ATRIAL FIBRILLATION AND THE USE OF ORAL ANTICOAGULANTS IN CHINESE PATIENTS

18th Conference on Healthcare of the Chinese in North America

October 8, 2016

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Disclosures

- Biotronik
  - Consulting-Moderate
  - Honorarium-Modest
- Boston Scientific
  - Honorarium-Modest
- CardioNet
  - Consulting-Moderate
- Zoll Medical
  - Research Support- Significant
- Apama
  - Research Support- Modest
- Medtronic
  - Research Support- Significant

88 year old Chinese woman presents for routine device check

- PMH: SSS, s/p DDD pacemaker, HTN, CRI, Parkinson's Disease
- Meds: Metoprolol XL 25mg daily, lisinopril 10mg daily, ASA 81mg daily
- PE: Unsteady gait
- Echo: Normal LV fxn
- Pacer interrogation: 3 AF episodes – lasting 5, 15 and 90 minutes.

Question
Anticoagulation therapy:

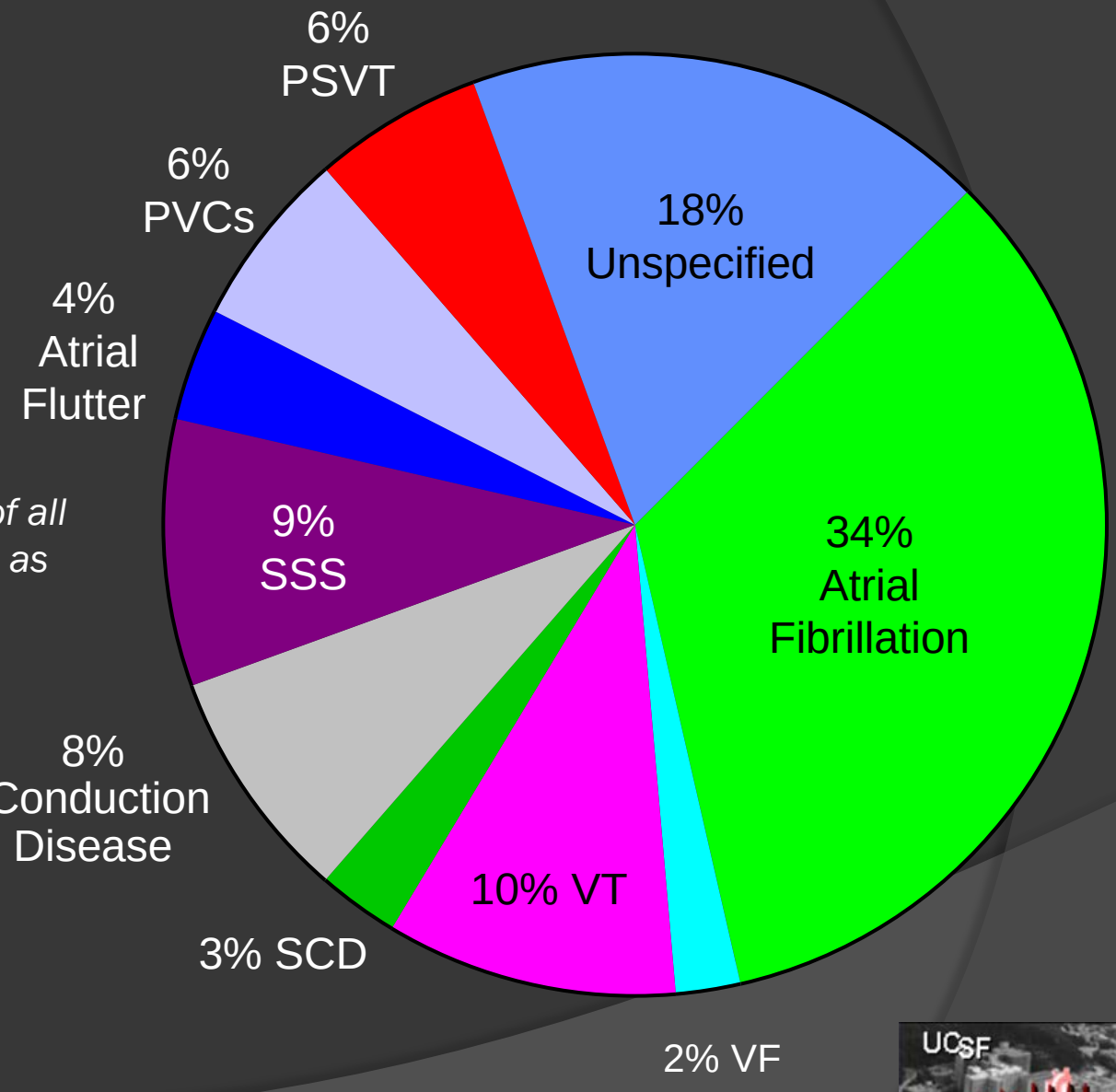
a) Do nothing
b) Increase to aspirin 325mg daily
c) Adjusted dose warfarin INR 2-3
d) Dabigatran 150mg bid
e) Rivaroxaban 20mg daily
f) Apixaban 2.5 mg twice daily

