Coronary artery Disease and TAVR

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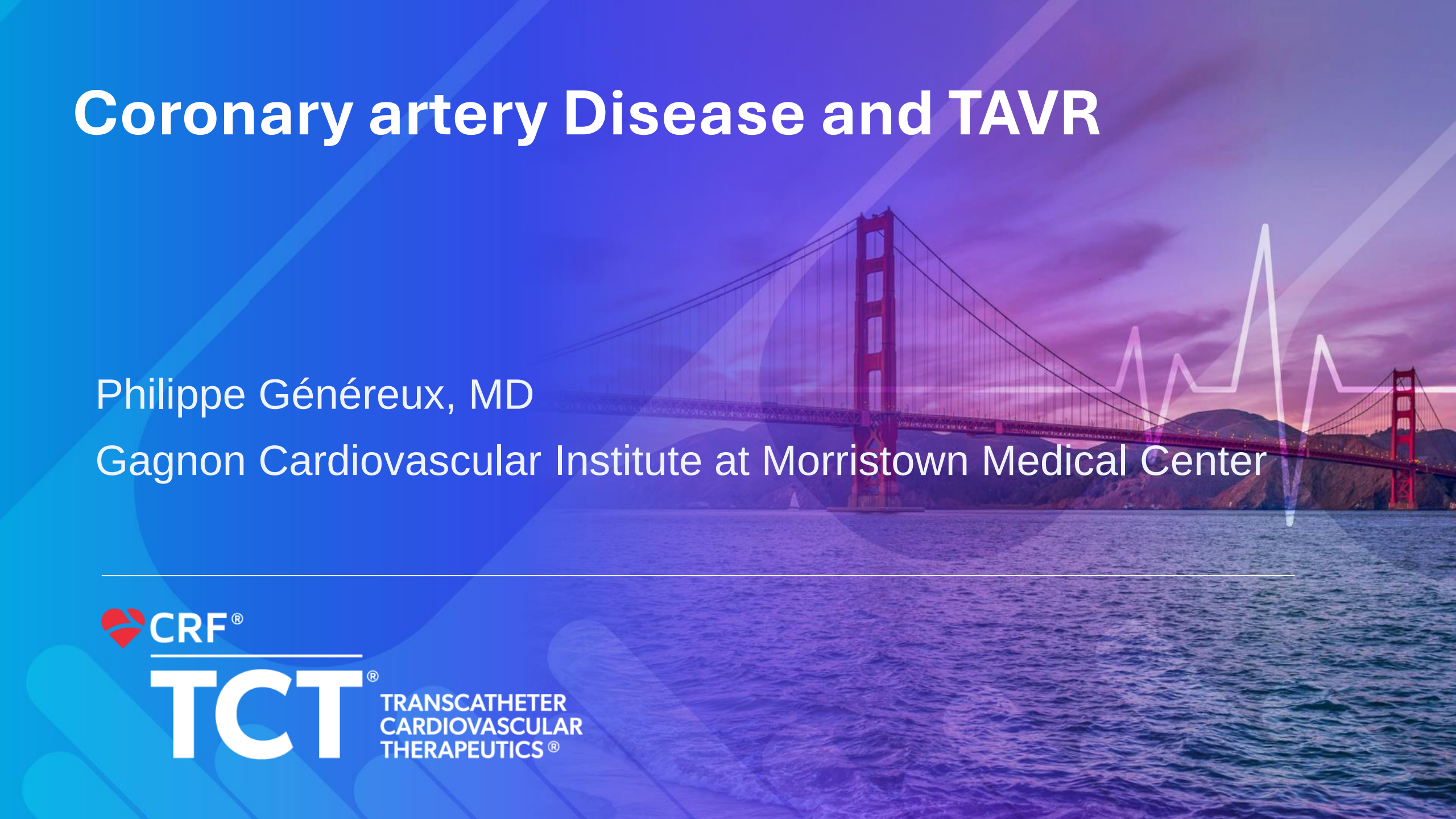

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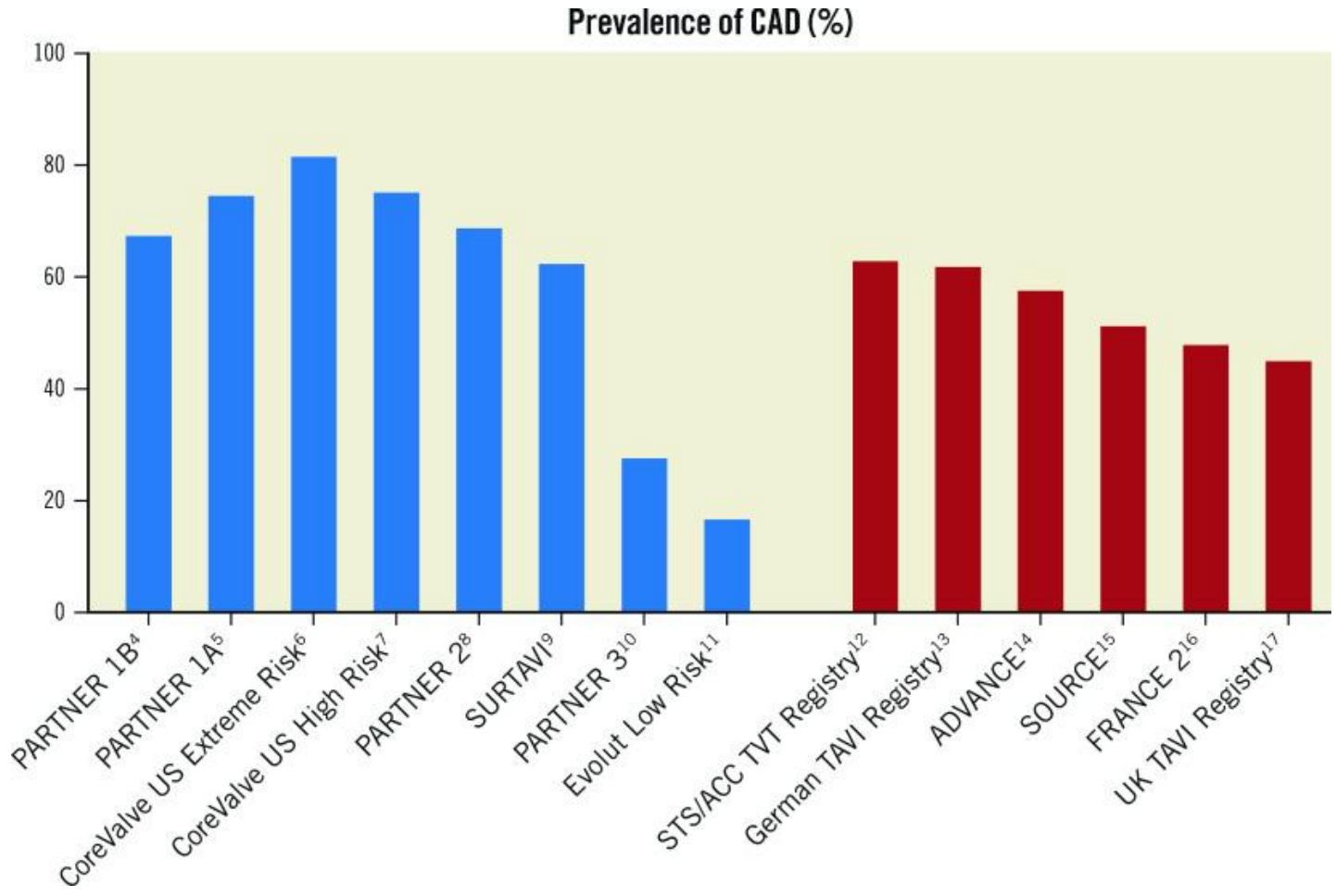
Prevalence of coronary disease: Frequent but Varies with definitions used and Population Studied



