TAVR System: Edward Sapien is Best

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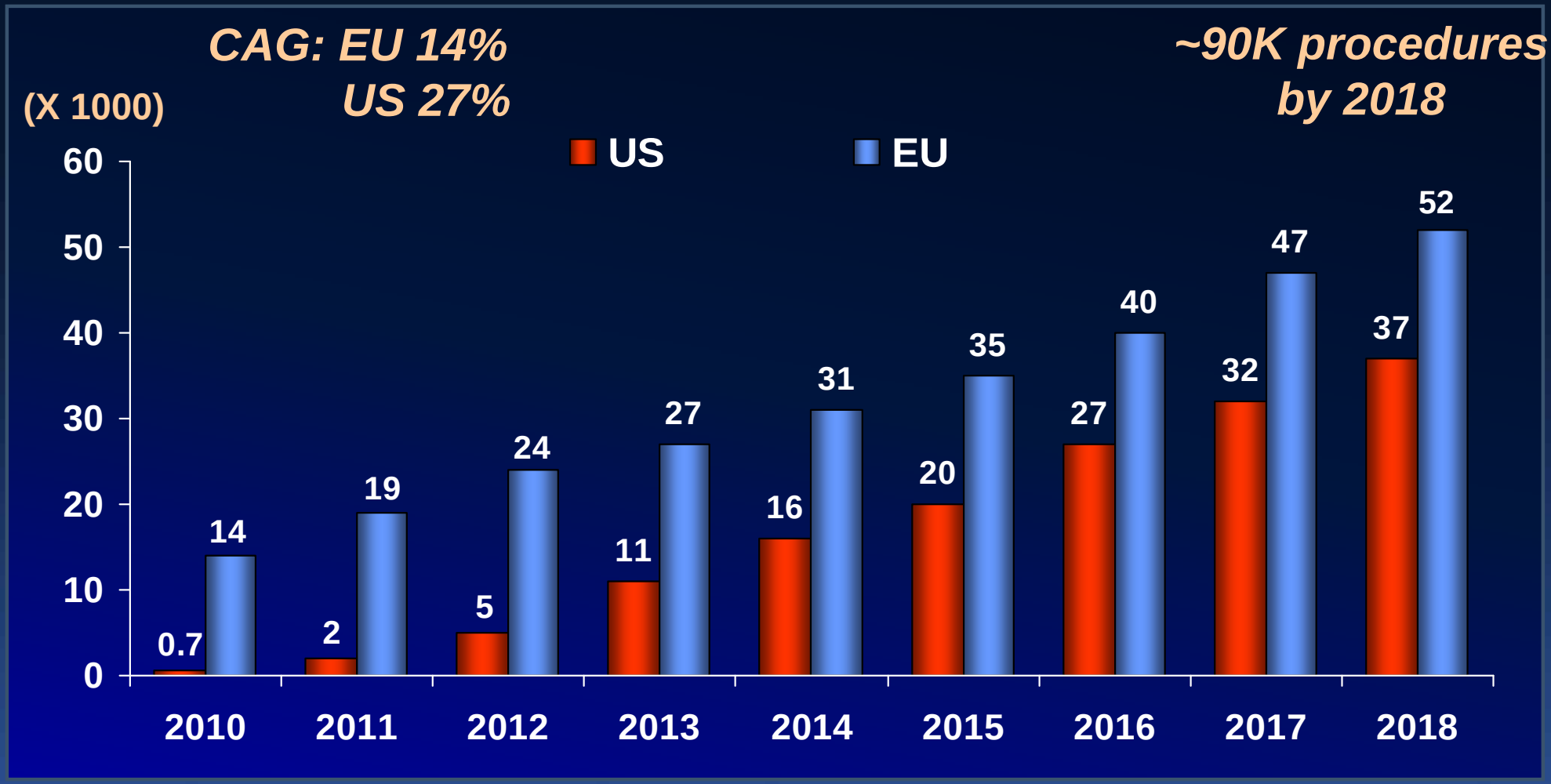
Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship	Company
• Grant/Research Support	• Edwards Lifesciences
• Grant/Scientific Advisory Board	• Medtronic
• Executive Physician Council	• Boston Scientific Corp

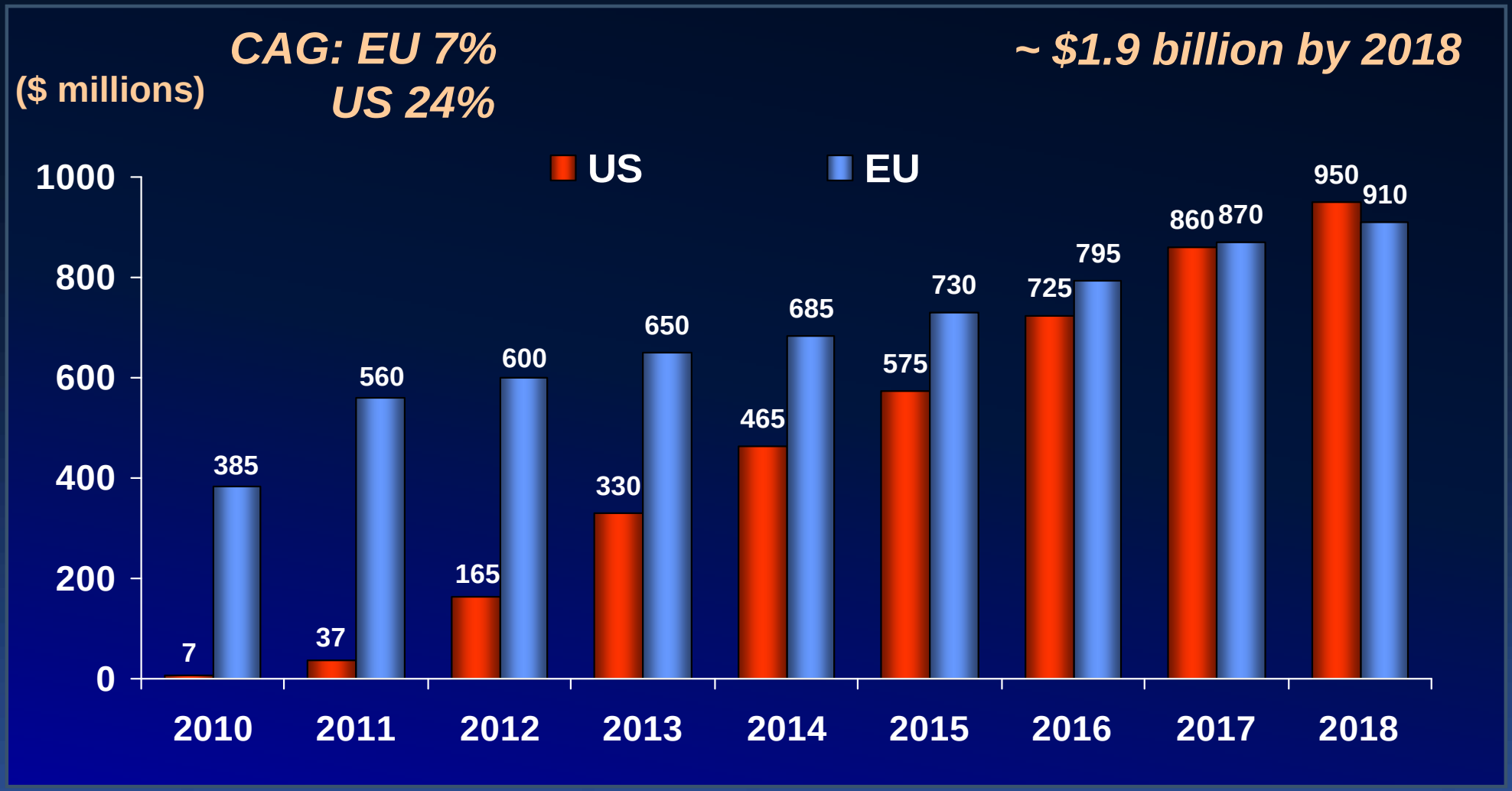
TAVR Procedures

Growth from 2010 - 2018



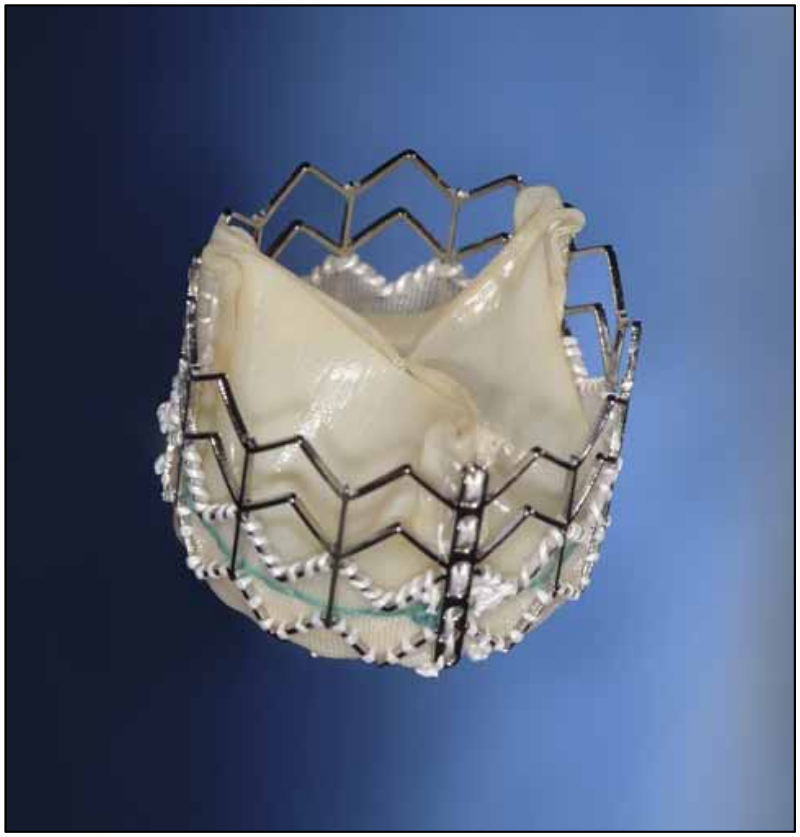
TAVR Revenue ($ millions)

