

Cerebral Protection in TAVR: Which Patient Category or Anatomical Subset?

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Disclosure Eberhard Grube, MD

Speaker Bureau/Advisory Board:

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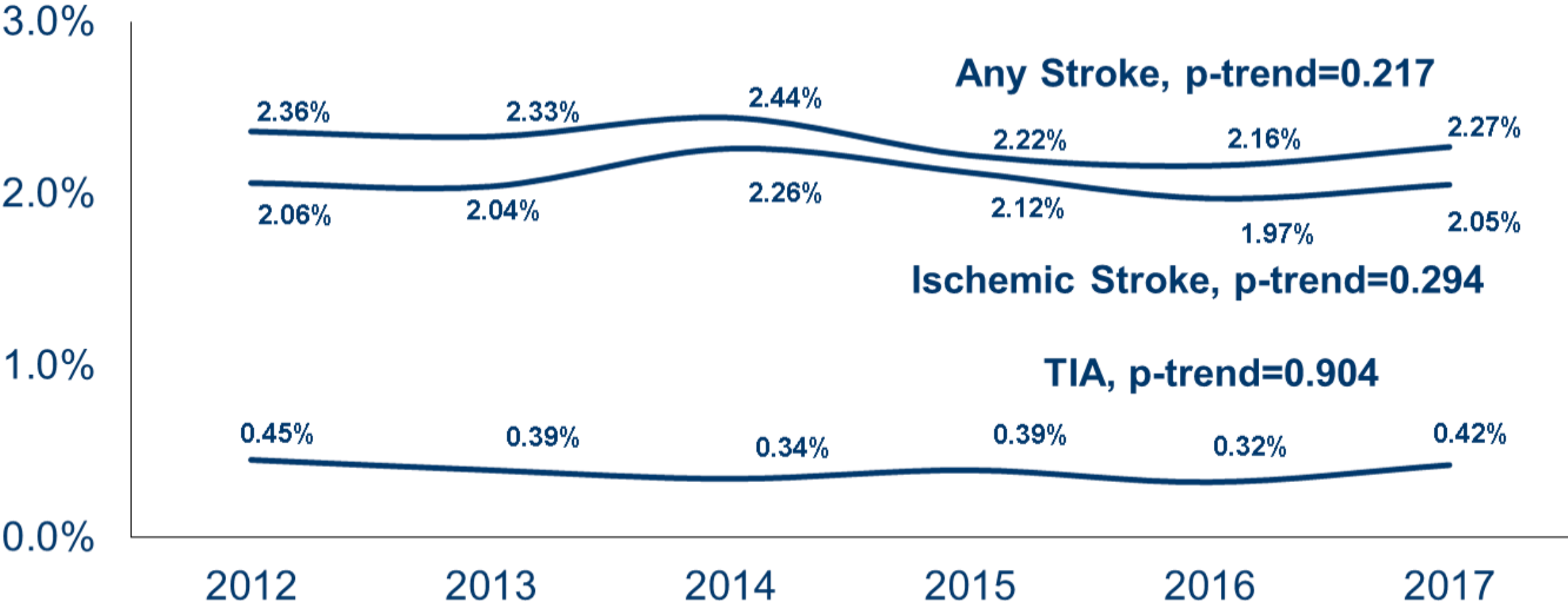
Equity Interest:

InSeal Medical: E, AB,
MTEx: E, AB, SB
Cardiovalve: E, SB,
Claret: E, AB
Shockwave: E, AB
Valve Medical: E, AB
Millipede E, AB, SB
Pie-Cardia: E, AB, SB
Imparative Medical: E, AB
Ancora: E, AB, SB

Key

G – Grant and or Research Support E – Equity Interests S – Salary, AB – Advisory Board
C – Consulting fees, Honoraria R – Royalty Income I – Intellectual Property Rights
SB – Speaker's Bureau O – Ownership OF – Other Financial Benefits

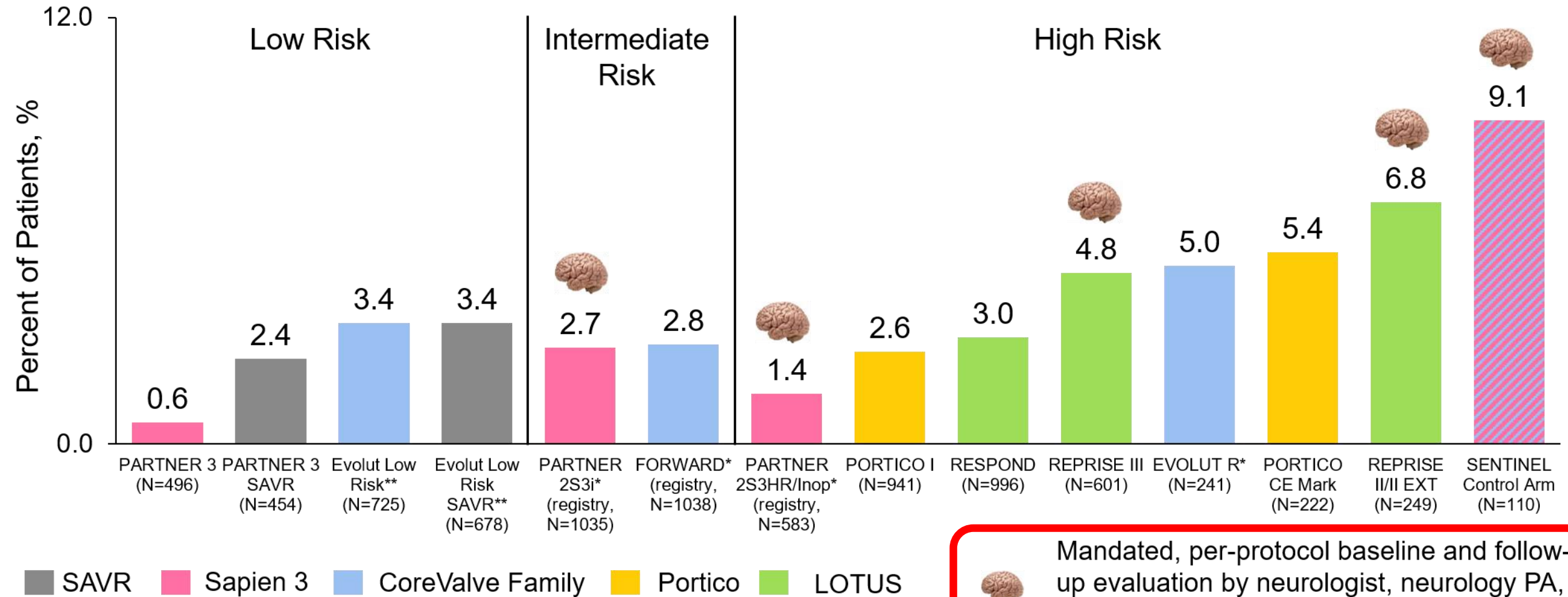
Real-World Results Demonstrate that Stroke Remains an Issue with TAVR



*2017 data through May

Data from the STS/ACC TVT Registry: 2290 30-day strokes reported among N=101,430 patients who underwent TAVR at 521 US sites from Nov 2011 – June 2017

Stroke Rates Problematic Amongst Contemporary TAVR Trials



Stroke is Associated with Significant Increases in 30-Day Outcomes including Mortality in the CENTER Collaboration

