Keystone Heart
Cerebral Embolic Protection
CMS March 2019

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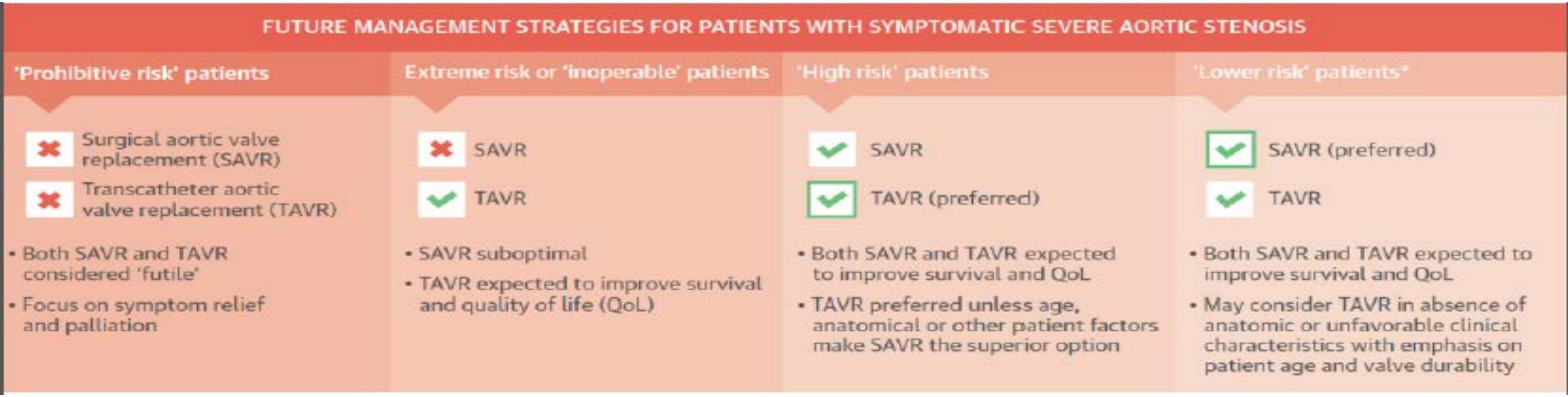
TAVR: Growing Indication

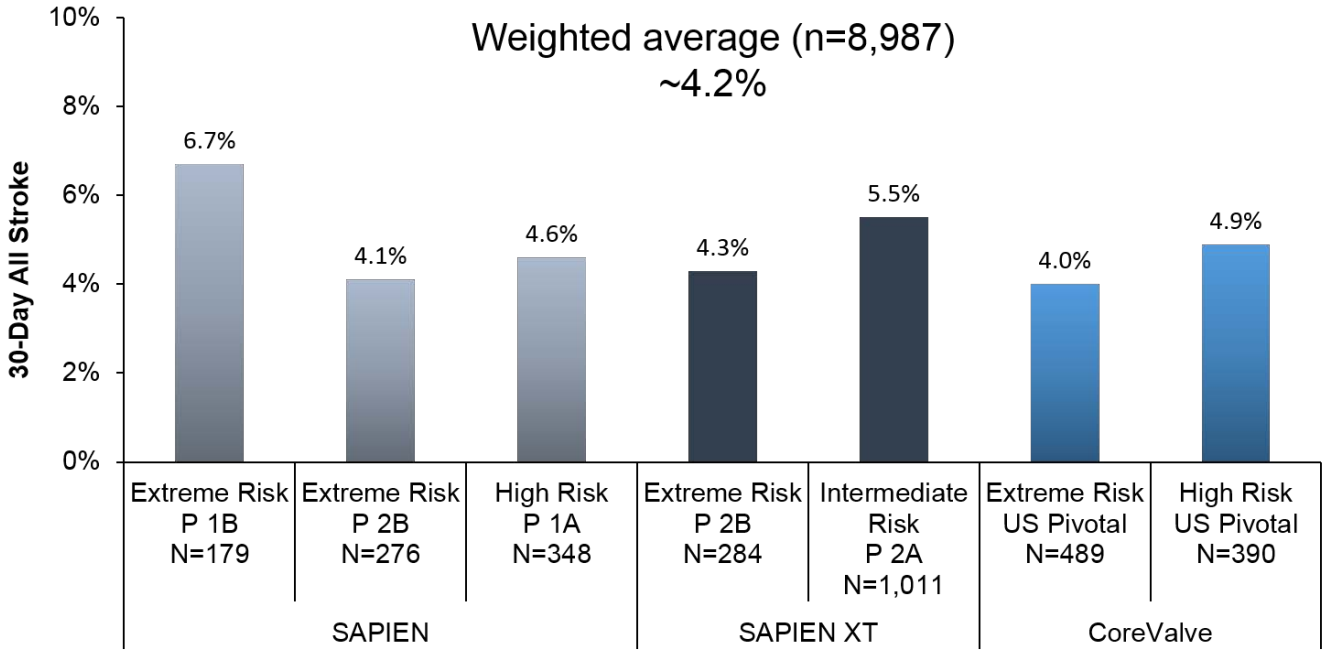


TAVR procedures continue to increase
This year > 125,000 and projected 300,000 by 2025

