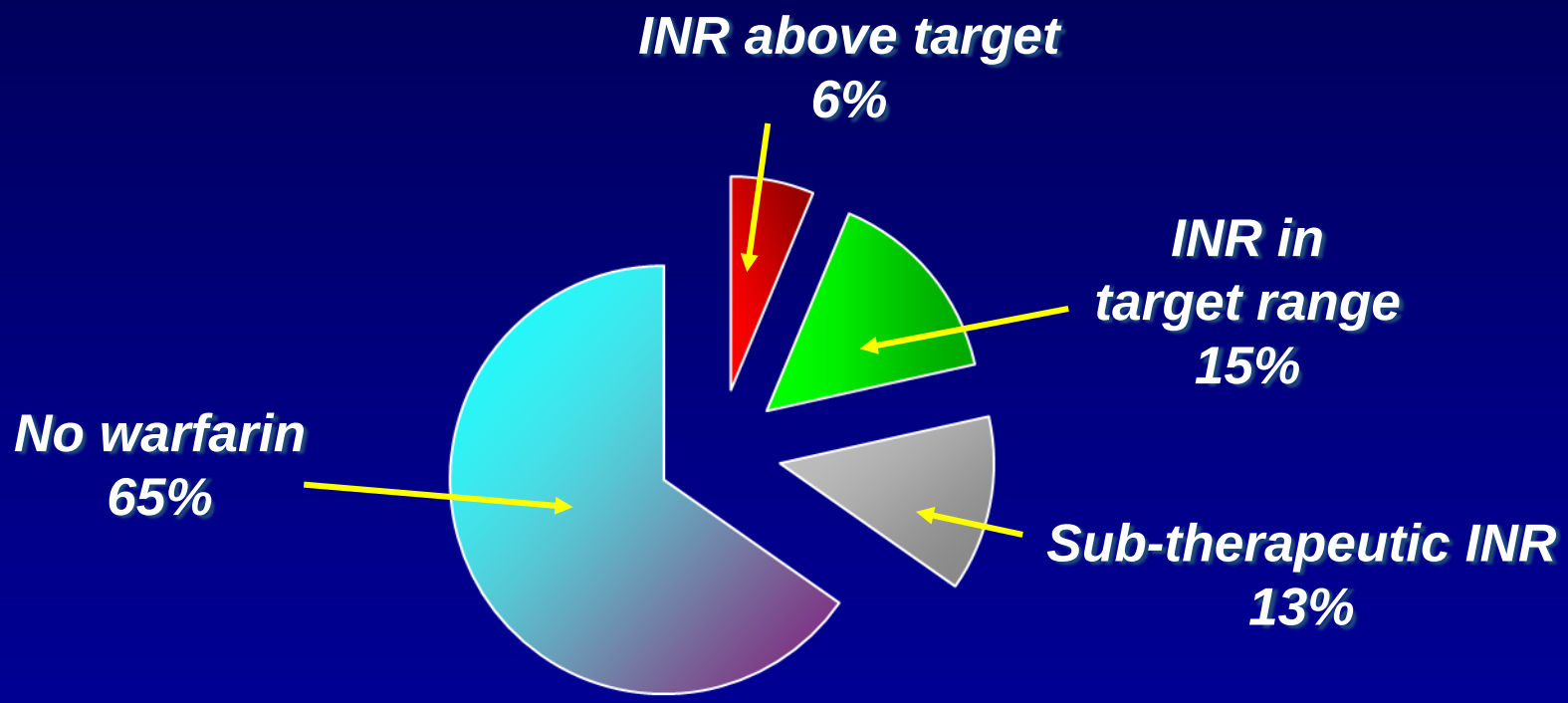
LAA Closure for Stroke Prevention in Atrial Fibrillation: Yes, Its Safe and Effective!

