What is the Current Role of EPD in TAVI?

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- I-Rhythm - Zoll/Therox

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- Medtronic - Edwards Lifesciences
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- Corvia - Impulse Dynamics

Embolic Protection for TAVR

- Is TAVR-related stroke really a problem?
- What is the benefit of EPD in current practice?
- Can we select appropriate patients?

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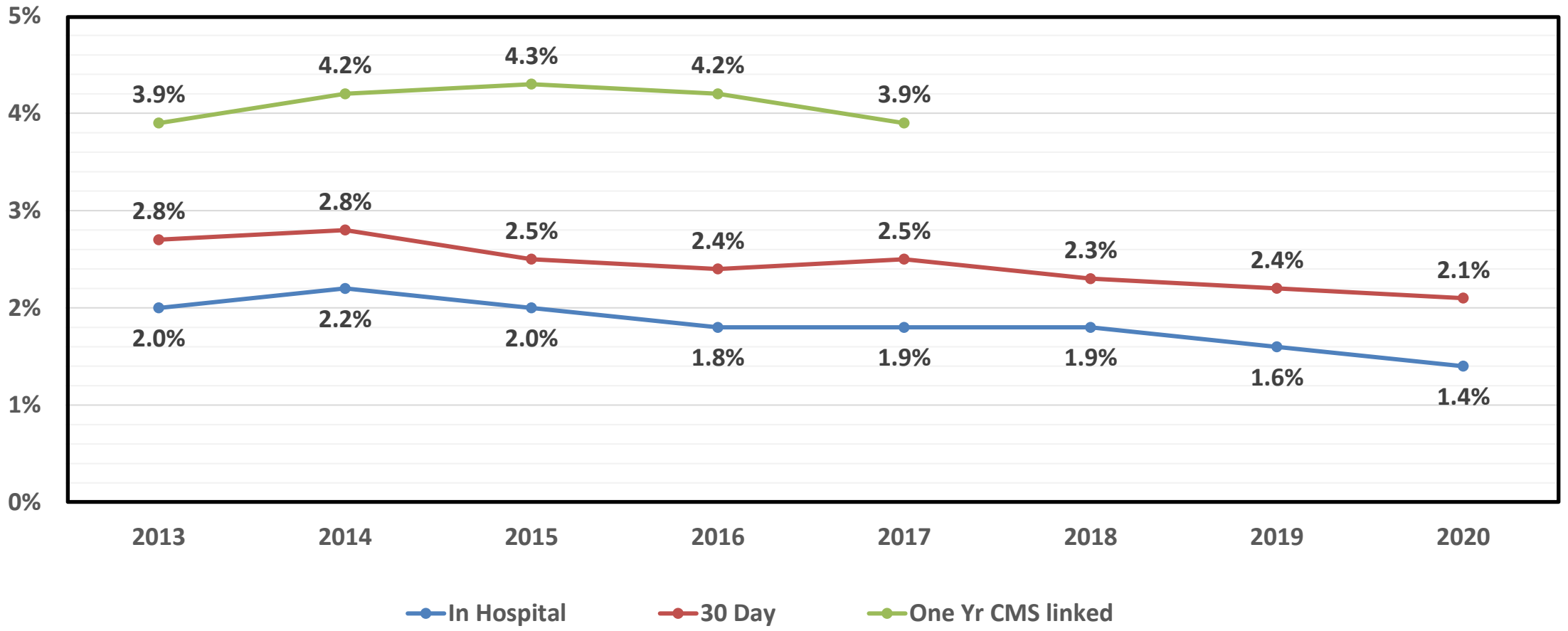
TVT Registry: TAVR-Related Stroke



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Impact of Stroke on Clinical and Economic Outcomes

Outcome	Adjusted HR or Diff. (95% CI)
Death	
30-day	3.2 (2.9 to 3.5)
1-year	1.5 (1.4 to 1.6)
5-year	1.2 (1.1 to 1.2)
Days at home	-16 (-18 to -14)
1-year cost	$9245 ($7665 to $10,825)

- Analysis of 129,000 TAVR procedures from Medicare Claims (2012-17)
- In-hospital stroke occurred in 4.3%
- Associated with increased risk of mortality (through 5 yrs) and ~$9000 increase in 1-year costs

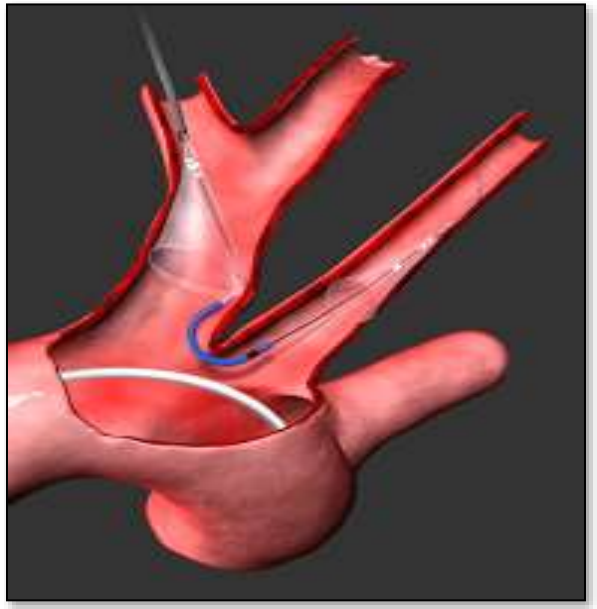
Almarzooq ZI, et al. EuroIntervention 2022; ;18:e335-e344. DOI: 10.4244/EIJ-D-21-00951

Current Cerebroembolic Protection Devices

Device	Access	Sheath Size	Approval Status
Sentinel	Right radial	6F	FDA Approved CE Mark
TriGuard 3	Femoral	8F	CE Mark
ProEmbo	Left radial	6F	Investigational
Emblok	Femoral	12F	Investigational
Emboliner	Femoral	9F	Investigational
Point-Guard	Femoral	10F	Investigational

