

Stroke Prevention in Atrial Fibrillation

{ A Comprehensive Review of the Options }

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October 31, 2022

KING'S
DAUGHTERS



Faculty Disclosures

- Serve as a clinical expert to teach others how to use the Watchman device

Definitions/Abbreviations

- DOAC = Direct Oral Anticoagulant
 - Edoxaban
 - Apixaban
 - Rivaroxaban
 - Dabigatran
- OAC = Oral Anticoagulant
 - DOAC or warfarin
- LAAO = Left Atrial Appendage Occlusion



Course Objectives

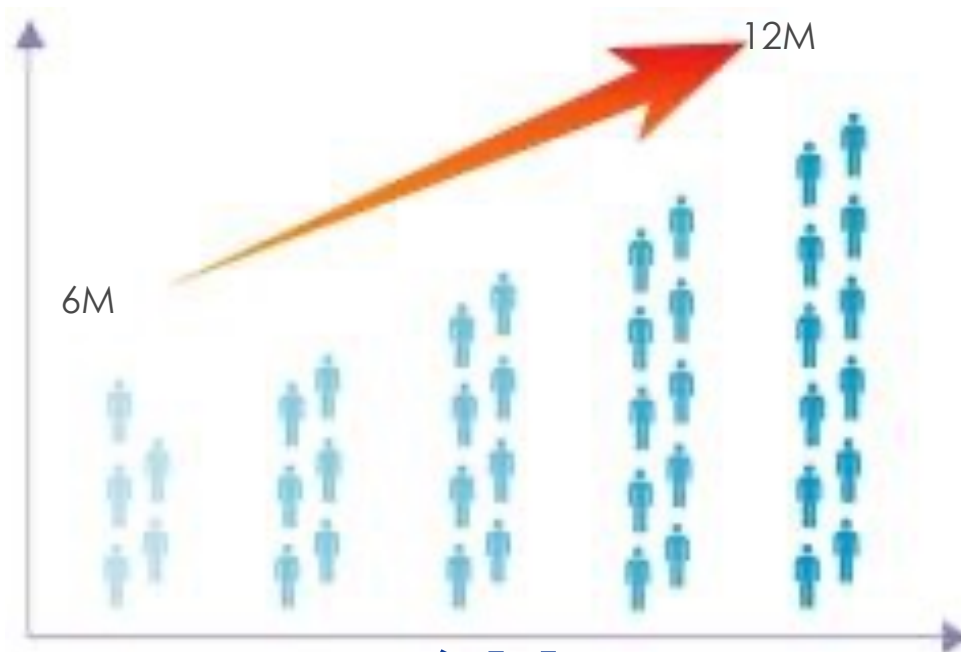
- Options for Stroke Risk Reduction
- OAC in ESRD Patients
- Stroke prevention strategies in patients hospitalized for bleeding
- Clinical data
- Guideline Review



Stroke in Atrial Fibrillation

**Need for a Device-Based Alternative for Stroke
Risk Reduction**

Atrial Fibrillation: An Independent Risk Factor for Stroke



~6M

people with AF in U.S.,
expected to more than
double by 2030¹

5X

increased
risk of stroke
for AF
patients²



1 in 6 strokes
occur in patients
with AF³

~2X

greater likelihood
of stroke
recurrence in AF
patients (within 6
months)⁴

¹Benjamin EJ, et al, Heart Disease and Stroke Statistics—2018 Update: A Report From the American Heart Association. Circulation. 2018; 137: e67-e492.

²Holmes DR, Atrial Fibrillation and Stroke Management: Present and Future, Seminars in Neurology 2010;30:528–536

³Hart RG, Halperin JL. Atrial fibrillation and thromboembolism: a decade of progress in stroke prevention. Ann Intern Med. 1999.

⁴Wolf PA et al, Duration of Atrial Fibrillation and the Imminence of Stroke: The Framingham Study, Stroke 1983; 14:664-667

AF-Related Strokes are Debilitating

Stroke

#1 cause of **adult disability** worldwide¹

AF-related Stroke

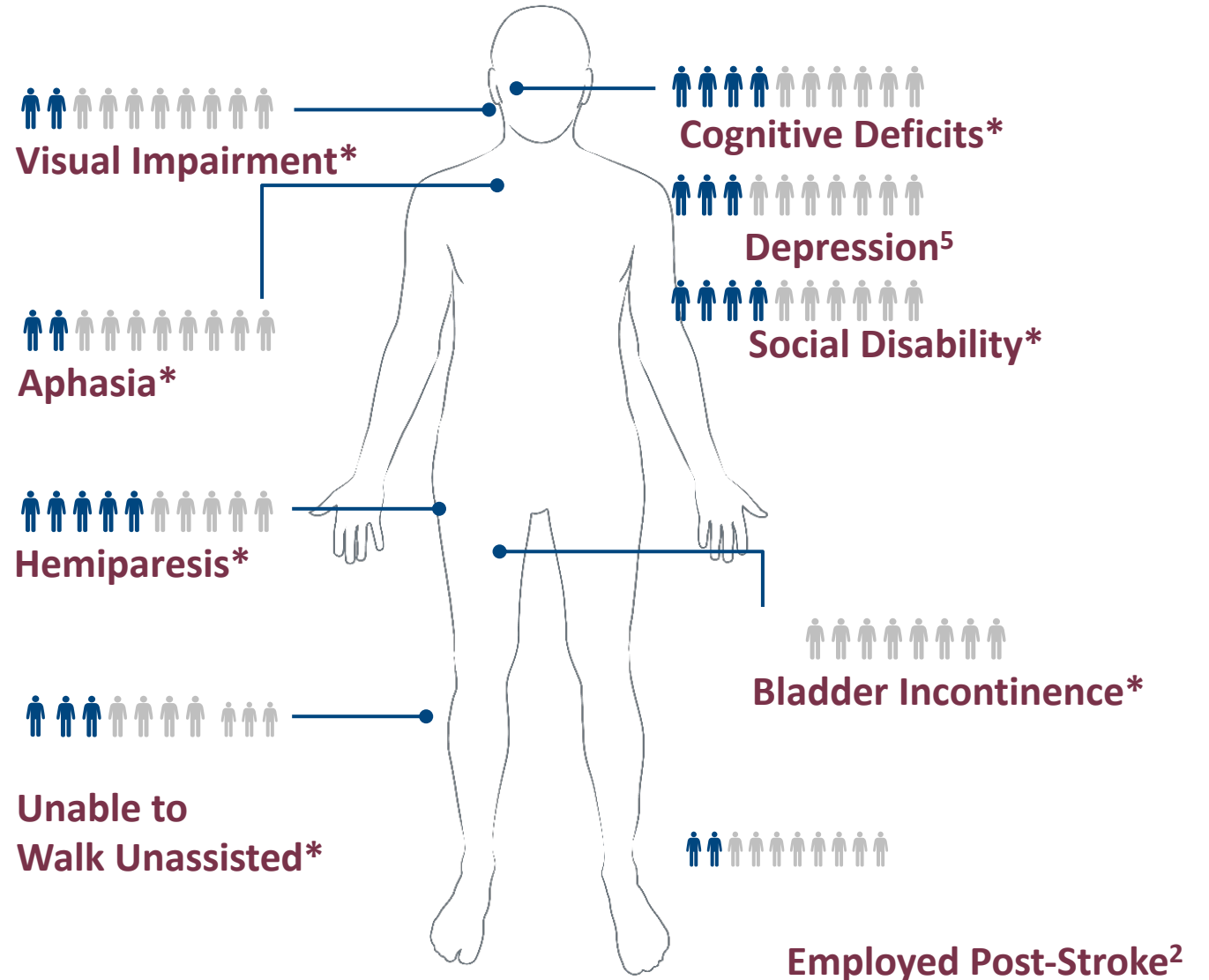
1.5X higher **disability**^{3**}

2X higher **mortality**^{3**}

70% result in **death or permanent disability**⁶

*at 6 months post-stroke⁴

**compared with stroke patients without AF



Connection Between Afib, Stroke, and the Left Atrial Appendage



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

AF Creates Environment for Thrombus Formation in Left Atrium

- In Afib >90% of stroke-causing clots that come from the left atrium are formed in the left atrial appendage



1. Stoddard et al. Am Heart J. (2003)
2. Goldman et al. J Am Soc Echocardiogr (1999)
3. Blackshear JL, Odell JA., *Annals of Thoracic Surg* (1996)

2014 ACC/AHA/HRS Treatment Guidelines on Anticoagulation in Afib & 2019 Focused Update

Assess stroke risk with CHA₂DS₂-VASc score

- Score 1 in men & 2 in women: Annual stroke risk 1%-2%, oral anticoagulants or aspirin may be considered
- Score ≥2 in men & ≥3 in women: Annual stroke risk 2%-15%, oral anticoagulants are recommended

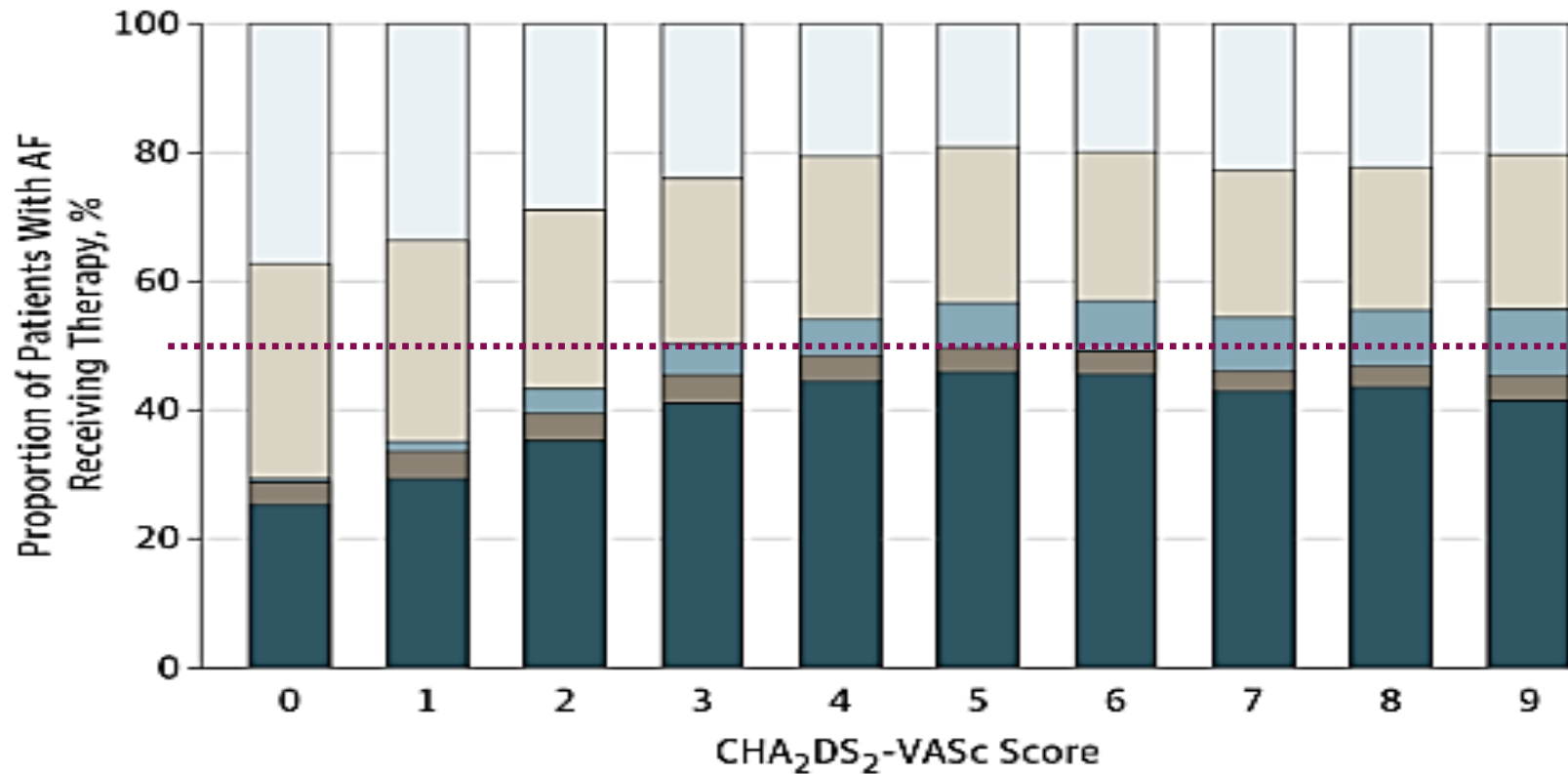
&

Balance stroke risk reduction benefit vs. bleeding risk

CHA ₂ DS ₂ -VASc Score in Men	CHA ₂ DS ₂ -VASc Score In Women	Recommendation
0	0	No anticoagulant
1	2	Aspirin (81-325 mg daily) or oral anticoagulants may be considered
≥ 2	≥ 3	Oral anticoagulants are recommended*