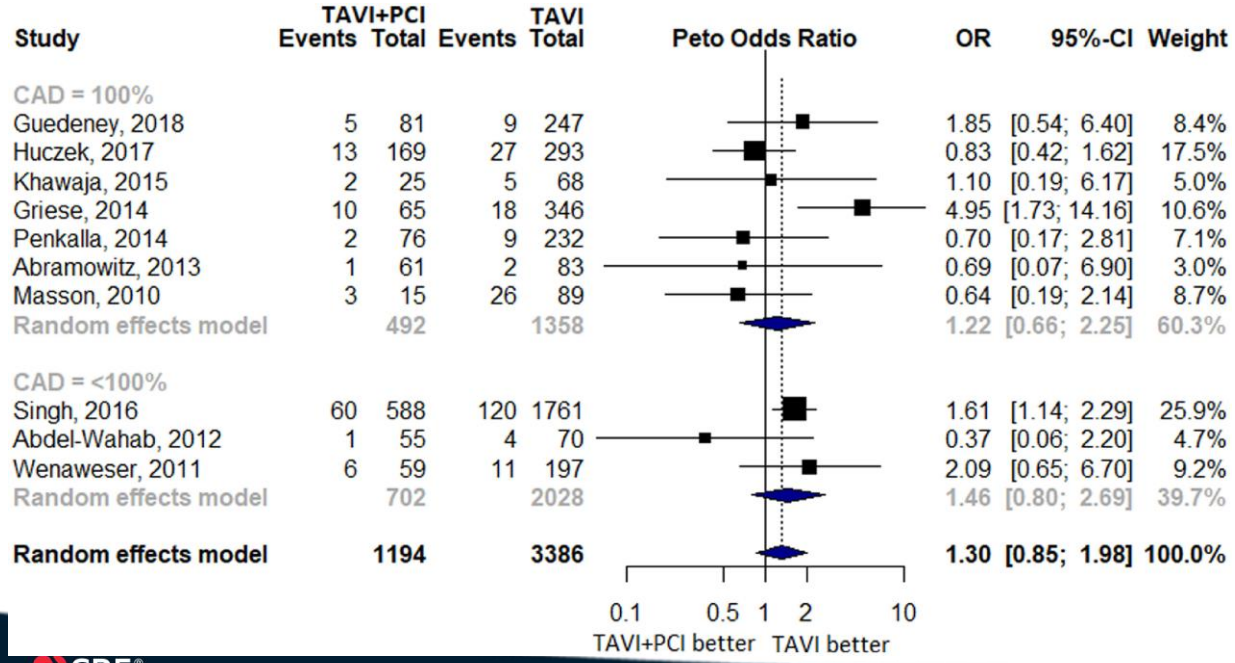
Stefanini, Eurointervention 2013

CAD Management and AVR

- **Is there a need to treat?**
  - Age
  - Severity, complexity, and extent of CAD
  - Causing symptoms or impacting survival?
- **How?**
  - PCI vs. CABG
- **When?**
  - Before vs. After vs. During?

TAVI and PCI vs. TAVI alone

No differences in 30-day all-cause mortality (OR 1.30 [0.85 to 1.98], p = 0.22, I^2 = 37.5%), stroke (OR 0.7 (0.36 to 1.45), p = 0.36, I^2 = 32.8%), MI (OR 2.71 [0.55 to 12.23], p = 0.22, I^2 = 41.3%), acute kidney injury (OR 0.7 [0.46 to 1.06], p = 0.08, I^2 = 14.4%) and 1-year all-cause mortality (OR 1.19 [0.92 to 1.52], p = 0.18, I^2 = 0.0%)



Meta-Analysis Comparing Outcomes in Patients Undergoing Transcatheter Aortic Valve Implantation With Versus Without Percutaneous Coronary Intervention