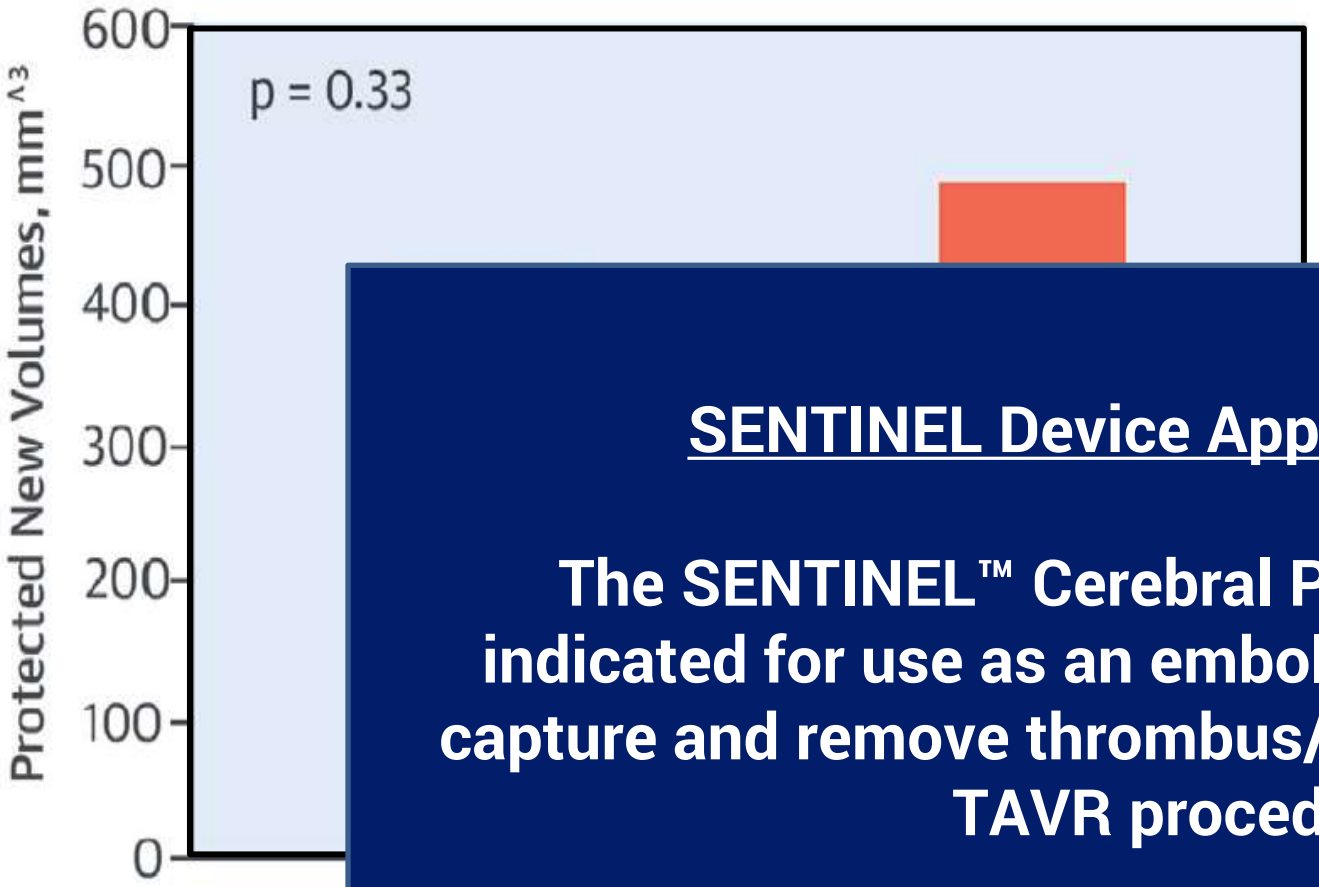
SENTINEL Device

- Two independent polyurethane filters (pore size 140 µm) deployed in the right brachiocephalic trunk and left common carotid artery



- Delivered through 6Fr sheath via right radial artery

SENTINEL IDE Trial



- **Design:** 363 high-risk TAVR patients randomized to Sentinel or no Sentinel

duction
n
s on MRI

2% (p=0.05)
p=0.25)

