PROTECTED -TAVR
Statistical or Clinical Interpretation
My Take Home Messages

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Disclosures

- **PI of the trial**
- **No financial conflict**

How to Interpret Data from PROTECTED - TAVR

- **Brief Overview of PROTECTED TAVR data**
- **Data not covered in the main manuscript**
- **Data in context with other data**
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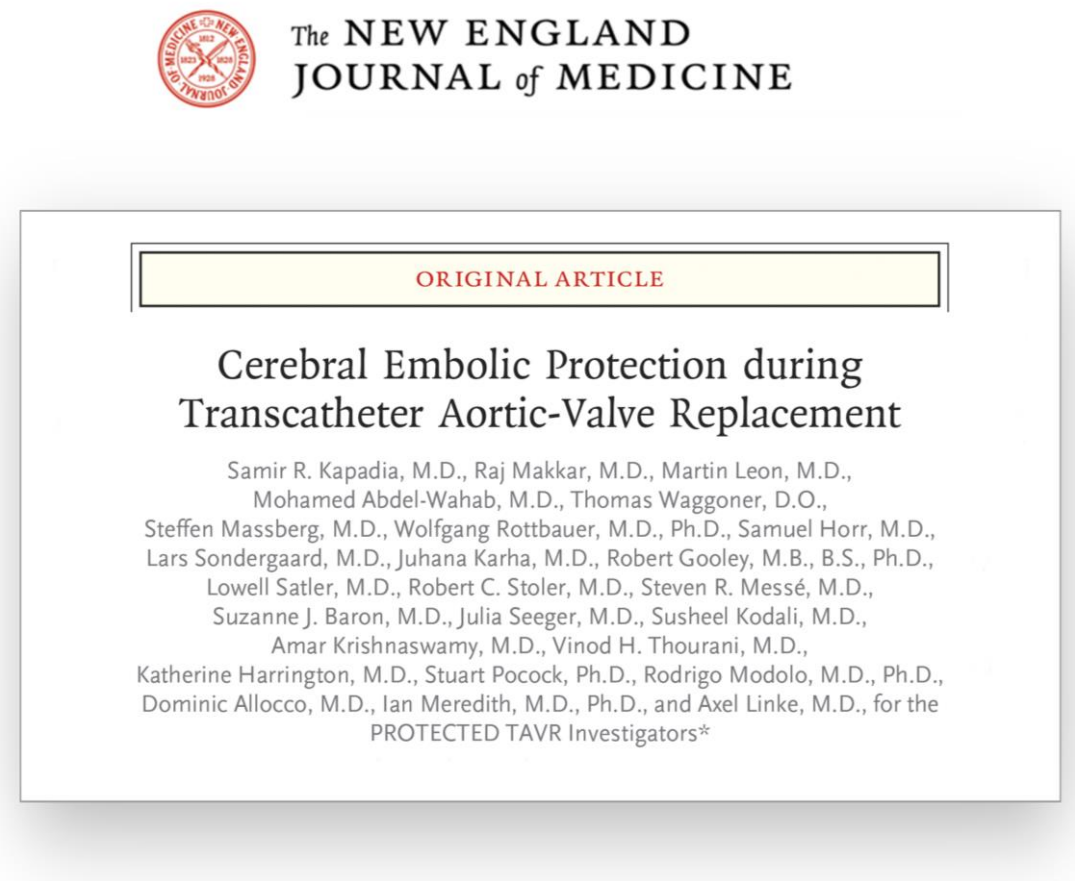
PROTECTED TAVR Study



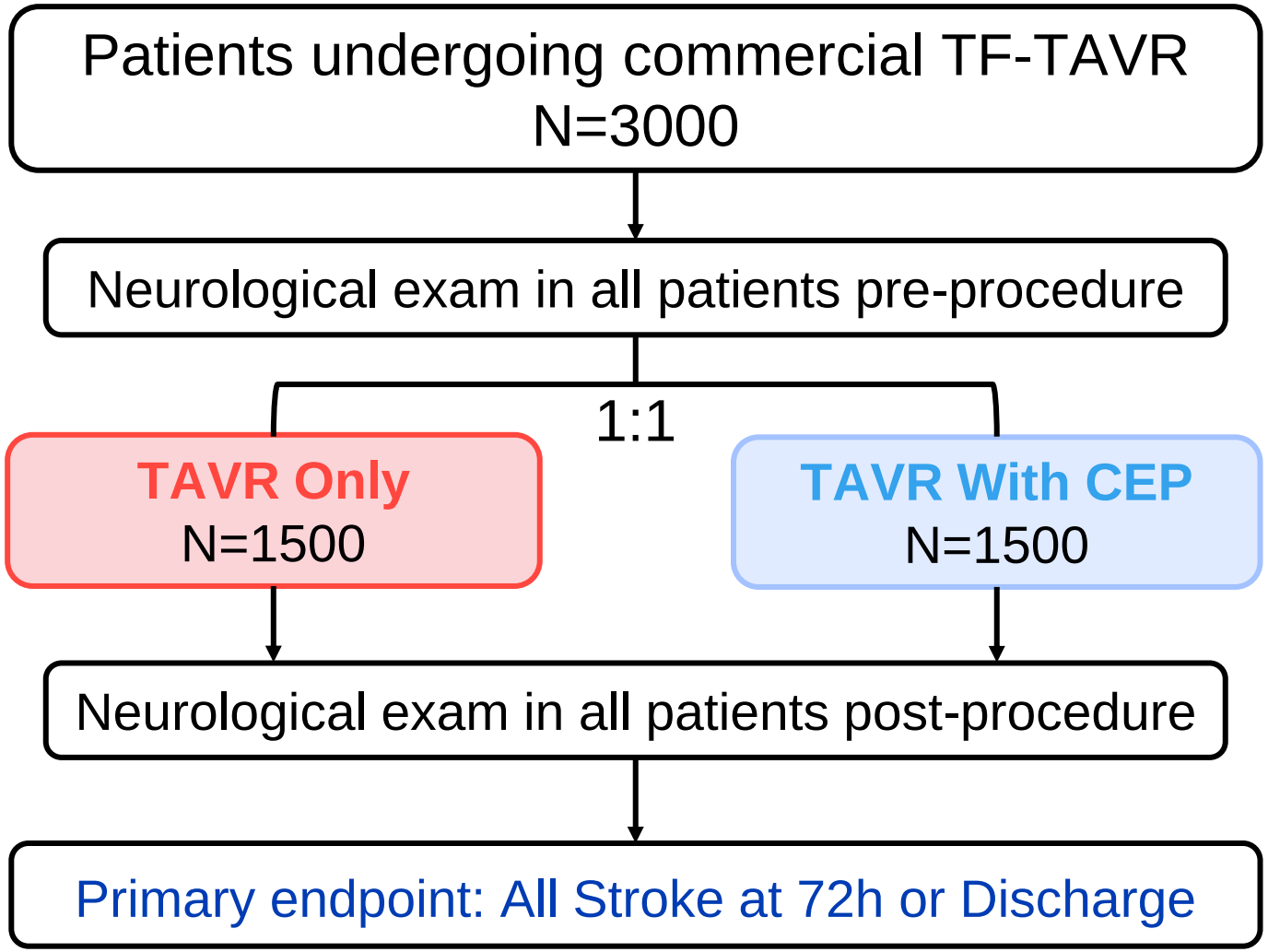
OBJECTIVE

To study whether clinical stroke in transfemoral TAVR is reduced with CEP, across all risk groups and all commercially available devices

DESIGN

Prospective, post-market, multicenter randomized controlled trial at 51 centers in North America, Europe, and Australia

PROTECTED TAVR Study Design



- Patients of all risk categories eligible
- Any commercially available TAVR device

Neurological examination

- At baseline
- Discharge or 72 hours after TAVR (whichever comes first)
- Performed by a neurology professional
- mRS, NIHSS, MoCA, CAM-ICU

- Adaptive study design with interim analysis at 70% enrollment

mRS, Modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; MoCA, Montreal Cognitive Assessment; CAM-ICU, Confusion Assessment Method for Intensive Care Unit Patients

