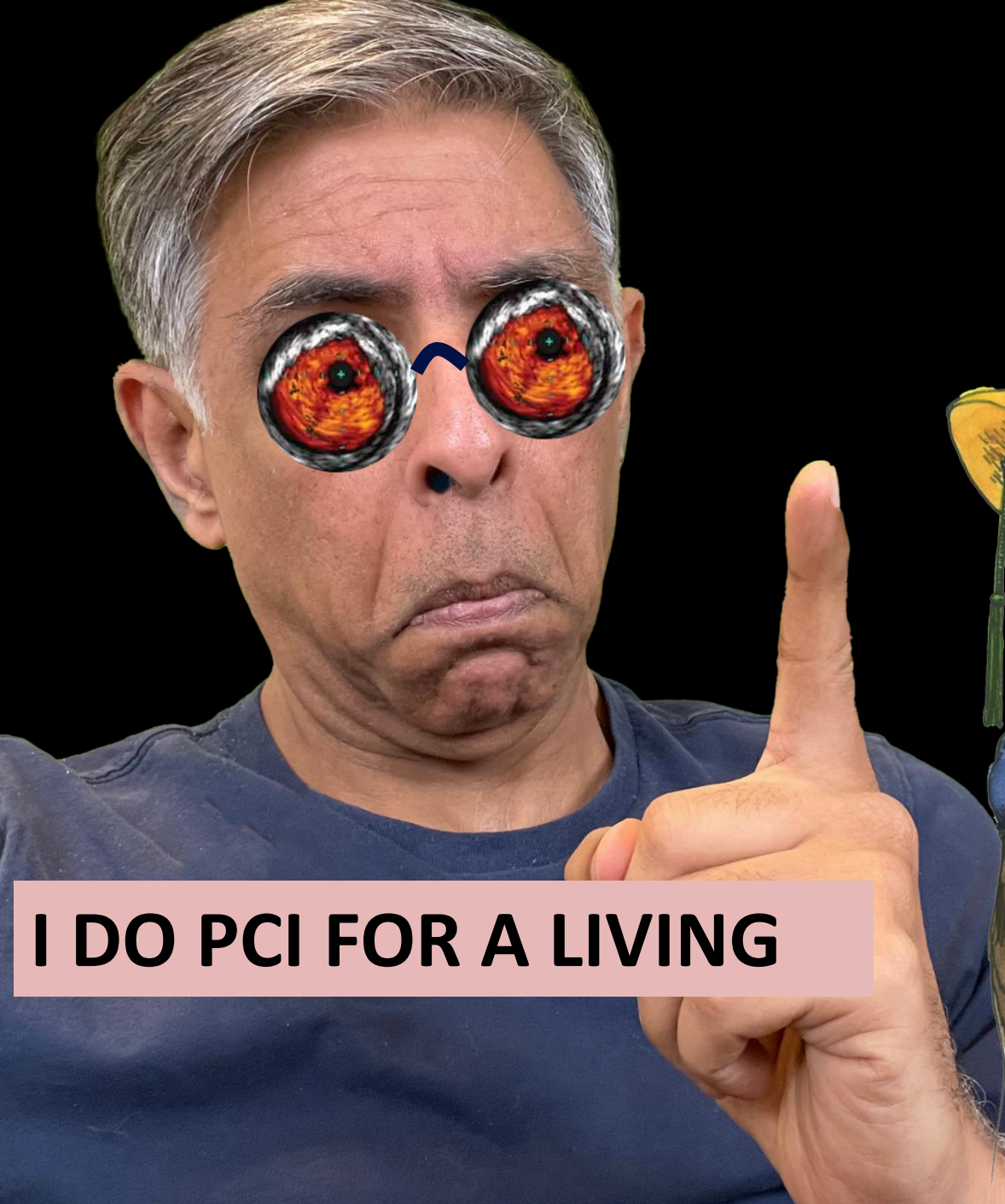
Senior Consultant

Department of Cardiology

NHG Heart Institute, Tan Tock Seng Hospital, Singapore

Disclosures

- No conflicts of interest



INTERVENTIONAL CARDIOLOGIST

CT CARDIOLOGIST

NUCLEAR CARDIOLOGIST

I DO PCI FOR A LIVING

My 'hats'

HAS **ISCHEMIA** CHANGED PRACTICE
FOR **LEFT MAIN DISEASE**?

HAS **ISCHEMIA** CHANGED PRACTICE
FOR **MULTIVESSEL DISEASE**

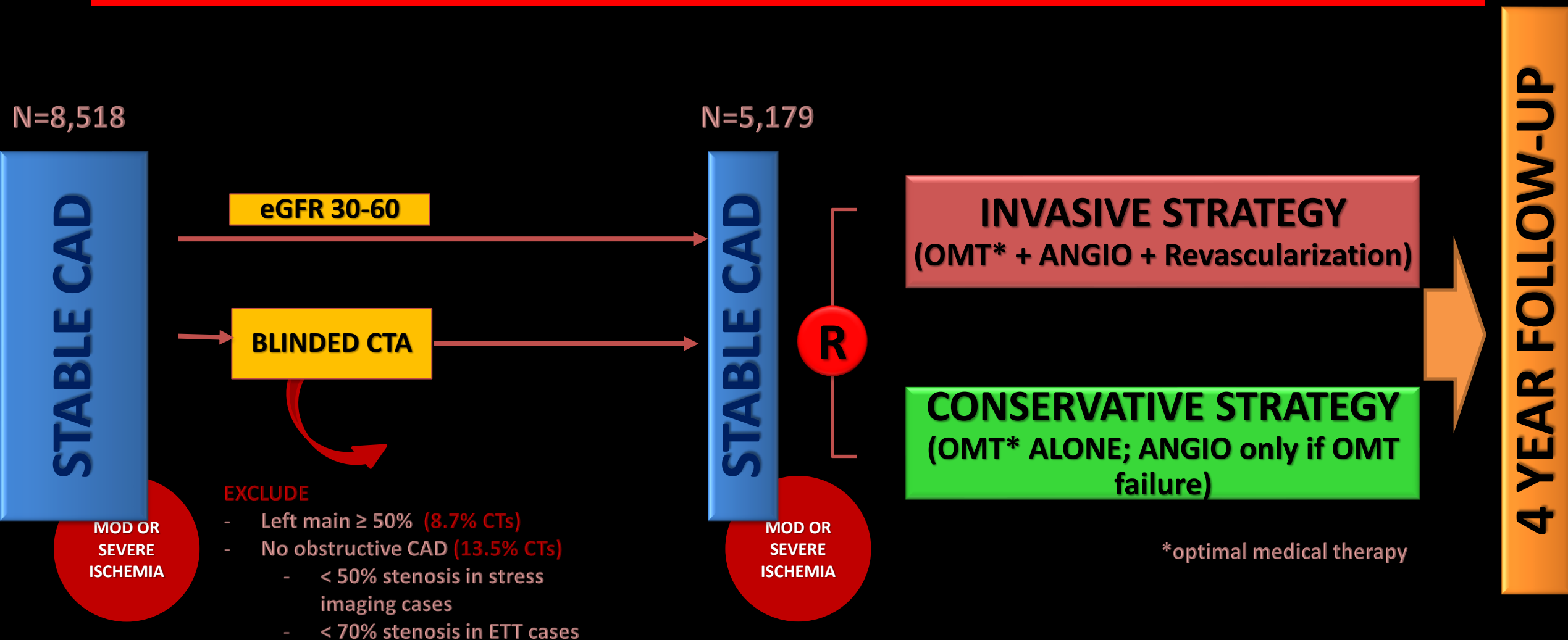
Non-left main disease



HAS **ISCHEMIA** CHANGED PRACTICE
FOR LEFT MAIN DISEASE?