Matthew J. Price MD
Scripps Clinic, La Jolla, CA

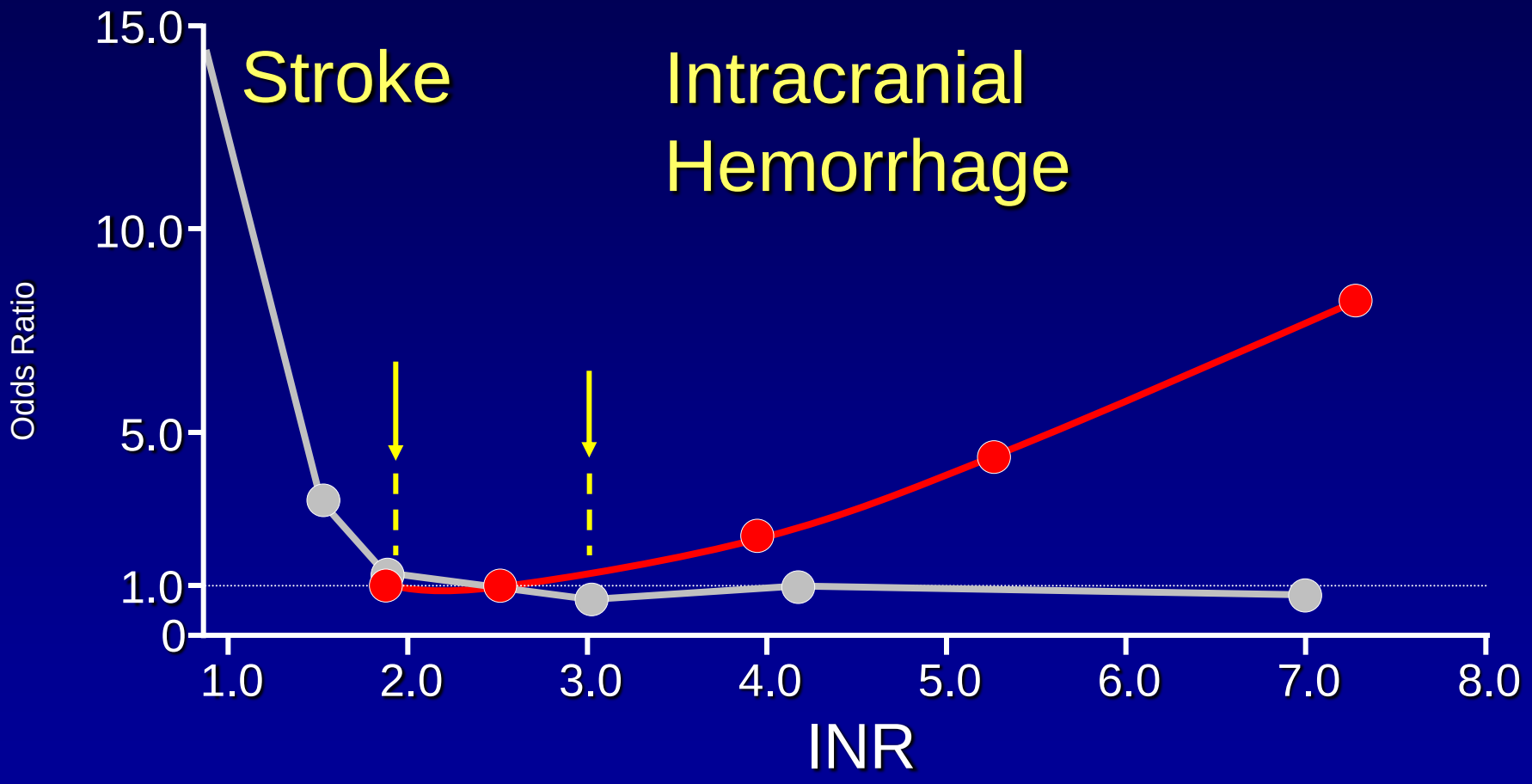
Patients *Don't Get Adequate Medical Treatment To Begin With!*

Adequacy of Anticoagulation in Patients with AF in Primary Care Practice



Therapeutic Range for Warfarin

INR Values at Stroke or ICH



Fuster et al. *J Am Coll Cardiol*. 2001;38:1231-1266.

Dabigatran: Bleeding in RE-LY

	D 110mg	D 150mg	warfarin	D 110mg vs. Warfarin		D 150mg vs. Warfarin	
	Annual rate	Annual rate	Annual rate	RR 95% CI	p	RR 95% CI	p
Total	14.6%	16.4%	18.2%	0.78 0.74-0.83	<0.001	0.91 0.86-0.97	0.002
Major	2.7 %	3.1 %	3.4 %	0.80 0.69-0.93	0.003	0.93 0.81-1.07	0.31
Life-Threatening major	1.2 %	1.5 %	1.8 %	0.68 0.55-0.83	<0.001	0.81 0.66-0.99	0.04
Gastro-intestinal Major	1.1 %	1.5 %	1.0 %	1.10 0.86-1.41	0.43	1.50 1.19-1.89	<0.001

Major bleed = ↓Hgb ≥2 g/dl, transfusion ≥2U PRBC, or symptomatic bleeding in a critical area or organ.

Primary Safety Outcomes (Bleeding)

	Rivaroxaban	Warfarin		
	Event Rate	Event Rate	HR (95% CI)	P-value
Major and non-major Clinically Relevant	14.91	14.52	1.03 (0.96, 1.11)	0.442
Major	3.60	3.45	1.04 (0.90, 1.20)	0.576
Non-major Clinically Relevant	11.80	11.37	1.04 (0.96, 1.13)	0.345

*Major Bleed = fatal outcome, involvement of a critical anatomic site, ↓Hgb ≥2 g/dl, transfusion ≥2U PRBC or permanent disability.

Event Rates are per 100 patient-years
Based on Safety on Treatment Population

ROCKET AF

Apixiban: Bleeding Outcomes in ARISTOTLE

Outcome	Apixaban (N=9088) Event Rate (%/yr)	Warfarin (N=9052) Event Rate (%/yr)	HR (95% CI)	P Value
Primary safety outcome: ISTH major bleeding*	2.13	3.09	0.69 (0.60, 0.80)	<0.001
Intracranial	0.33	0.80	0.42 (0.30, 0.58)	<0.001
Gastrointestinal	0.76	0.86	0.89 (0.70, 1.15)	0.37
Major or clinically relevant non-major bleeding	4.07	6.01	0.68 (0.61, 0.75)	<0.001
GUSTO severe bleeding	0.52	1.13	0.46 (0.35, 0.60)	<0.001
TIMI major bleeding	0.96	1.69	0.57 (0.46, 0.70)	<0.001
Any bleeding	18.1	25.8	0.71 (0.68, 0.75)	<0.001

*clinically overt bleed w/↓Hgb ≥2 g/dl or transfusion ≥2U PRBC, occurring at a critical site, or resulting in death.

