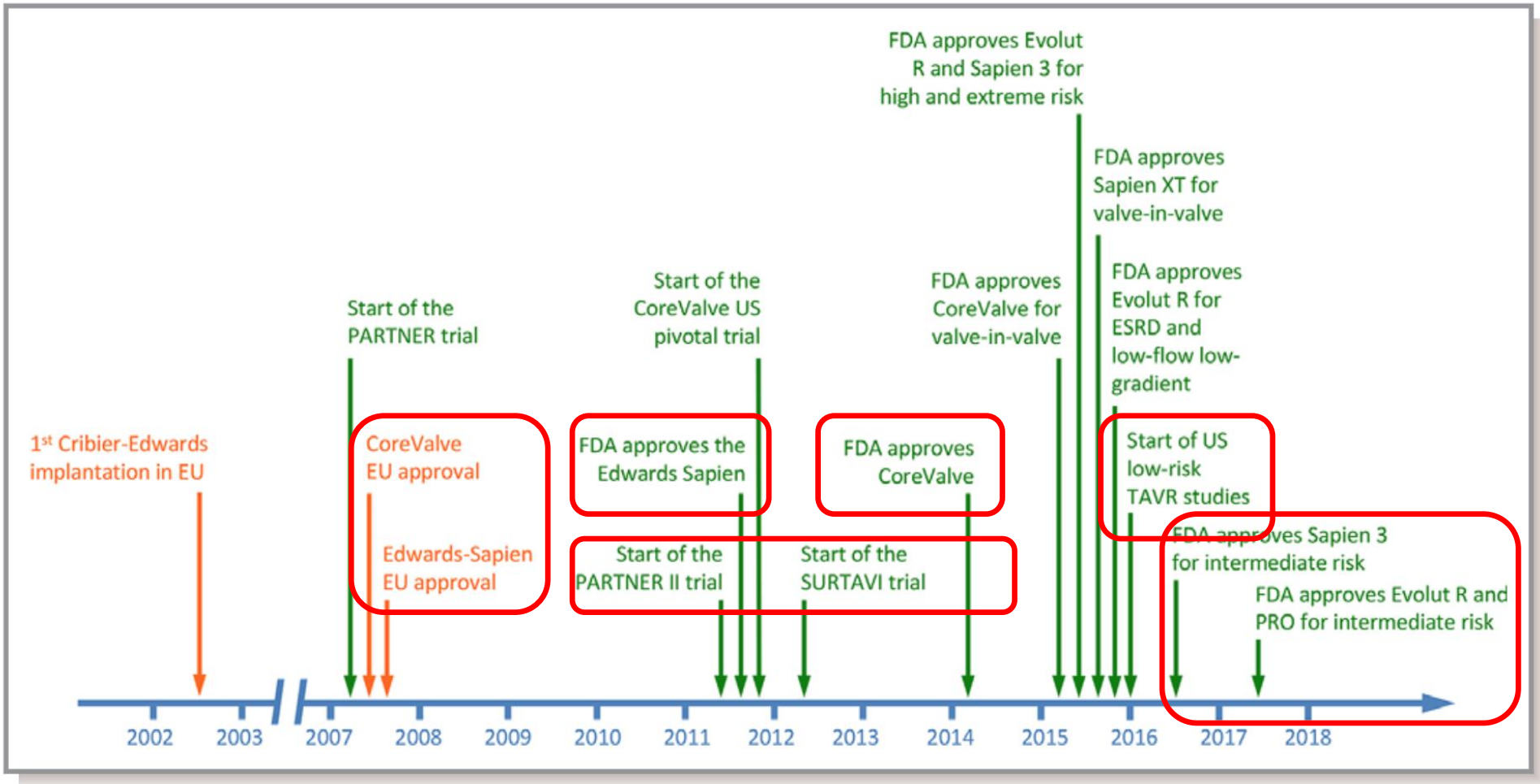
TAVI LOW RISK TRIAL IMPLICATIONS
and the role of Heart Team

Nguyễn Hoàng Định, Vũ Hoàng Vũ, Võ Tuấn Anh, Trương Quang Bình and UMC Heart Team

- Alain Cribier, 2002, first THV implantation
- FDA approved, 2012, 5000 TAVR in the US
- 2018: 59,200 TAVR vs. 25,274 SAVR

