



PLATFORM OF LABORATORIES FOR ADVANCES IN CARDIAC EXPERIENCE

**ROMA**

Centro Congressi  
di Confindustria

**Auditorium  
della Tecnica**

**9ª Edizione**

**30 Settembre**

**1 Ottobre**

**2022**



# Indications and evidence on Left Main treatment

**Luca Testa, MD, PhD**

Head of Coronary Revasc Unit, IRCCS Policlinico S. Donato, Milan

Head of Clinical Research Unit, IRCCS Policlinico S. Donato, Milan

Contract Professor of Cardiology, «Vita e Salute» Univ. San Raffaele Hospital, Milan



# Conflict of interest disclosure

## **Consulting fees, honoraria personal and Institutional, advisory board participation from:**

- Abbott,
- Boston Scientific Corporation,
- Cardionovum,
- Concept Medical,
- Medtronic,
- Meril,
- Terumo Lifesciences

## **Proctoring Activity:**

- TAVR (Abbott, Boston Scientific, Meril)
- CTOs (Boston Scientific)
- IVUS/coronary physiology (Boston Scientific)
- OCT (Abbott)
- Rotablator (Boston Scientific)



# Basics for the LM

- The LM roughly supplies 2/3 of the myocardium
- 4.8% of patients undergoing coronary angiogram
- Male gender and Age are the only independent predictors of LM disease
- Associated with 3-VD in approx 50% of the cases
- Isolated LMCA stenosis in 5% (more frequent in women)

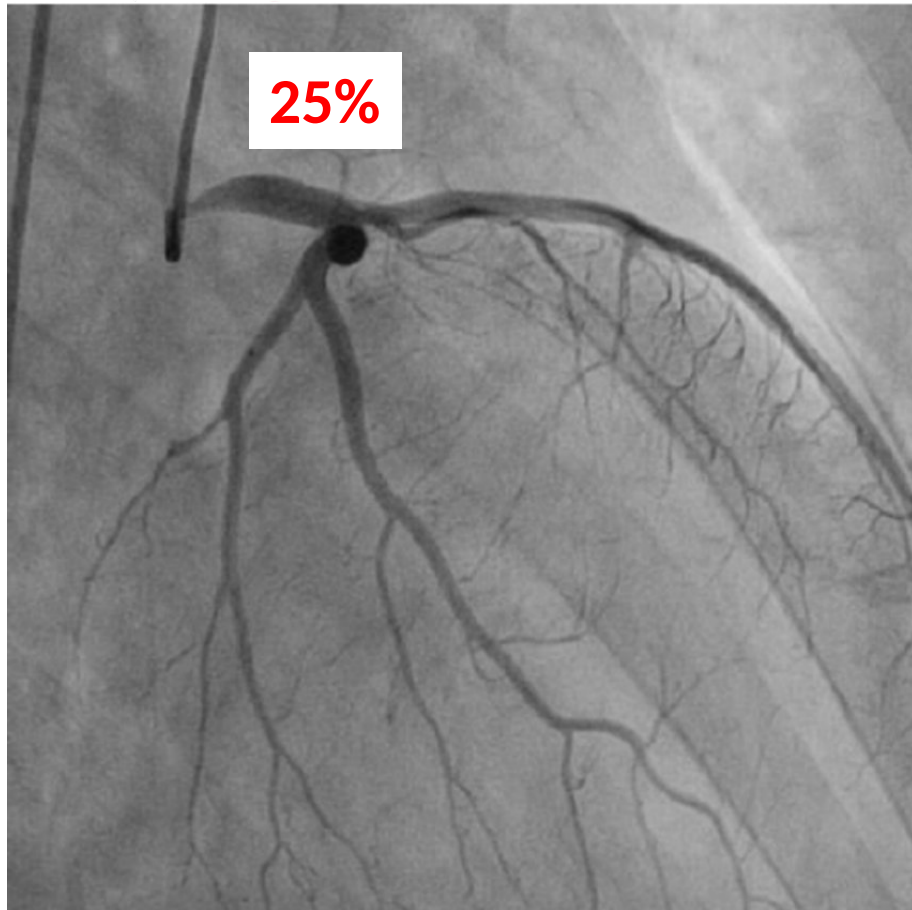


# LM assessment

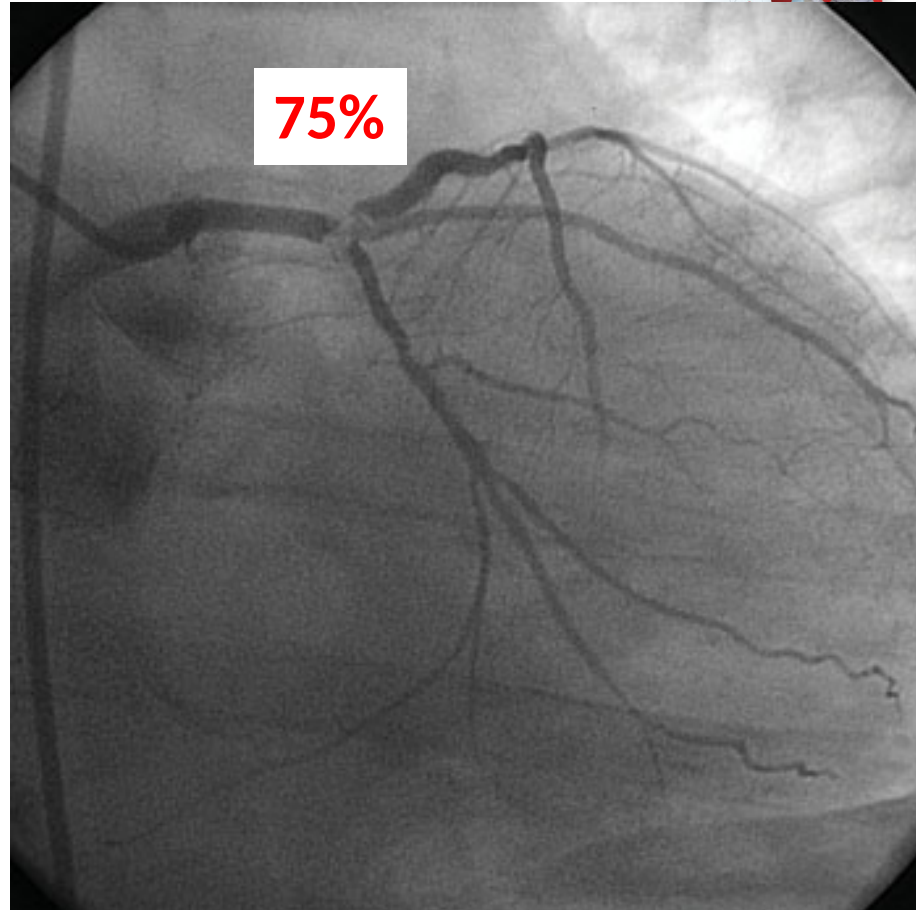
- LM is particularly prone to intra and interobserver variability
- Physiology but mostly Imaging (IVUS +, OCT  $\pm$ ) are helpful for a better understanding
  - Cut off pre & post (?)