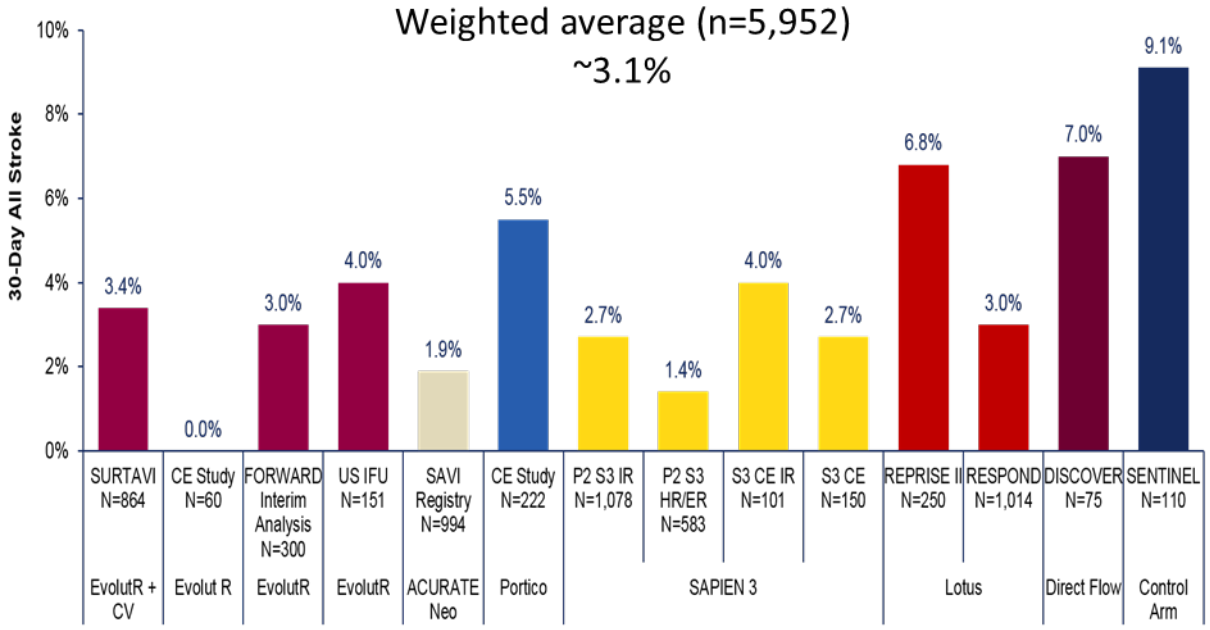
Vahl T et al. J Am Coll Cardiol 2016

Major Stroke Rates in Randomized TAVR Trials Constant over time

1st Generation Devices



Current Generation Devices



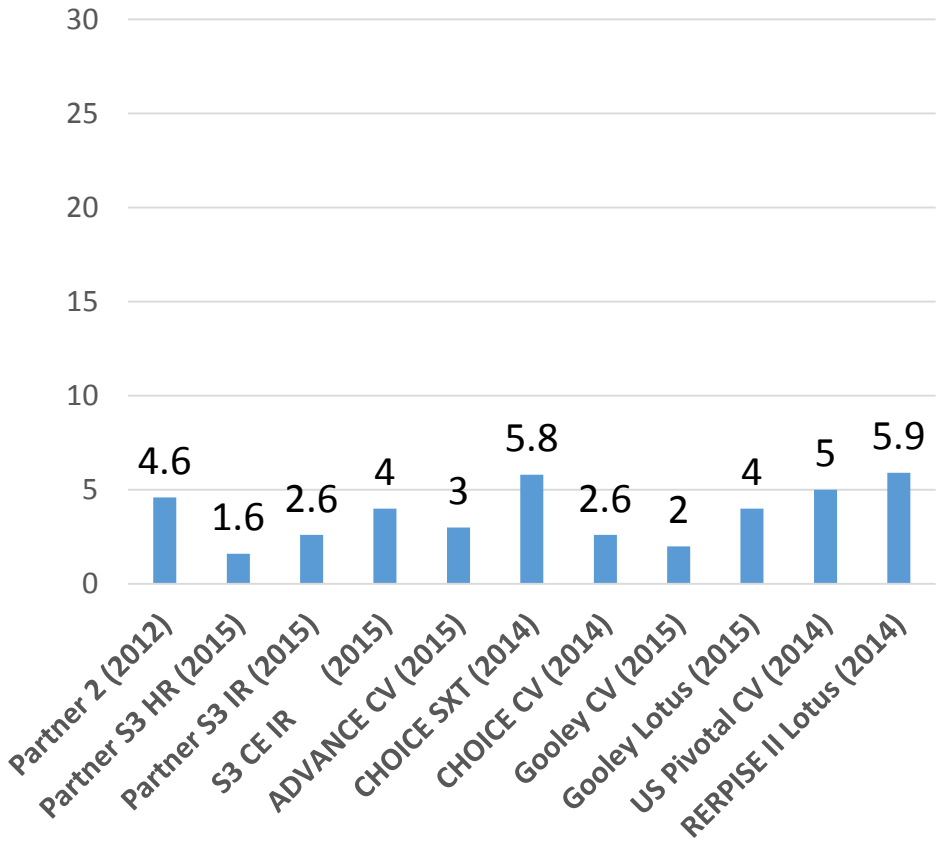
[1]Leon, et al., *N Engl J Med* 2010;363:1597-1607; [2]Webb, et al., *J Am Coll Cardiol Intv* 2015;8:1797-806; [3]Smith, et al., *N Engl J Med* 2011;364:2187-98; [4]Leon, et al., *N Engl J Med* 2016;374:1609-20; [5]Popma, et al., *J Am Coll Cardiol* 2014;63:1972-81; [6]Adams, et al., *N Engl J Med* 2014;370:1790-8;;

[1]Manoharan, et al., *J Am Coll Cardiol Intv* 2015; 8: 1359-67; [2]Moellman, et al., presented at PCR London Valves 2015; [3]Linke, et al., presented at PCR London Valves 2015; [4]Kodali, et al., *Eur Heart J* 2016; doi:10.1093/eurheartj/ehw112; [5]Vahanian, et al., presented at EuroPCR 2015; [6]Webb, et. al. *J Am Coll Cardiol Intv* 2015; 8: 1797-806; [7]DeMarco, et al, presented at TCT 2015; [8]Meredith, et al., presented at PCR London Valves 2015; [10]Falk, et al., presented at EuroPCR 2016; [11]Kodali, presented at TCT 2016; Reardon, M Published in NEJM March 2017

Major Stroke Under Represent all Strokes in TAVR Studies

Severe Stroke

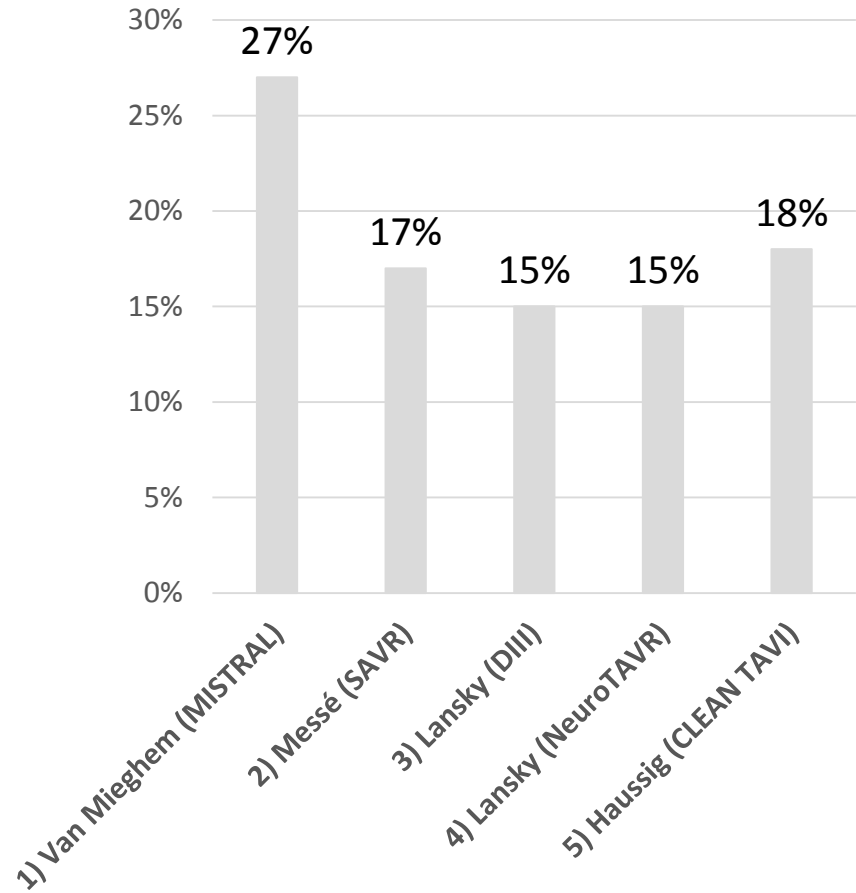
Major and disabling stroke rates range from 1.6%-5.9%



Mild, Moderate and Severe Stroke

Stroke rate is 15-27% by current AHA/ASA definitions

Neurologist identified deficits with new brain MRI lesions



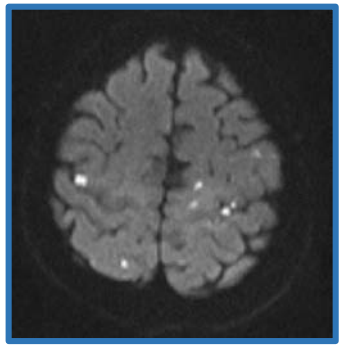
[1]Van Mieghem NM, EuroIntervention. 2016;12:499. [2]Messe S, Circulation. 2014;129:2253. [3]Lansky AJ, Eur Heart J. 2015; 36:2070.
[4]Lansky AJ, AJC 2016. [5]Haussig S, JAMA. 2016;316:592.

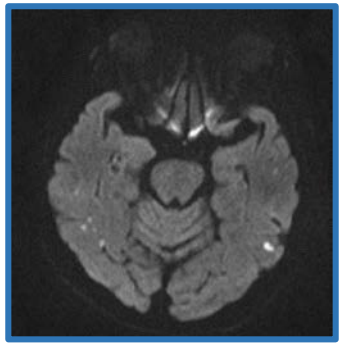
After TAVR Cerebral Embolization is Ubiquitous and Stroke is Unpredictable

Brain Injury

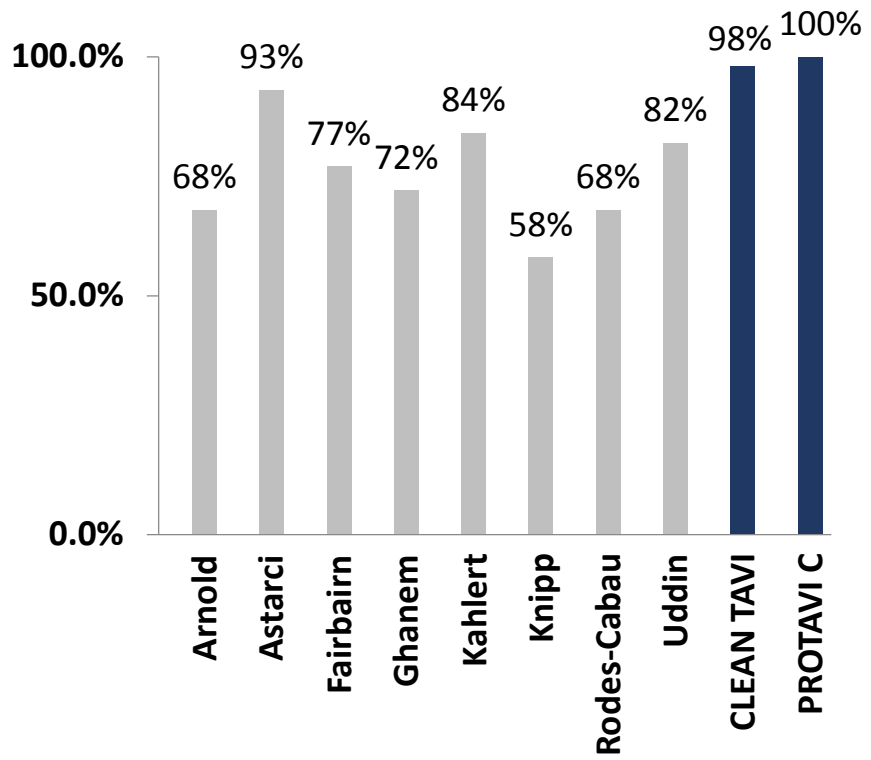
- "Silent" infarcts are associated with adverse neurological and cognitive consequences:
  - Impaired mobility
  - Physical decline
  - Depression
  - Cognitive dysfunction
  - Dementia
  - Alzheimer disease

