



Stroke Prevention in Non-Valvular Atrial Fibrillation

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TCTAP 2018

Seoul, Korea

April 2018

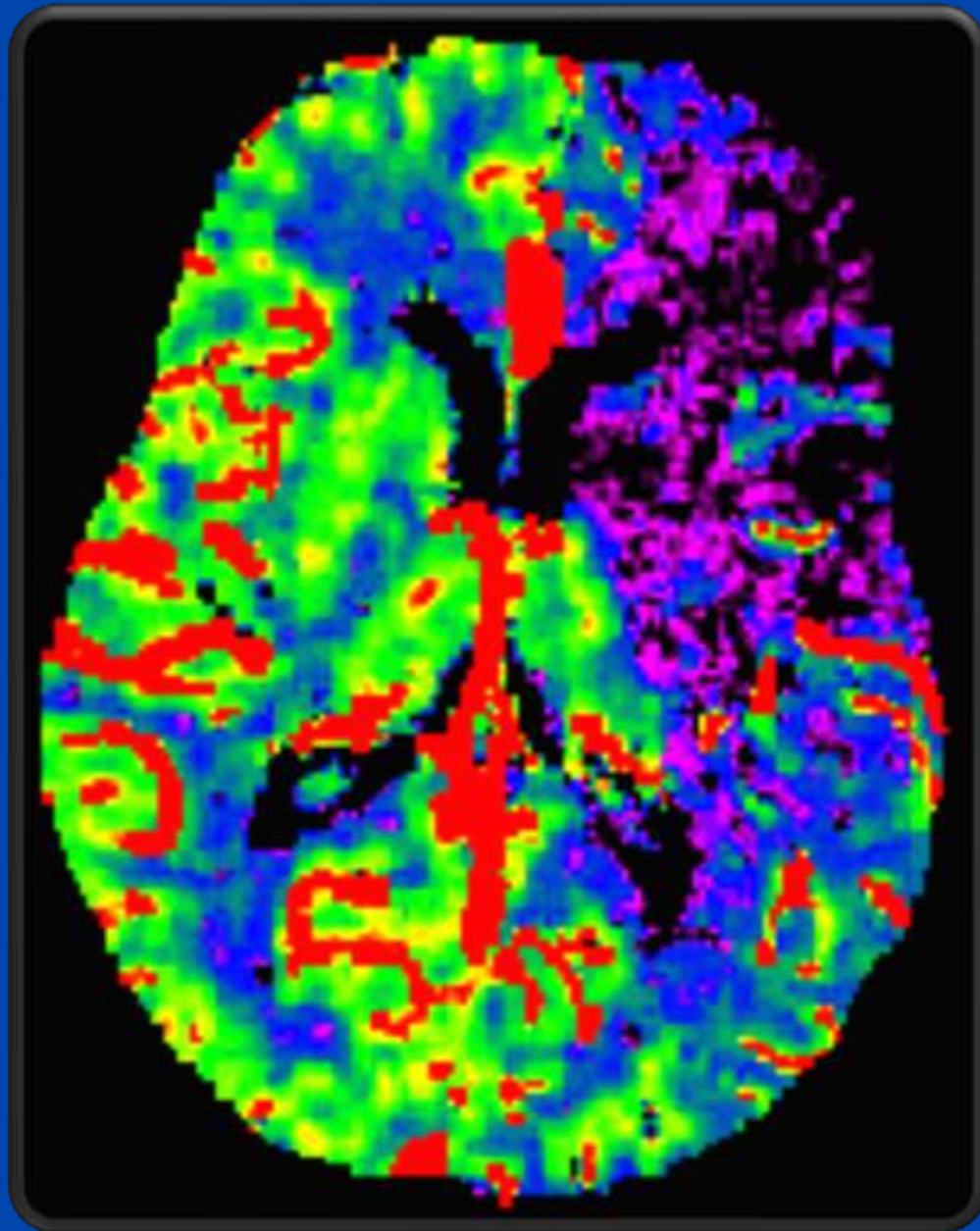
Presenter Disclosure Information

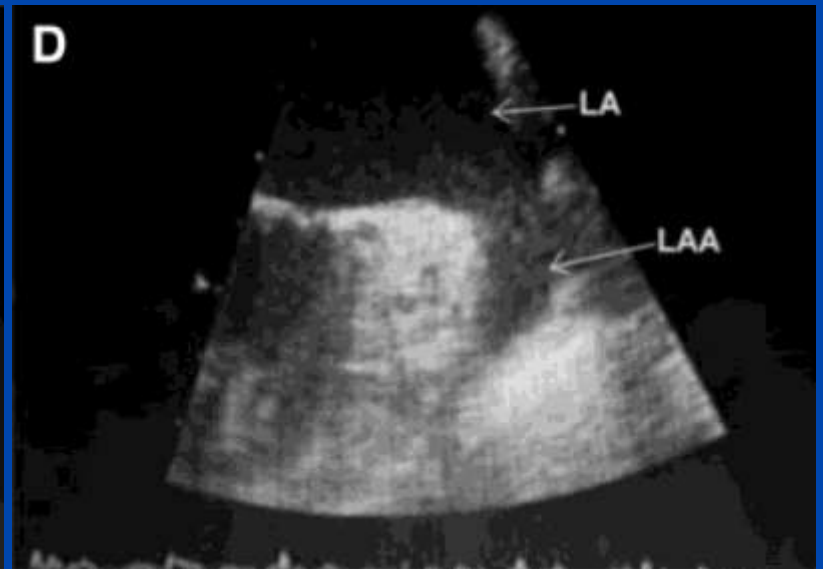
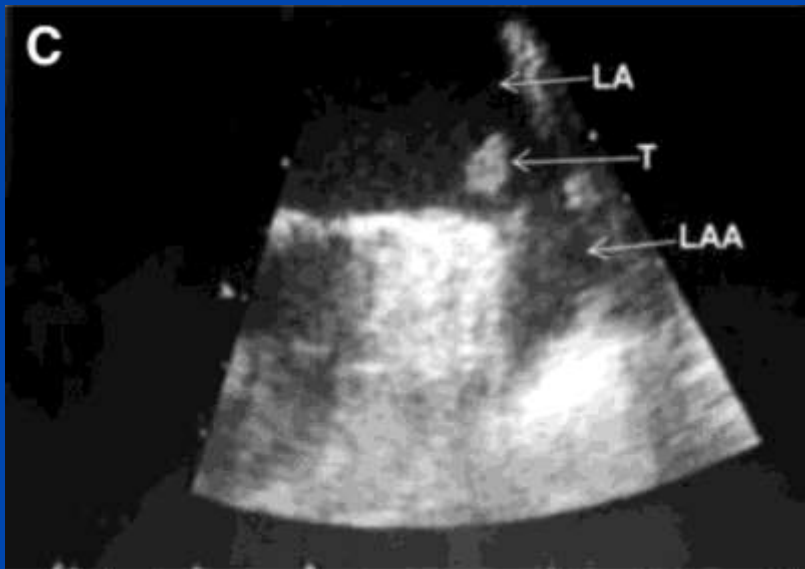
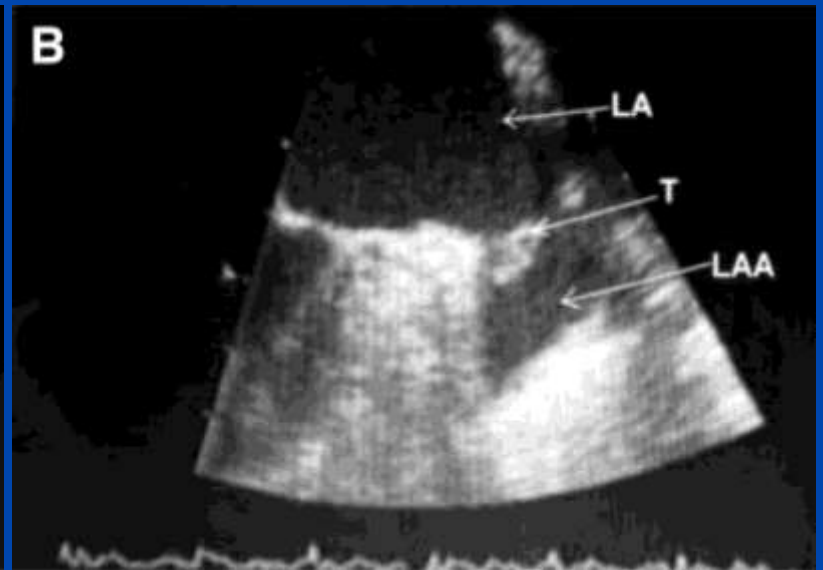
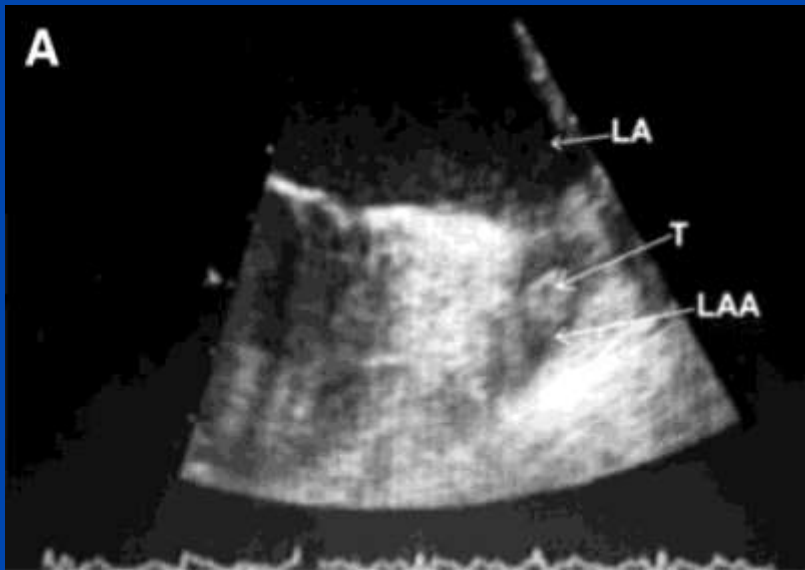
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“Stroke Prevention in Non-Valvular Atrial Fibrillation”

The following relationships exist related to this presentation:

None





Parekh A, Ezekowitz M et al: *Circ* 114:e513, 2006

Atrial Fibrillation Patients

- **Stroke is single most feared complication of CV disease**
- **Higher mortality and morbidity than non-embolic strokes**
- **20-40% of all strokes are related to NVAF**
- **Up to 15-20% AF strokes fatal**
- **High recurrence rates**
- **Cost of treatment**
- **Cost of prevention**

EQUIPOISE?



Equipoise

- **A state of genuine uncertainty is a requisite for randomized clinical trials**
- **Complex**
 - **Theoretical equipoise**
 - **Clinical equipoise**

Nonvalvular Atrial Fibrillation Concepts

- Although risk scores are imperfect – all patients with nonvalvular atrial fibrillation should be evaluated for risk of stroke/systemic embolism and bleeding
- There are several strategies for stroke prevention in high risk patients
- Patients should be given the information about these strategies in a way that they can understand them
- Patients increasingly are at the center of shared decision making

MENU

- Coumadin
- Dabigatran
- Rivaroxaban
- Apixaban
- Edoxaban
- Watchman
- Amulet
- LARIET

Stroke Prevention Strategies

Anticoagulation

- Studied and found effective in large studies
- Is associated with bleeding