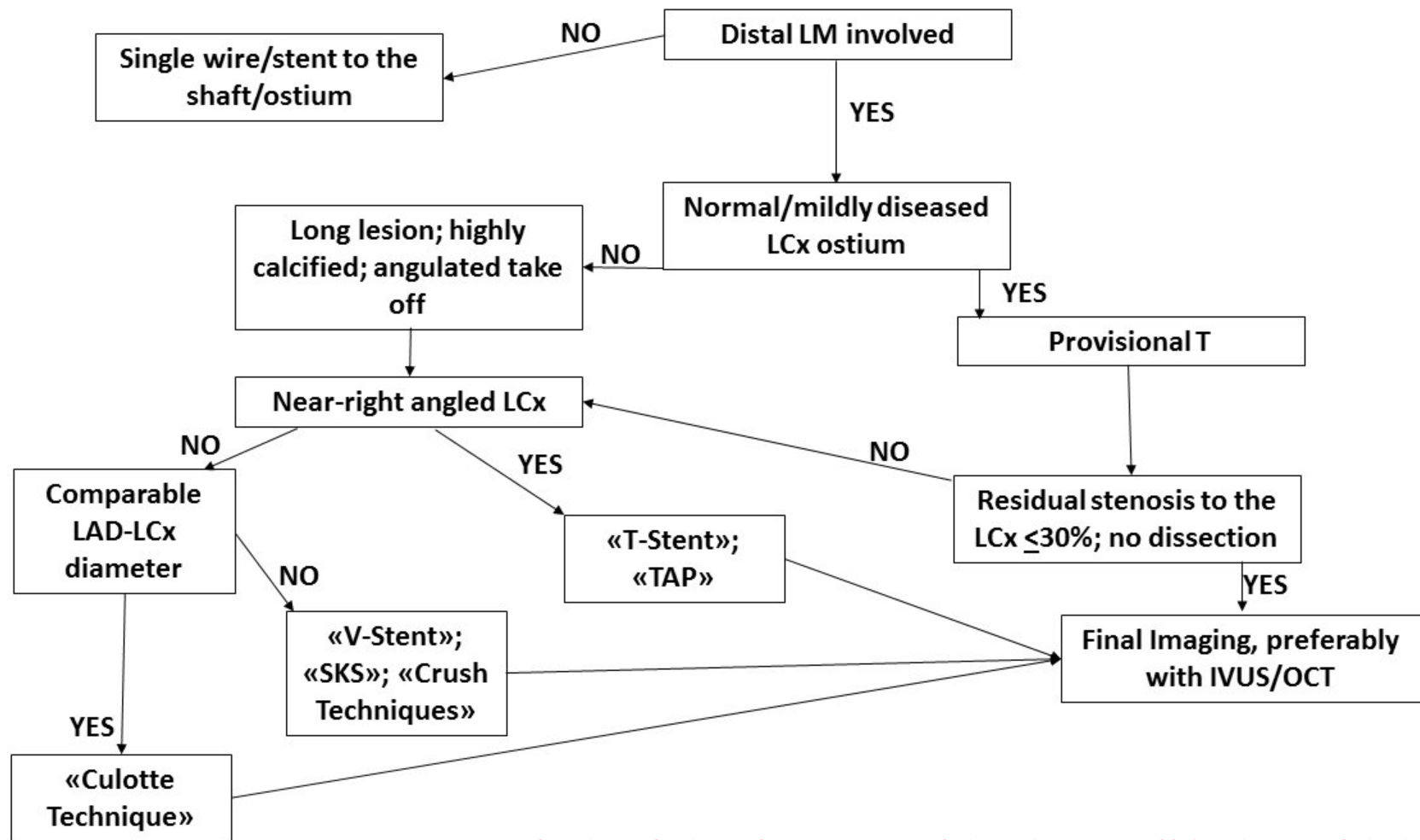


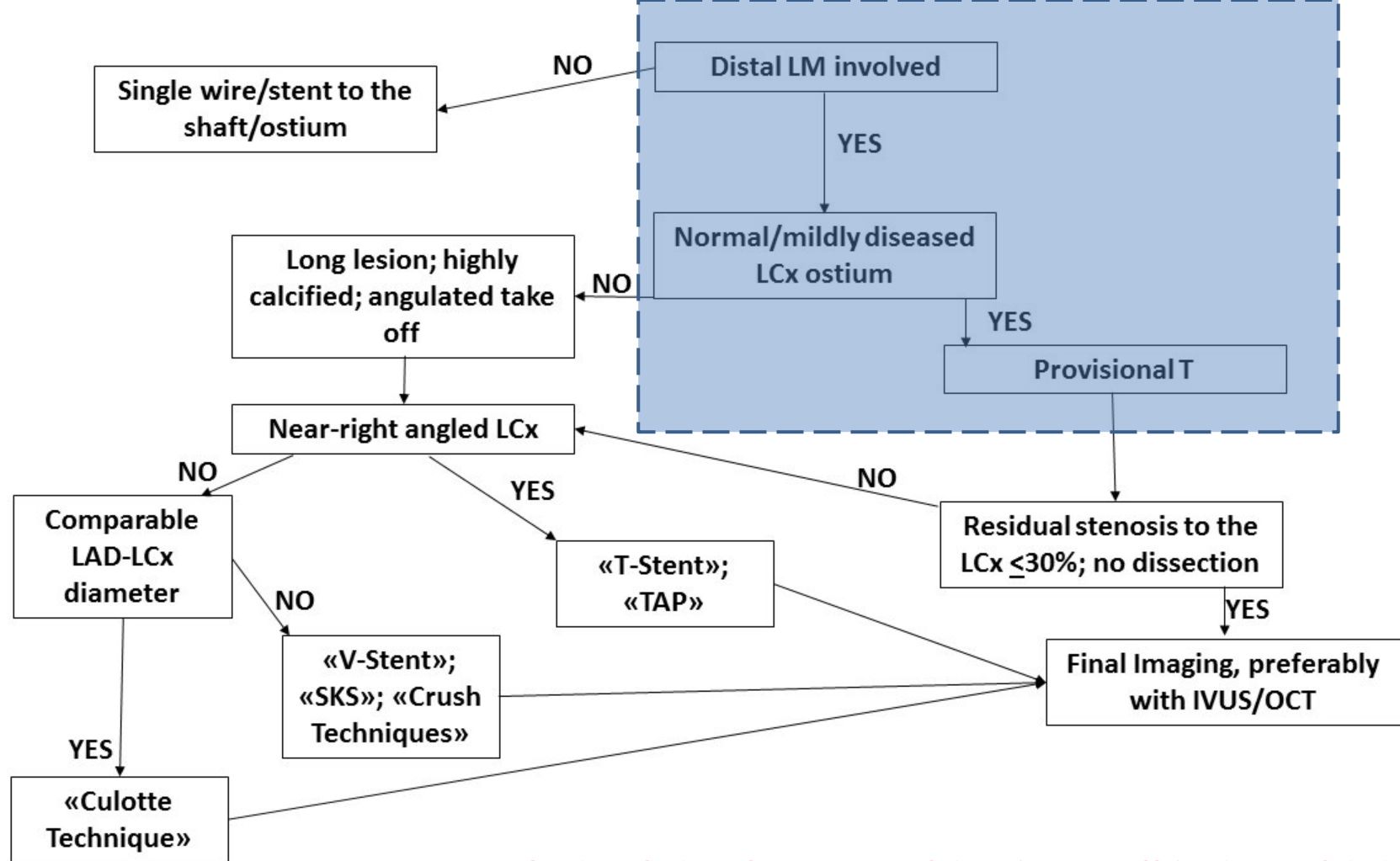
**25%**

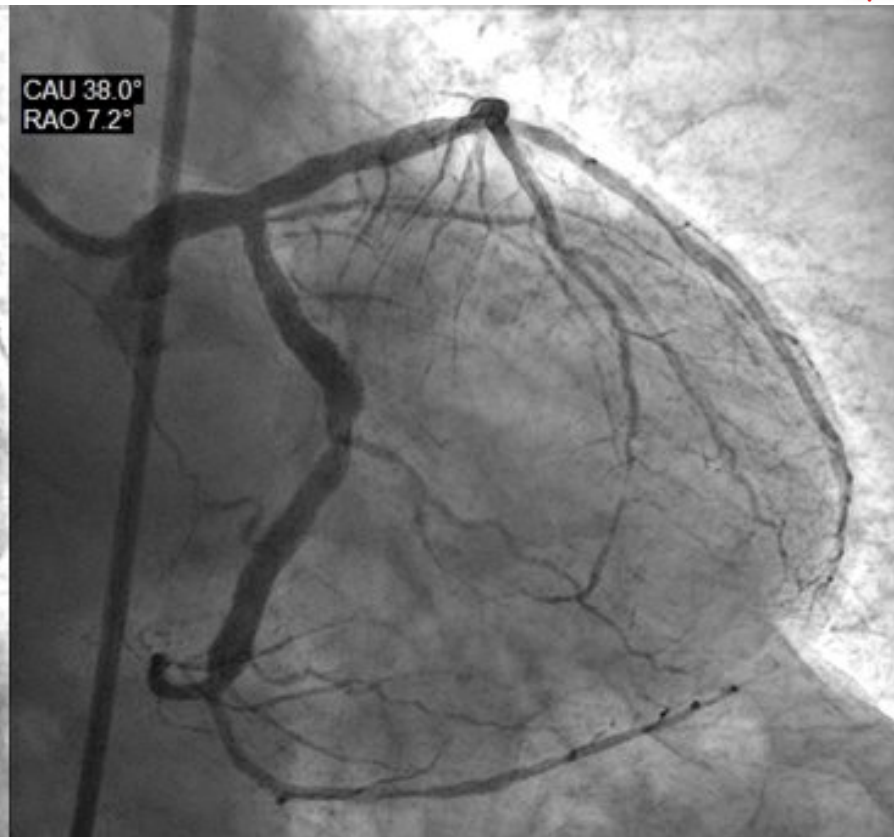
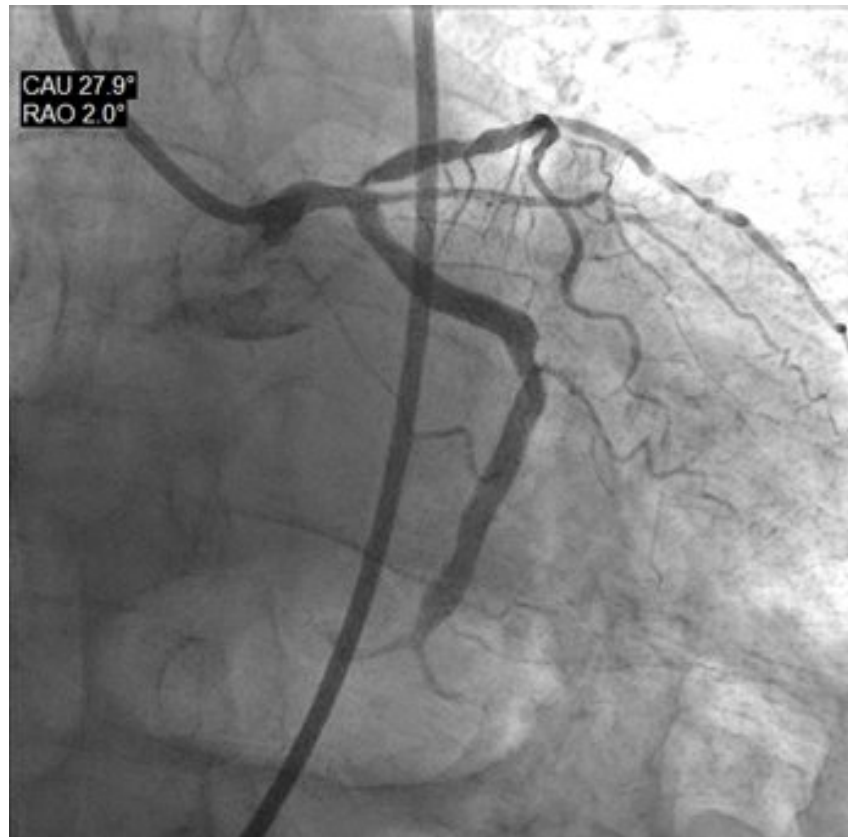