Baseline Demographics

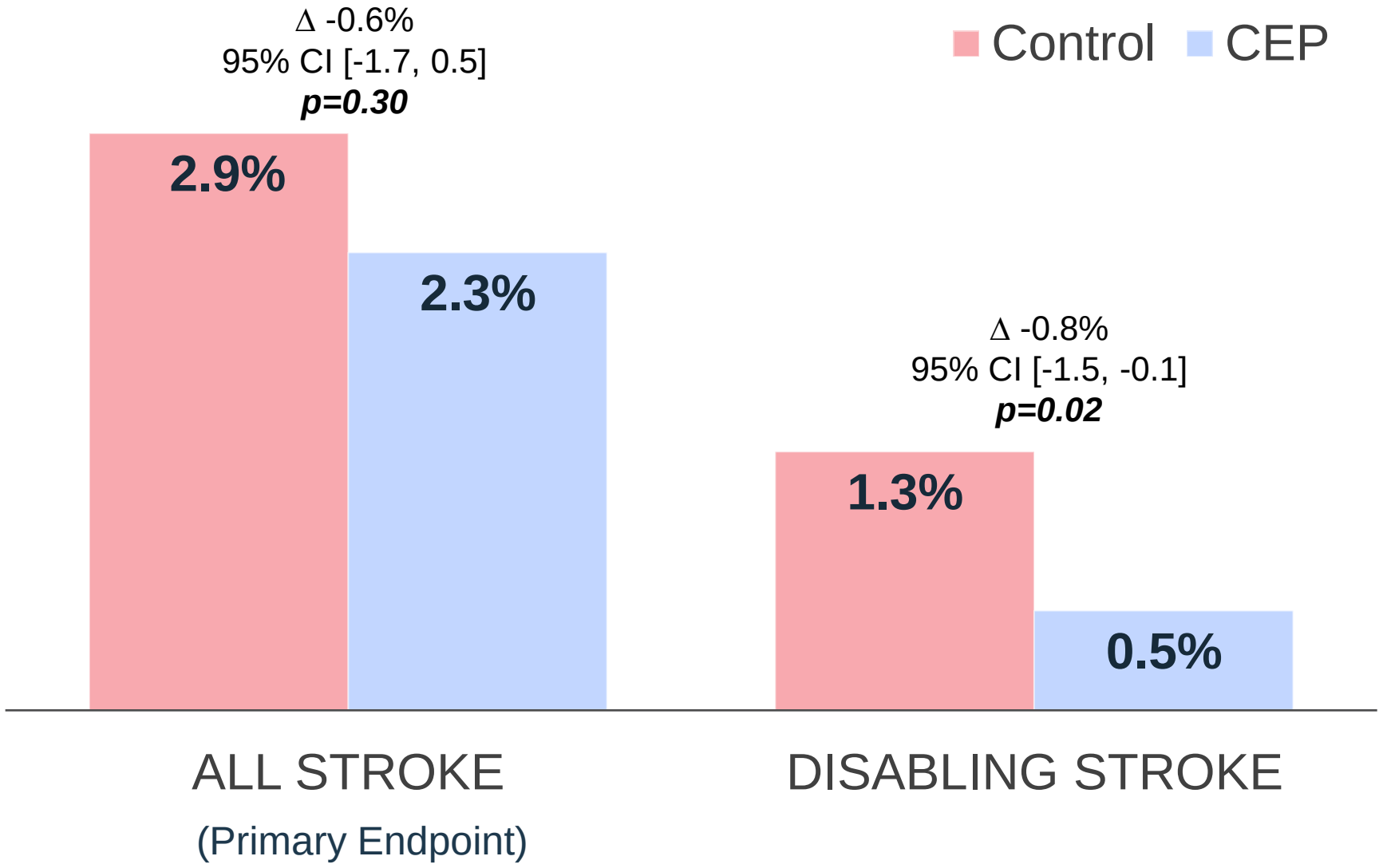
	Control (N=1499)	CEP (N=1501)
Age (years)	78.9±7.8	78.9±8.0
Female Sex	37.8%	42.0%
Society of Thoracic Surgeons score, %	3.4±2.8	3.3±2.7
STS score <3%	58.2%	55.6%
Surgical Risk (per Heart Team)		
Extreme/High Risk	30.4%	30.4%
Intermediate Risk	34.2%	33.2%
Low risk	35.4%	36.3%
Native Valve Calcification Severity (site-reported)		
None/Mild	15.2%	16.2%
Moderate	29.5%	29.4%
Severe/Extreme	55.3%	54.4%
CHA_2DS_2-VASC score	4.2±1.3	4.2±1.3

Operative risk was well-balanced

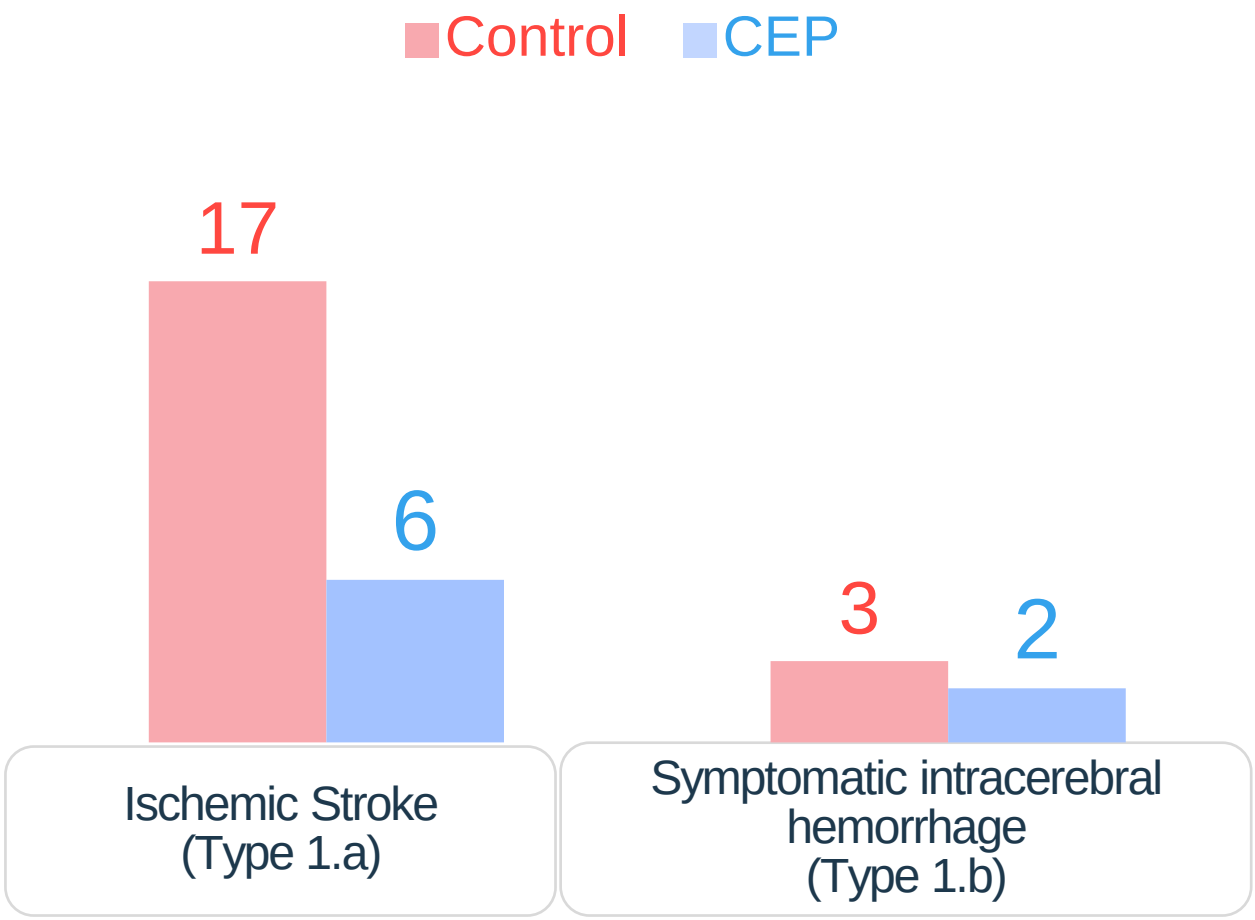
Procedural Characteristics

	Control (N=1499)	CEP (N=1501)
Anesthesia		
General Anesthesia	26.4%	26.8%
Local or Conscious Sedation	73.6%	73.2%
Valve Anatomy		
Tricuspid Valve	89.5%	87.5%
Bicuspid Valve	8.1%	8.7%
Bio-prosthesis	2.5%	3.7%
Prosthetic Valve Type		
Balloon Expandable Valve	63.7%	64.3%
Non-Balloon Expandable Valve	36.3%	35.7%
Balloon Dilatation		
Pre-dilatation	41.9%	38.5%
Post-dilatation	25.7%	26.2%