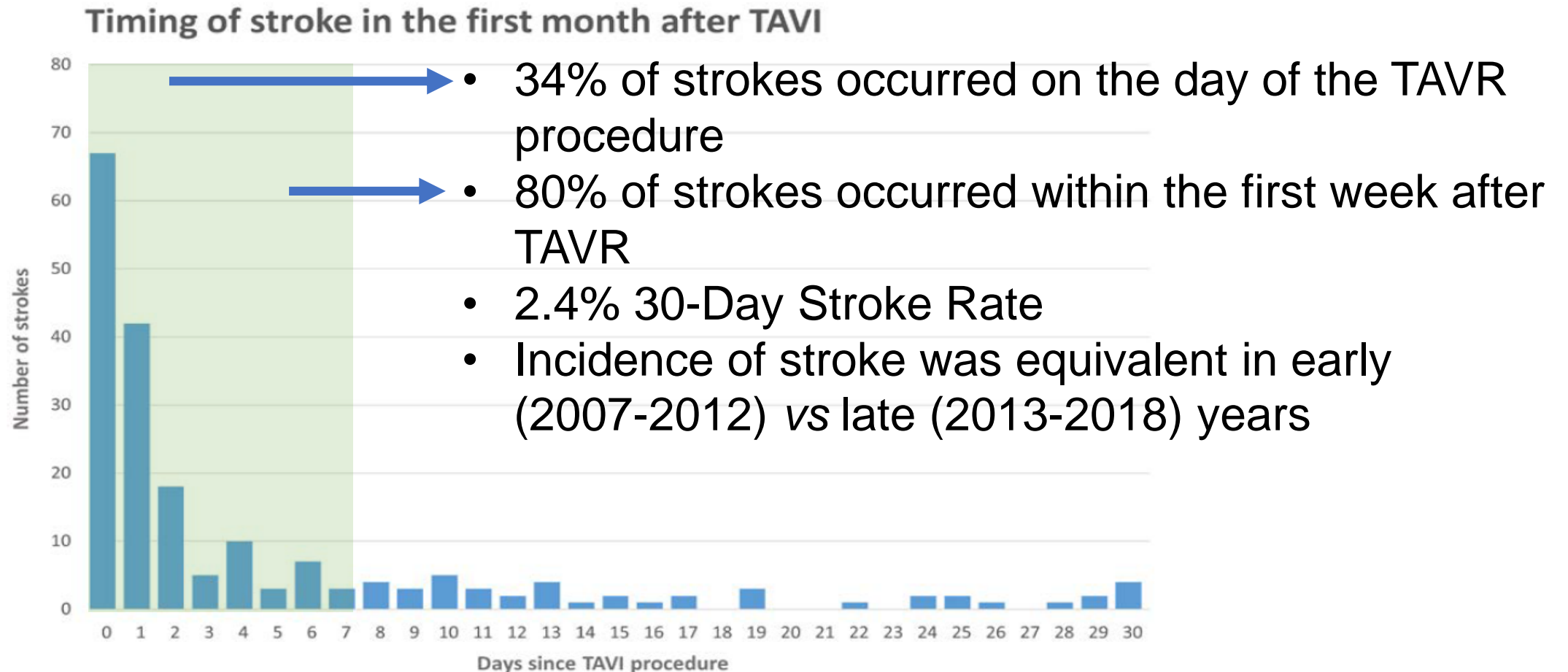
	No Stroke at 30 d (n=10 721)	Stroke at 30 d (n=261)	OR (95% CI)	P Value
Mortality	570 (5%)	61 (25%)	6.0 (4.4–8.1)	<0.001
Major or life-threatening bleeding	592 (7%)	24 (12%)	1.9 (1.3–3.0)	0.003
Myocardial infarction	71 (0.9%)	2 (0.8%)	1.2 (0.3–5.0)	0.79
New-onset atrial fibrillation	51 (3%)	5 (16%)	5.2 (1.9–14.1)	0.001
Permanent pacemaker implantation	1178 (14%)	24 (14%)	1.0 (0.6–1.5)	0.81

Incidence and OR (95% CI). OR indicates odds ratio.

Independent predictors of stroke at 30 days: 1.History of cerebrovascular events/TIA and 2.Glomerular filtration rate of <30 mL/min per 1.73m².

N=10982 patients undergoing TF-TAVR with Edwards’ balloon-expandable valves or Medtronic self-expanding valves between 2007-2018 from 3 national registries and 7 local registries or prospective clinical trials

CENTER Collaboration Demonstrated that 80% of TAVR-Related Stroke Occurred in the First Week After TAVR



N=10982 patients undergoing TF-TAVR with Edwards' balloon-expandable valves or Medtronic self-expanding valves between 2007-2018 from 3 national registries and 7 local registries or prospective clinical trials

Stroke Rates Not Declining with Newer Generation Valves

	Early generation TAVI devices	Newer generation TAVI devices	Newer generation vs early generation	
			Crude	
	n=391	n=391	HR (95% CI)	P value
30-day follow-up				
Early safety composite end point, n (%)	83 (21.2)	81 (20.8)	0.98 (0.72 to 1.33)	0.876
All-cause death, n (%)	19 (4.9)	15 (3.9)	0.80 (0.41 to 1.58)	0.519
Cardiovascular death, n (%)	18 (4.6)	11 (2.8)	0.62 (0.29 to 1.31)	0.210
CVE, n (%)	17 (4.4)	17 (4.4)	1.00 (0.51 to 1.97)	0.989
Stroke	16 (4.1)	15 (3.9)	0.94 (0.47 to 1.91)	0.868
Disabling stroke	14 (3.6)	9 (2.3)	0.64 (0.28 to 1.49)	0.301
Non-disabling stroke	2 (0.5)	6 (1.6)	3.05 (0.61 to 15.09)	0.172
Transient ischaemic attack	1 (0.3)	2 (0.5)	2.02 (0.18 to 22.25)	0.567
Myocardial infarction, n (%)	2 (0.5)	2 (0.5)	1.00 (0.14 to 7.10)	1.000
All-cause death or CVE, n (%)	26 (6.7)	29 (7.5)	1.13 (0.66 to 1.91)	0.661

Prospective, real-world registry with propensity-matched populations, 30-day safety and efficacy study of 782 patients undergoing TAVR between 2007 and 2016 at a single center in Switzerland. All adverse outcomes were adjudicated by an independent CEC. Early-generation devices: CoreValve, SAPIEN, SAPIEN XT. Newer-generation devices: SAPIEN 3, LOTUS, Evolut R

Stroke Rate Not Decreasing with Number of Procedures Performed by a Team

- Retrospective observational study
- 8,771 TAVR procedures performed in the state of New York
- 5,916 elective TAVR procedures
- 207 operators
- Jan 2012- Dec 2016

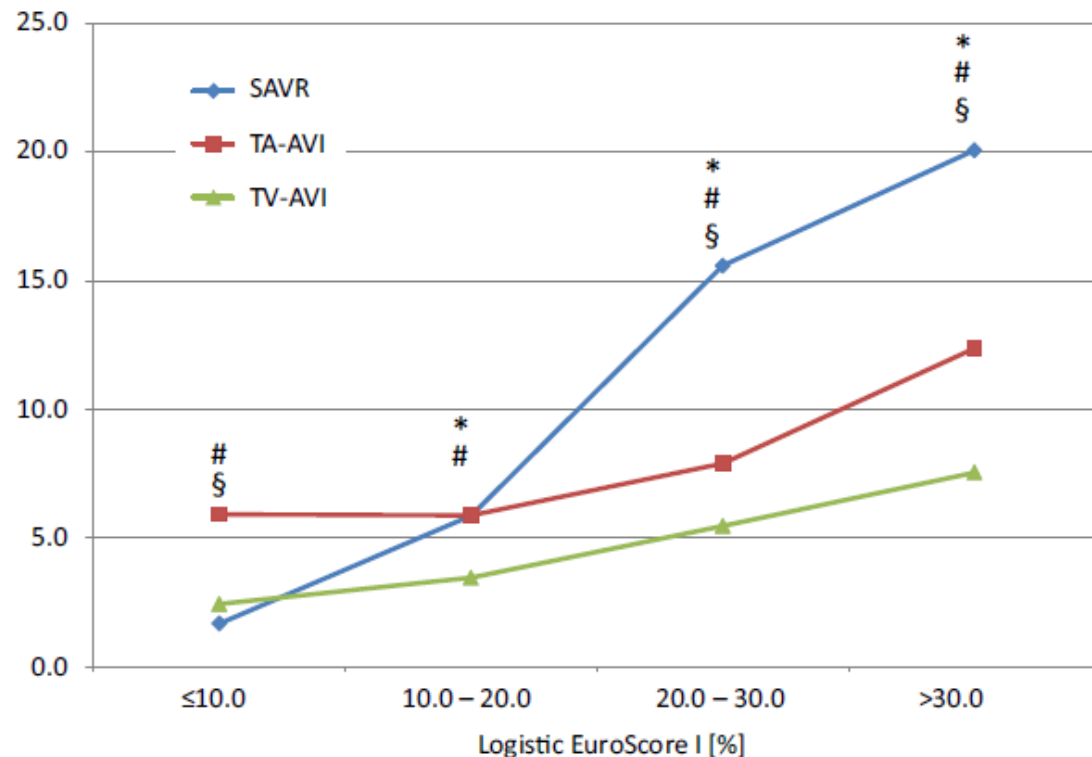
In-Hospital Outcomes for Elective TAVR

		By Volume Groups		
	All Patients (N = 5,916)	Low (1-23) (n = 1, 973)	Medium (24-79) (n = 1, 860)	High (≥80) (n = 2,083)
In-hospital death		Trend toward lower mortality		
Events (%)	115 (1.9%)	53 (2.7%)	32 (1.7%)	30 (1.4%)
OR (95% CI)	—	Reference	0.69 (0.42-1.13)	0.59 (0.32-1.08)
Stroke		No trend toward lower stroke rate		
Events (%)	94 (1.6%)	29 (1.5%)	37 (2.0%)	28 (1.3%)
OR (95% CI)	—	Reference	1.11 (0.63-1.95)	0.62 (0.30-1.30)
Death, MI, or stroke		Significantly lower risk for death, stroke or acute MI		
Events (%)	202 (3.4%)	79 (4.0%)	68 (3.7%)	55 (2.6%)
OR (95% CI)	—	Reference	0.90 (0.62-1.31)	0.59 (0.37-0.93)