Growth from 2010 - 2018

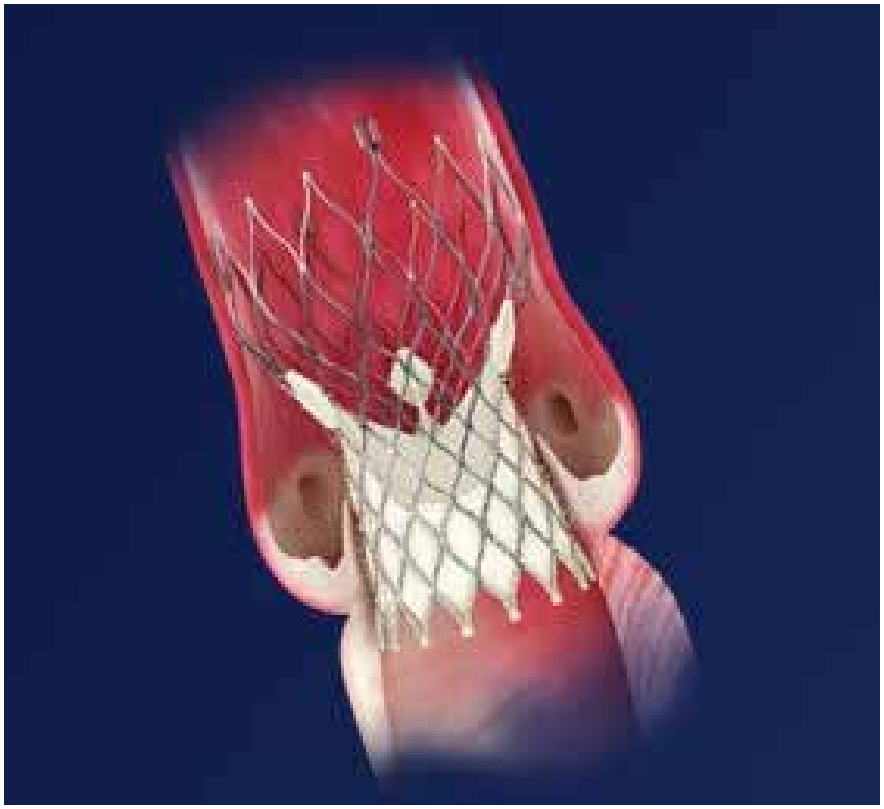


Multiple Industry Sources - 2013

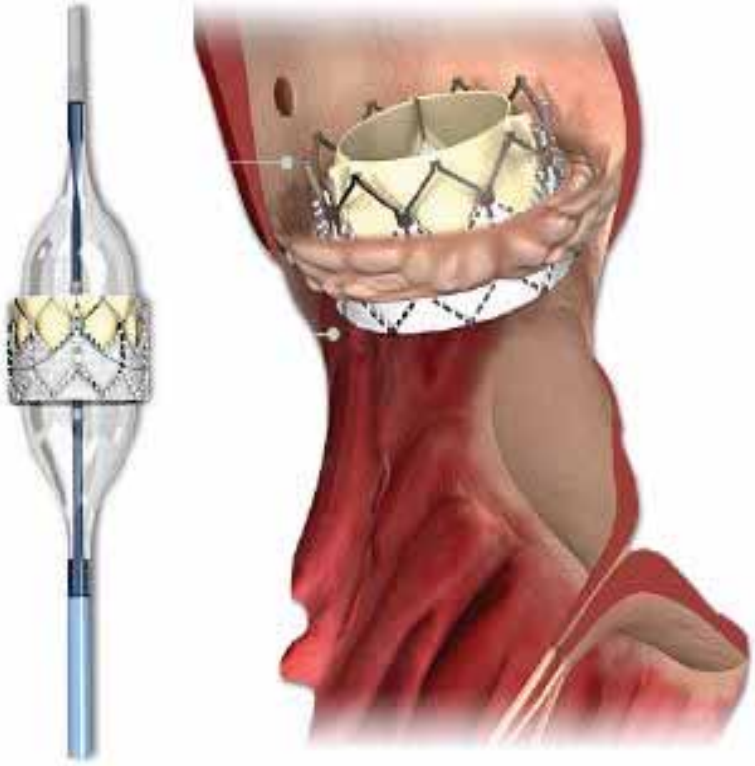
Balloon-expandable THV
Edward Sapien
(Stainless Steel stent frame, bovine pericardium)



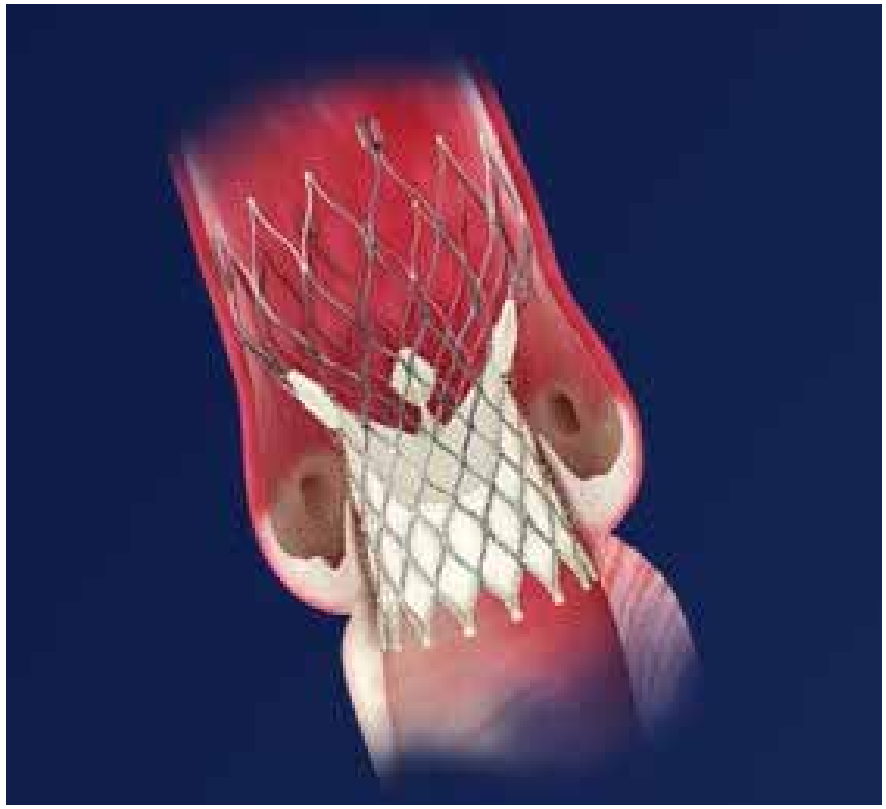
Self-expandable THV
Medtronic CoreValve
(Nitinol stent frame, porcine pericardium)



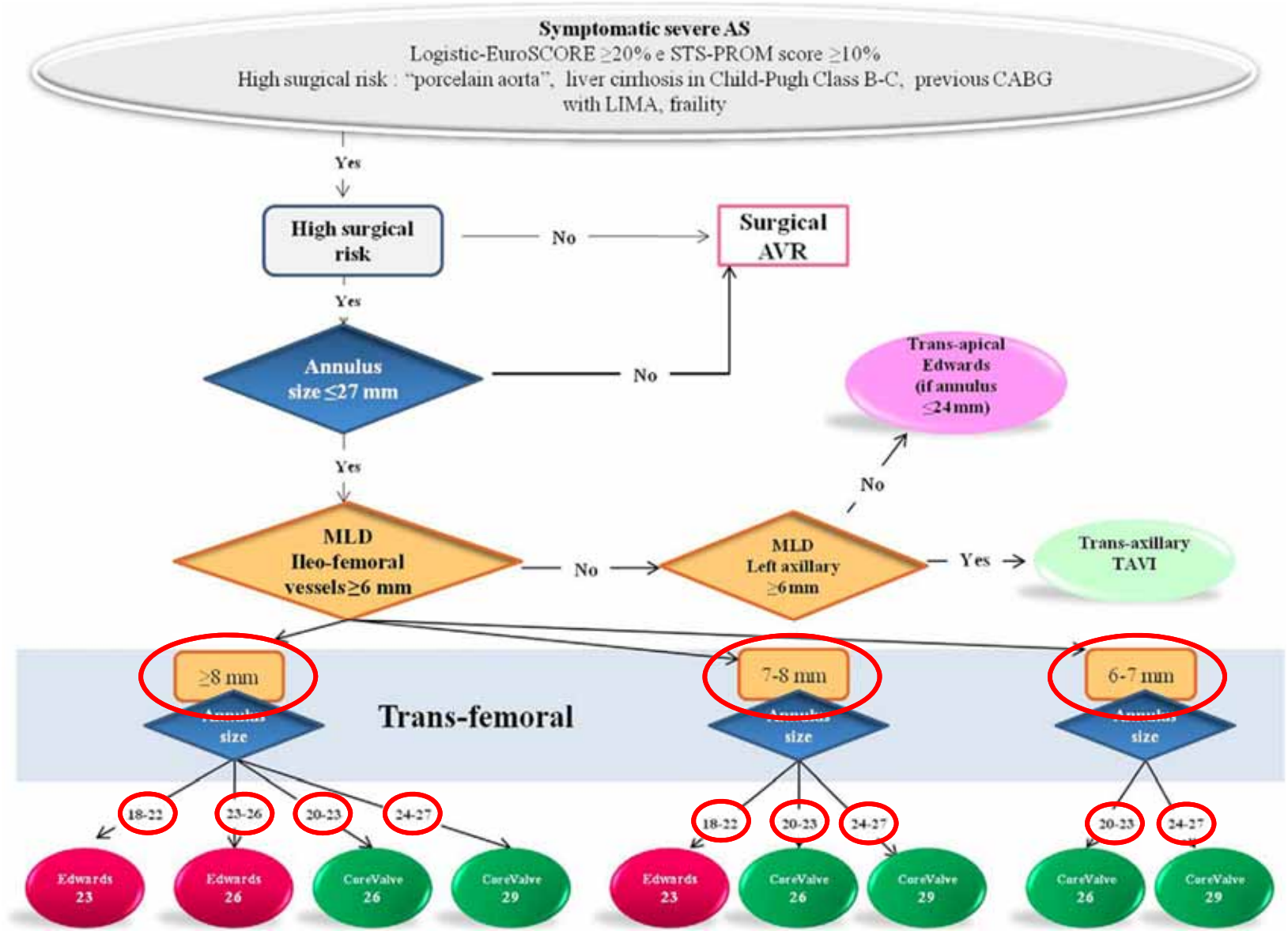
Balloon-expandable THV
Edwards Sapien XT
(Cobalt chromium stent frame, bovine pericardium)



Self-expandable THV
Medtronic CoreValve
(Nitinol stent frame, porcine pericardium)



TAVR vs. TAVR: Europe 2007-2010

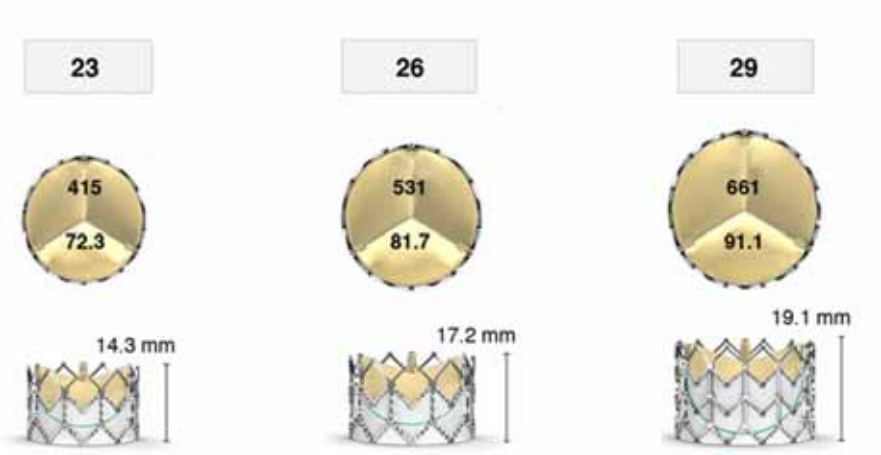


Godino et al. JACC Cardiovasc Interv 2010;3:1110-21

The (TF) TAVR landscape in Europe: 2010-2013

Balloon-expandable system

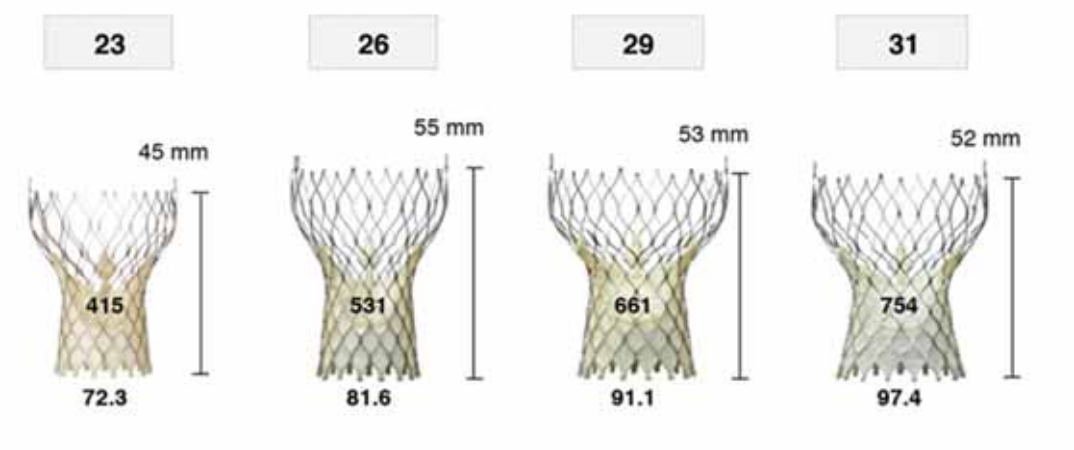
Edwards Sapien XT



- Sheath size: 16-20 F (e-sheaths)
- Annulus range: 18-27 mm

Self-expandable system

Medtronic CoreValve



- Sheath size: 18 F
- Annulus range: 18-29 mm

The frequency of use of each device depended strongly on :