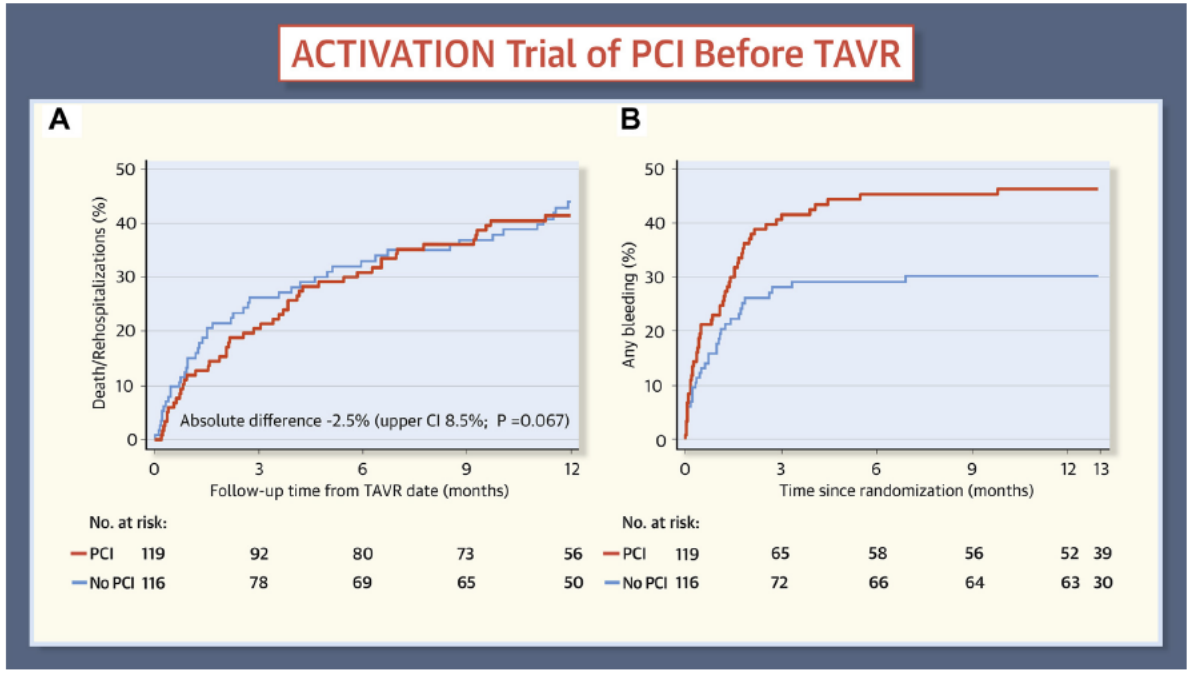
Noman Lateef, MD[a], Muhammad Shahzeb Khan, MD[b], Salil V. Deo, MD[c], Naser Yamani, MD[b], Haris Riaz, MD[d], Hafeez Ul Hassan Virk, MD[e], Safi U. Khan, MD[f], David P. Hedrick, MD, PhD[d,g], Anmar Kanaan, MD[d,g], Grant W. Reed, MD[d], Amar Krishnaswamy, MD[d], Rishi Puri, MBBS, PhD[d], Samir R. Kapadia, MD[d], Ankur Kalra, MD[d,g,*]

Lateef et al. Am J Cardiol. 2019

Activation Trial

No Benefits in PCI for death-Rehospitalization
Increased Bleeding risk at 1 year

CENTRAL ILLUSTRATION The ACTIVATION Trial of PCI Compared With No PCI Prior to TAVR Demonstrated No Difference in the Primary Endpoint of Death or Rehospitalization at 1 Year and Increased Bleeding Events in the PCI Arm



Patterson, T. et al. J Am Coll Cardiol Intv. 2021;14(18):1965-1974.

TABLE 2 Angiographic and Procedural Characteristics

	PCI (n = 119)	No PCI (n = 116)
Coronary artery disease		
Left anterior descending artery >70%	73 (61.3)	69 (60.5)
Circumflex artery >70%	42 (35.3)	38 (33.3)
Right coronary artery >70%	47 (39.5)	59 (51.8)
Left main stem coronary artery >70%	3 (2.5)	6 (5.3)
Bare-metal stent implantation		
Number of patients	21 (17.6)	
Number of stents/lesions	39/194 (20)	

RESULTS

PATIENTS. A total of 235 participants were recruited between December 4, 2012, and January 11, 2019,

Bleeding at 30 d			
Any bleed	49 (41.2)	31 (26.7)	1.46 (0.93-2.29); 0.098
During TAVR procedure	8 (6.7)	4 (3.4)	
Major bleed	31 (26.1)	21 (18.1)	1.23 (0.68-2.22); 0.49
During TAVR procedure	7 (5.8)	2 (1.7)	

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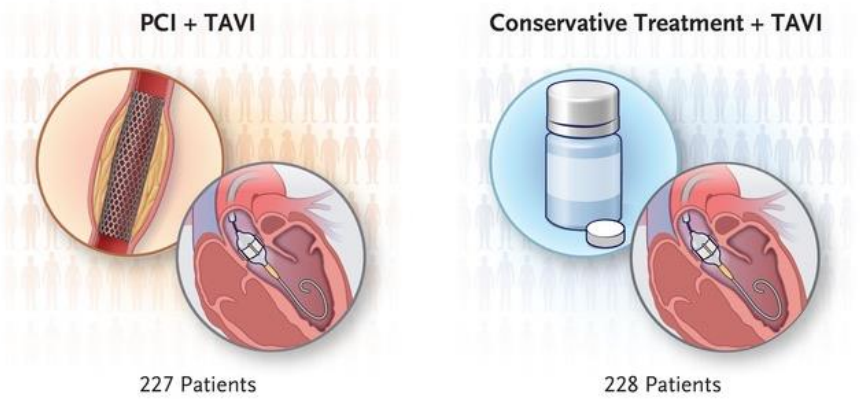