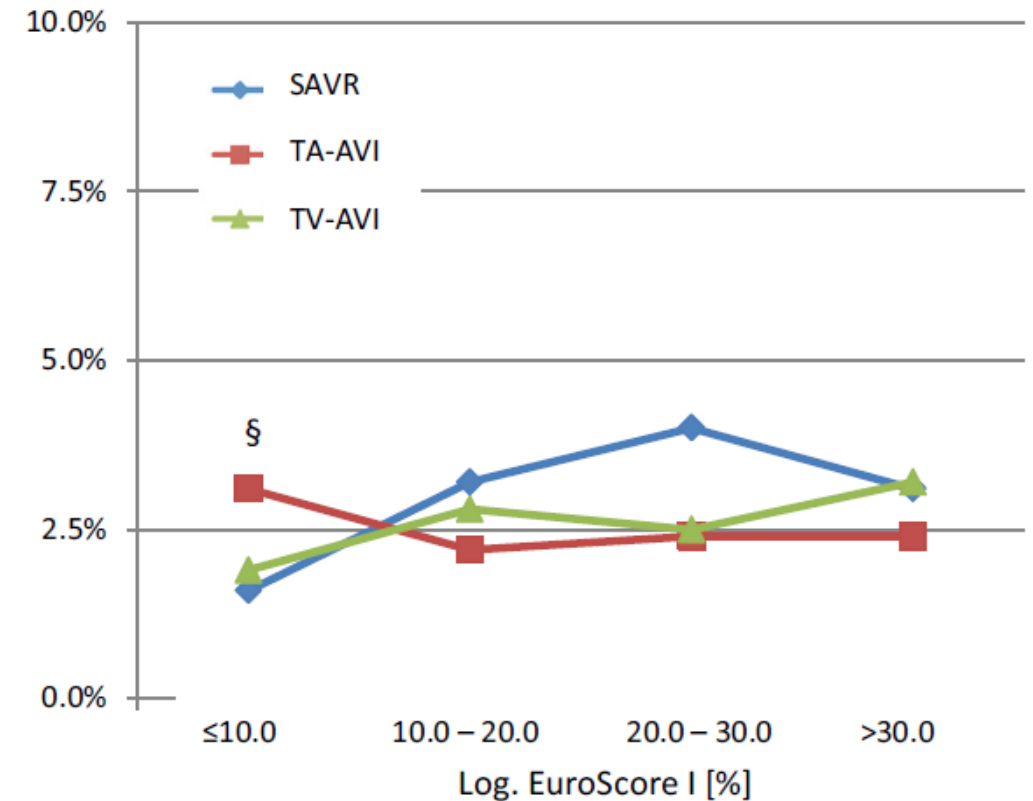
Events (%) and ORs from adjusted analyses are presented.
CI = confidence interval; MI = myocardial infarction; OR = odds ratio; TAVR = transcatheter aortic valve replacement.

Stroke Not Associated with Surgical Risk Score in TAVR or SAVR

In-Hospital Mortality



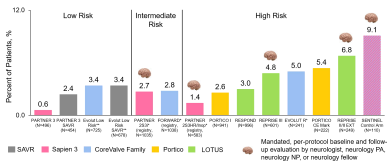
In-Hospital Stroke



20,340 patients receiving TAVR or SAVR in Germany in 2013

TA-AVI=transapical aortic valve implantation; TV-AVI=transvascular aortic valve implantation. Statistical significance ($p < 0.05$) between groups are marked with asterisk for TV-AVI vs. SAVR; hash symbol for TV-AVI vs. TAAVI; section sign for TA-AVI vs. SAVR. Möllmann, H. et al. *Clin Res Cardiol* (2016) 105:553–559.

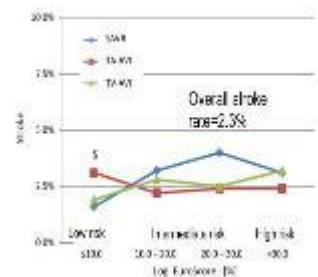
Stroke in TAVR: Bottom Line



- Stroke rates in real-world registries and contemporary trials range from ~1-9%.



- Rates are not declining with newer generation valves.¹
- Stroke is independent of experience and operator volume.²⁻⁴
- Surgical risk score not associated with stroke risk in TAVR or SAVR.⁵⁻⁸


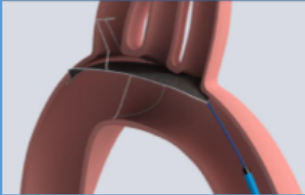





What can be done to improve this?

¹Pilgrim et al. *Open Heart* 2018;5:e000695; ²Bestehorn K et al. 2017 *EuroIntervention*;13:914-920; ³Carroll J., presented at TAVI 2017; ⁴Salemi et al. 2018. *J Am Coll Cardiol Interv.* 2019 Jan 14;12(1):90-97.

⁵Williams C. presented at ACC 2016; ⁶Kodali S, presented at ACC 2015; ⁷Zein M et al, ACTA 2015; ⁸Möhlmann, H. et al. *Clin Res Cardiol* (2016) 105:553–559

Cerebral Embolic Protection Devices to Reduce Peri-Procedural Strokes with TAVR

Company and Product	Boston Scientific Sentinel 	Keystone TriGuard 	Edwards Embrella 	ICS Emblok 	Transverse Point-Guard 
EU Status	CE Mark 97% market share	CE Mark 3% market share	CE Mark <3% market share	FIM first clinical case March 15, 2017	Pre-clinical/prototype
US Status	IDE study completed Positive FDA Panel Feb 23, 2017	IDE trial underway	No IDE yet	No IDE yet	No IDE yet
Access	6 Fr Right Radial	9Fr TF	Right Radial	12Fr TF sheath	TF
Debris	Captures and removes	Deflects downstream	Deflects downstream	Captures and removes	Deflects downstream
Placement and Interaction with TAVR devices	Not in aortic arch	Sits in aortic arch. Devices must pass over and back across	Sits in aortic arch. Devices must pass over and back across	Sits in ascending aorta Devices must pass over and back across	Sits in aortic arch. Devices must pass over and back across