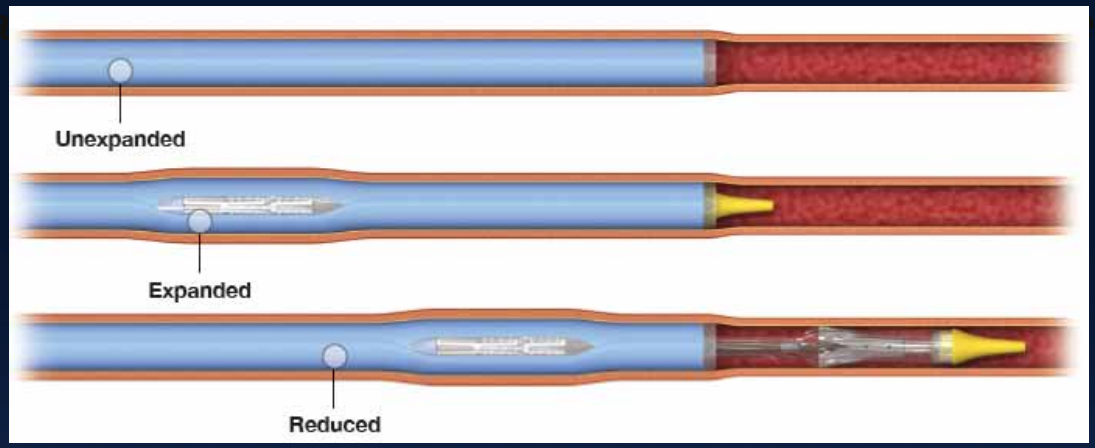
1) operators' familiarity / experience
2) anatomical and clinical factors (e.g. distance to coronaries, LV function)

Figures modified from Kasel et al. JACC Cardiovasc Imaging 2013;6:249-62

Three Areas

- Ease of use…
- Long term data
- Comparative studies

Edwards Expandable Introducer Sheath



THV	eSheath I.D. (unexpanded)	eSheath OD (unexpanded)	Minimum Vessel Diameter*
23 mm SAPIEN 3	**14F (4.6 mm)**	**6.0 mm**	**5.5 mm**
26 mm SAPIEN 3	**14F (4.6 mm)**	**6.0 mm**	**5.5 mm**
29 mm SAPIEN 3	**16F (5.3 mm)**	**6.7 mm**	**6.0 mm**
23 mm SAPIEN XT	16F (5.3 mm)	6.7 mm	6.0 mm
26 mm SAPIEN XT	18F (5.9 mm)	7.2 mm	6.5 mm
29 mm SAPIEN XT	20F (6.6 mm)	8.0 mm	7.0 mm

CoreValve and EnVeoR Sheath

Ease of Use

- Sheath Size
- Preparation
- One vs 2 persons
- Pre-dilation
- Post-dilation
- Failure mode

Three Areas

- Ease of use…sheath size, one person operation
- Long term data
- Comparative studies

Background

The PARTNER Trial demonstrated:

- In severe symptomatic aortic stenosis
  - Inoperable
    - TAVR decreased mortality by 20% compared to standard therapy
  - High risk operable patients
    - TAVR was non-inferior to surgical AVR

PARTNER Manuscripts in NEJM (October, 2010 – May, 2012)

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 21, 2010 VOL. 363 NO. 17

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JUNE 9, 2011 VOL. 364 NO. 23

Transcatheter and Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Babaliaros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Transcatheter Aortic-Valve Replacement for Inoperable Severe Aortic Stenosis

Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Hasan Jilaihawi, M.D., Samir Kapadia, M.D., Augusto D. Pichard, M.D., Pamela S. Douglas, M.D., Vinod H. Thourani, M.D., Vasilis C. Babaliaros, M.D., John G. Webb, M.D., Howard C. Herrmann, M.D., Joseph E. Bavaria, M.D., Susheel Kodali, M.D., David L. Brown, M.D., Bruce Bowers, M.D., Todd M. Dewey, M.D., Lars G. Svensson, M.D., Ph.D., Murat Tuzcu, M.D., Jeffrey W. Moses, M.D., Matthew R. Williams, M.D., Robert J. Siegel, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Stuart Pocock, Ph.D., Craig R. Smith, M.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement

Susheel K. Kodali, M.D., Mathew R. Williams, M.D., Craig R. Smith, M.D., Lars G. Svensson, M.D., Ph.D., John G. Webb, M.D., Raj R. Makkar, M.D., Gregory P. Fontana, M.D., Todd M. Dewey, M.D., Vinod H. Thourani, M.D., Augusto D. Pichard, M.D., Michael Fischbein, M.D., Wilson Y. Szeto, M.D., Scott Lim, M.D., Kevin L. Greason, M.D., Paul S. Teirstein, M.D., S. Chris Malaisrie, M.D., Pamela S. Douglas, M.D., Rebecca T. Hahn, M.D., Brian Whisenant, M.D., Alan Zajarias, M.D., Duolao Wang, Ph.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., and Martin B. Leon, M.D., for the PARTNER Trial Investigators*

Recently Published

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Sex-Related Differences in Outcomes After Transcatheter or Surgical Aortic Valve Replacement in Patients With Severe Aortic Stenosis

Insights From the PARTNER Trial (Placement of Aortic Transcatheter Valve)

Mathew Williams, MD,* Susheel K. Kodali, MD,* Rebecca T. Hahn, MD,*
Karin H. Humphries, DS, DSc,† Vuyisile T. Nkomo, MD,‡ David J. Cohen, MD, MS,§
Pamela S. Douglas, MD,|| Michael Mack, MD,¶ Thomas C. McAndrew, MS,#
Lars Svensson, MD, PhD,** Vinod H. Thourani, MD,†† E. Murat Tuzcu, MD,**
Neil J. Weissman, MD,‡‡ Ajay J. Kirtane, MD, SM,* Martin B. Leon, MD*

New York, New York; Vancouver, British Columbia, Canada; Rochester, Minnesota; Kansas City, Missouri; Durham, North Carolina; Dallas, Texas; Cleveland, Ohio; Atlanta, Georgia; and Washington, DC

Transcatheter versus Surgical Aortic Valve Replacement in Patients with Diabetes and Severe Aortic Stenosis at High Risk for Surgery

PARTNER I, High-risk Cohort

Brian R. Lindman, MD

on behalf of The PARTNER Trial Investigators

ESC 2013 | Amsterdam | September 3, 2013

THE PARTNER TRIAL

Transcatheter versus surgical aortic valve replacement in patients with prior coronary artery bypass graft operation

A PARTNER Trial subgroup analysis

Kevin L. Greason, Verghese Mathew, Rakesh M. Suri

on behalf of The PARTNER Trial Investigators and The PARTNER Publications Office

• STS | Orlando | January 27, 2013

Left Ventricular Ejection Fraction Improves Less after Trans-Apical vs. Trans-Femoral Transcatheter Aortic Valve Replacement:

A PARTNER Trial Echo Substudy

William F. Fearon, MD

on behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office

• TCT 2013 | San Francisco | October 29, 2013

THE PARTNER TRIAL

Impact of Paravalvular Leak Following Transcatheter Aortic Valve Replacement on One-Year Mortality

Analysis of the Combined PARTNER Cohorts

Susheel K. Kodali

on behalf of The PARTNER Publications Office and the PARTNER Trial Investigators

• ESC 2013 | Amsterdam | September 2, 2013

THE PARTNER TRIAL

Predictors and Clinical Consequences of Permanent Pacemaker Implantation after TAVR: The PARTNER Experience

Tamim Nazif, MD

on Behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office

TCT 2013 | San Francisco | October 29, 2013

THE PARTNER TRIAL

Atrial Fibrillation is Associated with Increased Mortality in Patients Undergoing TAVR:
Insights from The PARTNER Trial

Angelo Biviano, MD, MPH
New York-Presbyterian Hospital
Columbia University Medical Center
on behalf of The PARTNER Trial Investigators
and The PARTNER Publications Office:

Angelo B. Biviano, Jose Dizon, Tamim Nazif, Samir Kapadia, Vasilis Babaliaros, Ke Xu, Josep Rodes-Cabau, Wilson Y. Szeto, William F. Fearon, Danny Dvir, Todd Dewey, Mathew Williams, Michael Mack, John G. Webb, D. Craig Miller, Craig Smith, Martin B. Leon, Susheel Kodali

ACC 2014 | Washington, DC | March 29, 2014

Regression of LV Mass after Transcatheter or Surgical Aortic Valve Replacement for Aortic Stenosis in the PARTNER I Trial: Amount and Predictors

William J. Stewart, MD, FASE, FACC
Cleveland Clinic; Cleveland, Ohio
Lindman B, Pibarot P, Weissman N, Hahn R, McAndrew T, Xu K, Goldstein S, Rubenson D, Liang D, Leon M, Kodali S, Mack M, Svensson L, Thourani V, Herrmann H, Douglas P

On Behalf of The PARTNER Trial Investigators
with thanks to all involved!

THE PARTNER TRIAL

Transcatheter Aortic Valve Replacement for Failed Surgical Bioprostheses

Early Results from the PARTNER II Valve-in-Valve Registry

John Webb, MD
Michael Mack, MD

on behalf of The PARTNER II Trial Investigators
and The PARTNER Publications Office

• ACC 2014 | Washington, D.C. | March 30, 2014

THE PARTNER II TRIAL

MAYO CLINIC

One Year Outcomes from the STS/ACC Transcatheter Valve Therapy (TVT) Registry

David R. Holmes, Jr., J. Matthew Brennan, John S. Rumsfeld, David Dai, Fred Edwards, John Carroll, David Shahian, Fred Grover, E. Murat Tuzcu, Eric Peterson, Ralph Brindis, Michael J. Mack

March 2014
On behalf of the TVT Registry
ACC 2014
Washington, D.C.

 |

Patient Population

- 5,980 Patients enrolled in the STS/ACC TVT registry November 2011 – July 2013
- Age > 65 years
- Medicare insurance
- Part A & B and non-HMO during month of index procedure
- Index admission linked to inpatient Medicare claims using direct patient identifiers (97% successful record linkage rate)

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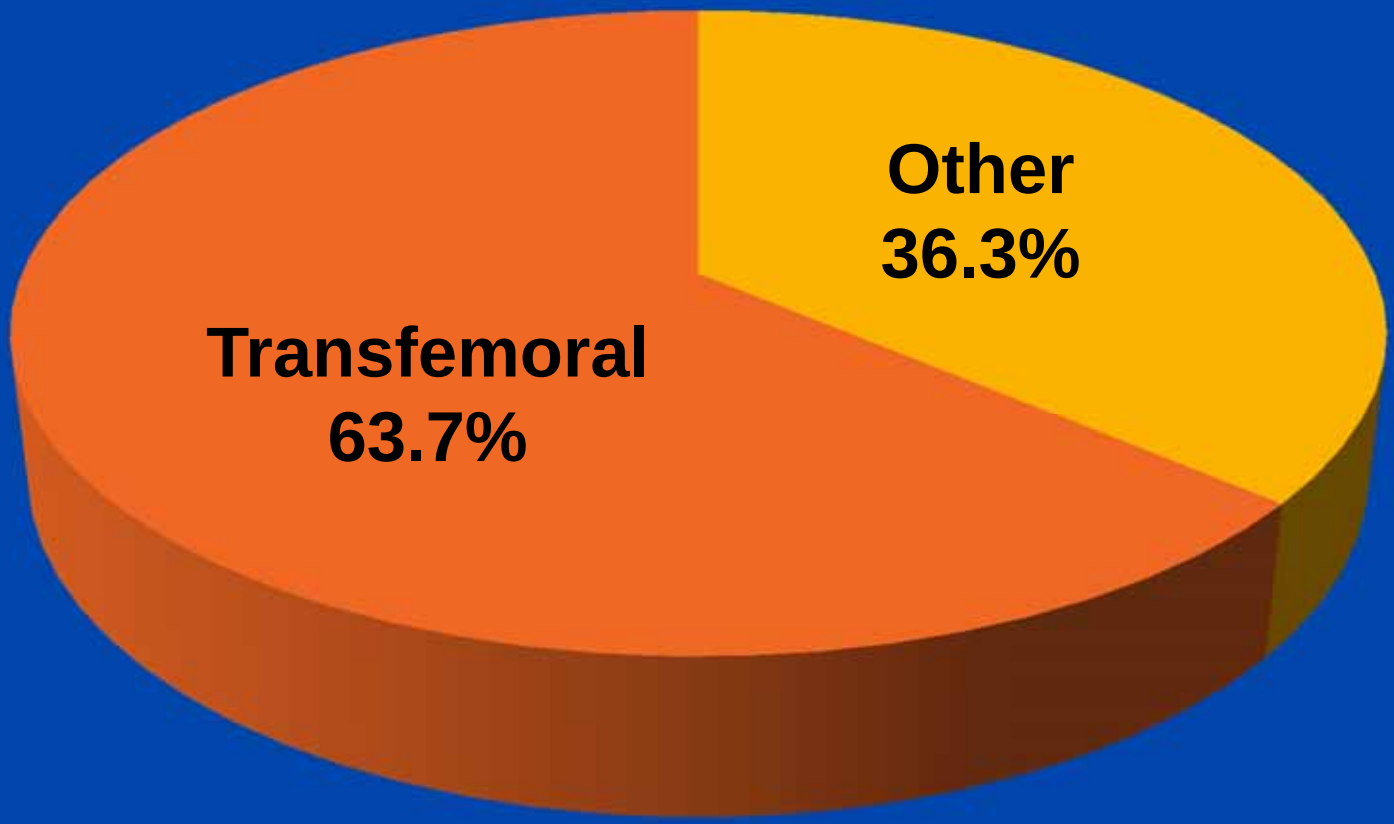
Procedural Performance
Access Site