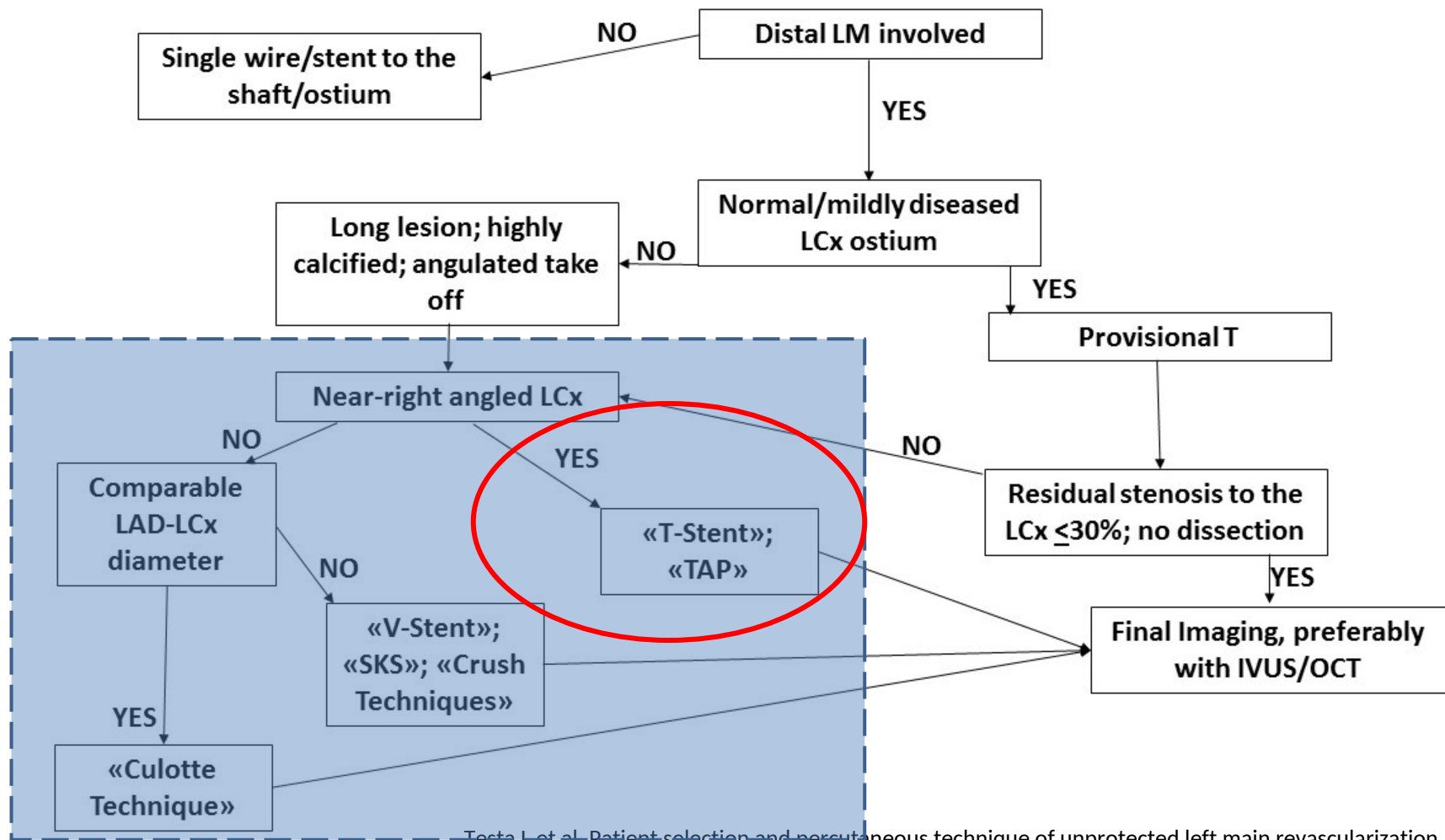
**75%**

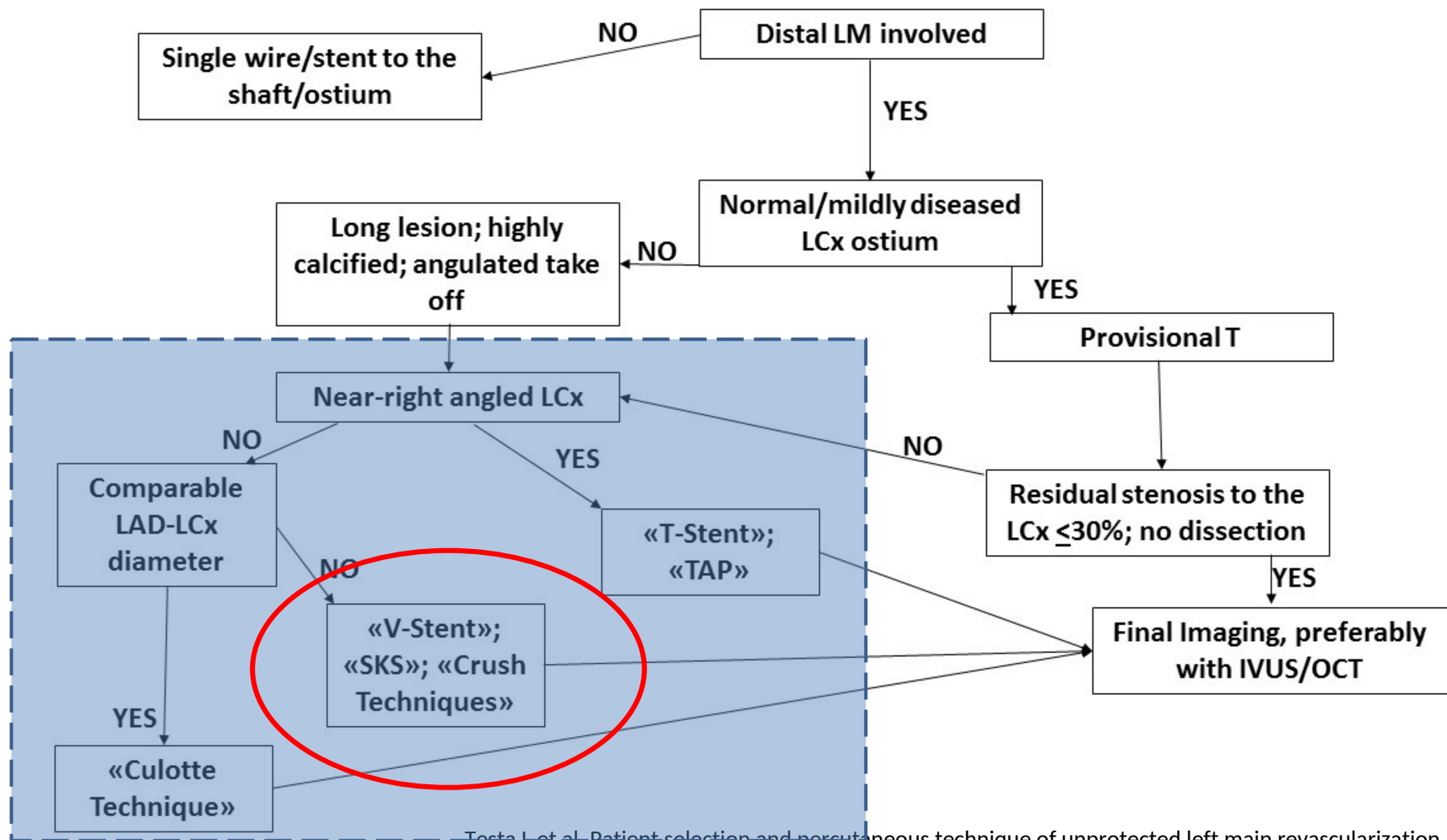


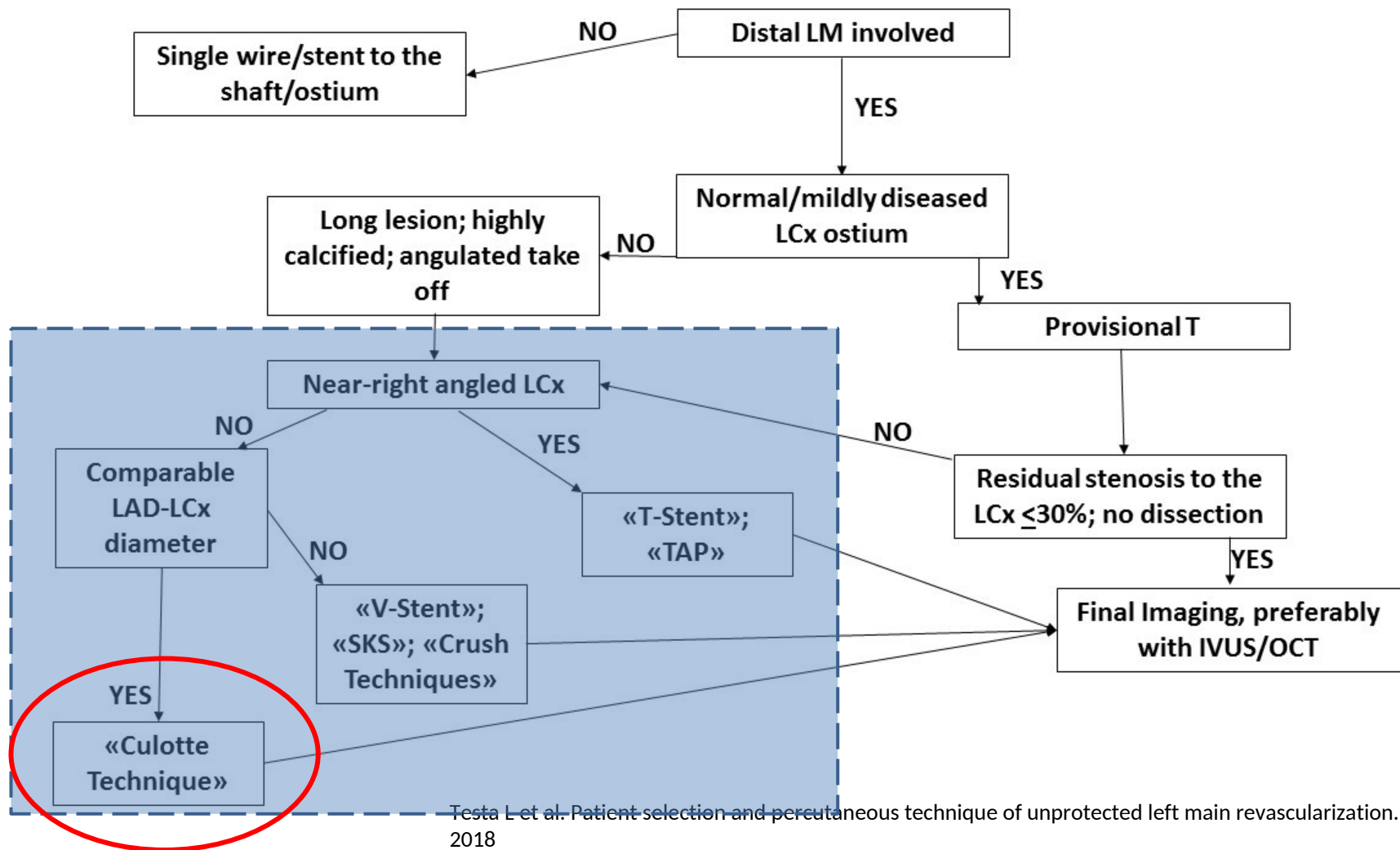




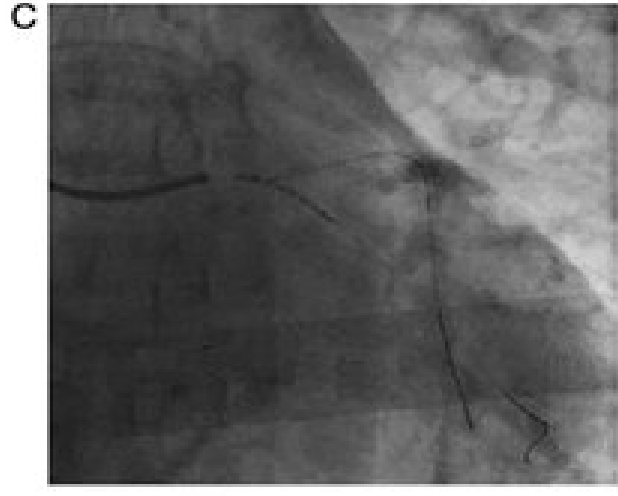
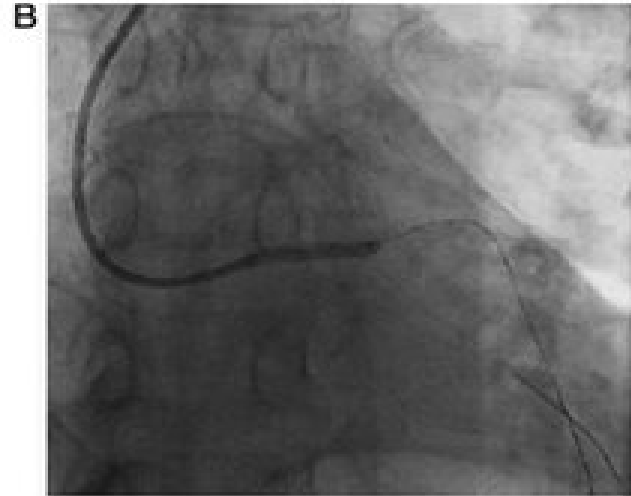
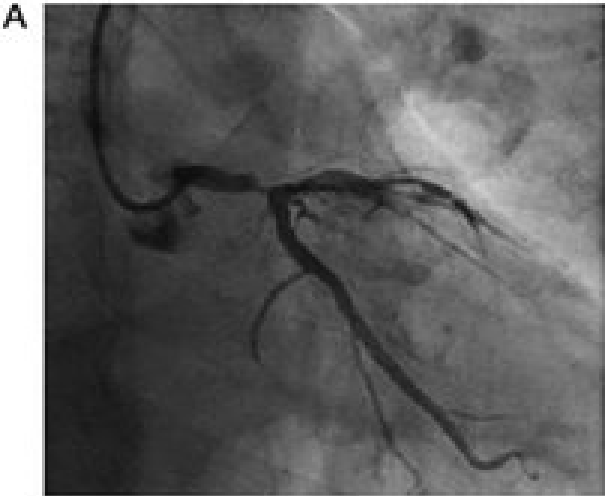












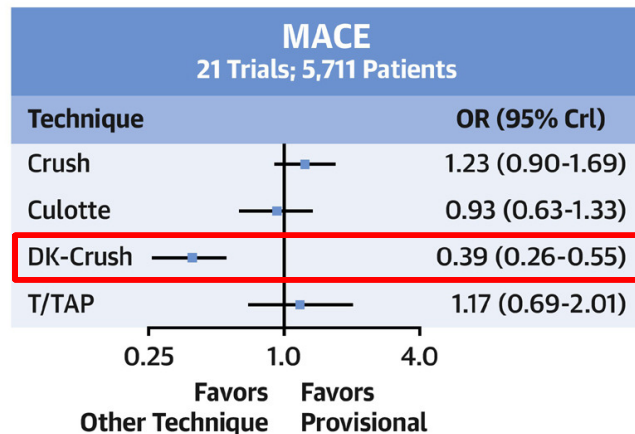
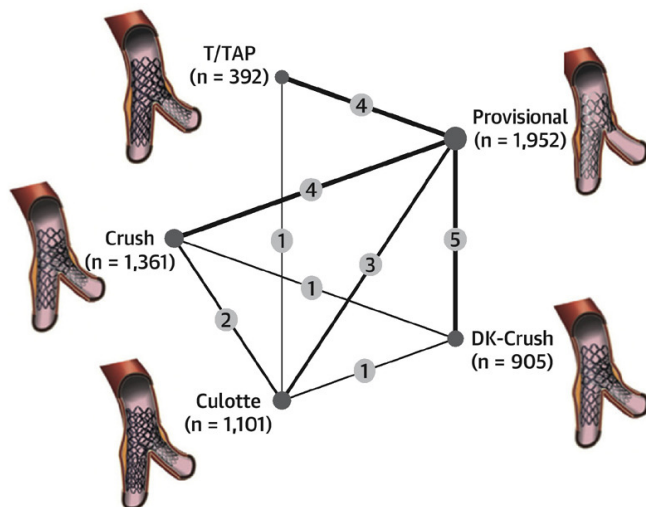


# Clinical Outcomes Following Coronary Bifurcation PCI Techniques

A Systematic Review and Network Meta-Analysis Comprising  
5,711 Patients (JACC 2020)



## CENTRAL ILLUSTRATION: Network Plot and Forest Plot for the Primary Outcome of Interest



Di Gioia, G. et al. J Am Coll Cardiol Interv. 2020;13(12):1432-44.



# General Remarks (1)

- PCI to LM can be demanding, particularly with respect to lesion preparation and side branch re-wiring when the SB is diseased
- When the SB is relatively healthy, the overall complexity considerably decreases, regardless the specific segment of the coronary tree
- ***So, the Side Branch matters!!!! Because the technique is CONSEQUENCE of the Side Branch (anatomy & disease burden)***



# General Remarks (2)

- The selection of the appropriate “gear” (catheter, wires, balloons, stents..) MUST be mainly based on routine
- **Dedicated bifurcation devices?** Not much evidence or even failed...