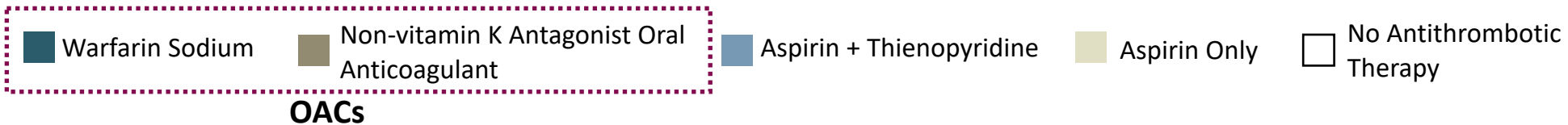
*DOACS (dabigatran, rivaroxaban, apixaban, and edoxaban) recommended over warfarin in DOAC-eligible patients

Oral Anticoagulation is Standard of Care, but Gaps in Care Remain



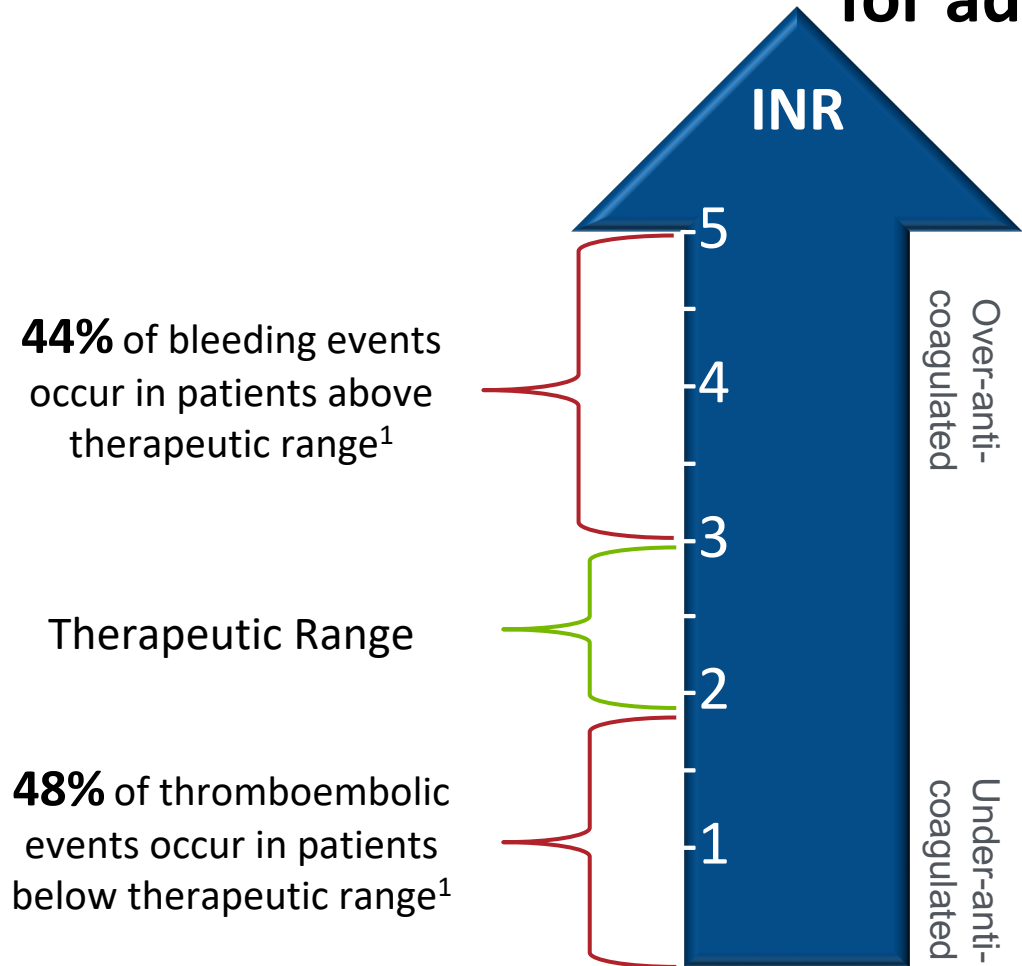
Despite increasing risk of stroke, the use of OAC in AF patients peaks at ~50%

No. 12348 36976 61557 87008 97878 70212 37314 17814 6385 1161



Stroke Treatment Option: Warfarin

Warfarin tops the list for emergency hospitalizations for adverse drug events in older Americans².



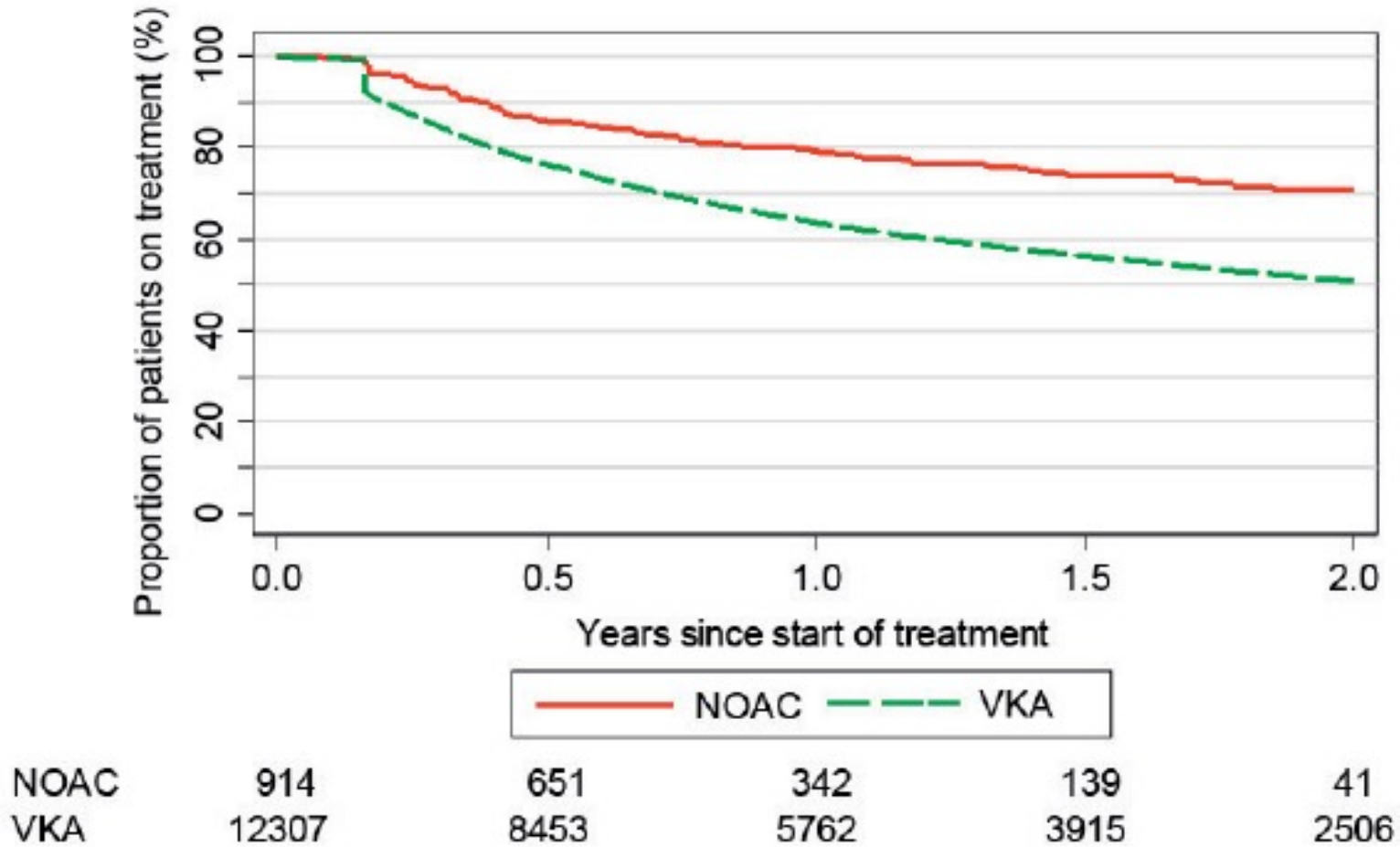
Many patients spend a significant amount of time outside of the therapeutic range.

¹ Oake N, et al. *Can Med Assoc J.* 2007;176(11);1589–1594

² Budnitz, MD, MPH. et al. *Annals of Internal Medicine.* 2007;147(11); 229

DOAC Use, Adherence Is Poor

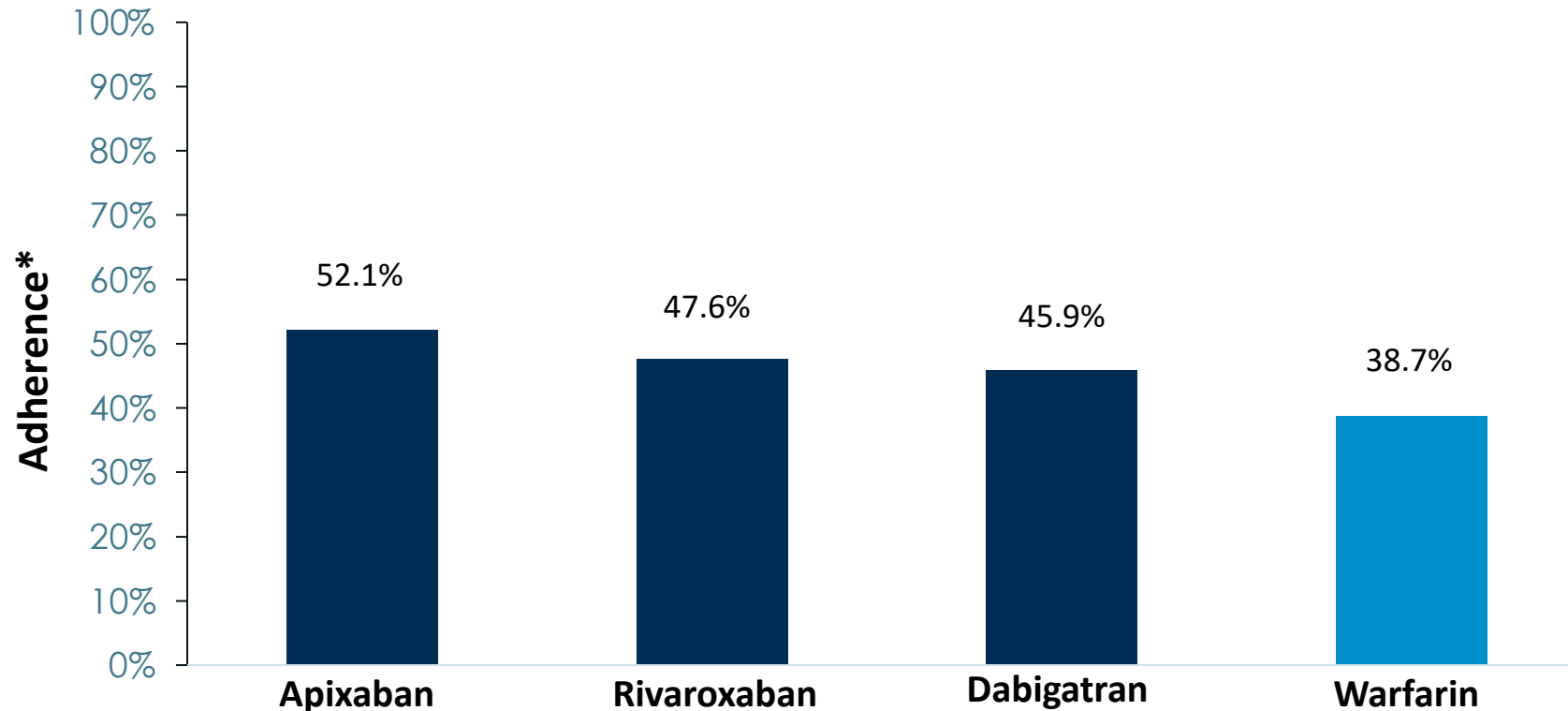
About 30% of DOAC patients discontinue treatment at 2 years