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 |

In-Hospital Outcome

Characteristic	Study Cohort N = 5,980
In-hospital death	319 (5.3)
Any in-hospital stroke	99 (1.7)
Any in-hospital TIA	22 (0.4)
Any in-hospital valve complication	125 (2.1)
Conversion to open heart surgery	83 (1.4)
Discharge location	
Home	3,455 (61.1)
Extended care/TCU/rehab	1,788 (31.6)
Other acute care hospital	34 (0.6)
Nursing home	328 (5.8)
Hospice	31 (0.5)
Other	22 (0.4)

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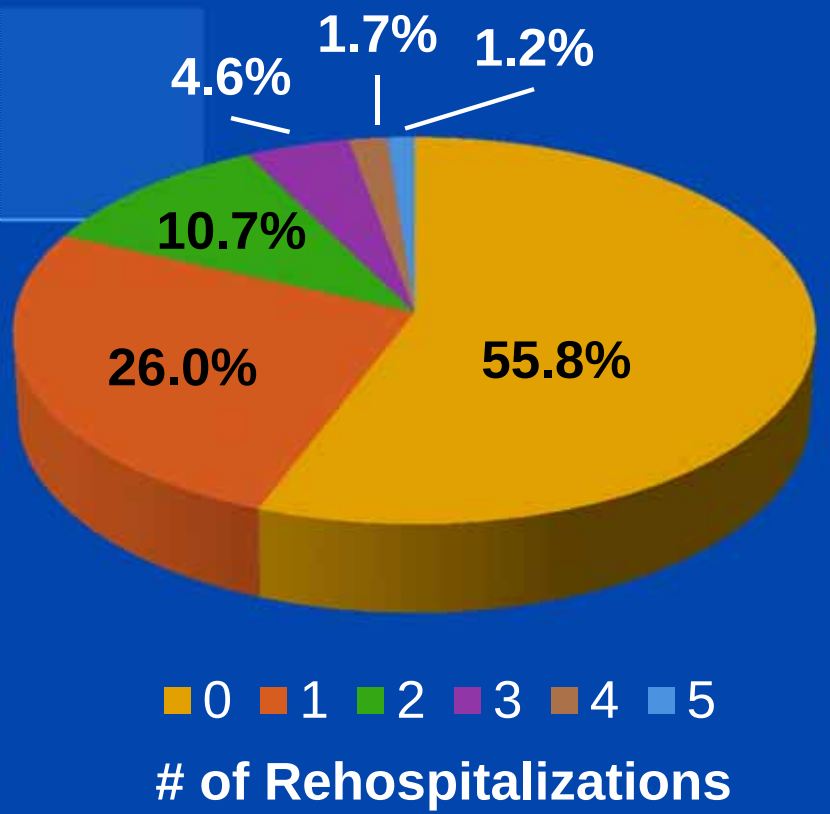
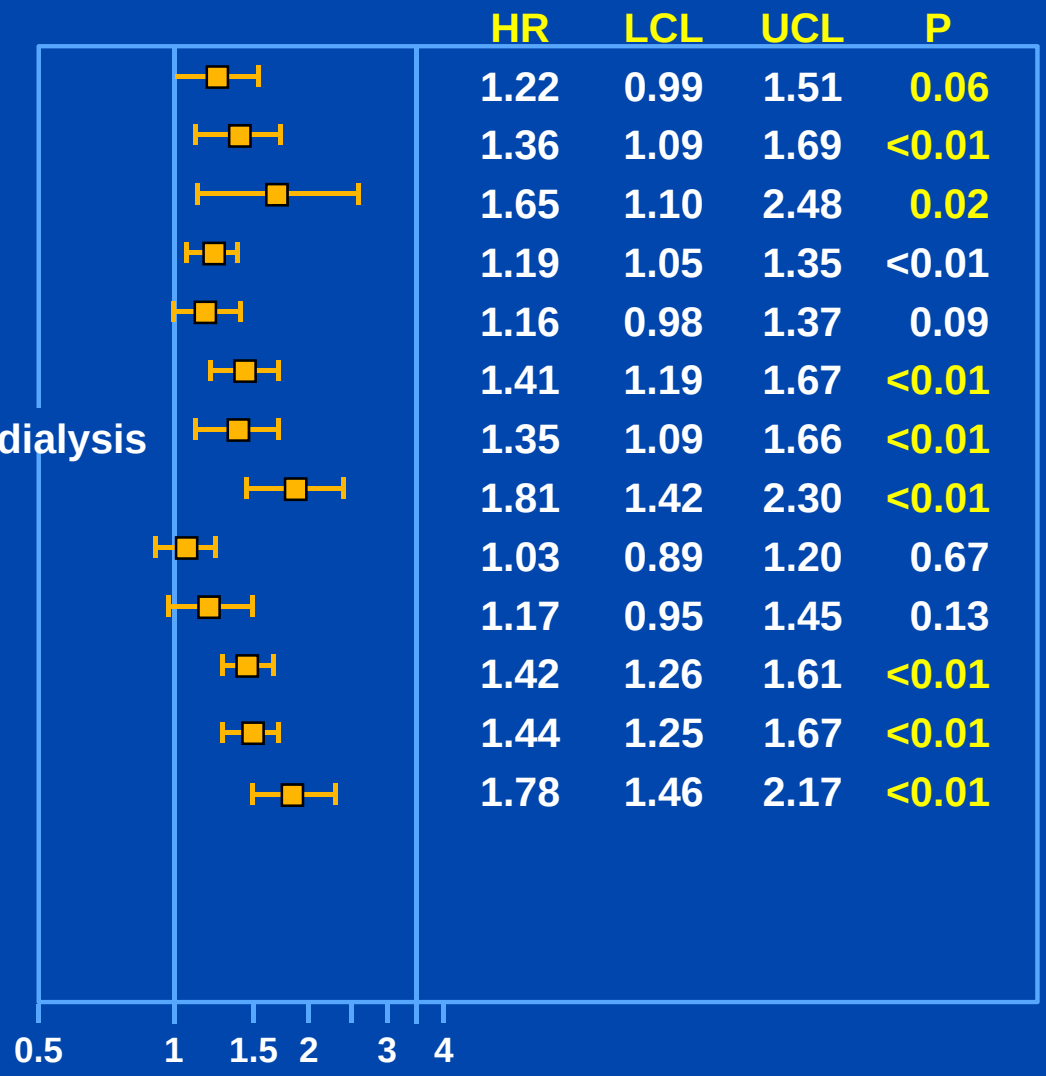
One Year Outcome

Mortality	26.2% (24.7%, 27.8%)
Stroke	3.6% (3.1%, 4.2%)
Death or stroke	28.4% (26.9%, 30.0%)
Incidence & frequency of repeat hospitalization within 6 months	



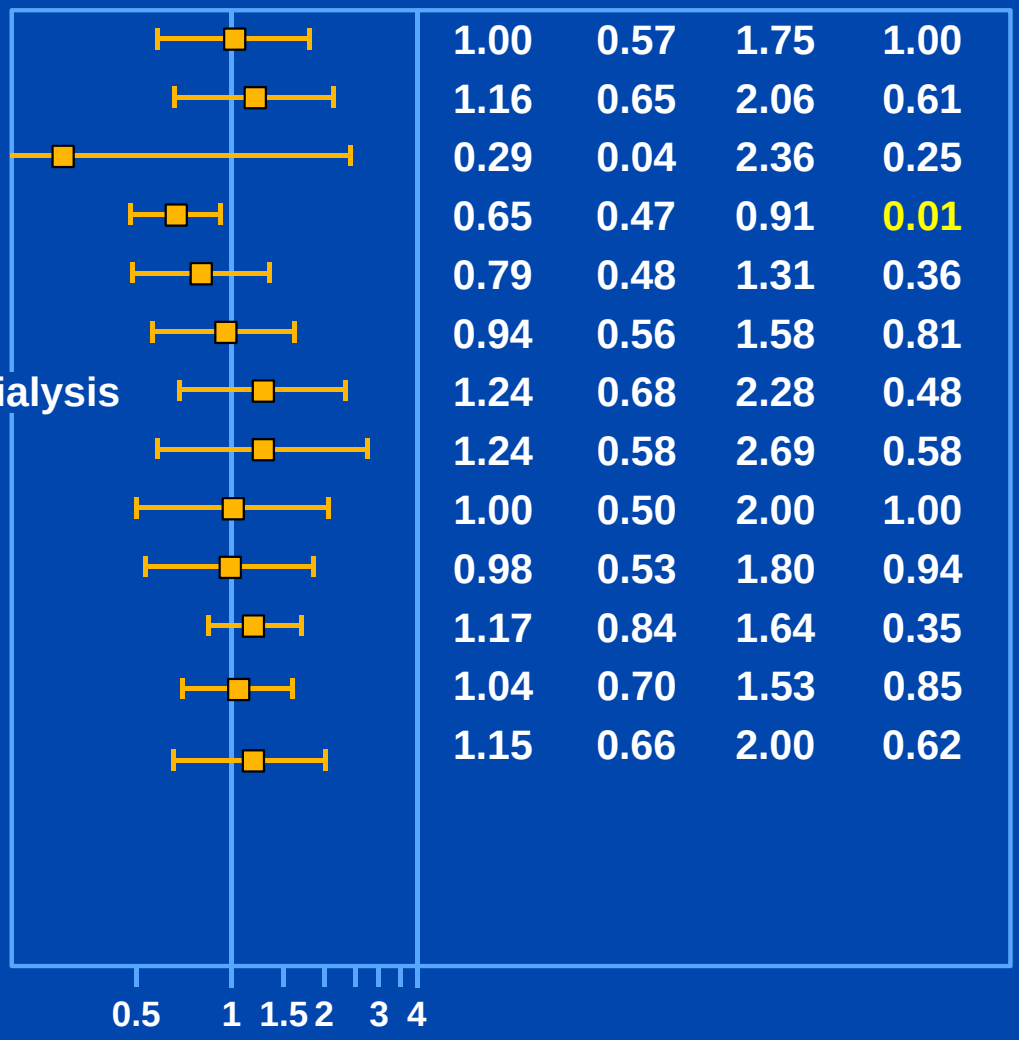
MAYO CLINIC

Multivariable Model of 1-Year Mortality after TAVR



MAYO CLINIC

Multivariable Model of 1-Year Stroke after TAVR



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Conclusions

- Different baseline demographics are significantly associated with 1 year mortality as compared with stroke

Mortality	Stroke
Age	Female gender
Male gender	
Severe COPD	
ESRD	
Access site	
STS PROM	

- Identification of these associations is essential for developing risk prediction models and will aid in patient selection criteria for TAVR

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TAVR
1 Year Outcomes

	Centers N	Patients N	Death %	Stroke %	Author
TVT/CMS	**230**	**5,980**	**26.2**	**3.6**	**TVT**
PARTNER B	21	179	30.7	11.2	Leon
PARTNER A	25	348	24.3	8.7	Smith
UK TAVI	25	870	21.4	NR	Moat
Canadian TAVI	6	339	24.0	NR	Rodes-Cabau
France 2	33	3,195	24.0	4.1	Gilard
Belgium	15	328	26.0	NR	Bosmans
Pragmatic	4	793	14.3	NR	Chieffo
SOURCE Reg	93	2,706	21.1	7.1	Treede