No!

ISCHEMIA trial



LEFT MAIN DISEASE WAS EXCLUDED

**FOR LEFT MAIN DISEASE,
REVASCULARIZATION REMAINS THE
PREFERRED STRATEGY**

Progress Study of 590 Consecutive Nonsurgical Cases of Coronary Disease Followed 5-9 Years

II. Ventriculographic and Other Correlations

By ALBERT V. G. BRUSCHKE, M.D., WILLIAM L. PROUDFIT, M.D.,
AND F. MASON SONES, JR., M.D.

Relation Between Coronary Arteriogram, Left Ventricular Angiogram, and Mortality

Coronary arteriogram	5-year cardiac mortality* (%)			
	Normal LV	Localized "scar" tissue	Aneurysm†	Diffuse "scar" tissue
Left main coronary involvement	57 (21)	50 (8)	50 (2)	100 (4)
1-vessel involvement	7 (100)	17 (49)	43 (14)	60 (10)
2-vessel involvement	33 (87)	31 (58)	50 (26)	57 (41)
3-vessel involvement	36 (45)	50 (30)	38 (8)	88 (24)

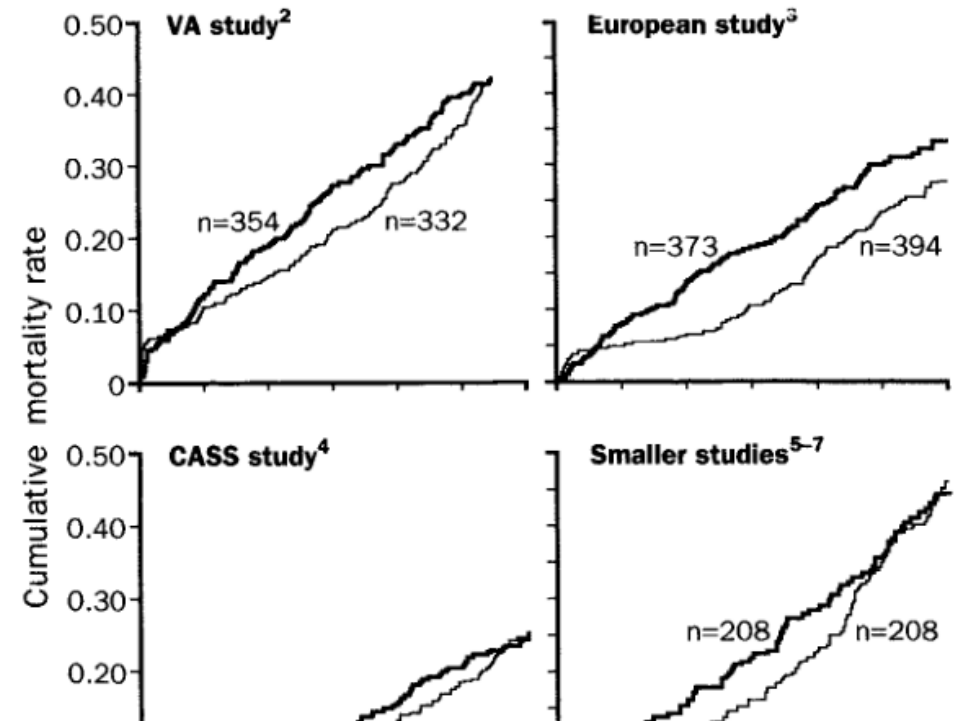
*Total number of cases in each category in parentheses.

†Cases with additional diffuse "scar" tissue included in the last category. See text.

5 YEAR MORTALITY WITH MEDICAL THERAPY ~ 50%

Effect of coronary artery bypass graft surgery of 10-year results from randomised trials by the Bypass Graft Surgery Trialists Collaboration*

Salim Yusuf, David Zucker, Peter Peduzzi, Lloyd D Fisher, Timothy Takaro, J Ward Kent, Thomas Killip, Eugene Passamani, Robin Norris, Cynthia Morris, Virendra Mathur, Ed



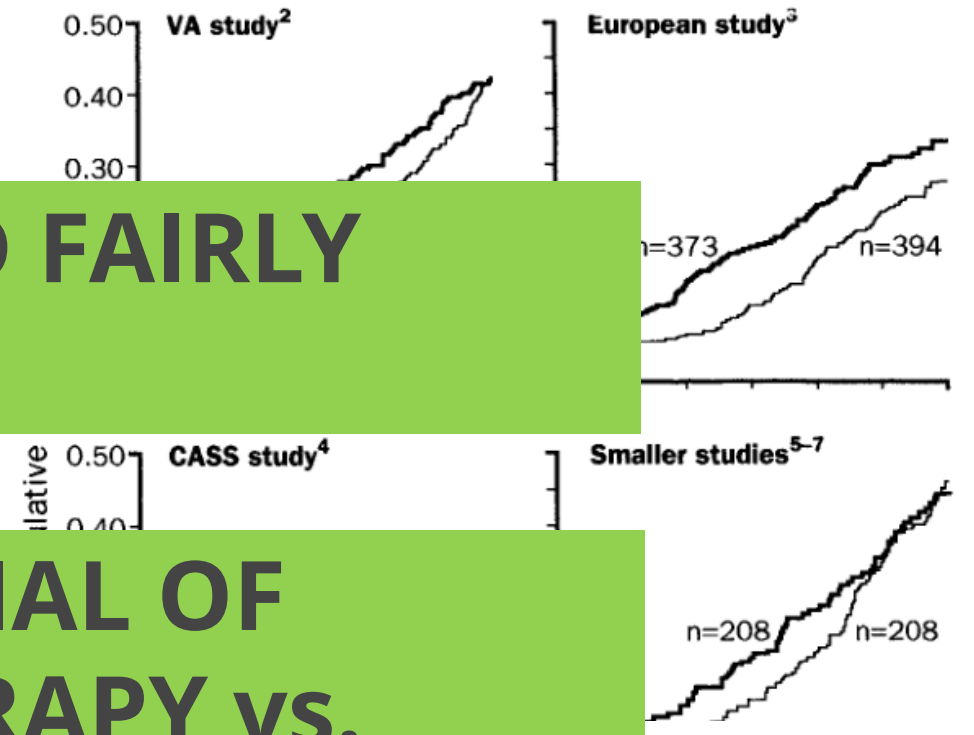
Subgroup	Overall numbers		Medical treatment mortality rate (%)	Odds ratio (95% CI)	p for CABG surgery vs medical treatment
	Deaths	Patients			
Vessel disease					
One vessel	21	271	9.9	0.54 (0.22-1.33)	0.18
Two vessels	92	859	11.7	0.84 (0.54-1.32)	0.45
Three vessels	189	1341	17.6	0.58 (0.42-0.80)	<0.001
Left main artery	39	150	36.5	0.32 (0.15-0.70)	0.004