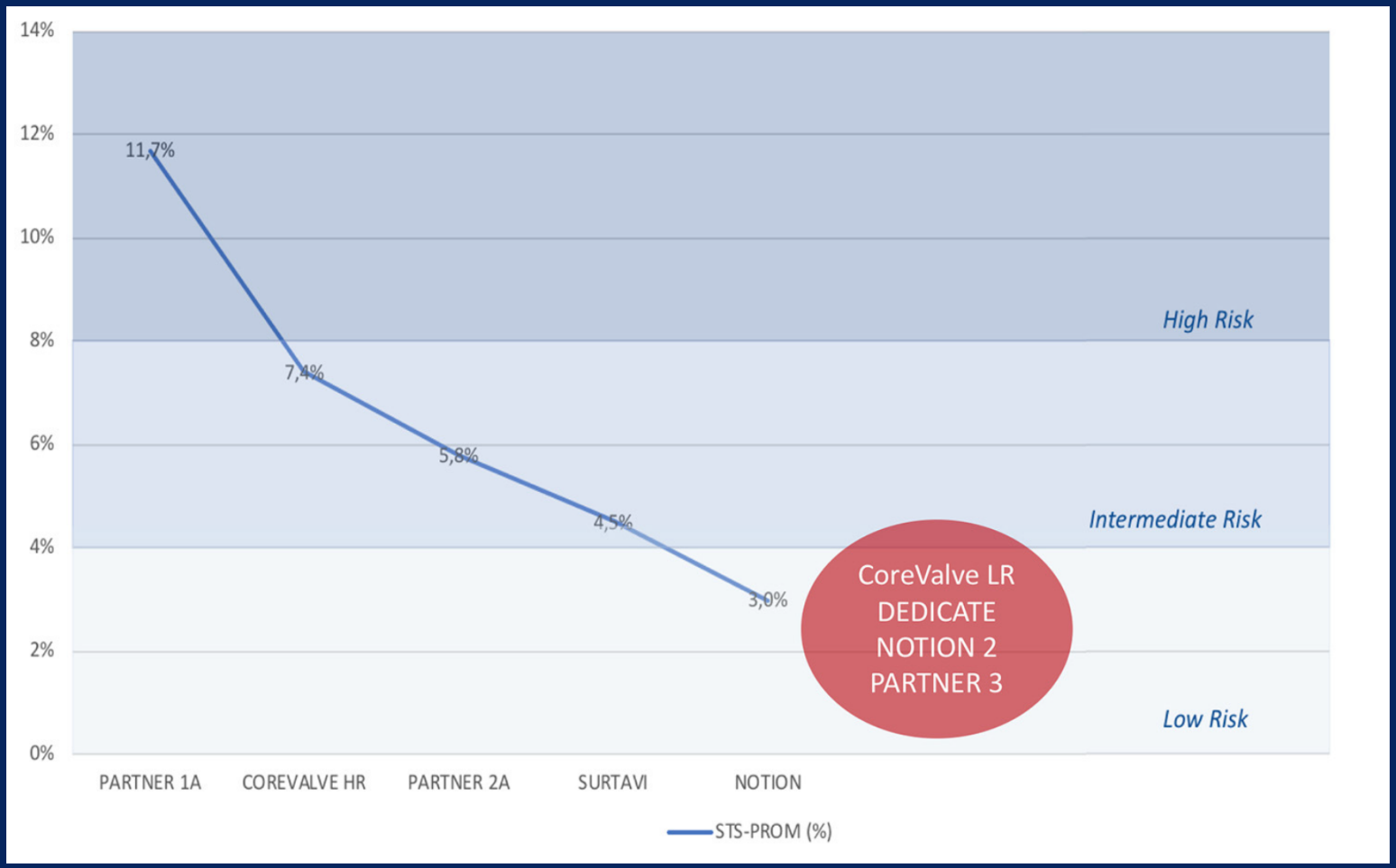
STS/ACC TVT Registry

US TAVR Regulatory Timeline



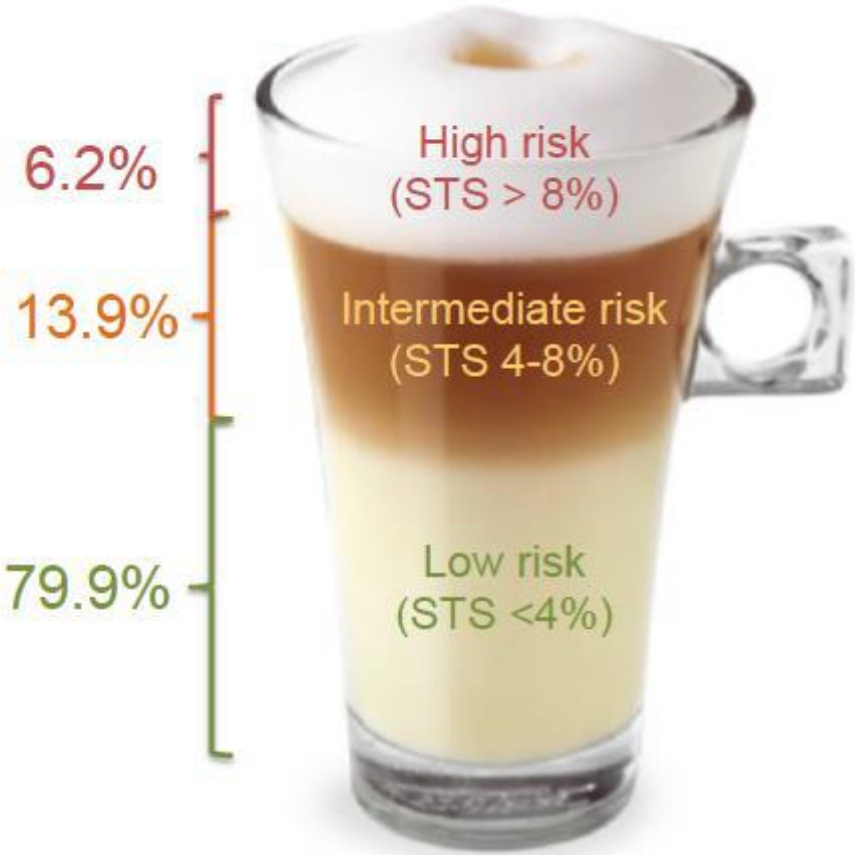
Rogers, J Am Heart Assoc, (2018)

Evolution of operative risk in major trials

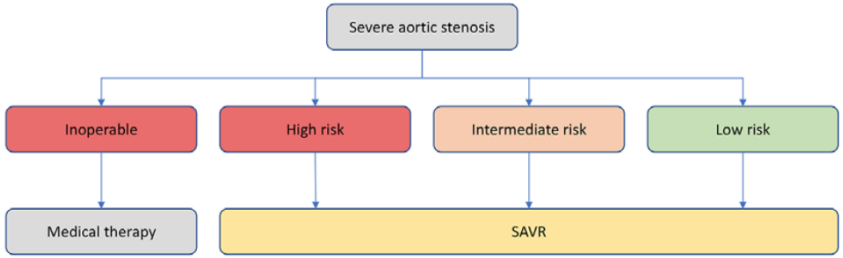


Voightlander, Front. Cardiovasc. Med. (2018)

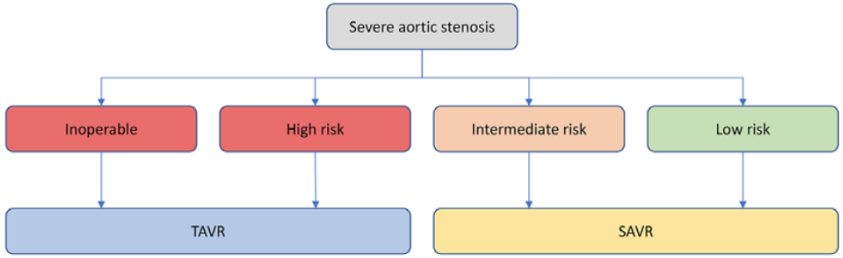
STS database 2002-2010
n=141,905



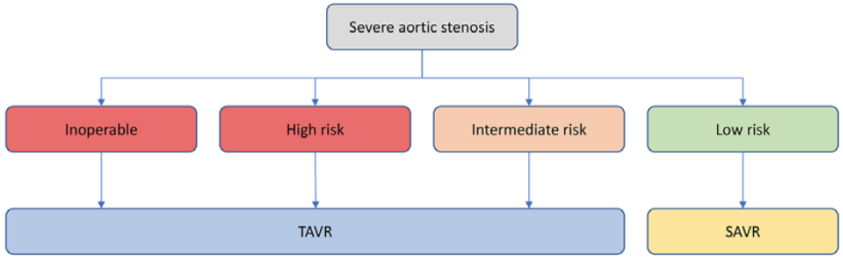
Before TAVR



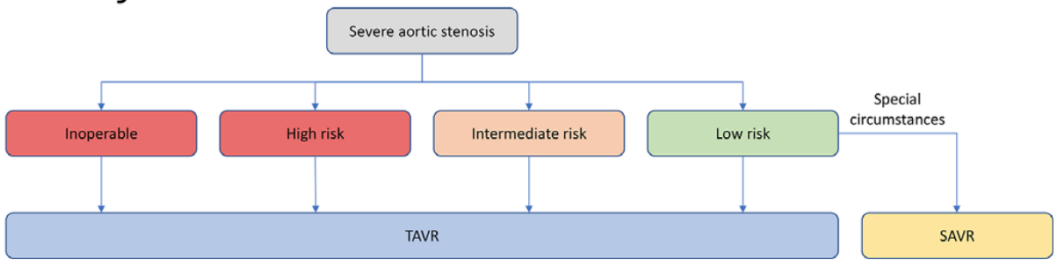
In 2011



In 2018



In the future…



Rogers, J Am Heart Assoc, (2018)

Do clinical trials of TAVR in low-risk patients herald the end of isolated SAVR?

