Cerebral Embolic Protection and TAVR Outcomes: Results from the TVT Registry

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Study Design

- **General Design:** Observational study of the relationship between use of EPDs and TAVR outcomes
- **Data Source:** TVT Registry
- **Inclusion Criteria:** TF TAVR between 1/18 and 12/19; includes all TAVR devices, bicuspid valve, ViV procedures
- **Exclusion Criteria:** Emergent procedure; alternative access; sites performing <20 TAVR/yr; concurrent mitral procedures
- **Primary Endpoint:** In-hospital stroke (site reported)

Analytic Approaches

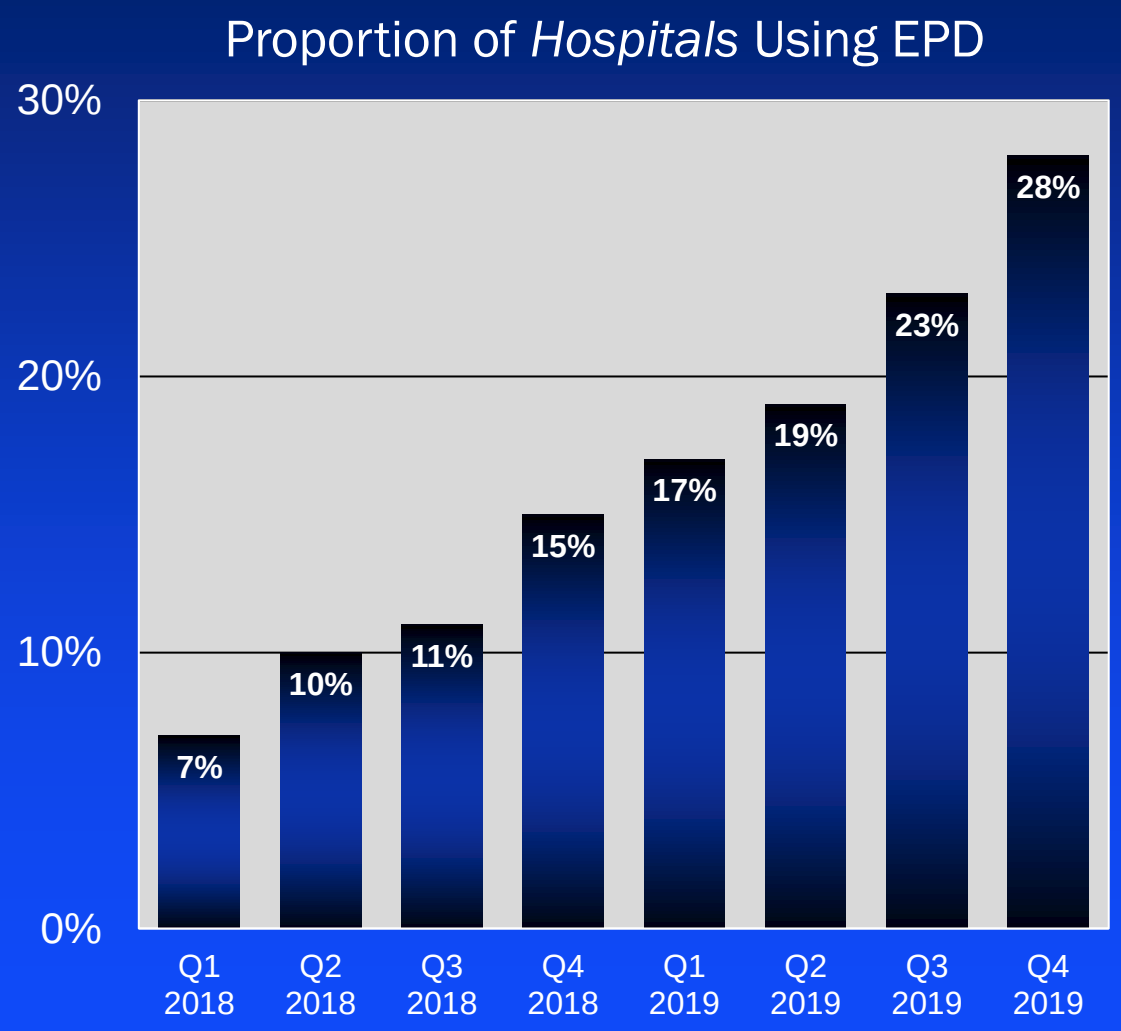
Primary: Instrumental Variable (IV) Analysis