# General Remarks (3)

- Imaging (overall):
  - IVUS (easy, reproducible, no contrast)
  - OCT (sometimes technically demanding, contrast issue for repeated runs, highest quality)



# ESC Guide Lines

Recommendation for the type of revascularization in patients with stable coronary artery disease with suitable coronary anatomy for both procedures and low predicted surgical mortality<sup>d</sup>

Recommendations according to extent of CAD	CABG		PCI	
	Class <sup>a</sup>	Level <sup>b</sup>	Class <sup>a</sup>	Level <sup>b</sup>
<b>One-vessel CAD</b>				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis. <sup>68,101,139–144</sup>	I	A	I	A
<b>Two-vessel CAD</b>				
Without proximal LAD stenosis.	IIb	C	I	C
With proximal LAD stenosis. <sup>68,70,73</sup>	I	B	I	C
<b>Left main CAD</b>				
Left main disease with low SYNTAX score (0–22). <sup>69,121,122,124,145–148</sup>	I	A	I	A
Left main disease with intermediate SYNTAX score (23–32). <sup>69,121,122,124,145–148</sup>	I	A	IIa	A
Left main disease with high SYNTAX score (≥33). <sup>c 69,121,122,124,146–148</sup>	I	A	III	B
<b>Three-vessel CAD without diabetes mellitus</b>				
Three-vessel disease with low SYNTAX score (0–22). <sup>102,105,121,123,124,135,149</sup>	I	A	I	A
Three-vessel disease with intermediate or high SYNTAX score (≥22). <sup>c 102,105,121,123,124,135,149</sup>	I	A	III	A
<b>Three-vessel CAD with diabetes mellitus</b>				
Three-vessel disease with low SYNTAX score 0–22. <sup>102,105,121,123,124,135,150–157</sup>	I	A	IIb	A
Three-vessel disease with intermediate or high SYNTAX score (≥22). <sup>c 102,105,121,123,124,135,150–157</sup>	I	A	III	A



## EXCEL: Study design



2905 pts with unprotected left main disease

↓  
SYNTAX Score  $\leq 32$

Consensus agreement of eligibility and equipoise by heart team

↓  
Yes (n= 1905)

→ No (n= 1000)

↓  
Enrollment registry

Stratified by diabetes, SYNTAX Score and center

R

↓  
PCI (Xience EES)  
N= 948

↓  
CABG  
N= 957

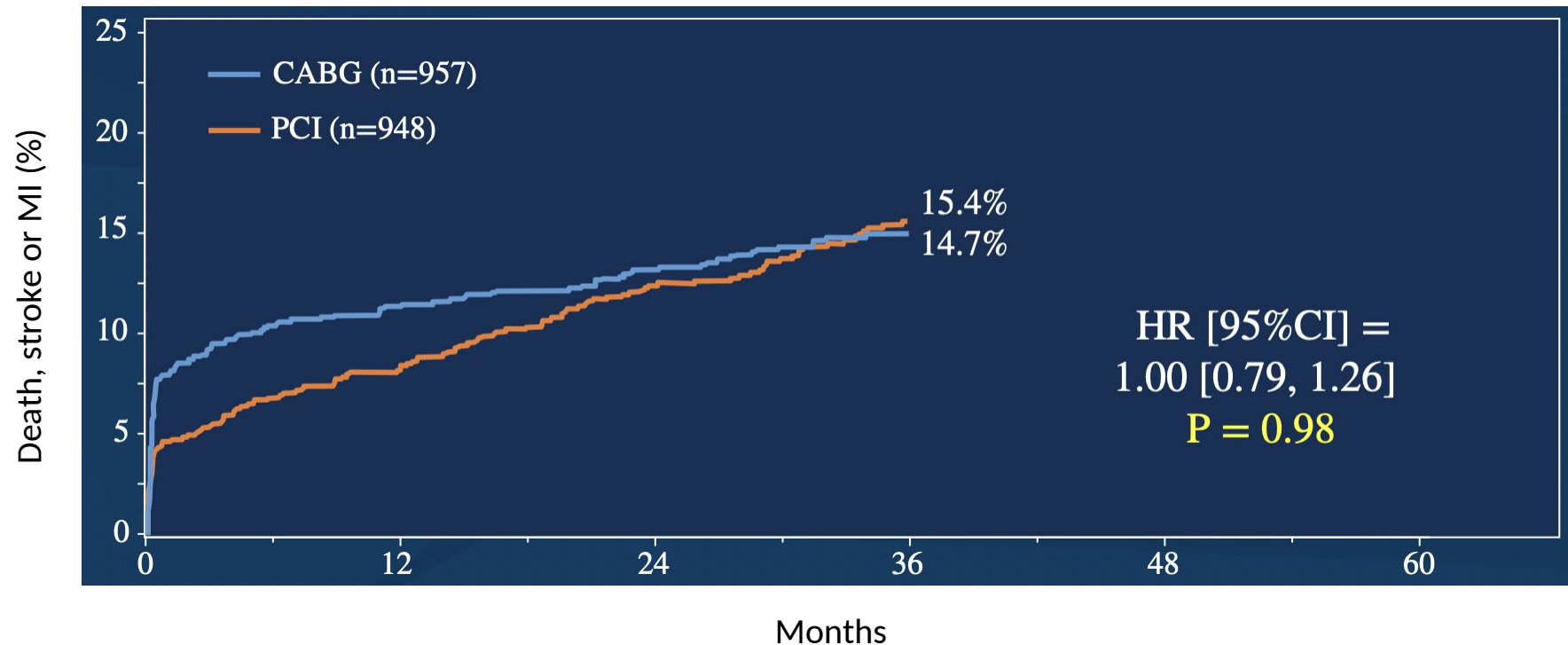
Follow-up: 1 month, 6 months, 1 year, annually through 5 years

Primary endpoint: death, MI or stroke measured at median 3-yr GU, min 2-yr FU



## PRIMARY ENDPOINT

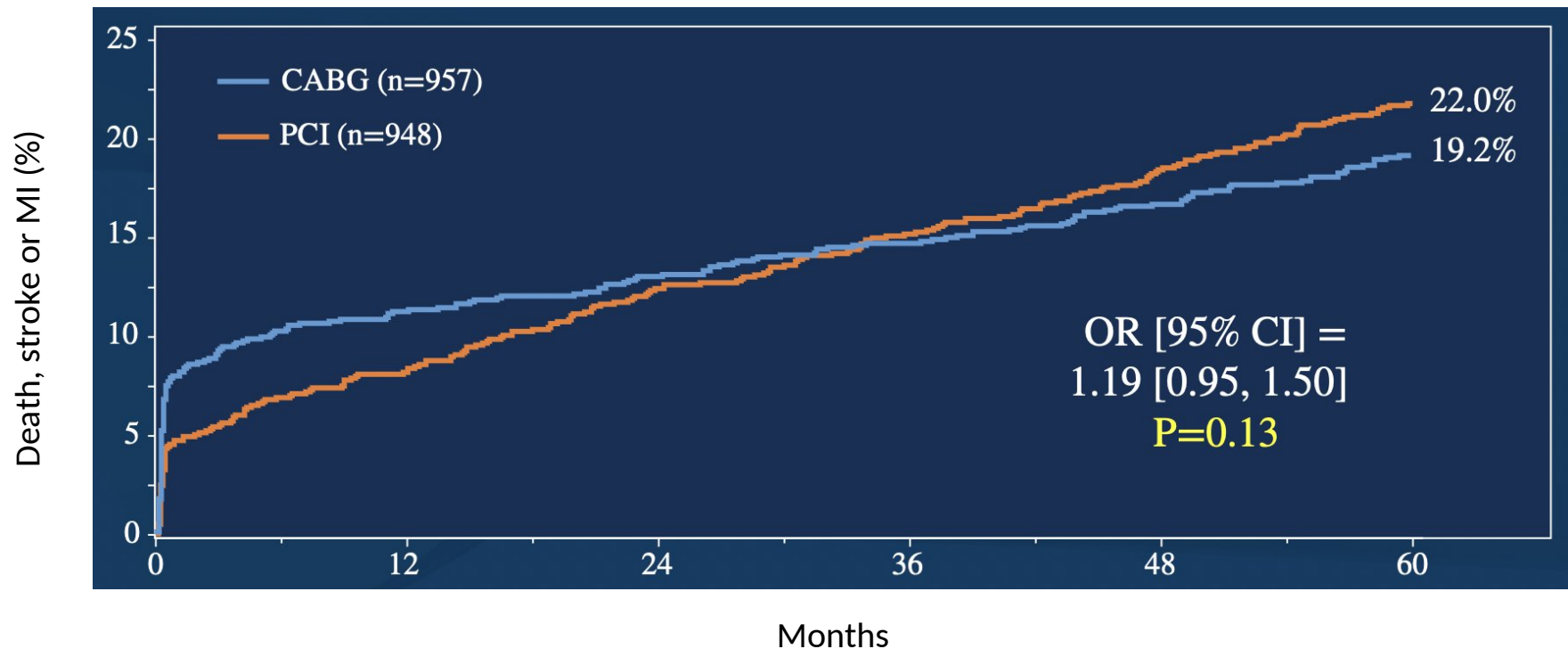
All-cause death, stroke or MI at median 3-yr FU





## PRIMARY ENDPOINT

All-cause death, stroke or MI at median 5-yr FU







**EXCEL was not powered for these outcomes**

- Prone to type II error (false negatives)

**Not adjusted for multiplicity**

- Prone to type I error (false positives)

**Not designed for hypothesis testing**



**Meta-analysis!**



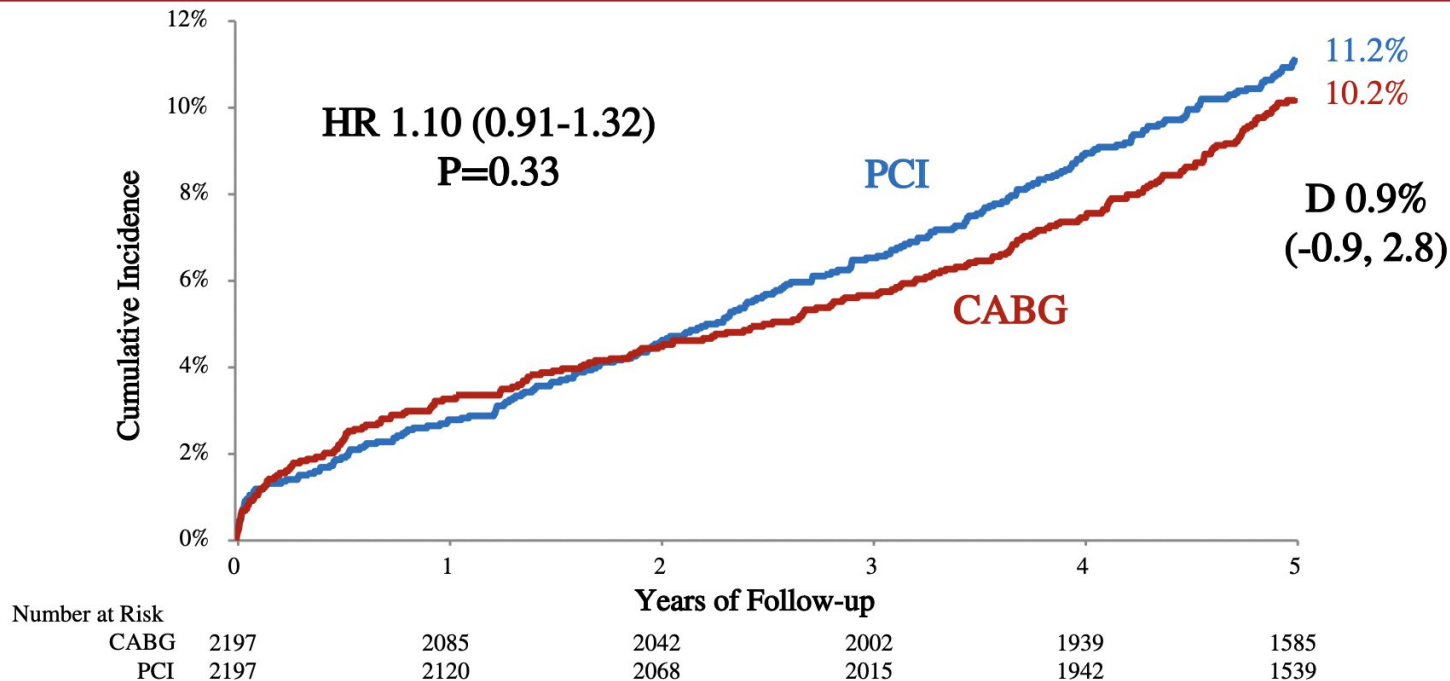
## Individual Patient Data Pooled Analysis from EXCEL, NOBLE, SYNTAX, and PRECOMBAT (n=4,394)