- ***After TAVR silent brain injury is associated with:***
  - ***Neurocognitive decline***
  - ***>2 fold risk of dementia***
  - ***>3 fold risk of stroke***





% of Subjects with New Lesions



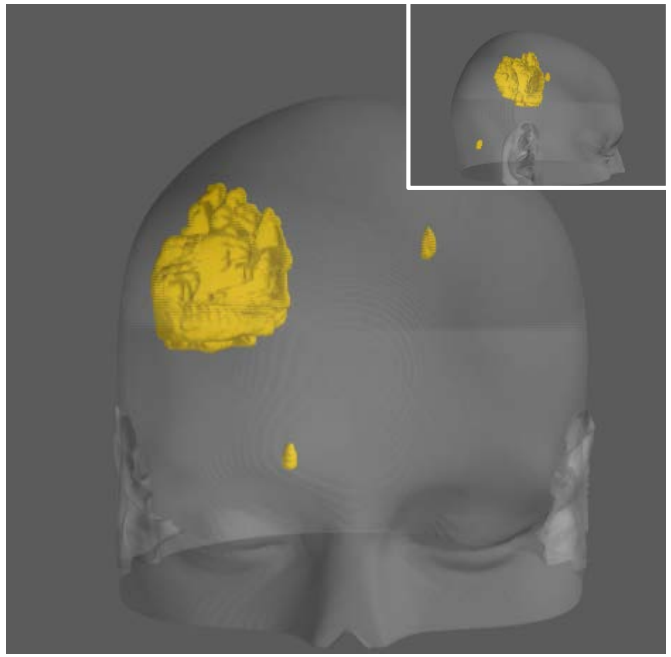
CLEAN TAVI and PROTAVI C exhibit the highest new lesion rates

Sources: Restrepo et al. *Stroke* 2002;33:2909, Lund et al. *Eur Heart J*. 2005;26:1269, Schwarz et al. *Am Heart J* 2011;162:756, Knipp et al. *Ann Thorac Surg* 2008;85:872, Vermeer et al. *NEJM 2003*; 348:1215, Vermeer et al. *Stroke* 2003; 34:1126, Arnold et al. *JACC Cardiovasc Interv*. 2010;3:1126, Astarci et al. *J Heart Valve Dis*. 2013;22:79, Fairbairn et al. *Heart* 2012;98:18, Ghanem et al. *EuroIntervention*. 2013;8:1296, Kahlert et al. *Circ*. 2010;121:870, Knipp et al. *Interact Cardiovasc Thorac Surg*. 2013;16:116, Linke et al. TCT 2014, Rodes-Cabau et al. *JACC Cardiovasc Interv* 2014;7:1146.

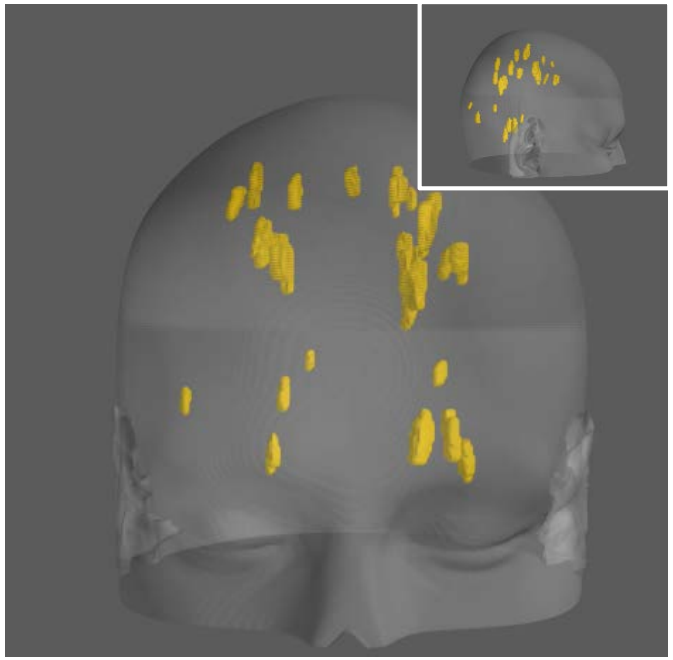
Strokes cannot be predicted by lesion size, number or location OR clinical characteristics

2-7 day DWI from the SENTINEL Trial

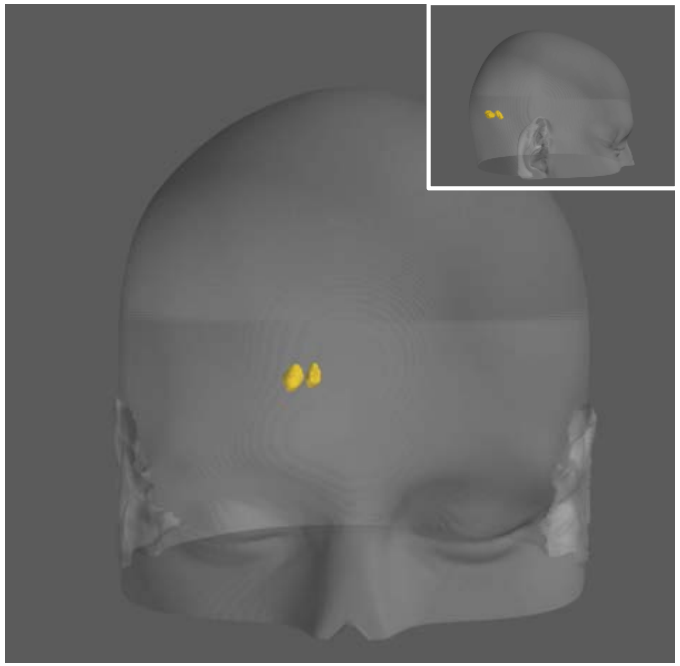
Size



Number



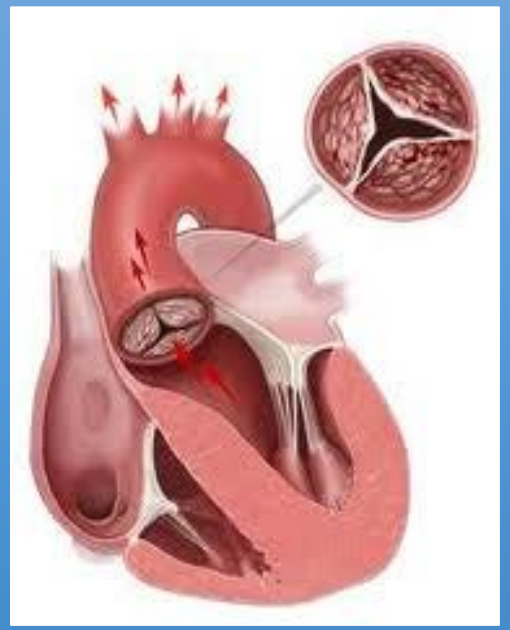
Location



3 Control Arm Stroke Patients

Calcific Aortic Valve Stenosis

Primary source of embolic material following TAVR



Calcified stenotic aortic valve

Large irregular masses of dystrophic calcification prevent normal valve opening

Sizeable calcific deposits prevent normal valve function

Consequences of Stroke

Mortality

- Disabling stroke after TAVR increased mortality (1-year mortality of 67% vs. 12% and 2-year mortality of 83% vs. 20%.[1])

Physical Functioning

- 40% of patients with overt ischemic strokes have moderate to severe permanent disability and
- 55%-75% of "fully recovered" patients will have residual dysfunction in at least one limb.[2-3]