CABG ↓ MORTALITY (VS. MEDICAL THERAPY) BY 68% IN LEFT MAIN DISEASE

Effect of Coronary Artery Bypass Grafting of 10-year Mortality

THIS IS HISTORICAL AND FAIRLY OBSOLETE DATA

THERE HAS BEEN NO TRIAL OF MODERN MEDICAL THERAPY vs. REVASCULARIZATION FOR LEFT MAIN DISEASE



Subgroup
Vessel disease
One vessel
Two vessels
Three vessels
Left main artery

Subgroup	n	n	Relative mortality (%)	Relative mortality (95% CI)	p-value
One vessel	92	859	11.7	0.84 (0.54-1.32)	0.18
Two vessels	189	1341	17.6	0.58 (0.42-0.80)	0.45
Three vessels	39	150	36.5	0.32 (0.15-0.70)	<0.001
Left main artery					0.004

CABG ↓ MORTALITY (VS. MEDICAL THERAPY) BY 68% IN LEFT MAIN DISEASE

Percutaneous coronary intervention with drug-eluting stents versus coronary artery bypass grafting in left main coronary artery disease: an individual patient data

HOW TO TREAT LEFT MAIN DISEASE

PATIENT LEVEL METAANALYSIS

SYNTAX

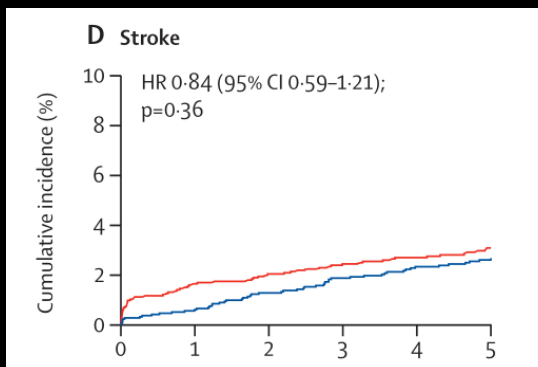
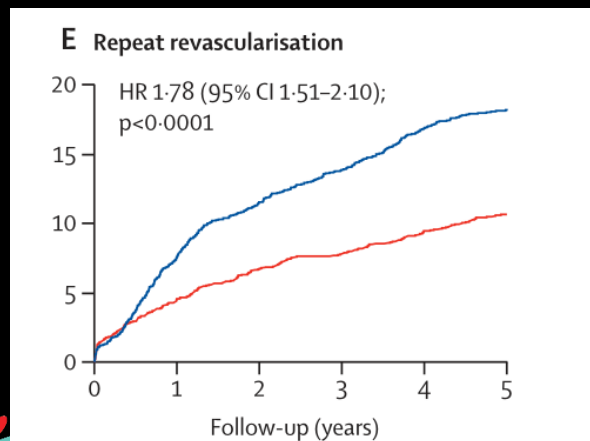
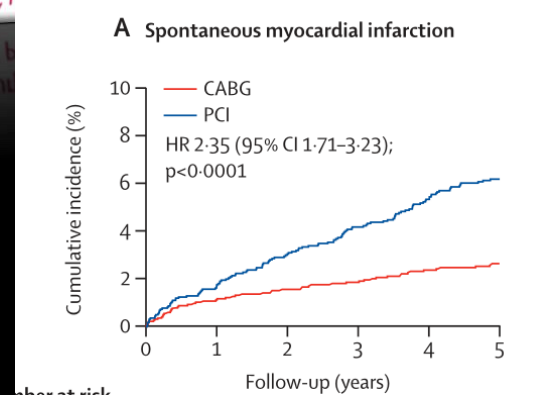
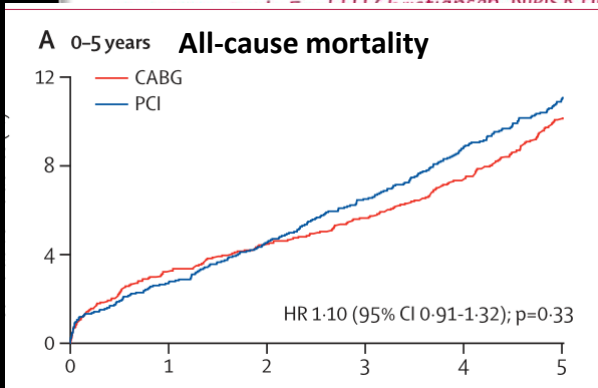
PRECOMBAT,

NOBLE,

EXCEL

5 YEAR FOLLOW-UP

Marc S Sabatine, Dharm A Bergin, ...



MORTALITY SAME OR MARGINALLY ↓

SPONTANEOUS MI ↓

REPEAT REVASCULARIZATION ↓

STROKE ↑

WITH CABG

2018 ESC/EACTS Guidelines on myocardial revascularization

Recommendations according to extent of CAD	CABG		PCI	
	Class ^a	Level ^b	Class ^a	Level ^b
Left main CAD				
Left main disease with low SYNTAX score (0 - 22).	I	A	I	A
Left main disease with intermediate SYNTAX score (23 - 32).	I	A	IIa	A
Left main disease with high SYNTAX score (≥33). ^c	I	A	III	B

Neumann FJ et al. European Heart Journal (2019) 40, 87–165

ACC/AHA/SCAI CLINICAL PRACTICE GUIDELINE

2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

Left main CAD		
1	B-R	3. In patients with SIHD and significant left main stenosis, CABG is recommended to improve survival. ⁹⁻¹²
2a	B-NR	4. In selected patients with SIHD and significant left main stenosis for whom PCI can provide equivalent revascularization to that possible with CABG, PCI is reasonable to improve survival. ⁹

“... for whom PCI can provide equivalent revascularization to that possible with CABG...”

Lawton JS et al. Circulation. 2022;145:e18–e114

HAS **ISCHEMIA** CHANGED PRACTICE
FOR MULTIVESSEL DISEASE?

Yes and No!

HAS **ISCHEMIA** CHANGED PRACTICE
FOR MULTIVESSEL DISEASE?

FOR SYMPTOM RELIEF

No!

FOR IMPROVING PROGNOSIS

Yes

HAS **ISCHEMIA** CHANGED PRACTICE
FOR MULTIVESSEL DISEASE?

FOR SYMPTOM RELIEF

No!