TAVI in low-intermediate risk trials

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 28, 2016 VOL. 374 NO. 17

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael J. Mack, M.D., Raj R. Makkar, M.D., Lars G. Svensson, M.D., Ph.D., Susheel K. Kodali, M.D., Vinod H. Thourani, M.D., E. Murat Tuzcu, M.D., D. Craig Miller, M.D., Howard C. Herrmann, M.D., Darshan Doshi, M.D., David J. Cohen, M.D., Augusto D. Pichard, M.D., Samir Kapadia, M.D., Todd Dewey, M.D., Vasilis Babaliaros, M.D., Wilson Y. Szeto, M.D., Mathew R. Williams, M.D., Dean Kereiakes, M.D., Alan Zajarias, M.D., Kevin L. Greason, M.D., Brian K. Whisenant, M.D., Robert W. Hodson, M.D., Jeffrey W. Moses, M.D., Alfredo Trento, M.D., David L. Brown, M.D., William F. Fearon, M.D., Philippe Pibarot, D.V.M., Ph.D., Rebecca T. Hahn, M.D., Wael A. Jaber, M.D., William N. Anderson, Ph.D., Maria C. Alu, M.M., and John G. Webb, M.D., for the PARTNER 2 Investigators*

	PPM Implantation		Stroke		Moderate or Severe PVL		New Atrial Fibrillation	
	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR	TAVR	SAVR
PARTNER 2[12]	8.5%	6.9%	3.2%	4.3%	3.7%*	0.6%*	9.1%*	26.4%*
SURTAVI[14]	25.9%*	6.6%*	1.2%	2.5%	3.5%*	0.7%*	12.9%*	43.4*
NOTION[11]	34.1%*	1.6%*	1.4%	3.0%	15.3%*	1.8%*	16.9%*	57.8%*
SAPIEN 3 IR[13]	10.2%	7.3%	1.0%*	4.4%*	3.8%*	0.6%*	3.2%*	28.5%*

TAVI in low risk trials

Name	Unique Identifier	Population	Study Design	Primary End Point	THV in TAVR Arm	Sample Size
LRT[23]	NCT02628899	No age restriction STS ≤3%	Feasibility study Prospective TAVR arm with historical SAVR controls	All-cause mortality at 30 d	Transfemoral SAPIEN 3 or Evolut R/PRO	200 TAVR in main arm Up to 100 TAVR in bicuspid arm
PARTNER 3[24]	NCT02675114	Age ≥65 y STS <4%	Noninferiority Randomized TAVR vs SAVR	All-cause mortality, all stroke, and rehospitalization at 1 y	Transfemoral SAPIEN 3	614 TAVR 614 SAVR
Medtronic TAVR in low risk patients[25]	NCT02701283	No age restriction STS <3%	Noninferiority Randomized TAVR vs SAVR	All-cause mortality or disabling stroke at 2 y	Transfemoral or subclavian Evolut R	625 TAVR 625 SAVR
NOTION 2[26]	NCT02825134	Age 18 to 75 y STS <4%	Noninferiority Randomized TAVR vs SAVR	Composite rate of all-cause mortality, myocardial infarction and stroke at 1 y	Transfemoral Any CE-approved THV	496 TAVR 496 SAVR

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 2, 2019 VOL. 380 NO. 18

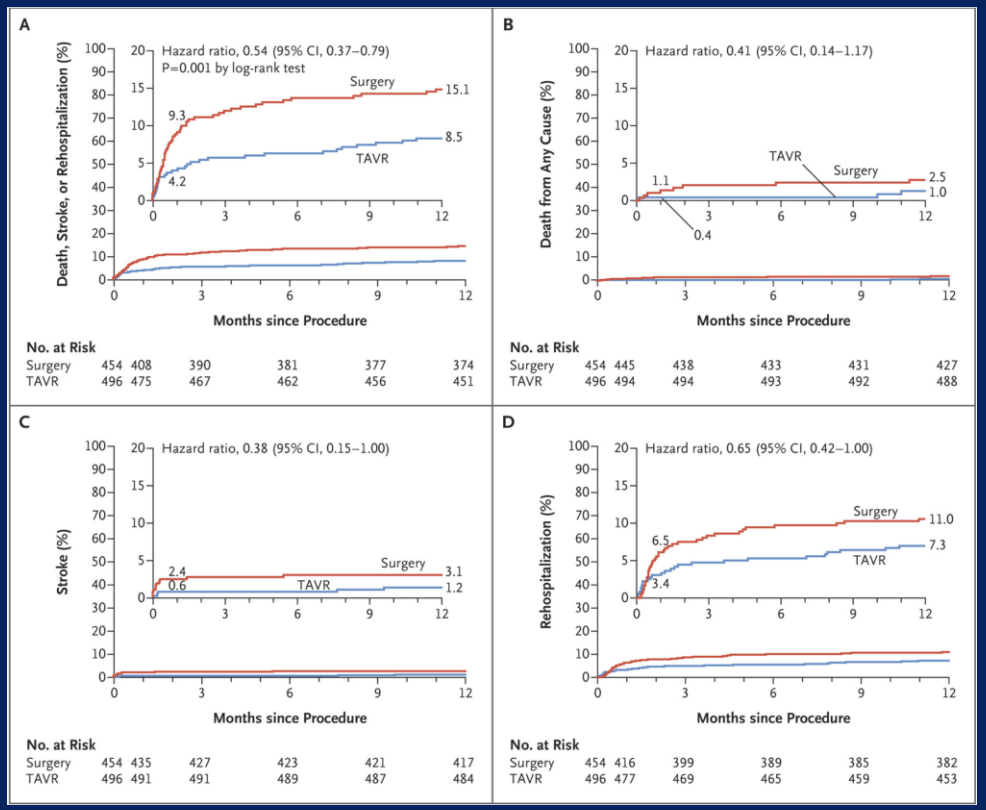
Transcatheter Aortic-Valve Replacement with a Balloon-Expandable Valve in Low-Risk Patients

M.J. Mack, M.B. Leon, V.H. Thourani, R. Makkar, S.K. Kodali, M. Russo, S.R. Kapadia, S.C.
P. Pibarot, J. Leipsic, R.T. Hahn, P. Blanke, M.R. Williams, J.M. McCabe, D.L. Brown, V. Ba
W.Y. Szeto, P. Genereux, A. Pershad, S.J. Pocock, M.C. Alu, J.G. Webb, and C.
for the PARTNER 3 Investigators*

- 71 centers, 1000 patients
- Mean age 73, STS 1.9%
- Composite death, stroke, rehospitalization at 1 year

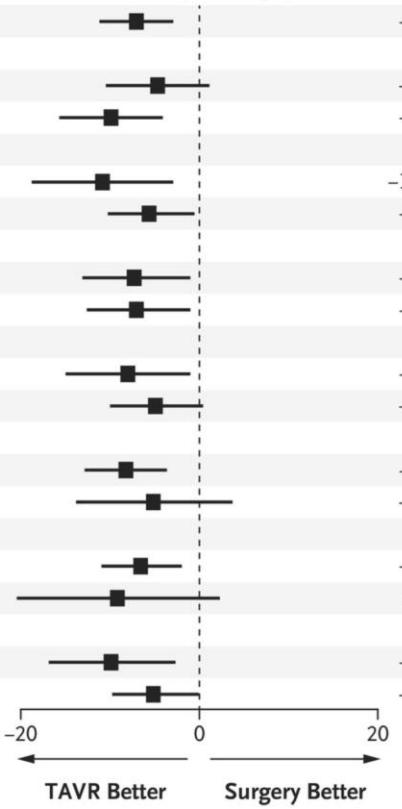
PARTNER 3 results

- TAVR has 46% lower rates of death, strokes, rehosp at 1 year, p=0.001
- Lower death or strokes at 30 days p=0.01
- Lower Afib (5% vs. 40%) p<0.001