- NOACs are better than Coumadin
- Compliance is an important issue (willpower)
- Issues of cost and convenience
- Do not prevent all strokes
- Hemorrhagic strokes have highest morbidity and mortality

Original Investigation

Oral Anticoagulant Therapy Prescription in Patients With Atrial Fibrillation Across the Spectrum of Stroke Risk Insights From the NCDR PINNACLE Registry

Jonathan C. Hsu, MD, MAS; Thomas M. Maddox, MD, MSc; Kevin F. Kennedy, MS; David F. Katz, MD; Lucas N. Marzec, MD; Steven A. Lubitz, MD, MPH; Anil K. Gehi, MD; Mintu P. Turakhia, MD, MAS; Gregory M. Marcus, MD, MAS

Results: The study cohort comprised 429,417 outpatients with AF. Their mean (SD) age was 71.3 (12.9) years, and 55.8% were male. Prescribed treatment consisted of an OCA (192,600 [44.9%]), aspirin only (111,134 [25.9%]), aspirin plus a thienopyridine (23,454 [5.5%]), or no antithrombotic therapy (102,229 [23.8%]). Overall, OAC prescription prevalence did not exceed 50% even in higher-risk patients with a CHADS₂ score exceeding 3 or a CHA₂DS₂-VASc score exceeding 4.

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IMPORTANCE Patients with atrial fibrillation (AF) are at a proportionally higher risk of stroke based on accumulation of well-defined risk factors.

OBJECTIVE To examine the extent to which prescription of an oral anticoagulant (OAC) in US

← Invited Commentary page 63

+ Author Audio Interview at jamacardiology.com

+ Supplemental content at jamacardiology.com

Conclusions and Relevance: In a large quality improvement registry of outpatients with AF, prescription of OAC therapy increased with a higher CHADS₂ score and CHA₂DS₂-VASc score. However, a plateau of OAC prescription was observed, with less than half of high-risk patients receiving an OAC prescription.