Effect of Stroke in Working Population

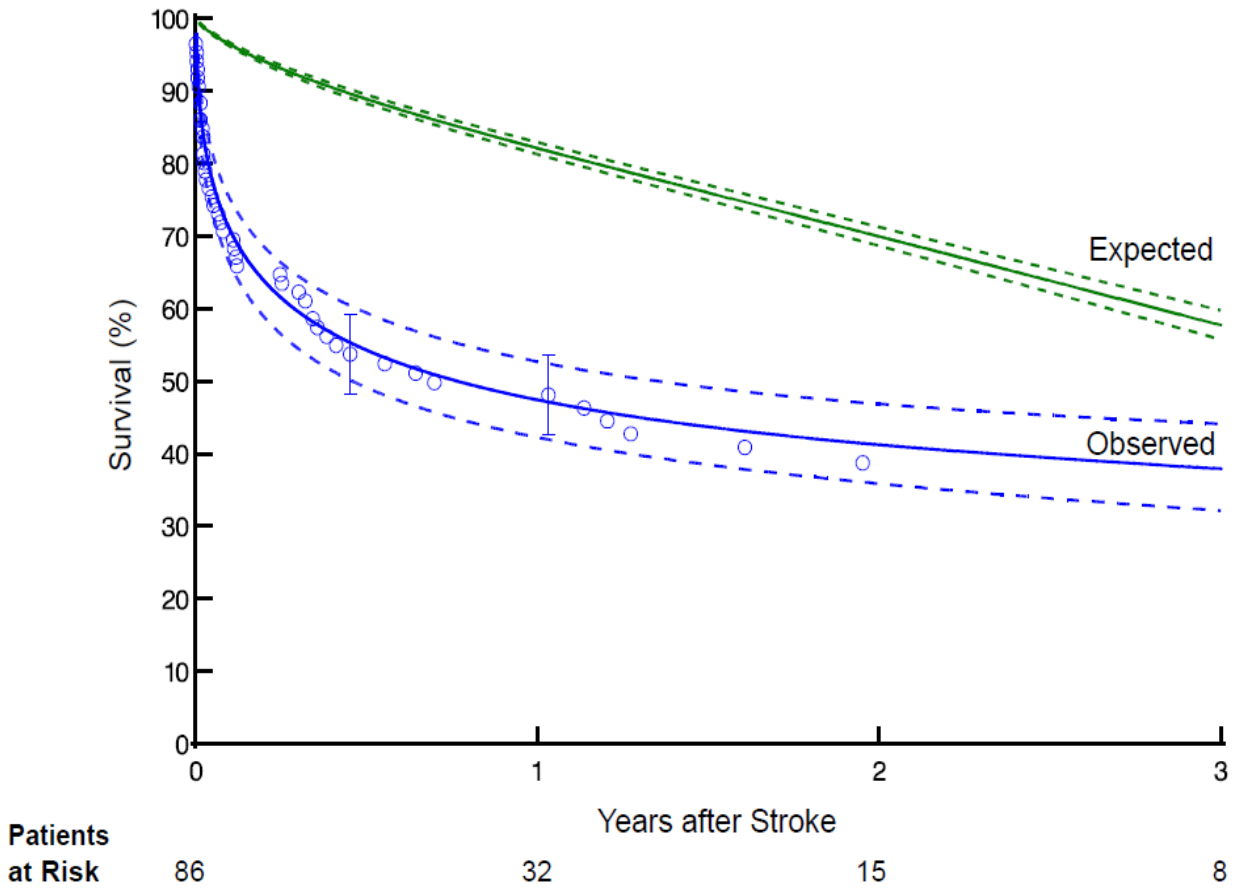
Only 44% of overt stroke patients are able to return to work,

33% report significant financial strains, and 79% reported a decrease in social activities.[4]

[1]Adams DH, N Engl J Med. 2014;370:1790.
[2]Connolly SJ, N Engl J Med. 2009;361:1139.
[3]Daniel K, Stroke. 2009;40:e431.
[4]Lai SM, Stroke. 2002;33:1840.

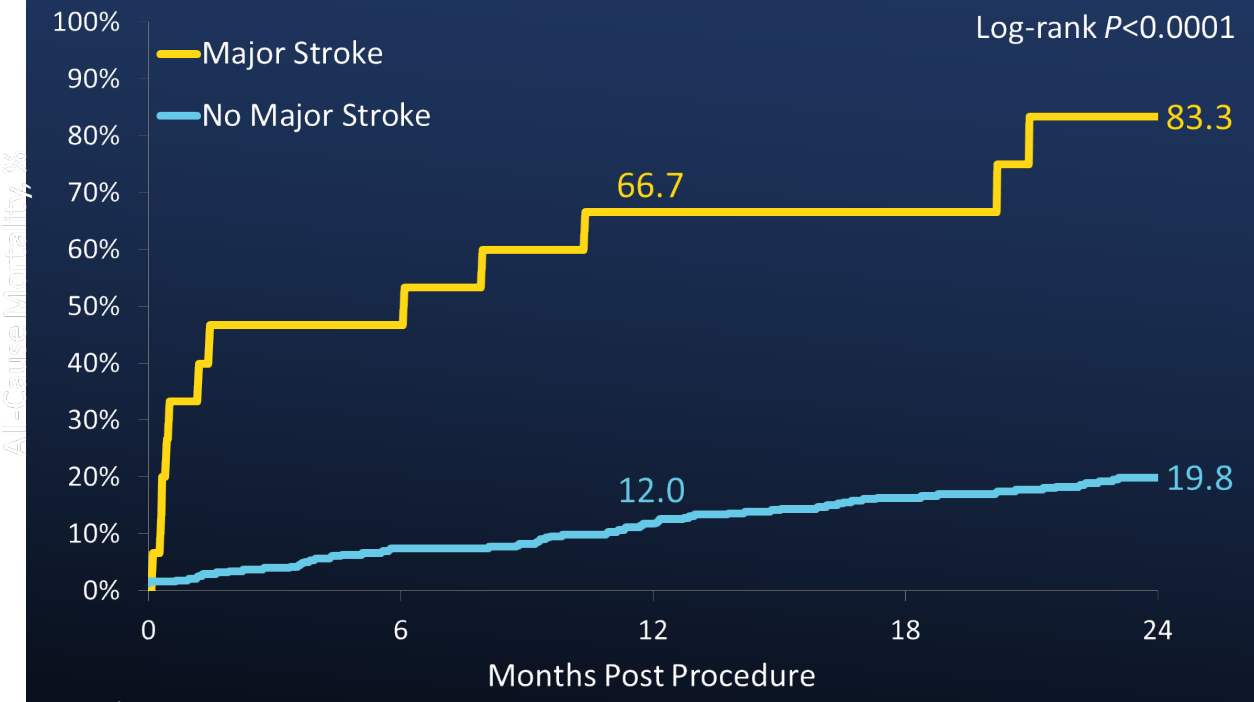
Major Stroke Increases Mortality 3-9 Fold

Partner Trials



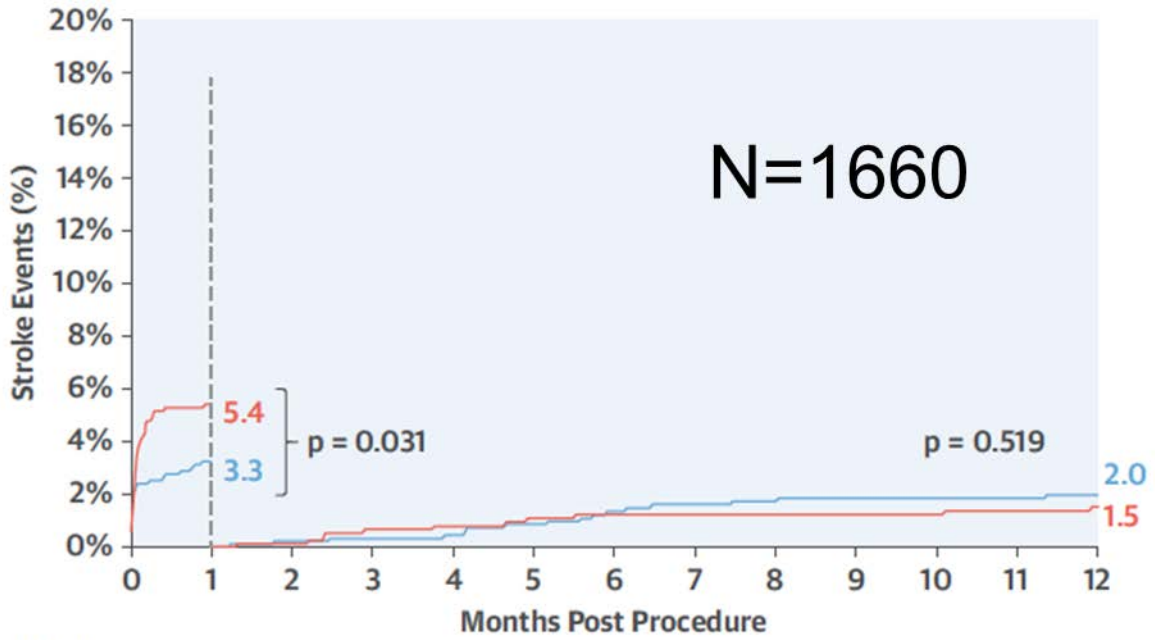
Kapadia et al, Circ Int 2016

CoreValve High Risk Trial



Stroke in Intermediate Risk Patients (SURTAVI Trial) Incidence and Outcomes Remain Constant