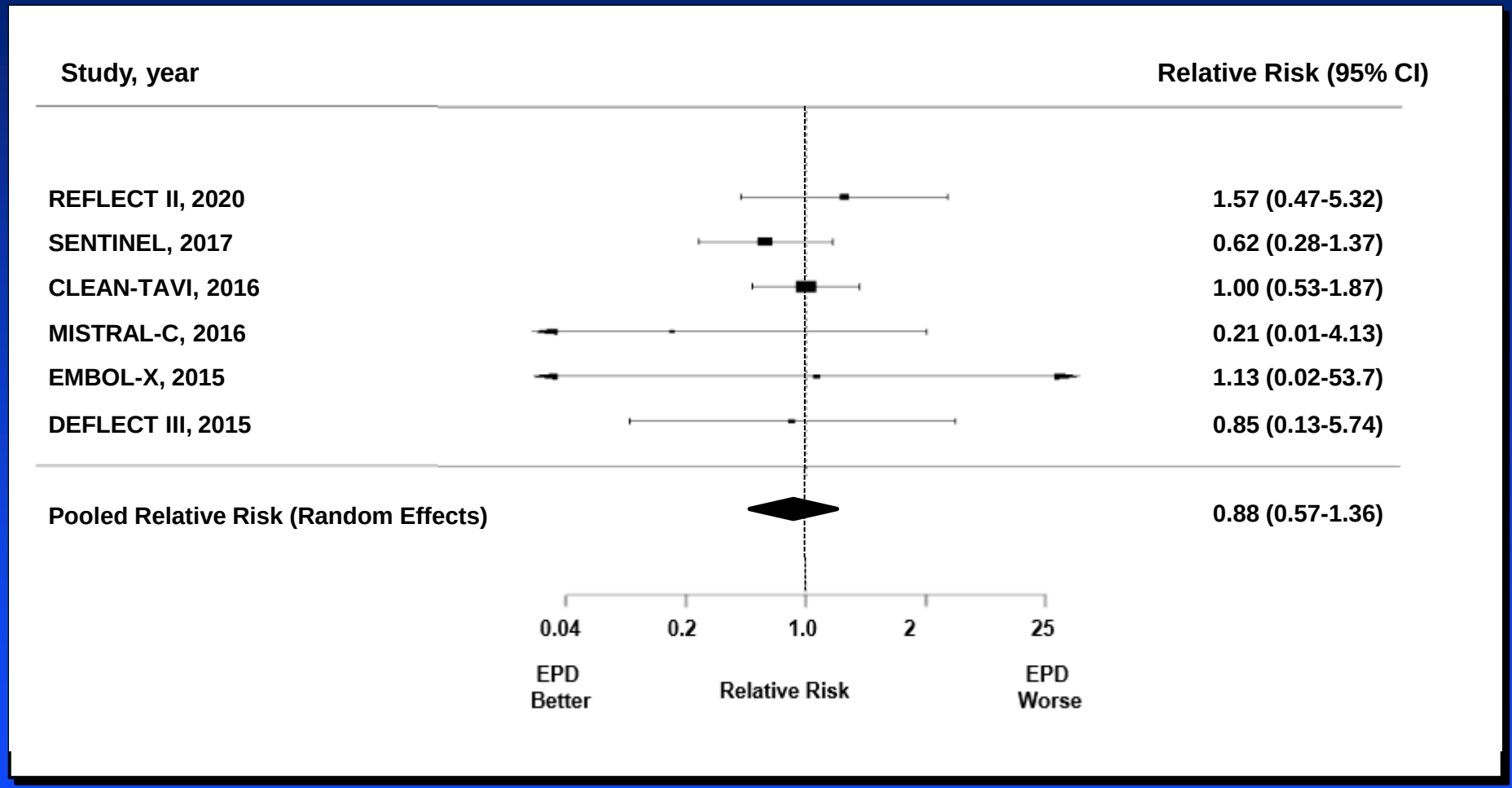
SENTINEL Device Approval Language

The SENTINEL™ Cerebral Protection System is indicated for use as an embolic protection device to capture and remove thrombus/debris while performing TAVR procedures.[1]

Kapadia et al. JACC 2017; 69: 367-77

EPD in TAVR: Meta-analysis of RCTs

Relative Risk of Any Stroke



Ahmad Y, et al. Am J Cardiol 2021;146:69-73

Ongoing RCTs Evaluating Stroke Prevention during TAVR with Cerebral Embolic Protection

PROTECTED-TAVR

- 3000 patients randomized to TAVR with or without SENTINEL
- ***Primary Endpoint*** – Stroke at 72 hrs or discharge
- All patients evaluated by neurologist before and after procedure

BHF- PROTECT TAVI

- 7730 patients randomized to TAVR with or without SENTINEL
- Primary Endpoint – Stroke at 72 hrs or discharge
- All pts undergo questionnaire to assess stroke-free status with subsequent stroke physician review

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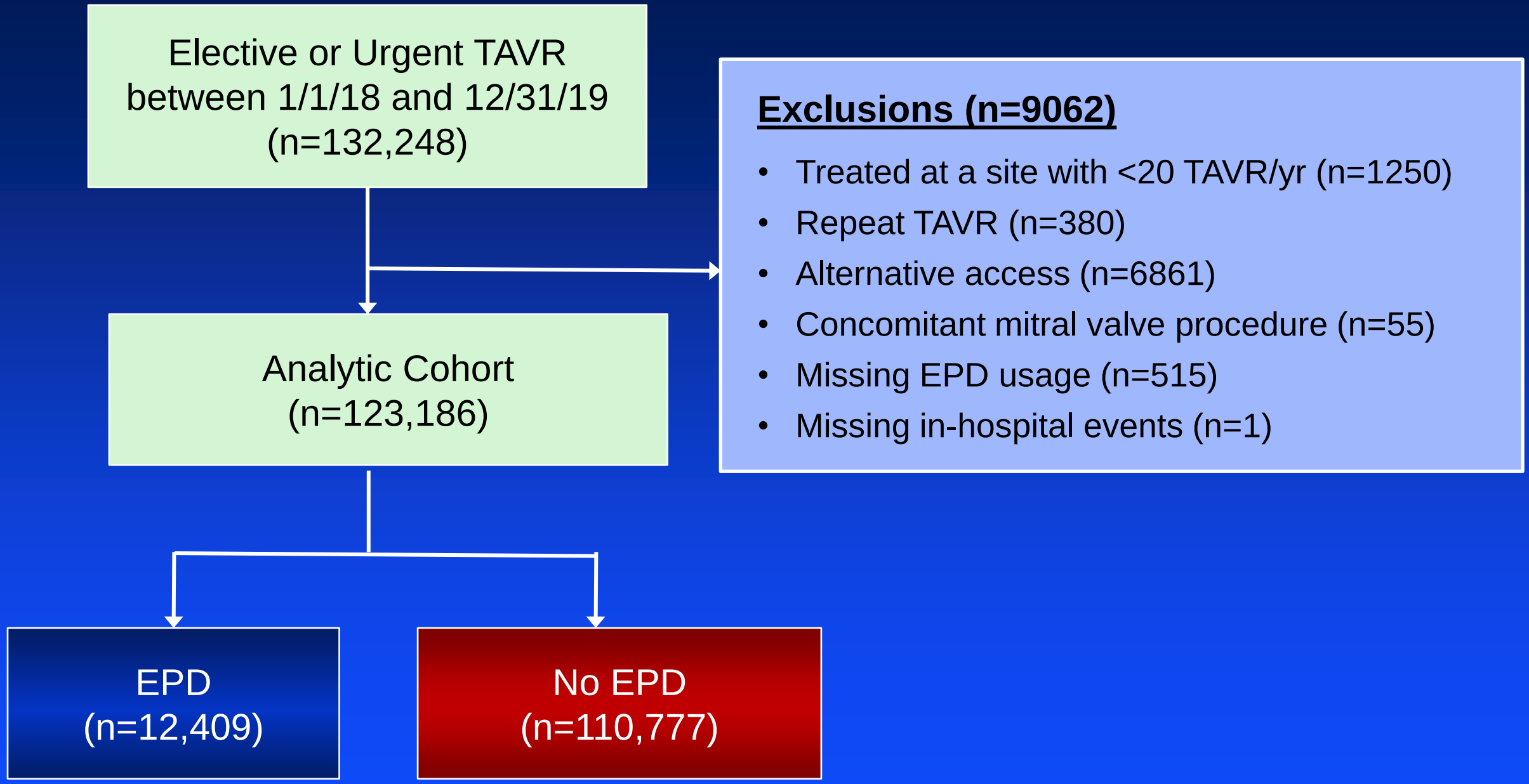

Elective or Urgent TAVR between 1/1/18 and 12/31/19 (n=132,248)
Exclusions (n=9062)
Treated at a site with <20 TAVR/yr (n=1250)
Repeat TAVR (n=380)
Alternative access (n=6861)
Concomitant mitral valve procedure (n=55)
Missing EPD usage (n=515)
Missing in-hospital events (n=1)
Analytic Cohort (n=123,186)
EPD (n=12,409)
No EPD (n=110,777)