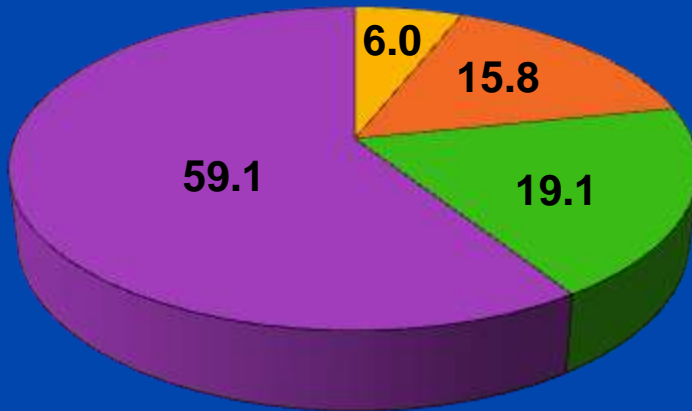
71.3 (12.9) years, and 55.8% were male. Prescribed treatment consisted of an OAC (192 600 [44.9%]), aspirin only (111 134 [25.9%]), aspirin plus a thienopyridine (23 454 [5.5%]), or no antithrombotic therapy (102 229 [23.8%]). Each 1-point increase in risk score was associated with increased odds of OAC prescription compared with aspirin-only prescription using the CHADS₂ score (adjusted odds ratio, 1.158; 95% CI, 1.144-1.172; *P* < .001) and the CHA₂DS₂-VASc score (adjusted odds ratio, 1.163; 95% CI, 1.157-1.169; *P* < .001). Overall, OAC prescription prevalence did not exceed 50% even in higher-risk patients with a CHADS₂ score exceeding 3 or a CHA₂DS₂-VASc score exceeding 4.

CONCLUSIONS AND RELEVANCE In a large quality improvement registry of outpatients with AF, prescription of OAC therapy increased with a higher CHADS₂ score and CHA₂DS₂-VASc score. However, a plateau of OAC prescription was observed, with less than half of high-risk patients receiving an OAC prescription.

Adherence to OAC

- U.S. commercial insurance data base (administrative claims)
66,661 patients with atrial fibrillation treated between
November 2010 and December 2014

■ Apixaban ■ Dabigatran
■ Rivaroxaban ■ Warfarin



CHA₂DS₂VASc score ≥2 ~90%

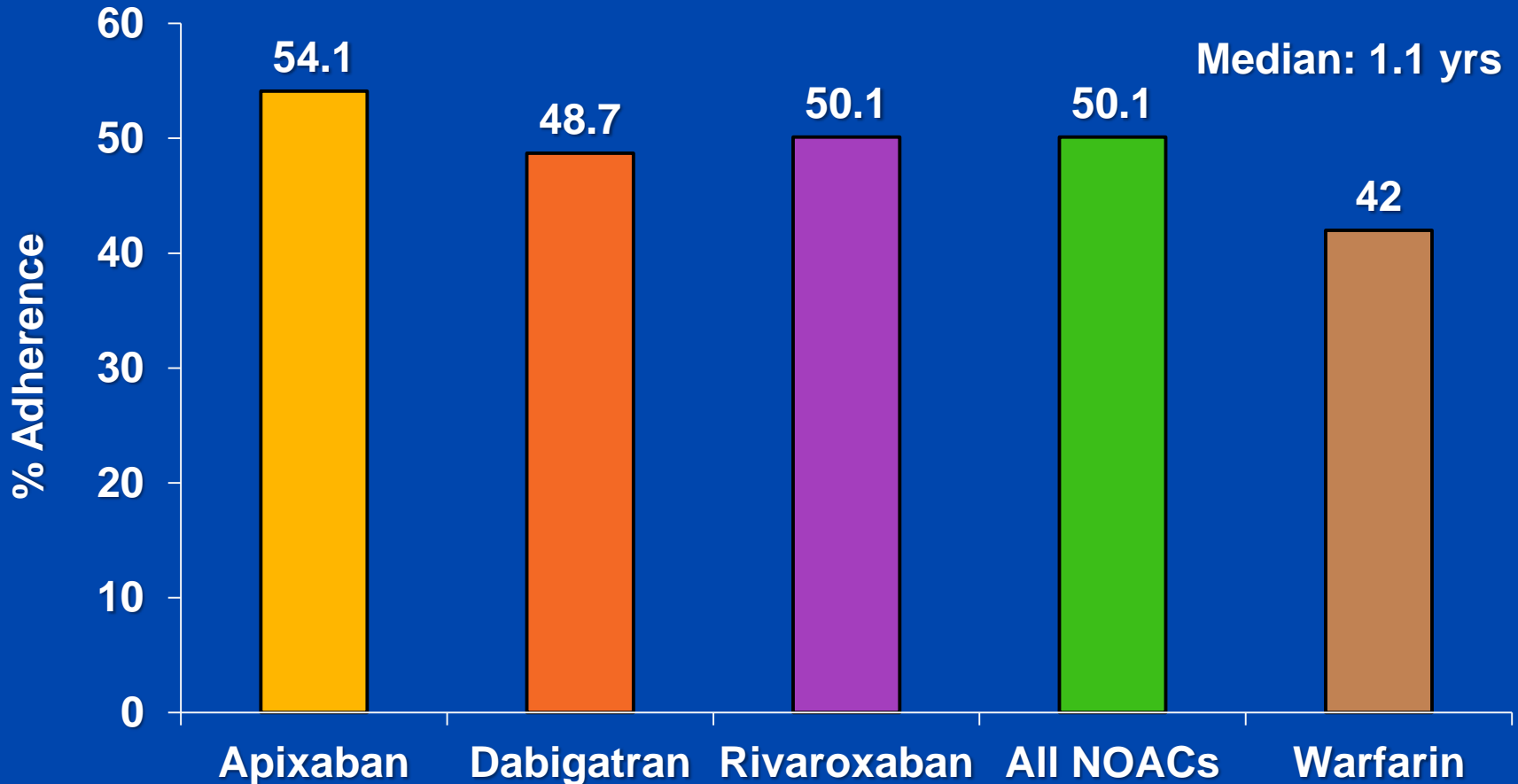
HAS-BLED ≥3 ~50%

Median F/U 1.1 yrs

Adherence to OAC

Proportion of Days Covered

CHA₂DS₂VASc score ≥ 4



RELY AF Registry

- Prospective registry patients presenting to ER with AF
- 164 sites, 64 countries
 - 15,400 patients
 - 2008-2011
- Use of oral anticoagulation prescribed
 - 58% of patients worldwide with $\text{CHADS}_2 \geq 2$
 - Range 11.2% - 65.7%