- Incidence and Disease Burden
- Indications for stroke prophylaxis
- Anticoagulant choice
- Novel devices to prevent stroke

Importance

- AF is the most common sustained arrhythmia in adults
- Affects
  - 4% of everyone over age 60
  - 10% of everyone over age 80
- Aging leads to atrial fibrosis which predisposes to AF

Hospitalization for Arrhythmias (USA)



Atrial fibrillation accounts for 1/3 of all patient discharges with arrhythmia as principal diagnosis.

Bialy D et al. JACC. 1992;19:41A

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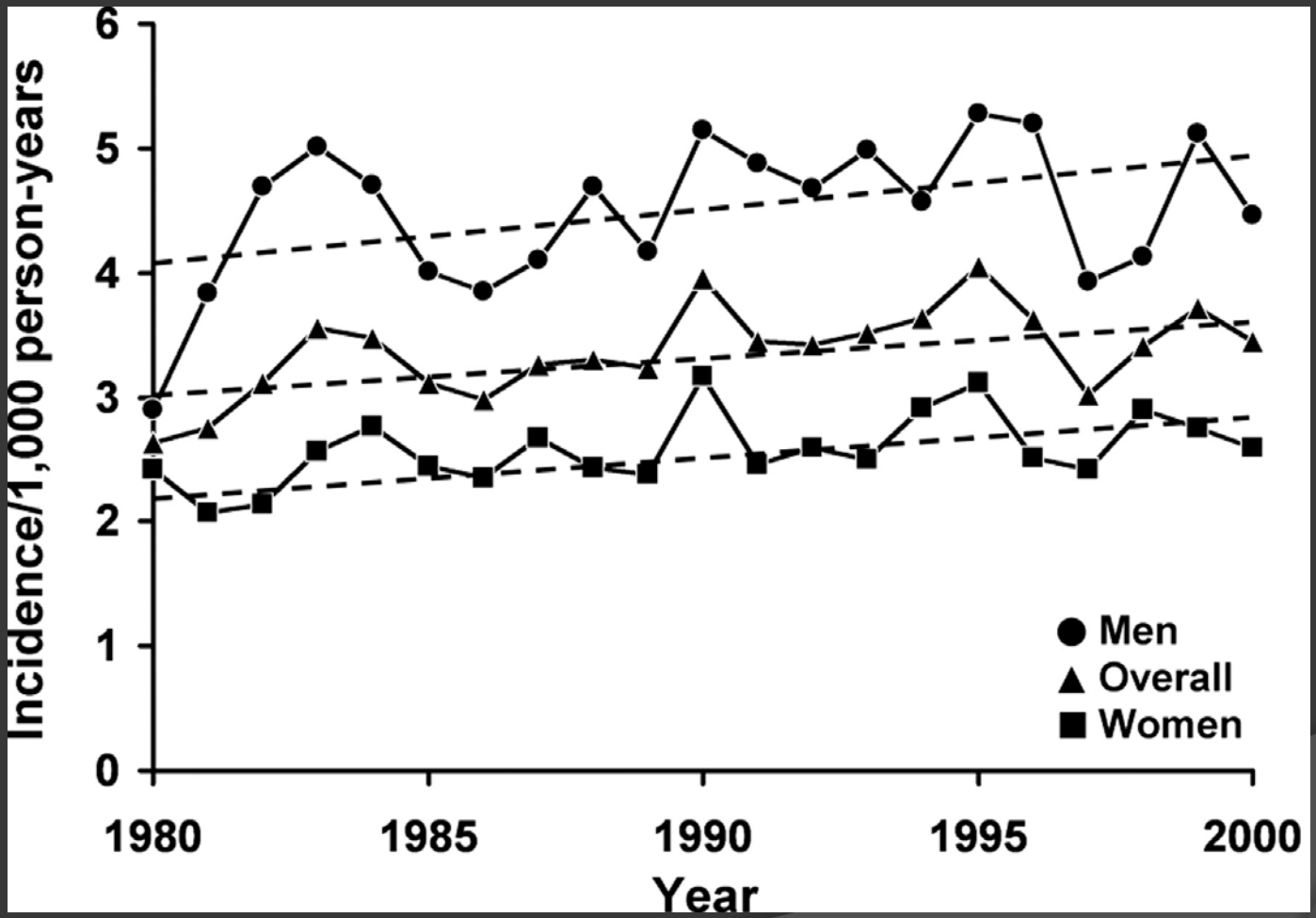
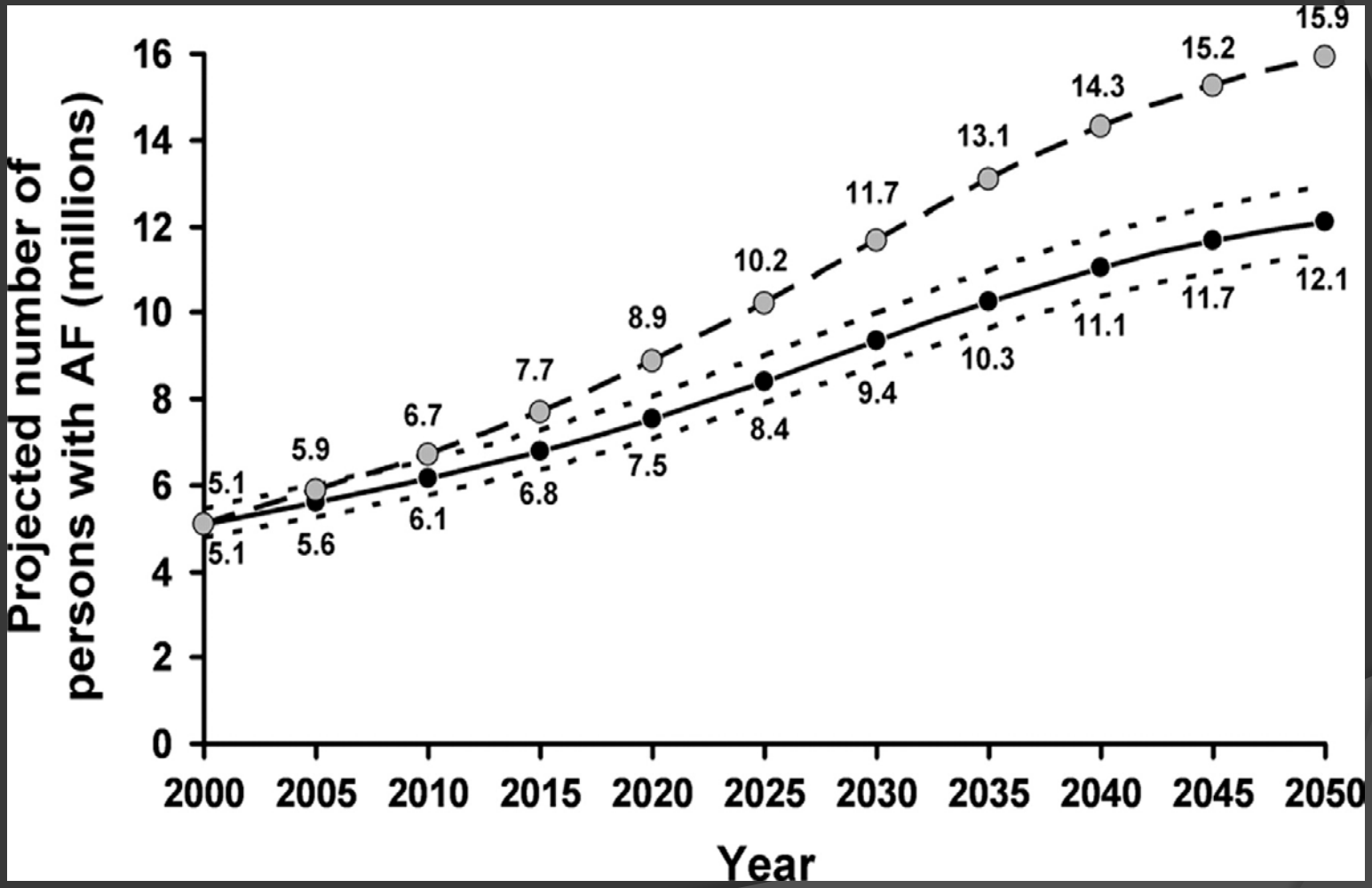
Overall and sex-specific trends in age-adjusted incidence of AF between 1980 and 2000 (age adjustment to the 1990 US population)



Miyasaka, Y. et al. Circulation 2006;114:119-125

Projected Prevalence of Atrial Fibrillation in United States between 2000 and 2050



Miyasaka, Y. et al. Circulation 2006;114:119-125

AF Symptoms[1]

- Feeling overtired or a lack of energy (most common)
- Pulse that is faster than normal or changing between fast and slow and feels irregular
- Shortness of breath
- Heart palpitations (feeling like your heart is racing, pounding, or fluttering)
- Trouble with everyday exercises or activities
- Pain, pressure, tightness, or discomfort in your chest
- Dizziness, lightheadedness, or fainting
- Increased urination (using the bathroom more often)