Analytic Approaches

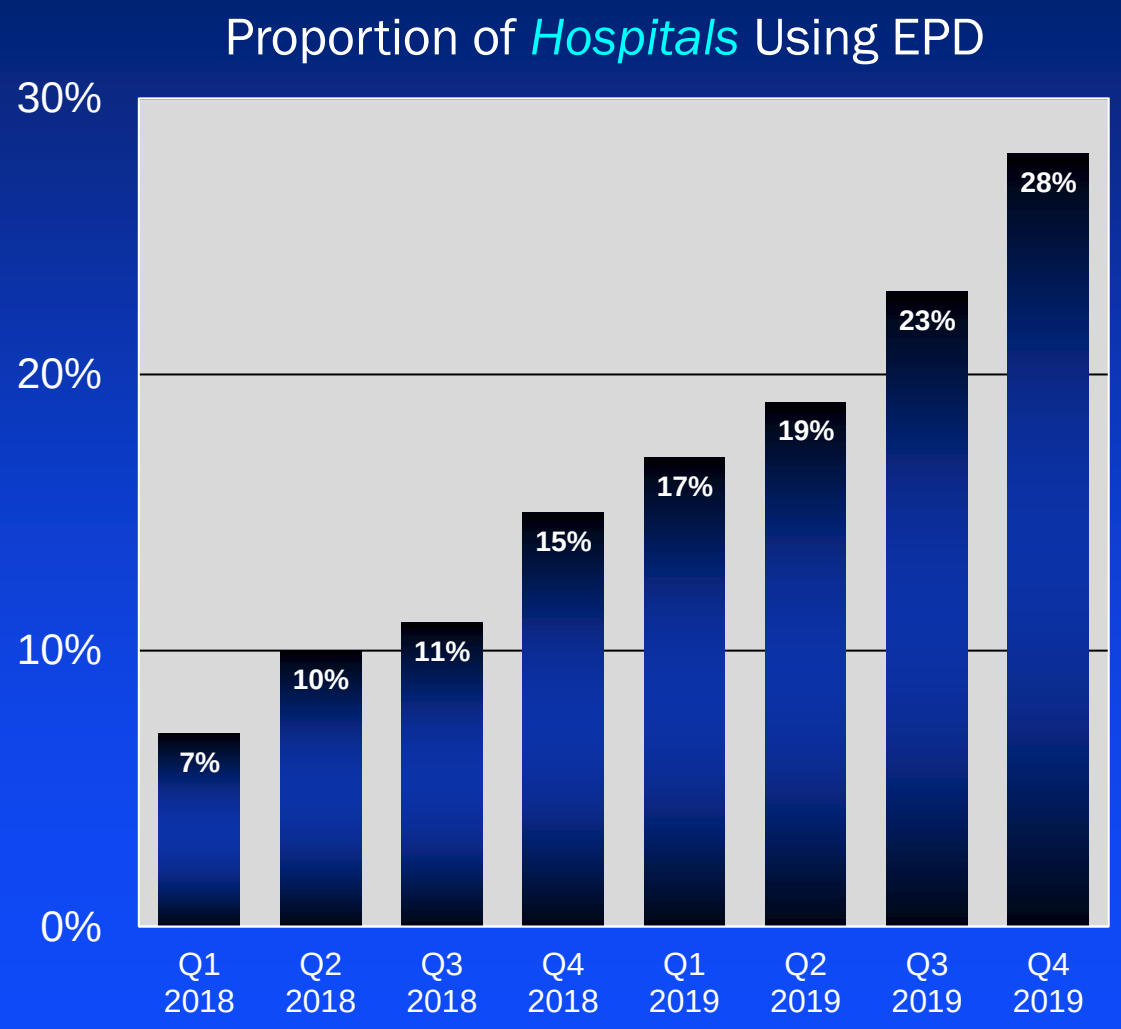
Primary: Instrumental Variable (IV) Analysis

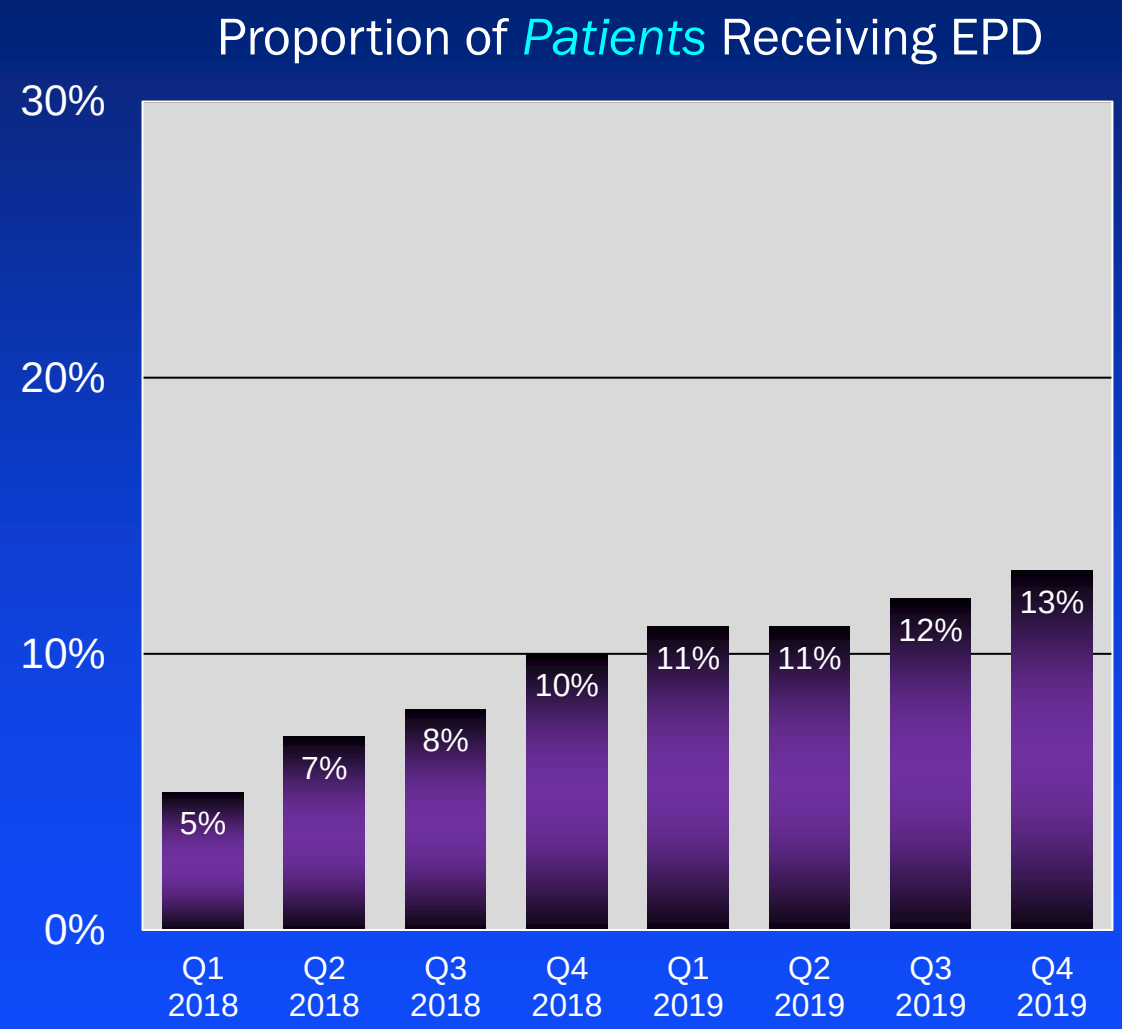
- Technique originally developed in economics that takes advantage of “natural experiments” to approximate randomization
- Unlike standard risk-adjustment technicques, IV analysis an account for both measured and unmeasured confounding
- Instrument = site-level preference for EPD use during the calendar quarter