Primary Endpoint: Stroke at 72h / Discharge



Mechanism of Disabling Stroke



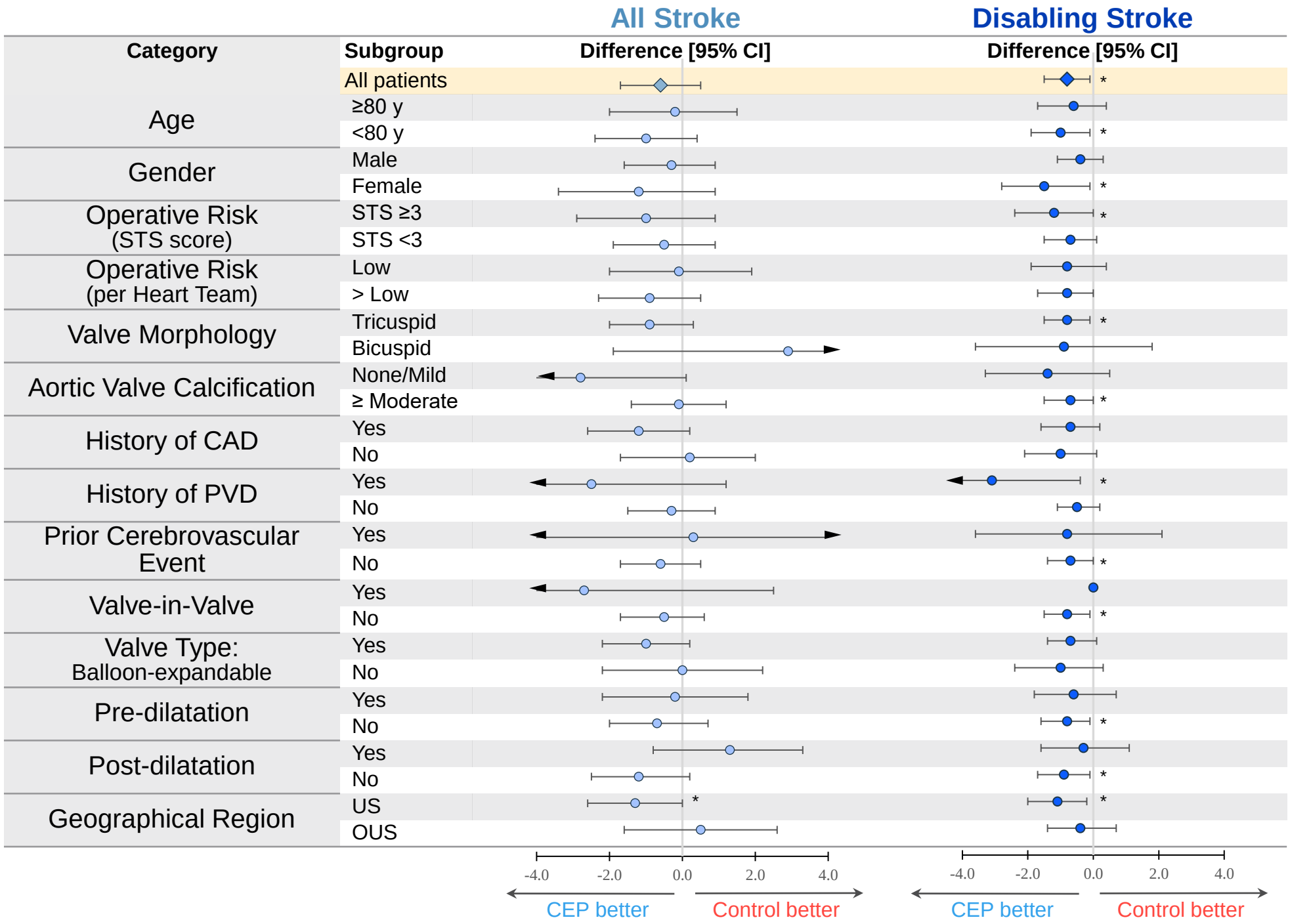
NeuroARC[1] definition of stroke

[1]Lansky AJ, et al. J Am Coll Cardiol 2017;69:679–91

Disabling Stroke in CEP-treated Patients

Stroke Etiology	NeuroARC subtype	Details of the Clinical Situation
Hemorrhagic	Type 1.b	Complicated TAVR (valve-in-valve, hemodynamic instability, CPR)
Hemorrhagic	Type 1.b	Uncomplicated TAVR, large cerebellar hemorrhage
Ischemic	Type 1.a	CEP not deployed (could not advance above brachial artery)
Ischemic	Type 1.a	Complicated TAVR (valve embolization, CPR, second valve placed), stroke symptoms apparent 2 hours post-TAVR
Ischemic	Type 1.a	Uncomplicated TAVR, right occipital stroke (vessel not fully protected by the device)
Ischemic	Type 1.a	Uncomplicated TAVR, occipital infarcts with vision difficulties (vessel not fully protected by the device)
Ischemic	Type 1.a	Uncomplicated TAVR, clinical symptoms consistent with stroke, but lesion localization uncertain
Ischemic	Type 1.a	Uncomplicated TAVR, stroke in left MCA territory (protected vessel)