*All 4394 patients judged by a Heart Team to be equally suitable candidates for either PCI or CABG*

Characteristic	PCI (N=2197)	CABG (N=2197)
Age, years	66 (59-73)	66 (59-72)
Male	77	77
Diabetes	26	25
LVEF <50%	12	12
SYNTAX score	25 (19-31)	24 (18-31)
Left main only	16	16
Left main + multivessel ( $\geq 2V$ ) disease	52	53
# stents / conduits	2 (1-3)	2 (2-3)
IVUS use	68	
LIMA		96
All arterial		23

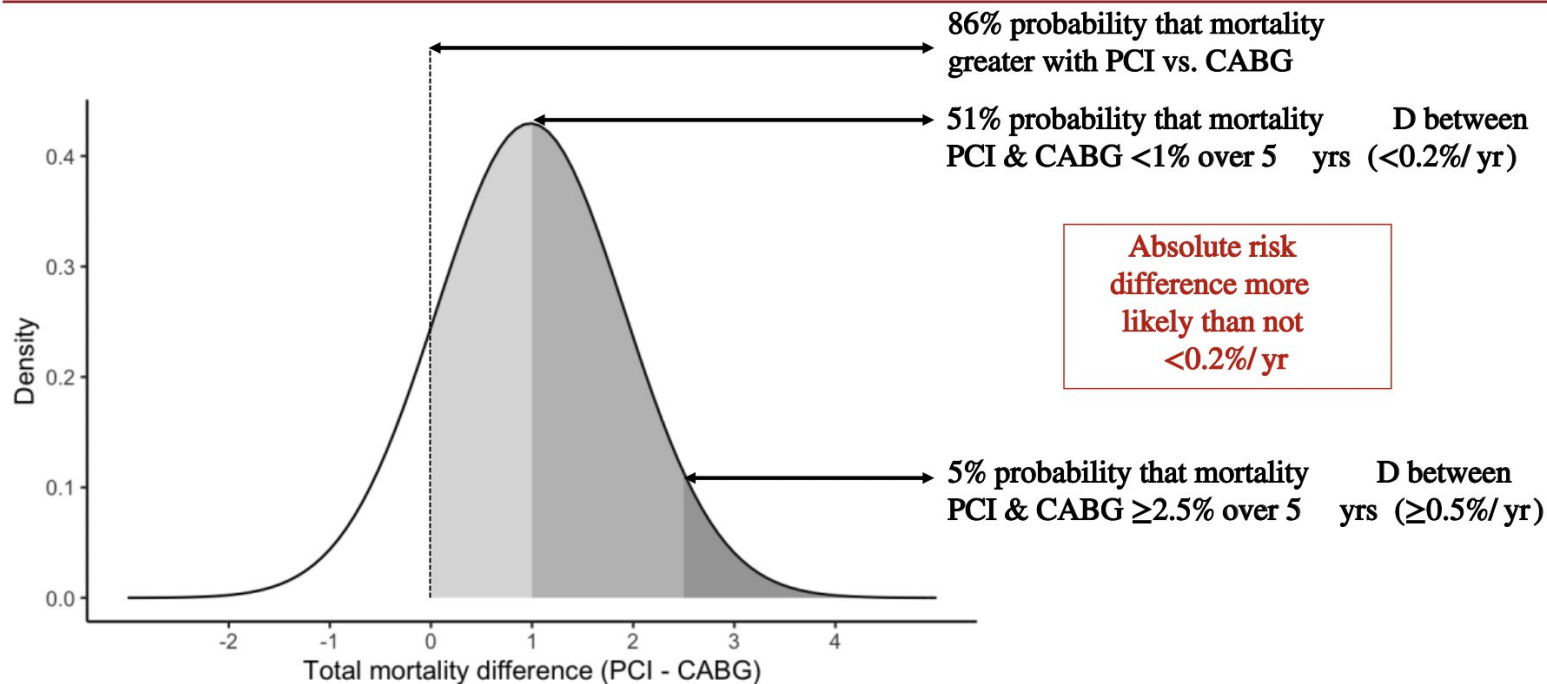


## PRIMARY ENDPOINT: All-cause Mortality



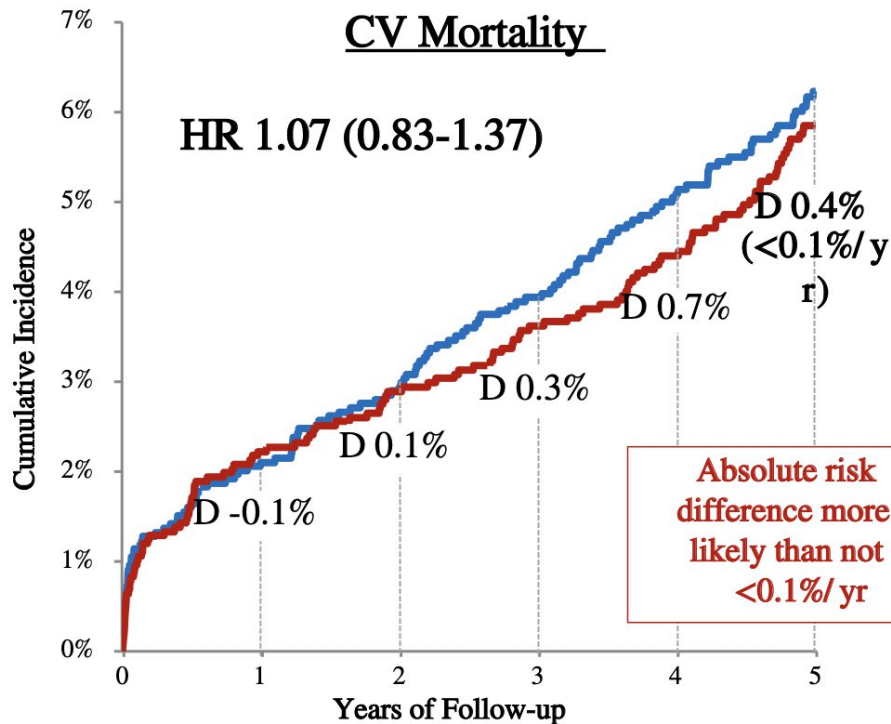


## Bayesian Analysis of Mortality





## CV and non-CV Mortality

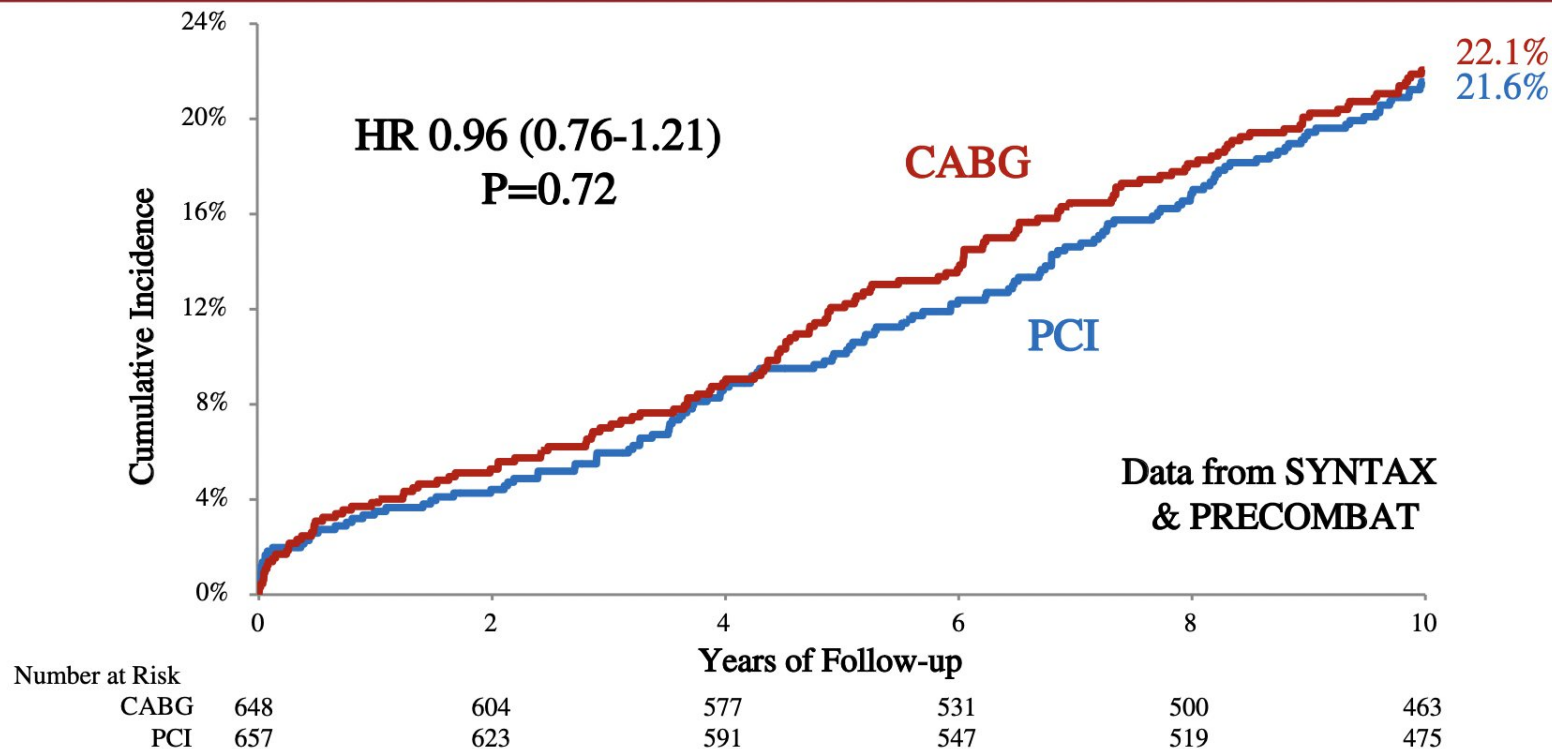


Type of Death	5-Year KM Rates		
	PCI	CABG	D
CV	6.2	5.9	0.4 (-1.1, 1.8)
Non-CV	5.2	4.5	0.7 (-0.6, 2.0)

Higher rate of non-CV death was driven by increased late (>1-year) rates of malignancy and sepsis in PCI-treated pts in EXCEL, with no evidence of increased risk in the other 3 trials or any prior trial of PCI vs. CABG.