All Stroke



Mortality at 12 months

	TAVR	SAVR	p Value
No early neurological events*	36/801 (4.5)	26/673 (3.9)	0.586
Early stroke (all)†	5/28 (17.9)	6/43 (14.0)	0.589
Early disabling stroke†	4/10 (40.0)	5/19 (26.3)	0.327
Early nondisabling stroke†	1/18 (5.6)	1/24 (4.2)	0.822
Early TIA†	2/12 (16.7)	0/8 (0.0)	0.254
Early encephalopathy†	3/14 (21.4)	11/62 (17.9)	0.716

1 in 5 patients (≈20%) with early stroke or encephalopathy will die at 1 year

Durco et al. JACC 2018; 72:2109-19

Patient Perceptions and Expectations

Health Expectations
An International Journal of Public Participation in Health Care and Health Policy

doi: 10.1111/hex.12393

Patient-defined goals for the treatment of severe aortic stenosis: a qualitative analysis

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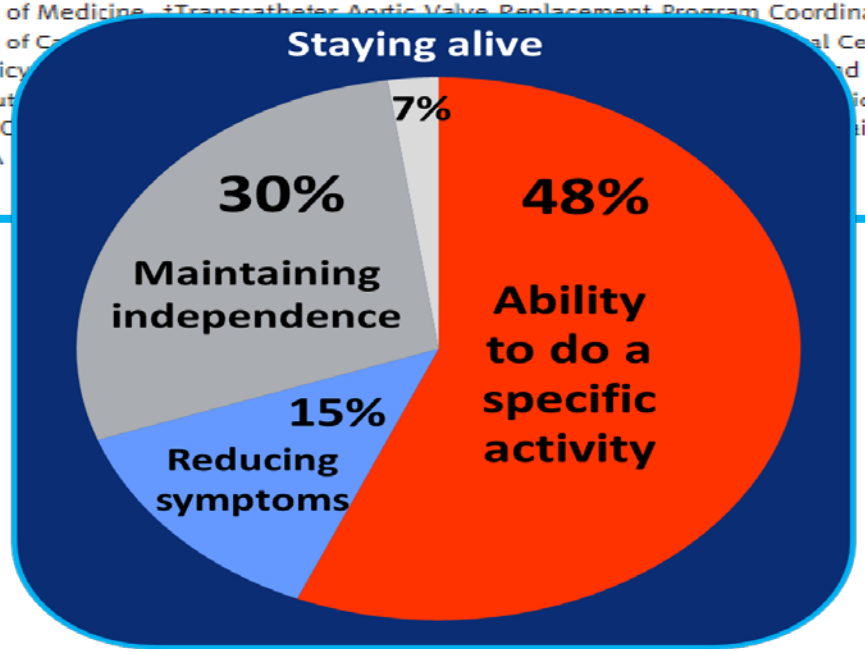
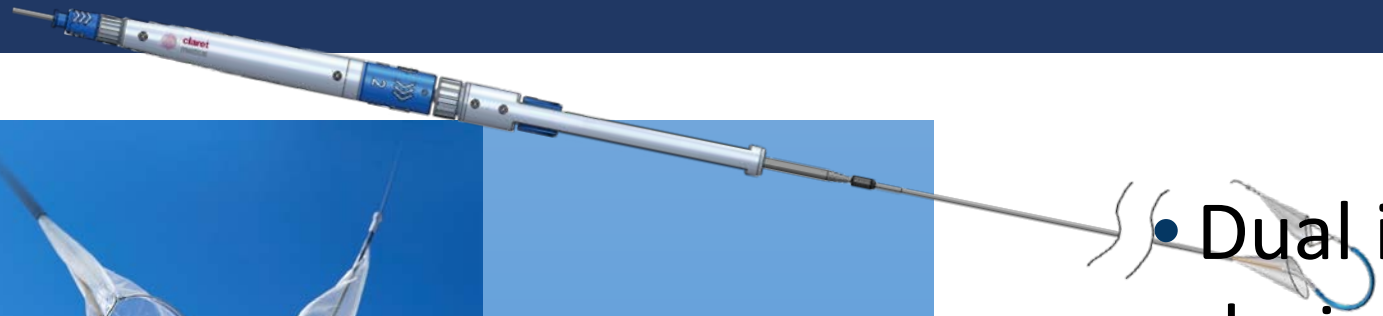
*Assistant Professor of Medicine, ‡Transcatheter Aortic Valve Replacement Program Coordinator, §Research Fellow, ¶Professor of Medicine, Section of C… …l Center, Lebanon, NH, †Assistant Professor of Health Policy … …d Clinical Practice, Geisel School of Medicine at Dartmout… …icine, School of Medicine, Yale University, New Haven, C… …irs Connecticut Healthcare System, West Haven, CT, USA

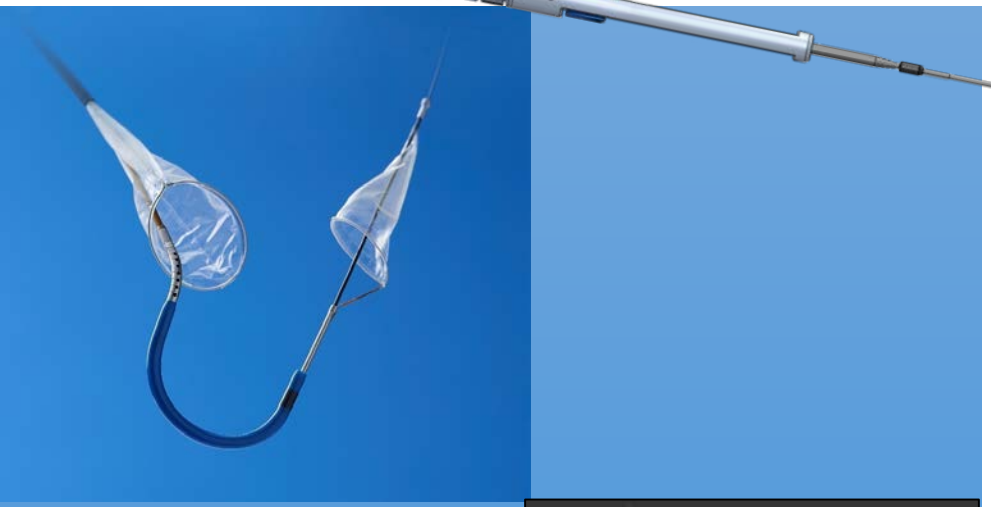


Elderly (higher risk):
"a stroke is worse than death"
"maintain independence and enjoy important activities"
"quality over longevity"

Younger (lower risk):
"more concerned about mortality"
"cognition and mental acuity"
"rapid return to normal quality life"