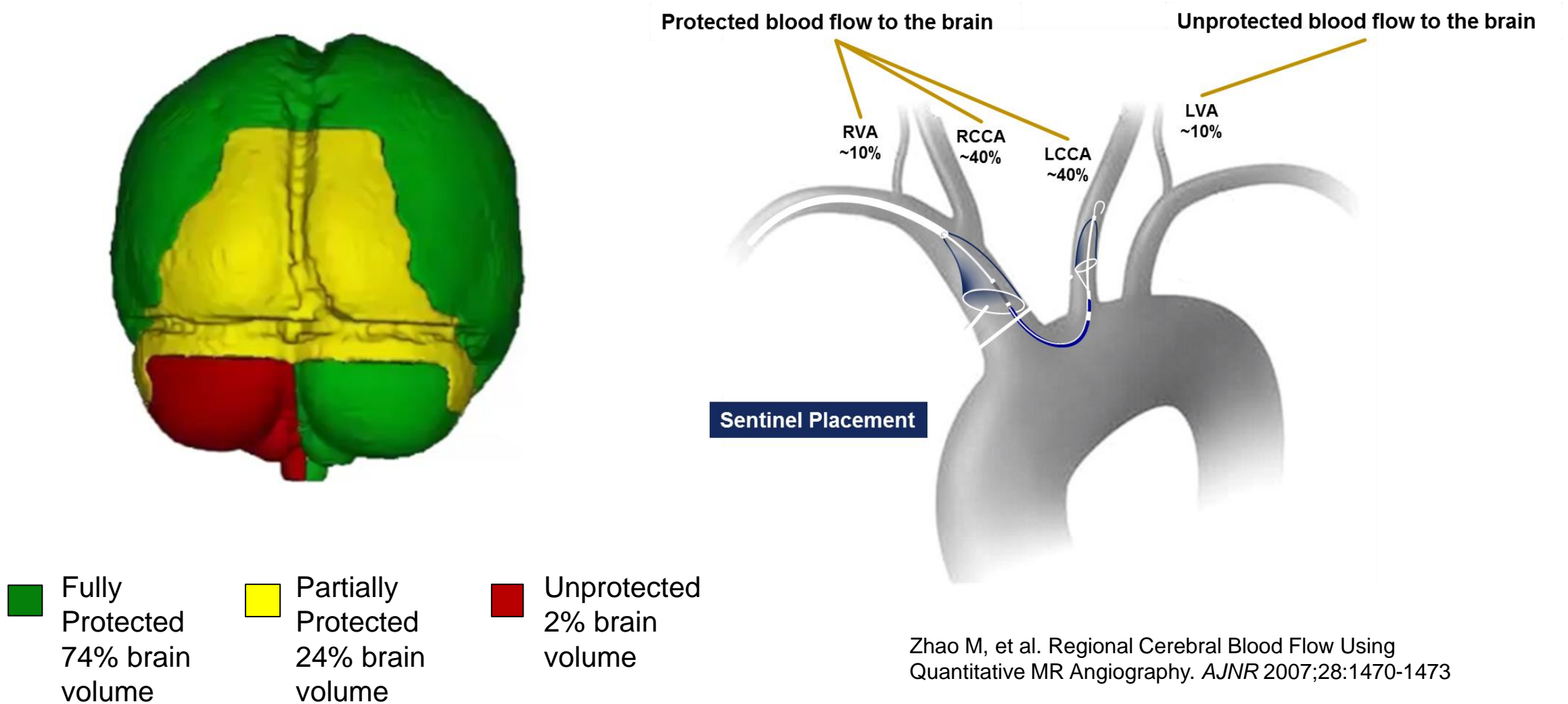
SENTINEL Cerebral Protection System (CPS)



- Two independent filters capture & remove embolic material
- Polyurethane filter, pore size = 140 μm
- Standard right trans-radial sheath access (6F)
- One size accommodates most vessel sizes; fits $\sim 90\%$ of anatomies
- Deflectable compound-curve catheter facilitates cannulation of LCC
- Minimal profile in aortic arch (little interaction with other devices)

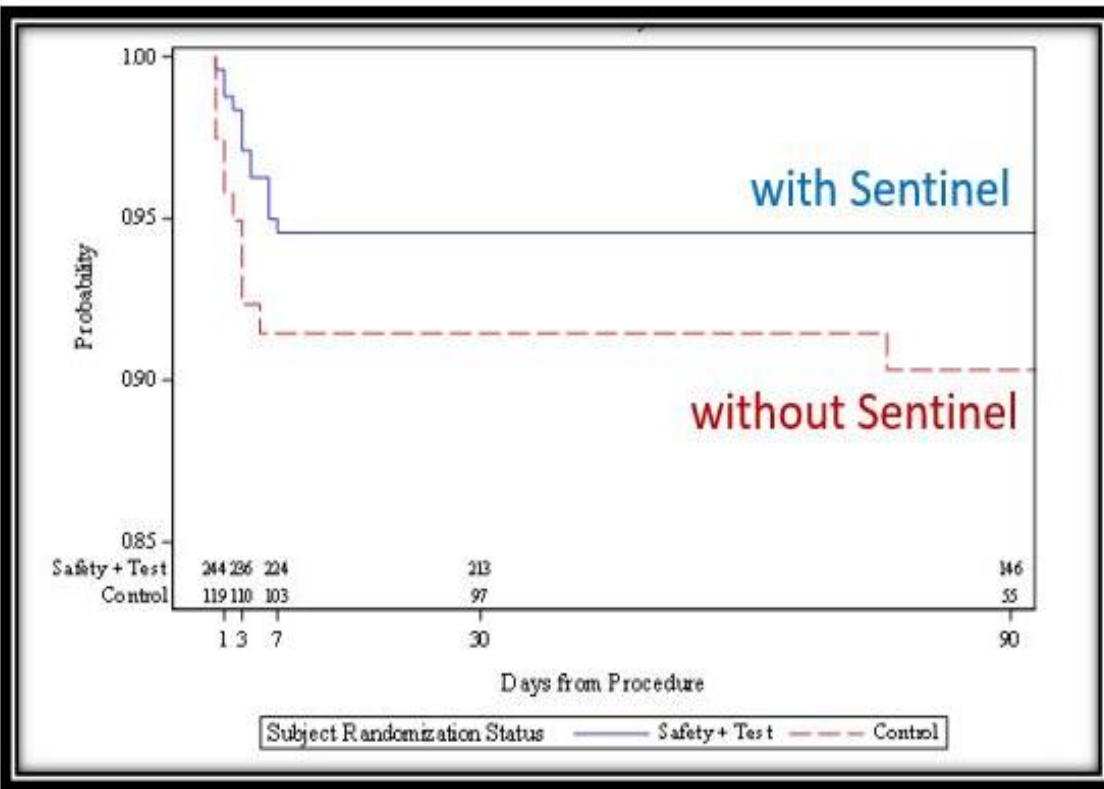


SENTINEL CPS Filters Protection

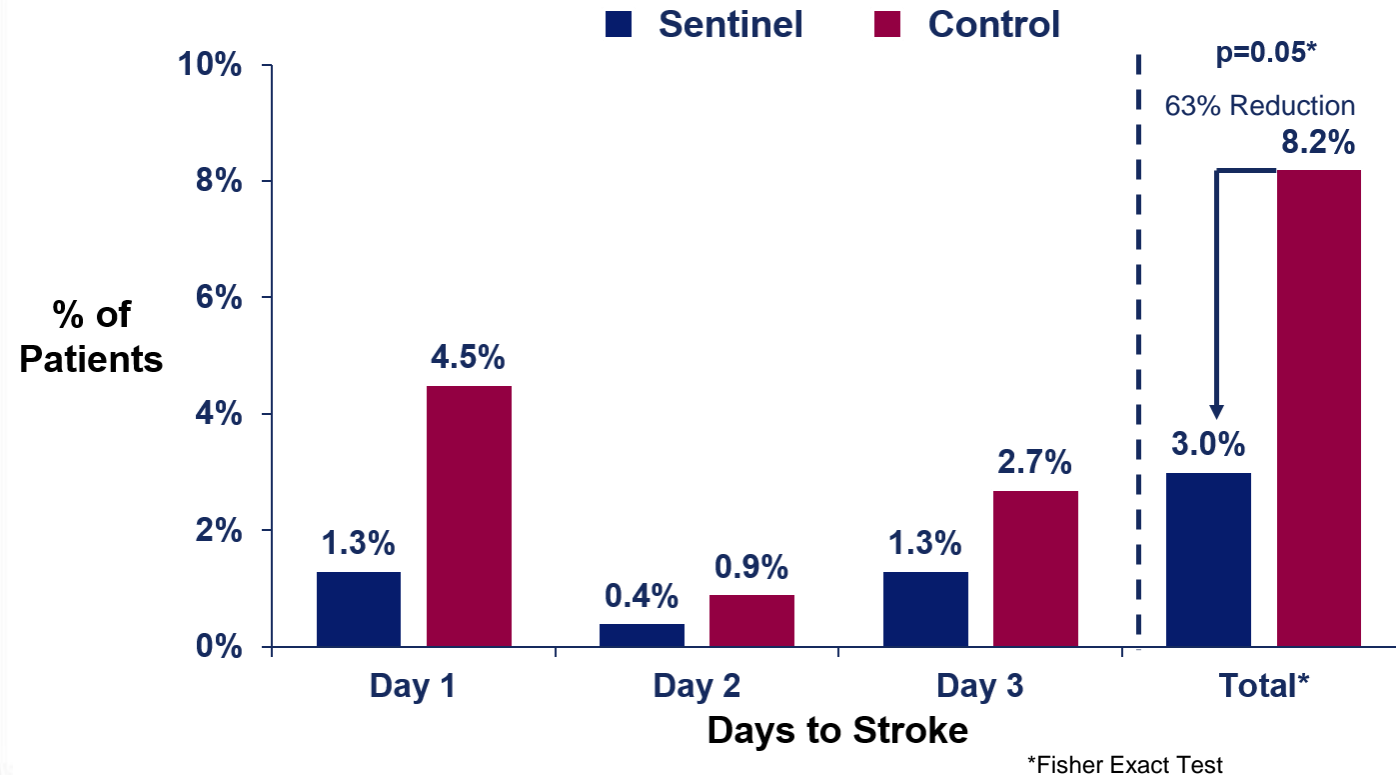


Zhao M, et al. Regional Cerebral Blood Flow Using Quantitative MR Angiography. *AJNR* 2007;28:1470-1473