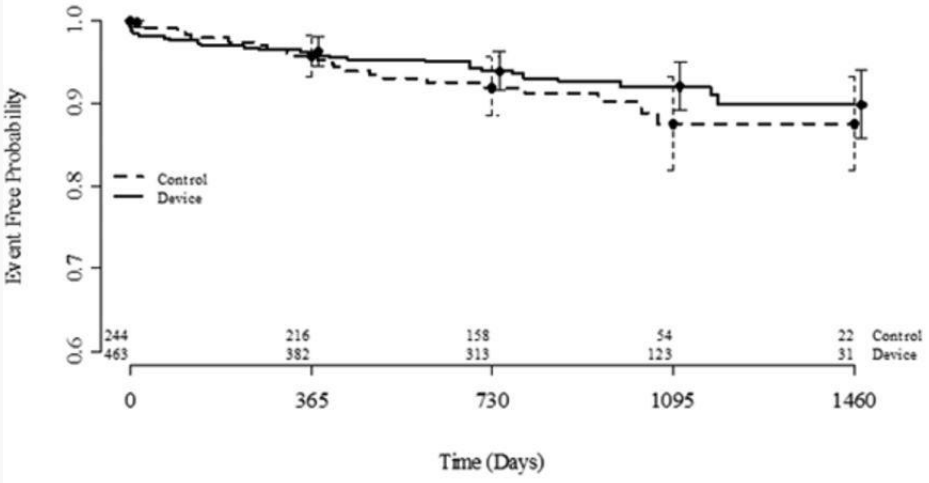
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Percutaneous Left Atrial Appendage Closure for Stroke Prophylaxis in Patients With Atrial Fibrillation : 2.3-Year Follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients With Atrial Fibrillation) Trial

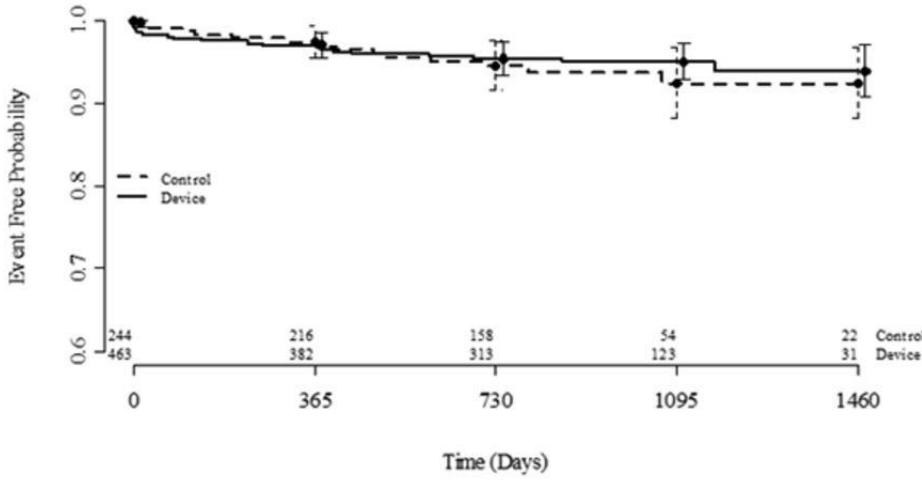
Vivek Y. Reddy, Shephal K. Doshi, Horst Sievert, Maurice Buchbinder, Petr Neuzil, Kenneth Huber, Jonathan L. Halperin and David Holmes
on behalf of the PROTECT AF Investigators