Secondary: Propensity Score Weighting

- Propensity score to predict EPD use developed based on 30 demographic, clinical, and hospital-level characteristics
- Risk-adjusted comparisons performed using overlap propensity weighting and generalized estimating equations to account for within-hospital clustering

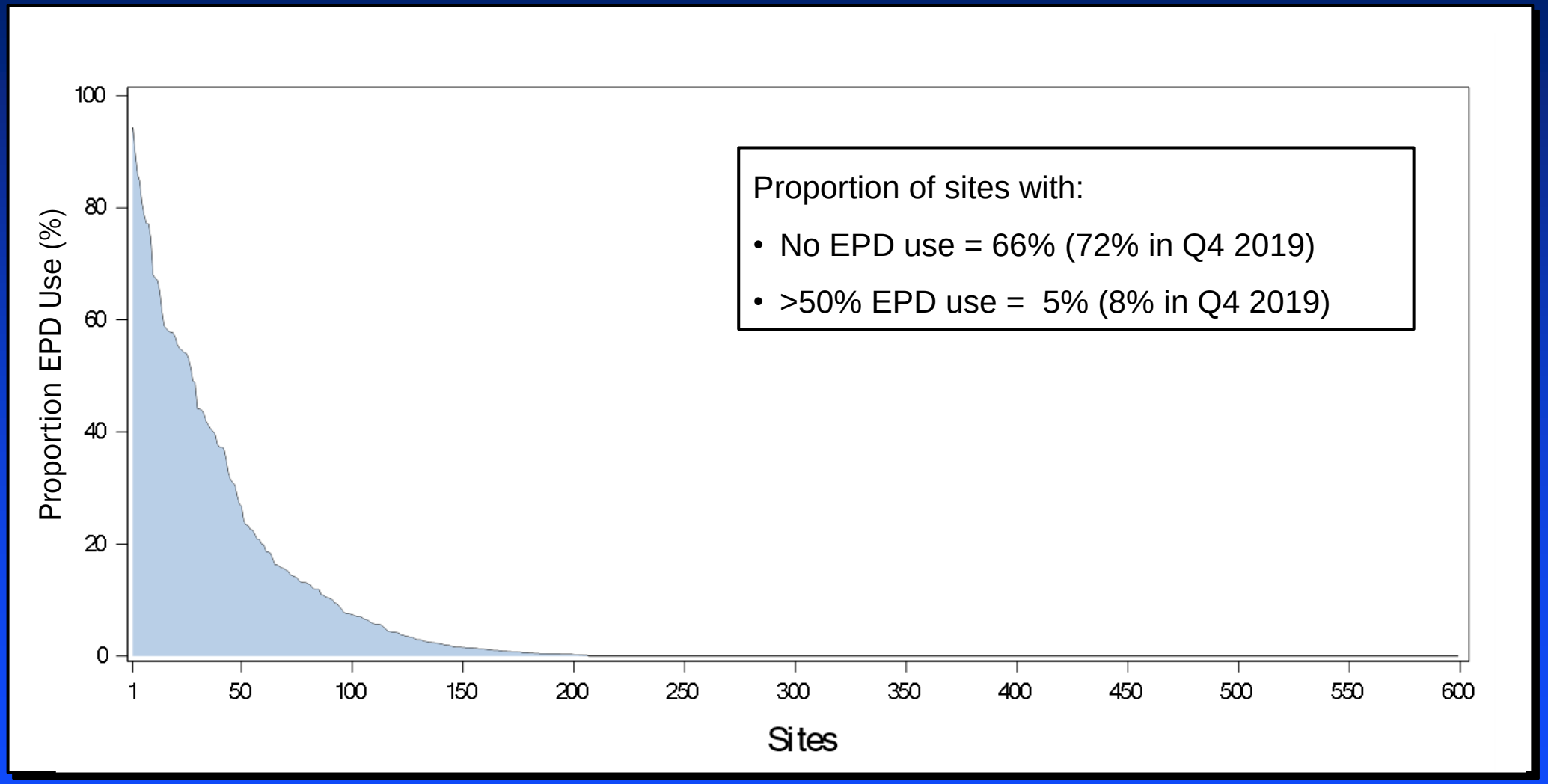
EPD Utilization by Calendar Quarter





Butala NM, et al. Circulation 2021; 143:2229–2240

Variation in EPD Use by Hospital (2018-2019)



Q1 2019-Q4 2019 (n=599 sites)