Challenges of Oral Anticoagulation

Less than Half of Patients on DOACS are Adherent

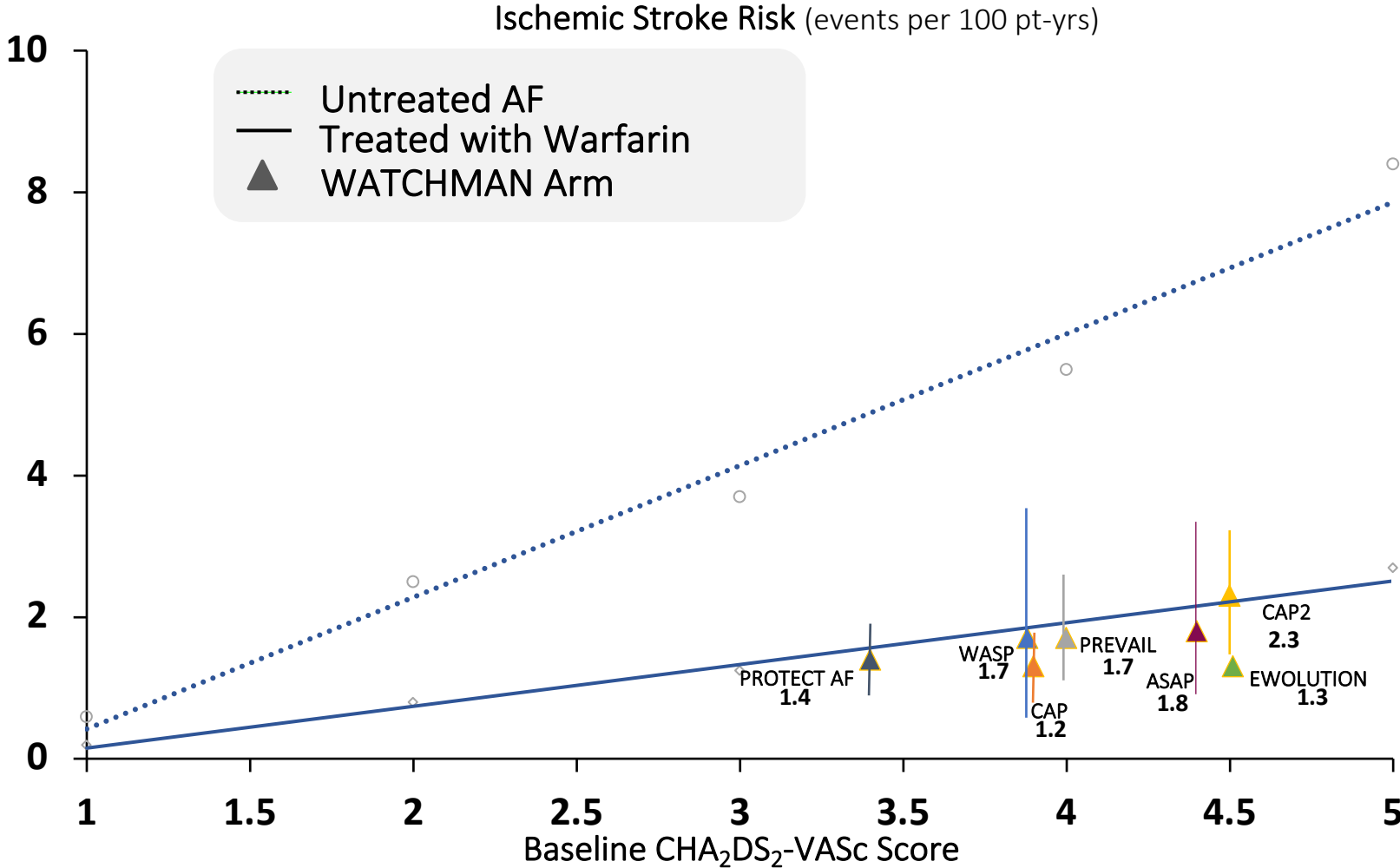
A retrospective study of 64,661 patients found that only 47.5% of patients had $\geq 80\%$ daily DOAC coverage during a median follow-up period of 1.1 years



*Predicted probability of adherence; reported adherence rates adjusted for confounders

Warfarin for Ischemic Stroke Risk Reduction

OAC cuts stroke risk by over 90% in PAF patients



Friberg. Eur Heart J (2012); NICE UK (2014). WATCHMAN FDA Panel Sponsor Presentation. Oct 2014; Reddy VY, et al. JACC 2017; 70(24): 2964-2975; Phillips, K et al. APHRS 2018. Taipei, Taiwan; Boersma LVA ECS 2018; LBCT; Sharma D et al. JACC 2016; 67(18): 2190-2192

OAC Clinical Data

(End Stage Renal Disease)

Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



Warfarin Use and the Risk for Stroke and Bleeding in Patients with Atrial Fibrillation Undergoing Dialysis

Mitesh Shah, Meytal Avgil Tsadok, Cynthia A. Jackevicius, Vidal Essebag, Mark J. Eisenberg, Elham Rahme, Karin H. Humphries, Jack V. Tu, Hassan Behlouli, Helen Guo and Louise Pilote

Circulation, published online January 22, 2014;

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

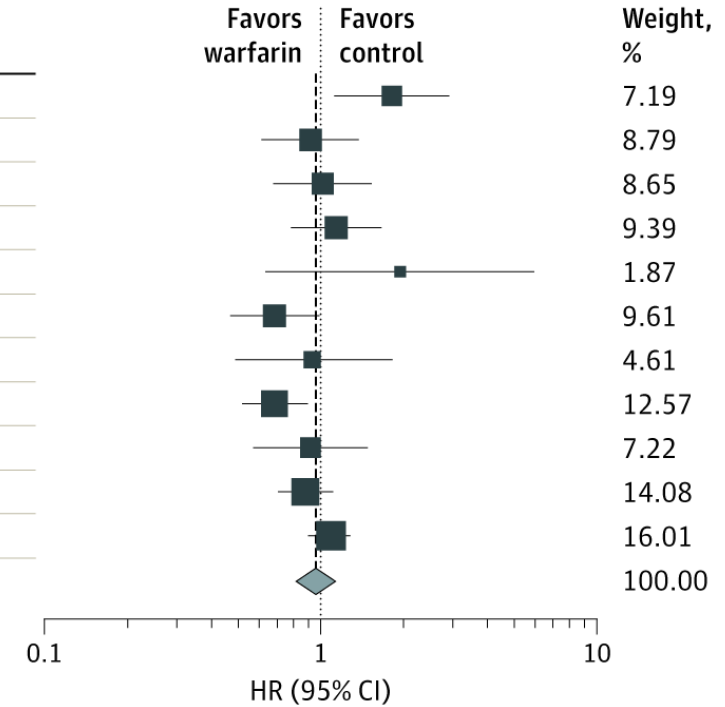
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

Warfarin for Atrial Fib in ESRD

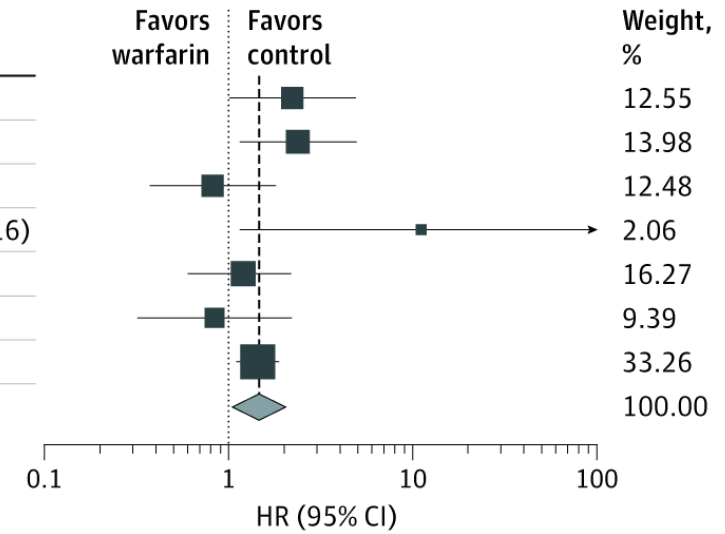
A Ischemic stroke

Source	HR (95% CI)
Chan et al, ⁸ 2009	1.81 (1.12-2.92)
Winkelmayer et al, ⁹ 2011	0.92 (0.61-1.37)
Chen J et al, ¹¹ 2014	1.02 (0.67-1.53)
Shah et al, ¹² 2014	1.14 (0.78-1.67)
Wakasugi et al, ¹³ 2014	1.94 (0.63-5.93)
Shen et al, ¹⁵ 2015	0.68 (0.47-0.99)
Garg et al, ¹⁶ 2016	0.93 (0.49-1.82)
Kai et al, ²⁰ 2017	0.68 (0.52-0.90)
Lee et al, ²² 2017	0.92 (0.57-1.48)
Tan et al, ¹⁹ 2019	0.88 (0.70-1.11)
Yoon et al, ²¹ 2017	1.09 (0.90-1.28)
Overall: $I^2 = 52.6\%$	0.96 (0.82-1.13)