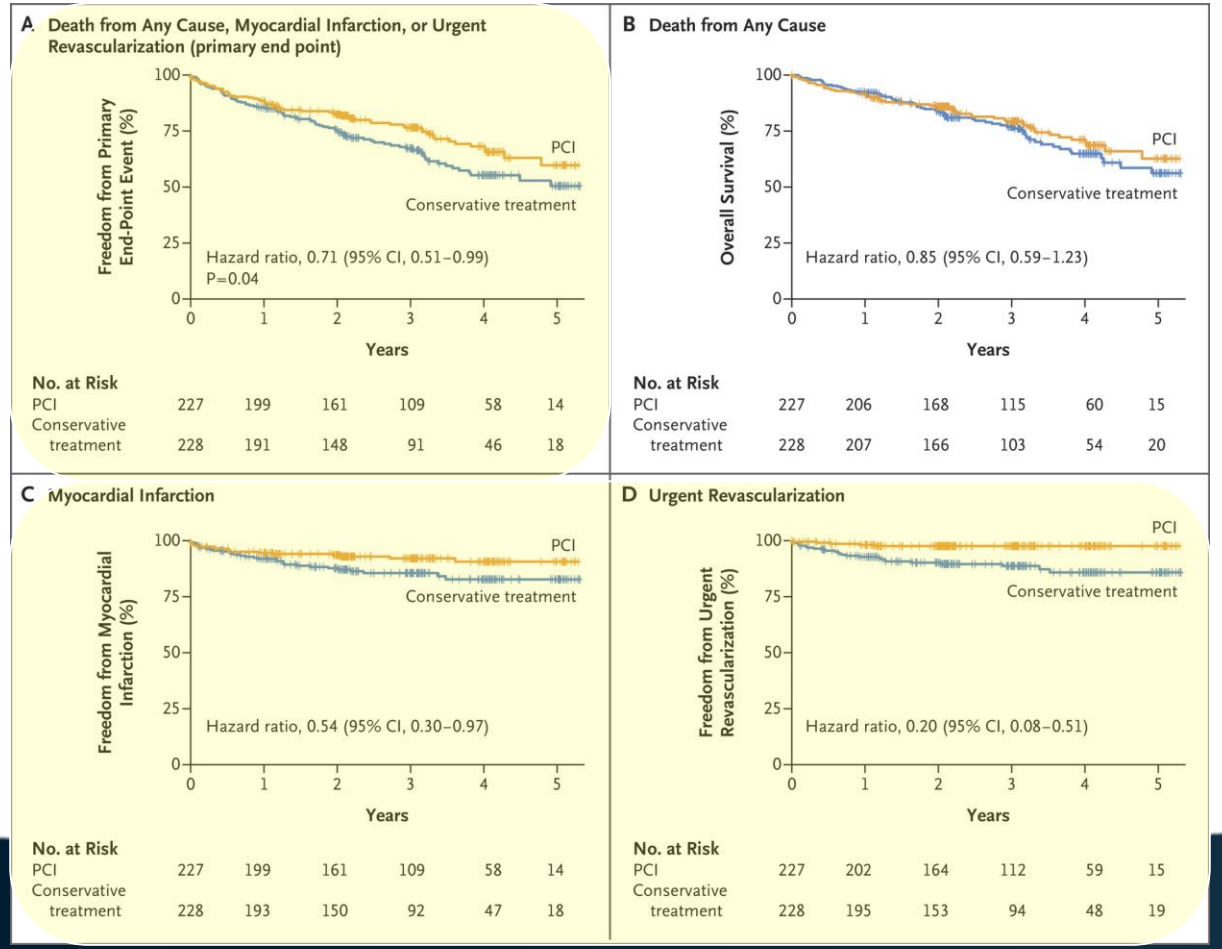
NOTION 3 TRIAL

Death-MI-Urgent Revasc

Criteria for PCI

1) All lesions DS ≥ 90%

2) if FFR ≤ 0.80 in lesions with DS <90%



Lønborg J et al. N Engl J Med2024;391:2189-2200

NOTION 3 TRIAL

Primary and Secondary End Points

Table 3. Primary and Secondary End Points.*

End Point	PCI (N=227)	Conservative Treatment (N=228)	Hazard Ratio (95% CI)	P Value
	number (percent)			
Primary end point: MACE†	60 (26)	81 (36)	0.71 (0.51–0.99)	0.04
Secondary end points				
Death from any cause	53 (23)	62 (27)	0.85 (0.59–1.23)	
Myocardial infarction‡	17 (7)	31 (14)	0.54 (0.30–0.97)	
Urgent revascularization§	5 (2)	25 (11)	0.20 (0.08–0.51)	
Death from cardiovascular causes¶	20 (9)	30 (13)	0.67 (0.38–1.19)	
Any revascularization	6 (3)	48 (21)	0.12 (0.05–0.27)	
Stroke	23 (10)	35 (15)	0.67 (0.39–1.14)	
Safety end points				
Any bleeding event‖	64 (28)	45 (20)	1.51 (1.03–2.22)	
Life-threatening or disabling	23 (10)	16 (7)		
Major	26 (11)	22 (10)		
Minor	53 (23)	36 (16)		
Stent thrombosis	1 (<1)	2 (1)	—	
Acute kidney failure	12 (5)	26 (11)	0.45 (0.23–0.89)	

* The widths of the confidence intervals for the secondary end points have not been adjusted for multiplicity and cannot be used to infer treatment effects.

† The primary end point was a major adverse cardiac event (MACE), defined as a composite of death from any cause, myocardial infarction, or urgent revascularization.

‡ Myocardial infarction included any spontaneous or periprocedural myocardial infarction that occurred less than 72 hours after TAVI and less than 48 hours after PCI.

§ Urgent revascularization included any revascularization that was performed during an unplanned hospital admission with acute coronary syndrome (myocardial infarction or unstable angina). Unstable angina was considered to require all the following factors: worsening ischemic discomfort, unscheduled hospitalization, objective evidence of myocardial ischemia, and cardiac biomarker levels not indicative of acute myocardial infarction.[16]

¶ Death from cardiovascular causes included death due to proximate cardiac cause (e.g., myocardial infarction, tamponade, or heart failure), death caused by a noncoronary vascular condition (e.g., neurologic condition, pulmonary embolism, or an aortic or other vascular condition), all procedure-related deaths, all valve-related deaths, sudden death, and death of unknown cause.[15,16]

‖ Bleeding was recorded according to the Valve Academic Research Consortium–2 criteria.[15] A patient may have had more than one bleeding event and thus may have events recorded in multiple categories.

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NOTION 3 TRIAL

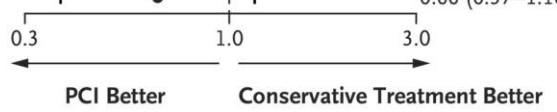
Criteria for PCI

1) *All lesions DS ≥ 90%*

2) *if FFR ≤ 0.80 in lesions with DS <90%*

FFR is in general <0.80 only in < 35% of lesions tested.
Therefore the trial strategy was tested only in a small number of patients with DS < 90%.
Concluding that there is no difference in lesions with DS < 90% based in such small tested lesions is potentially misleading.