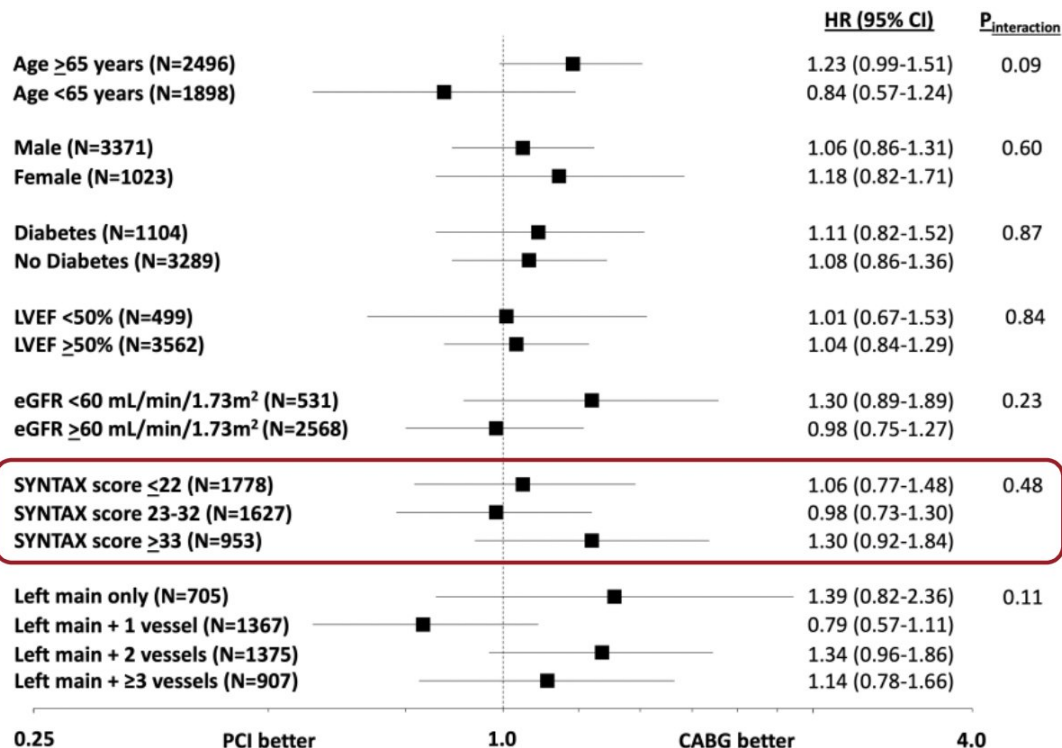


## Two Trials with 10-year Mortality Data



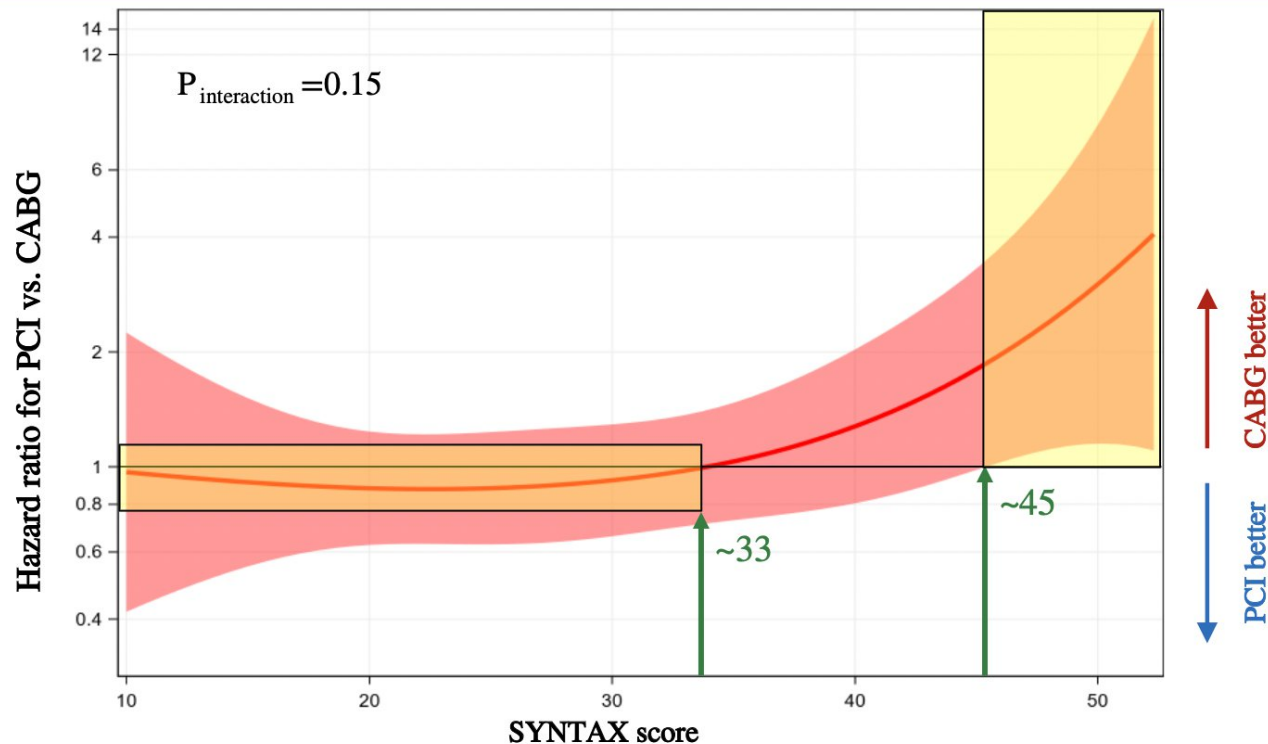


## Mortality Analysis Subgroups





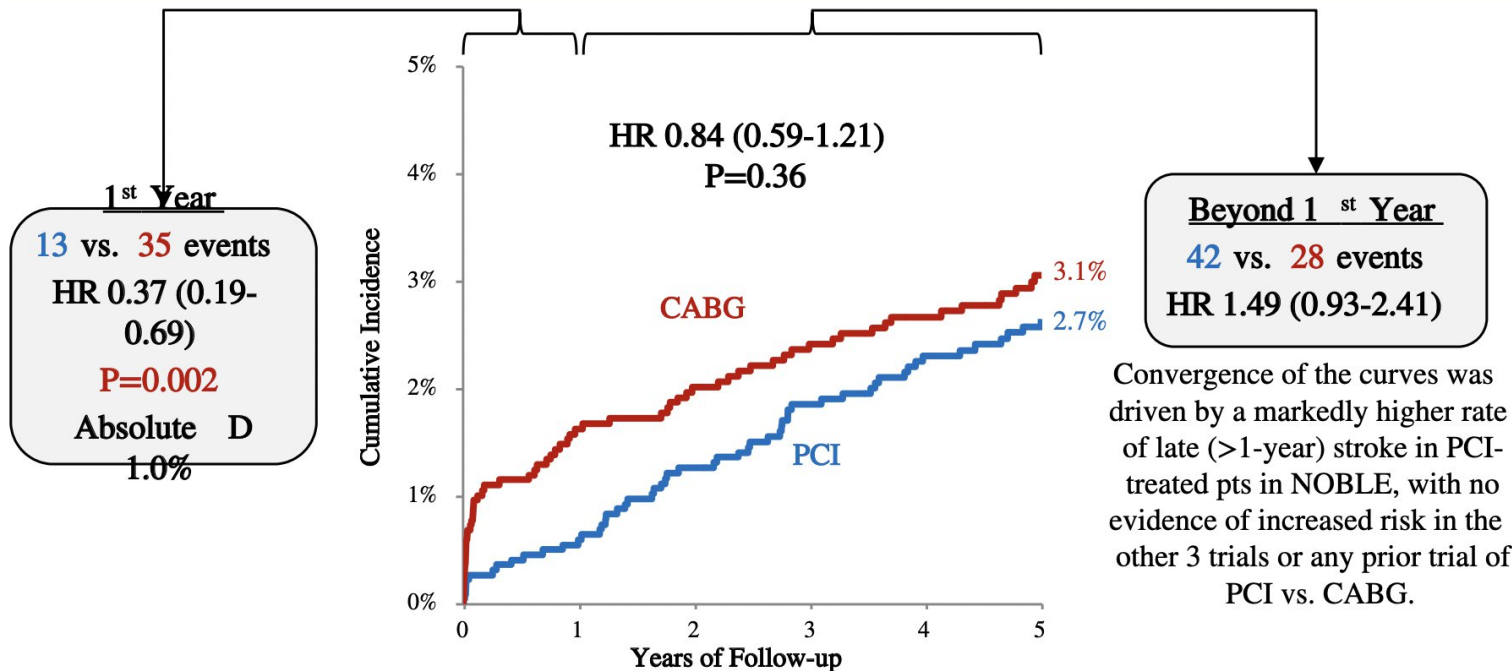
## 5-year CV Mortality and SYNTAX Score







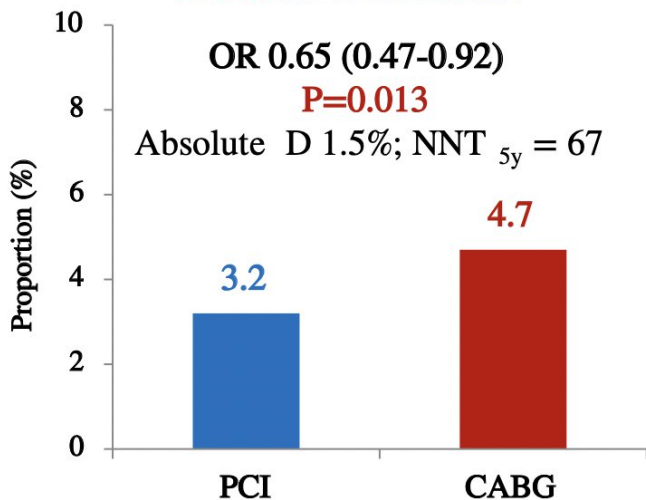
## Stroke





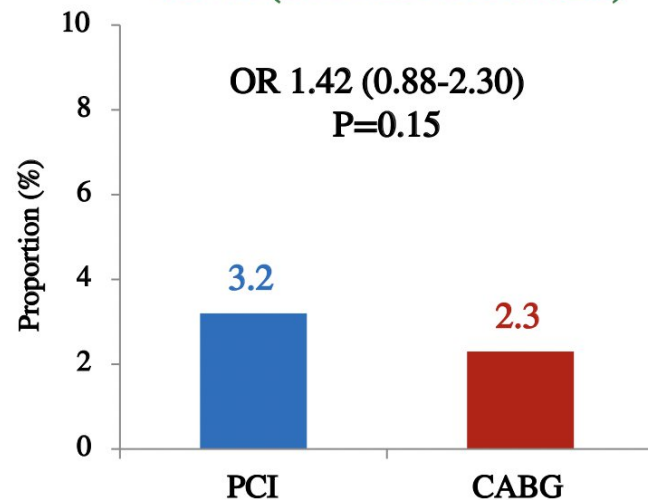
## Procedural MI

### Protocol Definition



- CK-MB >5× + new Qw [or angio or imaging in some trials]
- [CK-MB >10× in some trials]

### UDMI (SYNTAX & EXCEL)

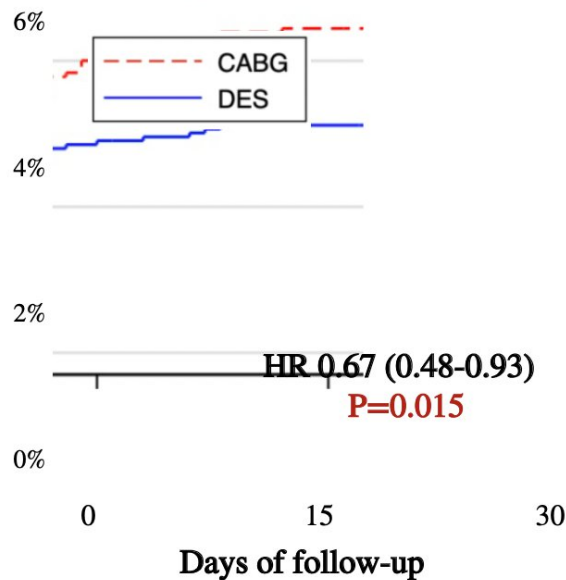


- **PCI:** cTn >5× + ST Ds, Qw, angio, or imaging [or sx]
- **CABG:** cTn >10× + Qw, angio, or imaging