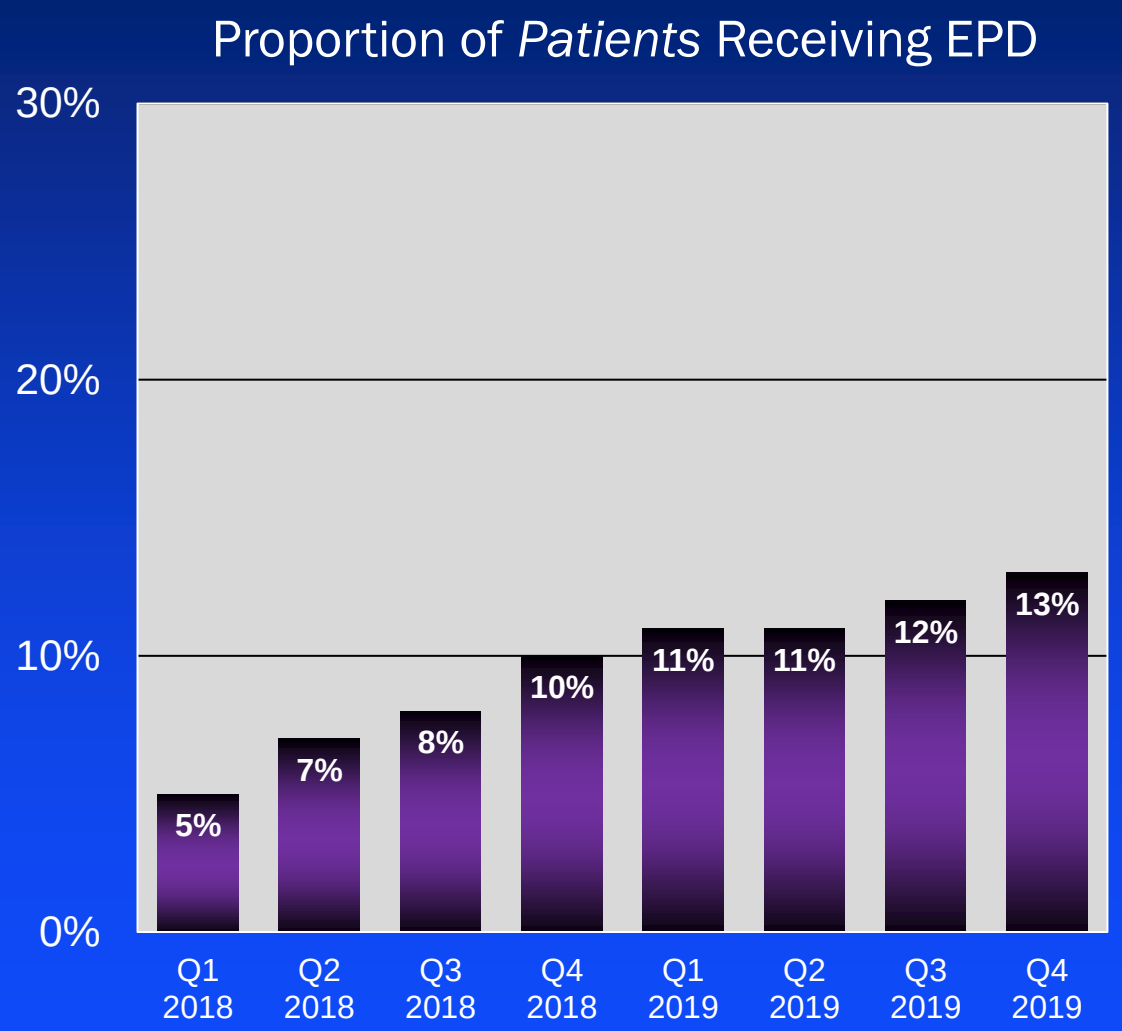
- Technique originally developed in economics that takes advantage of “natural experiments” to approximate randomization
- Under appropriate assumptions, can account for both measured and unmeasured confounding
- Instrument = site-level preference for EPD use during the calendar quarter