Subgroup Analyses



*p≤0.05

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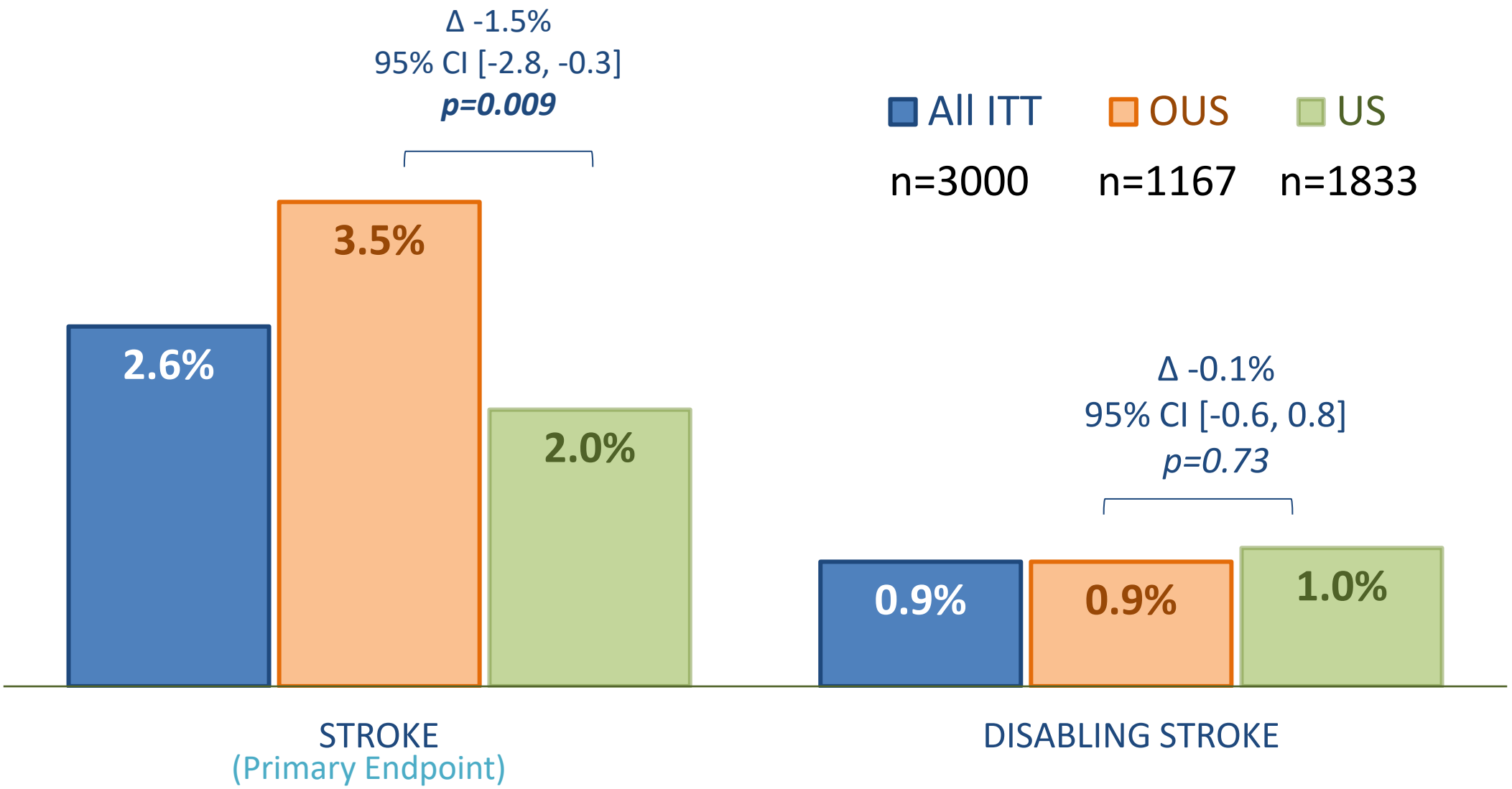
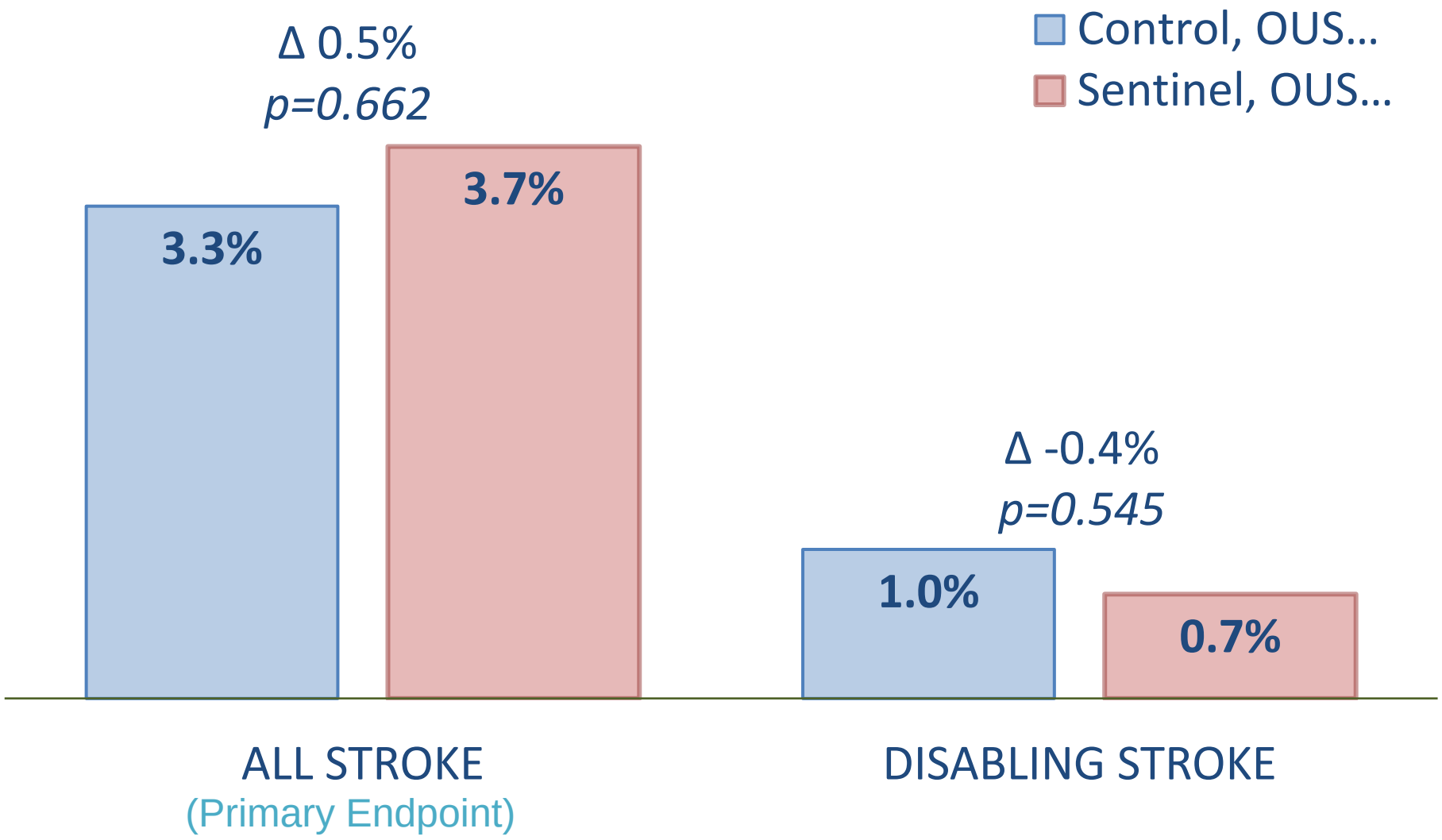
Regional Differences in Stroke & Disabling Stroke