Subgroup	PCI (N=227)	Conservative Treatment (N=228)	Hazard Ratio (95% CI)
	no. of patients with event/total no. (%)		
Age			
<82 yr	21/106 (20)	40/117 (34)	0.56 (0.33–0.95)
≥82 yr	39/121 (32)	41/111 (37)	0.81 (0.52–1.26)
Sex			
Male	43/154 (28)	56/153 (37)	0.73 (0.49–1.09)
Female	17/73 (23)	25/75 (33)	0.64 (0.35–1.19)
Diabetes			
No	40/168 (24)	55/167 (33)	0.67 (0.45–1.01)
Yes	20/59 (34)	26/61 (43)	0.79 (0.44–1.42)
Diameter of stenosis			
<90%	27/88 (31)	32/96 (33)	1.04 (0.62–1.73)
≥90%	33/139 (24)	49/132 (37)	0.53 (0.34–0.82)
LVEF			
>40%	50/194 (26)	72/196 (37)	0.65 (0.46–0.94)
≤40%	10/33 (30)	9/32 (28)	1.13 (0.46–2.79)
STS-PROM score			
>2.8	40/123 (33)	45/106 (42)	0.73 (0.48–1.13)
≤2.8	20/104 (19)	36/122 (30)	0.61 (0.35–1.05)
SYNTAX score			
>9	33/109 (30)	39/106 (37)	0.74 (0.47–1.18)
≤9	27/118 (23)	42/122 (34)	0.66 (0.41–1.07)
Balloon-expandable heart valve			
No	41/137 (30)	50/133 (38)	0.72 (0.48–1.09)
Yes	19/90 (21)	31/95 (33)	0.66 (0.37–1.16)



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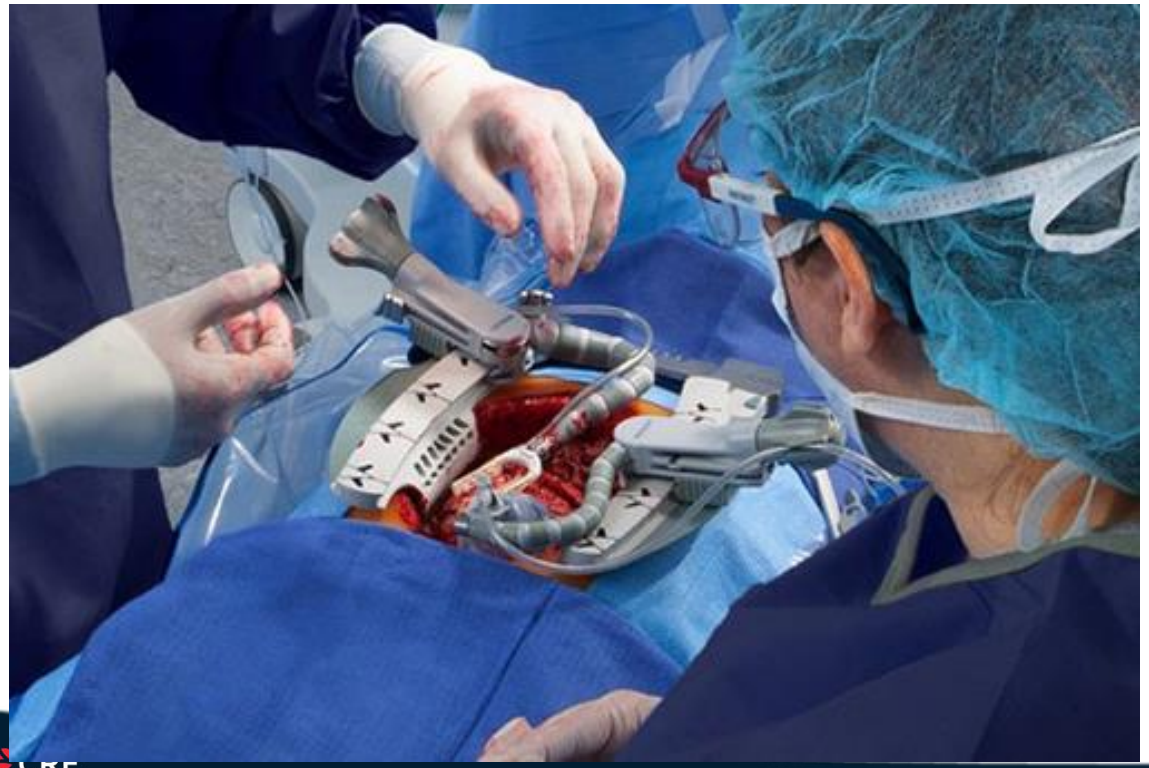
Second question: Surgical or Percutaneous (i.e. *SAVR & CABG* or *TAVI & PCI*)



ESC European Society of Cardiology
European Heart Journal (2022) 43, 561–632
https://doi.org/10.1093/eurheartj/ehab395

2021 ESC/EACTS Guidelines for the management of valvular heart disease

Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian * (ESC Chairperson) (France), Friedhelm Beyersdorf*[1] (EACTS Chairperson) (Germany), Fabien Praz (ESC Task Force Coordinator) (Switzerland), Milan Milojevic[1] (EACTS Task Force Coordinator) (Serbia), Stephan Baldus (Germany), Johann Bauersachs (Germany), Davide Capodanno (Italy), Lenard Conradi[1] (Germany), Michele De Bonis[1] (Italy), Ruggero De Paulis[1] (Italy), Victoria Delgado (Netherlands), Nick Freemantle[1] (United Kingdom), Martine Gilard (France), Kristina H. Haugaa (Norway), Anders Jeppsson[1] (Sweden), Peter Jüni (Canada), Luc Pierard (Belgium), Bernard D. Prendergast (United Kingdom), J. Rafael Sádaba[1] (Spain), Christophe Tribouilloy (France), Wojtek Wojakowski (Poland), ESC/EACTS Scientific Document Group

Indications for myocardial revascularization		
CABG is recommended in patients with a primary indication for aortic/mitral/tricuspid valve surgery and coronary artery diameter stenosis ≥70%.[e,f]	I	C
CABG should be considered in patients with a primary indication for aortic/mitral/tricuspid valve surgery and coronary artery diameter stenosis ≥50–70%.	IIa	C
PCI should be considered in patients with a primary indication to undergo TAVI and coronary artery diameter stenosis >70% in proximal segments.	IIa	C

TCW Trial Design

Patients ≥70 years
with <u>severe AS and ≥2VD or complex LAD</u>
Heart Team discussion