Primary Efficacy



RR: 0.71 (0.44–1.30), **Prob NI: >0.99**, Prob Sup: 0.88

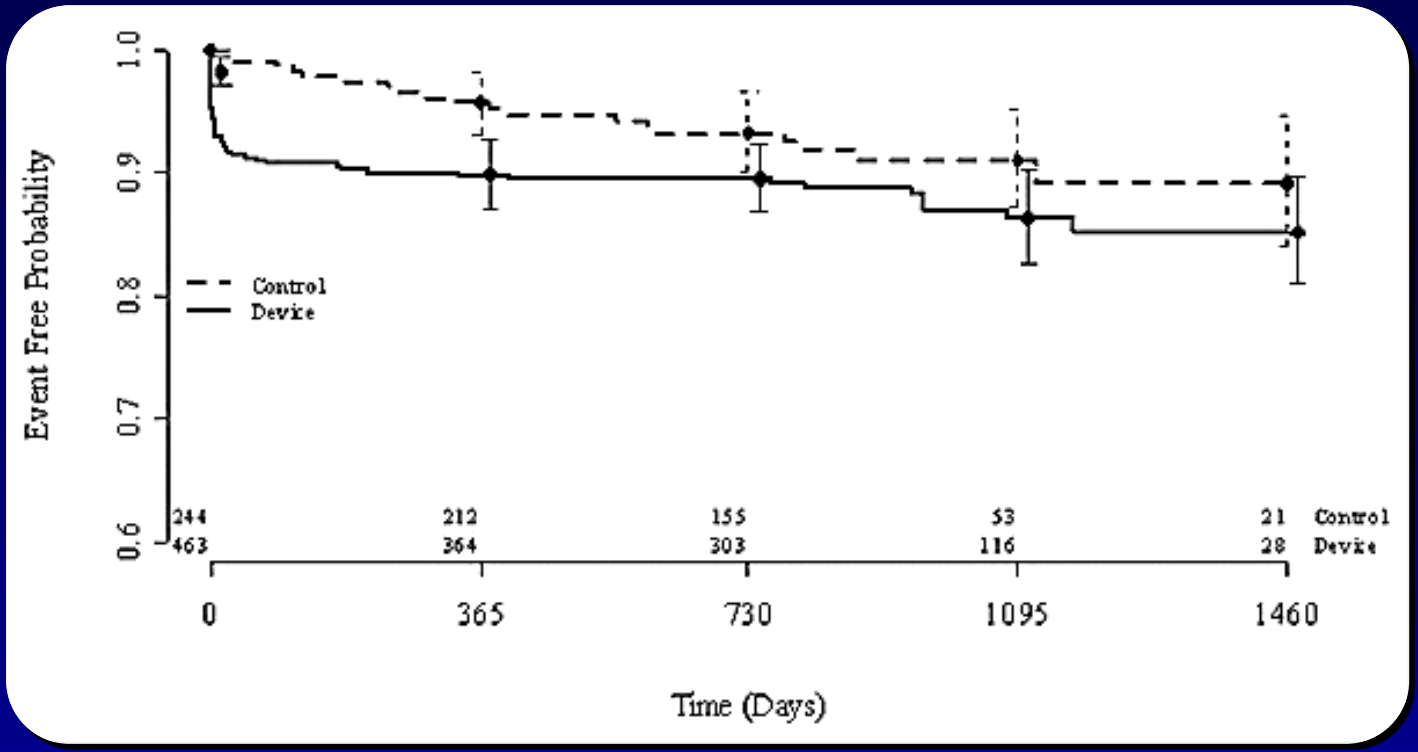
Stroke



RR: 0.77 (0.42–1.62), **Prob NI: >0.99**, Prob Sup: 0.73

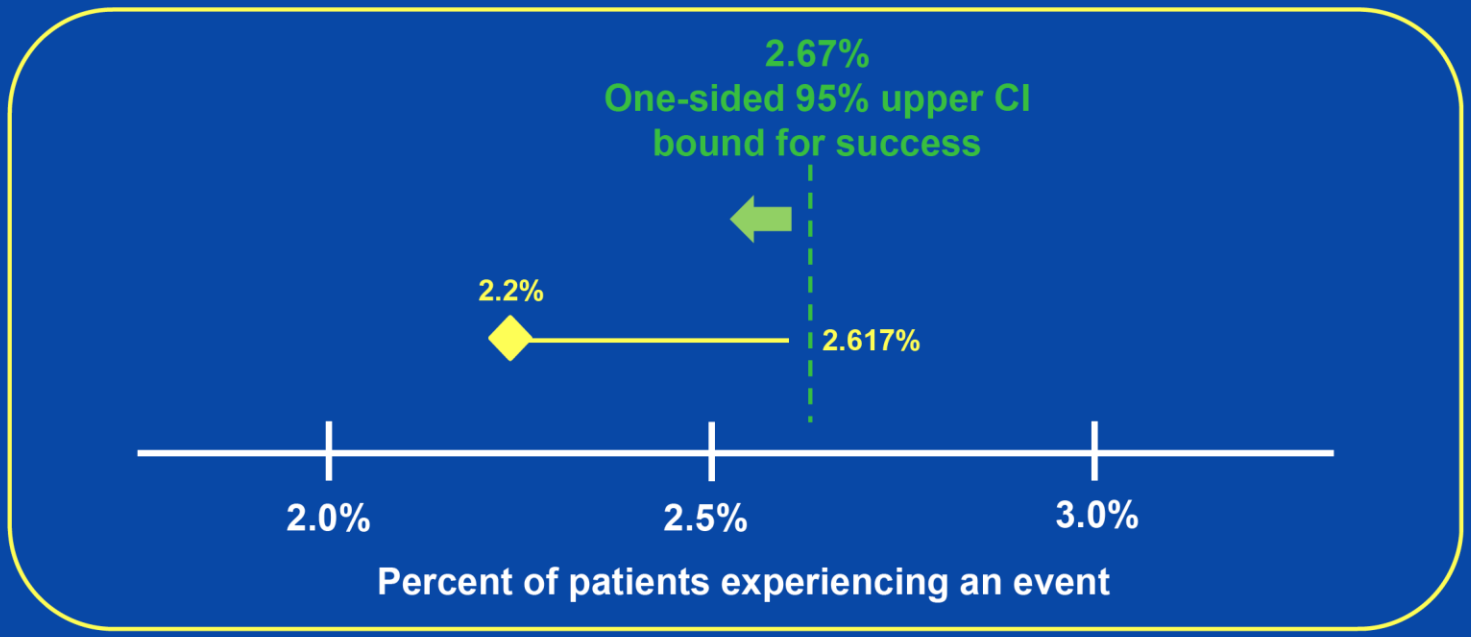
Reddy VY et al, Circulation. 2013; 127: 720-729

PROTECT-AF at 2.3 yr FU: Primary Safety Outcomes



Post-procedure primary event: 2.5% vs 4.3%
RR = 0.58 (0.35–1.09);
Probability of superiority = 95.5%