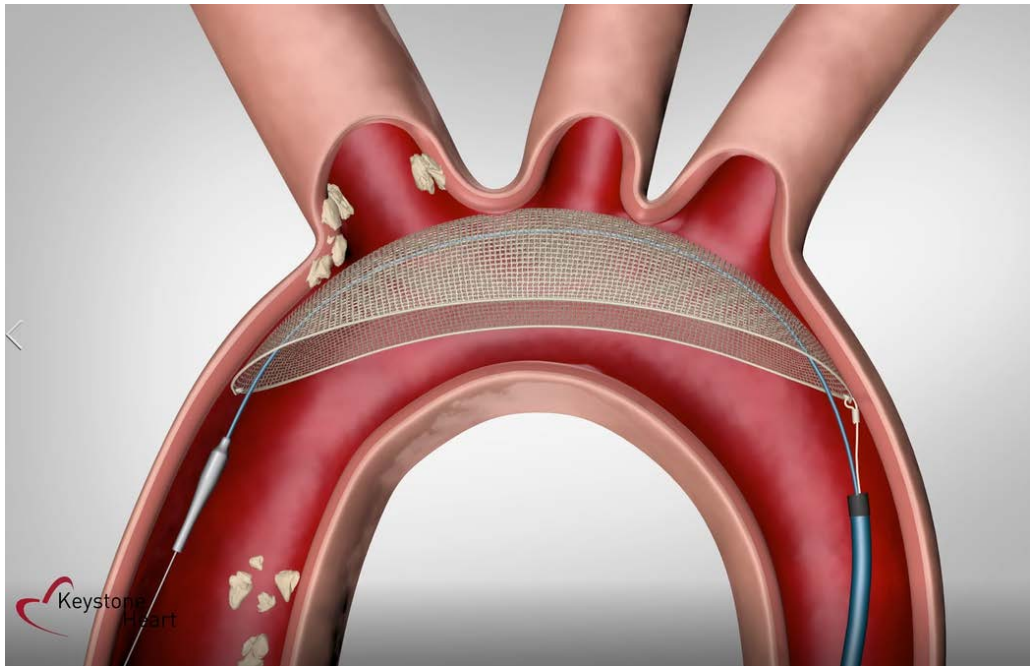
Sentinel Cerebral Protection Systems





- Dual independent filters designed for embolic debris capture and removal in two of the three cerebral branches
  - Innominate artery and left common carotid artery
- Right transradial 6F sheath access
- FDA approved

TriGuard 3: Cerebral Embolic Protection



Designed to cover ALL major cerebral vessels

- Deflection filter
- Protects entire cerebro-vascular system: innominate, left carotid, and subclavian
- Over the arch delivery vs down the carotids designed to minimize brain emboli

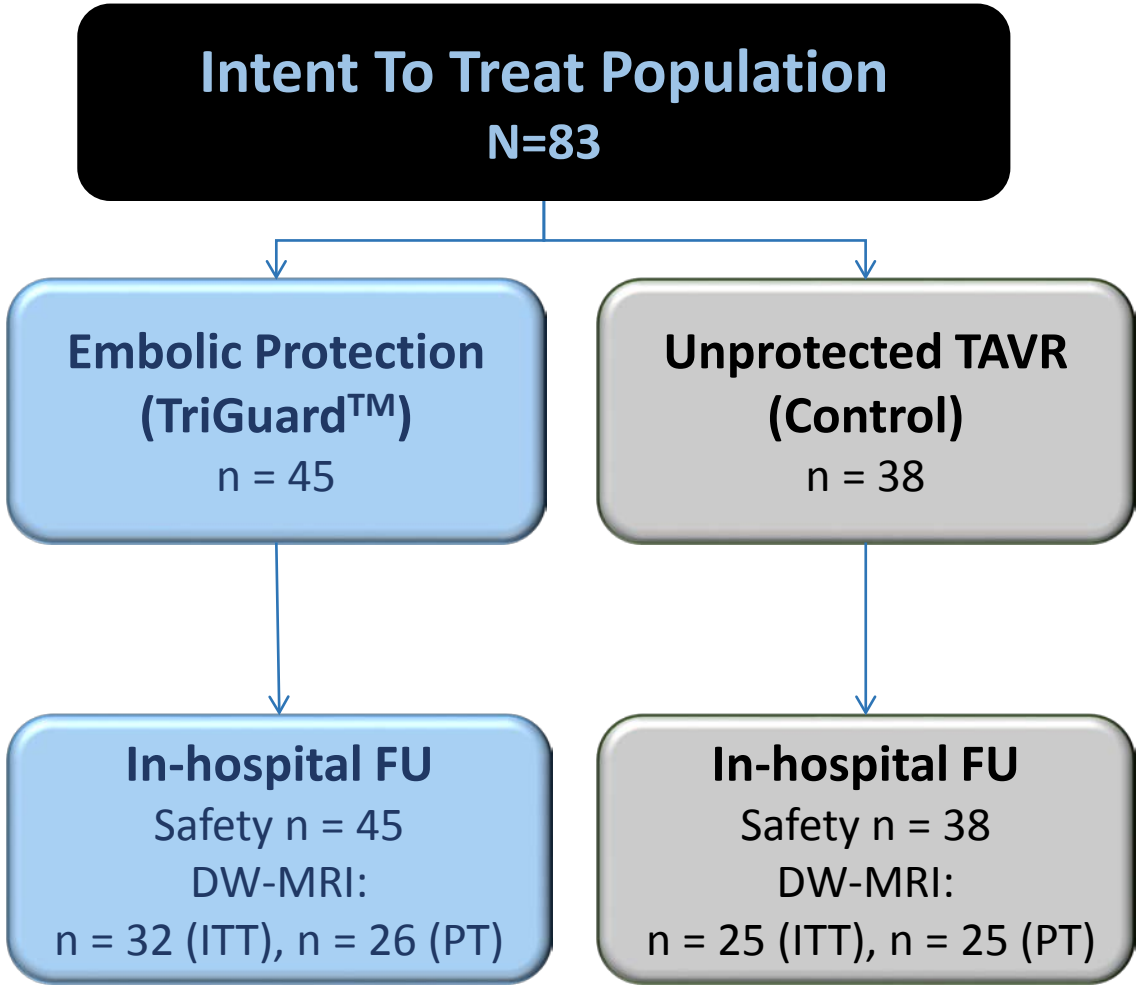
Broad Applicability

- No cerebral vessel size limitations
- No anatomic limitations

Unique Features of TriGUARD 3

	Sentinel CPS	TriGUARD 3
Filter design	Dual capture filter	Single deflection filter
Mechanism of action	Capture Filter: Filters and captures debris released during the cardiac procedure using filter-baskets positioned in 2 of 3 cerebral vessels. The baskets with debris are removed from the body at the end of the procedure	Deflection Filter: Filters and deflects debris released during the cardiac procedure using a filter-shield positioned in the aortic arch across the 3 cerebral vessels. Debris is deflected away from the brain.
Target Protection Area	Positioned in and protects 2/3 cerebral vessels (brachiocephalic and left common carotid arteries)	Position in aortic arch and protects 3/3 cerebral vessels (brachiocephalic, left common carotid, left subclavian artery)
Access Method	Device is introduced through the right arm	Device is introduced through the femoral artery
Technical method	Single use percutaneous catheter system	Single use percutaneous catheter system
Primary procedure	Transcatheter aortic valve replacement	Transcatheter aortic valve replacement