Baseline

Experimental arm (n=164):
FFR-guided PCI & TAVI
PCI for all lesions FFR≤0.80

1:1

Comparative arm (n=164):
CABG & SAVR

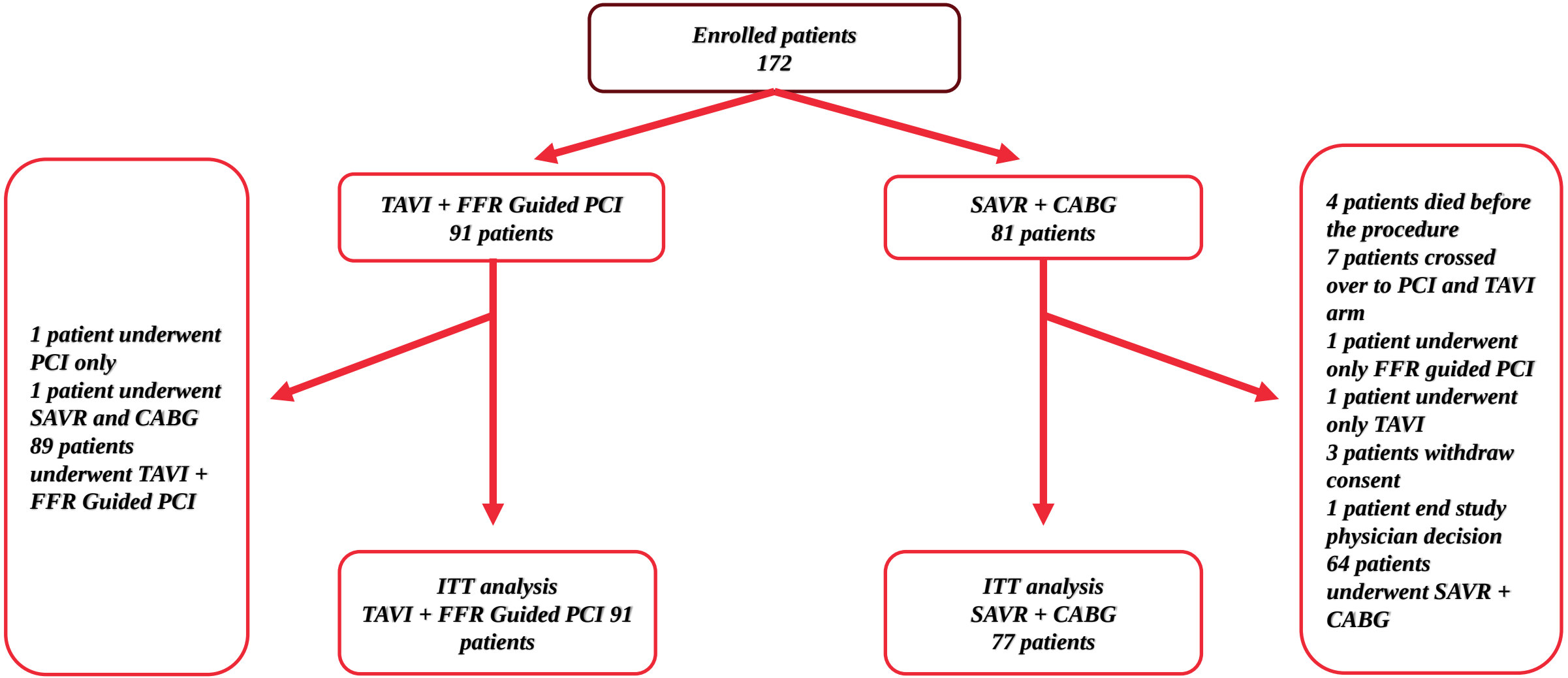
Follow up
30 days

<u>Evaluation of angina symptoms:</u>
Patients with persisting angina with known FFR ≤ 0.85 can undergo PCI if FFR ≤ 0.80 at FU

Follow up
12 months

<u>Primary endpoint:</u> A composite of all-cause mortality, myocardial infarction, disabling stroke, unscheduled clinically-driven target vessel revascularization, valve re-intervention, and life threatening or disabling bleeding