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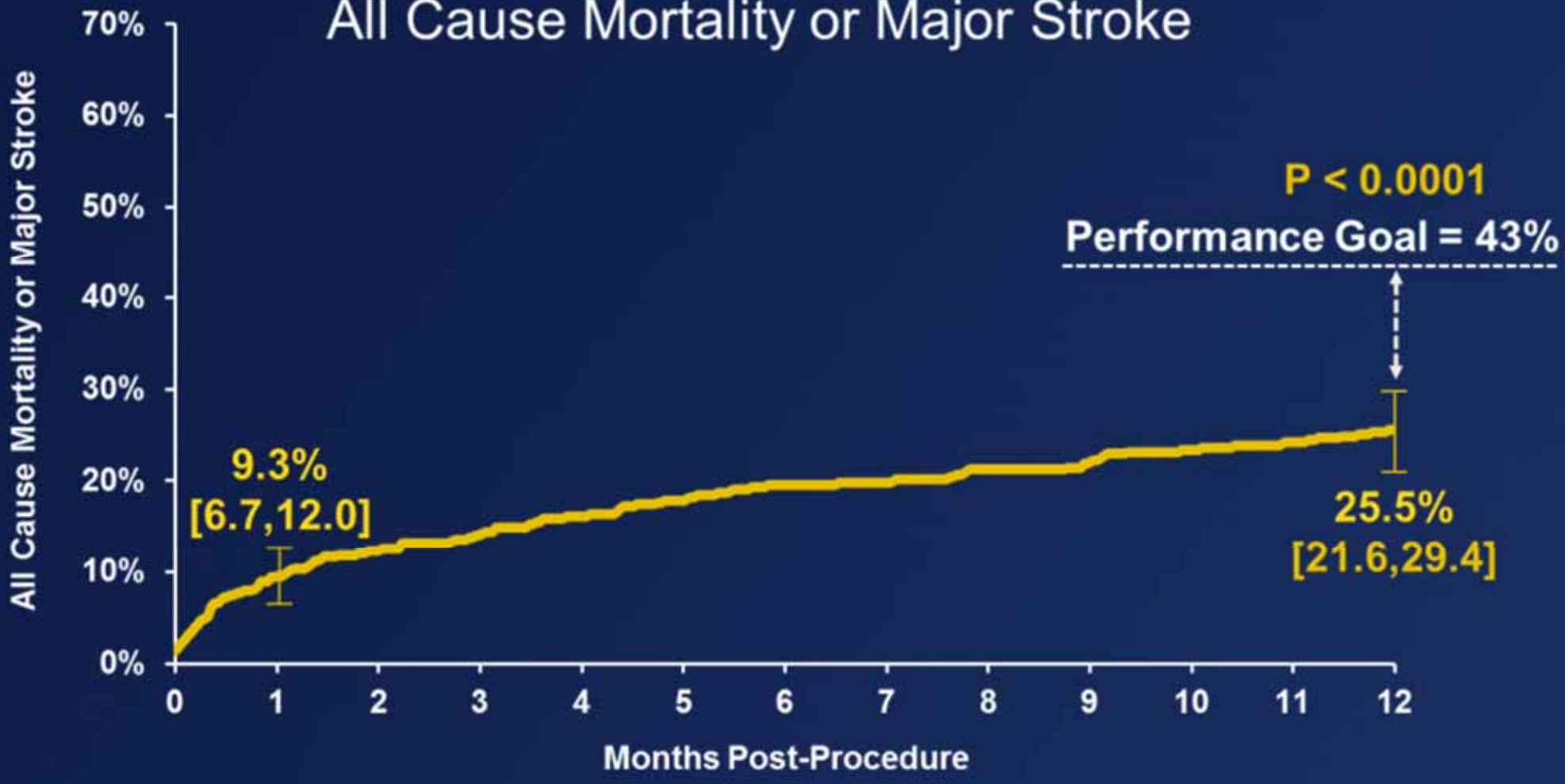
Pivotal Trial Design