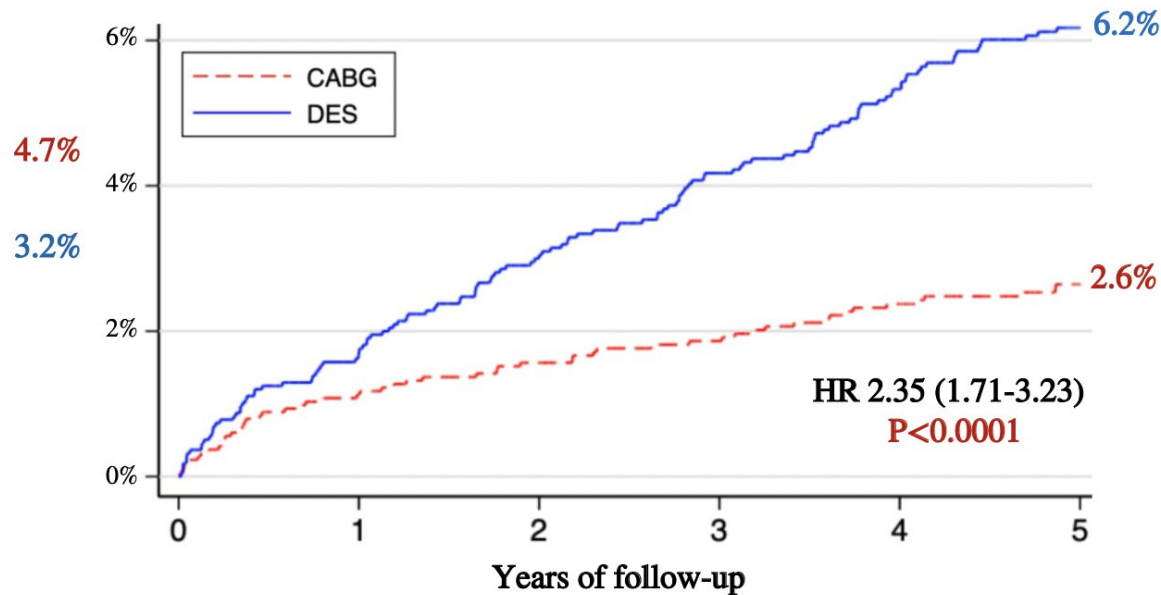


## Procedural and spontaneous MI

### Procedural MI (protocol definition)



### Spontaneous MI





## What about all other outcomes?

Recurrent angina

Chest pain

Musculoskeletal disorders

Infections/sepsis

Renal dysfunction

Atrial  
fibrillation/arrhythmias

Vascular complications

Major  
bleeding/transfusions

Repeat revascularization

Other reoperations

Rehospitalizations

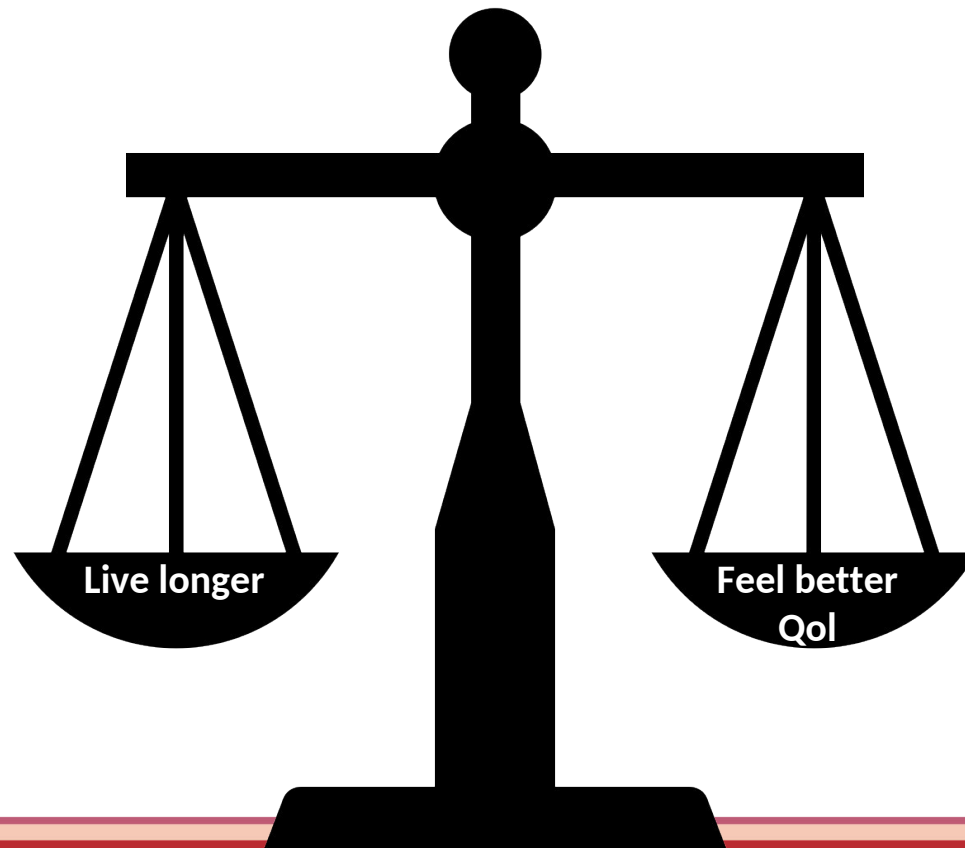
Cognitive decline

Depression

Time to recovery



## What do patients really want?



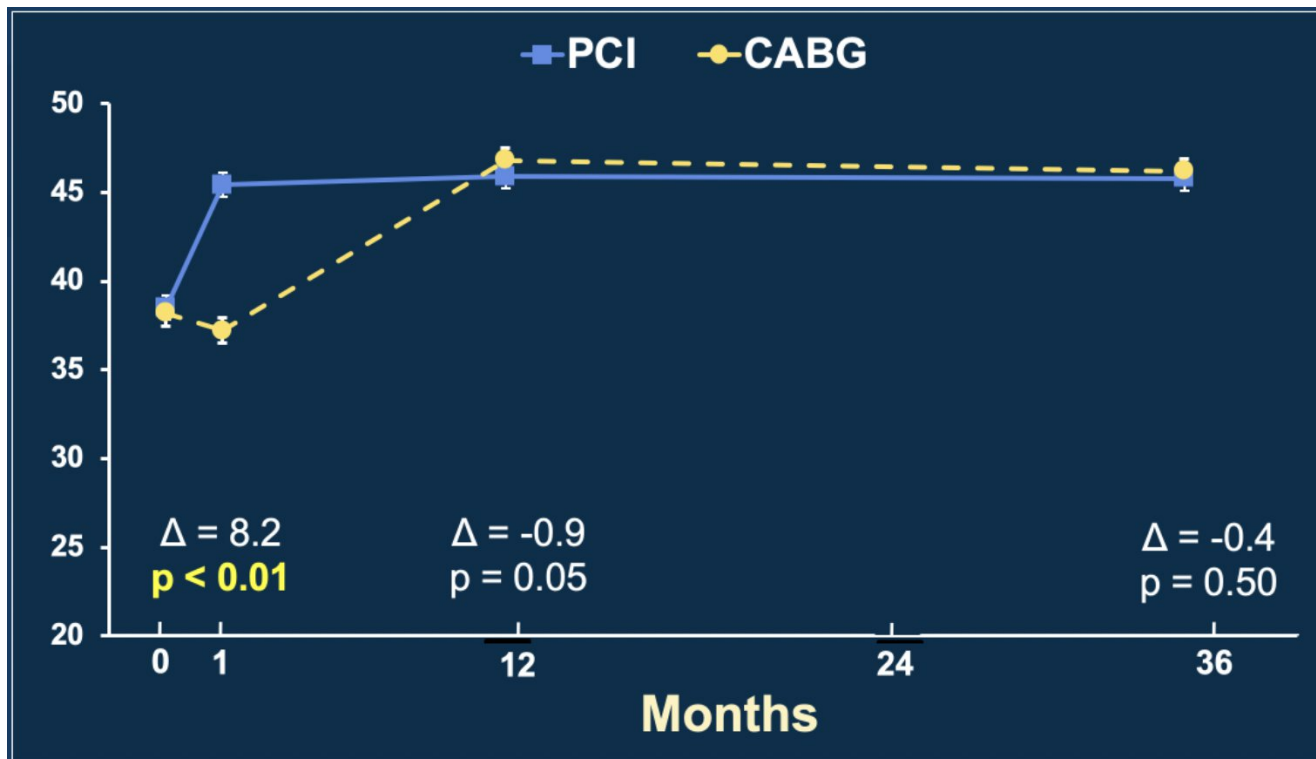


## LM PCI vs CABG controversies

**IS QUALITY OF LIFE  
DIFFERENT?**



## SF-12 Physical Summary Scale





## Major adverse events within 30 days

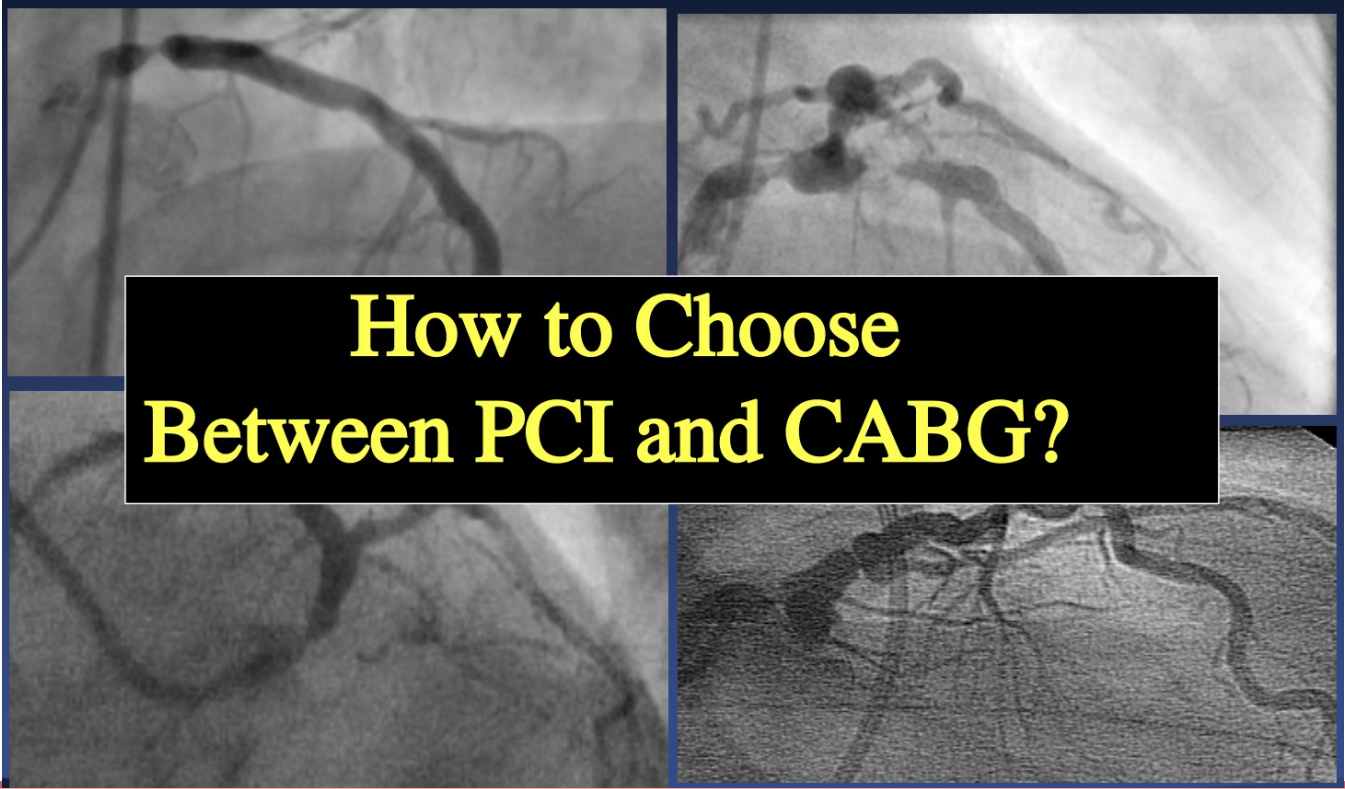
	PCI (n=948)	CABG (n=957)	RR [95%CI]	P-value
Peri-procedural MAE, any	12.4%	44.0%	0.28 [0.24, 0.34]	<0.001
- Death*	0.9%	1.0%	0.91 [0.39, 2.23]	0.83
- Stroke*	0.6%	1.3%	0.50 [0.19, 1.34]	0.16
- Myocardial infarction*	3.9%	6.2%	0.63 [0.42, 0.95]	0.02
- Ischemia-driven revascularization*	0.6%	1.4%	0.47 [0.18, 1.22]	0.11
- TIMI major/minor bleeding	3.7%	8.9%	0.42 [0.28, 0.61]	<0.001
- Transfusion ≥2 units	4.0%	17.0%	0.24 [0.17, 0.33]	<0.001
- Major arrhythmia**	2.1%	16.1%	0.13 [0.08, 0.21]	<0.001
- Surgery/radiologic procedure	1.3%	4.1%	0.31 [0.16, 0.59]	<0.001
- Renal failure <sup>†</sup>	0.6%	2.5%	0.25 [0.10, 0.61]	<0.001
- Sternal wound dehiscence	0.0%	2.0%	0.03 [0.00, 0.43]	<0.001
- Infection requiring antibiotics	2.5%	13.6%	0.18 [0.12, 0.28]	<0.001
- Prolonged intubation (>48 hours)	0.4%	2.9%	0.14 [0.05, 0.41]	<0.001
- Post-pericardiotomy syndrome	0.0%	0.4%	0.11 [0.01, 2.08]	0.12

\*Adjudicated events; others are site-reported. \*\*SVT requiring cardioversion, VT or VF requiring treatment, or bradyarrhythmia requiring temp or perm PM. <sup>†</sup>SCr increased by ≥0.5 mg/ dL from baseline or need for dialysis.