Sub-group analysis

Subgroup	No. of Patients	TAVR	Surgery	Difference (95% CI)	P Value for Interaction
		no. of events/total no. (%)		*percentage points*	
Overall	950	42/496 (8.5)	68/454 (15.1)	−6.6 (−10.8 to −2.5)	
Age					0.21
≤74 yr	516	29/273 (10.6)	36/243 (14.9)	−4.3 (−10.1 to 1.5)	
>74 yr	434	13/223 (5.8)	32/211 (15.3)	−9.5 (−15.3 to −3.7)	
Sex					0.27
Female	292	13/161 (8.1)	24/131 (18.5)	−10.4 (−18.3 to −2.5)	
Male	658	29/335 (8.7)	44/323 (13.8)	−5.1 (−9.9 to −0.3)	
STS-PROM score					0.98
≤1.8	464	21/232 (9.1)	36/232 (15.7)	−6.7 (−12.6 to −0.7)	
>1.8	486	21/264 (8.0)	32/222 (14.5)	−6.5 (−12.2 to −0.8)	
Left ventricular ejection fraction					0.48
≤65	384	20/208 (9.6)	30/176 (17.2)	−7.6 (−14.5 to −0.7)	
>65	524	21/264 (8.0)	32/260 (12.4)	−4.4 (−9.6 to 0.7)	
NYHA class					0.54
I or II	687	23/341 (6.8)	50/346 (14.5)	−7.8 (−12.4 to −3.2)	
III or IV	263	19/155 (12.3)	18/108 (16.9)	−4.7 (−13.5 to 4.1)	
Atrial fibrillation					0.67
No	786	33/418 (7.9)	51/368 (14.0)	−6.1 (−10.5 to −1.7)	
Yes	163	9/78 (11.6)	17/85 (20.3)	−8.7 (−19.9 to 2.5)	
KCCQ overall summary score					0.27
≤70	407	23/219 (10.5)	37/188 (19.9)	−9.4 (−16.5 to −2.4)	
>70	536	18/275 (6.5)	29/261 (11.2)	−4.6 (−9.2 to 0.2)	

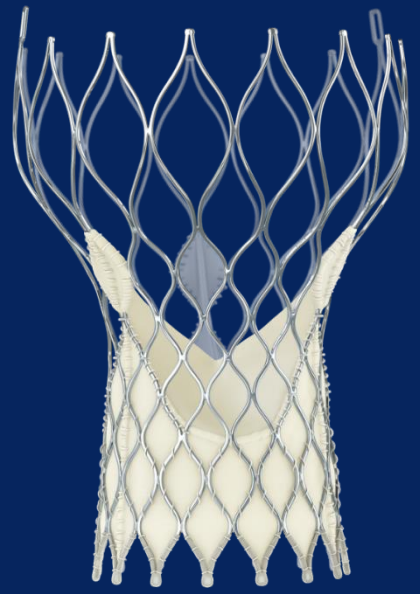


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

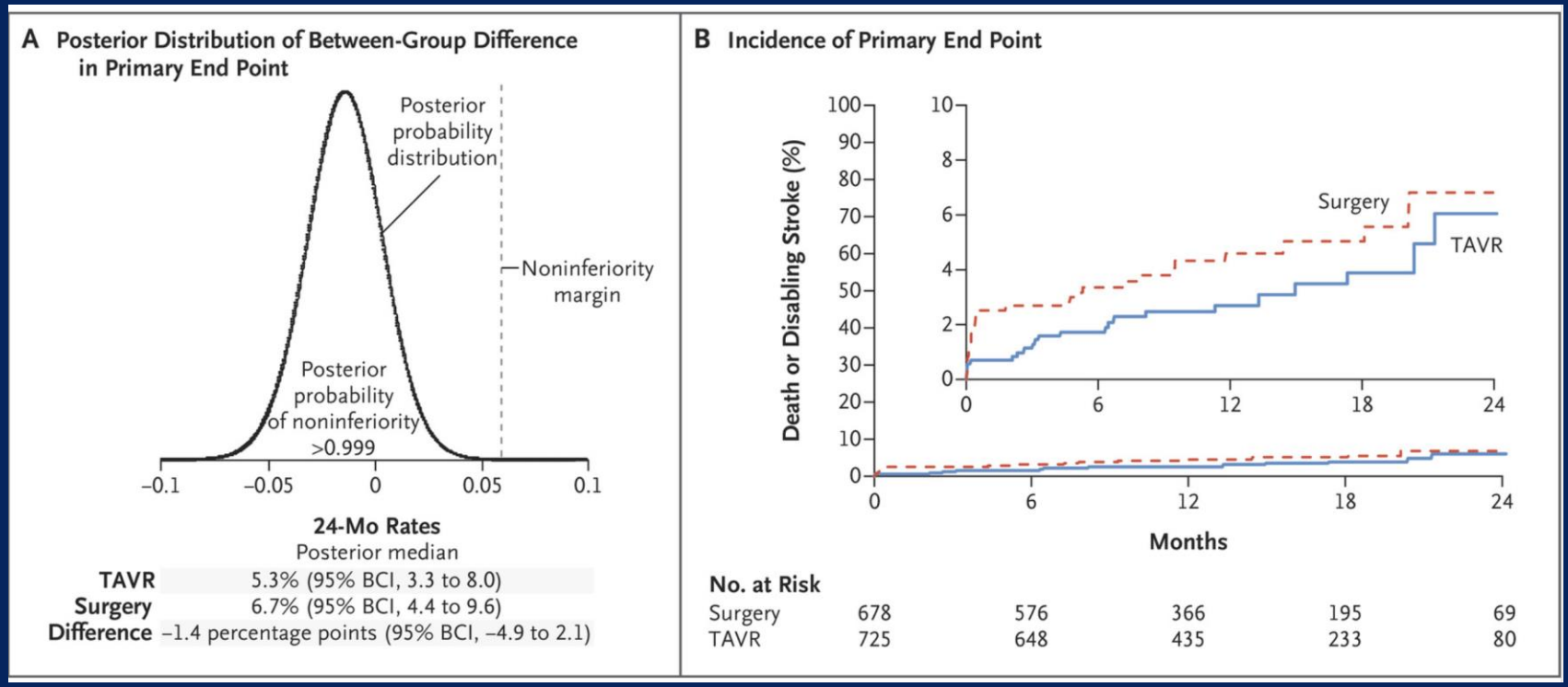
Transcatheter Aortic-Valve Replacement with a Self-Expanding Valve in Low-Risk Patients