1. http://www.hrsonline.org/Patient-Resources/Heart-Diseases-Disorders/Atrial-Fibrillation-

AF and Dementia

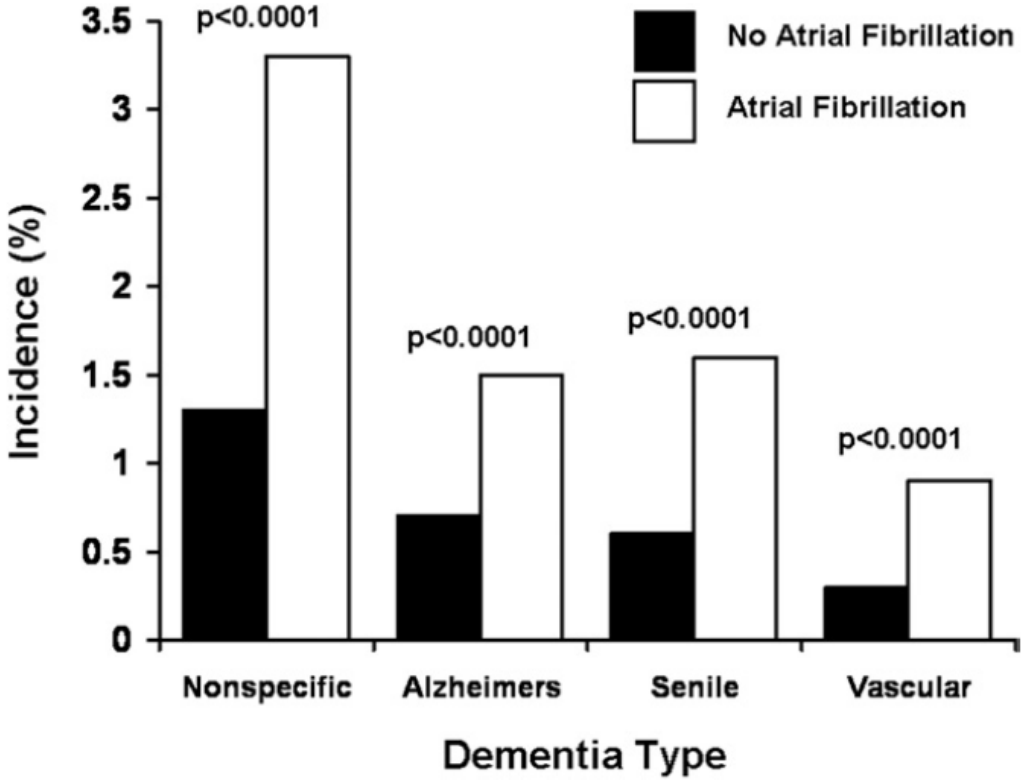


Figure 1 The incidence of dementia by the patient's AF status. There is a significant increase in dementia in general and in all subtypes in patients with AF.

Bunch TJ et al. Heart Rhythm 2010

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Atrial Fibrillation and Stroke

- AF is the most common cause of embolic stroke[1]
- 15% of all strokes in the US can be attributed to AF[1]

1. Nattel. Lancet 2006;367:262-272

- Incidence and Disease Burden
- Indications for stroke prophylaxis
- Anticoagulant choice
- Novel devices to prevent stroke