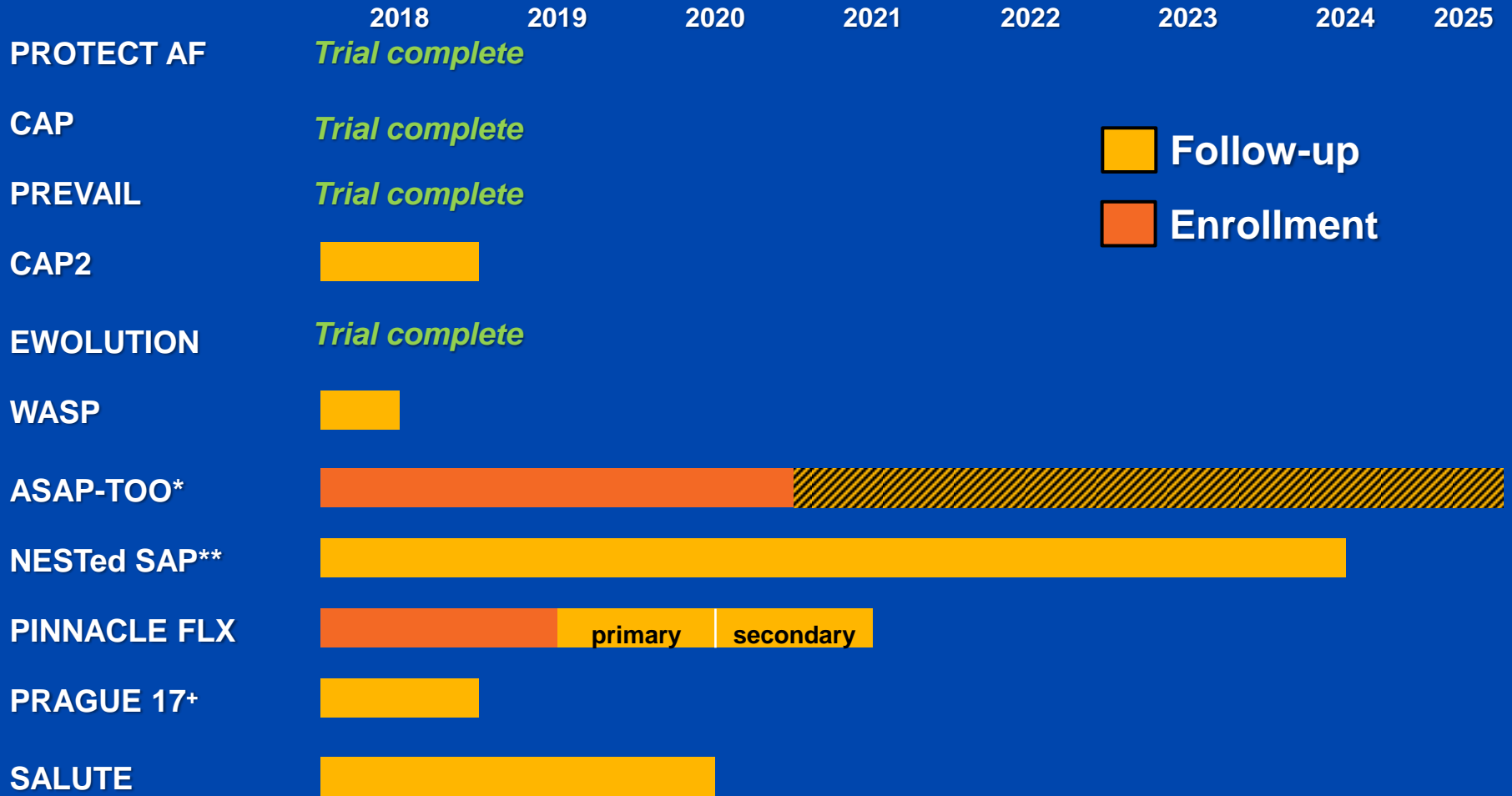
**Willpower lasts about 30 days
and is soluble in alcohol**

Stroke Prevention Strategies

Devices – Local Site Specific

- Studied and found effective in RCTs and registries
- Have small procedural adverse events
- Major reduction in hemorrhagic stroke
- Improvement in survival
- Are associated with decreased bleeding because AC is usually avoided
- Do not prevent strokes which are not related to LAA
- Eliminate noncompliance issues