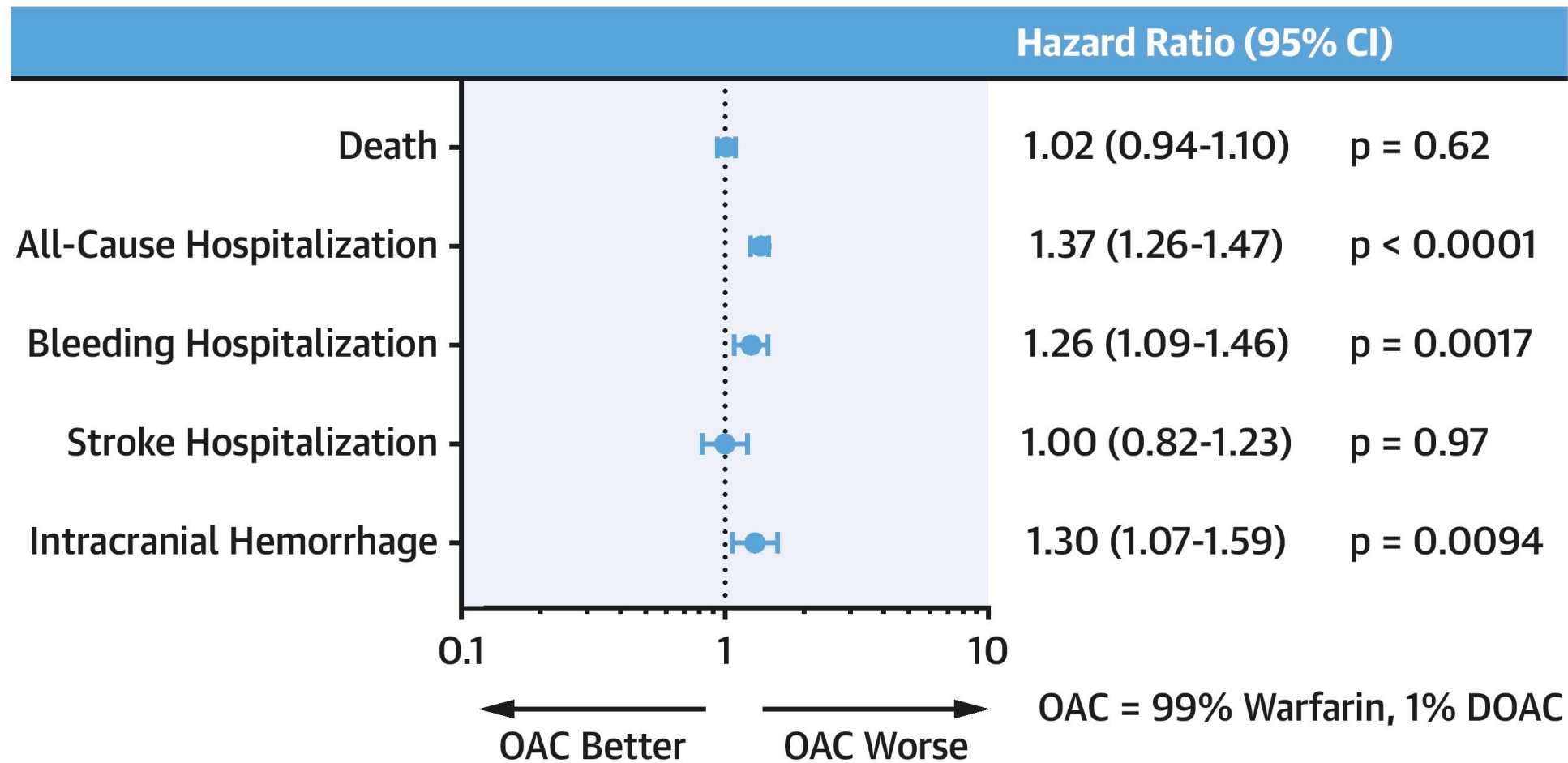
B Hemorrhagic stroke

Source	HR (95% CI)
Chan et al, ⁸ 2009	2.22 (1.01-4.91)
Winkelmayer et al, ⁹ 2011	2.38 (1.15-4.96)
Shen et al, ¹⁵ 2015	0.82 (0.37-1.81)
Wang et al, ¹⁷ 2016	11.11 (1.15-107.16)
Kai et al, ²⁰ 2017	1.20 (0.60-2.20)
Lee et al, ²² 2017	0.84 (0.32-2.19)
Yoon et al, ²¹ 2017	1.44 (1.10-1.88)
Overall: $I^2 = 37.0\%$	1.46 (1.05-2.04)



Randhawa MS et al. Association Between Use of Warfarin for Atrial Fibrillation and Outcomes Among Patients With End-Stage Renal Disease: A Systematic Review and Meta-analysis. *JAMA Netw Open*. 2020;3(4):e202175.

CENTRAL ILLUSTRATION: Adjusted Outcomes Among Matched End-Stage Renal Disease-Atrial Fibrillation Patients by Anticoagulant Use at 2 Years



Pokorney, S.D. et al. J Am Coll Cardiol. 2020;75(11):1299-308.

OAC Clinical Data

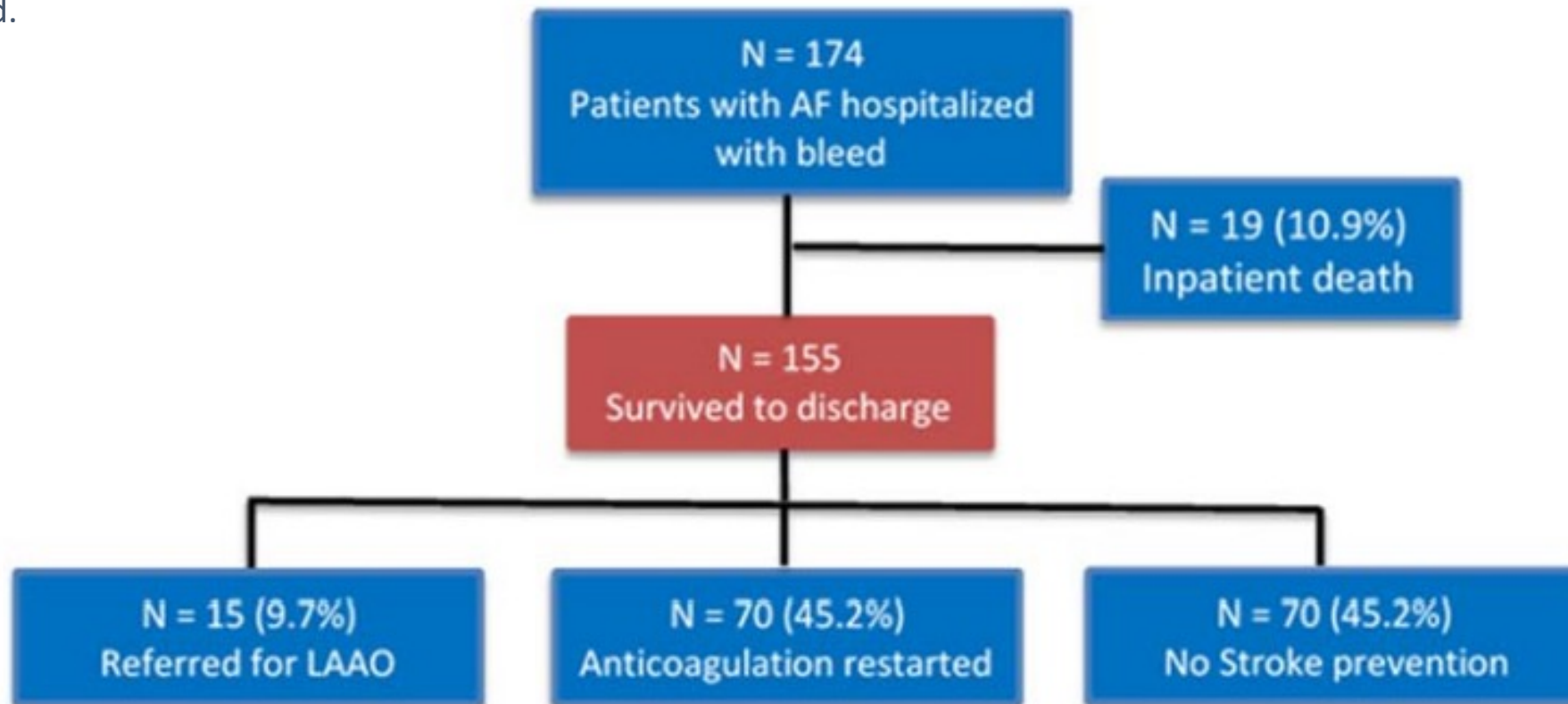
(Patients on OAC admitted for bleeding)

Method:

Patients with AF on OAC admitted for bleeding: January 2016 and August 2019.

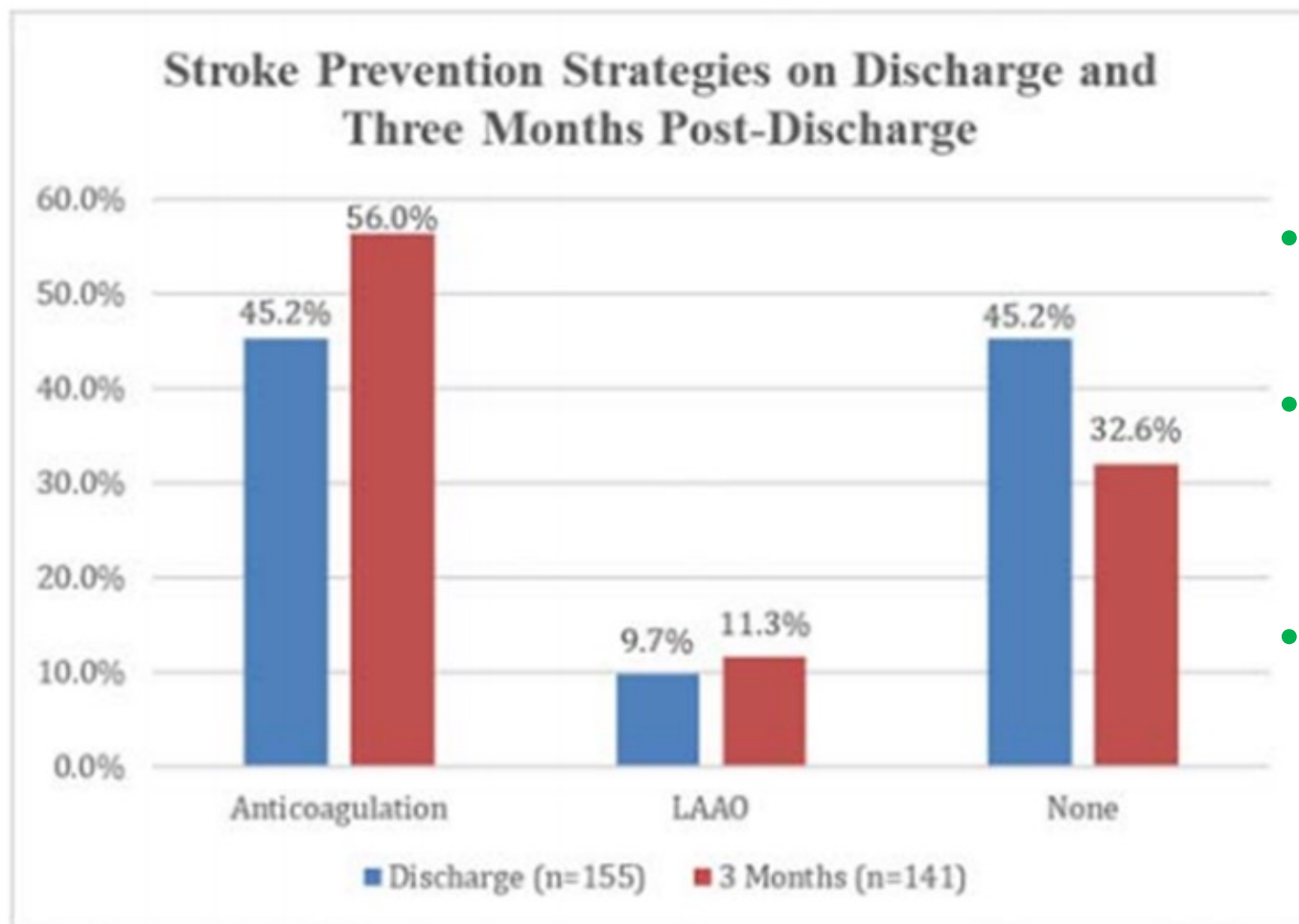
The type of AC, form of bleeding, and CHA2DS2VASc were collected. Stroke prevention strategies upon discharge and at 3 months were noted.