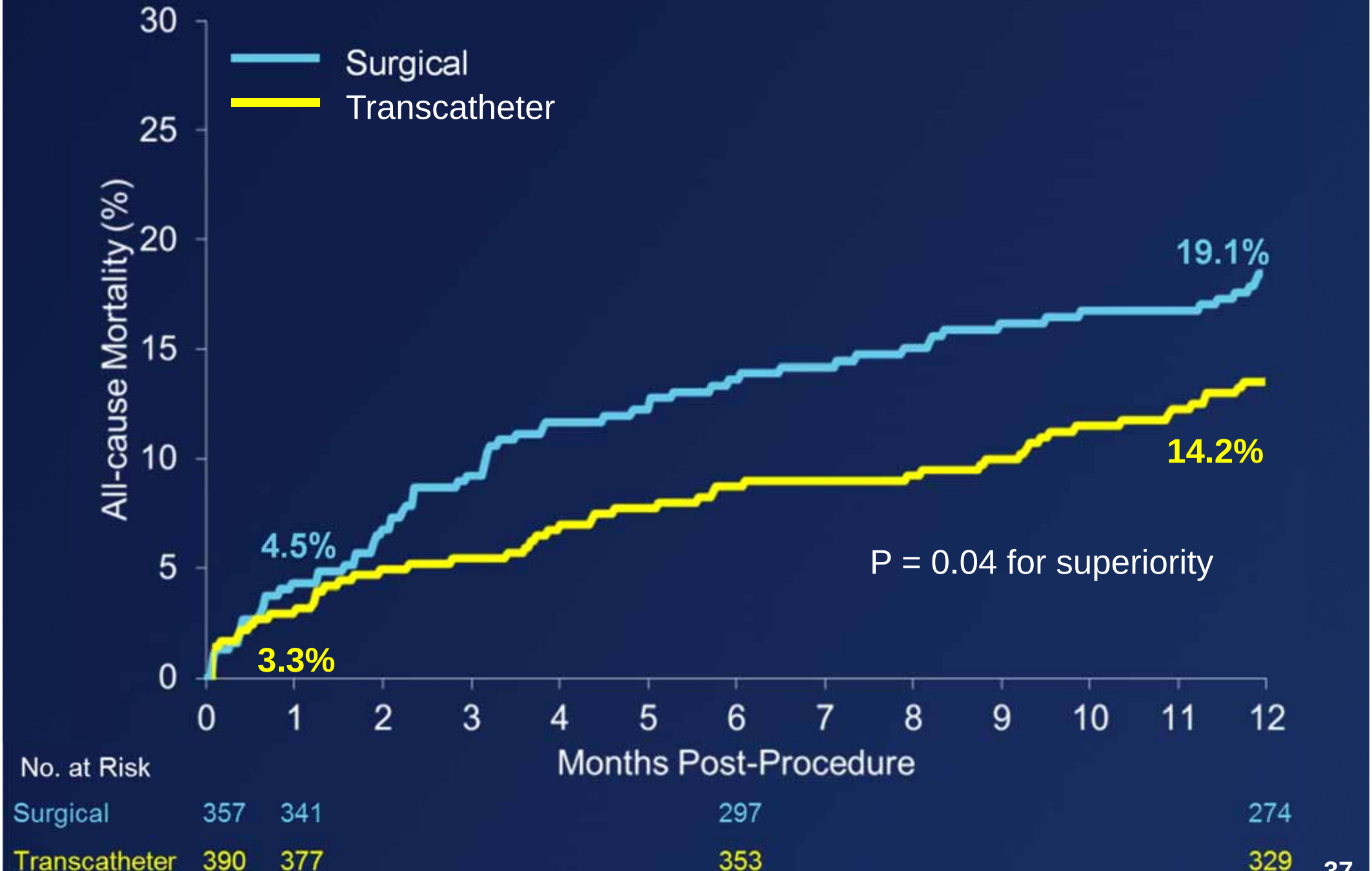
Primary Endpoint



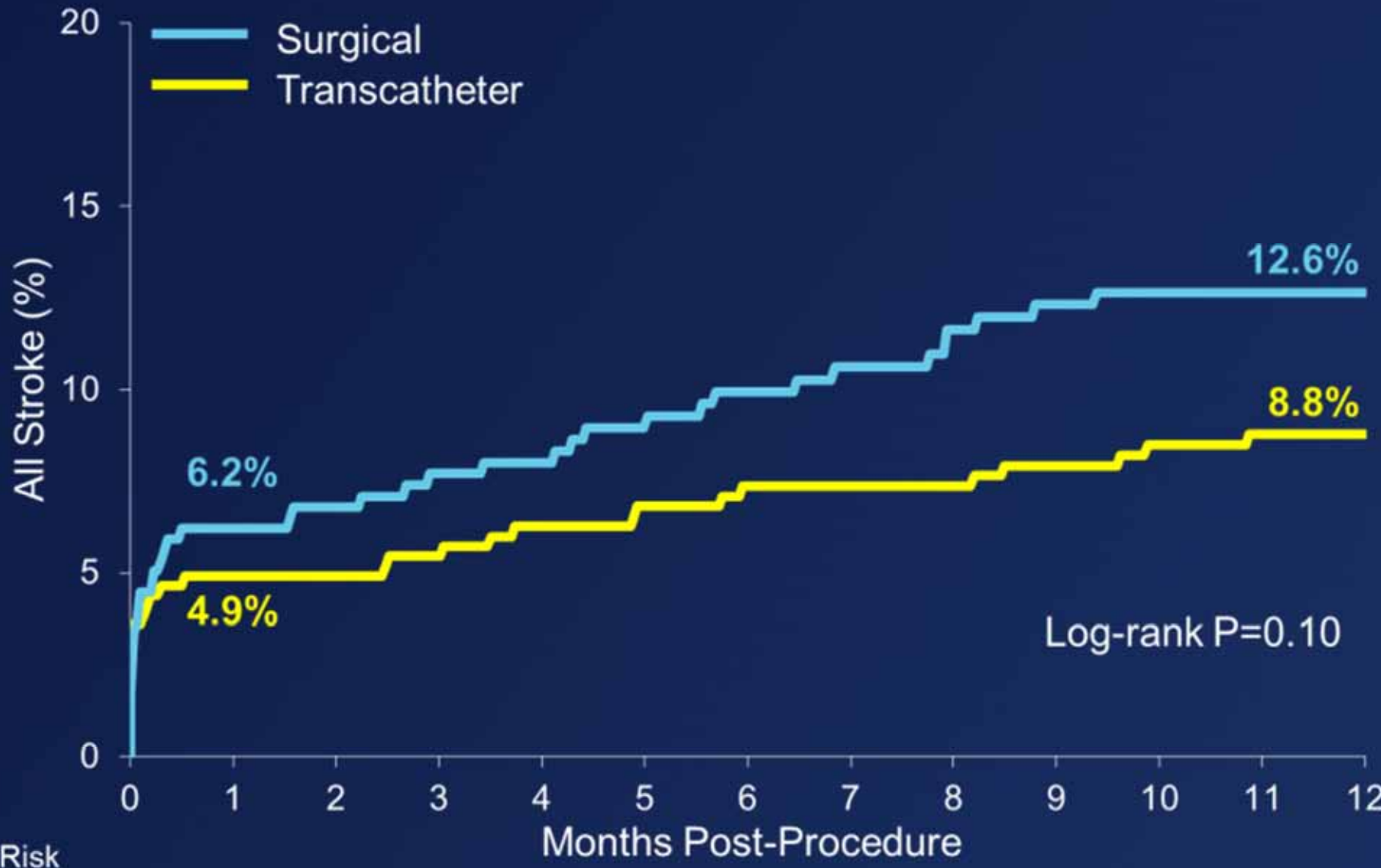
Pivotal Trial Design

* Randomization stratified by intended access site

Primary Endpoint: 1 Year All-cause Mortality



All Stroke



No. at Risk

Surgical	357	322	274	249
Transcatheter	390	363	334	314

All-Cause Mortality after TAVR

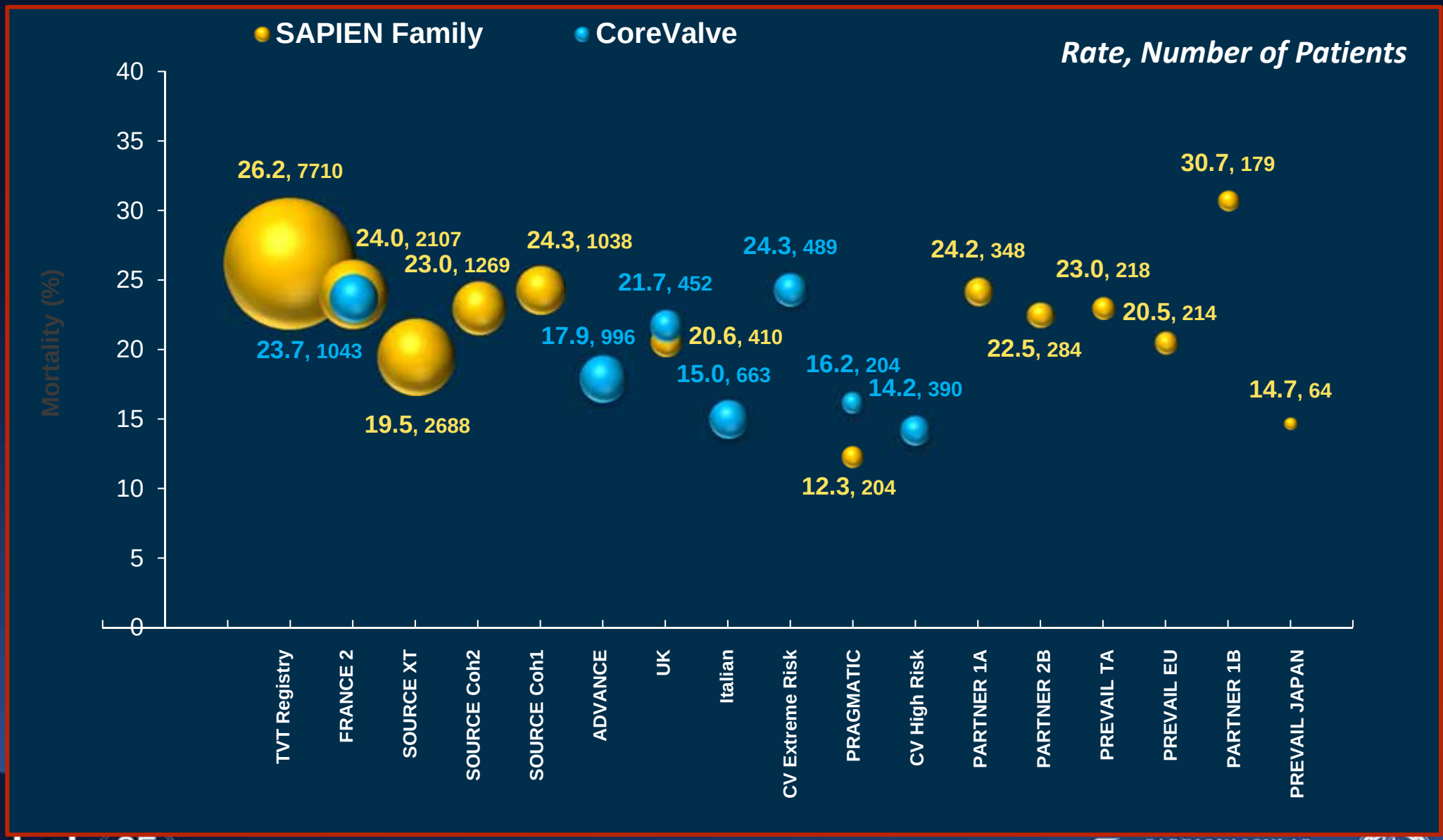
	Death at 1	Death at 2	Death at 3
High risk operable			%
Inoperable			%
High risk Operable	14%		
Extreme Risk	24%		

Since CoreValve showed a lower mortality than surgery in the U.S. high-risk study and Sapien didn't in PARTNER, then CoreValve has a lower mortality than SAPIEN…

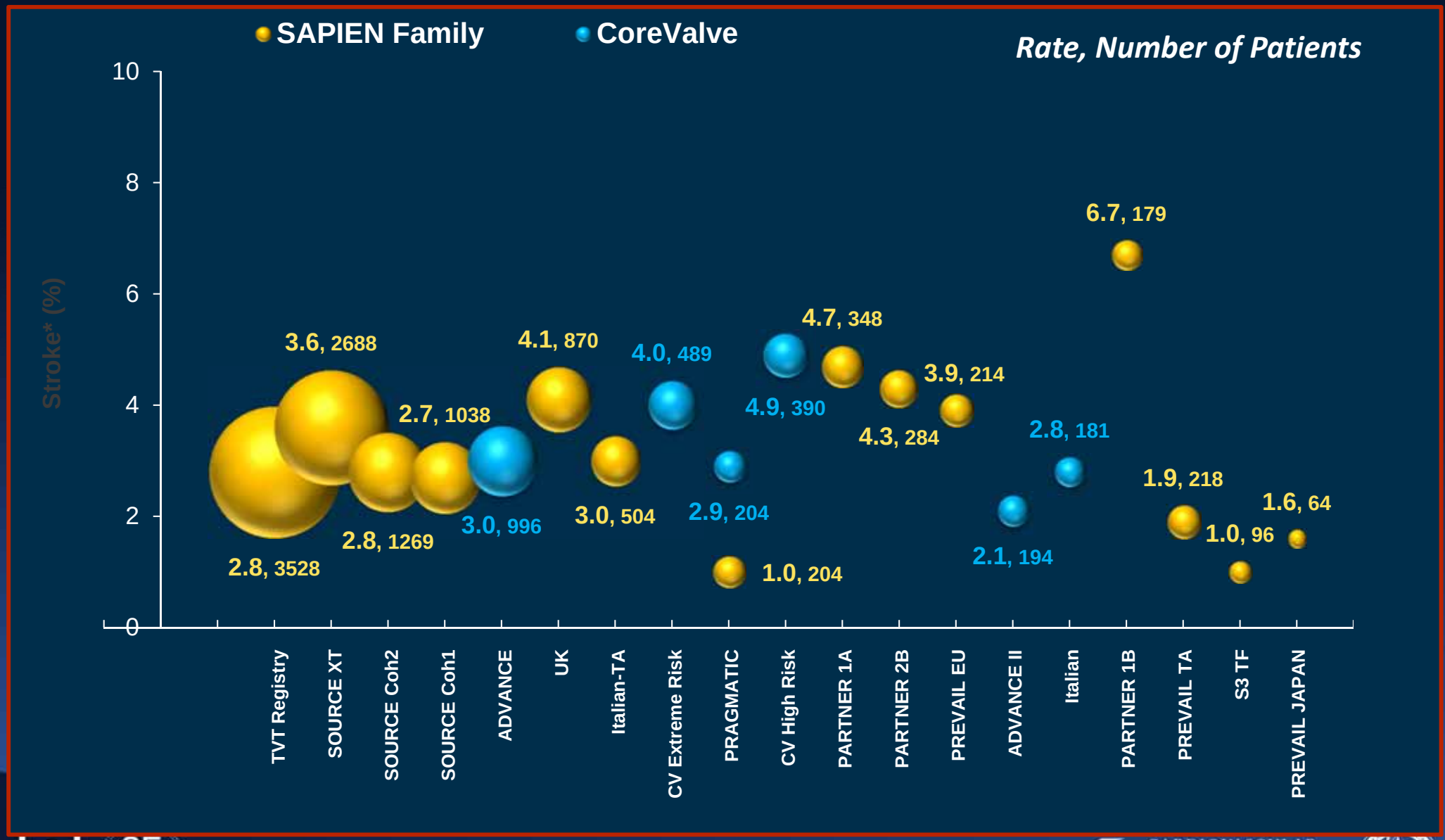
Three Areas

- Ease of use…sheath size, one person operation
- Long term data
- Comparative studies

No Differences in Mortality at 1 Year in High Risk and Inoperable Patients



No Differences in All Strokes at 30 days in High Risk and Inoperable Patients



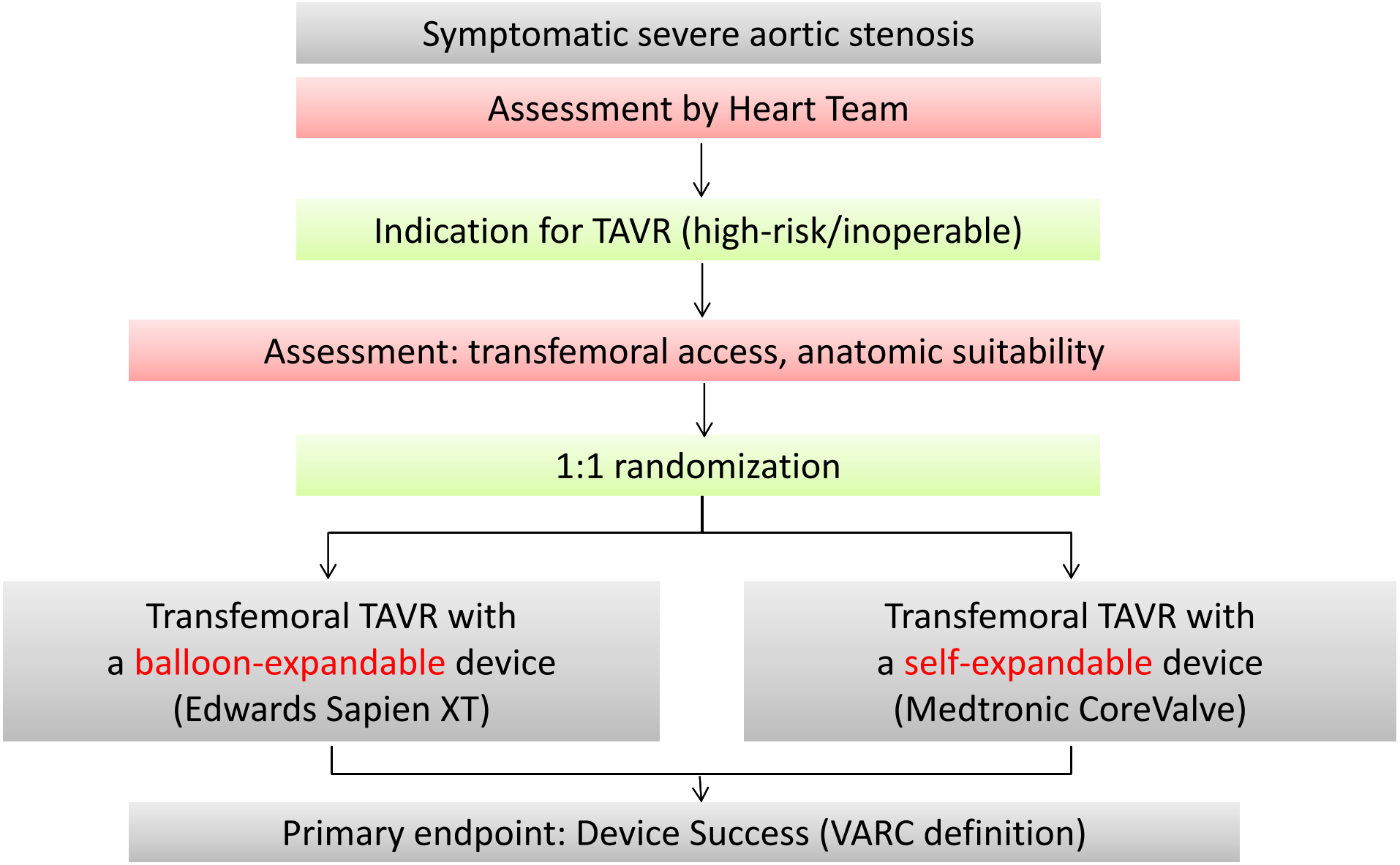
*Rate of All Stroke or Major Stroke + Minor Stroke

TAVR

Perm Pacer/Aortic Regurgitation (mod/Severe)

	Sapien N	Core N	PP S/C	AI S/C	Method
UK TAVI	410	452	7.4/24.4	9.6/17.3	Angio
FRANCES 2	2107	1043	11.5/24.2	13/21.5	Echo
Sentinel	2604	1943	6/23.4	6.7/12.2	Echo
PRAGMATIC +	204	204	5.9/22.5	0.5/1.5	Echo