Clinical Trial Timelines

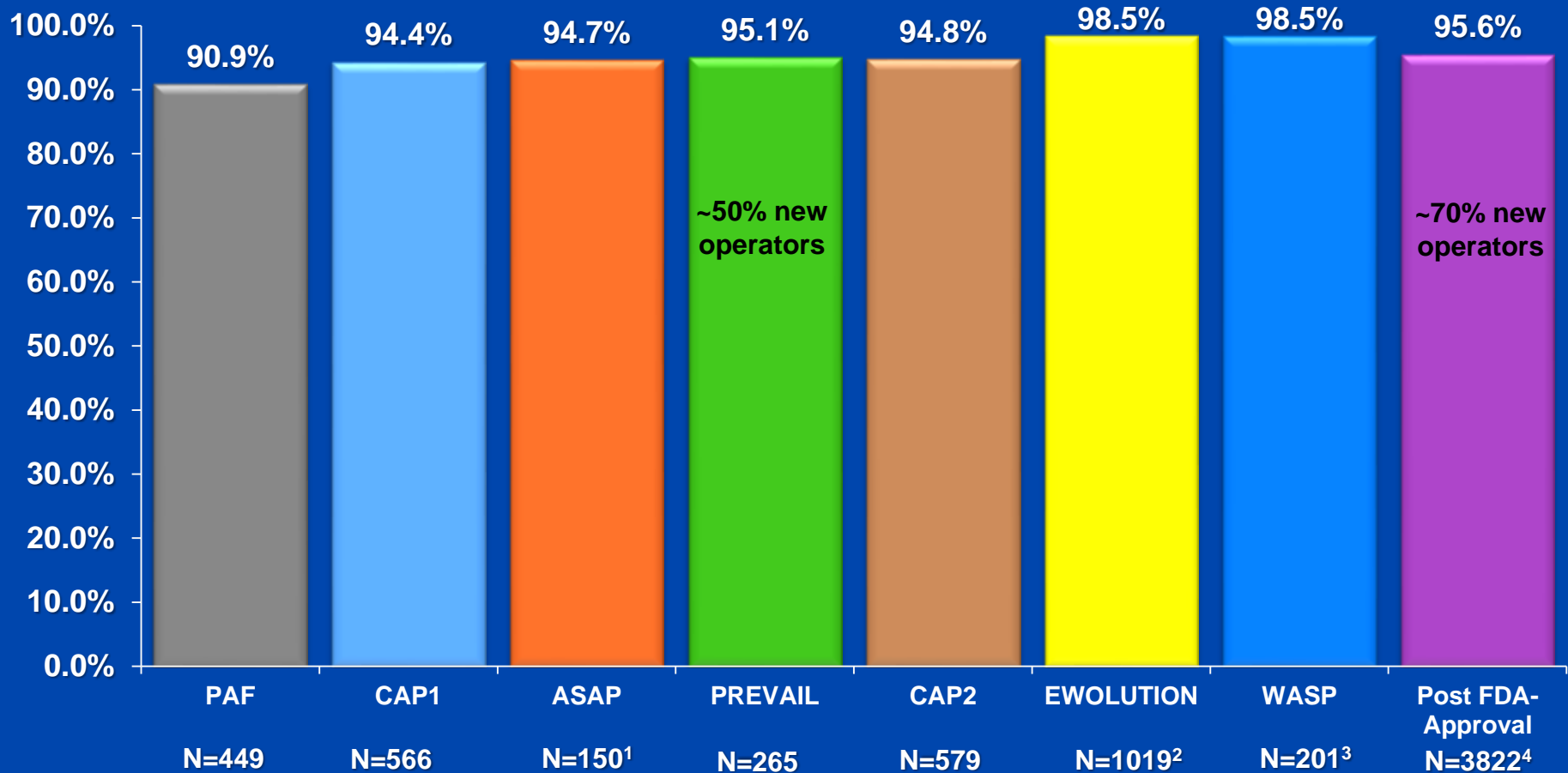


*ASAP TOO is event-driven, so follow-up timelines are variable

**Novel Evaluation of the WATCHMAN LAA Closure Therapy Surveillance Analysis Plan

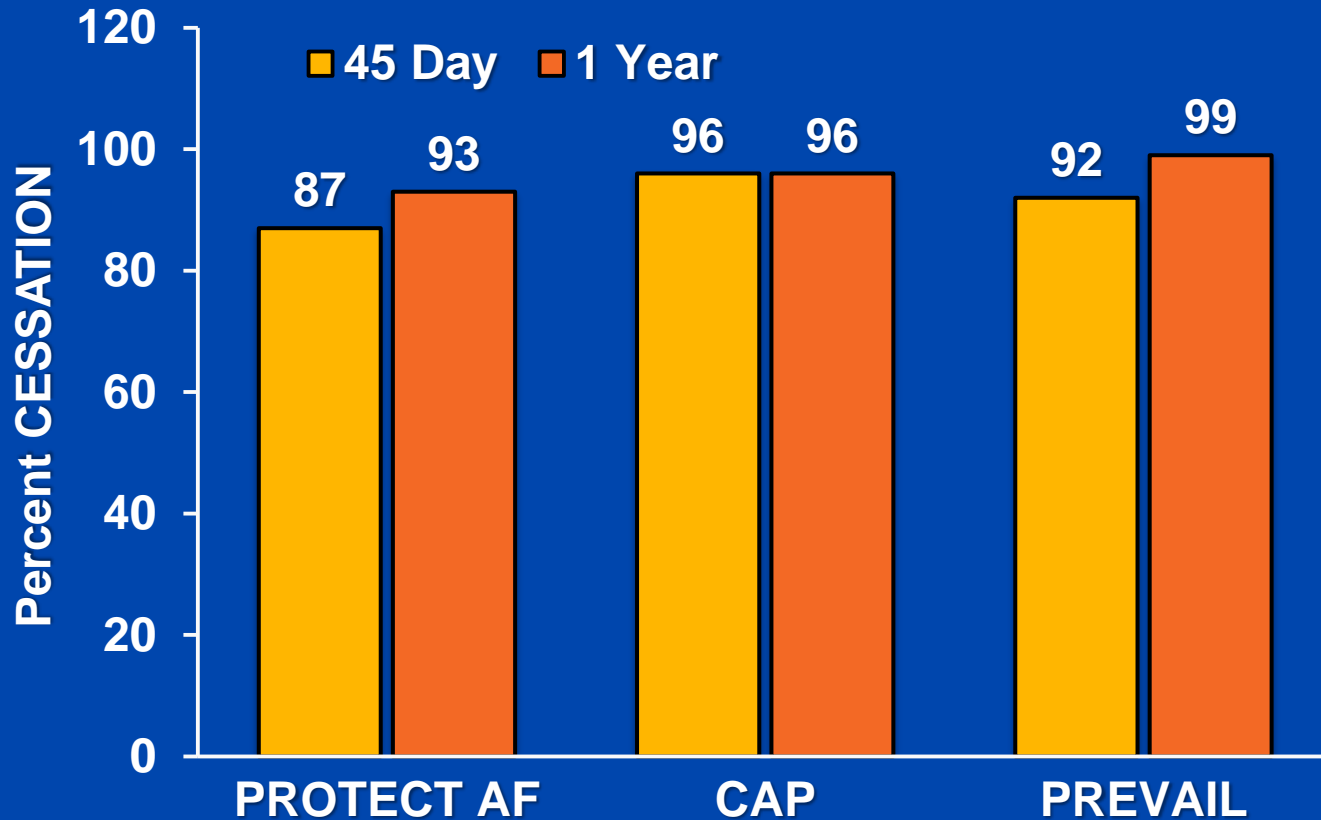
+ Czech Ministry of Health sponsored study

Consistent Procedural Success

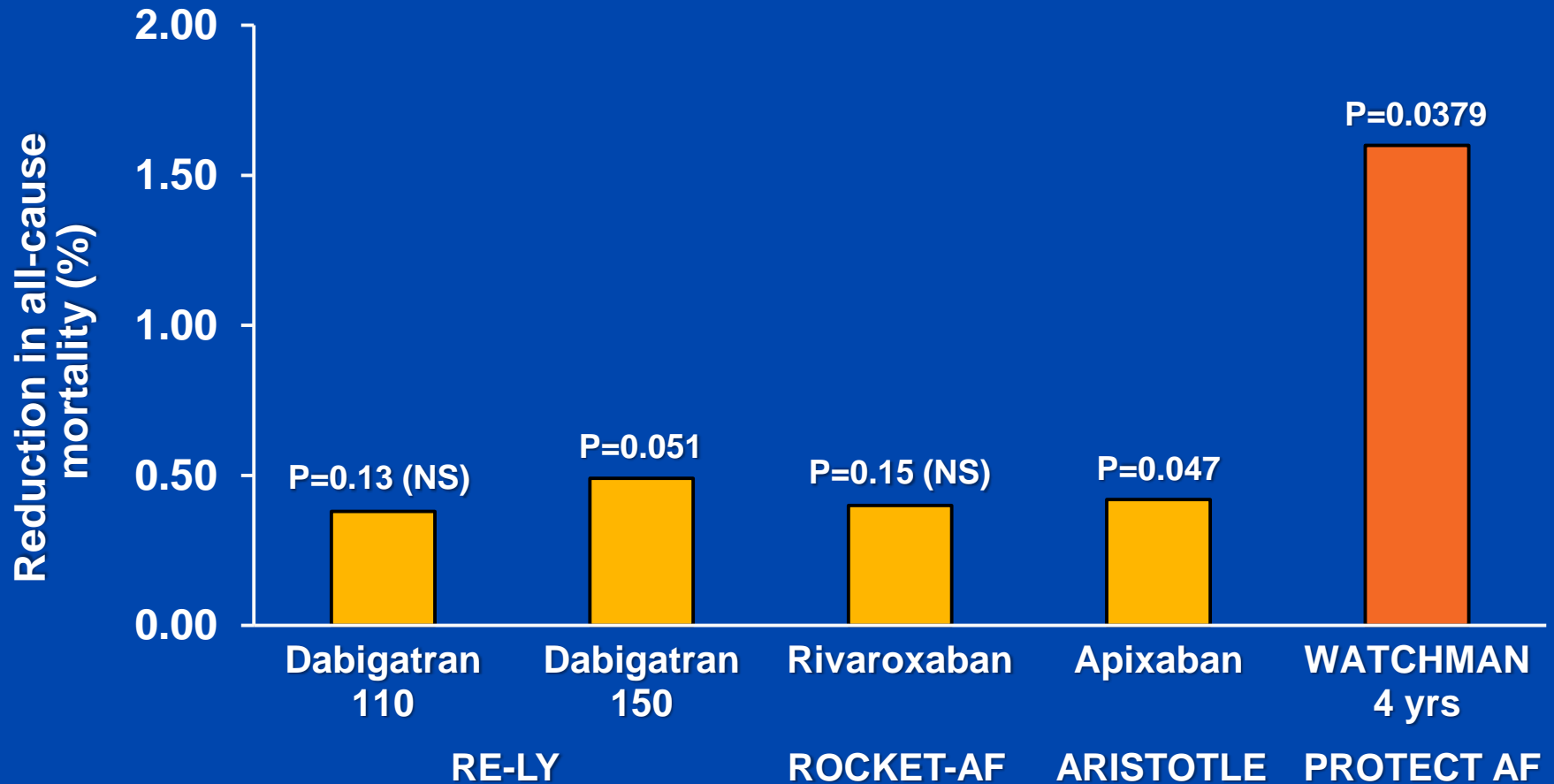


Implant success defined as deployment and release of the device into the LAA; no leak \geq 5 mm