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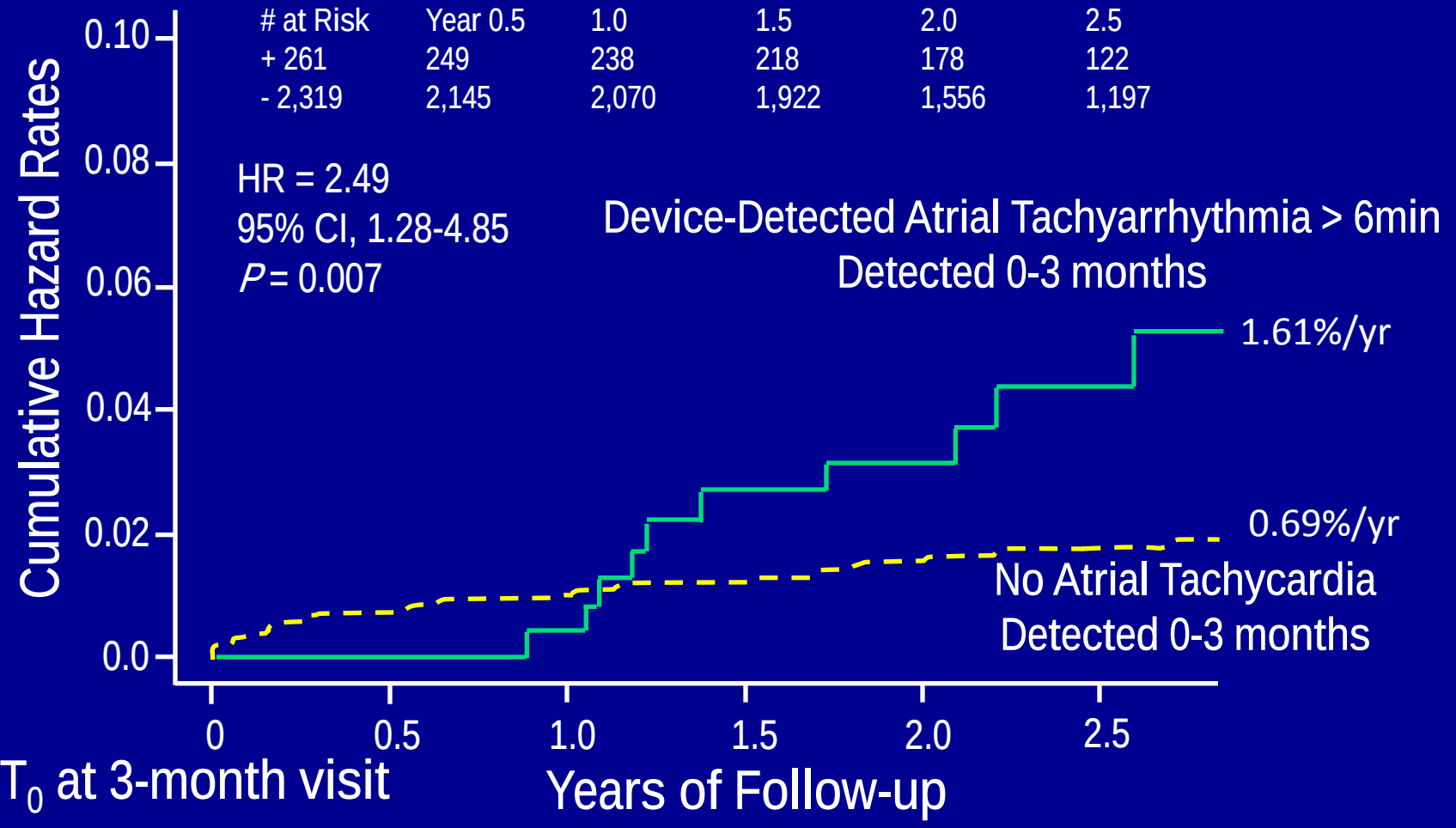
TRENDS Trial
AF Burden & Thromboembolic Events

	Annualized Rate (Stroke & TIA)	Annualized Rate (Stroke only)
Zero burden	1.1%	0.5%
Low burden < 5.5 hours	1.1%	1.1%
High burden **≥ 5.5 hours**	2.4%	1.8%

Glotzer TV, et al. Circ Arrhythm Electrophysiol. 2009;474-480.

ASSERT Trial
Stroke or Systemic Embolism



Healy JS, et al. *N Engl J Med*. 2012;366:120-129.

Device Detected Atrial Fibrillation and Stroke Risk:

Analysis of more than 10,000 patients from the SOS AF project

Giuseppe Boriani, MD, Ph.D, *Taya V. Glotzer, MD*, Massimo Santini, MD, Teena M. West, MSc, Mirko De Melis, Ph.D, Milan Sepsi, MD, Ph.D, Maurizio Gasparini, MD, Thorsten

Lewalter, MD, John A. Camm, MD, Daniel E. Singer, MD

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Patient Population

- TRENDS: 2,553 pts enrolled to assess the relationship between device detected AF and TE events
- PANORAMA: 3,556 pts (developing countries) enrolled to investigate the clinical outcome of CIEDs
- Clinical Service Project: 3,907 pts national cardiovascular data repository aimed at describing the use of CIEDs in 150 Italian cardiology centers

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Study Design/Methods

- Pts were characterized according to the highest daily burden achieved on any single day during follow-up
- *Dichotomized analysis*

  < 5 min vs ≥ 5 min
  < 1 hr vs ≥ 1 hr
  < 6 hr vs ≥ 6 hr
  < 12 hr vs ≥ 12 hr
  < 23 hr vs ≥ 23 hr

- Results were adjusted for $CHADS_2$ classification and use of OAC (at baseline)

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AF Burden and Risk of Stroke

AF Burden value	Hazard Ratio	95% Confidence Interval	P value
< 5 vs. ≥ 5 min	1.76	1.02-3.02	p=0.041
< 1 vs. ≥ 1 hr	2.11	1.22 to 3.64	p=0.008
< 6 vs. ≥ 6 hr	1.74	0.96 to 3.41	p=0.067
< 12 vs. ≥ 12 hr	1.72	0.92 to 3.22	p=0.090
< 23 vs. ≥ 23 hr	1.44	0.69 to 3.01	p=0.332