First Primary Endpoint
Acute (7-day) Procedural Safety



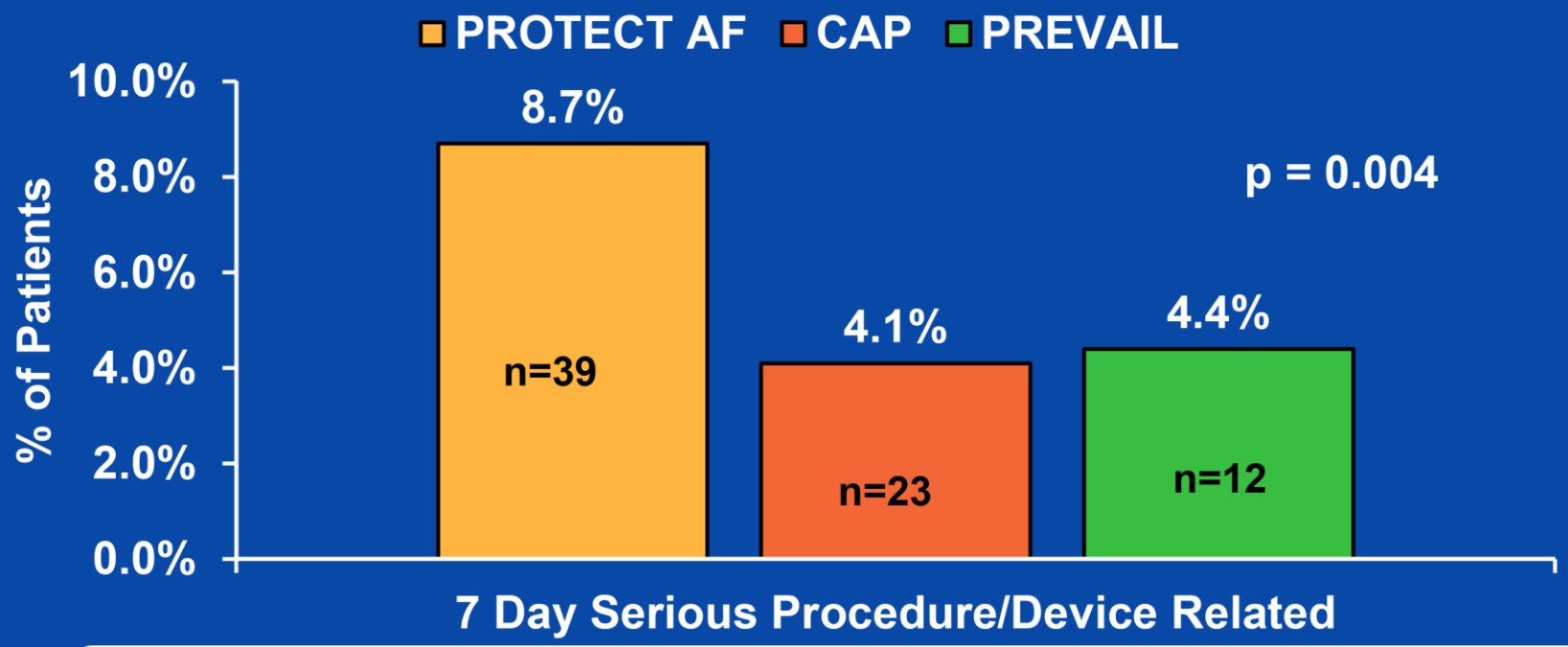
- 6 events in device group = 2.2% (6/269)
- Pre-specified criterion met for first primary endpoint (95% Upper confidence bound < 2.67%)
  - 95% CI = 2.618%

Results are preliminary; final validation not yet complete

Death, ischemic stroke, SE and procedure or device related complications requiring major CV or endovasc intervention

Vascular Complications

- Composite of vascular complications includes cardiac perforation, pericardial effusion with tamponade, ischemic stroke, device embolization, and other vascular complications[1]



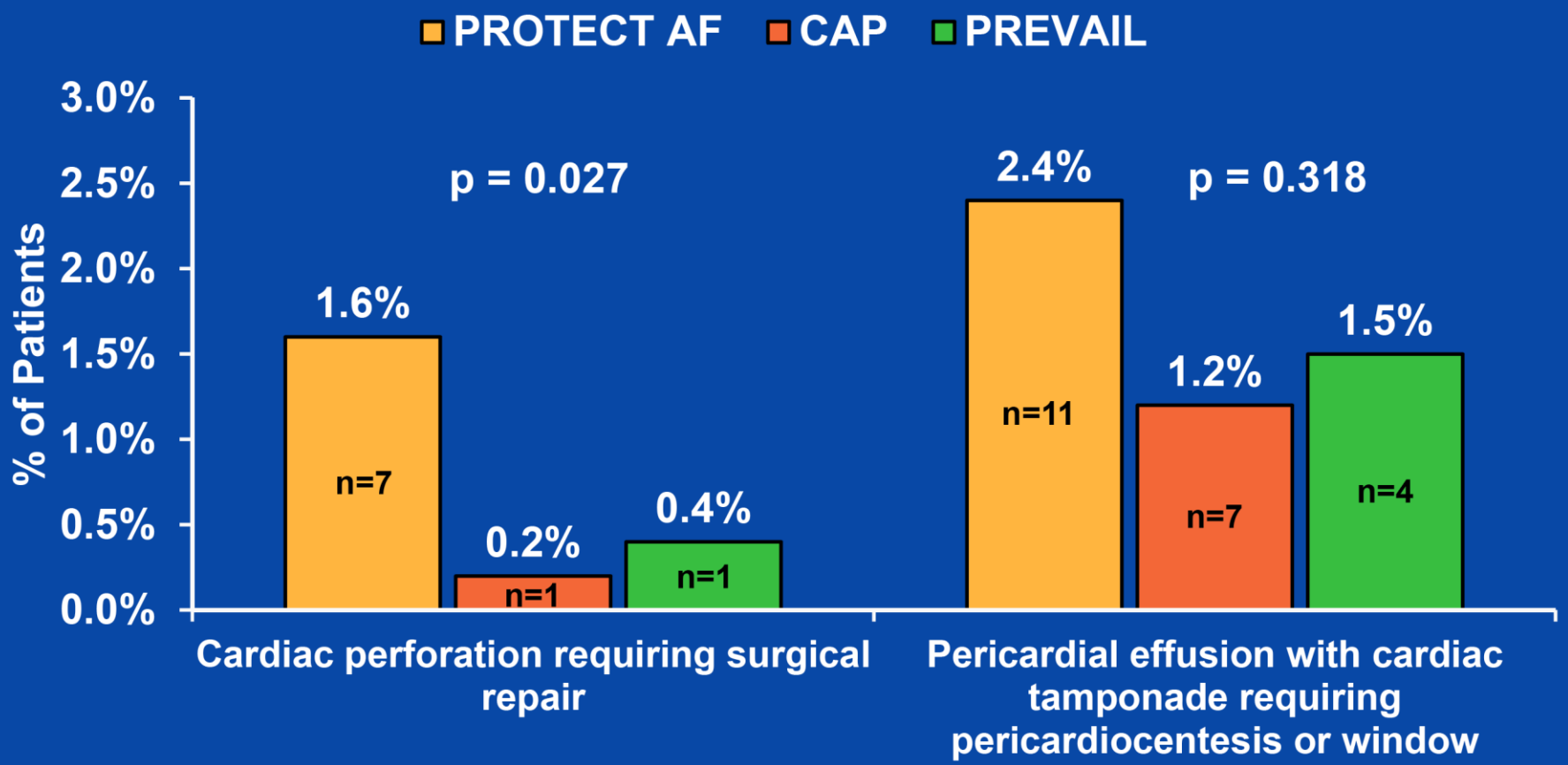
No procedure-related deaths reported in any of the trials