Jeffrey J. Popma, M.D., G. Michael Deeb, M.D., Steven J. Yakubov, M.D., Mubashir Mumtaz, M.D., Hemal Gada, M.D., Daniel O'Hair, M.D., Tanvir Bajwa, M.D., John C. Heiser, M.D., William Merhi, D.O., Neal S. Kleiman, M.D., Judah Askew, M.D., Paul Sorajja, M.D., Joshua Rovin, M.D., Stanley J. Chetcuti, M.D., David H. Adams, M.D., Paul S. Teirstein, M.D., George L. Zorn III, M.D., John K. Forrest, M.D., Didier Tchétché, M.D., Jon Resar, M.D., Antony Walton, M.D., Nicolo Piazza, M.D., Ph.D., Basel Ramlawi, M.D., Newell Robinson, M.D., George Petrossian, M.D., Thomas G. Gleason, M.D., Jae K. Oh, M.D., Michael J. Boulware, Ph.D., Hongyan Qiao, Ph.D., Andrew S. Mugglin, Ph.D., and Michael J. Reardon, M.D., for the Evolut Low Risk Trial Investigators*



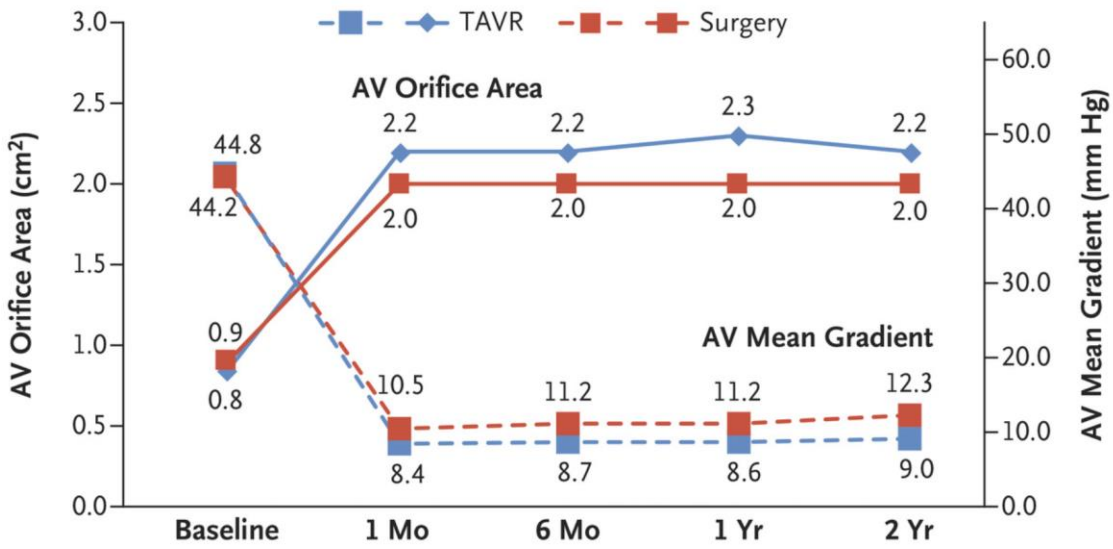
- 86 centers, 1403 patients
- Mean age 74, STS 1.9%
- Composite of death and disabling strokes at 24 mo

EVOLUT results



- At 30 days, TAVR has lower rates of disabling strokes, bleedings, AKI and Afib
- Higher rates of AR and PPI

EVOLUT results



No. of Patients with Echocardiographic Data					
AV mean gradient					
TAVR	712	699	619	409	71
Surgery	673	634	542	339	62
AV orifice area					
TAVR	632	610	544	341	59
Surgery	590	541	467	293	53

- At 12 months: lower AV gradients and larger EOA

PARTNER 3 and EVOLUT Exclusion Criteria

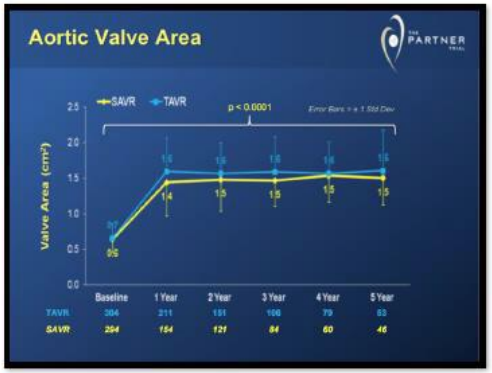
- Iliofemoral vessel diseases
- Bicuspid, unicuspid AV
- AA dilatation
- Highly severe AV calcification
- LVOT calcification
- Low coronary take-off
- Complex CAD (Syntax score > 32)
- Severe AR, MR
- LVEF < 30%

THV durability and function

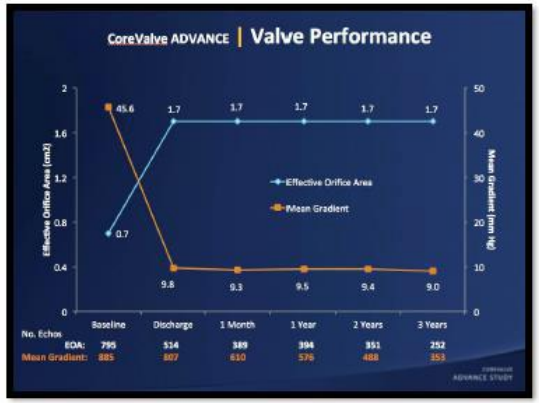
- Key challenge in expanding to lower risk and younger population.
- Solid long-term data: TAVR 5yrs follow-up vs. SAVR 15 yrs.
- Leaflet thrombosis: significantly higher in TAVR

PARTNER I
Arora, Am J Cardiol, (2017)
Chakravaty, Lancet, (2017)