AF Burden and Risk of Stroke

- Device detected AF burden is associated with an increased risk of stroke in this population of 10,000 pts with CIEDs
- Dichotomized Analysis: 1 hour of AF burden had the highest hazard ratio doubling the risk of stroke
- Continuous Analysis: every additional hour of daily maximum of AF burden increases the relative risk for stroke by about 3%

DS_2 Score	
Failure	1
40/90mmHg)	1

S_2	Prior T

- Class IIa: If just one risk
  assessment of bleeding
  patient preference
  - → aspirin (81-325 mg) o
- Class I: If more than one
  - → warfarin or NOAC

Fuster *et al.*
ACC/AHA/ESC Practice Guidelines

JACC Vol. 48, No. 4, 2006
August 15, 2006:e149–246

Cardiac Electrophysiology

(b) Risk factor-based approach expressed as a point based scoring system, with the acronym CHA_2DS_2-VASc

(Note: maximum score is 9 since age may contribute 0, 1, or 2 points)

Risk factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75	2
Diabetes mellitus	1
Stroke/TIA/thrombo-embolism	2
Vascular disease[a]	1
Age 65–74	1
Sex category (i.e. female sex)	1
Maximum score	**9**

European Heart Journal (2010) **31**, 2369–2429
doi:10.1093/eurheartj/ehq278

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CHA_2DS_2-VASc Improves Risk Stratification of AF Patients With a $CHADS_2$ Score of 0–1

	1 Year Follow-up			
	Person-years	Events	Stroke Rate	(95% CI)
$CHADS_2$ score=0	17,327	275	1.59	(1.41-1.79)
CHA_2DS_2-VASc=0	6919	58	0.84	(0.65-1.08)
CHA_2DS_2-VASc=1	6811	119	1.75	(1.46-2.09)
CHA_2DS_2-VASc=2	3347	90	2.69	(2.19-3.31)
CHA_2DS_2-VASc=3	250	8	3.20	(1.60-6.40)
$CHADS_2$ score=1	22,945	1130	4.92	(4.65-5.22)
CHA_2DS_2-VASc=1	2069	40	1.93	(1.42-2.64)
CHA_2DS_2-VASc=2	8516	345	4.05	(3.65-4.50)
CHA_2DS_2-VASc=3	11,223	652	5.81	(5.38-6.27)
CHA_2DS_2-VASc=4	1137	93	8.18	(6.68-10.02)

Olesen JB.Tromb Haemost 2012;107:1172-1179

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CHA_2DS_2-VASc score

CHA_2DS_2-VASc score	Patients (n = 73538)	Stroke and thromboembolism event rate at 1 year follow-up (%)
0	6369	0.78
1	8203	2.01
2	12771	3.71
3	17371	5.92
4	13887	9.27
5	8942	15.26
6	4244	19.74
7	1420	21.50
8	285	22.38
9	46	23.64

Score	Risk	Anticoagulation Therapy	Considerations
0	Low	No antithrombotic therapy (or Aspirin)	No antithrombotic therapy (or Aspirin 75-325mg daily)
1	Moderate	Oral anticoagulant (or Aspirin)	Oral anticoagulant, either new oral anticoagulant drug eg dabigatran or well controlled warfarin at INR 2.0-3.0 (or Aspirin 75-325mg daily, depending on factors such as patient preference)
2 or greater	High	Oral anticoagulant	Oral anticoagulant, using either a new oral anticoagulant drug (eg dabigatran) or well controlled warfarin at INR 2.0-3.0