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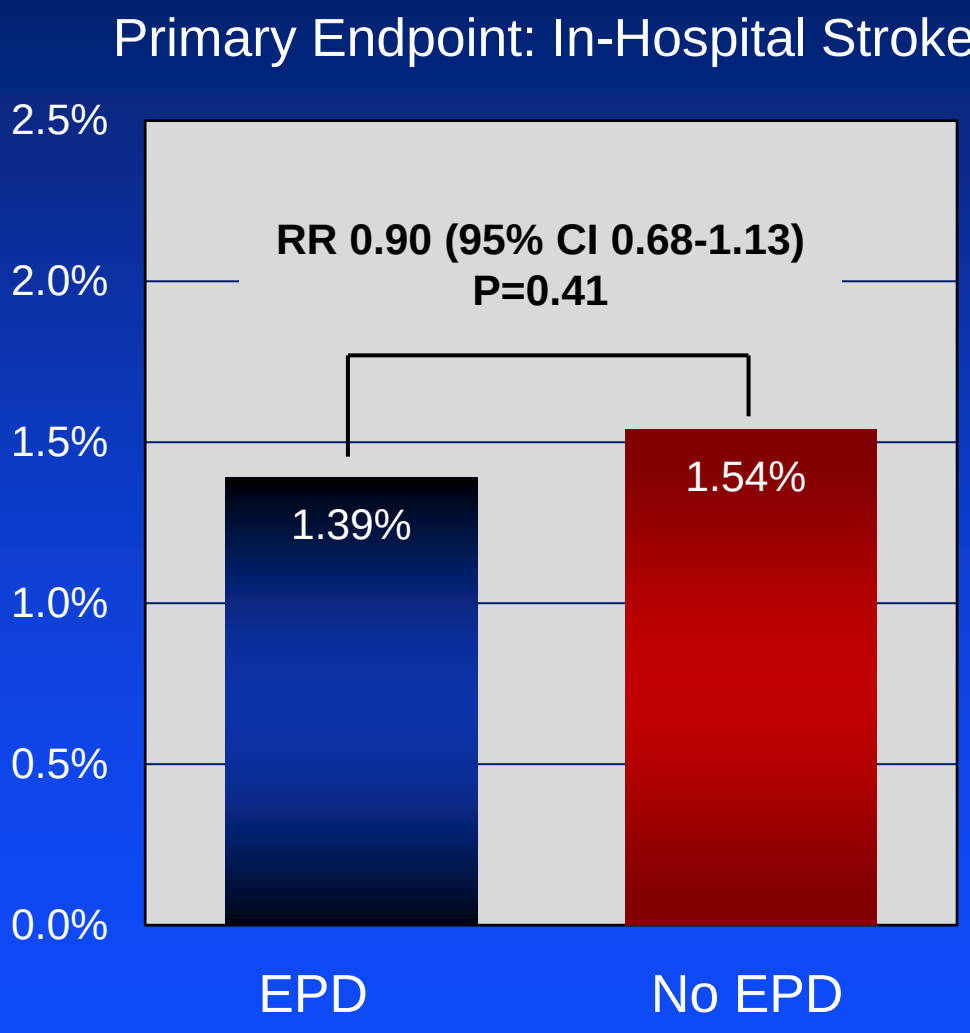
Results: Instrumental Variable Analysis



	EPD	No EPD	RR (95% CI)	P-Value
In-Hosp Outcomes				
Death or Stroke	2.4%	2.6%	0.93 (0.76-1.11)	0.47
Death	1.1%	1.2%	0.92 (0.66-1.19)	0.58
TAVR Success	97.0%	97.2%	1.00 (0.99-1.00)	0.41
GI or GU Bleed*	0.6%	0.4%	1.34 (0.91-1.80)	0.11
30-day Outcomes				
Stroke	2.0%	2.1%	0.92 (0.72-1.12)	0.42
Death	1.9%	2.2%	0.84 (0.65-1.04)	0.11

* Falsification Endpoint

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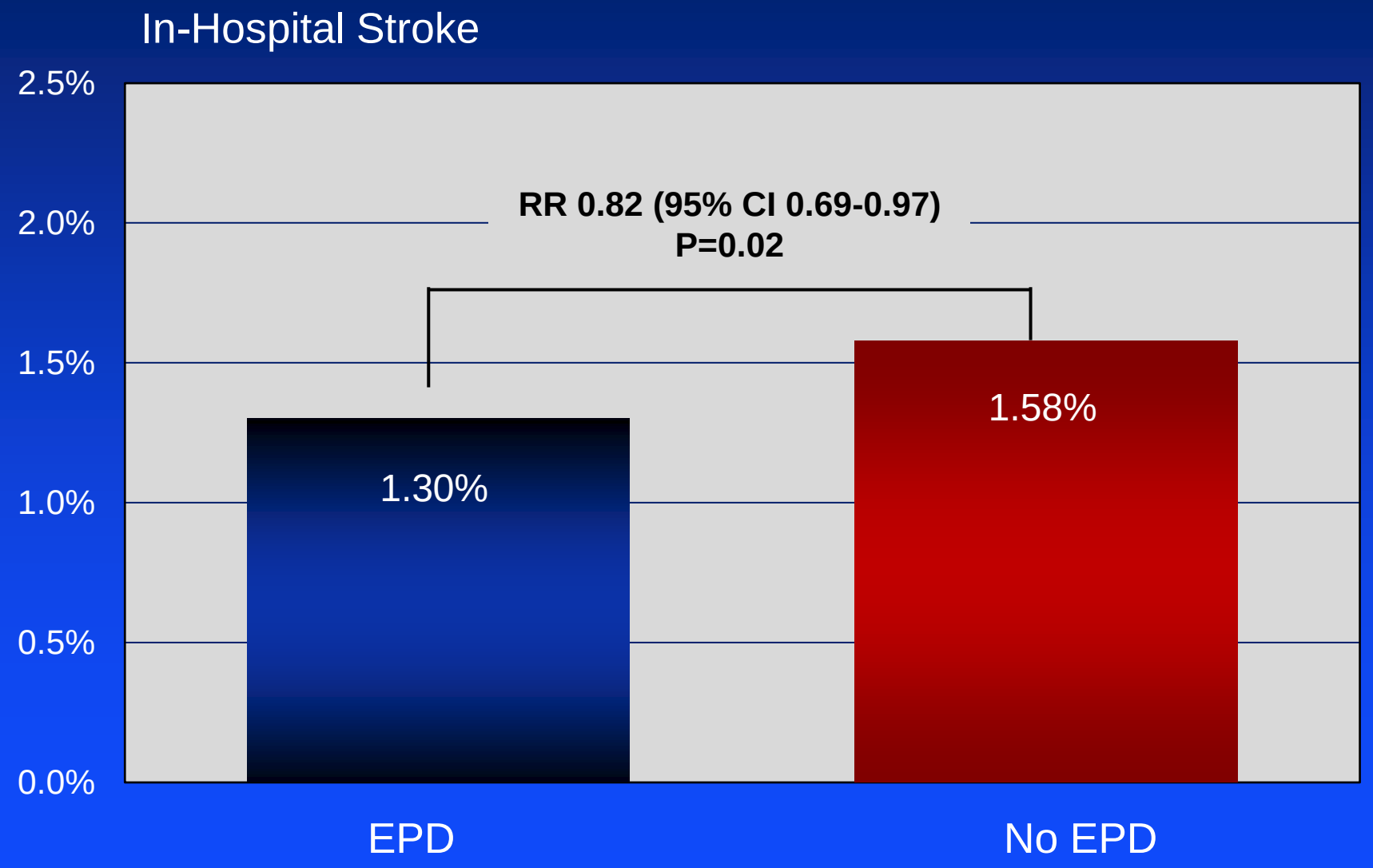
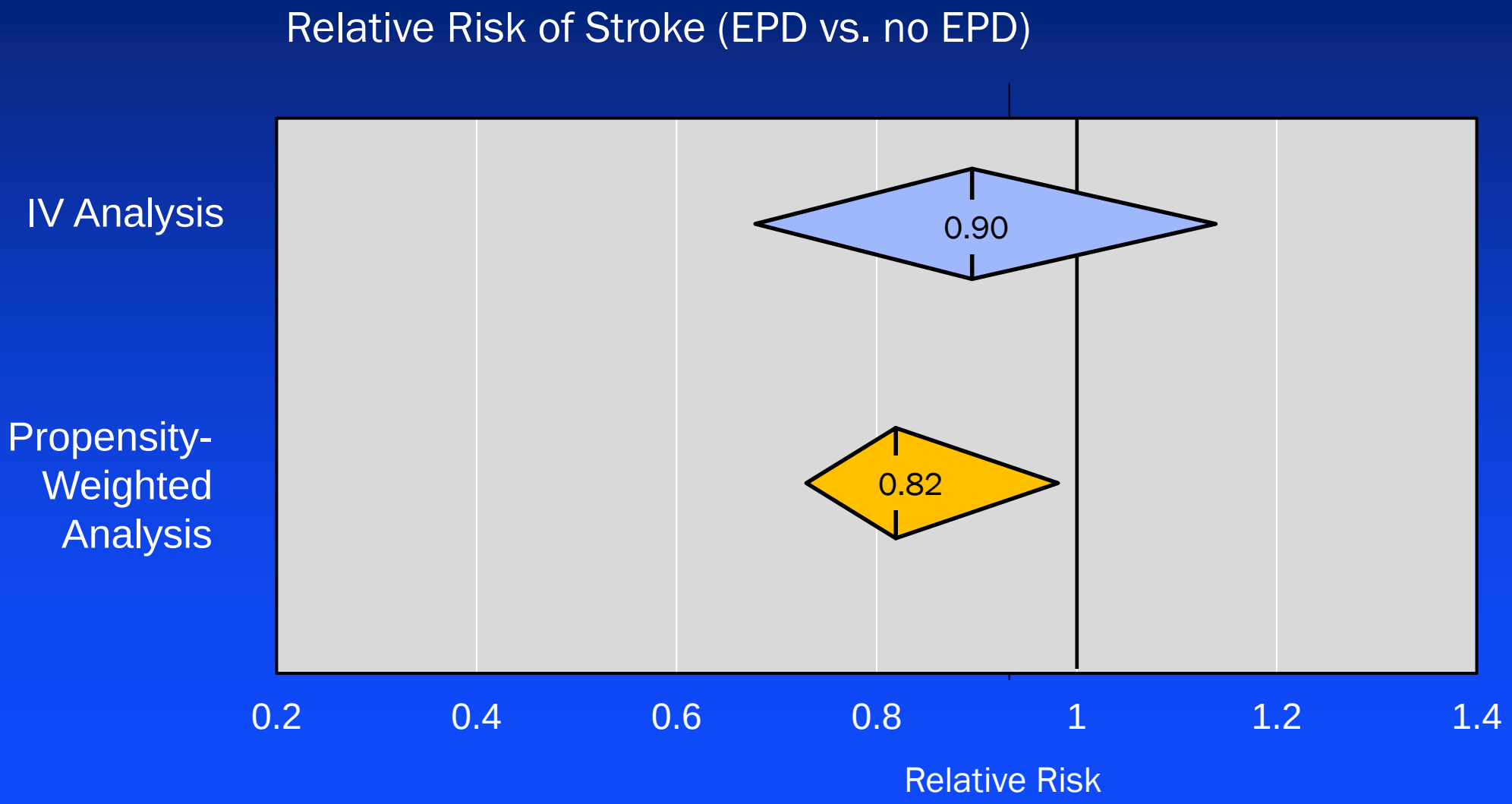
Results: Propensity-Weighted Analysis