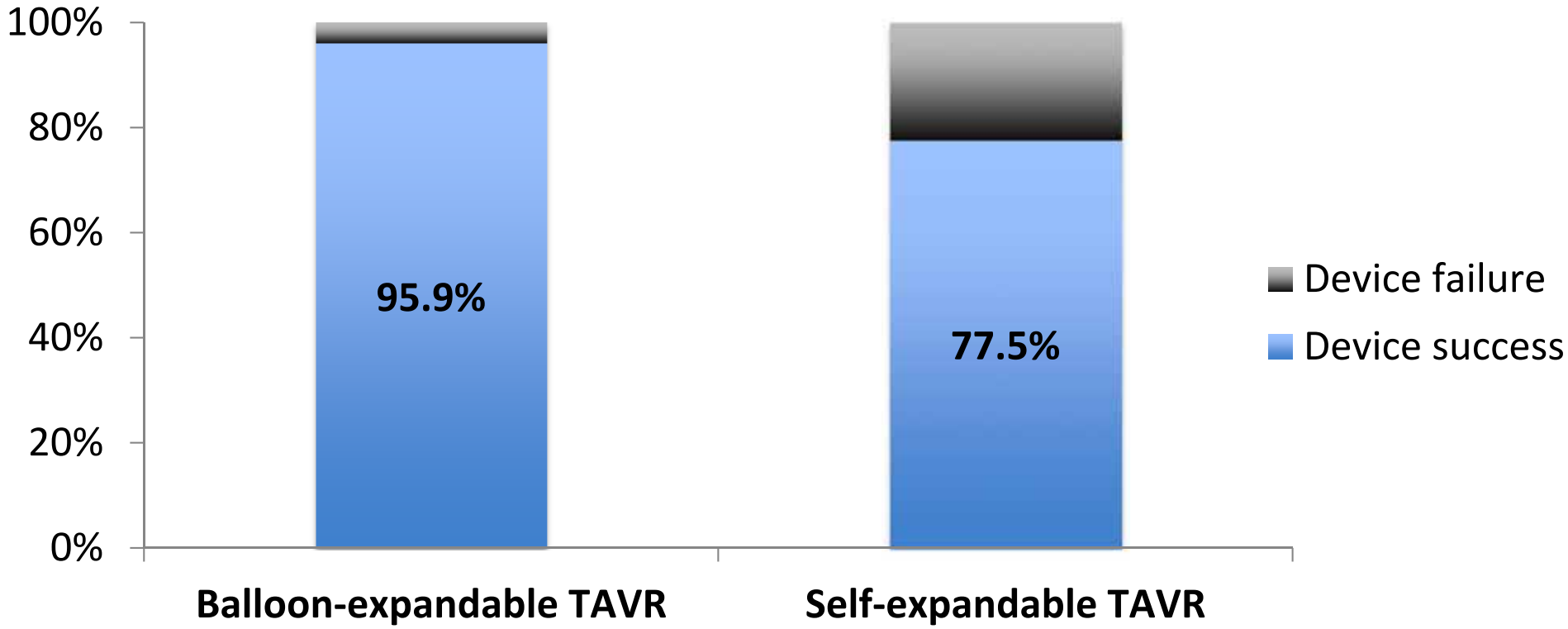
CHOICE: Study Design



Abdel-Wahab et al. JAMA 2014;311:1503-14

CHOICE: Device Success (Primary Endpoint)

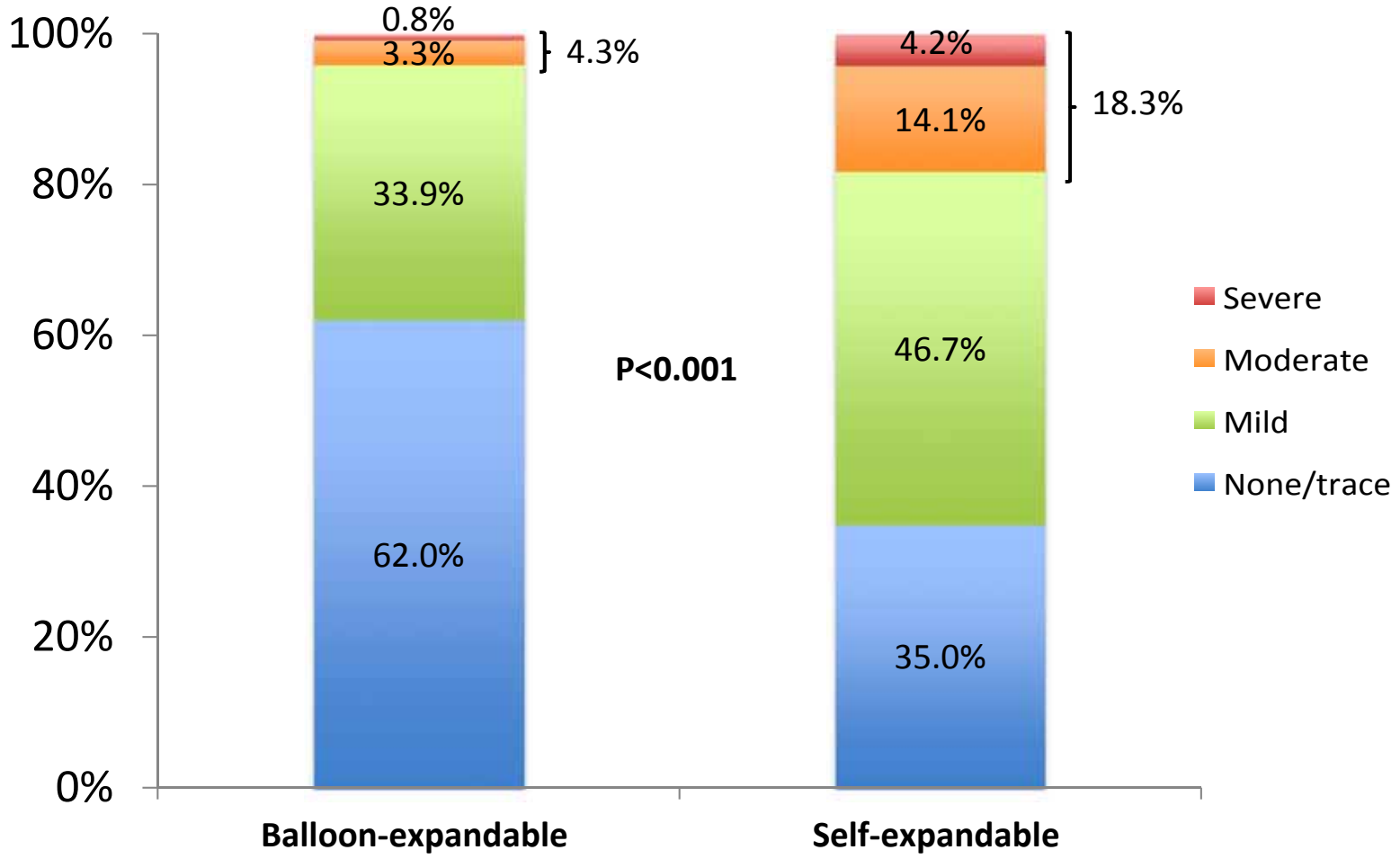
Relative risk 1.24, 95%CI 1.12-1.37, p<0.001



Causes of device failure	Balloon-expandable (n=121)	Self-expandable (n=120)
Unsuccessful vascular access, delivery and deployment	0/121 (0)	0/120 (0)
Incorrect position with implantation of more than one valve	1/121 (0.8)	7/120 (5.8)
Inadequate performance of the prosthetic heart valve - Aortic valve area < 1.2 cm^2 or mean aortic valve gradient > 20 mmHg	0/121 (0)	0/120 (0)
- Moderate or severe prosthetic valve regurgitation	5/121 (4.1)	22/120 (18.3)
Total (hierarchical)	5/121 (4.1)	27/120 (22.5)

CHOICE: Aortic Regurgitation

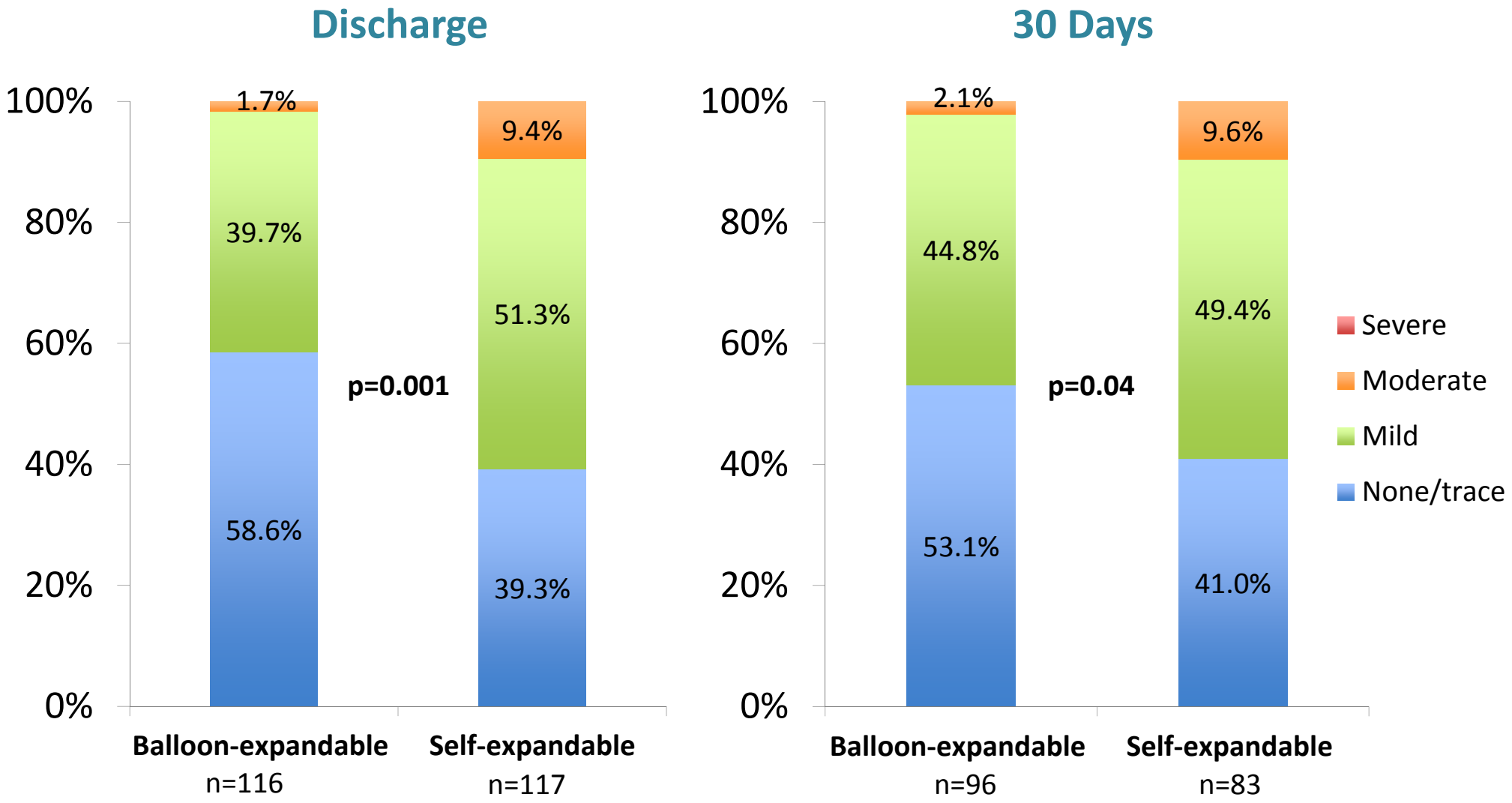
AR by Angiography (core-lab)



	Balloon-expandable (n=116)	Self-expandable (n=114)	p-value
Dimensionless AR Index	29.0±7.1	27.3±7.2	0.08

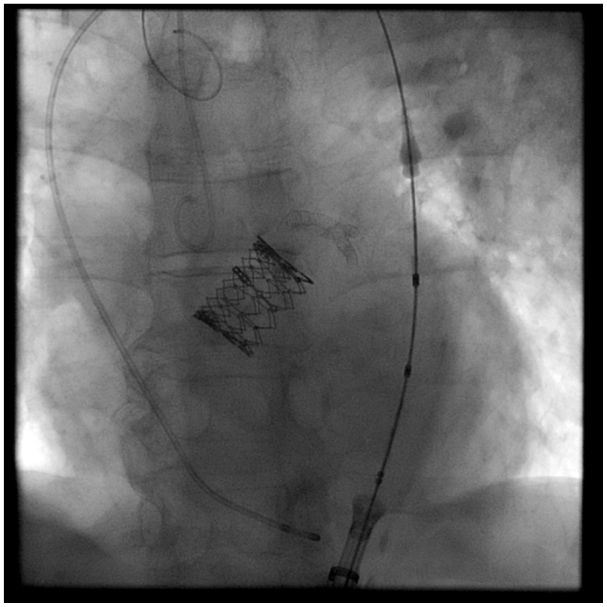
CHOICE: Aortic Regurgitation

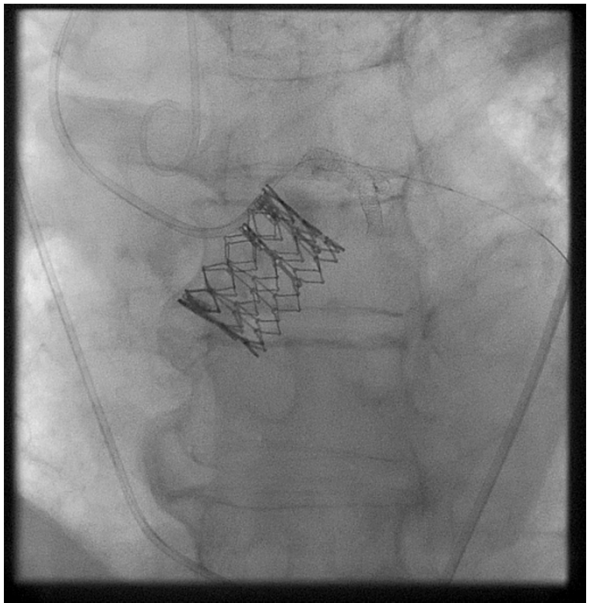
AR by Echo (site-reported)