Adapted from ***Olesen JB. BMJ 2011;342:d124***

Since 2010, further validation of the CHA2DS2-VASc score

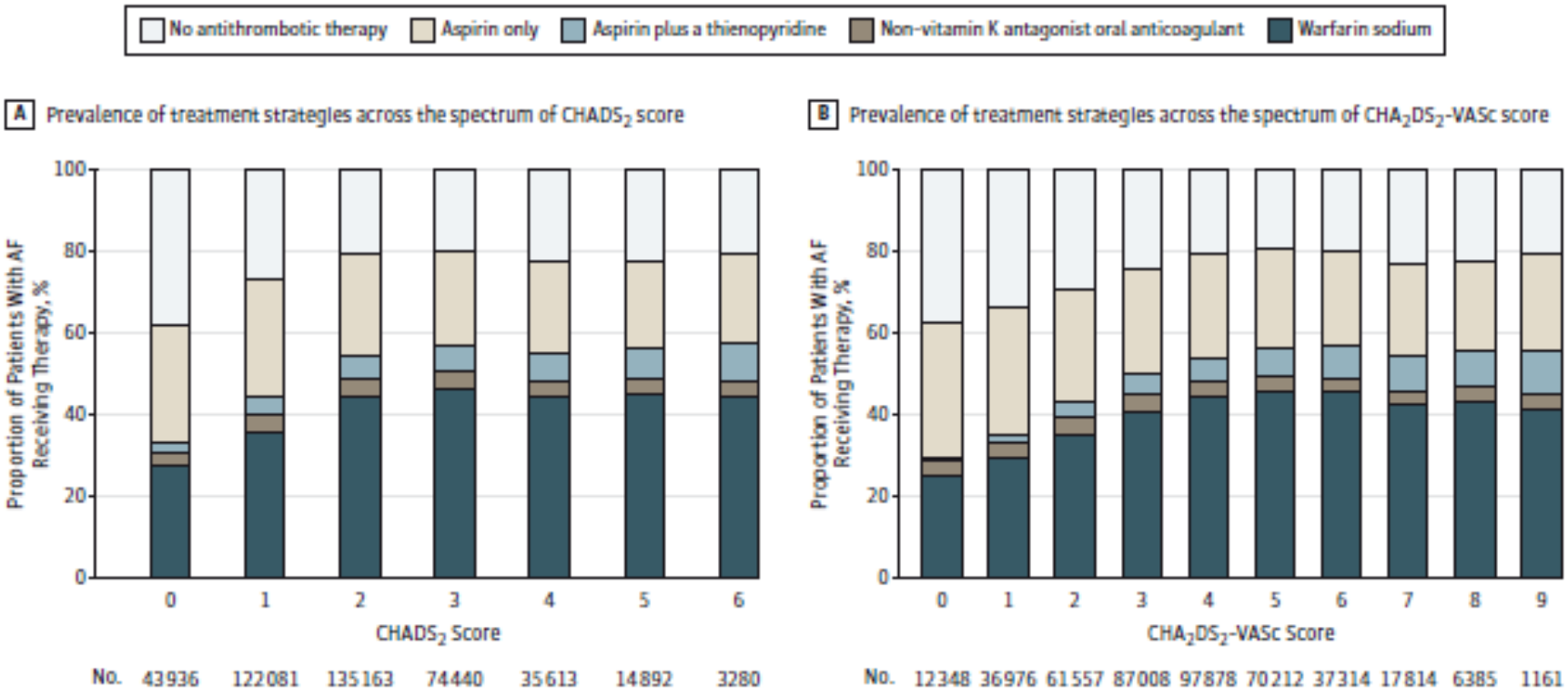
Lip GY. *J Thromb Haemost* 2011;**9** Suppl 1:344–351.
Potpara TS, et al. *Circ Arrhythm Electrophysiol* 2012;**5**:319–326.
Olesen JB, et al. *Thromb Haemost* 2012;**107**:1172–1179
Van Staa TP, et al. *J Thromb Haemost* 2011;**9**:39–48.
Abu-Assi E, et al. *Int J Cardiol.* 2011
January CT, et al. 2014 AHA/ACC/HRS Guideline for the Management of Patients with Atrial Fibrillation. 2014

Recommendations for prevention of thromboembolism in non-valvular AF - general		
Recommendations	**Class**	**Level**
The CHA_2DS_2-VASc score is recommended as a means of assessing stroke risk in non-valvular AF.	I	A