PROTECT-AF and CAP data from Reddy, VY et al. *Circulation.* 2011;123:417-424.

[11]Includes observed PE not necessitating intervention, AV fistula, major bleeding requiring transfusion, pseudoaneurysm, hematoma and groin bleeding

Caution: In the United States, WATCHMAN is an investigational device limited by Federal law and investigational use only. Not for sale in the US. Prior to use please review device indications, contraindications, warnings, precautions, adverse events, and operational instructions. Only available according to applicable local law.

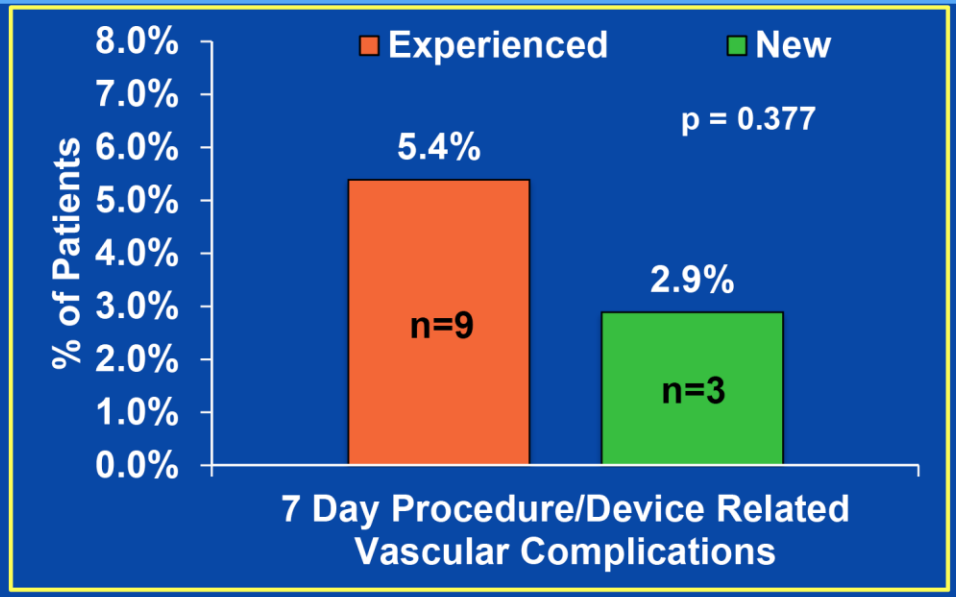
Pericardial Effusions Requiring Intervention