RESULTS:



Almost half of patients with AF on OAC discharged without stroke prophylaxis protection or plan

45.2% of Patients were discharged **without** a STROKE PREVENTION PLAN



Reasons for no stroke prophylaxis

- Provider fear of rebleeding due multiple episodes of prior bleeding, hemorrhagic shock, or need of reversal agent
- Patient reluctance to restart OAC
- Deferral of the decision to restart outpatient
- Lack of awareness of LAAO as an alternative to OAC

WATCHMAN

[Clinical Study Overview]

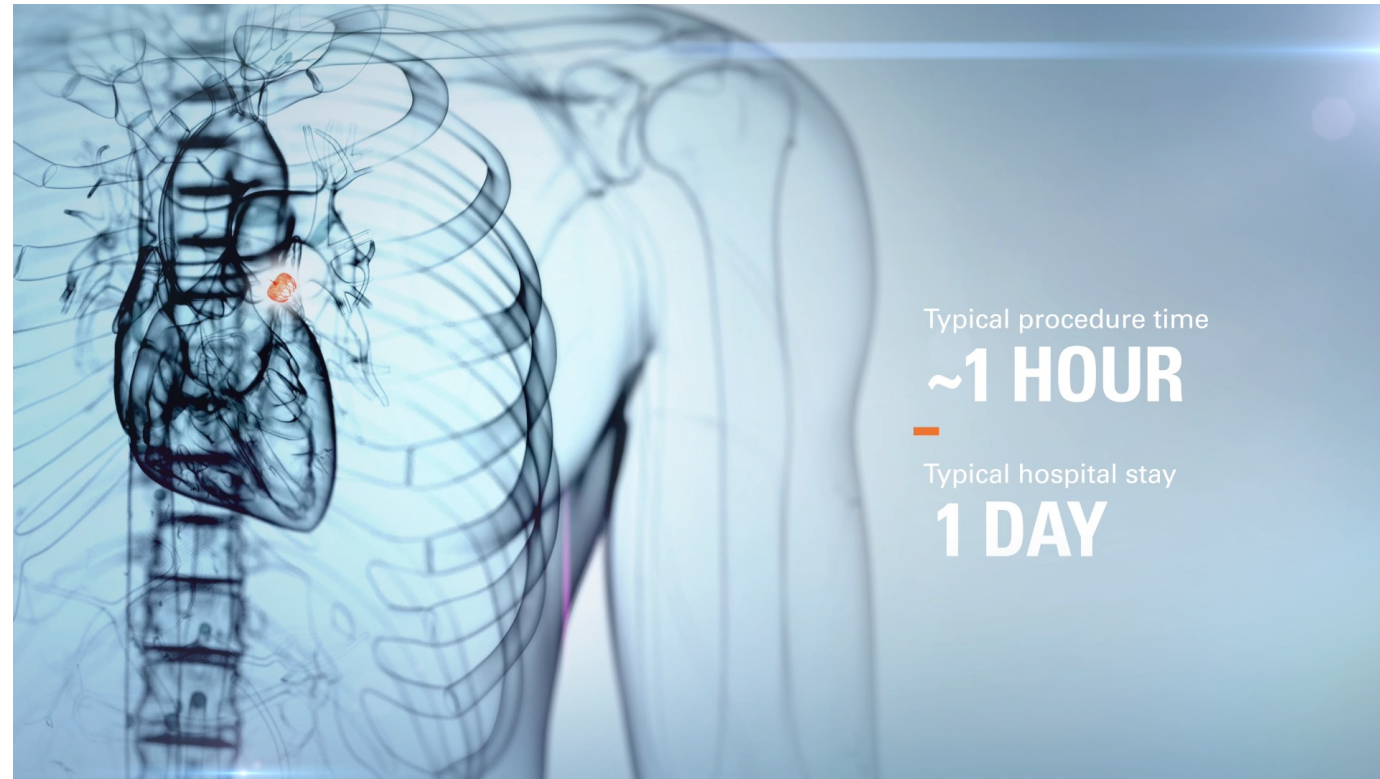


WATCHMAN™ Left Atrial Appendage Closure (LAAC) Device Procedure



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

- One-time implant that does not need to be replaced
- Performed by a Heart Team
 - IC/EP, TEE, General Anesthesia, WATCHMAN Clinical Specialist
- Transfemoral Access
- General anesthesia
- 1 hour procedure
- Same day discharge



Typical procedure time

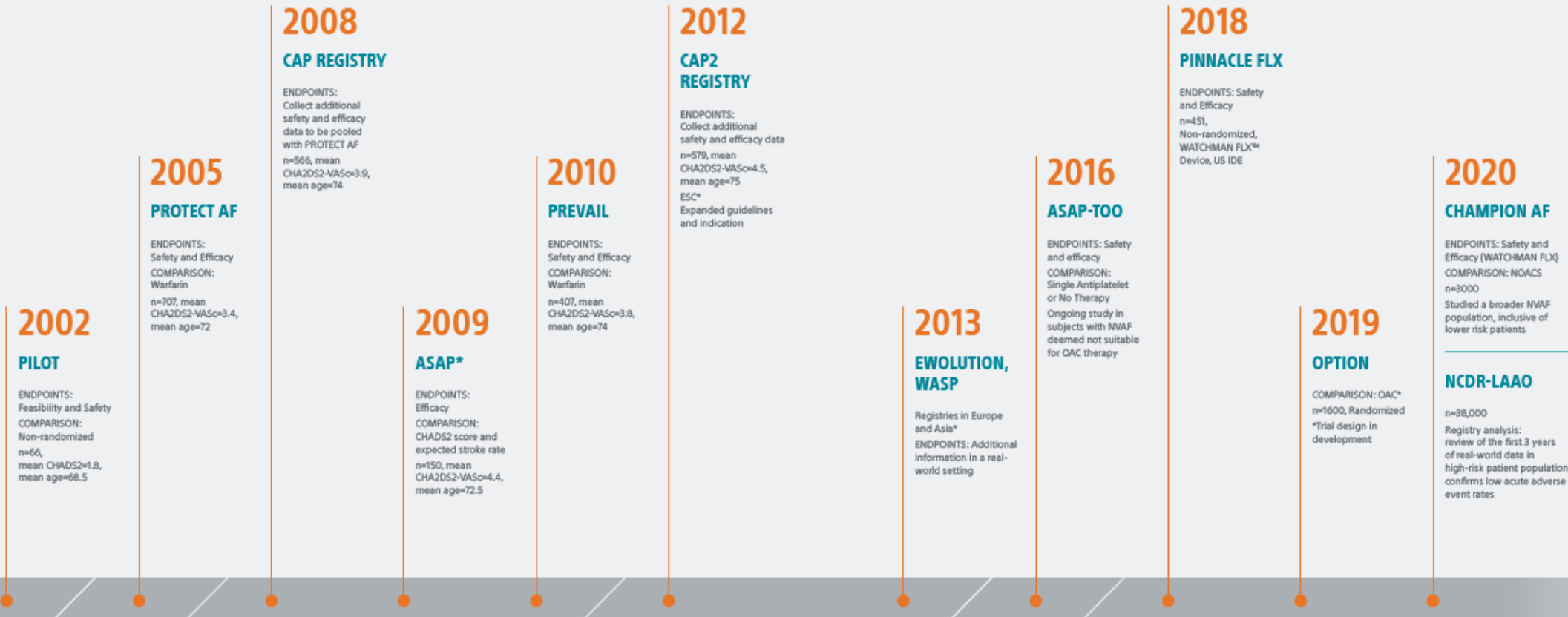
~1 HOUR

Typical hospital stay

1 DAY

WATCHMAN is the Most Studied LAAC Device

Globally, WATCHMAN has been implanted in more than 150,000 patients and studied in more than 10 clinical studies. WATCHMAN is a safe, proven, and effective option for stroke risk reduction and enables patients to discontinue OAC therapy for a lifetime.



WATCHMAN™ IS PROVEN.