DEFLECT III Patient Disposition

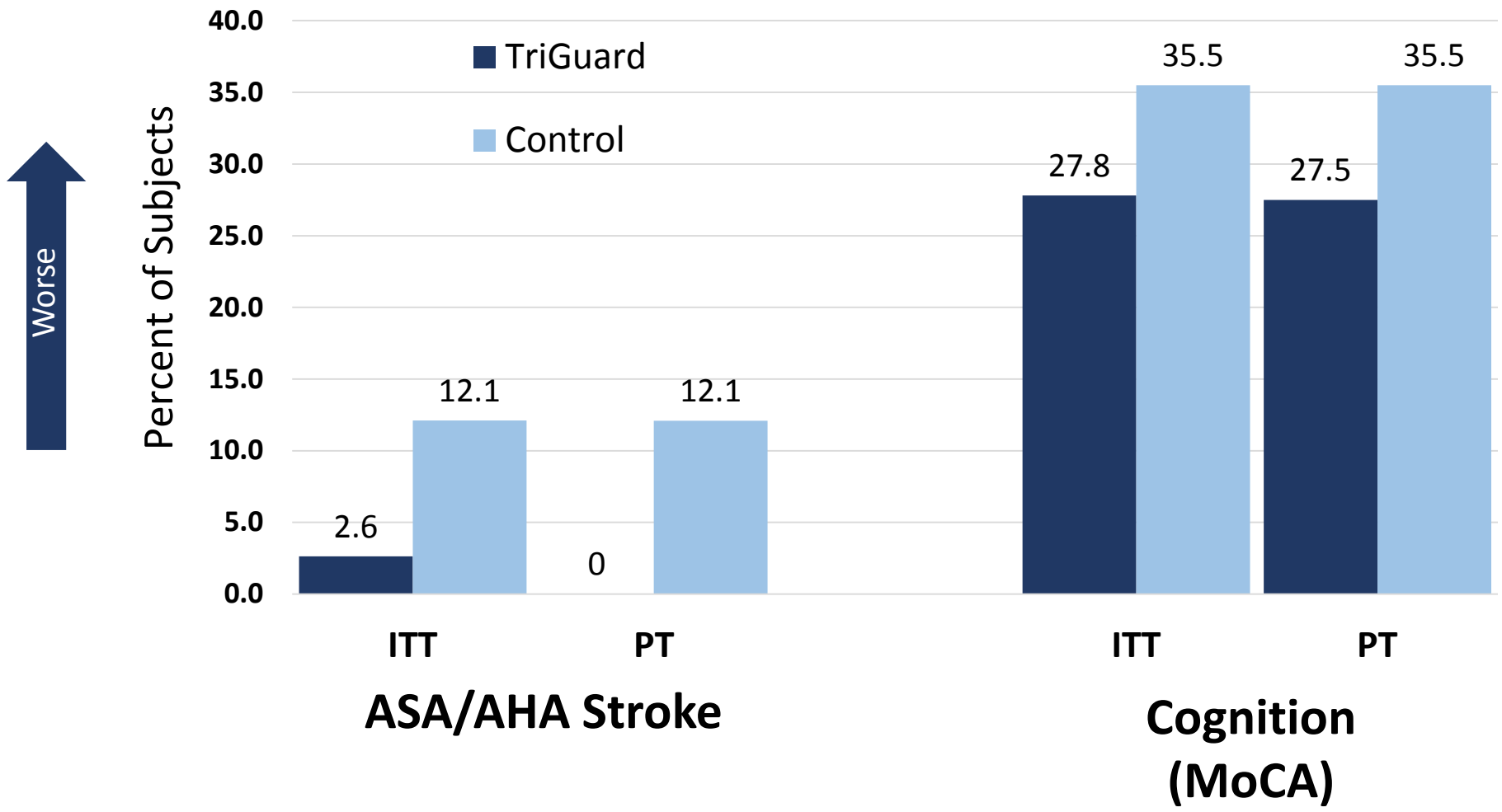


- Deployment Success: 93.5%
- **Successful positioning: 87%**(complete 3-vessel coverage until final valve deployment of first valve, verified by QCA)

Lansky AJ, Eur Heart J. 2015; 36:2070.

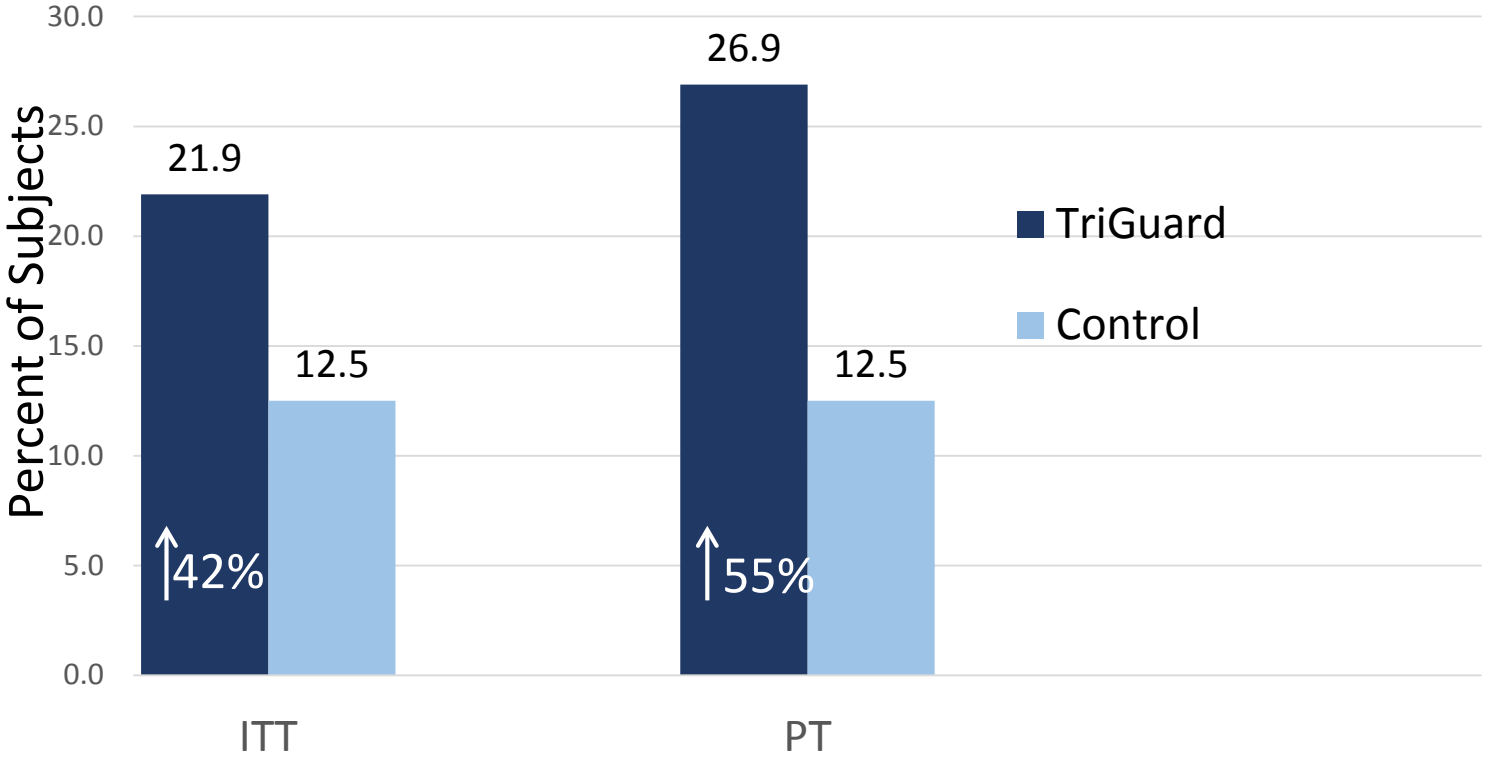
Clinical Efficacy Outcomes – Stroke and Cognition

Protection reduces worsening of neurologic and cognitive outcomes

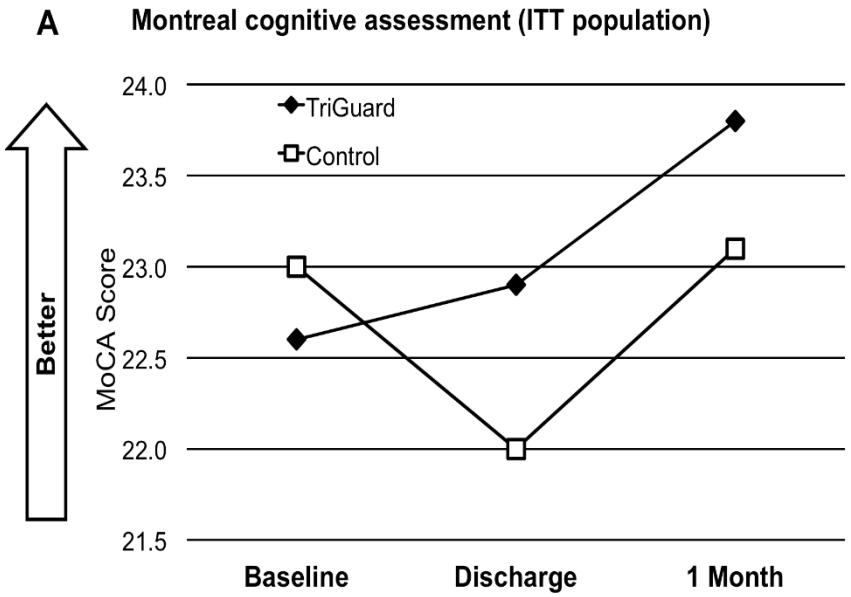


Neurologic Injury and Cognition

Free from ischemic lesions (DW MRI)



Cognition (MOCA)