Warfarin Cessation after WATCHMAN



Mortality Reduction (vs warfarin)



Results from different clinical trials:

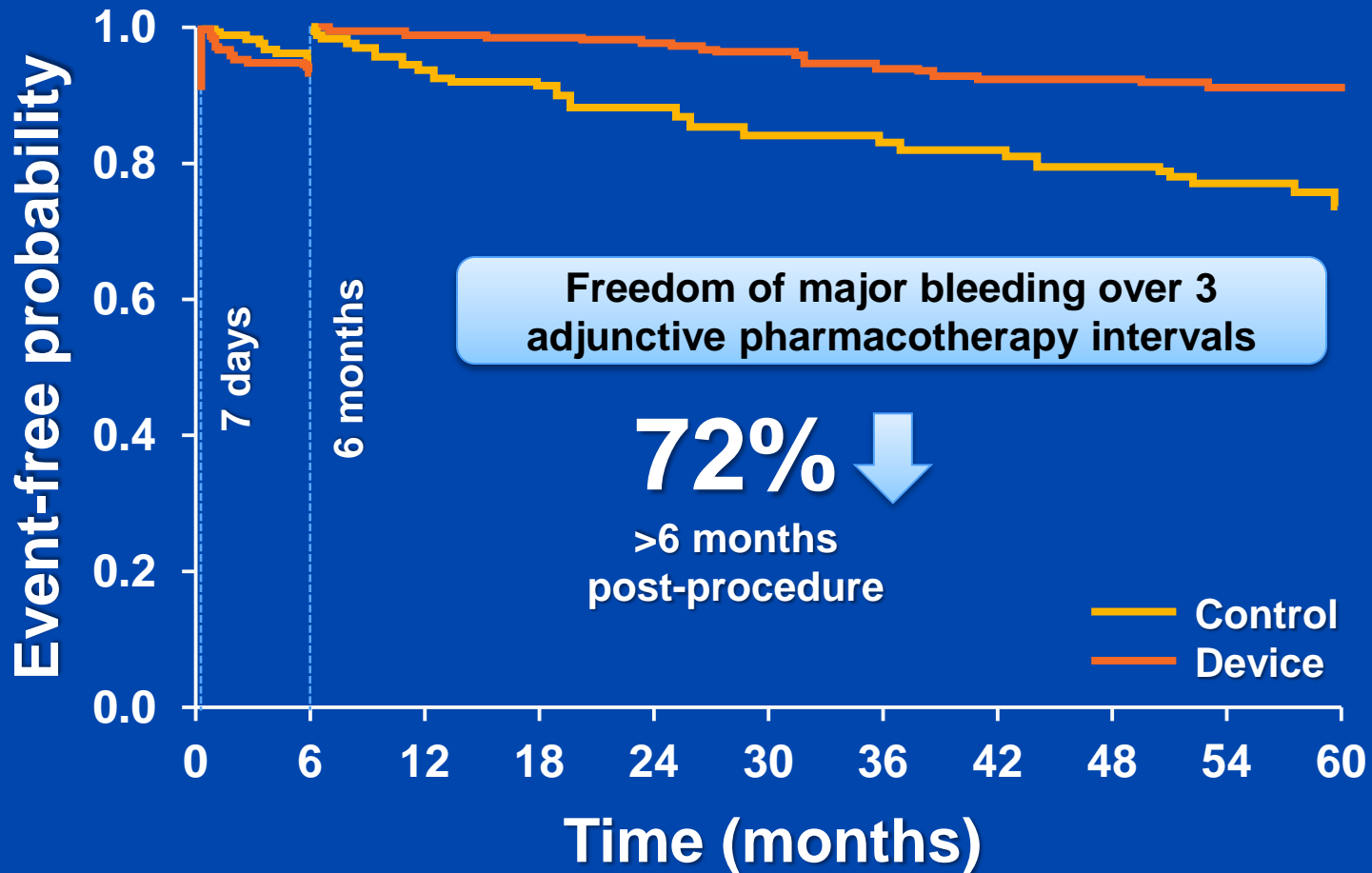
¹Connolly, S. NEJM 2009; 361:1139-1151 – 2 yrs f-up