Are these 2 analyses inconsistent?



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Predictors of In-Hospital Stroke after TAVR

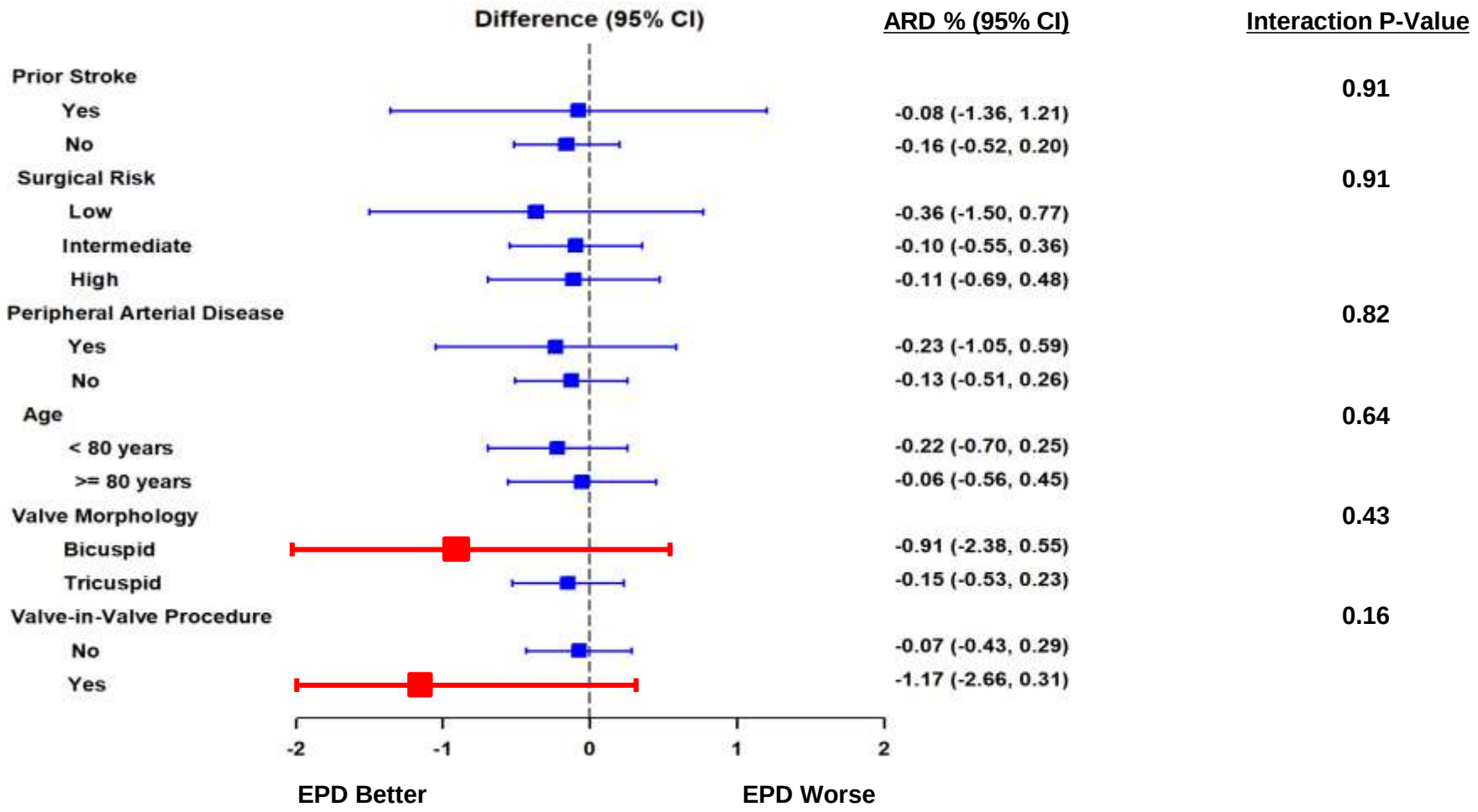
Variable	Odds Ratio	P-Value
Age (per 5 yrs > 75 yrs old)	1.11	< 0.001
BSA (men/women; per m2)	0.55/0.43	< 0.001
GFR (per 5ml/min)	0.97	< 0.001
TA access	1.44	< 0.001
Non TA/TF access	1.77	< 0.001
Prior Stroke	1.57	< 0.001
Prior TIA	1.50	< 0.001
PAD	1.21	< 0.001
Smoker	1.28	0.008
Porcelain Aorta	1.23	0.04
Pre-procedure Shock	1.48	< 0.001