PATIENTS IMPLANTED



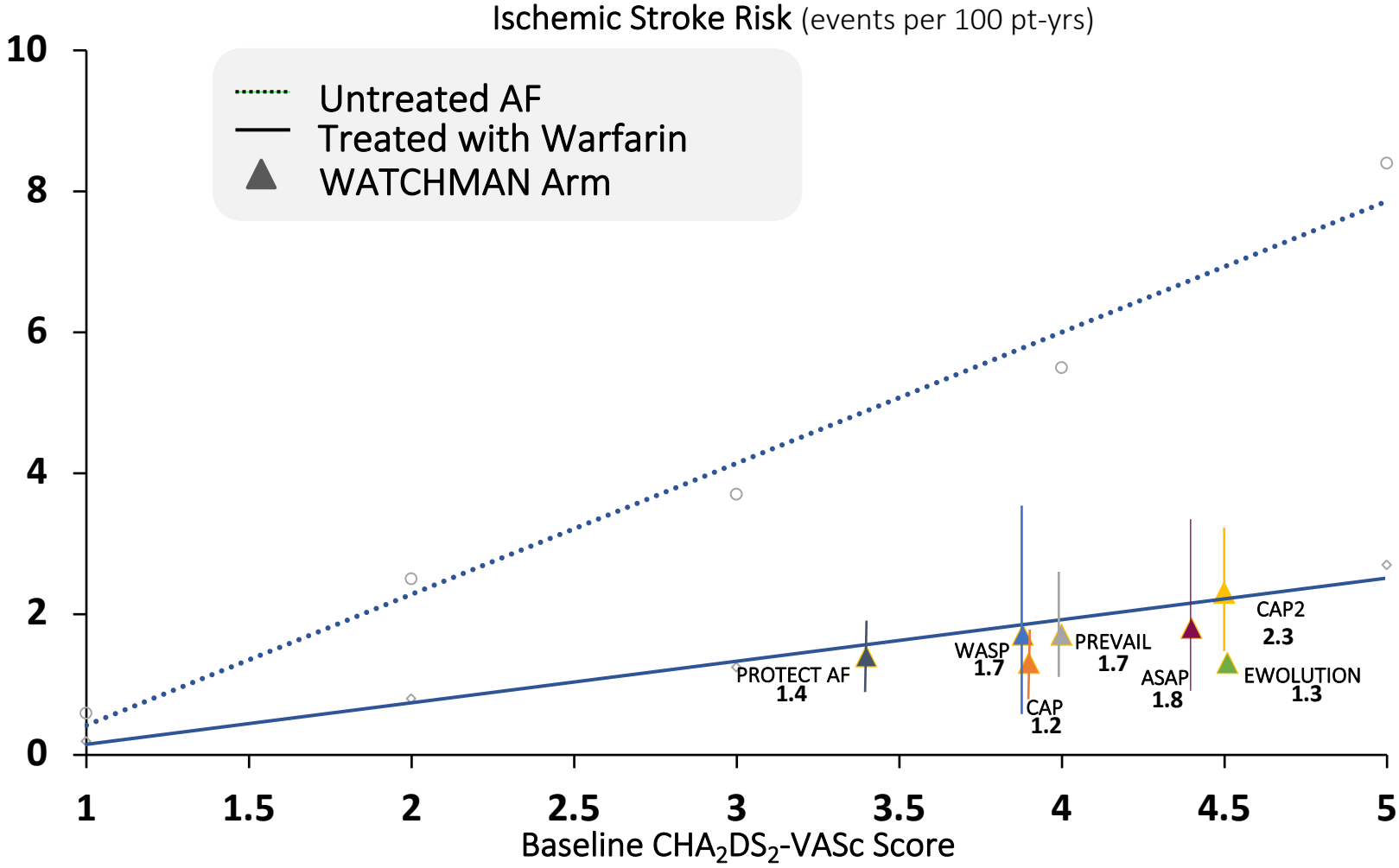
CLINICAL AND REAL-WORLD EXPERIENCE



CLINICAL STUDIES

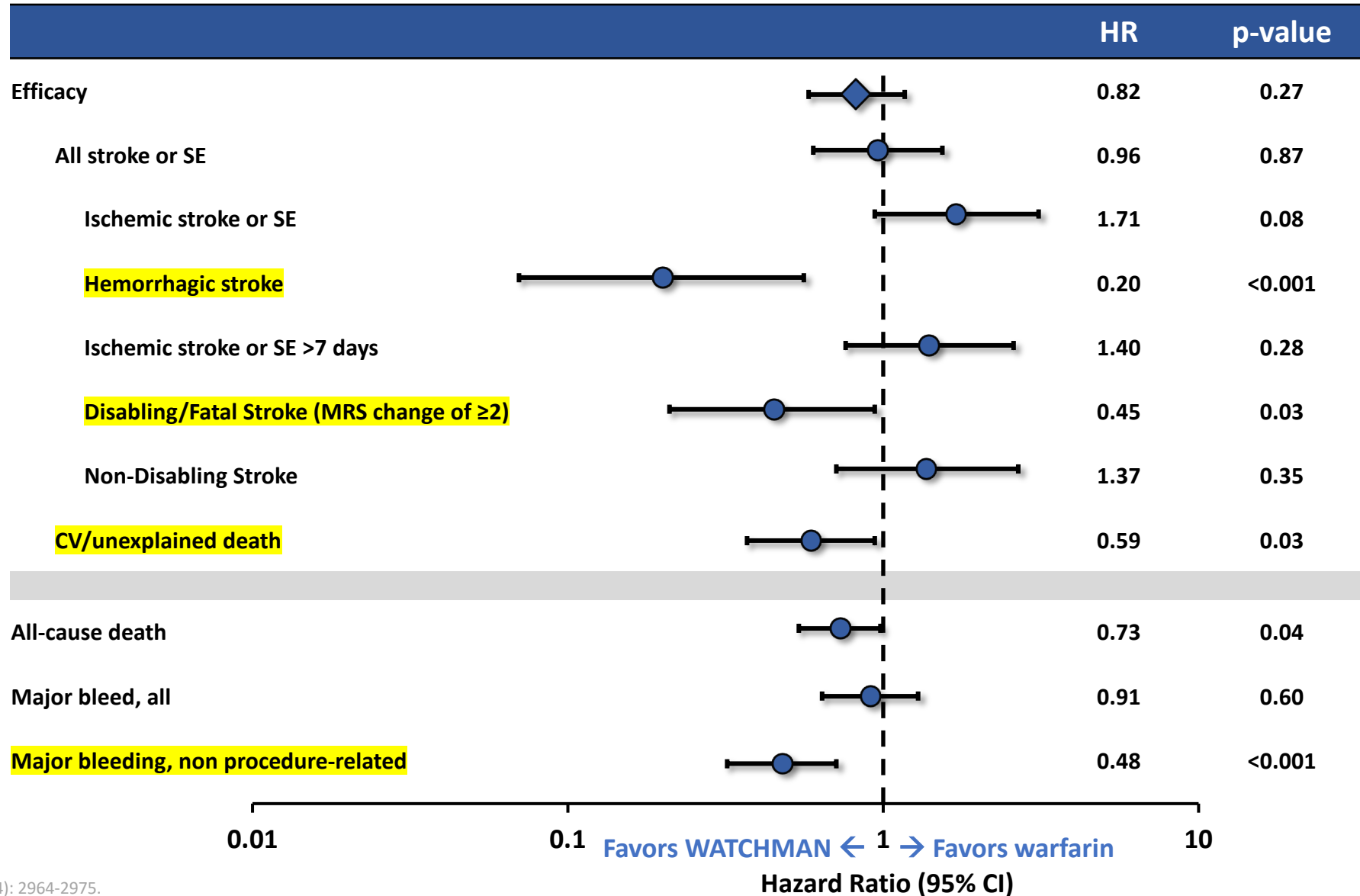
Warfarin for Ischemic Stroke Risk Reduction

Watchman cuts stroke risk by over 90% in PAF patients



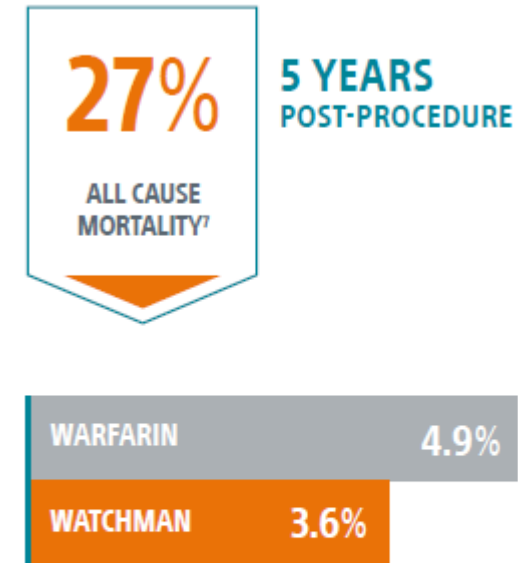
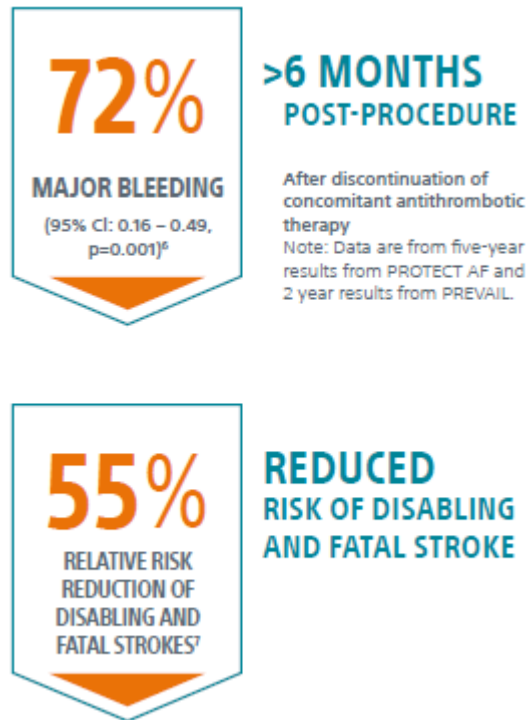
Friberg. Eur Heart J (2012); NICE UK (2014). WATCHMAN FDA Panel Sponsor Presentation. Oct 2014; Reddy VY, et al. JACC 2017; 70(24): 2964-2975; Phillips, K et al. APHRS 2018. Taipei, Taiwan; Boersma LVA ECS 2018; LBCT; Sharma D et al. JACC 2016; 67(18): 2190-2192

PROTECT AF & PREVAIL 5 Year Patient Level Meta-Analysis



The WATCHMAN Difference

Long-term results demonstrated WATCHMAN reduced risk of disabling stroke, post-procedure bleeding, and mortality vs. warfarin



- Bleed Reduction Findings from PROTECT AF & PREVAIL Meta Analysis (3 Year)
- Disabling Stroke & All Cause Mortality Finding from PROTECT AF & PREVAIL Meta Analysis (5 Year)

*Major bleeding defined as adverse event that was assigned one of several bleeding codes and was adjudicated by an independent Clinical Events Committee as significant (life-threatening or resulting in hospitalization, prolongation of hospitalization, substantial disability, or death).

WATCHMAN Clinical Summary

A **safe alternative** to long-term OAC therapy which offers **comparable stroke risk reduction** and enables patients to **stop taking OAC**^{1,2}

Demonstrated **statistically superior reductions** in **disabling/fatal strokes, major non-procedure related bleeding** and **cardiovascular death** compared to OAC^{2,3,5}

Demonstrated **95% implant success rate** and a **1.5% major procedural complication rate** with both new and experienced operators⁴

> 92% OAC cessation after 45 days, > 99% after 1 year¹

2019 ACC/AHA/HRS Focused Update on Atrial Fibrillation

WATCHMAN included in AF Guidelines

4.4. Nonpharmacological Stroke Prevention

4.4.1. Percutaneous Approaches to Occlude the LAA

Recommendation for Percutaneous Approaches to Occlude the LAA		
Referenced studies that support the new recommendation are summarized in Online Data Supplement 4 .		
COR	LOE	Recommendation
Ib	B-NR	1. Percutaneous LAA occlusion may be considered in patients with AF at increased risk of stroke who have contraindications to long-term anticoagulation (S4.4.1-1–S4.4.1-5). NEW: Clinical trial data and FDA approval of the Watchman device necessitated this recommendation.

Which Patients are Eligible?



WATCHMAN™
LEFT ATRIAL APPENDAGE
CLOSURE DEVICE

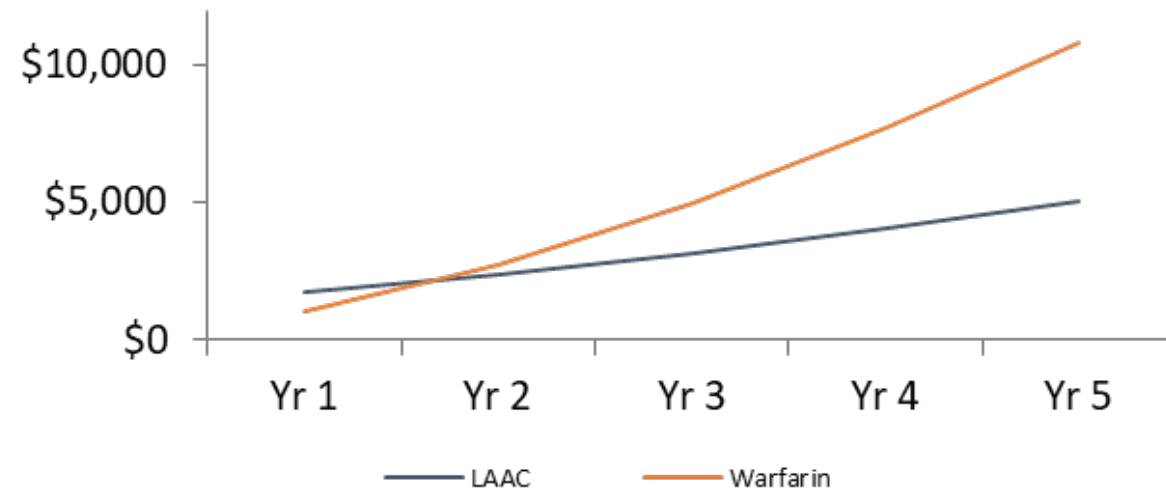
Insurance covers percutaneous LAAC implants for patients with :

- CHADS₂ score ≥ 2 or a CHA₂DS₂-VASc score ≥ 3
(virtually anyone over 65 yo)

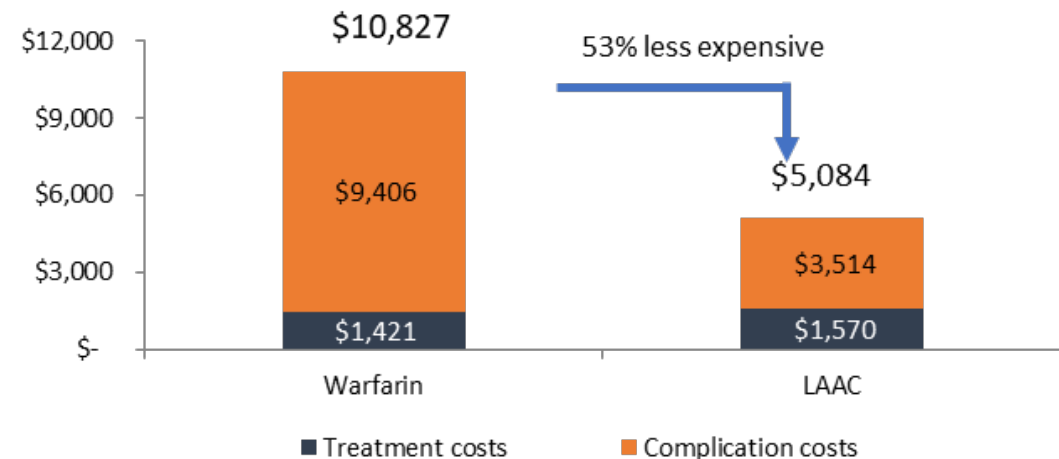
How Much Does WM Cost?