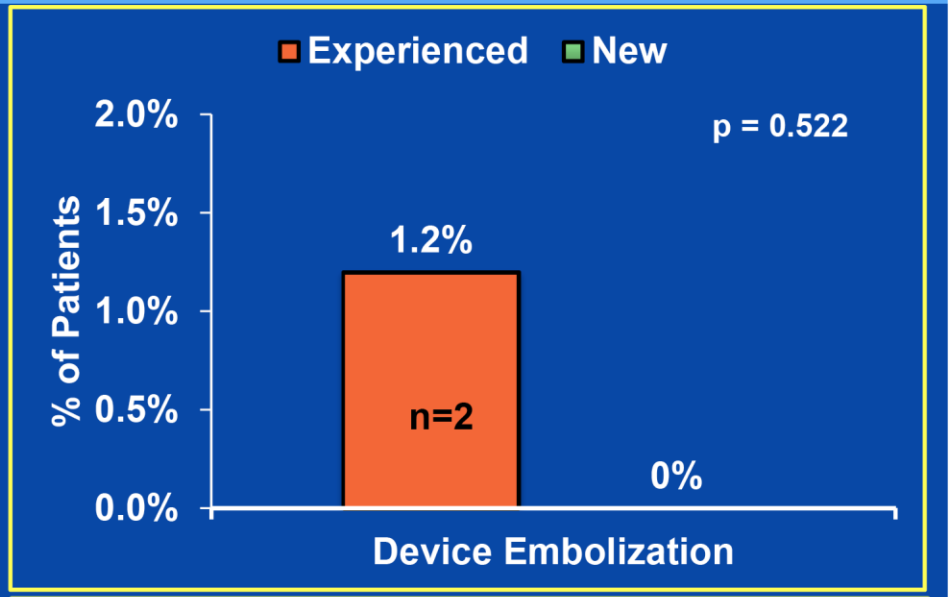


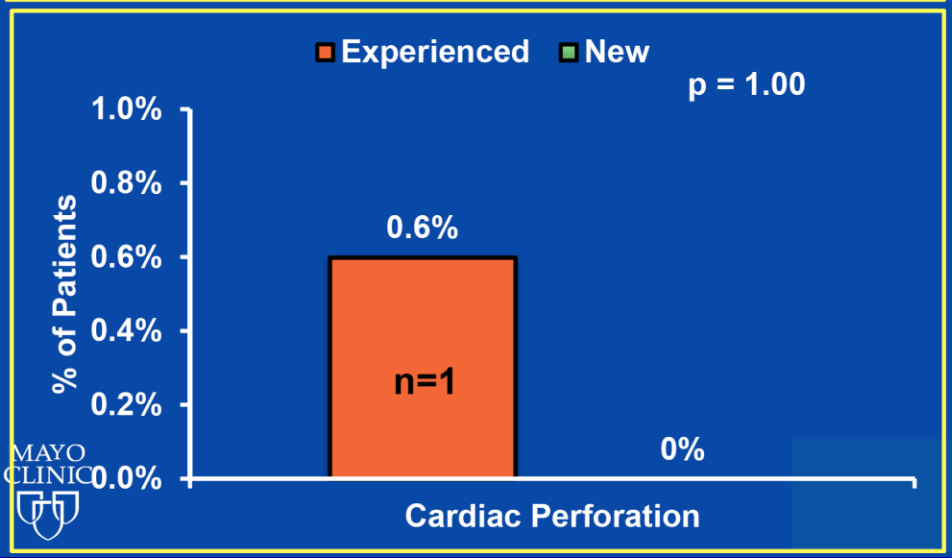
MAYO CLINIC

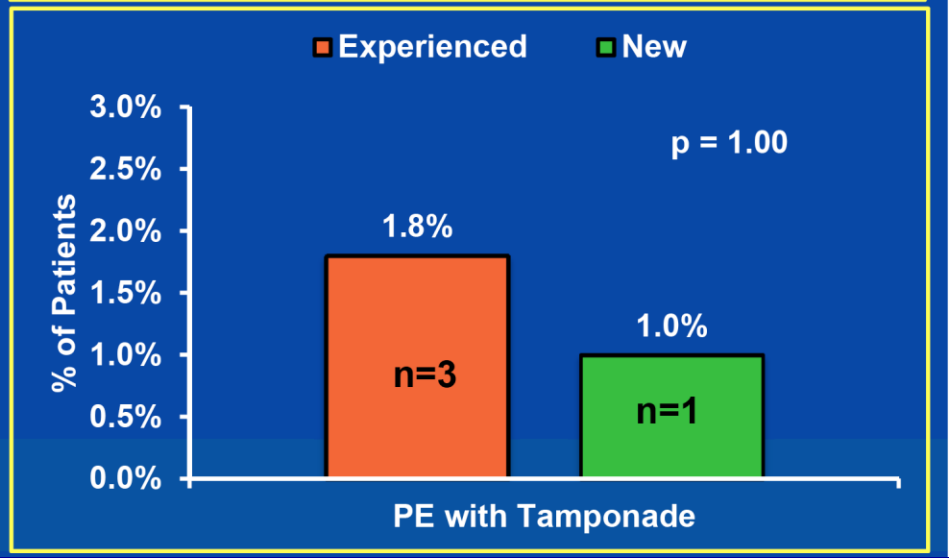
PROTECT AF and CAP data
from Reddy, VY et al. *Circulation*. 2011;123:417-424.