SENTINEL Study: “Procedural Stroke”

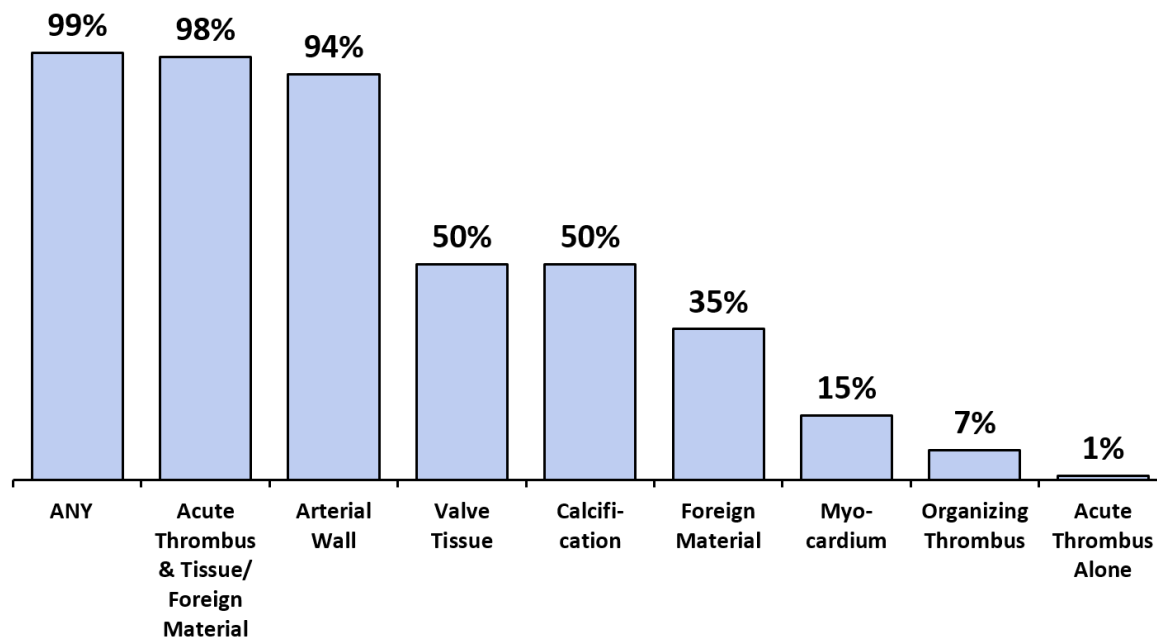


95% of SENTINEL patients were evaluated by neurologists
Clinical Events Committee included 2 stroke neurologists

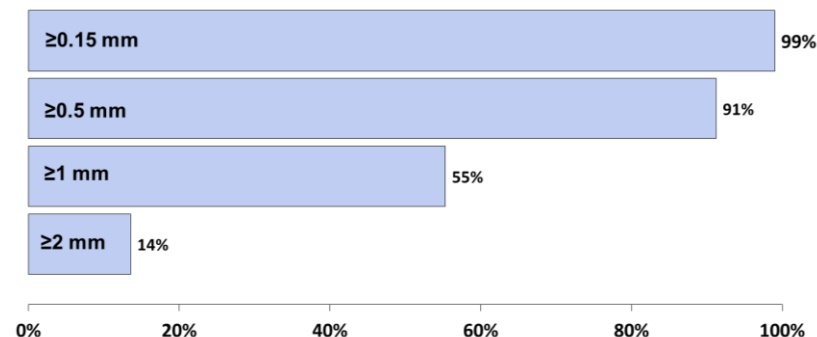


Debris Captured in 99% of TAVR Patients in the SENTINEL IDE

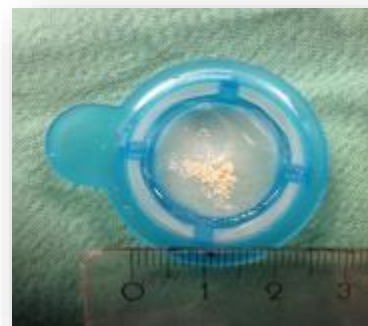
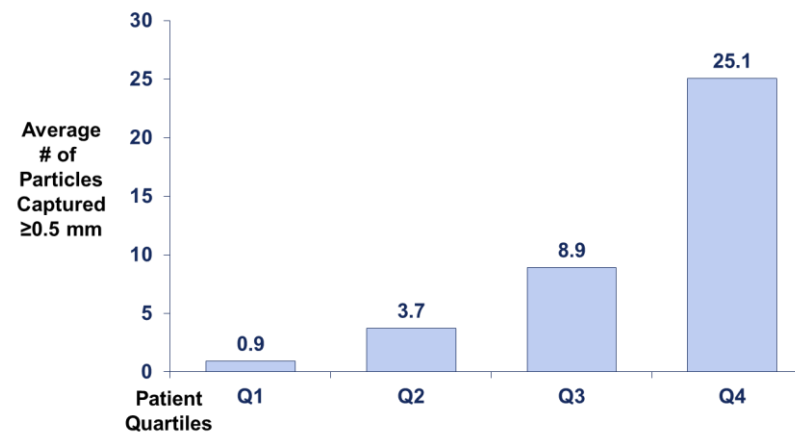
Patients with Captured Debris (%)