Secondary: Overlap 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





Patient Characteristics– by EPD Use

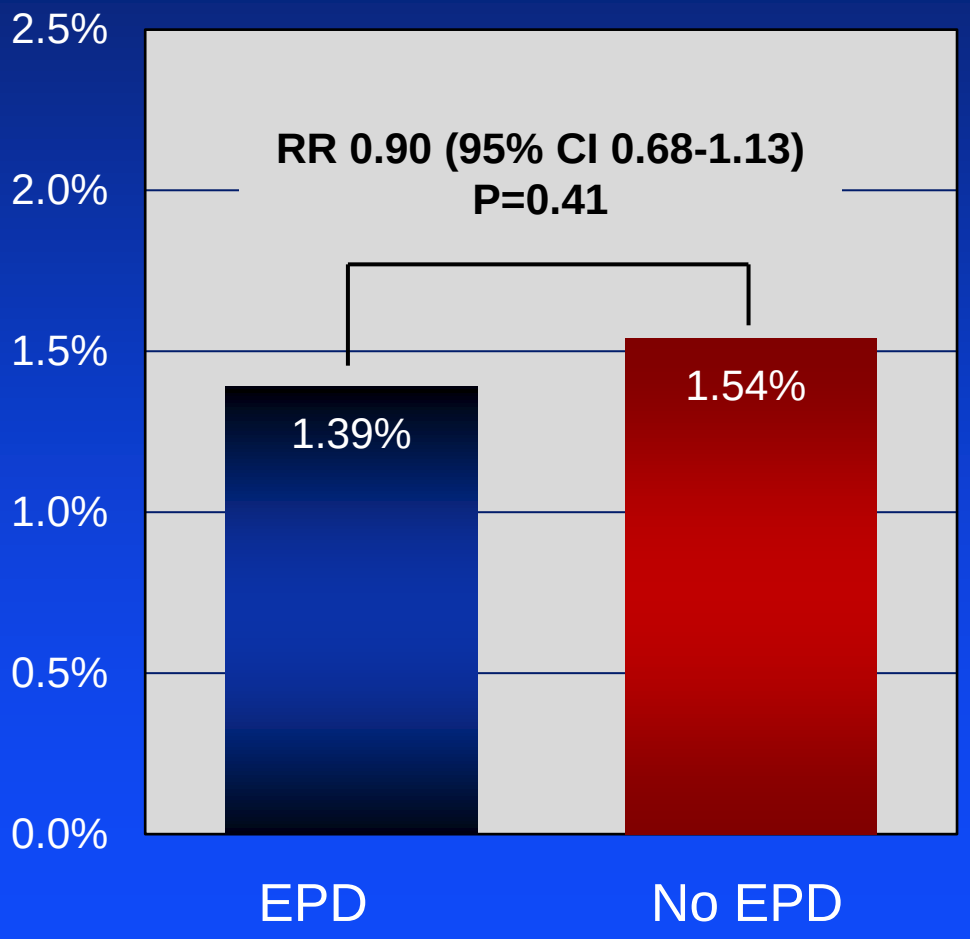
	EPD (n=12,409)	No EPD (n=110,777)
Age, yrs	79 ± 9	79 ± 9
Female	40.8%	45.3%
Prior stroke	11.8%	10.7%
Dialysis*	2.1%	3.9%
Bicuspid Valve*	6.8%	4.4%
ViV Procedure	6.8%	6.1%
Surgical Risk		
Low	7.4%	7.6%
Intermediate	46.5%	45.5%
High/Extreme	46.1%	46.9%

- No significant differences in other pt characteristics including BSA, smoking, NYHA Class, severe lung dz, or valve type used