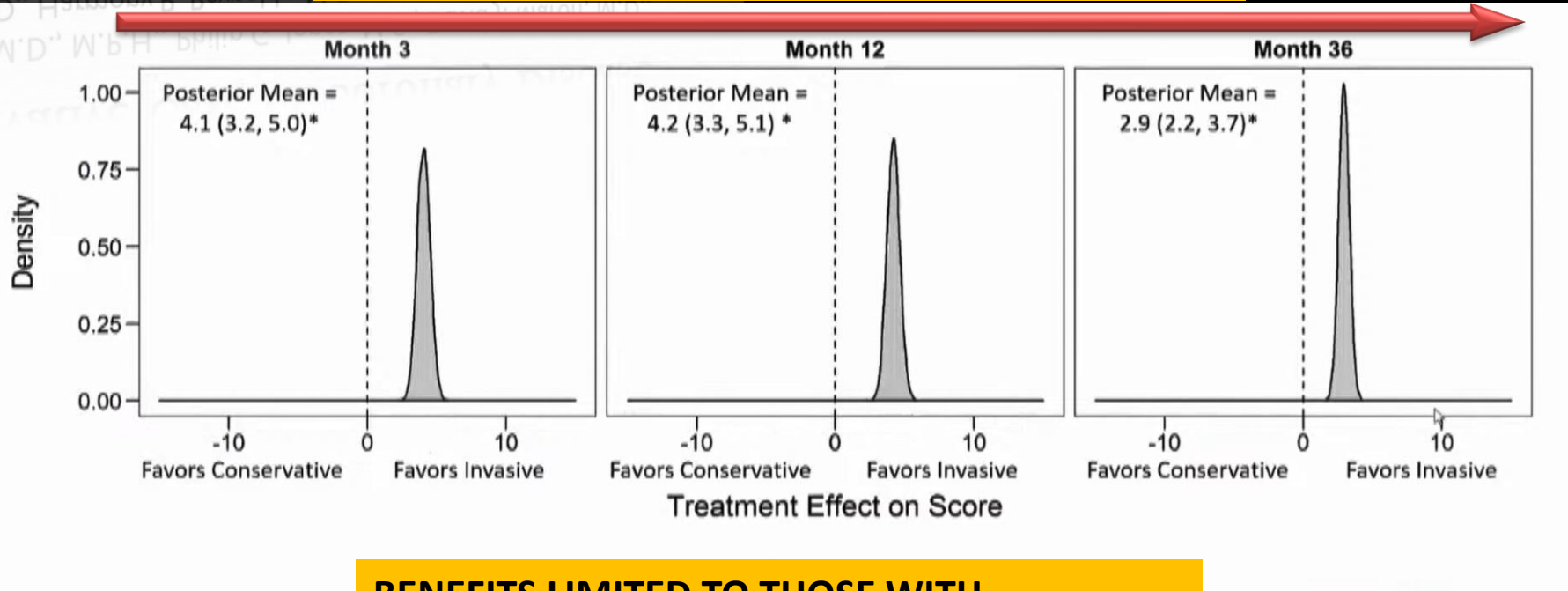
PCI ALWAYS APPROPRIATE WHEN
SYMPTOMATIC

ORIGINAL ARTICLE

Health-Status Outcomes with Invasive or Conservative Care in Coronary Disease

John A. Spertus, M.D., M.P.H., Philip G. Jones, M.S., David J. Maron, M.D., Sean M. O'Brien, Ph.D., Harmony R. Reynolds,

DURABLE BENEFIT IN ↓ ANGINA

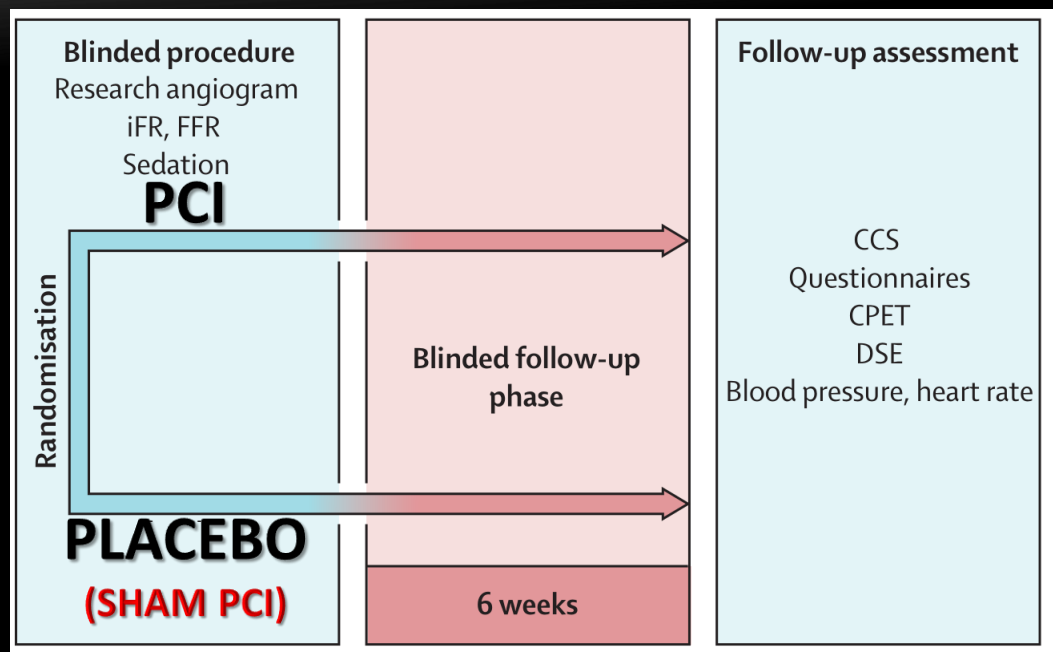


BENEFITS LIMITED TO THOSE WITH DAILY OR WEEKLY ANGINA (21% OF SUBJECTS)

Percutaneous coronary intervention in stable angina (ORBITA): a double-blind, randomised controlled trial

Rasha Al-Lamee, David Thompson, Hakim-Moulay Dehbi, Sayan Sen, Kare Tang, John Davies, Thomas Keeble, Michael Mielewczik, ...

STABLE CAD



~ 200 patients, single lesion

Primary EP : change in total exercise time

	PCI	Placebo
Exercise time (s)	EXERCISE TIME ↑ EVEN AFTER SHAM PCI	
Patients assessed	104	90
Pre-randomisation	528.0 (178.7)	490.0 (195.0)
Follow-up	556.3 (178.7)	501.8 (190.9)
Increment (pre-randomisation to follow-up)	28.4 (95% CI 11.6 to 45.1)	11.8 (95% CI -7.8 to 31.3)
Difference in increment between groups	16.6 (95% CI -8.9 to 42.0)	..
p value	0.200	..

DIFFERENCE BETWEEN PCI / SHAM GROUPS NOT STATISTICALLY SIGNIFICANT

HAS **ISCHEMIA** CHANGED PRACTICE
FOR MULTIVESSEL DISEASE?

FOR SYMPTOM RELIEF

No!