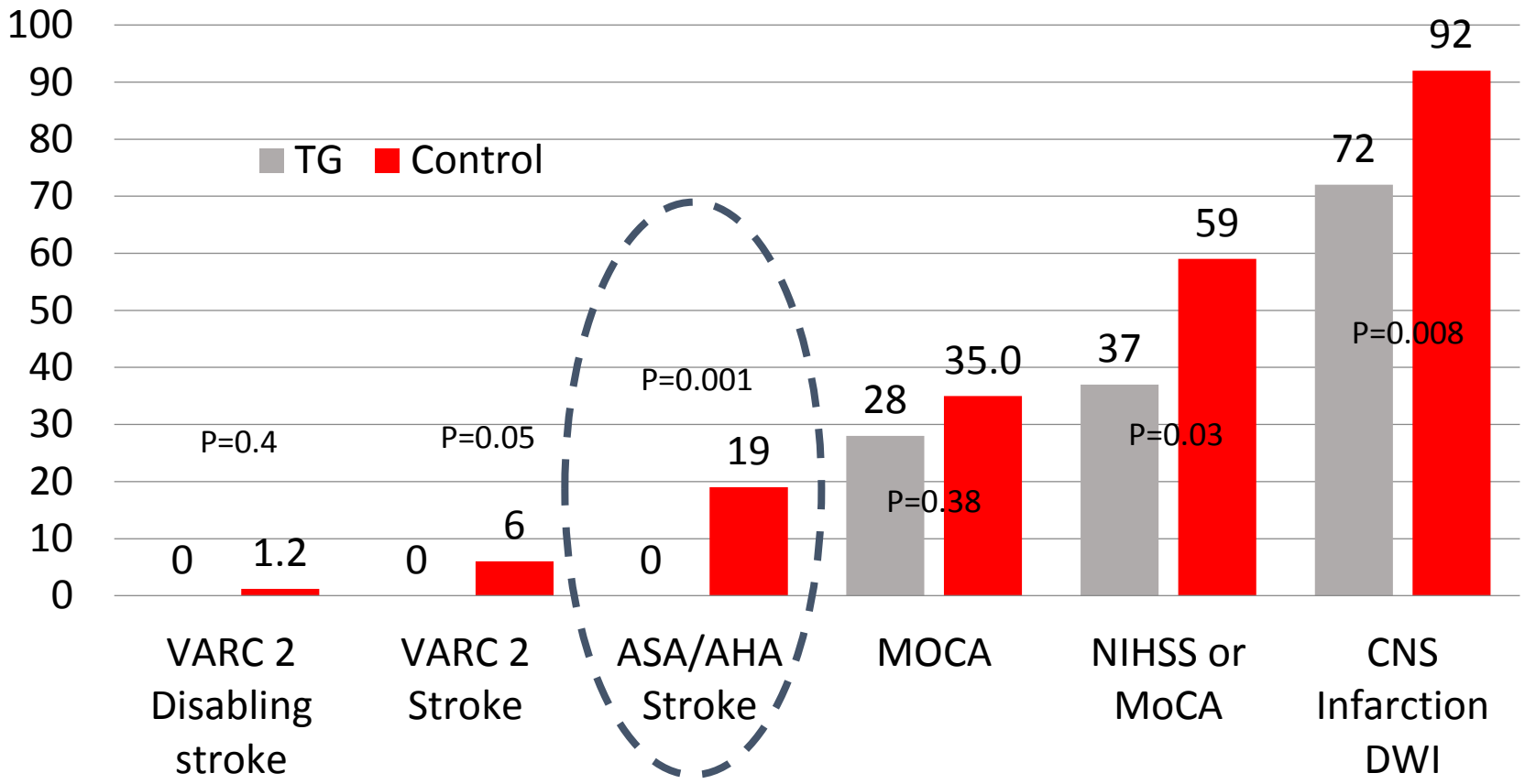
>2 fold recovery of cognitive function with protection vs Controls at 30 days

Age Normalized MoCA Score: 45% TG vs 20% of controls RR 2.27 95%CI [1.01-5.10]

TriGuard Pooled Analysis: Reduction in all Measures of Neurologic Injury

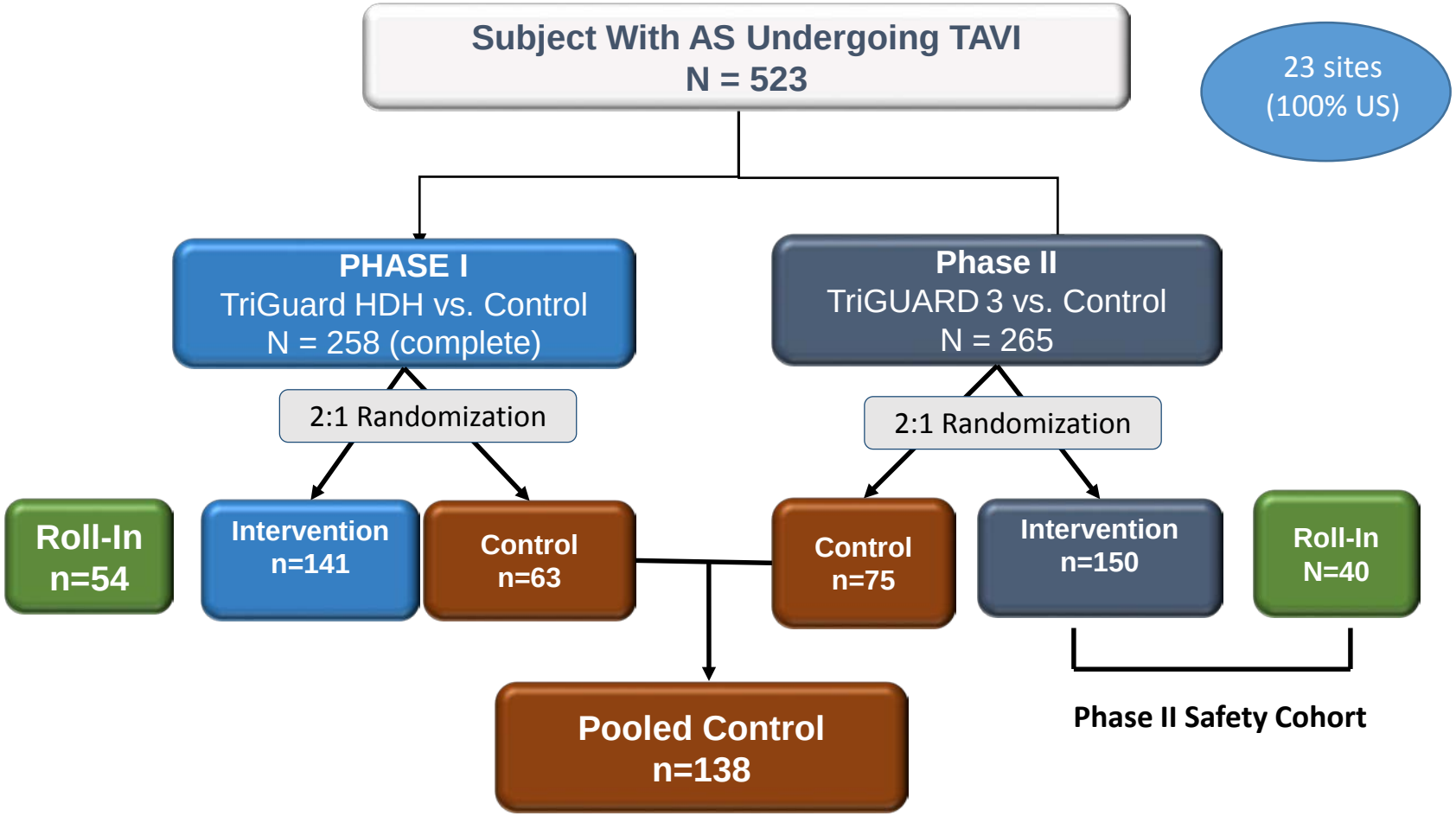
Primary Safety Endpoint of 30 day MACCE: 18.2% TG vs 24.1% Control, p=0.44

Patient level pooled analysis from the TriGuard Trials (N=142)[1]



Lansky et al PCR 2016

Ongoing REFLECT IDE Trial Design



Modified to include a clinical evaluation of the TriGUARD 3 device while leveraging existing blinded data and trial infrastructure

SAFETY

- Combined safety endpoint (VARC-2) at 30 days
- TriGuard vs. Performance Goal

- **EFFICACY**
- • **Hierarchical composite endpoint (Finkelstein-Schoenfeld)**:
  - - CV Death or stroke (30 d)
  - NIHSS (30 d)
  - Freedom from DWI lesions
  - - TLV (DWI)
- • TriGuard vs. Control

PI: Nazif T, Lansky A, Makar R

Conclusions

1. Stroke is unpredictable and incidence has been constant after TAVR
2. TriGuard use is safe and provides complete cerebral coverage with no anatomic limitations
3. TriGuard reduces stroke risk, cerebral injury and measures of cognition
4. Current ICD-10-PCS codes do not uniquely identify cerebral embolic protection procedures that
   - protect all three branches of the aortic arch (innominate, left carotid, and subclavian) OR
   - differentiate dual filter capture from single filter deflection devices
5. Modification with more granular coding is needed for accurate reporting and outcome-tracking of different cerebral embolic protection approaches and devices.