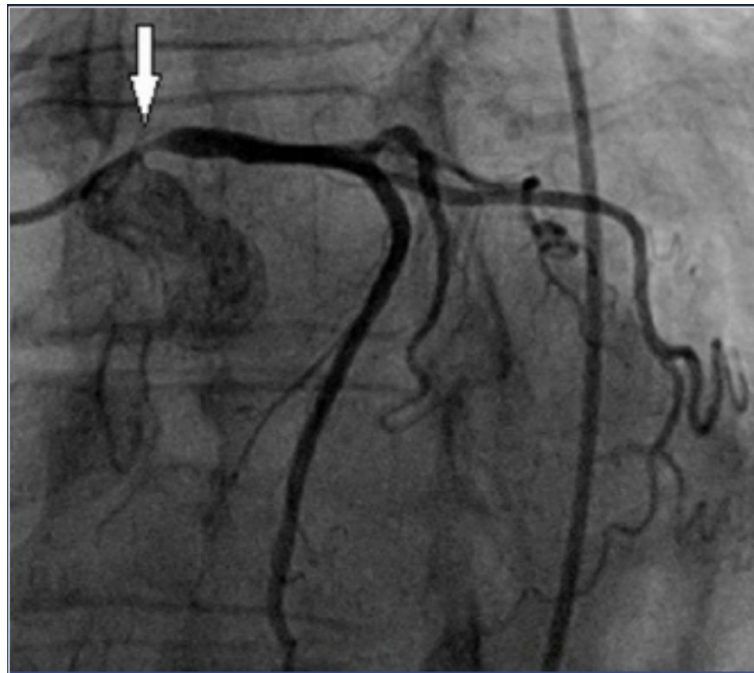
# The spectrum of Left Main coronary artery disease



**How to Choose  
Between PCI and CABG?**

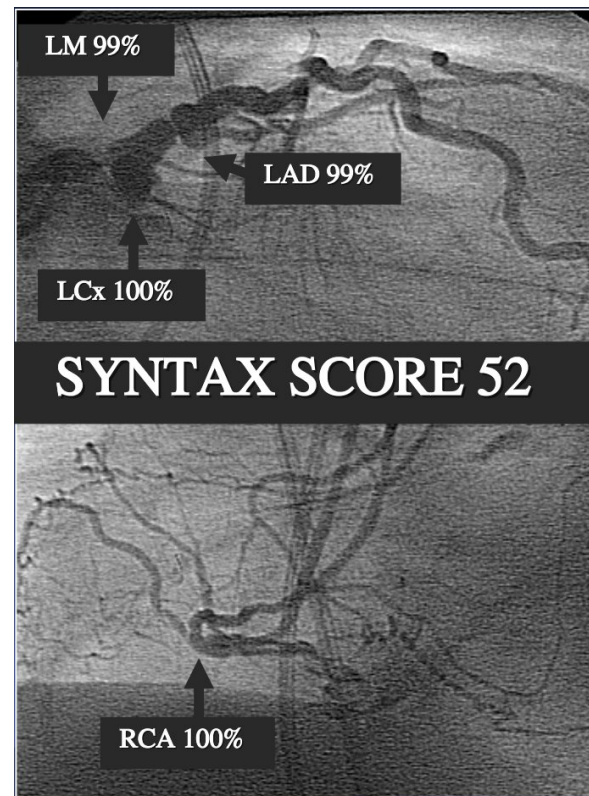


## Obvious choices



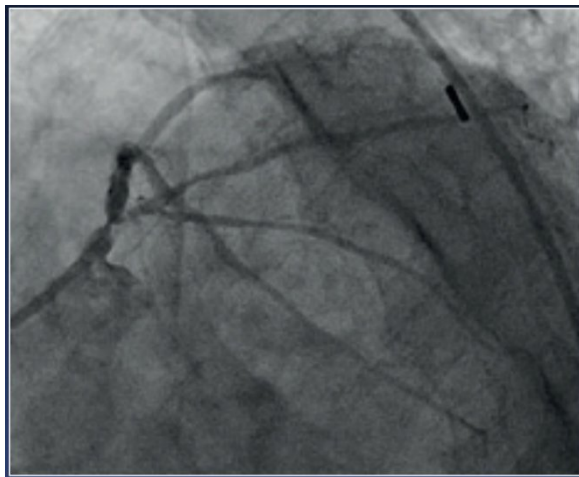
VS

## Equipoise





## Obvious choices



VS

## Equipoise





## Left Main PCI vs CABG Two Very Different Procedures

### PCI

#### EARLY ADVANTAGES

- Less invasive
- Fewer peri-procedural complications (stroke, MI, Afib, bleeding, AKI, etc.
- Lower 30-day MACE
- More rapid recovery with better early QoL and earlier angina relief



### CABG

#### LATE ADVANTAGES

- More durable
- Fewer adverse events beyond 1 year
  - particularly MI and repeat revascularization procedures

## PCI and CABG

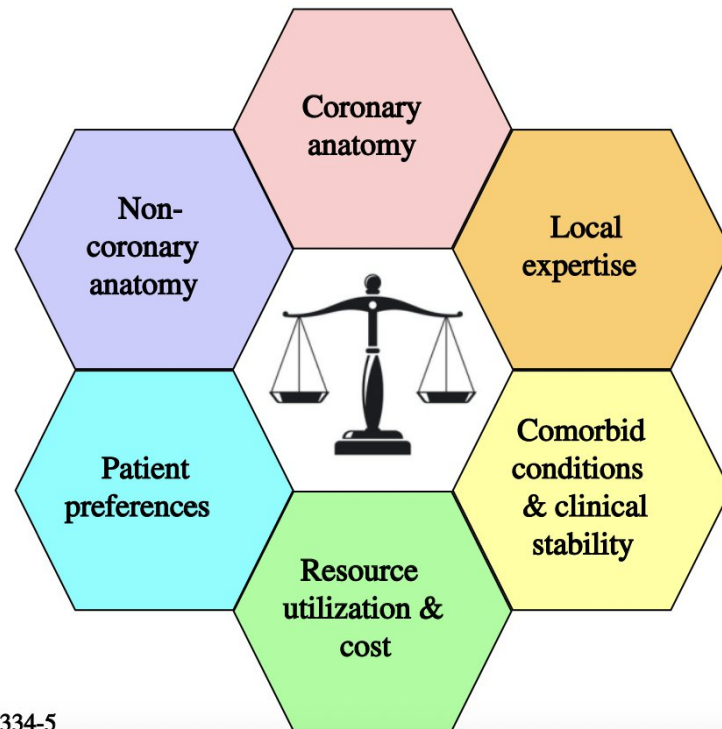
**No significant major differences in long-term survival, MACE (death, MI or stroke) or QoL**



## Revascularization of the Left Main CAD

### Critical Role of the Heart Team

The nuances of these data emphasize the importance of a Heart Team approach *to assist patients in reaching a treatment decision that is best for them.*



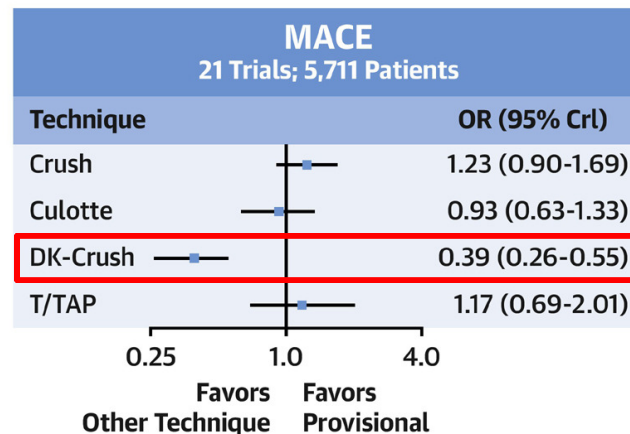
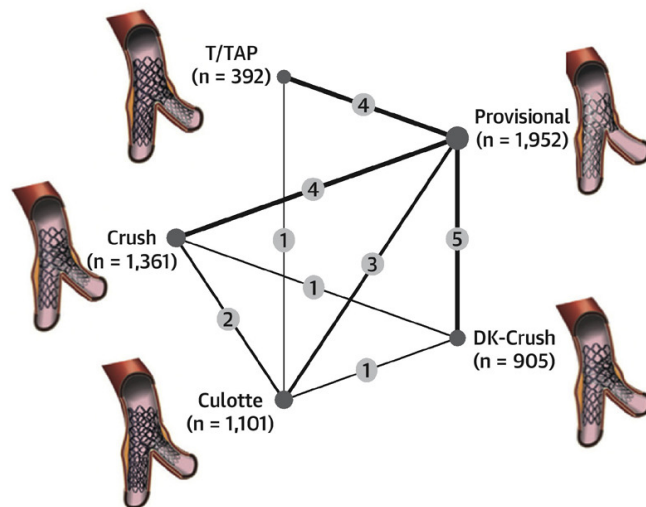


# Clinical Outcomes Following Coronary Bifurcation PCI Techniques

A Systematic Review and Network Meta-Analysis Comprising 5,711 Patients (JACC 2020)



## CENTRAL ILLUSTRATION: Network Plot and Forest Plot for the Primary Outcome of Interest



Di Gioia, G. et al. J Am Coll Cardiol Interv. 2020;13(12):1432-44.



# Intravascular ultrasound in the evaluation and treatment of left main coronary artery disease: a consensus statement from the European Bifurcation Club

Gary S Mintz <sup>1</sup>, Thierry Lefèvre, Jens Flensted Lassen, Luca Testa, Manuel Pan, Jag Singh, Goran Stankovic, Adrian P Banning

Affiliations + expand

PMID: 29688182 DOI: [10.4244/EIJ-D-18-00194](https://doi.org/10.4244/EIJ-D-18-00194)

**Free article**



# 2018 ESC/EACTS Guidelines on myocardial revascularization

	Class	Level
IVUS should be considered to optimize treatment of unprotected left main lesions. <sup>35</sup>	<b>IIa</b>	<b>B</b>

**Why not a class I ?**



# Optimization of Left Main PCI with Intravascular Ultrasound. The OPTIMAL Randomized Controlled Trial



**PI: Luca Testa**



**PI: Adrian Banning**



**Spain P.I. : Jose M de la Torre Hernandez**



- 800 patients in approximately 30 sites (UK, Italy, Spain)
- Randomized, controlled, multicenter, international, post-market strategy study in patients with indication for PCI of the Left Main coronary artery
- Patients will be followed up to 2 years after the index procedure

The Half way  
Point



# Thanks for the attention

**Luca Testa, MD, PhD**

**Head of Coronary Revasc Unit, IRCCS Policlinico S. Donato, Milan**

**Head of Clinical Research Unit, IRCCS Policlinico S. Donato, Milan**

**Contract Professor of Cardiology, «Vita e Salute» Univ. San Raffaele Hospital, Milan**