- For many it is totally covered (100%) as many meet their deductibles for their other medical conditions
- For "healthier patients" they experience significant savings versus cost of warfarin or DOAC

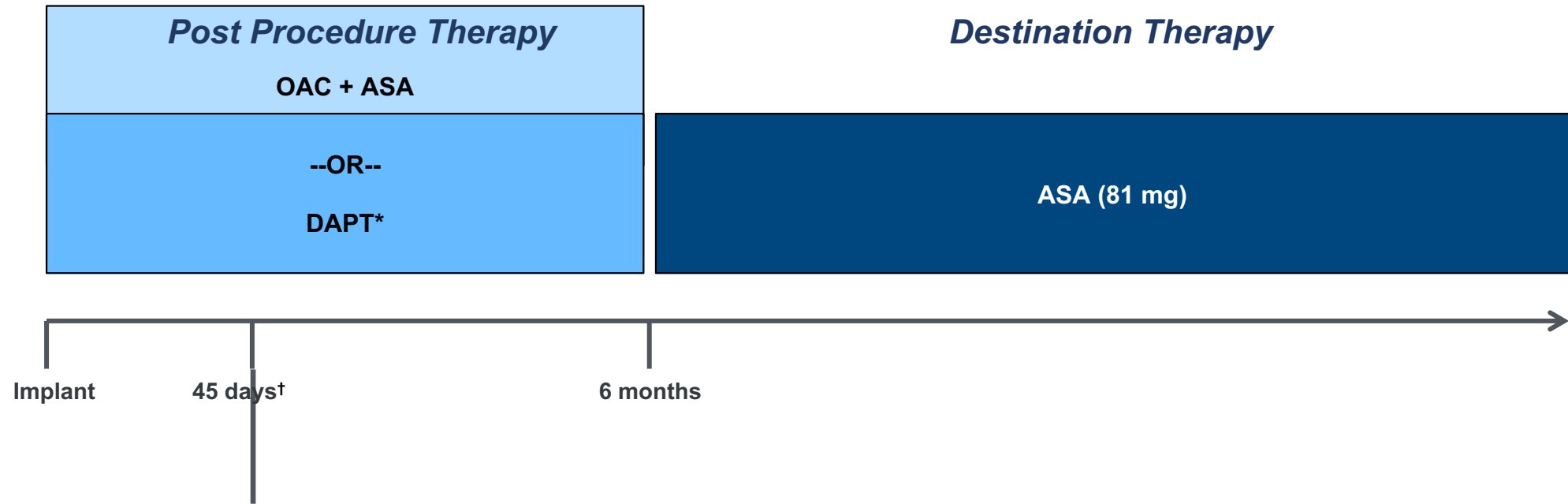
WATCHMAN had lower patient out of pocket costs than Warfarin by year 2.¹
Annual Cumulative Patient Out of Pocket Costs¹



WATCHMAN was 53% less expensive than warfarin by year 5.¹
Average Total Out of Pocket Costs at Year 5¹



Post-Implant Drug Regimen



>96%
Of Patients
Discontinued OACs
at 45 Days

April 2020: FDA-approved electronic Directions for Use (eDFU) update specifies patients can be placed on OAC (either NOAC or warfarin) for 45 days along with aspirin after a WATCHMAN device implant.

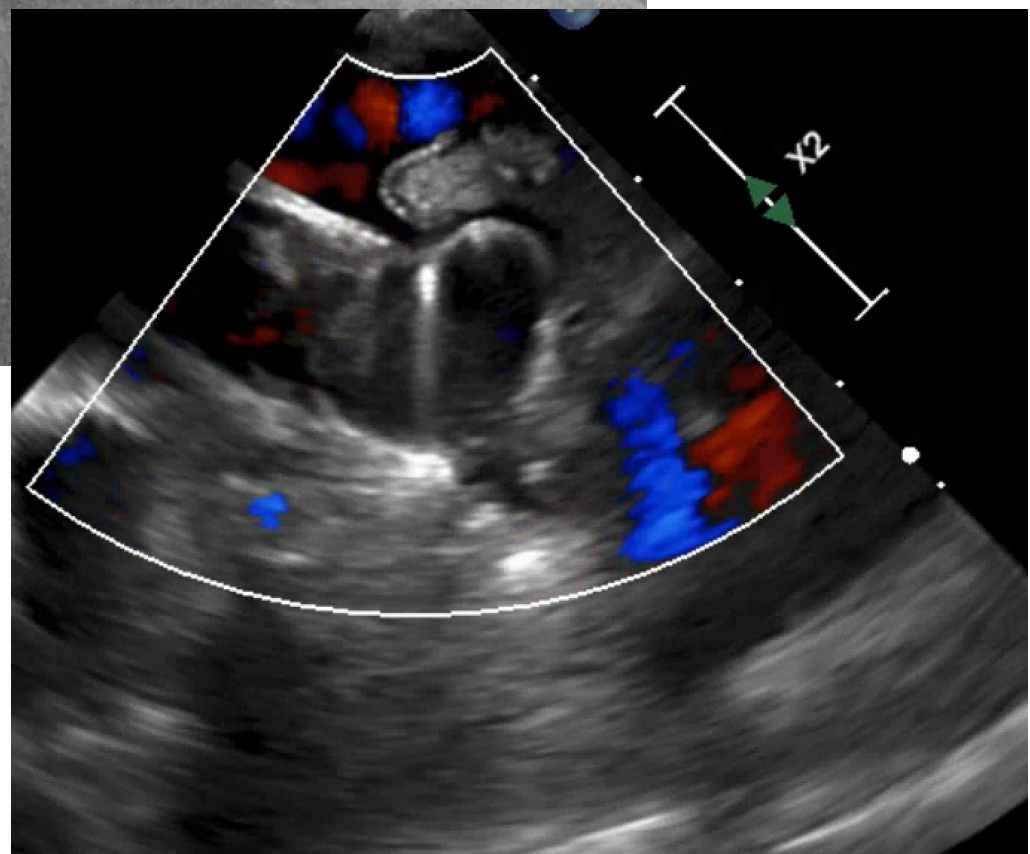
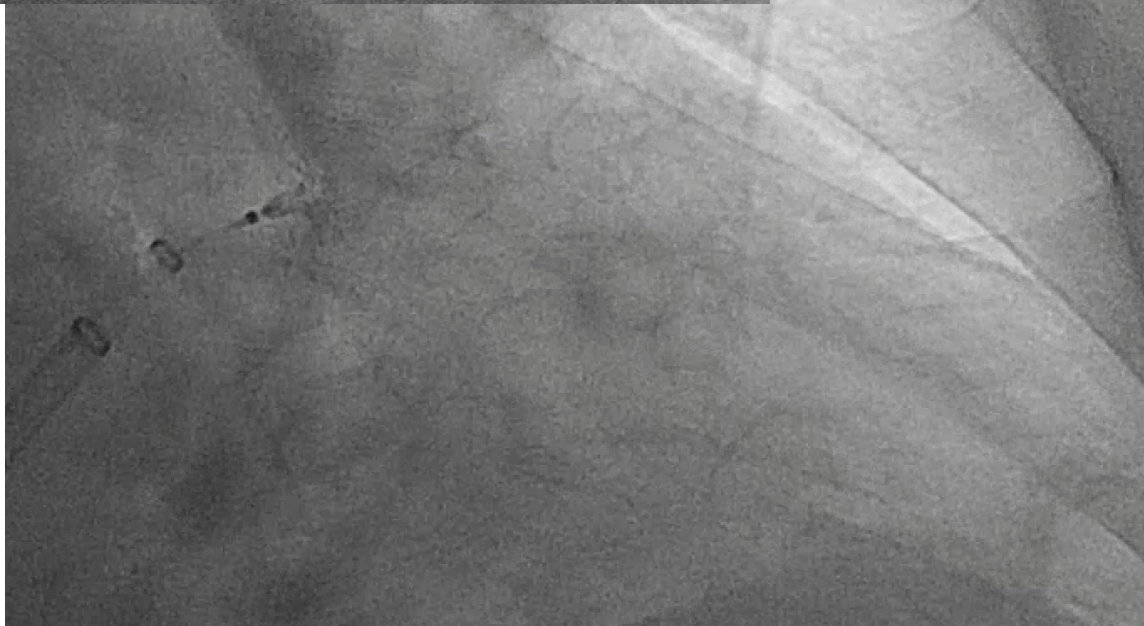
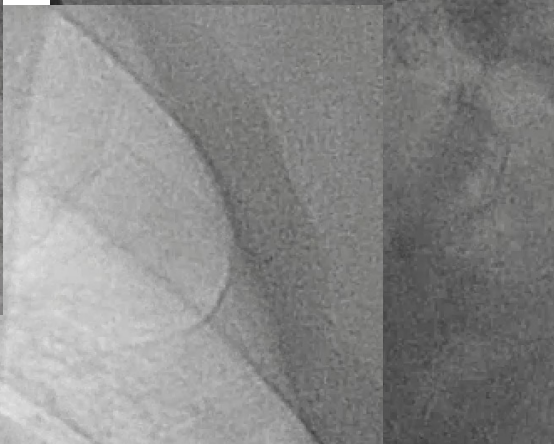
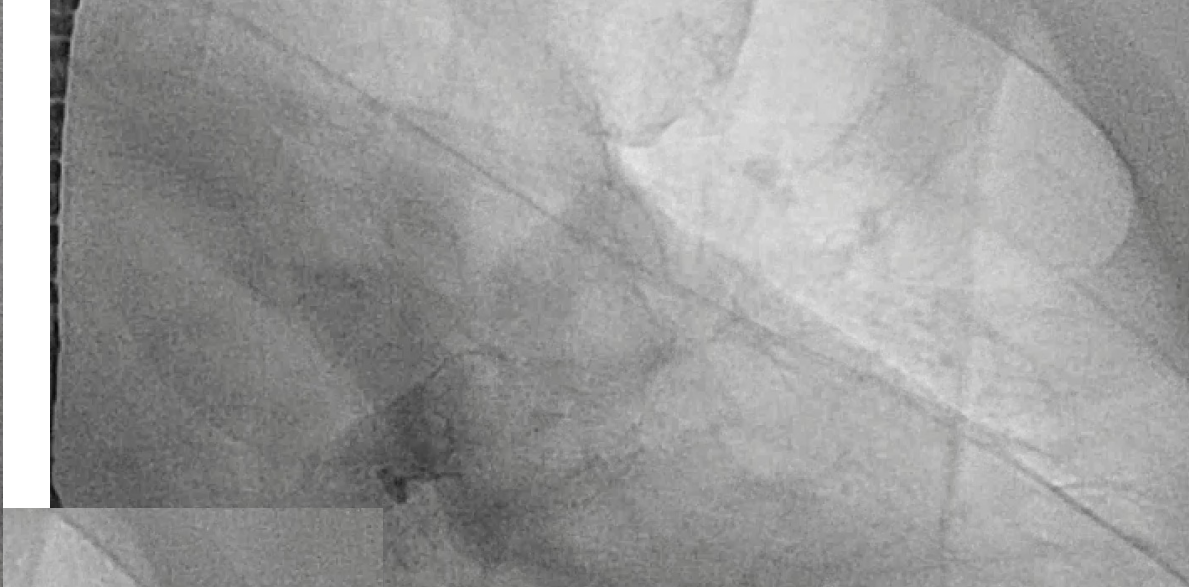
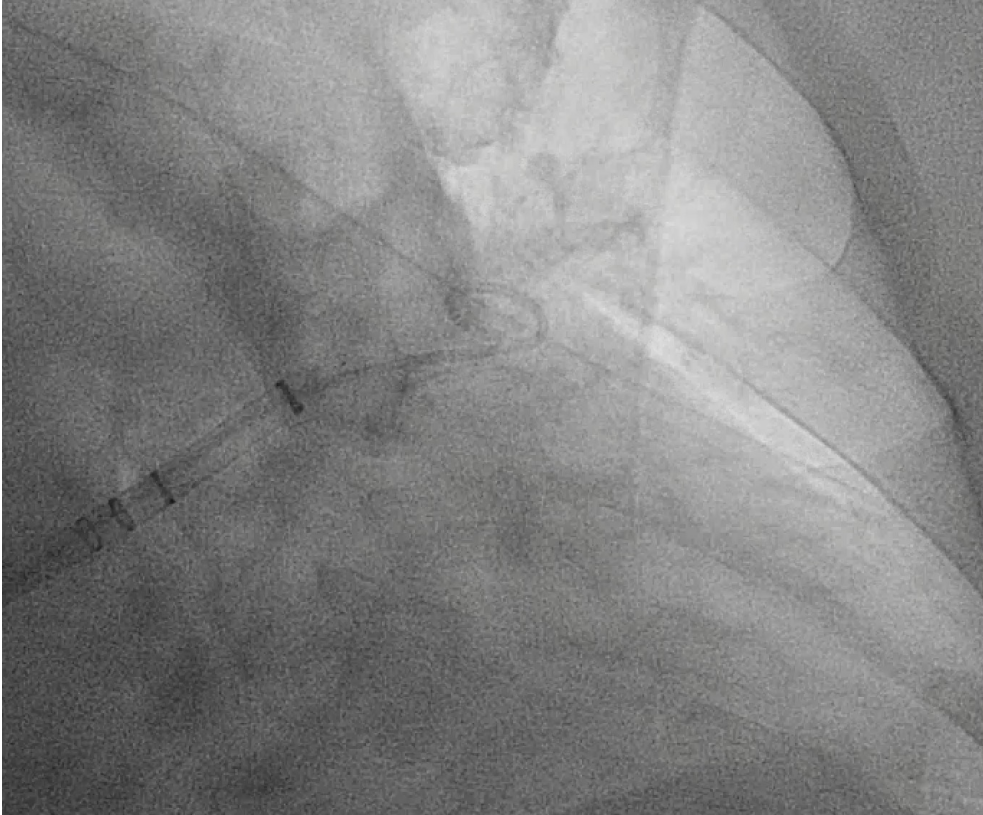
* Any P2Y12 inhibitor and ASA