FOR IMPROVING PROGNOSIS

Yes

PCI FOR **MOST PATIENTS** WITH
STABLE CAD DOES NOT ALTER
PROGNOSIS

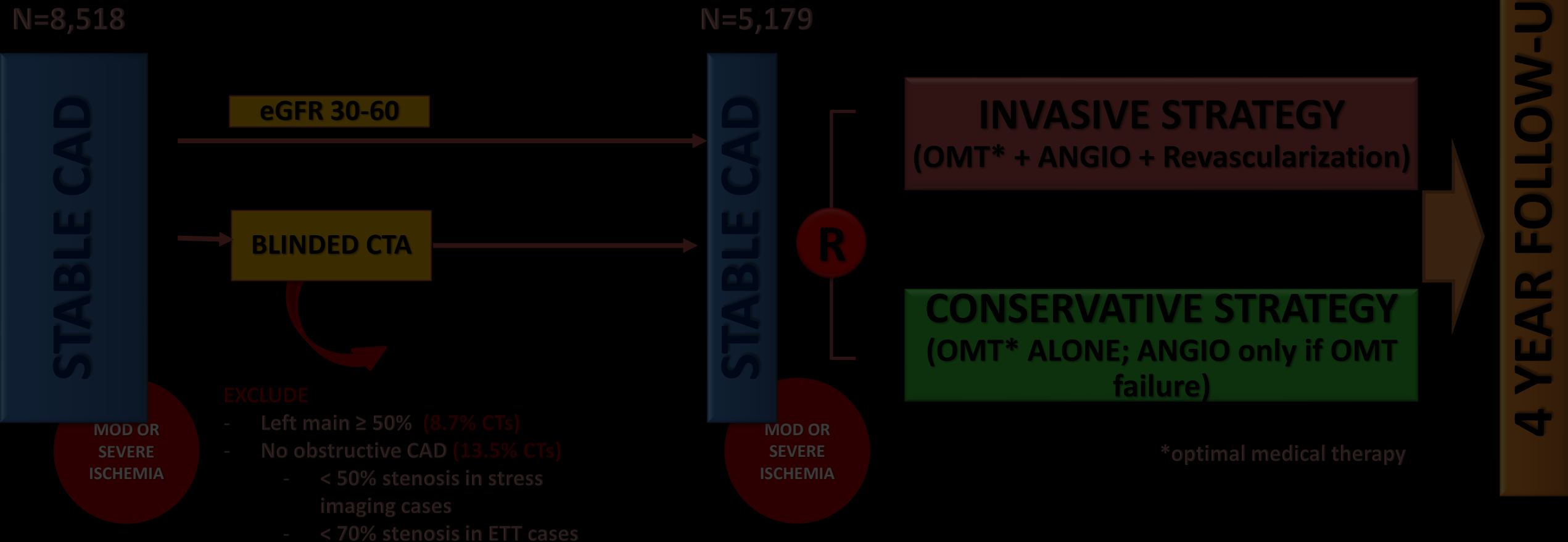
ISCHEMIA trial

ENROLLED PATIENTS BEFORE ANGIOGRAPHY

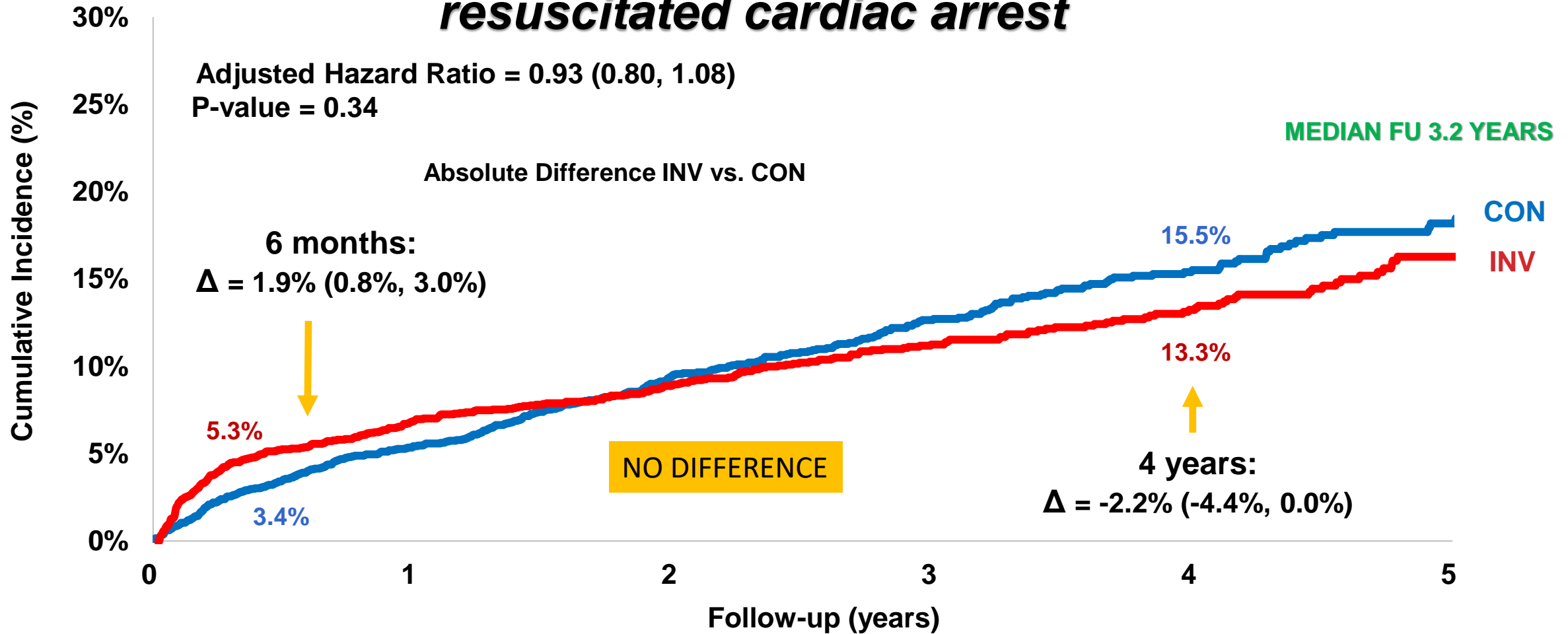
MODERATE OR SEVERE ISCHEMIA

87% HAD LAD DISEASE

>75% HAD MULTIVESSEL DISEASE



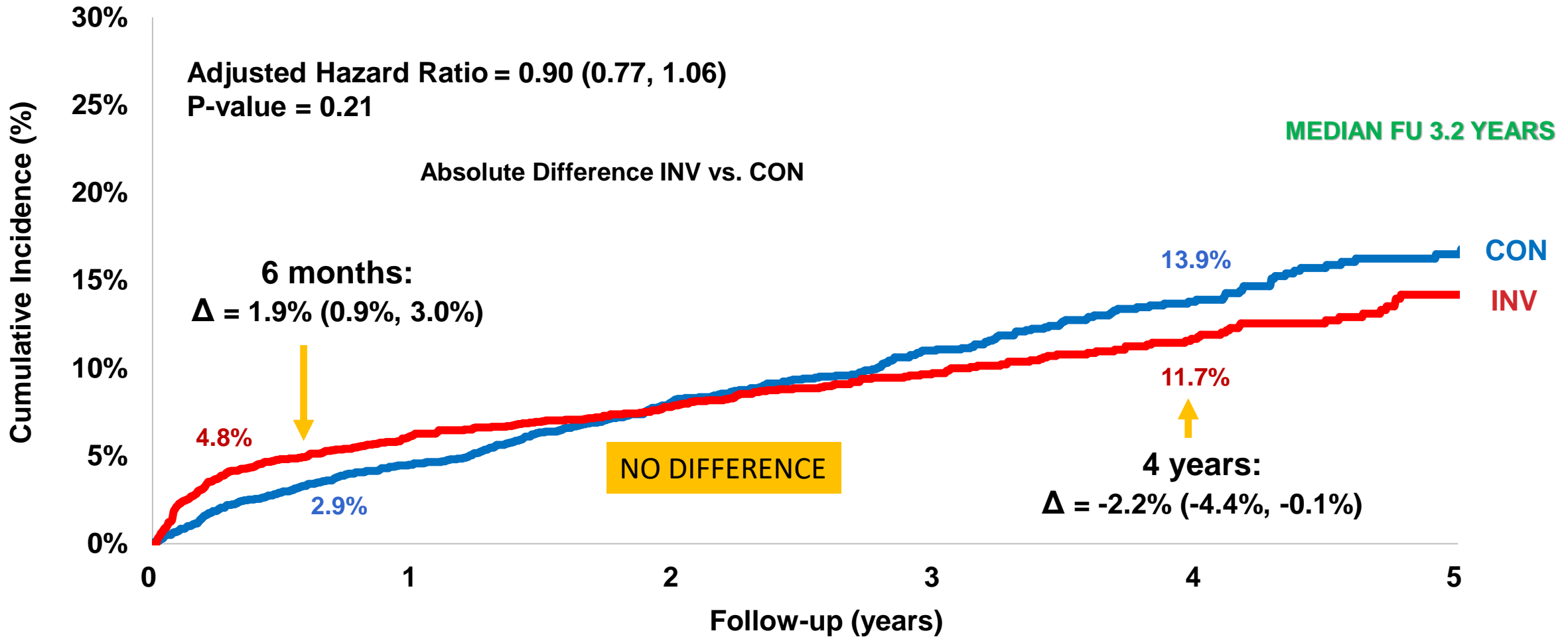
Primary Outcome: CV Death, MI, hospitalization for UA, HF or resuscitated cardiac arrest