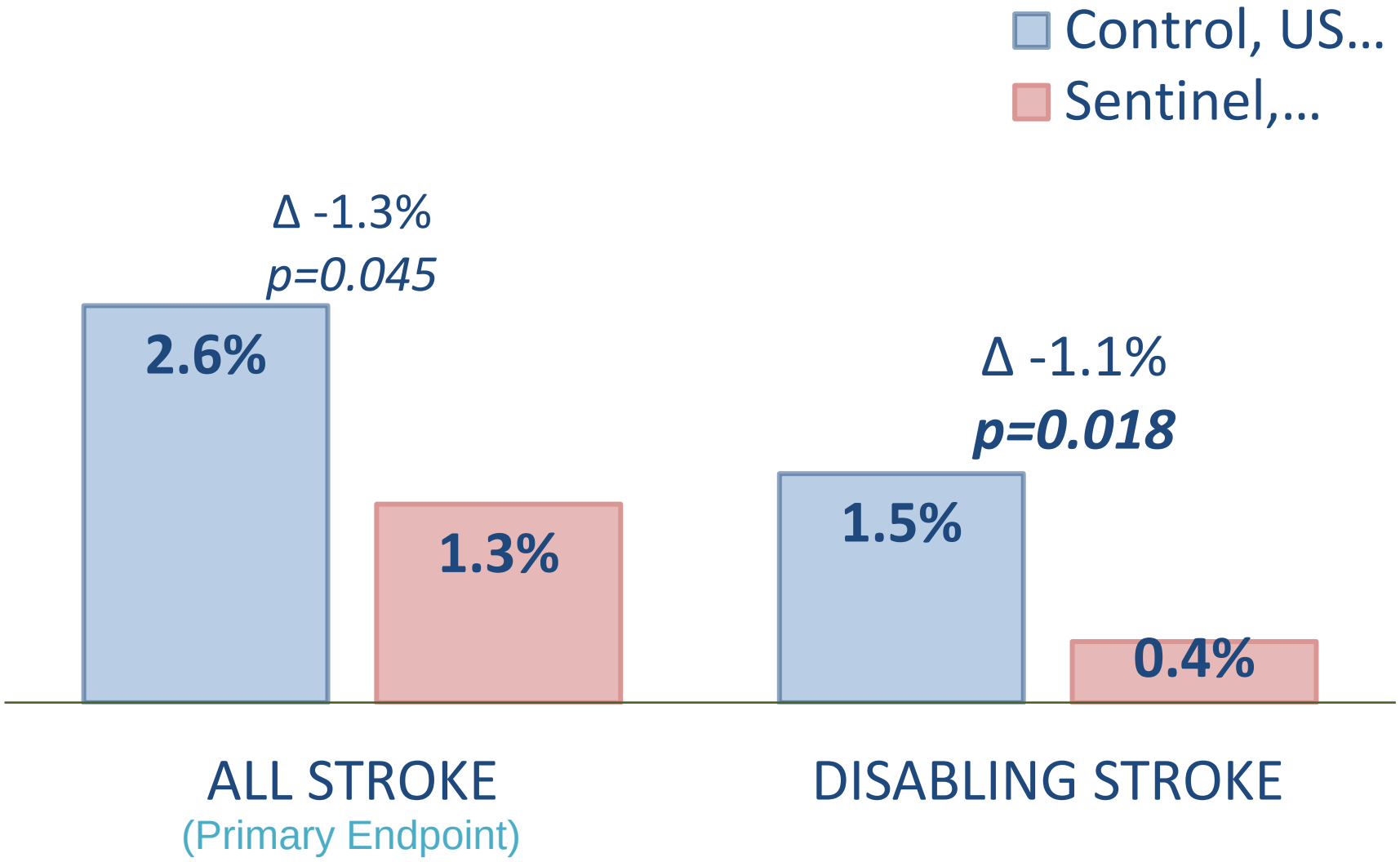
72h Stroke by Treatment Arm

OUS cohort



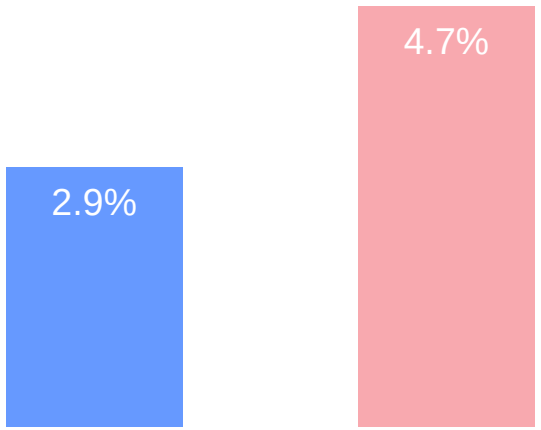
72h Stroke by Treatment Arm

US cohort

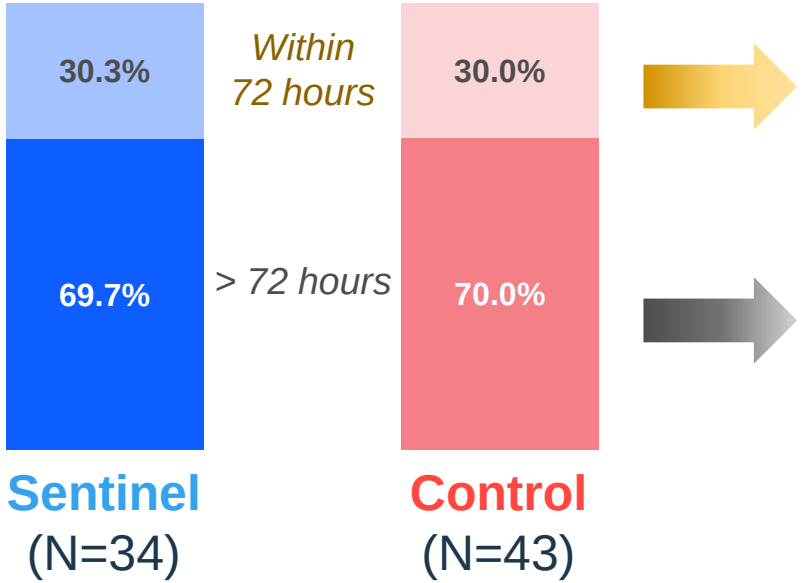


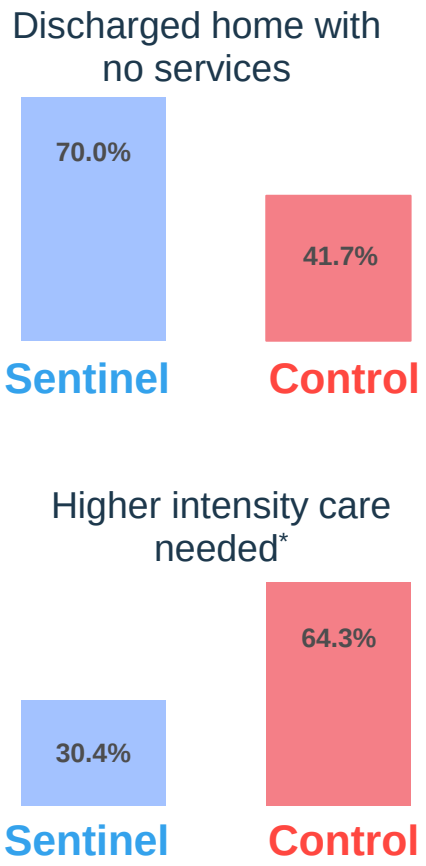
Clinical Outcomes in Patients with Stroke

Mortality at 72h/Discharge



Discharge / Length of Stay





*ICU, med/surg ward, rehab, step-down care

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Real World Data

Transcatheter Valve Therapy registry[1]
(N=123,186)

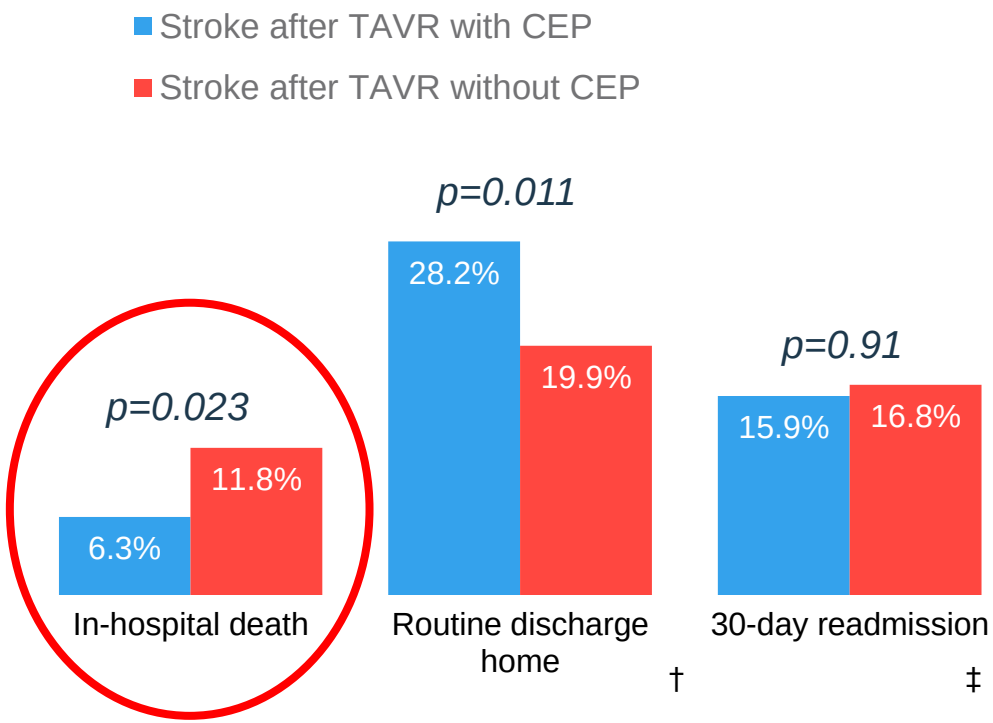
- No association between CEP and in-hospital stroke
- Mortality (in-hospital and 30-day) is lower with CEP