²Patel, M. NEJM 2011; 365:883-891 – 1.9 yrs f-up, ITT

³Granger, C NEJM 2011; 365:981-992 – 1.8 yrs f-up

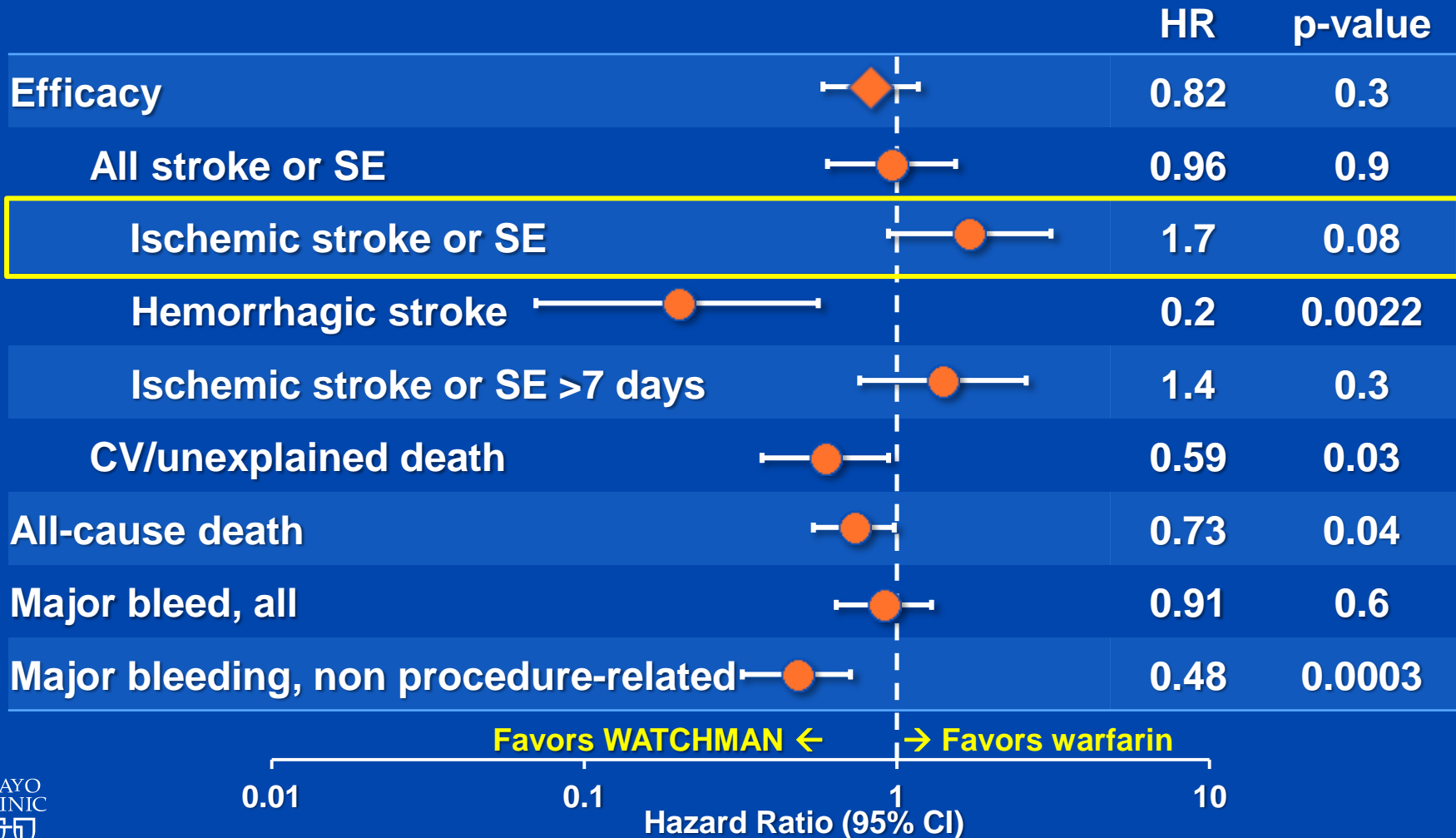
⁴Reddy, V. LBCT HRS 2013 – 4 yrs f-up

Bleeding Outcomes After LA Appendage Closure Compared with Long-term Warfarin



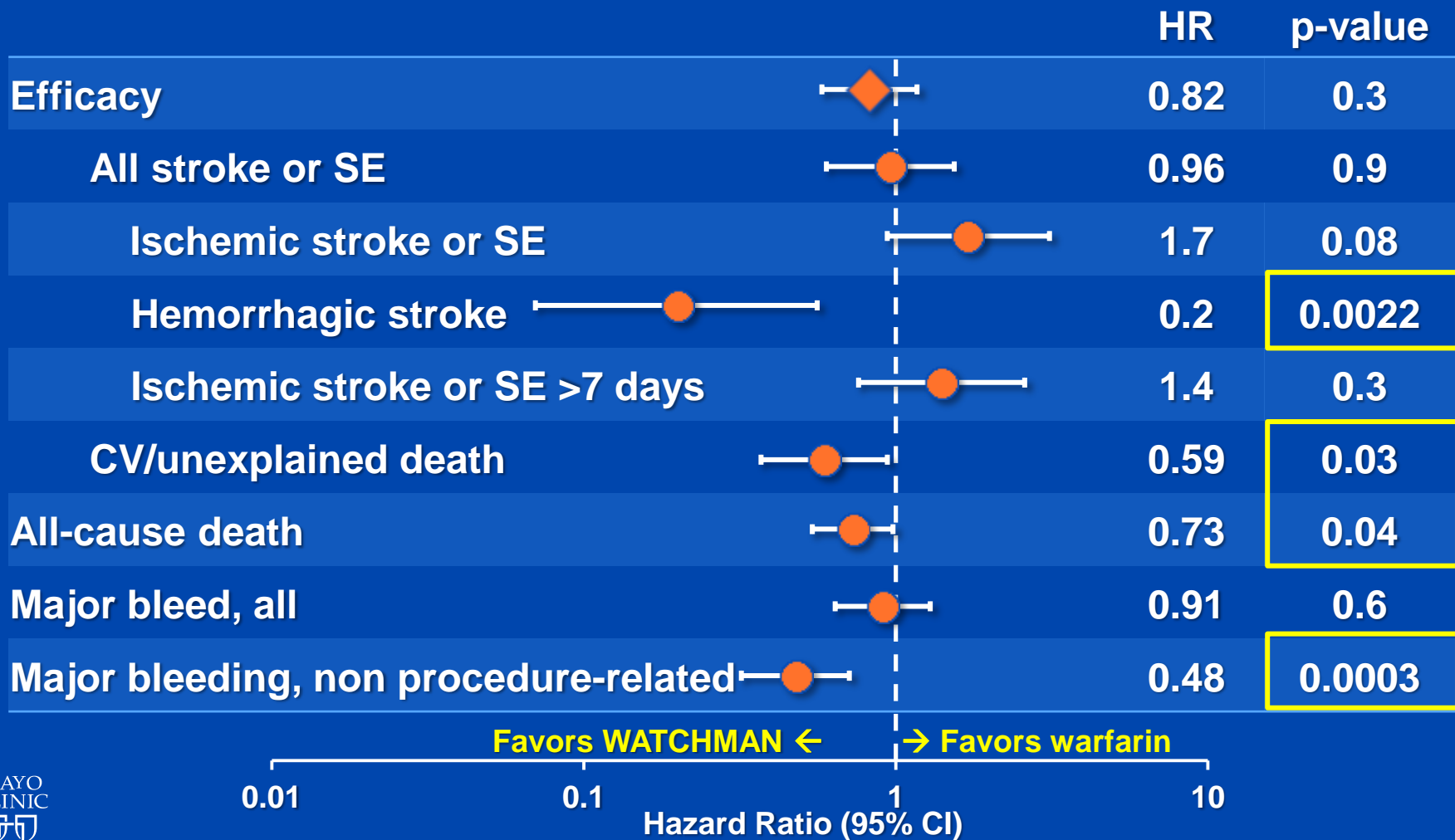
Patient-Level Meta-Analysis

PROTECT AF and PREVAIL 5 years



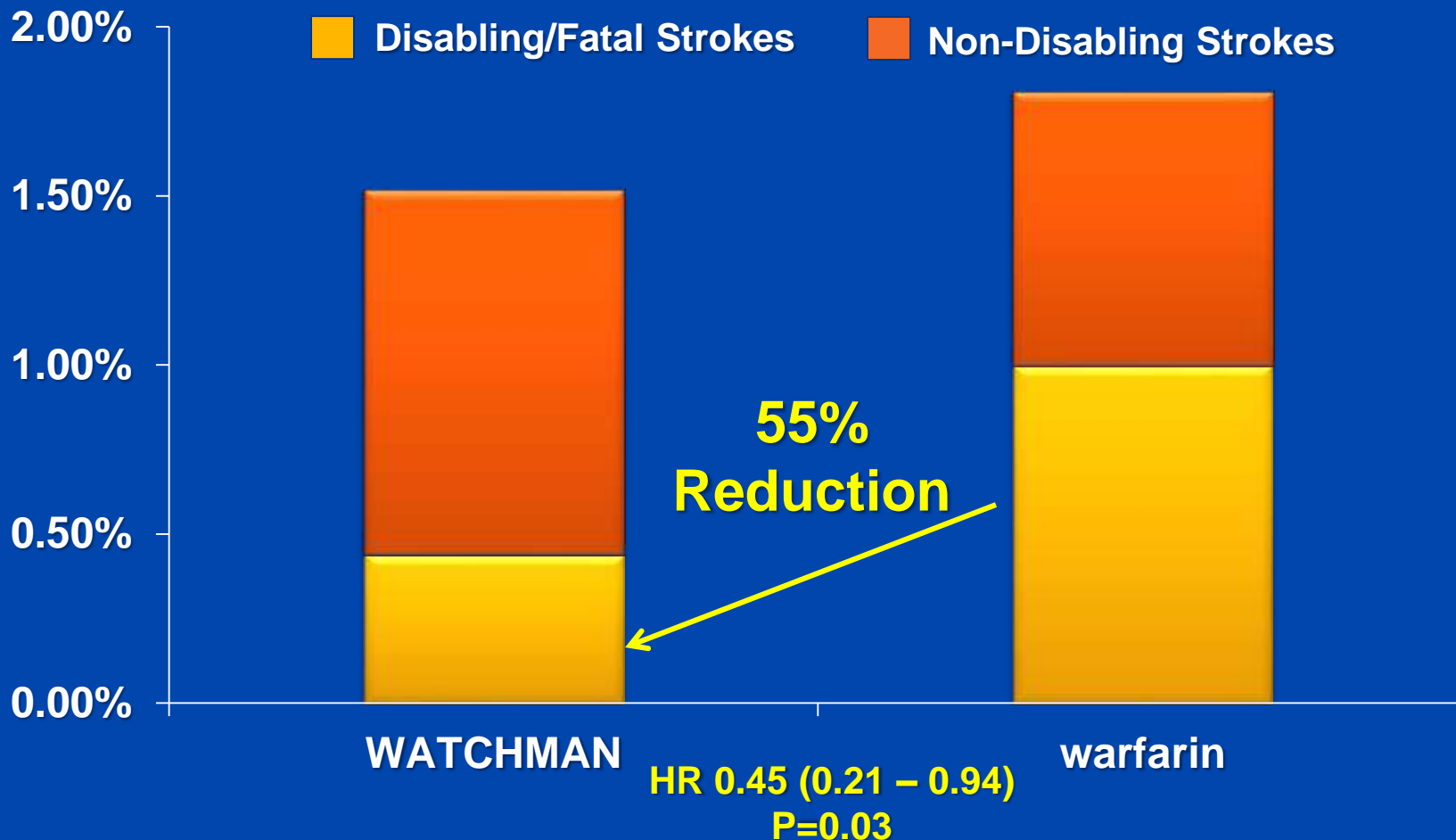
Patient-Level Meta-Analysis

PROTECT AF and PREVAIL 5 years



Patient-Level Meta-Analysis

WATCHMAN Superior Reduction in Disabling Strokes



Disabling Stroke defined as MRS ≥ 2

Two strokes in PREVAIL are excluded because the baseline MRS score was unavailable

What Then Can We Say?

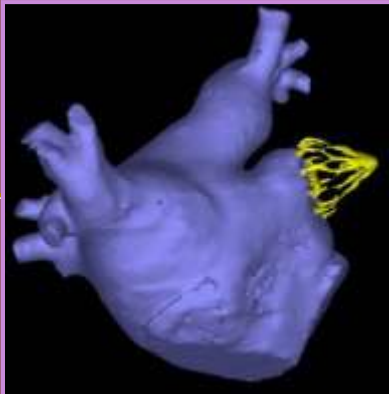
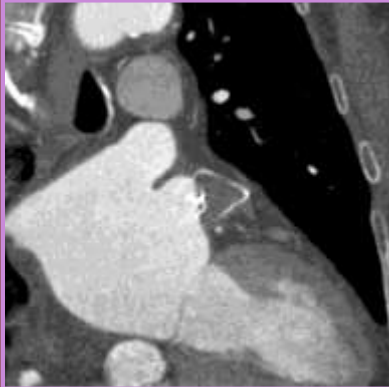
LAAC

- **Atrial fibrillation and stroke prevention is a global unmet need**
- **Has been used mainly as second line therapy; first line therapy anticoagulation has significant gaps**