* Standardized Difference > 10%

Results: Instrumental Variable Analysis

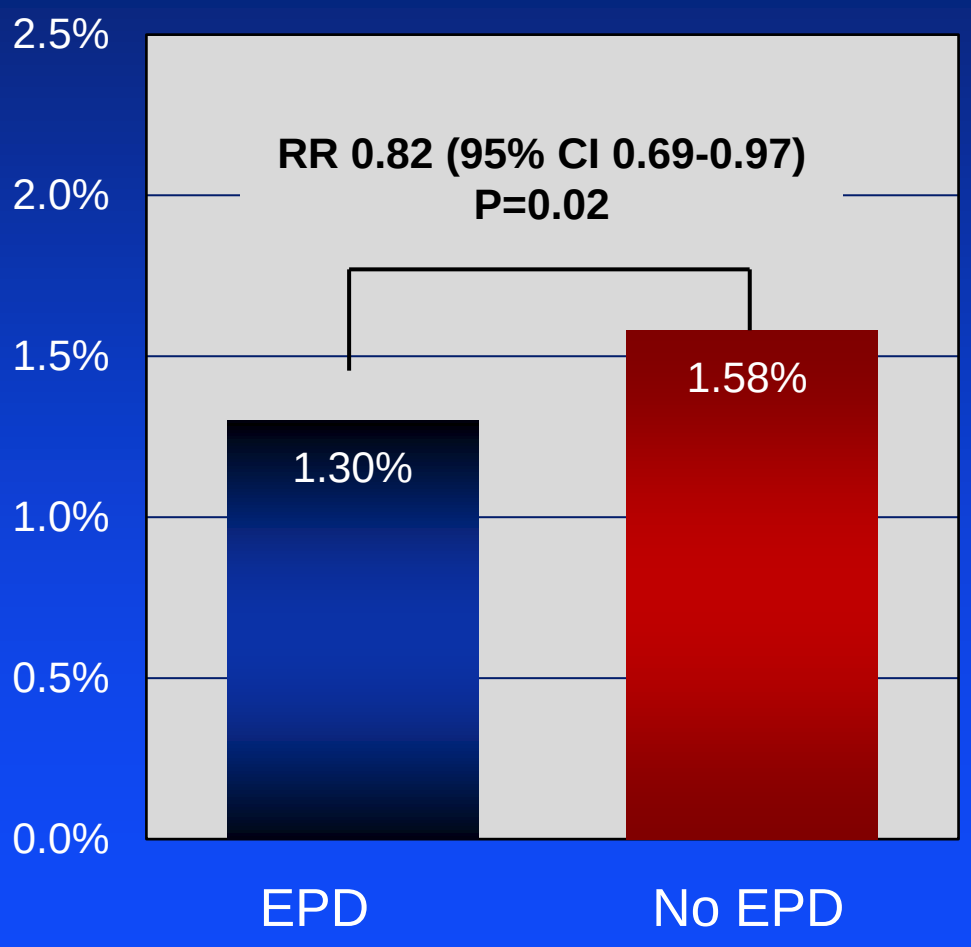
Primary Endpoint: In-Hospital Stroke



	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
Major Bleed	4.0%	4.4%	0.90 (0.79-0.97)	0.12
Device 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