CHOICE: Life-Threatening Complications

	Balloon-expandable (n=121)	Self-expandable (n=120)	p-value
Coronary obstruction	2/121 (1.6%)	0/120 (0.0%)	0.49
Annular rupture	0/121 (0%)	0/120 (0%)	--
Left-to-right shunt	2/121 (1.6%)	2/120 (1.7%)	0.99





CHOICE: Clinical Outcome at 30 Days

	Balloon-expandable (n=121)	Self-expandable (n=117)	p-value
Death			
From any cause	5/121 (4.1%)	6/117 (5.1%)	0.77
From CV causes	5/121 (4.1%)	5/117 (4.3%)	0.99
Stroke	7/121 (5.8%)	3/117 (2.6%)	0.33
Major	3/121 (2.5%)	3/117 (2.6%)	0.99
Minor	4/121 (3.3%)	0/117 (0.0%)	0.12
Bleeding			
Life threatening	10/121 (8.3%)	14/117 (12.0%)	0.35
Major	23/121 (19.0%)	17/117 (14.5%)	0.36
Vascular complications			
Major	12/121 (9.9%)	13/117 (11.1%)	0.76
Combined safety endpoint	22/121 (18.2%)	27/117 (23.1%)	0.42
Rehospitalization for HF	0/119 (0.0%)	5/117 (4.3%)	0.02
NYHA class improvement	100/106 (94.3%)	91/105 (86.7%)	0.06
New permanent pacemaker	19/110 (17.3%)	38/101 (37.6%)	0.001

Device-Dependent Association Between Paravalvular Aortic Regurgitation (AR) and Outcome After TAVI

UK TAVI registry: 2,440 TAVR cases (52.7% CoreValve; 47.2% Sapien) performed at 25 centers, 2007-2011.

- On multivariable analysis, use of CoreValve predicted risk of moderate/severe vs mild/no AR (OR 1.61; 95% CI 1.21-2.13)
- Patients with moderate/severe AR had higher 30-day mortality (11.1%) than those with mild AR (5.8%) or no AR (5.2%; *P* = .006)
- Moderate/severe AR predicted mortality in the Sapien group (HR 1.97; 95% CI 1.47-2.61) but not in the CoreValve group

Implications: Risk of AR after TAVR and its association with mortality depends on the type of device implanted.

Dworakowski R, et al. *Heart.* 2014;Epub ahead of print.

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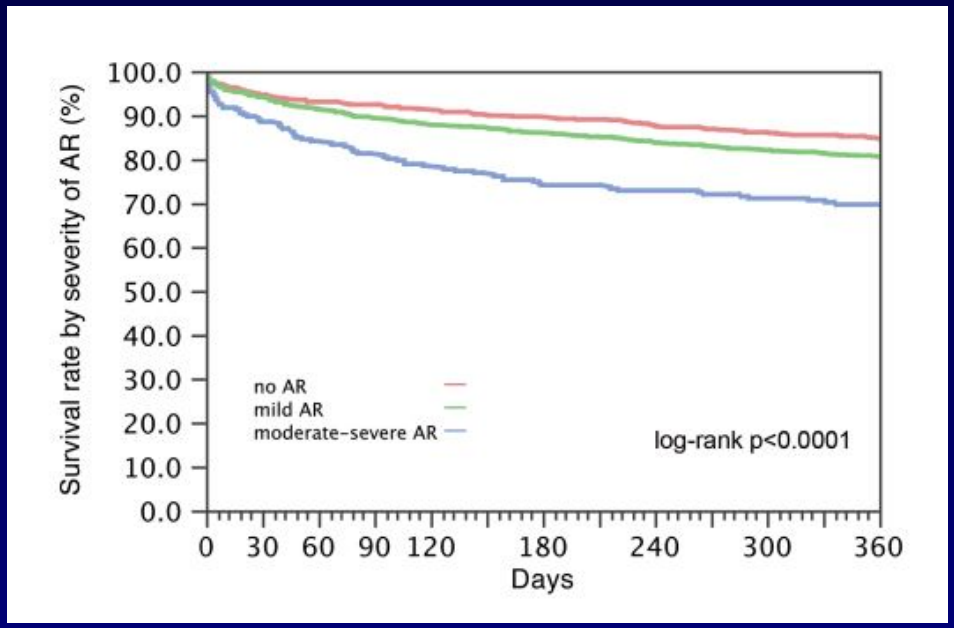
ORIGINAL ARTICLE

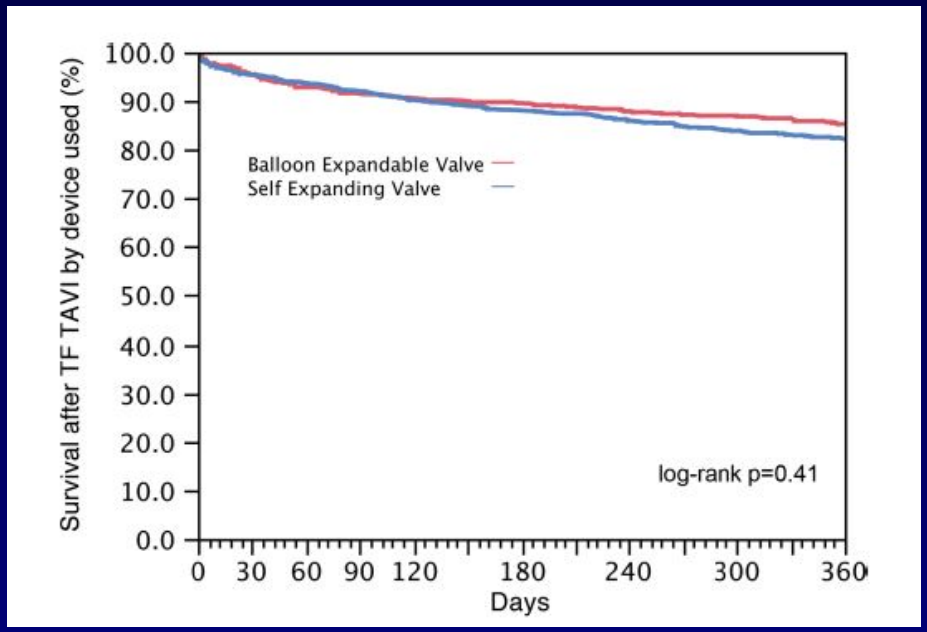
Device-dependent association between paravalvar aortic regurgitation and outcome after TAVI

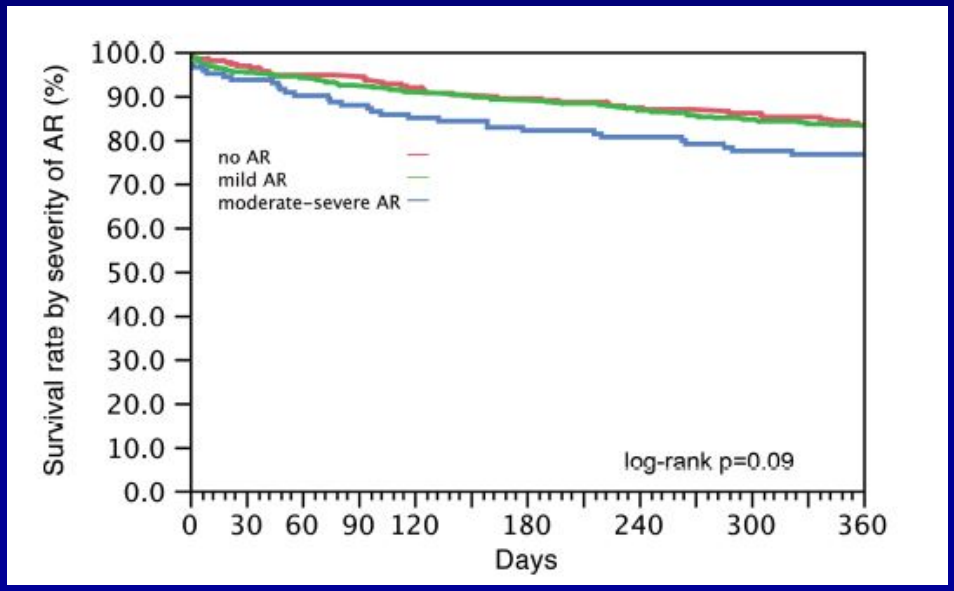
Rafal Dworakowski,[1] Olaf Wendler,[1] Brian Halliday,[1] Peter Ludman,[2] Mark DeBelder,[3] Simon Ray,[4] Neil Moat,[5] Jan Kovac,[6] Tomasz Spyt,[6] Uday Trivedi,[7] David Hildick-Smith,[7] Dan Blackman,[8] Damian Marlee,[9] David Cunningham,[9] Philip A MacCarthy[1]

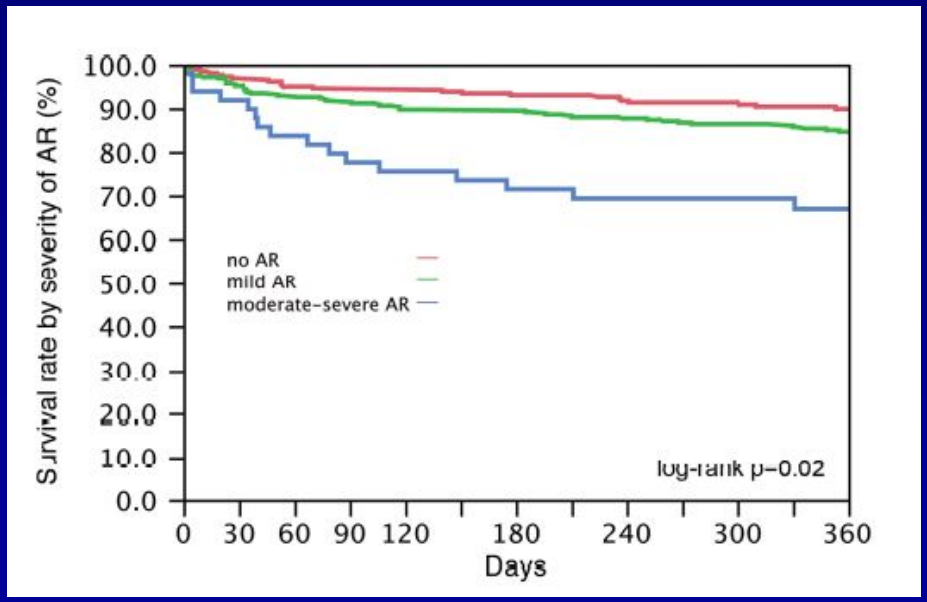
Table 3 Predictors of moderate/severe aortic regurgitation versus no/mild AR (nominal logistic regression, effect likelihoods ratio test for multivariate analysis, χ^2=43.3, p<0.0001)

	Multivariate analysis		
Variables	OR	95% CI	p Value
Height (per 0.01 m increase)	0.12	0.02 to 0.54	0.006
Aortic annulus dimension (per 1 mm increase)	0.92	0.86 to 0.99	0.02
Aortic peak pressure gradient (per 1 mm Hg increase)	0.99	0.98 to 0.99	0.012
Self-expanding valve used	1.61	1.21 to 2.13	0.008


Survival rate by severity of AR (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
no AR
mild AR
moderate-severe AR
log-rank p<0.0001
0 30 60 90 120 180 240 300 360
Days


Survival after TF TAVI by device used (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
Balloon Expandable Valve
Self Expanding Valve
log-rank p=0.41
0 30 60 90 120 180 240 300 360
Days


Survival rate by severity of AR (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
no AR
mild AR
moderate-severe AR
log-rank p=0.09
0 30 60 90 120 180 240 300 360
Days


Survival rate by severity of AR (%)
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0
no AR
mild AR
moderate-severe AR
log-rank p=0.02
0 30 60 90 120 180 240 300 360
Days

TAVR

SAPIEN vs COREVALVE

	Sapien N	Core N
Ease of Use	**+**	**+**
Data, data..	**+**	
Comparison	**+**	