- **LAAC is effective**
 - **Dramatic reduction in hemorrhagic stroke**
 - **Significant reduction in mortality**
 - **Significant reduction in bleeding**
 - **Can be used in patients in whom anticoagulation is either contraindicated or not optimal**
- **Multiple devices are either approved or CE mark available**

EQUIPOISE?



Certificate of Compliance

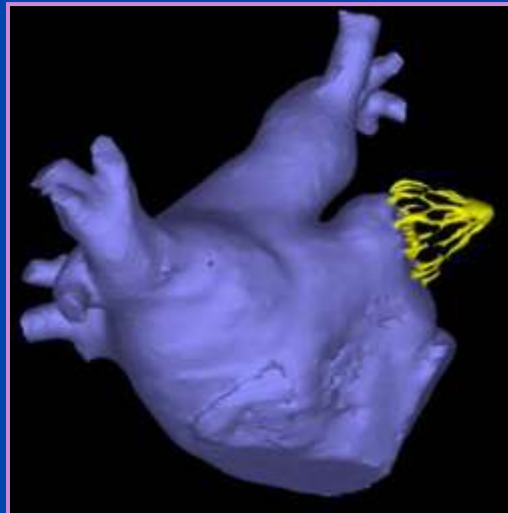
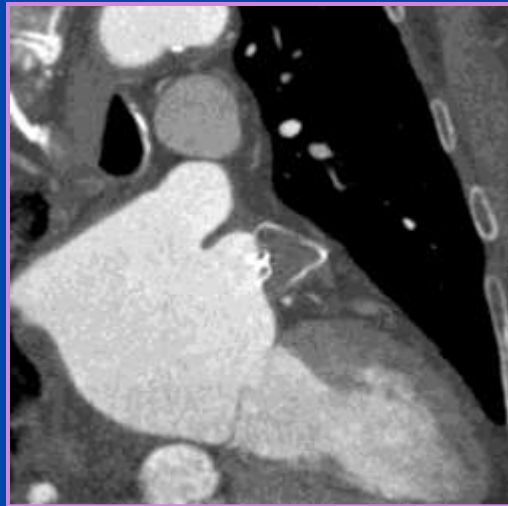


- Patients who could be treated with warfarin/NOACS
- Patients who choose not to be treated with warfarin/NOACS
- Contraindications to warfarin/NOACS
- In concert with ablation



Stroke and Atrial Fibrillation

Alternative to Warfarin or NOACS



- Patients who could be treated with warfarin/NOACS
- Patients who choose not to be treated with warfarin/NOACS
- Contraindications to warfarin/NOACS
- In concert with ablation