	CEP N=12,409	No CEP N=110,777	Odds Ratio [95% CI]	P-value
In-hospital stroke	1.3%	1.5%	0.82 [0.65-1.03]	0.083
In-hospital death	0.8%	1.2%	0.67 [0.51-0.88]	0.005
30-day death	1.4%	2.2%	0.62 [0.49-0.78]	<0.001

Table reflects unadjusted outcomes

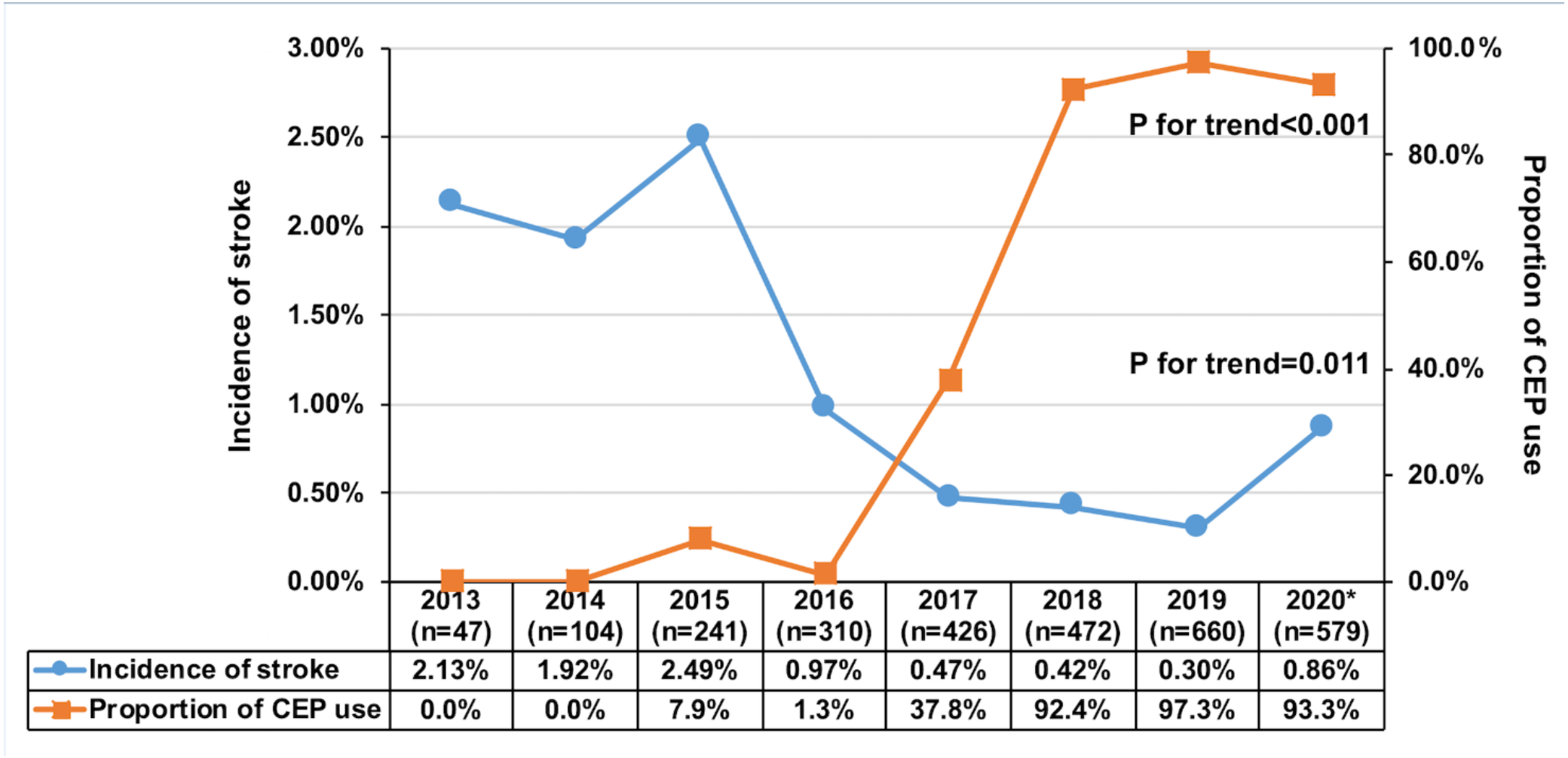
Nationwide Readmission Database[2]
(N=136,382)

Mortality after stroke is lower in patients protected with CEP



[1]Butala NM, et al. Circulation 2021;143:2229–40. [2]Isogai T, et al. JACC Cardiovasc Interv 2022;15:569–71.†Includes only patients discharged alive (CEP n=177, non-CEP n=2,159). ‡Includes only patients discharged alive before December of each year (CEP n=145, non-CEP n=1,964)

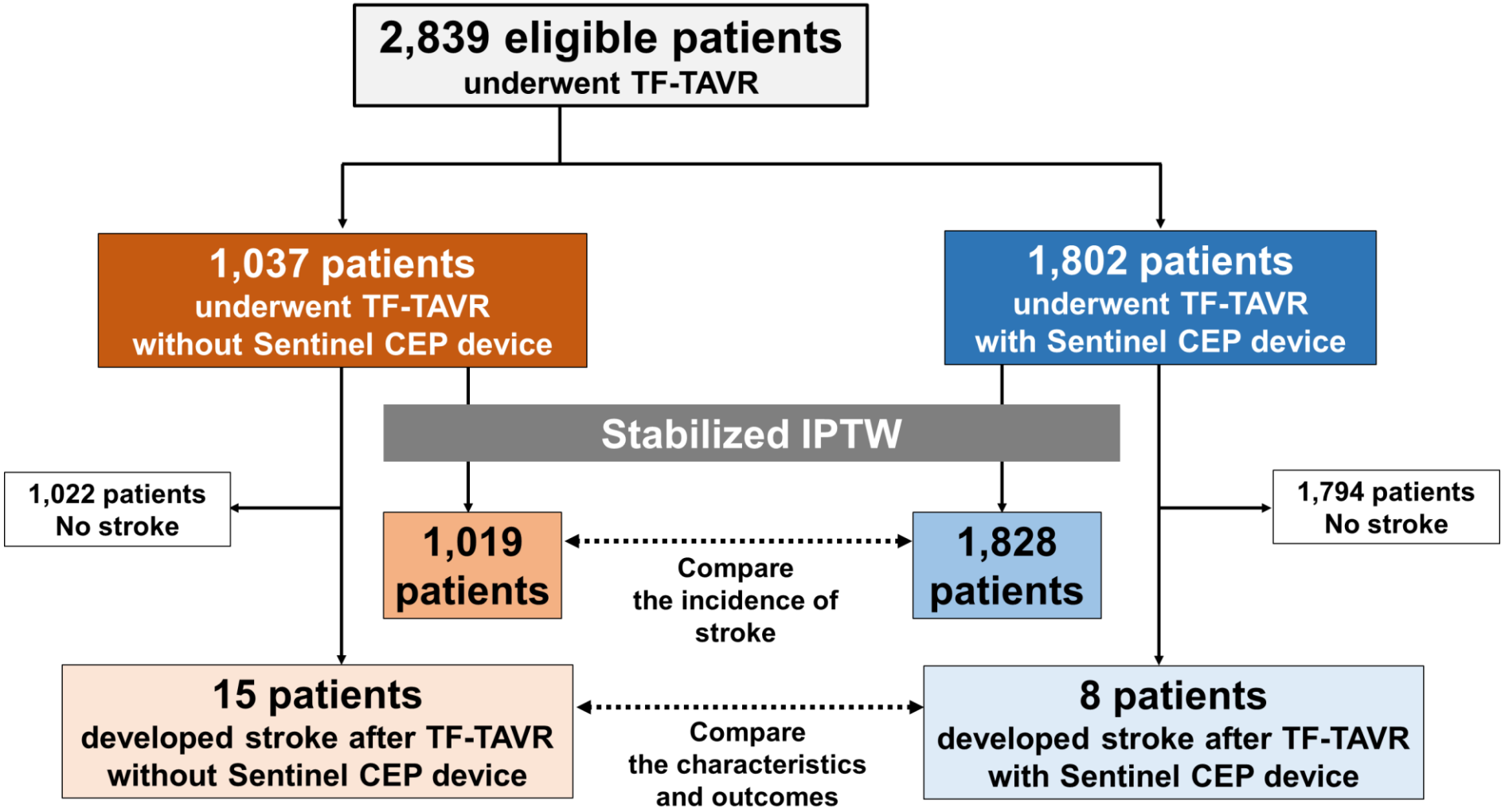
Cleveland Clinic Experience



	2013 (n=47)	2014 (n=104)	2015 (n=241)	2016 (n=310)	2017 (n=426)	2018 (n=472)	2019 (n=660)	2020* (n=579)
Incidence of stroke	2.13%	1.92%	2.49%	0.97%	0.47%	0.42%	0.30%	0.86%
Proportion of CEP use	0.0%	0.0%	7.9%	1.3%	37.8%	92.4%	97.3%	93.3%