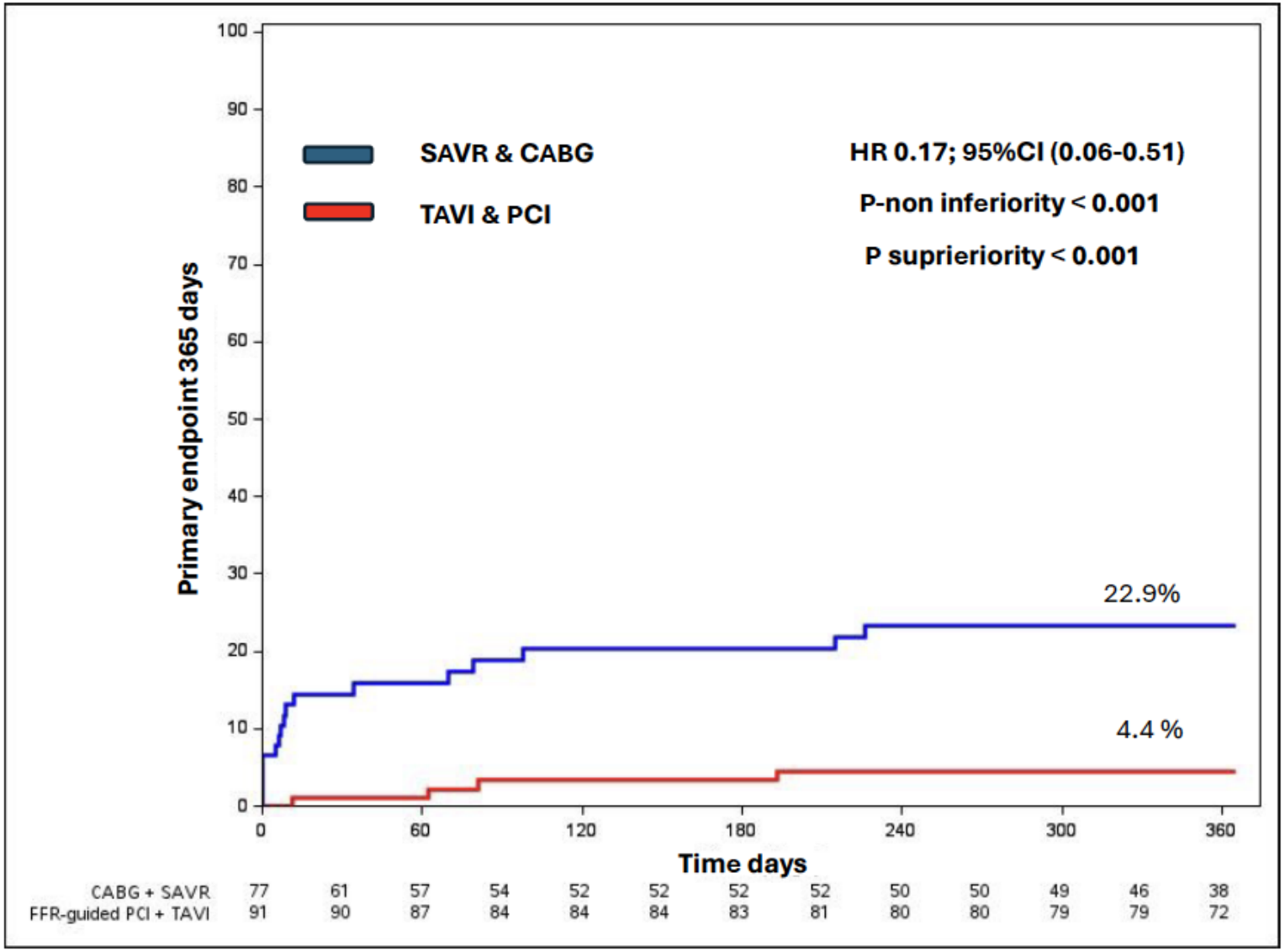
Patient Flow Chart



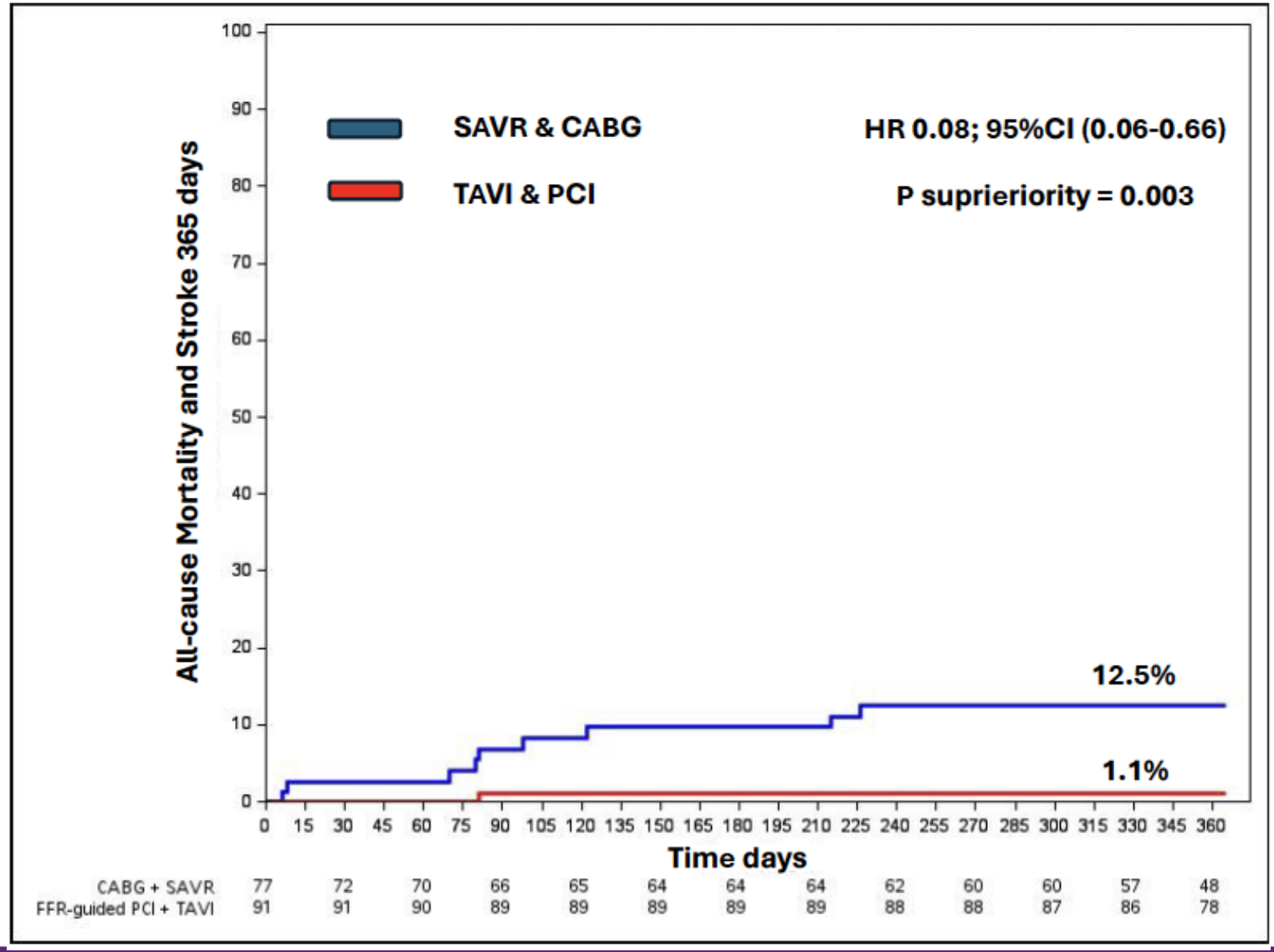
Primary Endpoint outcomes IT analysis

1 Year Primary Endpoint:

all-cause mortality,
myocardial infarction,
disabling stroke,
unscheduled clinically-driven TVR
valve reintervention, and
life threatening or disabling bleeding



All Cause Mortality and Stroke



Outcomes at 30 days

	FFR-Guided PCI + TAVI (n= 91)	SAVR+CABG (n= 77)	HR (95% CI)	P value
Primary endpoint	1 (1.10)	11(14.42)	0.07 (0.01-0.55)	***0.001***
Secondary endpoint MACE	1 (1.10)	4 (5.23)	0.20 (0.02-1.82)	0.16
Secondary endpoint All-cause mortality and stroke	1 (1.10)	3 (3.93)	0.27 (0.03-2.62)	0.23
Death – all cause	0 (0)	1 (1.30)		0.28
Death - cardiovascular	0 (0)	1 (1.30)		0.28
Stroke or TIA	0 (0)	2 (2.70)		0.12
Disabling stroke	0 (0)	1 (1.35)		0.28
Non-disabling stroke	0 (0)	0 (0)		
TIA	0 (0)	1 (1.35)		0.28
Myocardial infarction (any)	1 (1.10)	1 (1.30)	0.82 (0.05-13.18)	0.89