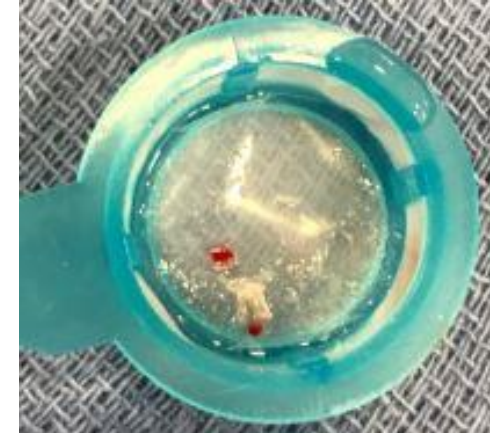
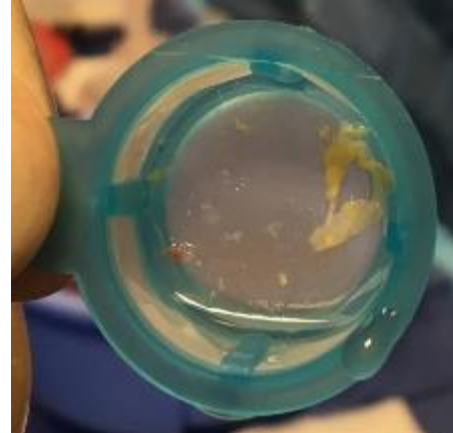
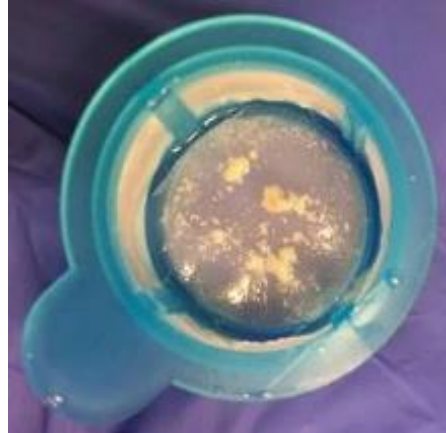
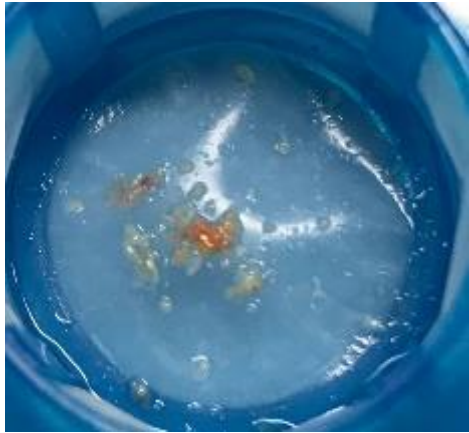
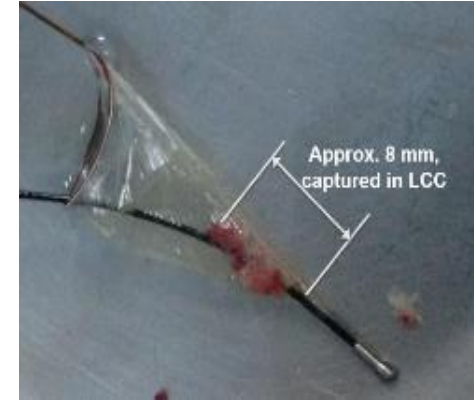
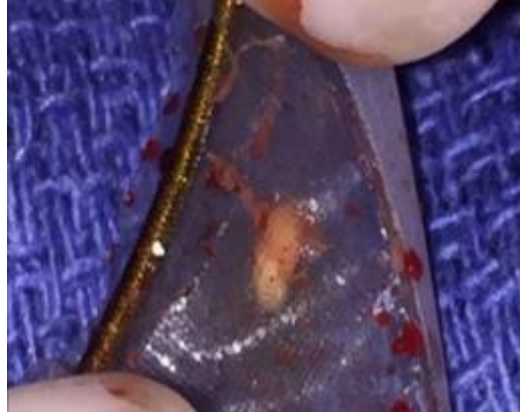
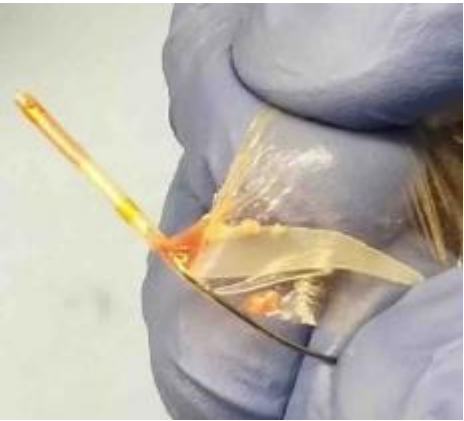
Percent of Patients with at Least One Particle of Given Size



1 in 4 Patients had an average of 25 Particles ≥ 0.5 mm in Size Captured and Removed



Debris Captured and Removed by SENTINEL CPS



Real-world Results at Cleveland Clinic Reiterate Low Occurrence of Stroke with Routine Use of SENTINEL CPS

TAVR by the numbers at Cleveland Clinic in 2018

- Sentinel used in ~470 (95%) of 494 patients who underwent TAVR
- 60% High risk, 40% Intermediate risk
- 90% Conscious Sedation

30-Day Outcomes

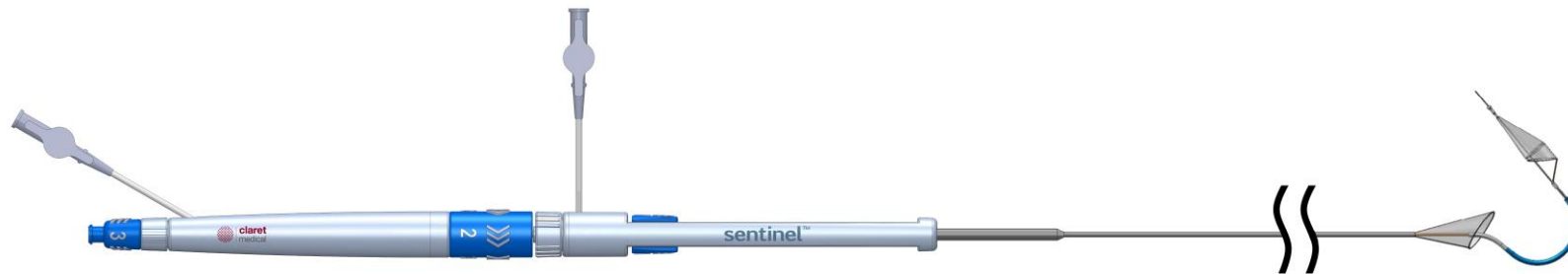
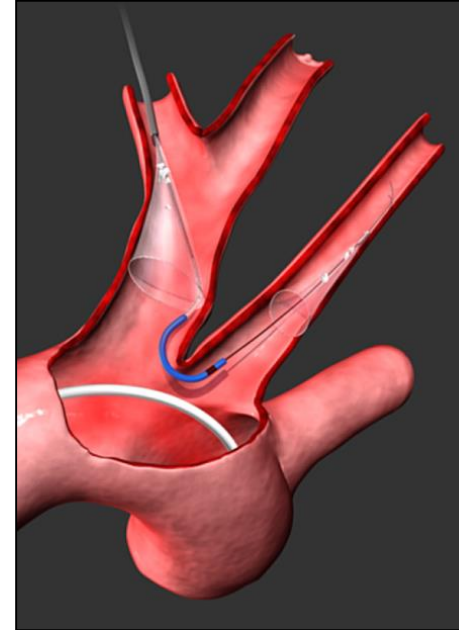
0.2% Mortality

0.2% All Stroke

0.8% Aortic Regurgitation ($\geq 2+$)

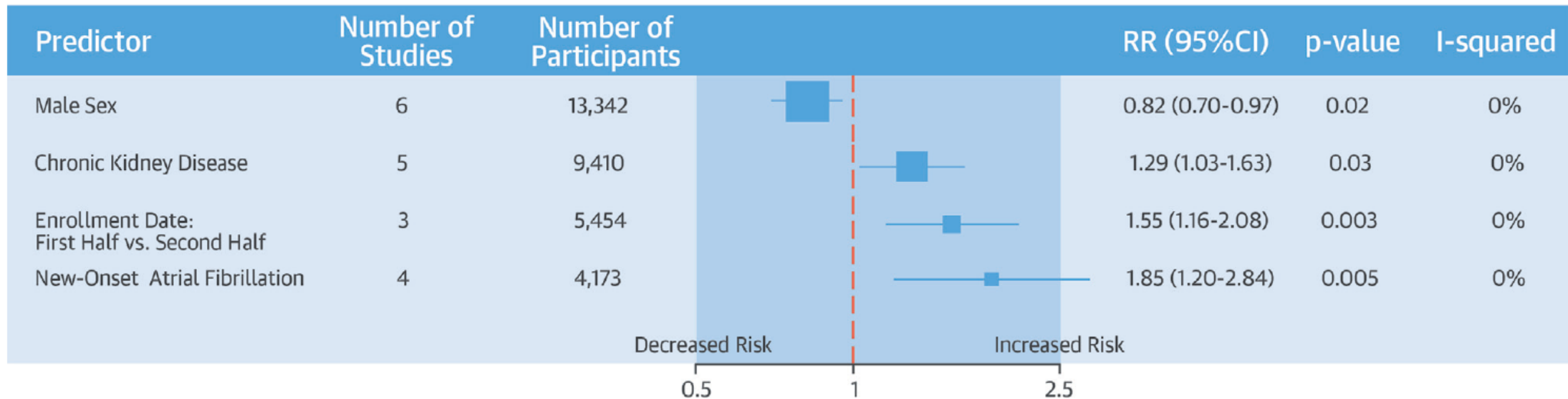
5% New PPM

Clinical data demonstrates efficacy of cerebral embolic protection.
Now the question is, who should get it?