Isogai et al, CCI, 2022

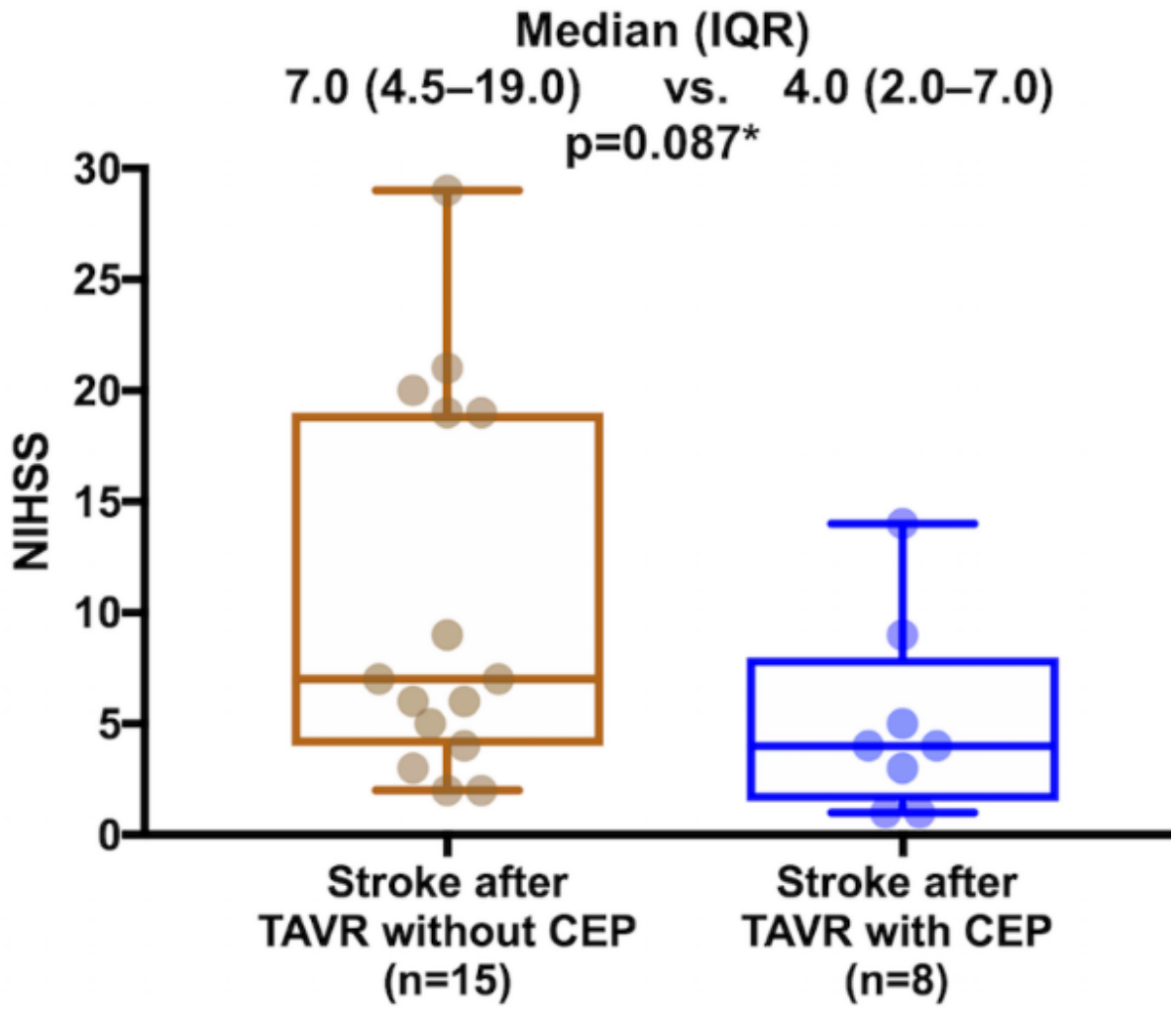
Results – Study Patients



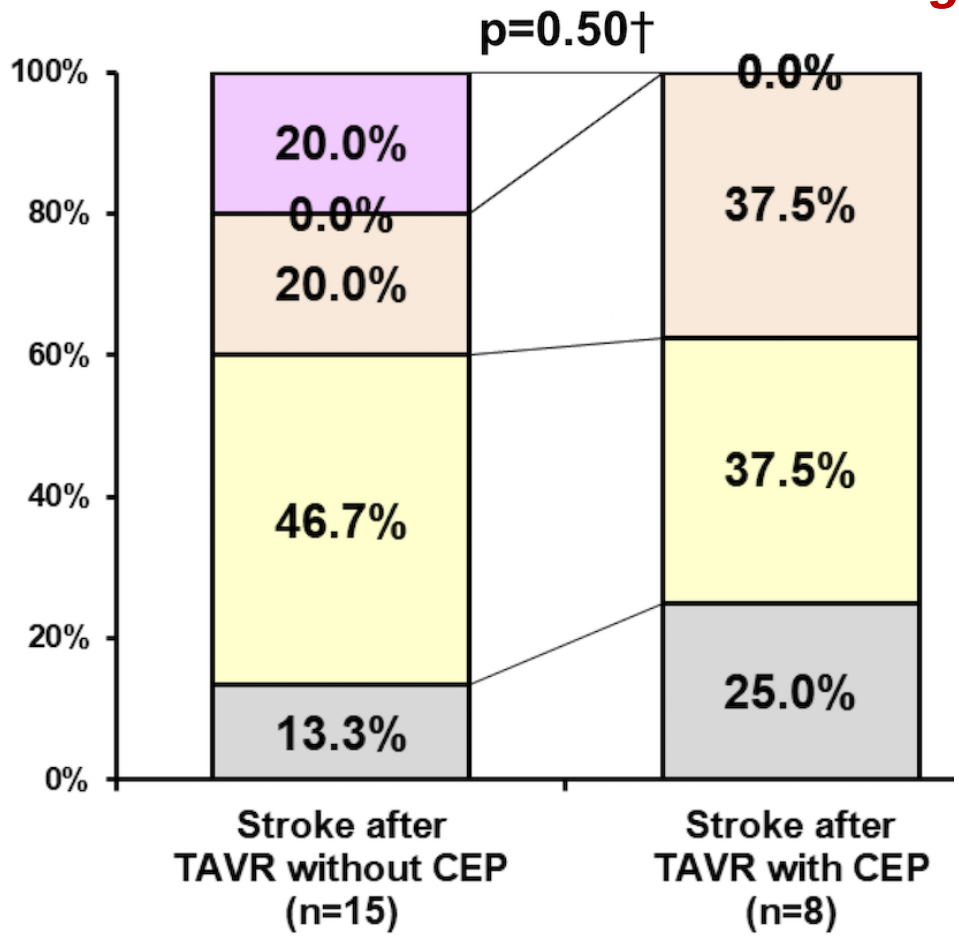
Isogai et al, CCI, 2022

NIHSS and modified Rankin Scale among stroke patients

NIHSS at the time of diagnosis and severity of stroke



Modified Rankin Scale at discharge



Isogai et al, CCI, 2022

Treatment and Mortality of Stroke

	Stroke after TAVR without CEP (n=15)	Stroke after TAVR with CEP (n=8)	p value
Treatment			1.00
Conservative medical management	11 (73.3)	7 (87.5)	
Thrombolysis alone	0 (0.0)	0 (0.0)	
Thrombectomy alone	3 (20.0)	1 (12.5)	
Both thrombolysis and thrombectomy	1 (6.7)	0 (0.0)	
Outcomes			
In-hospital death	3 (20.0)	0 (0.0)	0.53
Discharge disposition†			0.16
Home	2/12 (16.7)	4/8 (50.0)	
Rehabilitation center or SNF	10/12 (83.3)	4/8 (50.0)	
30-day death	4 (26.7)	0 (0.0)	0.26