PARTNER 1A – 5 years

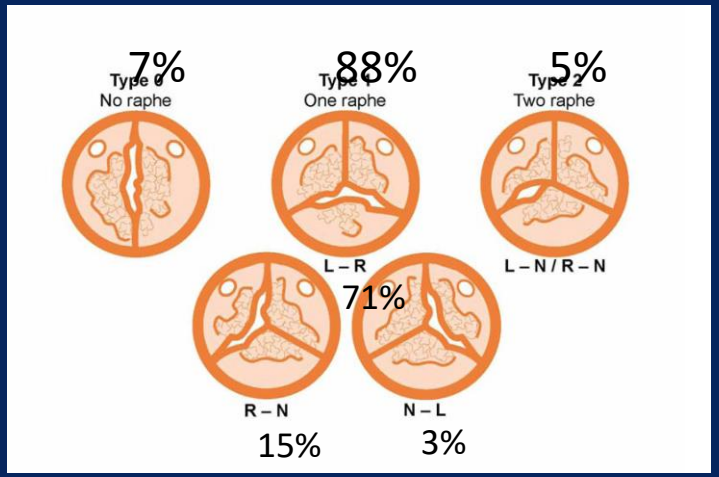


ADVANCE – 3 years



Bicuspid AS

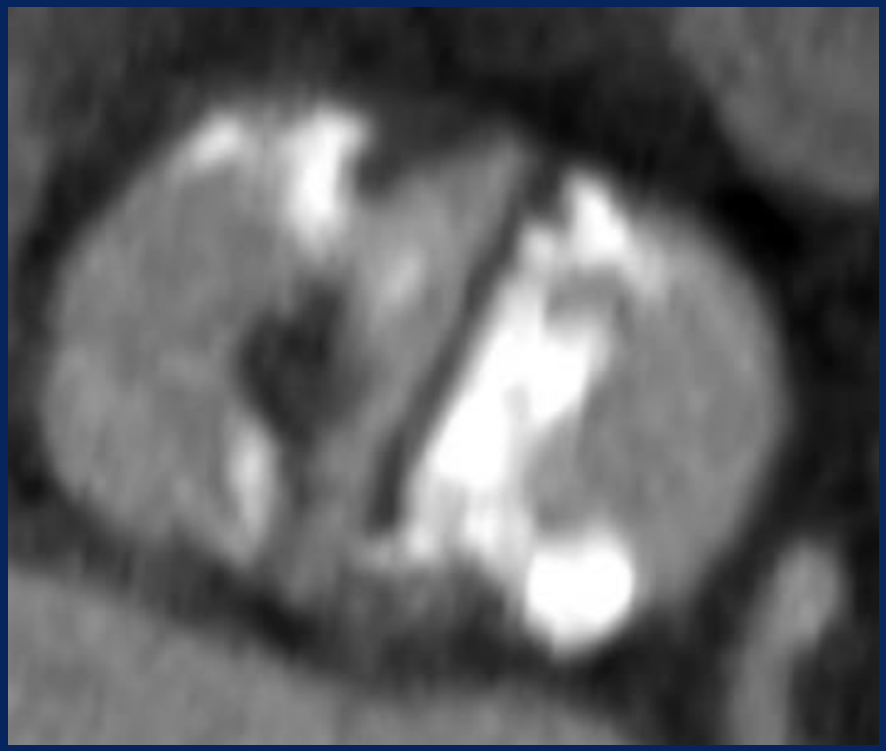
- Prevalence 1 – 2% in general population
- Stenotic at younger age, likely to fall into low and intermediate risk categories.
- Lower procedural succes, higher PPM, PVL (9.6-28.4%)
- Concomittant dilatation of ascending aorta: 40% meet criteria for surgical repair



Mylotte, J Am Cardiol (2014)
Yoon, J Am Cardiol (2017)

Type I: L-R

Type 0

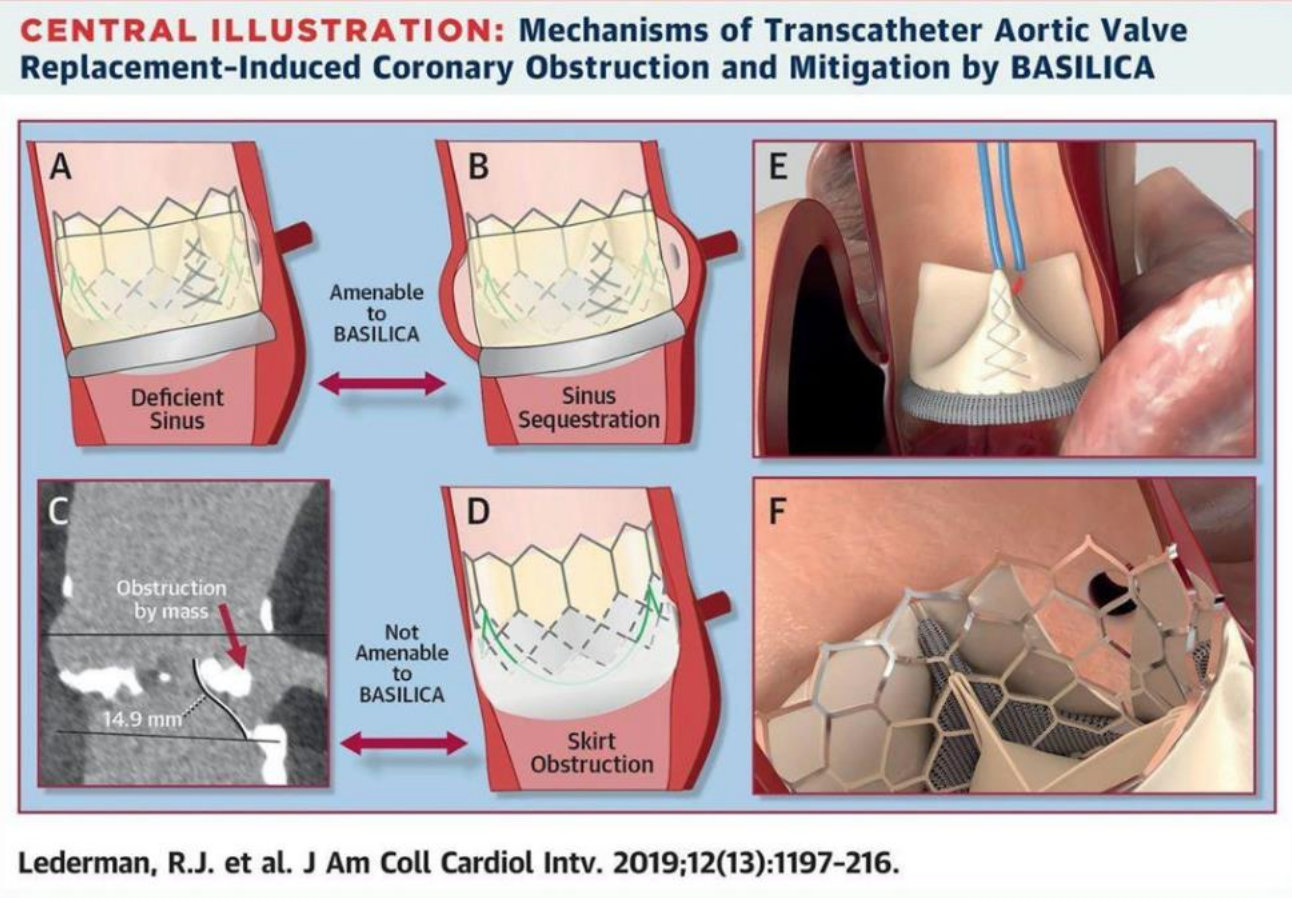


Very large aortic annulus

- THV comercially available for annuli up to 30mm (29mm Sapien 3, 34mm Evolut R)
- SAVR should be used for pts with very large annulus.

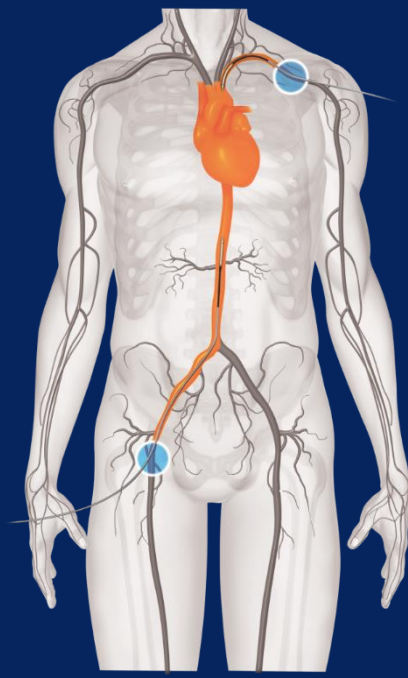
Low coronary take-off and deficient sinus

- <12 mm from annulus



Patients ineliglble for transfemoral access

- Small or diseased iliofemoral arteries
- PARTNER I, II: transthoracic access: risk factor of death HR 1.55
- Newer opitions: transcaval, subclavian, trans carotid



Multivessel CAD

- ACC expert consensus: limited PCI before TVR
- 3VD, LM: surgery

Weighing morbidity and mortality

- Distinct complication patterns after TAVR and SAVR
- Life threatening complications: annular rupture, valve migration, coronary obstruction, LV perforation)
- European Registry on Emergent Cardiac Surgery during TAVI (EuRECS-TAVI): 0.7%

How to weigh?
Not by predicted operative risk anymore!