TVT Stroke Model

- Model derived from 97,600 TAVR procedures performed between 2014 and 2017
- Good calibration but poor discrimination (c-statistic 0.62)
- Implications: Patient selection likely to be challenging

Thourani et al. Ann Thorac Surg 2019; 107: 1097-103

Subgroup Analyses



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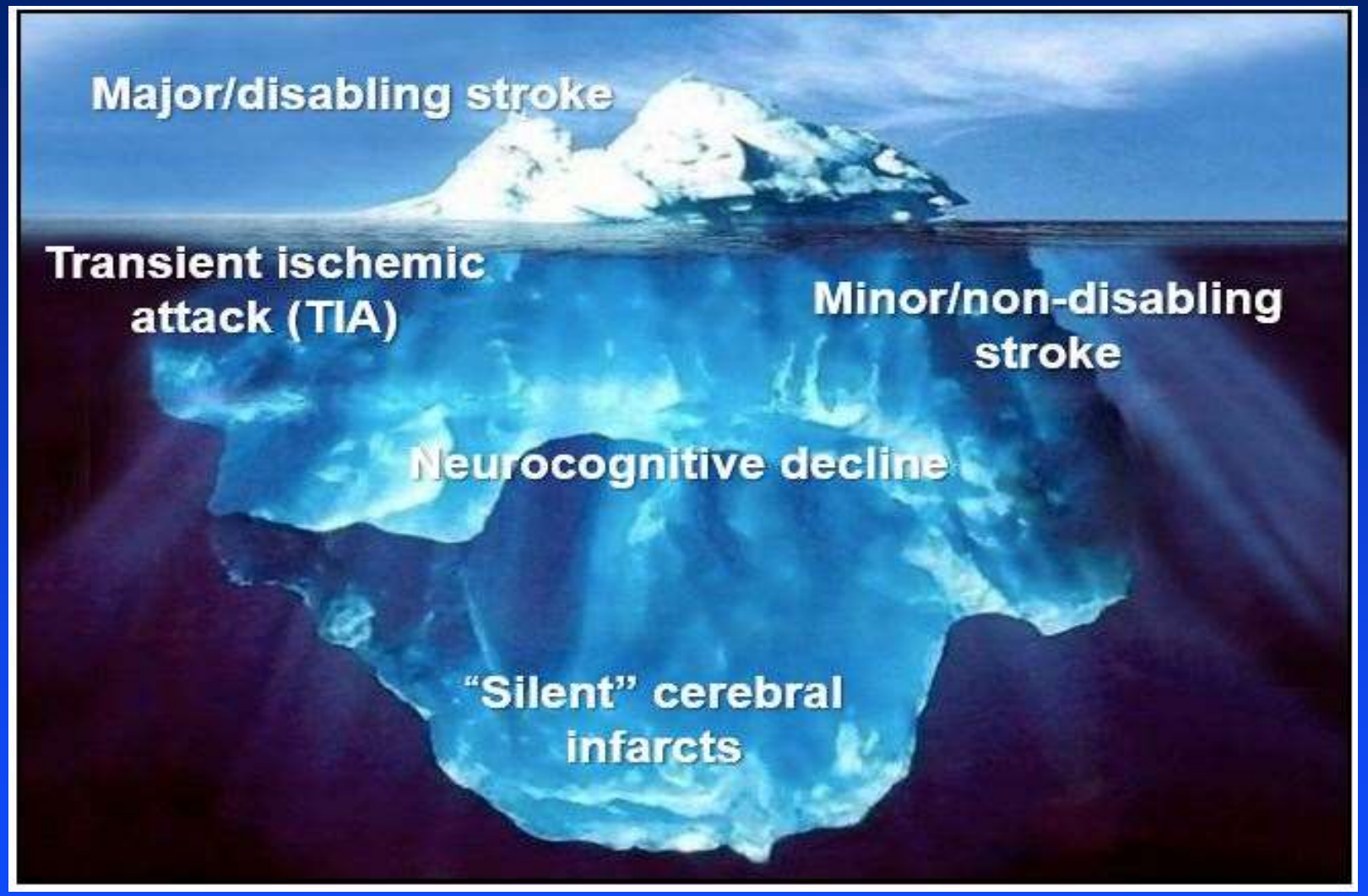
Are We Only Looking at the Tip of the Iceberg?



Summary

- Stroke remains a significant and unpredictable complication after TAVR
- Cerebroembolic protection devices capture procedure-related debris during the TAVR procedure and likely reduce volume of new brain lesions
- Clinical benefit of EPDs remains uncertain despite increasing use in the US → await definitive evidence from ongoing RCTs
- Selective use difficult to justify at present with the possible exception of ViV-TAVR and pts with bicuspid AS
- More research needed on long-term neurocognitive effects of non-disabling and clinically-silent strokes in TAVR and other structural cardiac procedures