Isogai et al, CCI, 2022

Summary

Consistent with “major stroke” reduction

Risk of mortality after stroke is reduced in patients with CEP compared to those without CEP

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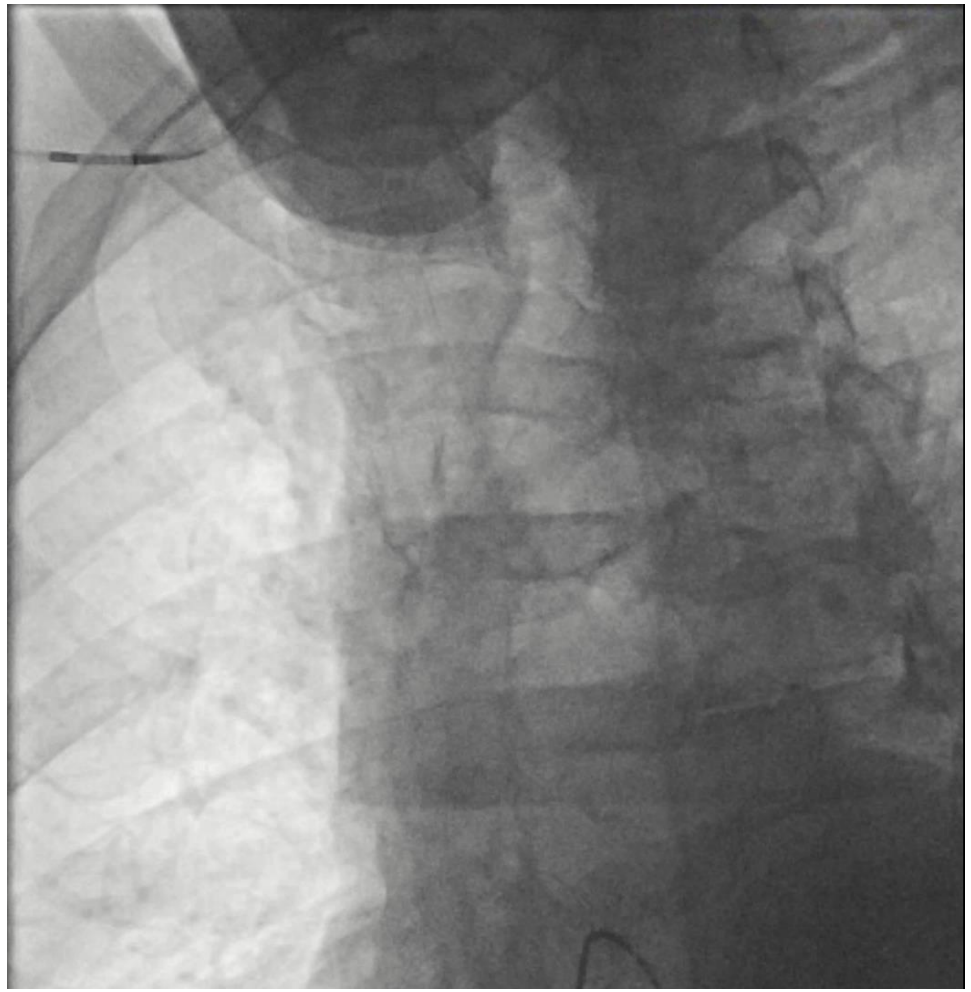
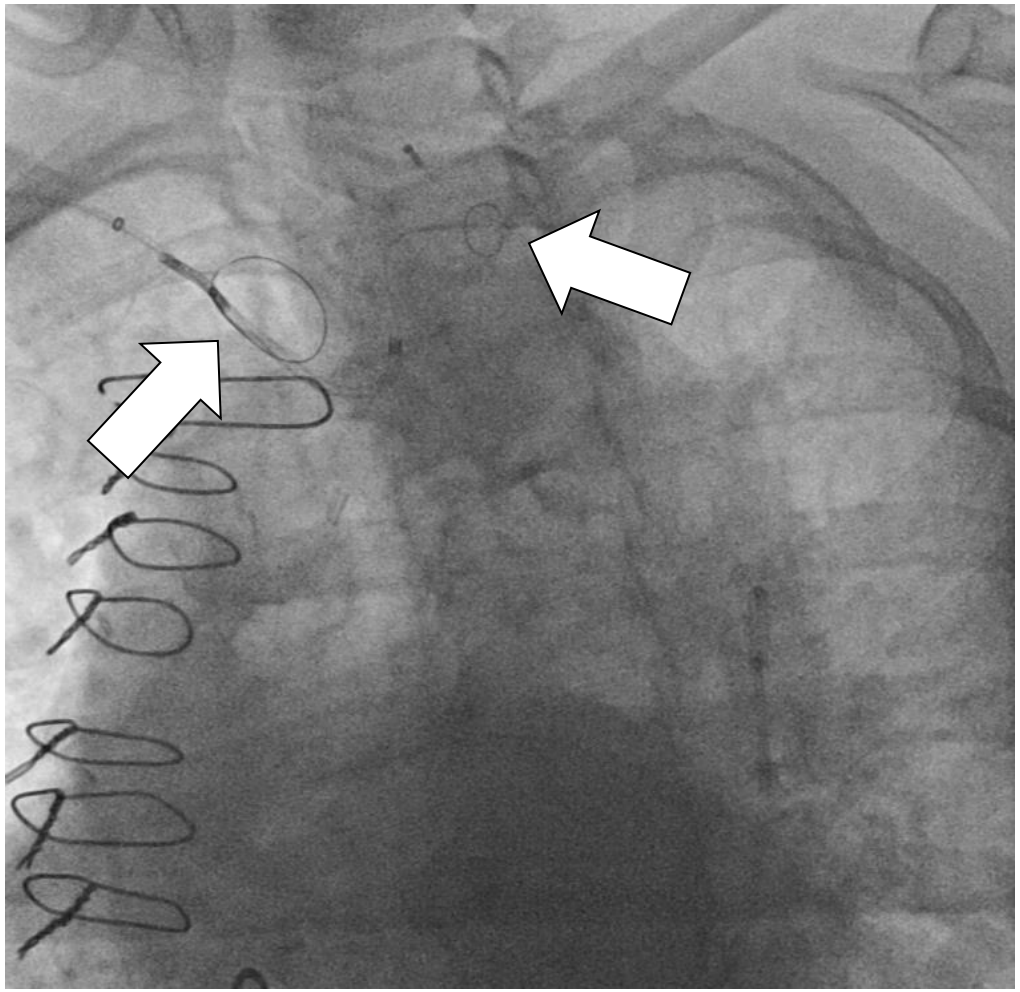
Sentinel: Short and Safe Procedure





Cleveland Clinic - Volume and Outcomes

	ALL	2018	2019	2020	2021	2022
n	3150	495	696	679	652	628
Mortality	0.4%	0.2%	0.0%	0.4%	0.6%	0.6%
Stroke	0.5%	0.2%	0.3%	1.0%	0.4%	0.6%
AR(>=2+)	0.4%	0.8%	0.3%	0.3%	0.4%	0.5%
New PPM	2.9%	5%	1.2%	2.5%	2.9%	3.5%

Take Home Messages

- Stroke is still a clinical problem although stroke risk is lower
- Sentinel use has been associated with lower risk of disabling or “major” strokes
- Device is safe
- Stroke remains unpredictable
- Use Sentinel in all patients (if you can afford it)