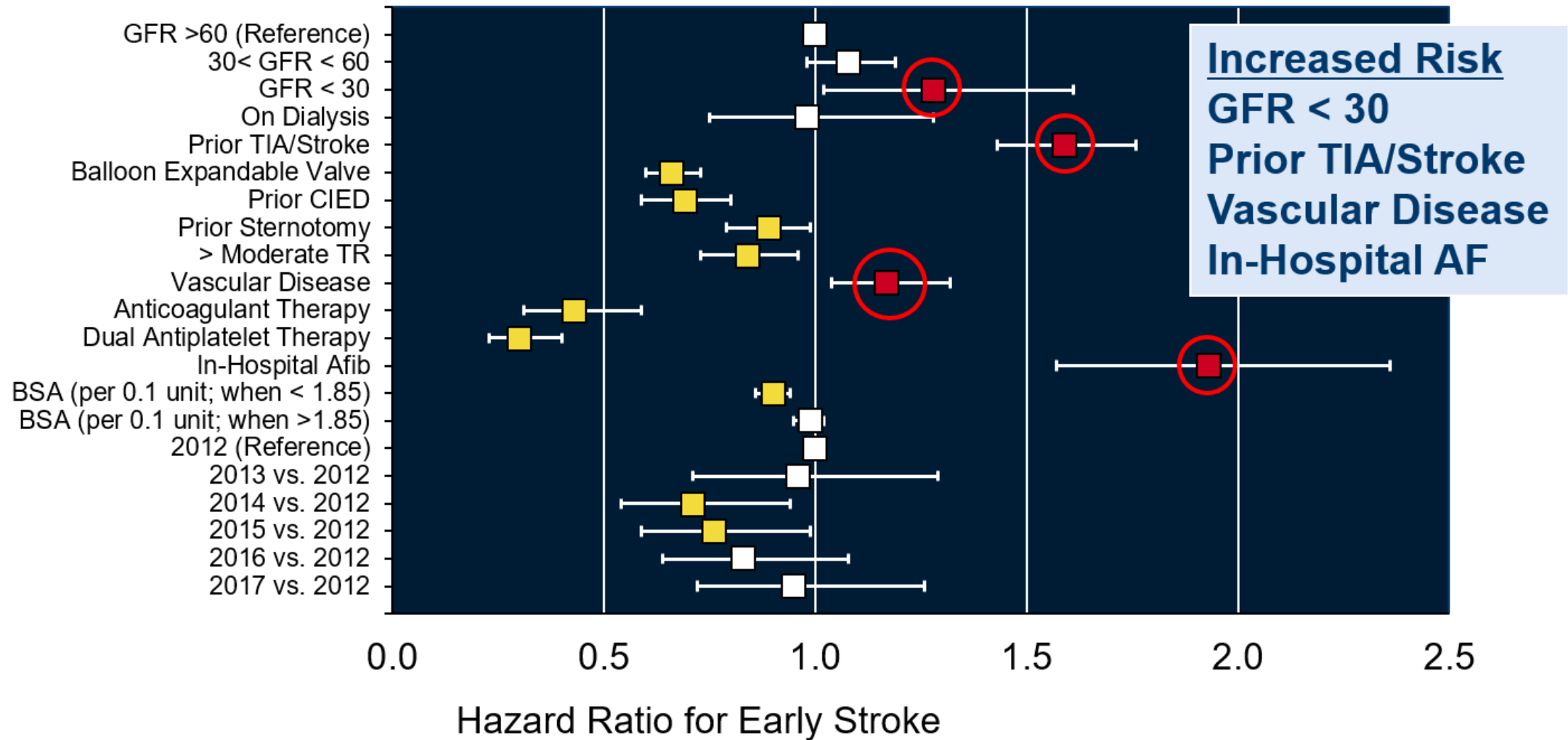
Meta-Analysis Identified Predictors of Stroke Post-TAVR:

Women, Patients with CKD, Patients treated in the second half of a center's experience, and Patients with New-Onset Atrial Fibrillation Post-TAVR



64 studies involving 72,813 patients (2,385 patients with a cardiovascular event within 30 days post-TAVR) were analyzed. Valve type (balloon-expandable vs self-expanding) and approach (TF vs non-TF) did not predict cerebrovascular events.

Risk Factors for Stroke Identified in the TVT Registry



Data from the STS/ACC TVT Registry: 2290 30-day strokes reported among N=101,430 patients who underwent TAVR at 521 US sites from Nov 2011 – June 2017. Data for TF-TAVR

Older and Sicker Patients May Benefit More From CEP in TAVR Based on In-Hospital Risk-Prediction Model

Development and Application of a Risk Prediction Model for In-Hospital Stroke After Transcatheter Aortic Valve Replacement: A Report From The Society of Thoracic Surgeons/American College of Cardiology Transcatheter Valve Therapy Registry



Vinod H. Thourani, MD, Sean M. O'Brien, PhD, John J. Kelly, MD, David J. Cohen, MD, MSc, Eric D. Peterson, MD, MPH, Michael J. Mack, MD, David M. Shahian, MD, Frederick L. Grover, MD, John D. Carroll, MD, J. Matthew Brennan, MD, MPH, Jessica Forcillo, MD, MSc, Suzanne V. Arnold, MD, Sreekanth Vemulapalli, MD, Susan Fitzgerald, RN, MS, David R. Holmes, MD, Joseph E. Bavaria, MD, and Fred H. Edwards, MD

Significant Predictors of Stroke Included:

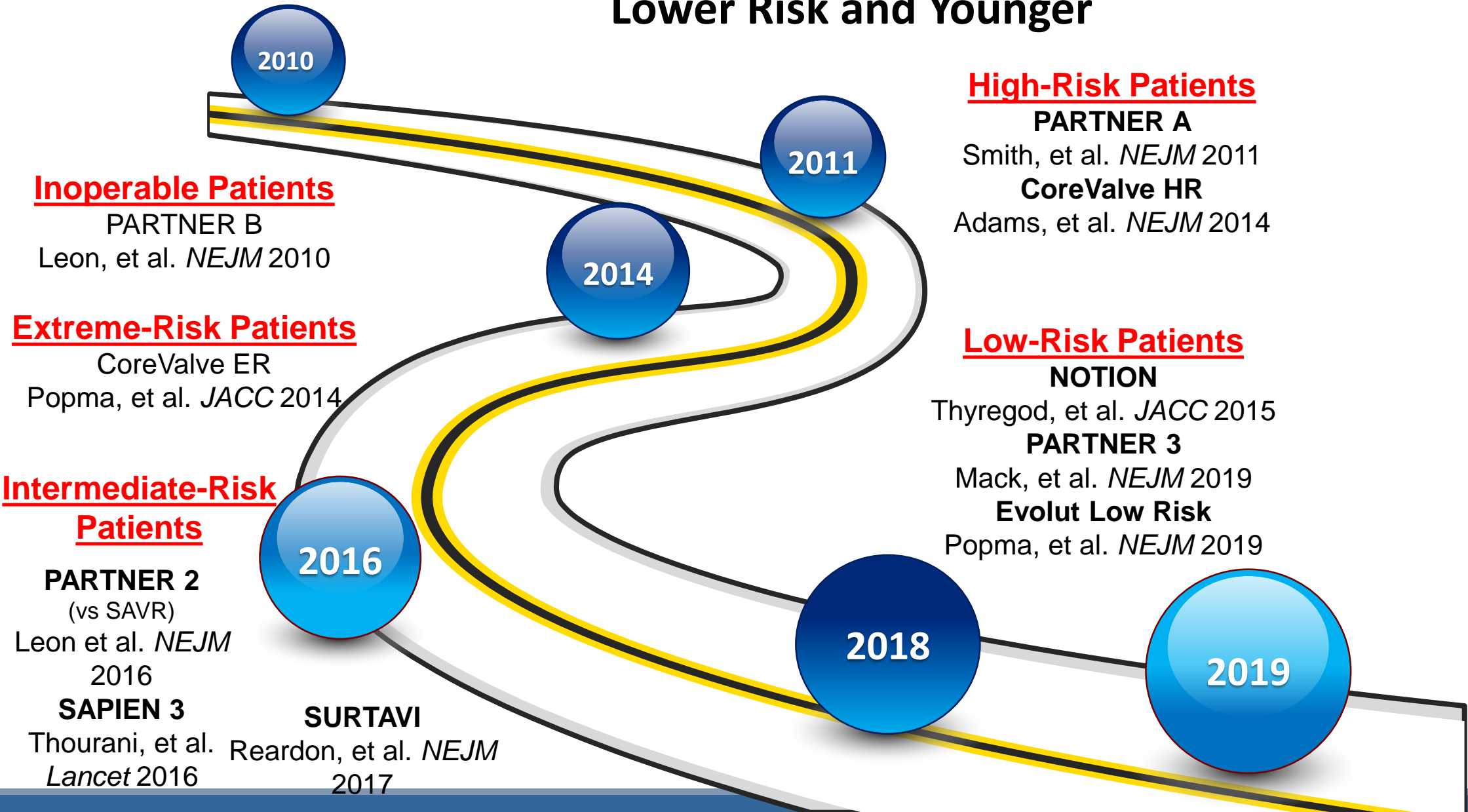
- Alternative access
- **Prior Stroke or TIA**
- Procedural acuity
- **Smoking**
- Porcelain aorta
- **Peripheral arterial disease**
- **Advanced age (>75)**

97,600 patients from 521 U.S. sites in the STS/ACC TVT Registry. Median age was 82 years.