	FFR-Guided PCI + TAVI (n= 91)	SAVR +CABG (n= 77)	HR (95% CI)	P value
Periprocedural MI	1 (1.10)	1 (1.30)	0.82 (0.05-13.18)	0.89
Spontaneous MI	0 (0)	0 (0)		
Any revascularization	0 (0)	1 (1.30)		0.28
CD-TVR	0 (0)	1 (1.30)		0.28
Valve reintervention	0 (0)	1 (1.30)		0.28
Life threatening or disabling bleeding (VARC-2)	1 (1.10)	7 (9.24)	0.11 (0.01-0.93)	***0.01***
Major bleeding (VARC-2)	2 (2.20)	6 (7.79)	0.28 (0.06-1.39)	0.09
Minor bleeding (VARC 2)	8 (8.79)	3 (3.90)	2.24 (0.59-8.44)	0.22
Permanent pacemaker implantation	8 (8.79)	1 (1.33)	6.74 (0.84-53.88)	***0.04***
Major Vascular Complication	4 (4.40)	1 (1.35)	3.36 (0.38-30.09)	0.25
Re-thoracotomy	0 (0)	4 (5.19)		***0.03***
Atrial Fibrillation	2 (2.20)	10(13.05)	0.16 (0.03-0.72)	***0.006***

Kedhi et al. Lancet. 2025 Dec 21;404(10471):2593-2602.

Other secondary endpoints at 365 days

	FFR-Guided PCI + TAVI (n= 91)	SAVR+CABG (n= 77)	HR (95% CI)	P value
Death – all cause	0 (0)	7 (9.74)		***0.002***
Death - cardiovascular	0 (0)	6 (8.35)		***0.005***
All Stroke and TIA	1 (1.11)	3 (4.20)	0.25 (0.03-2.45)	0.20
Disabling stroke	1 (1.11)	2 (2.85)	0.38 (0.03-4.19)	0.41
Non-disabling stroke	0 (0)	0 (0)		
TIA	0 (0)	1 (1.35)		0.27
Myocardial infarction (any)	2 (2.21)	1 (1.30)	1.58 (0.14-17.48)	0.71
Periprocedural myocardial infarction	1 (1.10)	1 (1.30)	0.82 (0.05-13.18)	0.89
Spontaneous myocardial infarction	1 (1.11)	0 (0)		0.40

	FFR-Guided PCI + TAVI (n= 91)	SAVR +CABG (n= 77)	HR (95% CI)	P value
CD-TVR	0 (0)	1 (1.30)		0.28
Valve reintervention	0 (0)	1 (1.30)		0.28
Life threatening or disabling bleeding (VARC-2)	2 (2.21)	9 (12.10)	0.17 (0.04-0.80)	***0.01***
Major bleeding (VARC-2)	5 (5.56)	7 (9.21)	0.57 (0.18-1.79)	0.32
Minor bleeding (VARC-2)	12 (13.27)	4 (5.40)	2.52 (0.81-7.81)	0.10
Permanent pacemaker implantation	9 (9.89)	2 (2.87)	3.74 (0.81-17.30)	0.07
Major Vascular Complication	4 (4.40)	1 (1.35)	3.36 (0.38-30.09)	0.25
Re-thoracotomy	0 (0)	4 (5.19)		***0.02***
Atrial Fibrillation	2 (2.20)	11 (13.05)	0.28 (0.09-0.88)	***0.03***

Kedhi et al. Lancet. 2025 Dec 21;404(10471):2593-2602.

The TCW trial, showed that FFR-guided PCI & TAVI as compared to CABG & SAVR was associated with significantly lower primary endpoint and mortality rates

Considering its limited trial size, these findings need corroboration from larger randomized trials

Kedhi et al. Lancet. 2025 Dec 21;404(10471):2593-2602.

Third Question

Optimal Timing of Transcatheter Aortic Valve Implantation and Percutaneous Coronary Intervention

Current opinion and considerations

	PCI before TAVI	PCI after TAVI	Combined PCI and TAVI
Advantages	- Easier coronary access (especially for self-expanding THV with a supra-annular leaflet position) - Lower risk of ischaemia-induced haemodynamic instability (i.e., during rapid pacing) - Reduced contrast use compared with concomitant PCI and TAVI	- More reliable FFR/iFR of intermediate lesions - Lower risk of haemodynamic instability during complex PCI (i.e., with rotational atherectomy and impaired LV function) - Reduced contrast use compared with concomitant PCI and TAVI	- Use of the same arterial access - Lower cost
Disadvantages	- Less reliable FFR/iFR assessments of borderline lesions - Higher risk of haemodynamic instability due to AS	- More challenging and potentially compromised coronary access - Less stability and support of the coronary guiding catheter - Potential THV dislodgement	- Larger amount of contrast and higher risk of AKI - Prolonged procedure - Need for DAPT at the time of TAVI, hence increased bleeding risk

AS: aortic stenosis; AKI: acute kidney injury; DAPT: dual antiplatelet therapy; FFR: fractional flow reserve; iFR: instantaneous wave-free ratio; LV: left ventricular; PCI: percutaneous coronary intervention; TAVI: transcatheter aortic valve implantation; THV: transcatheter heart valve

The TAVI PCI Trial (TAVI-PCI)

≥ 1lesion with DS ≥70% deemed amenable to PCI
within 45 days before or after TAVI

PCI + OMT Prior to TAVI

vs.

PCI+ OMT After successful TAVI

The primary outcome measure is a composite of:
All-cause death, Non-fatal myocardial infarction, Ischemia-driven revascularization, Rehospitalization (valve- or procedure-related including heart failure), Life-threatening/disabling or major bleeding (according to VARC-2)

Powered for superiority

FAITAVI trial

FFR Guided PCI

PCI if FFR values ≤0.80 only

vs.

Angiography guided PCI

PCI of all lesions with > 50% DS

Primary Endpoint: Composite of all-cause death, myocardial infarction, stroke, major bleeding, need for target vessel revascularization

Conclusions CAD and Aortic Stenosis

- Revascularisation of CAD is likely needed, particularly in younger patients with severe (truly ischemic) CAD
- TAVI and PCI is likely the best way to treat to this patients at least from 70 years and older
- Weather prior or post TAVI is a matter of debate and depends on multiple factors
- Role of ischemia detection (FFR)?
- **We need to complete the COMPLETE trial!**