* All results risk-adjusted based on 2-stage IV analysis

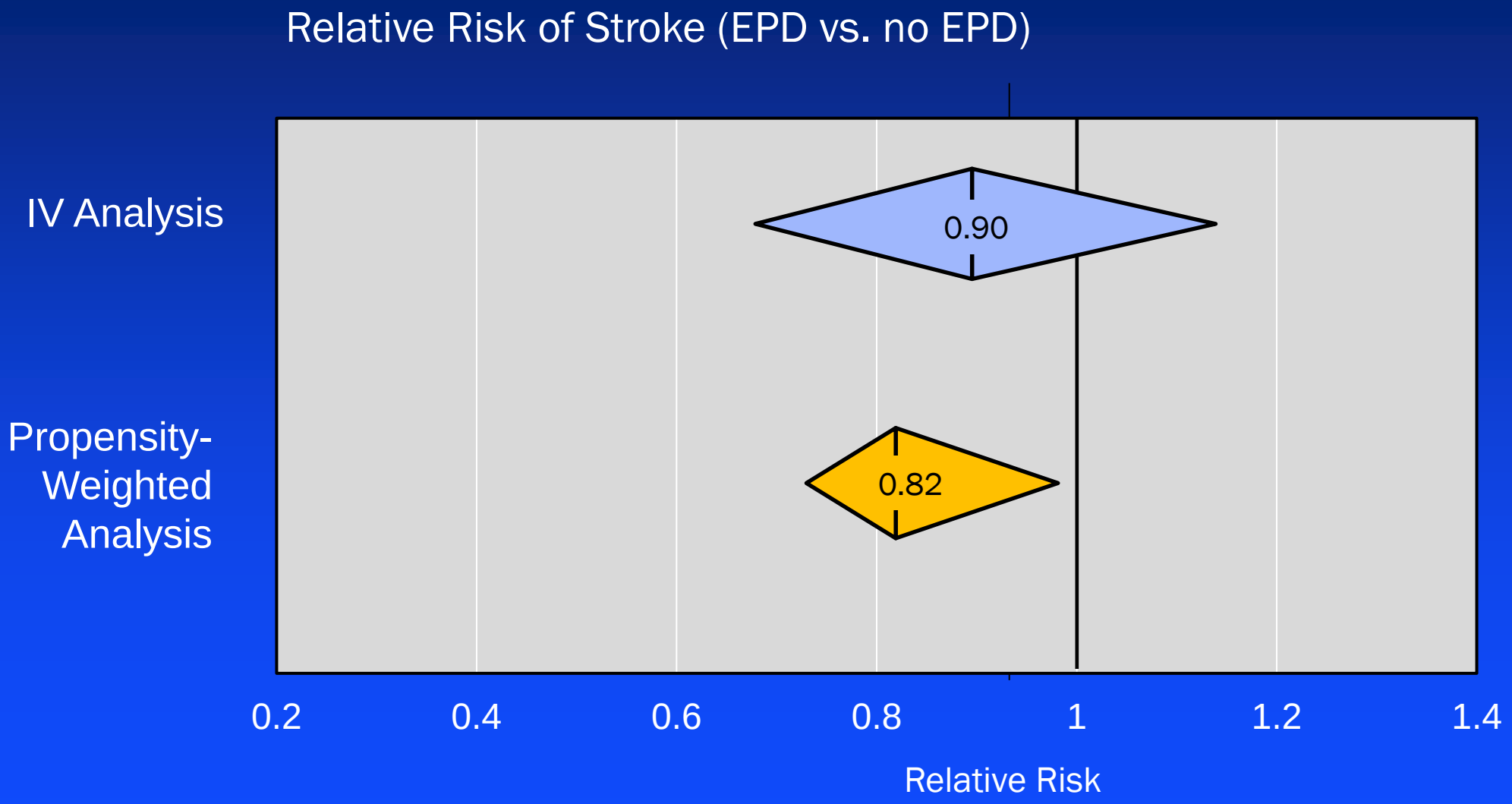
Results: Propensity-Weighted Analysis



	EPD	No EPD	RR (95% CI)	P-Value
In-Hosp. Outcomes				
Death or Stroke	2.1%	2.5%	0.84 (0.73-0.98)	0.03
Death	0.9%	1.1%	0.86 (0.66-1.10)	0.23
Major Bleeding	4.7%	4.3%	1.09 (0.95-1.24)	0.22
Device Success	97.3%	97.3%	1.01 (0.76-1.35)	0.93
GI or GU Bleed	0.6%	0.5%	1.29 (0.92-1.81)	0.14
30-day Outcomes				
Stroke	1.9%	2.2%	0.85 (0.73-0.99)	0.04
Death	1.7%	2.2%	0.78 (0.64-0.95)	0.01

Absolute risk differences converted to relative risks for comparison with propensity-weighted analyses

Are these 2 analyses inconsistent?



Summary-1

- Over the first 2 years after approval, use of cerebral EPDs has increased gradually across US centers. However, even by late 2019, EPDs were only used in 28% of hospitals and 13% of patients, with marked variation between centers
- Use of EPD was generally safe, with no evidence of increased vascular complications, major bleeding, or device failure
- Our prespecified primary analysis using an instrumental variable approach demonstrated no significant reduction in in-hospital or 30-day stroke

Summary-2

- Nonetheless, both the secondary (propensity-weighted) analysis and the confidence interval for the primary analysis are consistent with a possible modest reduction in stroke (~20% RRR, NNT ~300 for major stroke)
- These findings support clinical equipoise and provide a strong rationale for ongoing large-scale RCTs to test whether EPDs provide meaningful clinical benefit (i.e., reduced stroke, improved neurocognitive function) for patients undergoing TAVR

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