Limitations

- Neurologic exams were not standardized across sites; a higher site-specific odds ratio for in-hospital stroke may indicate a higher stroke rate or a more thorough neurologic evaluation.
- Patients enrolled in pivotal trials were not included in the TVT Registry which may have introduced selection bias.

Patients in Clinical Trials Have Evolved to be Lower Risk and Younger



Younger TAVR Patients with Strokes may have More Years to Live with a Disability

Evolut Low Risk

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

Average Age: 74 years

30-Day All-Stroke Rate: 3.4%

PARTNER 3

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

73 years

0.6%

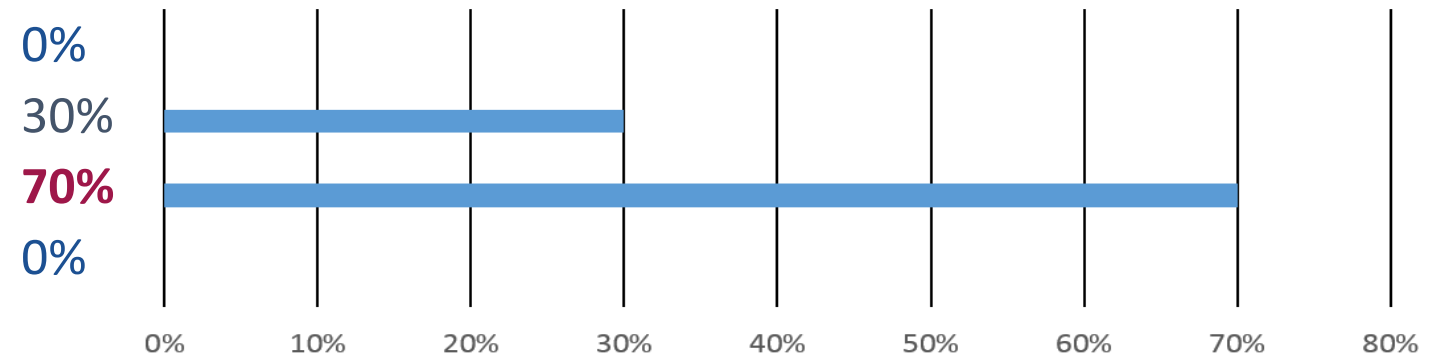
Stroke rates were low but not 0!

Procedural Strokes are a Significant Concern Among Patients

Audience Response from Cerebral Protection Session at ACC 2017:

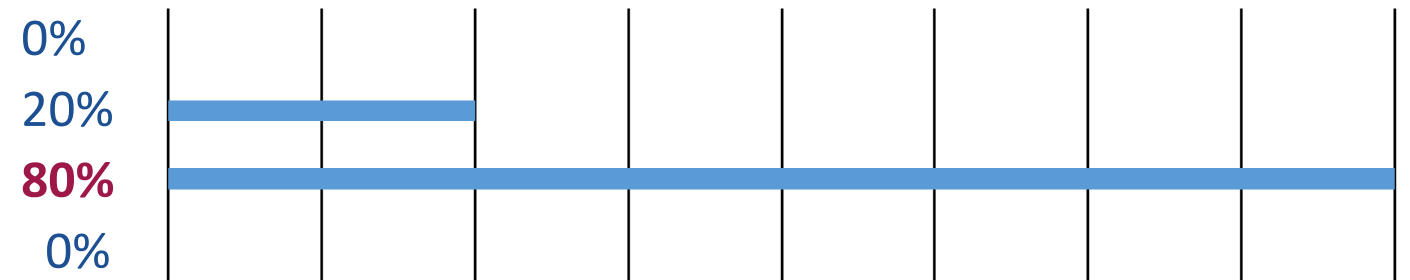
• *What is the biggest concern for your patients undergoing TAVR?*

1. Having general anesthesia:
2. Risk of dying:
- 3. Suffering stroke:**
4. Other:



• *Is cerebral protection necessary during TAVR?*

1. No, never:
2. Maybe (continue reviewing data):
- 3. Yes, in selected patients:**
4. Yes, always:



Who Should have Cerebral Embolic Protection with TAVR?

**Older, sicker
patients**

More predictors of
stroke

OR

**Younger, healthier
patients**

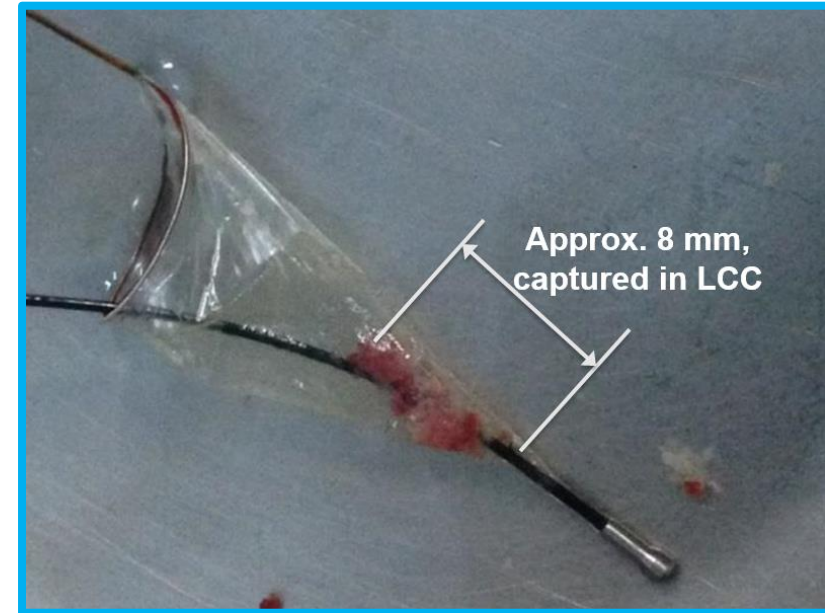
Longer to live with a
potential disability

Who Should have Cerebral Embolic Protection with TAVR?

Everyone!

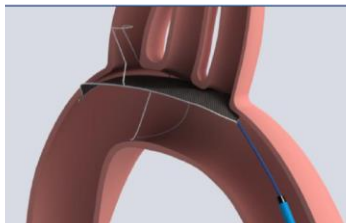
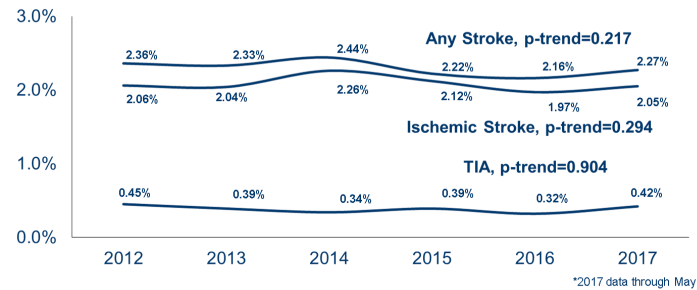


Would you take a chance and drive without a seatbelt?



You never know when You'll need protection!

Summary



- Stroke remains an issue in real-world registries and clinical trials with contemporary devices.
- Stroke has devastating consequences including higher risk of mortality and disability.
- Patients undergoing TAVR fear the risk of stroke over the risk of death.
- Cerebral embolic protection should be used in every eligible (anatomy-permitting) TAVR case.

Thank you very much for your attention!