Subjects at Risk

CON	2591	2431	1907	1300	733	293
INV	2588	2364	1908	1291	730	271

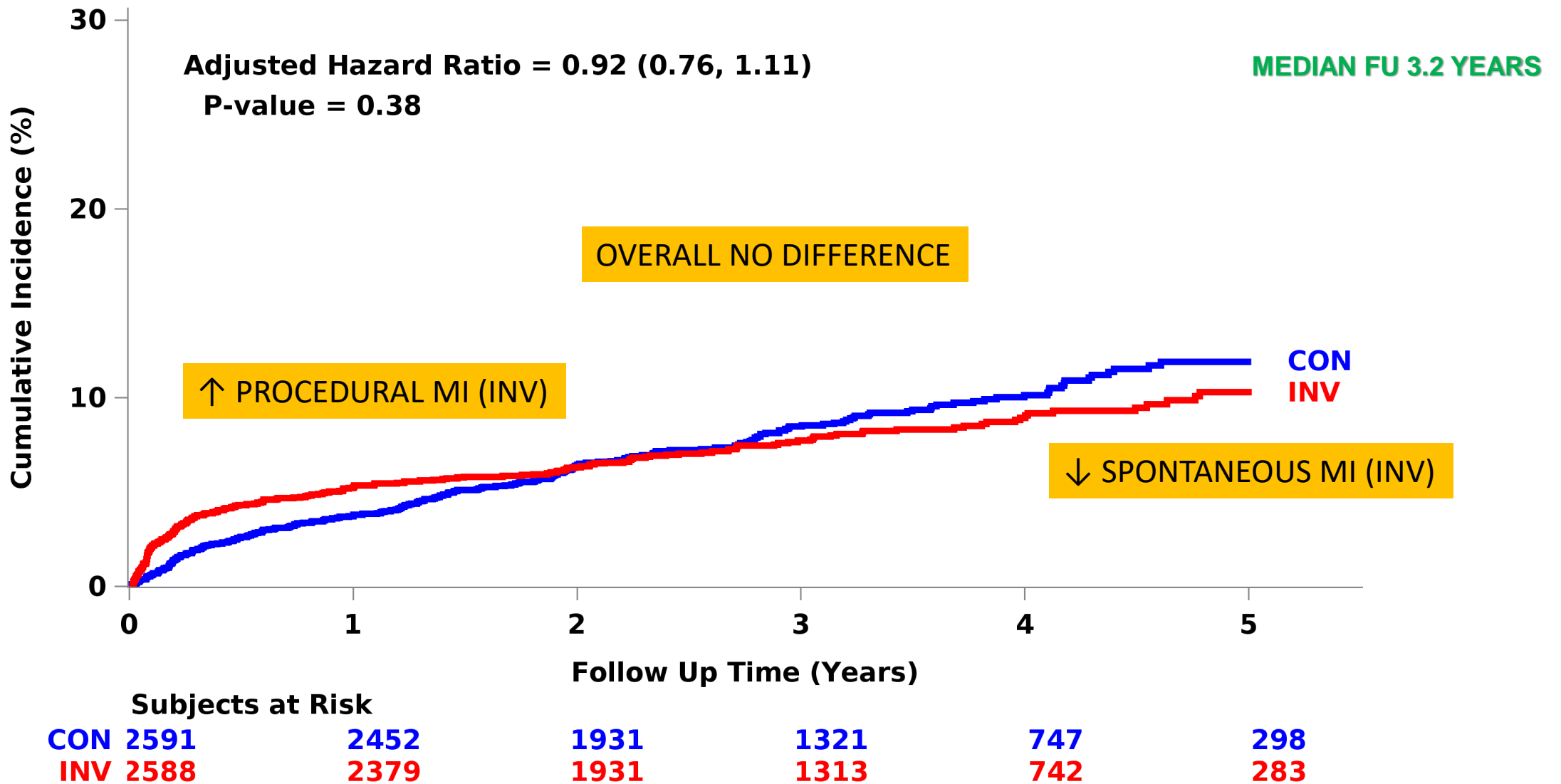
Secondary Outcome: CV Death or MI



Subjects at Risk

CON	2591	2453	1933	1325	746	298
INV	2588	2383	1933	1314	752	282

Myocardial Infarction

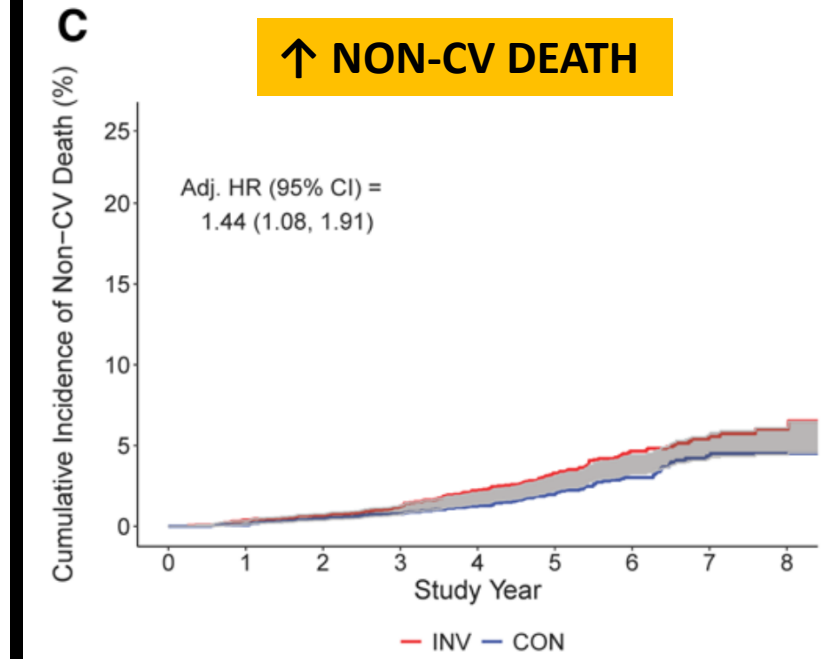
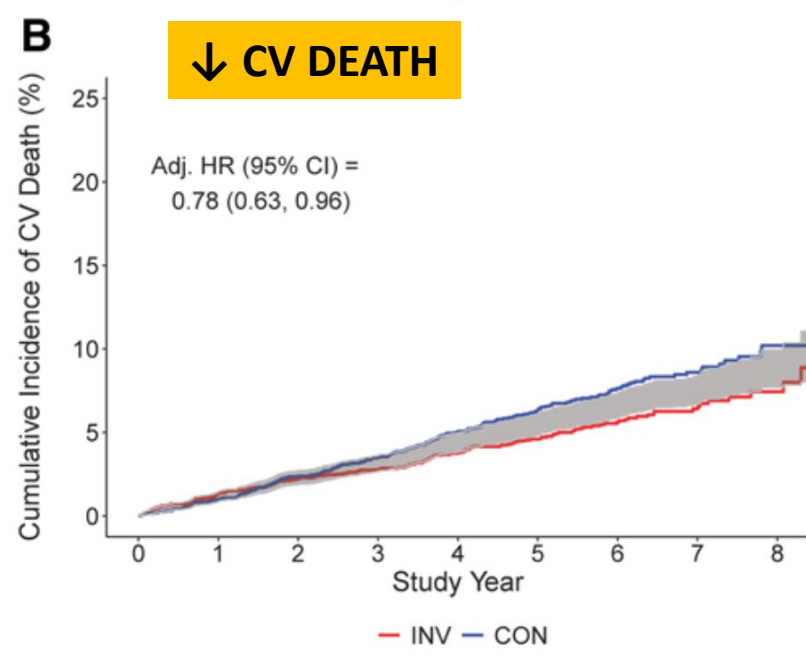
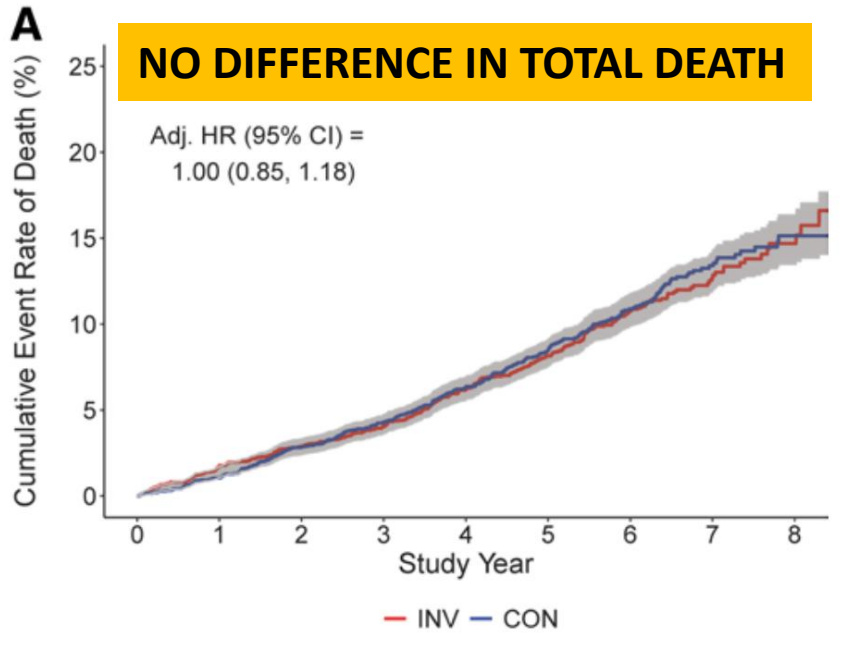