† At TEE, if leak >5mm, patients remain on OAC + ASA until seal is documented (leak < 5mm), skipping the P2Y12 inhibitor + ASA pharmacotherapy

CASE STUDIES

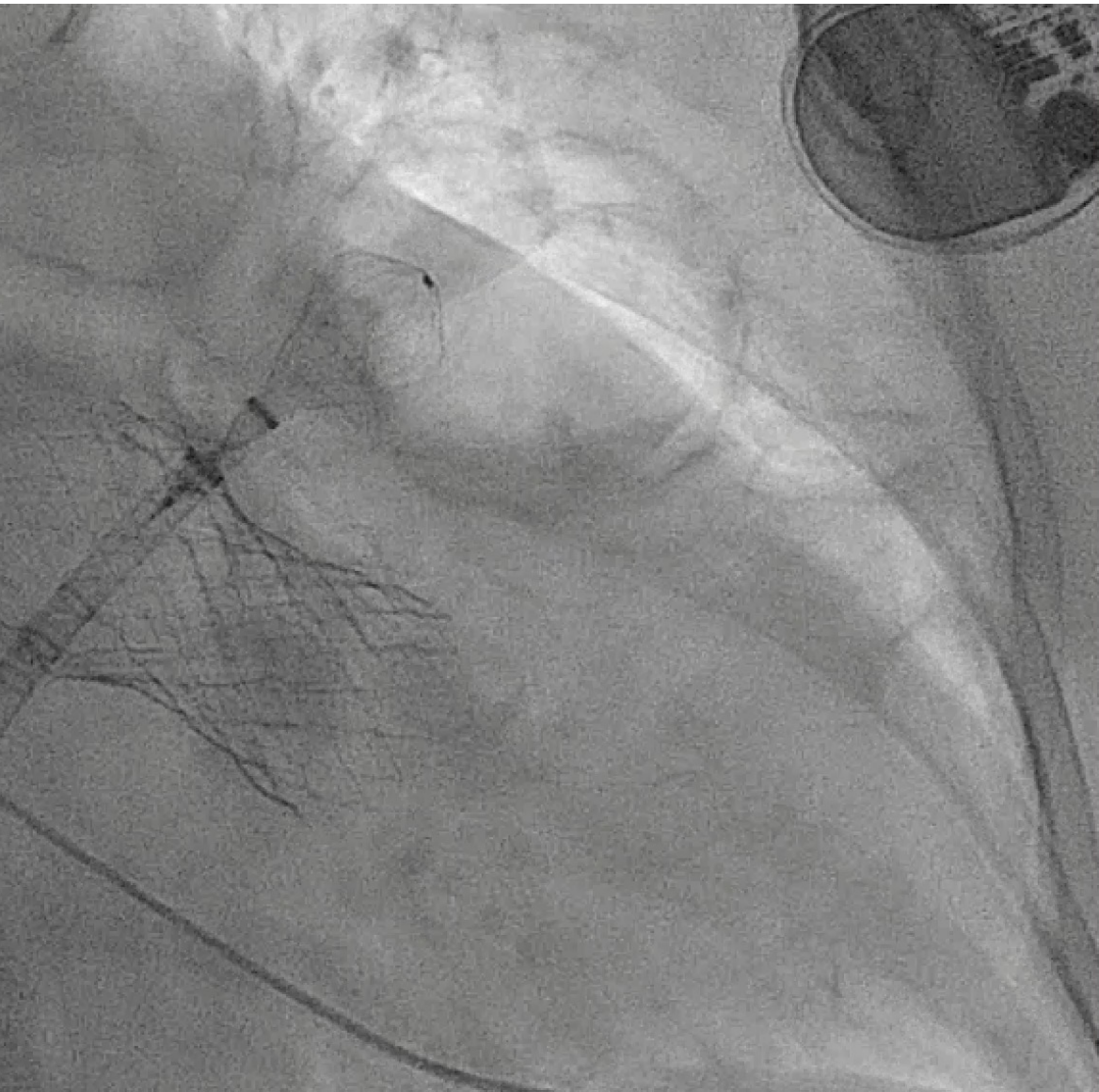
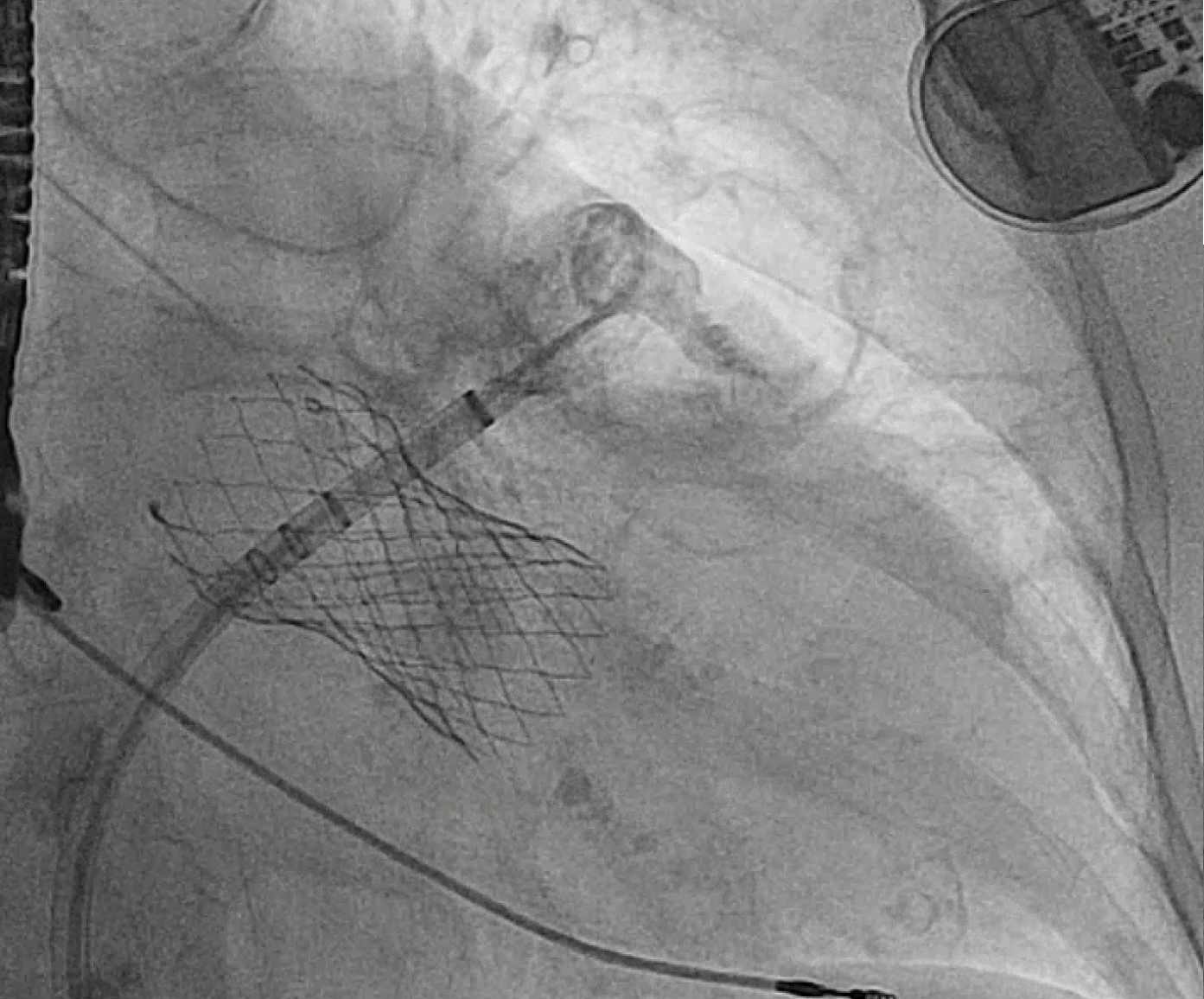
Case 1: 62 M with chronic Afib

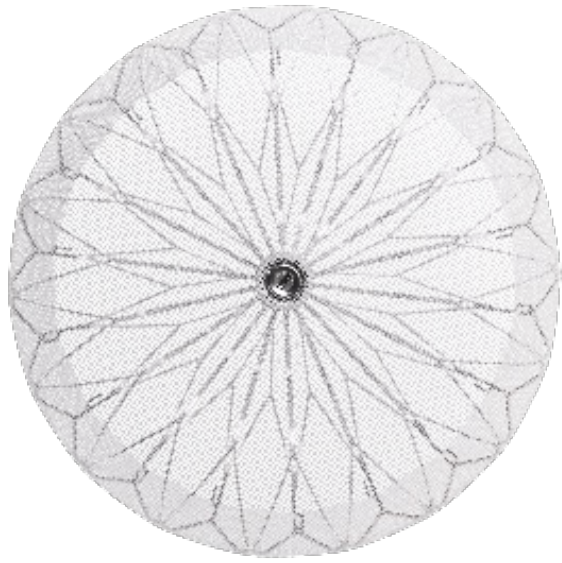
- Stroke in December 2019 and in a wheelchair
- Wants to get off of Xarelto due to large number of medications he is taking



Case 2: 93 yo F with paroxysmal Afib

- Wants to come off of Coumadin (she has taken it for 30 years)
- She gardens and when she nicks her skin she bleeds a long time
- Otherwise healthy





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KING'S
DAUGHTERS