PREVAIL Complications
New vs Experienced Operator



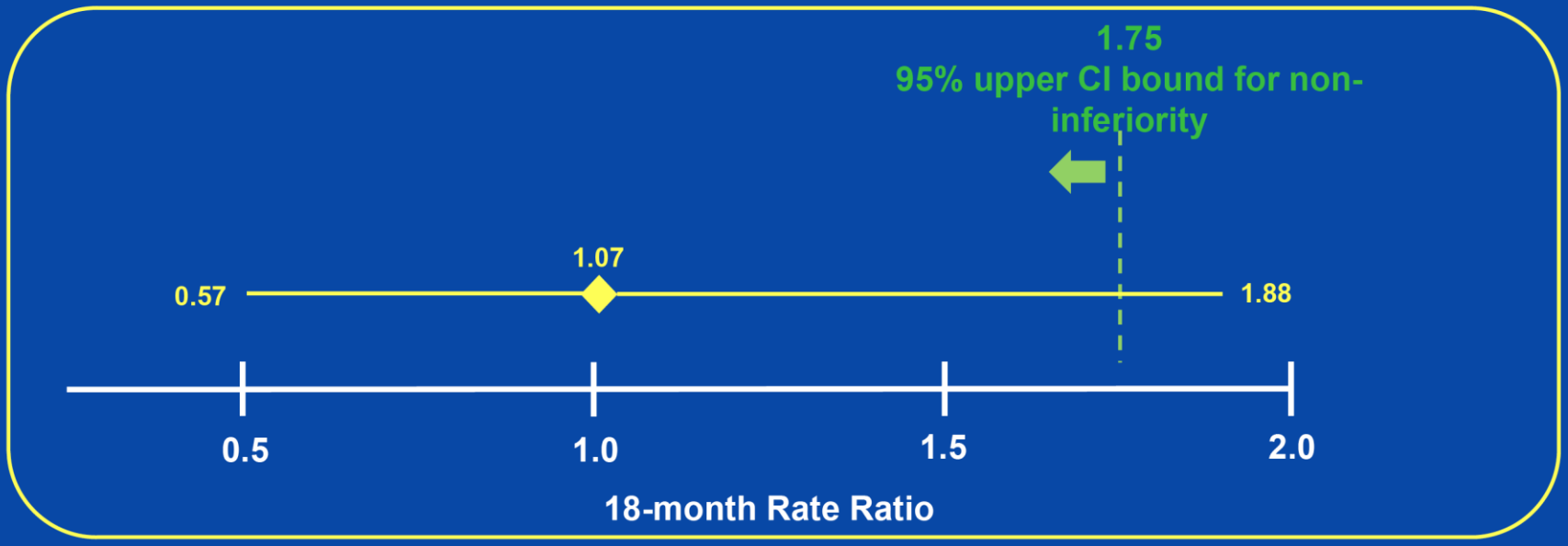






MAYO CLINIC

Second Primary Endpoint
Composite 18-month Efficacy

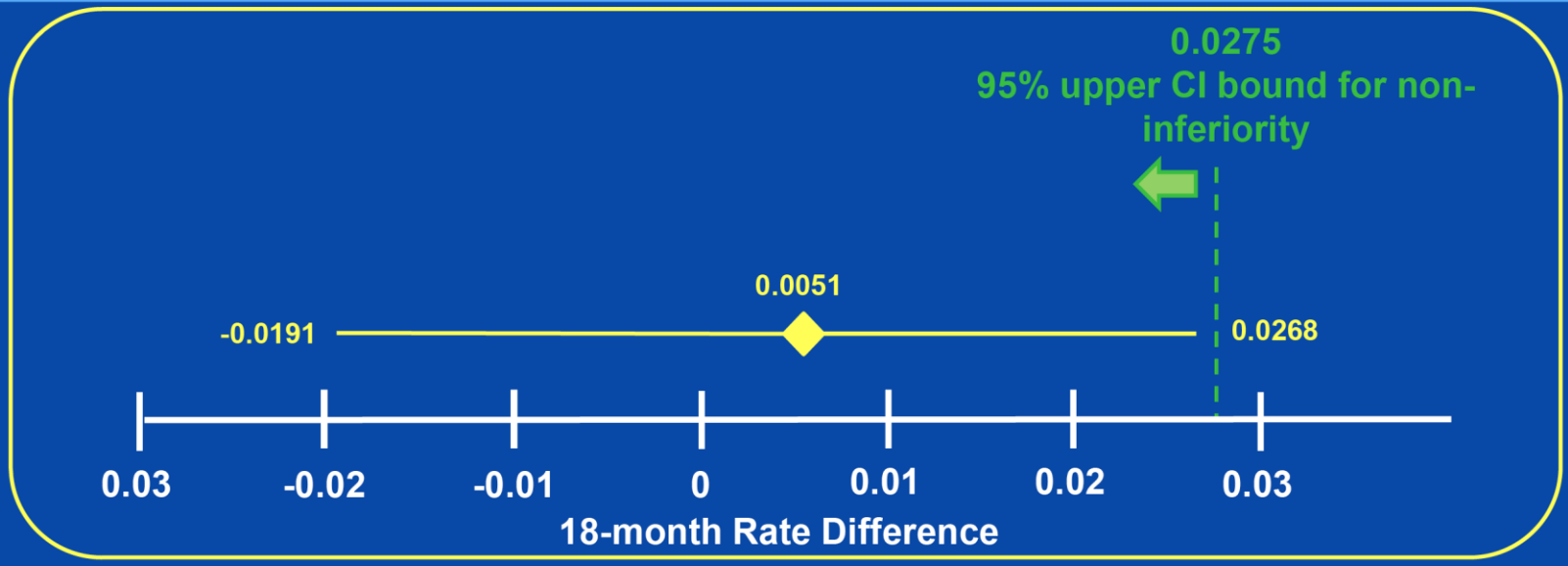


- Similar 18-month event rates in both control and device groups = 0.064
- Upper 95% CI bound slightly higher than allowed to meet success criterion (<1.75)
  - Limited number of patients with follow-up through 18 months thus far (Control = 30 pts, Device = 58 pts)

Results are preliminary; final validation not yet complete

MAYO CLINIC

Third Primary Endpoint
18-month Thrombolic Events



- **Endpoint success in the presence of an over performing control group**

Device 18-Month Rate	Control 18-Month Rate
0.0253	0.0201

- **Pre-specified non-inferiority criterion met for third primary endpoint (95% CI Upper Bound < 0.0275%)**

Results are preliminary; final validation not yet complete

Ischemic stroke or SE> 7days post procedure

LAA Closure/Occlusion/Excision

Recommendations for LAA closure/occlusion/excision		
Recommendations	**Class**	**Level**
Interventional, percutaneous LAA closure may be considered in patients with a high stroke risk and contraindications for long-term oral anticoagulation.	**IIb**	**B**
Surgical excision of the LAA may be considered in patients undergoing open heart surgery.	**IIb**	**C**

European Heart Journal 2012;33:2719-2747 - doi:10.1093/eurheartj/ehs253

Summary

- Chronic anticoagulation, including with the newer agents, is associated *with a significant hazard for bleeding.*
- Longer-term RCT data supports the efficacy of LAA occlusion, and suggests that LAA occlusion may be superior to warfarin after the post-procedure period
- PREVAIL supports the contention that the current approach to LAA occlusion is substantially safer, thereby tilting the balance toward closure.

Lets break the anticoagulant addiction!