Survival After Invasive or Conservative Management of Stable Coronary Disease

Judith S. Hochman¹, MD; Rebecca Anthopolos, DrPH; Harmony R. Reynolds², MD; Sripal Bangalore³, MD, MHA; Yifan Xu, MPH; Sean M. O'Brien, PhD; Stavroula Mavromichalis, MS; Michelle Chang, MPH; Aira Contreras, MA;

MEDIAN 5.7 YEAR
FOLLOW-UP



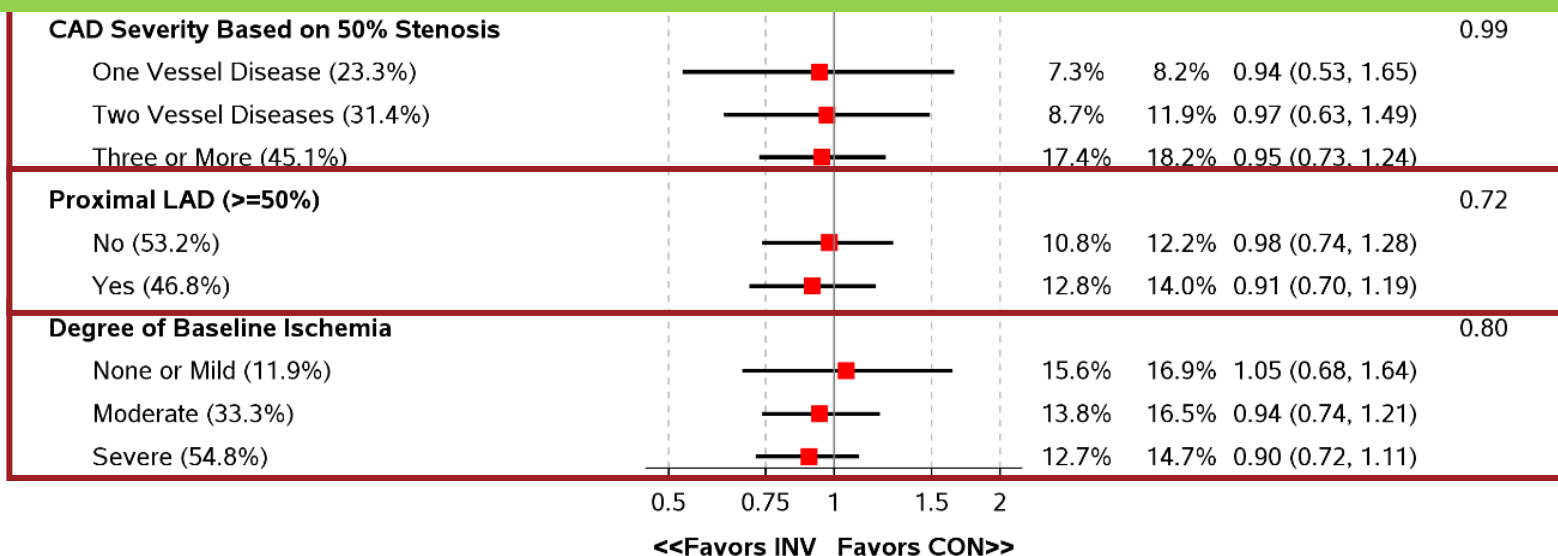
Primary Outcome: Influence of subgroups

Subgroup	Adjusted Hazard Ratio INV vs CON (95% CI)	Estimated 4-Yr Event Rate	Adjusted HR (95% CI)	Interaction P-Value
----------	--	------------------------------	-------------------------	------------------------

NO SUBGROUP SHOWED A BENEFIT OF INVASIVE

NO MATTER HOW MUCH ISCHEMIA OR EXTENT OF CAD....