Favoring TAVR

- Age >= 75
- Prior cardiac surgery
- Frailty
- Restricted mobility
- Transfemoral access
- Prior chest radiation
- Porcelain aorta
- Expected PPM

Favoring SAVR

- Age<75
- Suspicion endocarditis
- BAS
- Unfavorable anatomy for TAVR: access, low coro take-off, unfavorable root, calcified LVOT
- Concomittant cardiac surgery

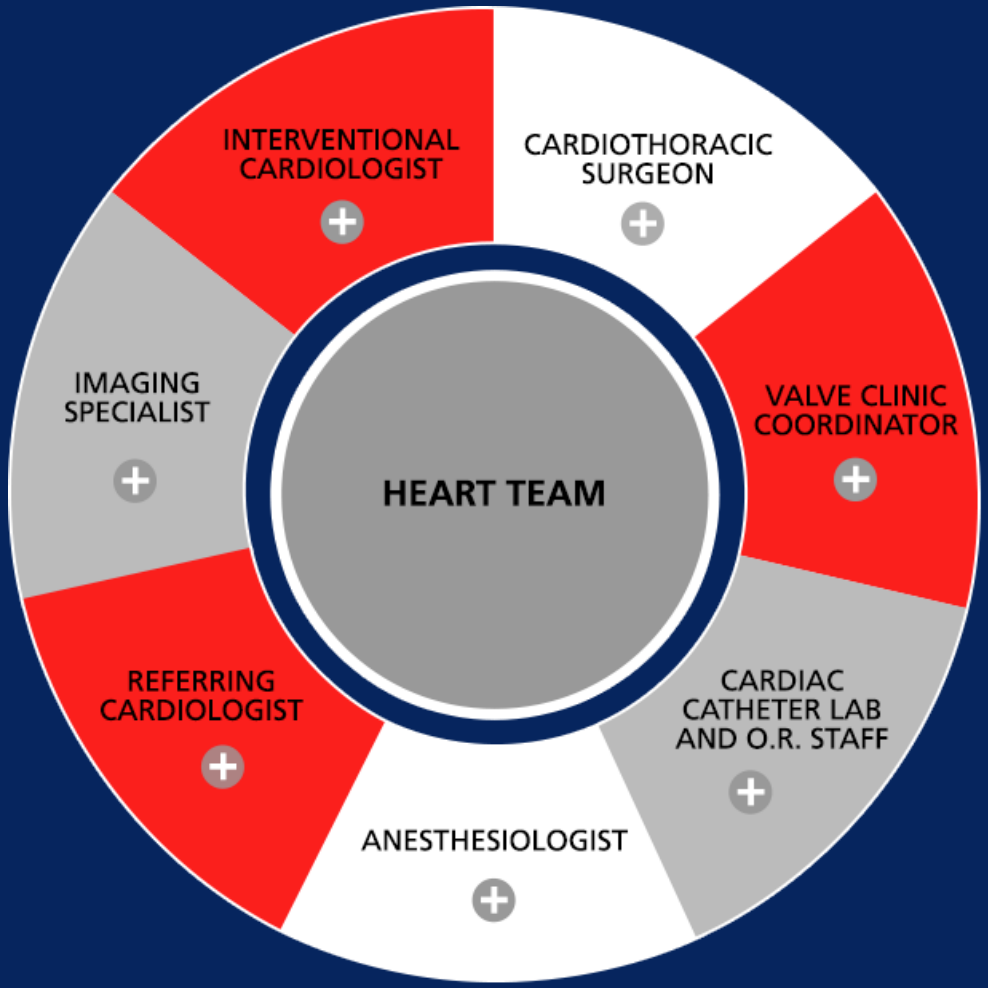
Alain Cribier, 2004

"The beauty and strength of TAVI has been to reinforce the relationship between interventionalists and surgeons

But it is not enough!

A dedicated Heart Team is crucial to ensure a successful program"

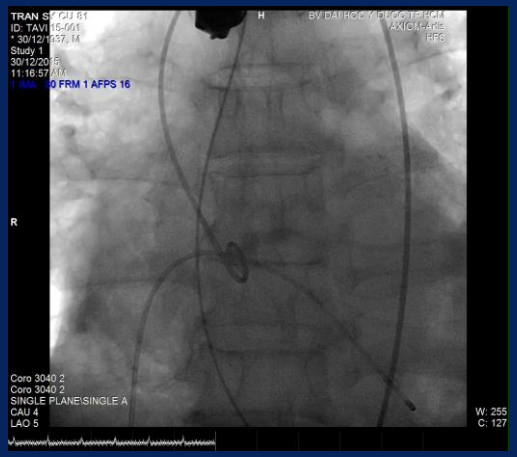
Heart team: the multidisciplinary team

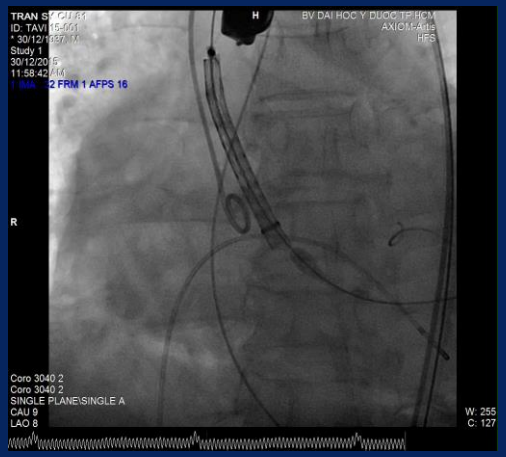


Cardiovascular Surgery – Cardiology (The Heart Team)

- Heart Team meeting every month:
  - Case review and decision
  - Inpatient review
  - Case and outcome discussion
  - Protocol development and discussion

Our data 2016 - 2018





Patients

	1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th
Age	77	81	76	85	78	74	79	81	65	83	56	74	76
Gender	F	M	F	F	M	M	F	M	M	F	M	M	F
Height	150	158	154	150	160	161	150	163	170	160	168	170	160
Weight	49	78	64	55	46	60	40	65	72	61	82	75	67
BMI	21.8	31.2	27	24.4	18	23.1	17.8	24.5	24.9	23.8	29.1	26	26
eGFR	67	74	82	60	87	30	70	61	80	59	95	78	19
DM	N	Y	N	N	N	N	Y	N	N	Y	Y	N	Y
HBP	N	Y	Y	N	N	Y	Y	Y	N	Y	N	Y	Y
Pulm. disease	N	N	N	N	COPD	COPD	N	N	N	N	N	N	N
CAD	N	N	Y	N	N	N	N	Y	N	N	N	Y	Y
PCI	N	N	Y	N	N	N	N	N	N	N	N	N	N