REVASCULARIZATION DID NOT ALTER PROGNOSIS



N=3739 for Prox LAD Y/N
N=2982 for # diseased vessels

PCI FOR **MOST PATIENTS** WITH
STABLE CAD DOES NOT ALTER
PROGNOSIS

LEFT MAIN EXCLUDED

LOW EF \leq 35% EXCLUDED

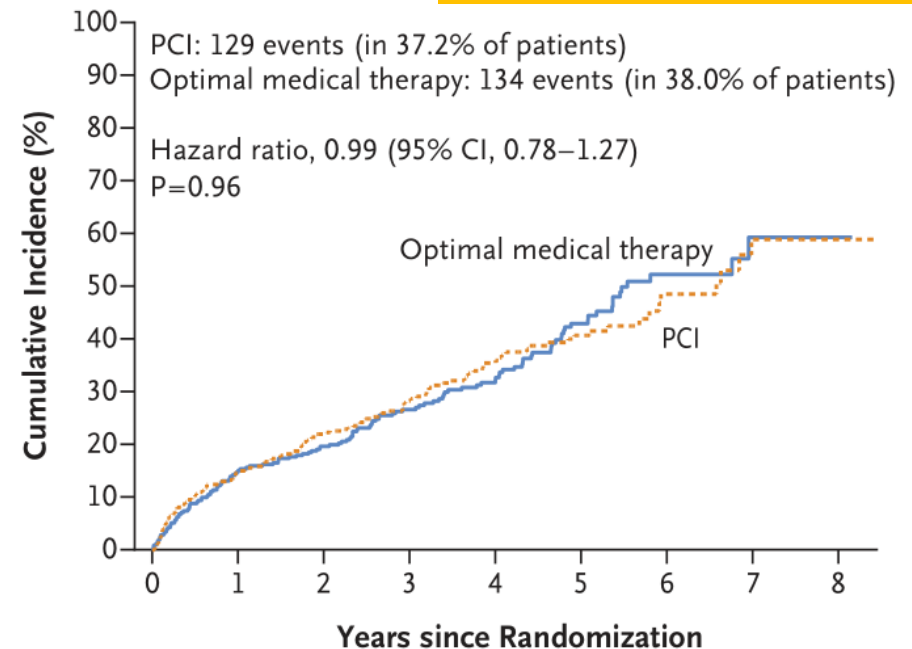
DISCLAIMER: NOT AN ISCHEMIA POPULATION

Percutaneous Revascularization for Ischemic Left Ventricular Dysfunction

NO BENEFIT OF REVASCULARIZATION OVER MEDICAL THERAPY

- ✓ EF ≤ 35%
- ✓ Extensive CAD - BCIS score ≥ 6 (out of 12)
- ✓ Viability in at least 4 dysfunctional segments
- ✓ No recent MI (> 4 weeks)
- ✓ No acute decompensated CHF
- ✓ No sustained ventricular arrhythmias

PCI vs. MEDICAL THERAPY



No. at Risk

	0	1	2	3	4	5	6	7	8
PCI	347	295	262	179	130	80	32	14	3
Optimal medical therapy	353	299	276	191	142	82	33	10	1

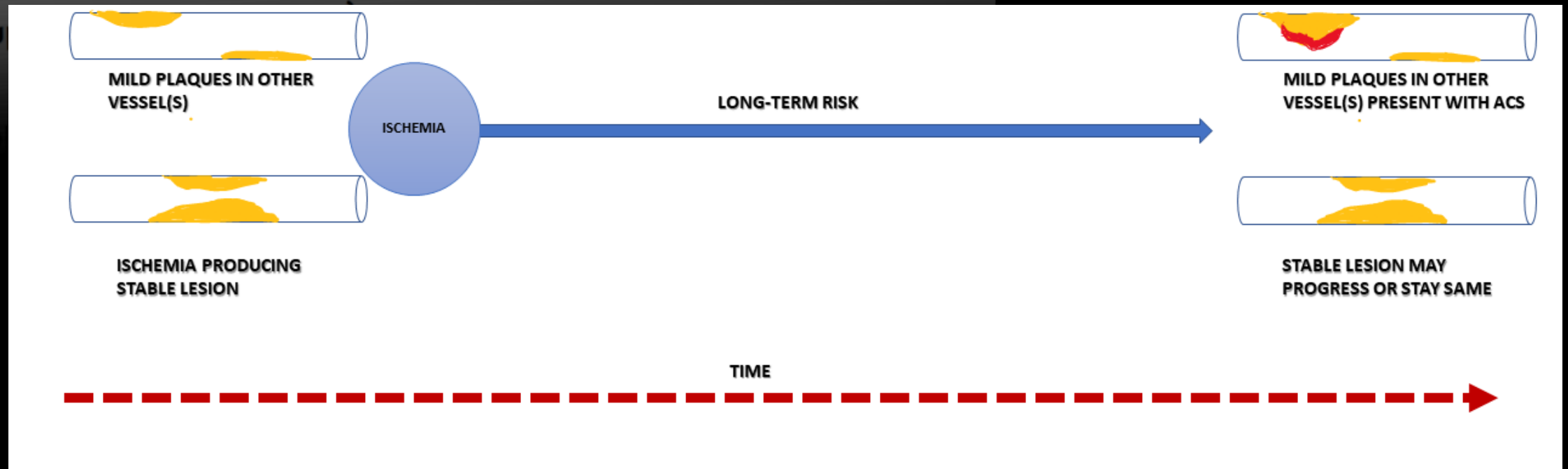
MEDIAN FOLLOW-UP 41 MONTHS

Why was treating ischemia NOT prognostic?

Ischemia Trial: Does the Cardiology Community Need to Pivot or Continue Current Practices?

Fahim H. Jafary¹ · Ali H. Jafary²

ISCHEMIA IS A SURROGATE FOR THE DISEASE PROCESS (ATHEROSCLEROSIS)





2021 ACC/AHA/SCAI Guideline for Coronary Artery Revascularization: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

2018 ESC/EACTS Guidelines on myocardial revascularization

		ESC 2018		ACC/AHA 2021	
		Class	Level	Class	Level
For Prognosis	Left main > 50%	I	A	I (CABG) IIA (PCI)	B-R B-NR
	Single or double vessel disease involving proximal LAD	I	A	IIB	B-R
	Single or double vessel disease NOT involving proximal LAD	I	C	III (no benefit)	B-NR
	Multivessel disease + EF ≤ 35%	I	A	I (CABG)	B-R
	Multivessel disease, EF 35-50%			IIA (CABG)	B-NR
	Multivessel disease, normal EF			IIB (CABG, PCI)	B-R
	Large ischemia (> 10%) or abnormal iFR/FFR	I	B		
	Single remaining vessel > 50%	I	C		
For reduction of events (MI, urgent revascularization)	Multivessel disease			IIA (CABG or PCI)	B-R
For Symptoms	Refractory angina	I	A	I	A

		ESC 2018		ACC/AHA 2021	
		Class	Level	Class	Level
For Prognosis	Left main > 50%	I	A	I (CABG) IIA (PCI)	B-R B-NR
	Single or double vessel disease involving proximal LAD	I	A	IIB	B-R
	Single or double vessel disease NOT involving proximal LAD	I	C	III (no benefit)	B-NR
	Multivessel disease + EF ≤ 35%	I	A	I (CABG)	B-R
	Multivessel disease, EF 35-50%			IIA (CABG)	B-NR
	Multivessel disease, normal EF			IIB (CABG, PCI)	B-R
	Large ischemia (> 10%) or abnormal iFR/FFR	I	B		
Single remaining vessel > 50%	I	C			
For reduction of events (MI, urgent revascularization)	Multivessel disease			IIA (CABG or PCI)	B-R
	For Symptoms				
	Refractory angina	I	A	I	A

DOWNGRADE

LESS ISCHEMIA CENTRIC

Conclusions – what's changed after ISCHEMIA?

- Clinical practice for ACS has not changed
- Clinical practice for left main disease has not changed → revascularize
- Clinical practice for non left main disease HAS changed
 - Revascularization is still reasonable to ↓ symptoms
 - Revascularization does not improve prognosis in MOST patients
 - So an initial medical therapy approach is reasonable
 - **CAUTION: doesn't mean revascularization is BAD, just means you can start with tablets**
- Unanswered questions:
 - Are the HIGHEST risk patients really medically manageable?
 - Will left main disease be “medically treatable” in the future?
 - What will the 10 year follow-up show?
 - Low EF without much angina