EuroSCORE II %	3.08	3.41	4.07	4.17	3.72	21.72	7.3	2.36	0.93	4.34	0.79	2.22	19.59
STS Score %	3.5	4.5	4.3	4.1	3.4	14.6	5	2.33	0.96	5.79	2.32	2.5	12.3
AVA pre	0.45	0.9	0.7	0.8	0.8	0.35	0.6	0.7	0.5	1	0.5	0.5	0.34
Bicuspid	N	N	Y	Y	N	N	Y	N	Y	N	Y	Y	N
Peak Gradient	92	100	105	86	77	94	95	73	89	43	77	130	79
Mean Gradient	43	41	54	40	48	61	50	49	52	28	43	119	74
Prev CABG	N	N	N	N	N	Y	N	N	N	N	N	N	N
CVA	N	N	N	N	N	N	N	N	N	N	N	N	N
PAD	N	N	N	N	N	N	N	N	N	N	N	N	N
LVEF pre %	0.63	0.7	0.64	0.6	0.69	0.28	0.18	0.60	0.60	0.67	0.66	0.61	0.43
AR pre	N	Mild	N	N	N	N	N	N	N	N	N	Mild	Mod
MR pre	Moderate	Moderate	Mild	Mild	N	Mild	Moderate	N	Mild	Mild	Mild	N	Mod

Valve size	26	26	31	29	29	31	29	26	29	29	29	29	26
Prev Val-Sur	N	N	N	N	N	N	N	N	N	N	N	N	N
Transfemo	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Vascular Compli	N	N	N	N	N	N	N	N	N	N	N	N	N
Device success	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
AVB III	N	N	Y	Y	N	Y	N	N	N	N	N	N	N
Stroke	N	N	N	N	N	N	N	N	N	N	Y	N	N
MI post	N	N	N	N	N	N	N	N	N	N	N	N	N
Major Bleeding	N	N	N	N	N	N	N	N	N	N	N	N	N
AKI	N	N	N	N	N	N	N	N	N	N	N	N	N
PPM	N	N	Y	N	Y	Y	N	N	N	N	N	N	N
LVEF post	0.63	0.65	0.65	0.65	0.6	0.5	0.3	0.2	0.55	0.64	0.58	0.54	0.50
LBBB	Y	Y	N	Y	N	N	N	N	N	N	N	N	N
Death	N	N	N	N	N	Y	N	N	N	N	N	N	N

Results

- Device success rate: 100%
- Mortality: 7.4%
- Paravalvular leak (<moderate): 24%
- PPM: 24%
- Stroke (transient): 7.4%
- Occlusion of coronaries: no
- Annular rupture: no
- Vascular complications: no
- Hospital stay: 4.5 days

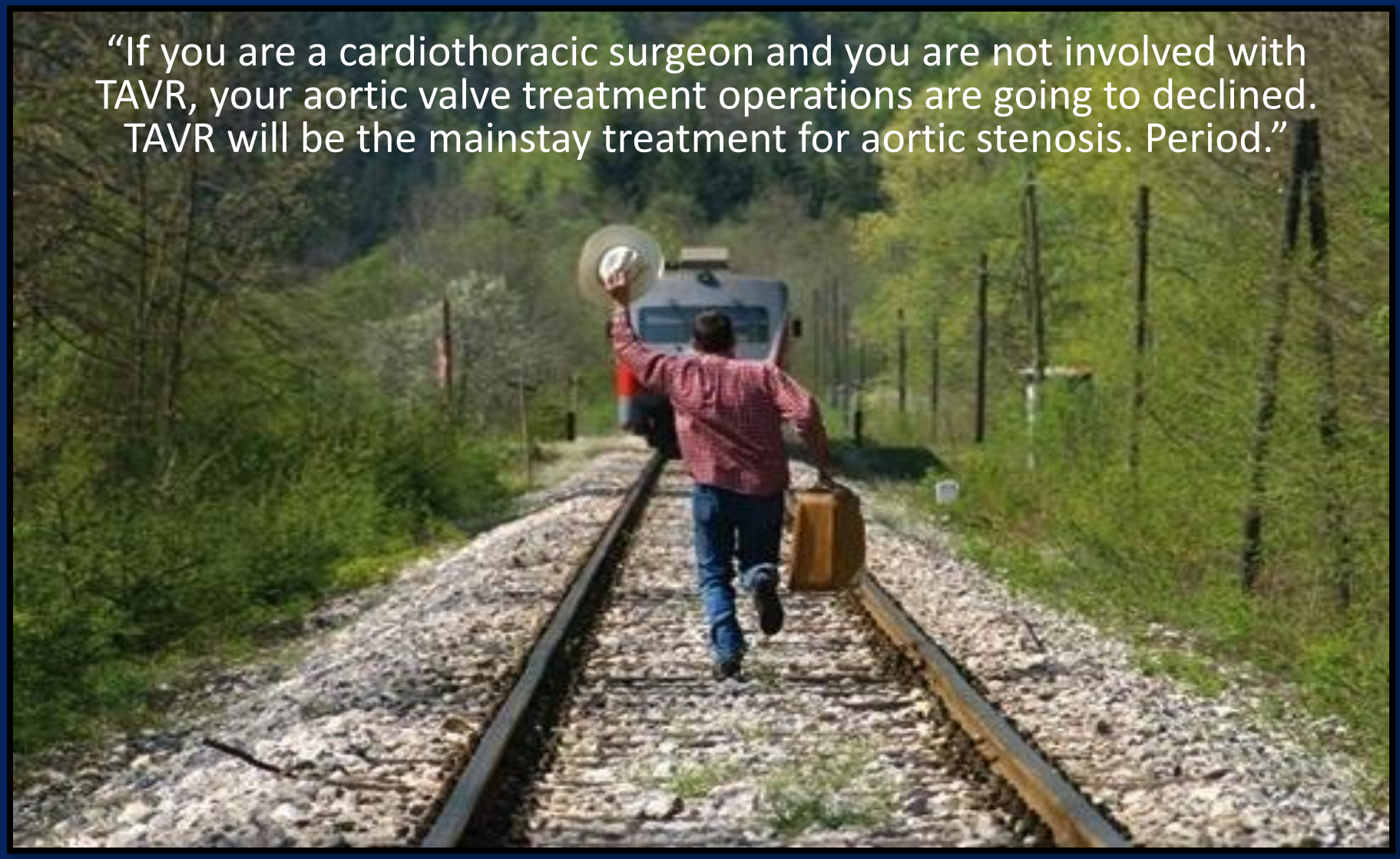
Results

- Avg follow-up time: 17.8 months
- All patients: markedly improved NYHA functional class
- No new PPM
- No reintervention

Conclusions

- TAVR has become the standard treatment in patients at increased surgical risk.
- TAVR is increasingly being performed in patients at intermediate to low risk.
- Joint decision of interdisciplinary Heart Team to select the best treatment for every individual patient while expanding TAVR to intermediate and low risk patients is crucial.

The TAVR train has left the station for multiple new stops



Thank you