Eur Heart J 2012;33:2719-2747

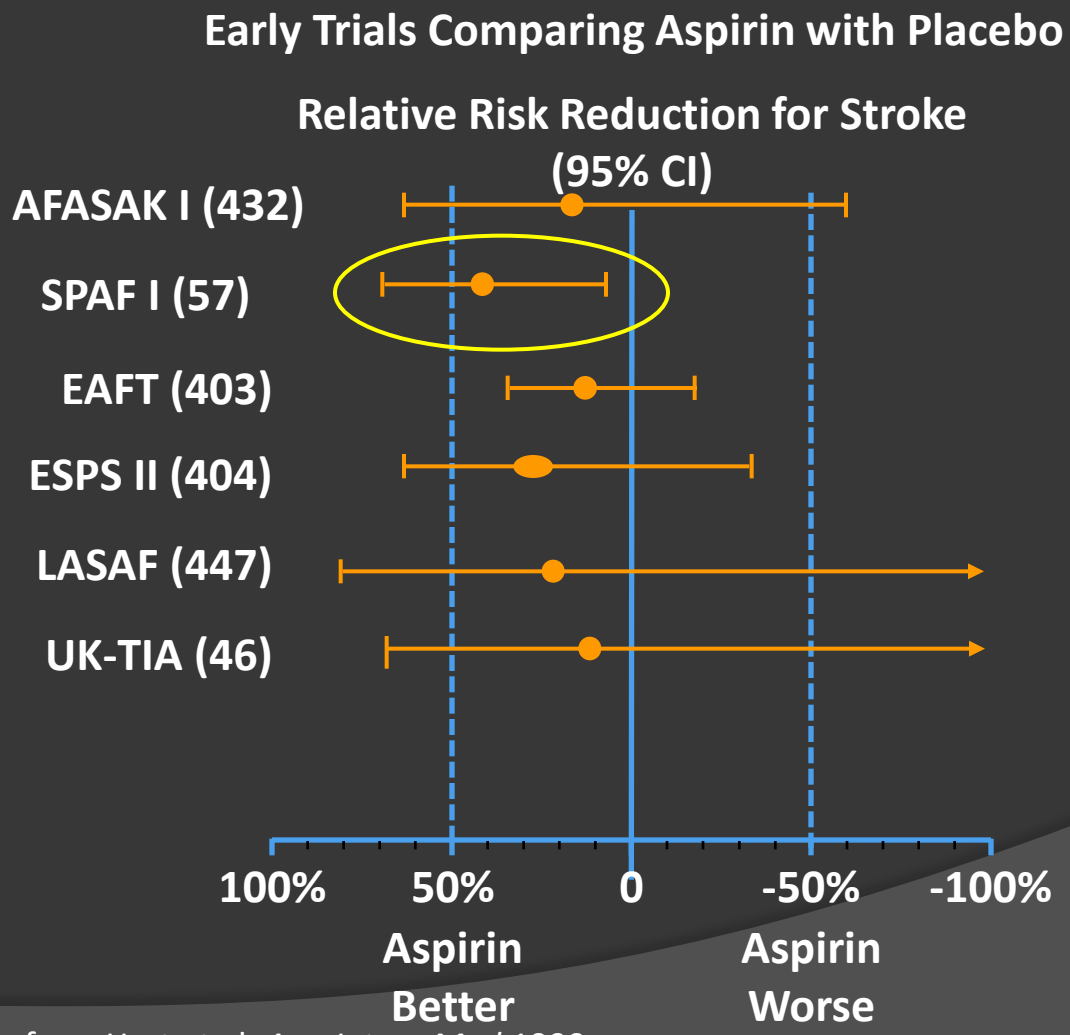
Courtesy Prof. R. de Caterina

Figure 2. Prevalence of Antithrombotic Therapies in Patients With Atrial Fibrillation (AF) Across the Spectrum of Stroke Risk by the $CHADS_2$ Score and the CHA_2DS_2-VASc Score



Hsu et al. JAMA Cardiology 20016

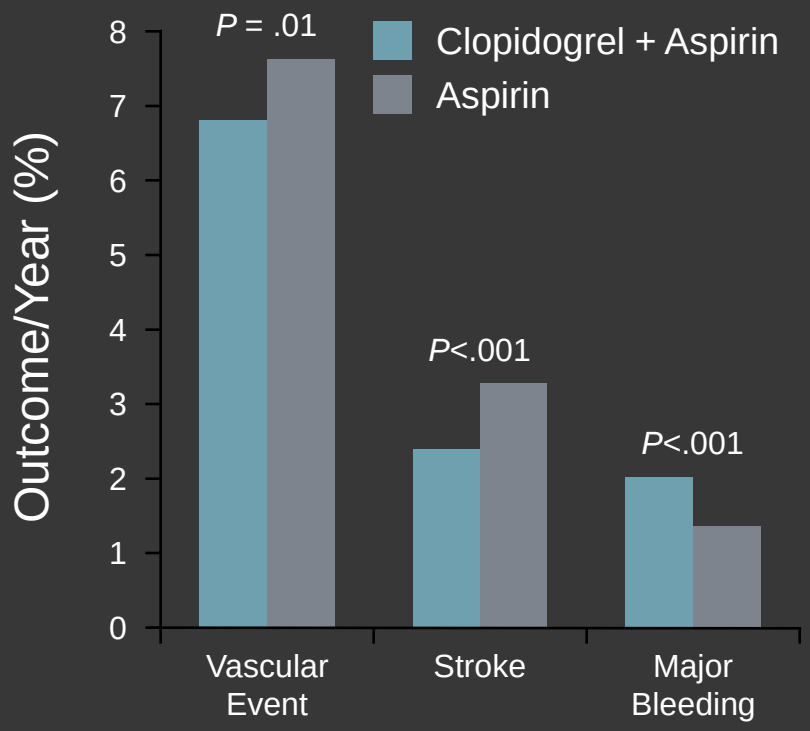
Aspirin Is Not an Effective Anticoagulation Therapy in AF



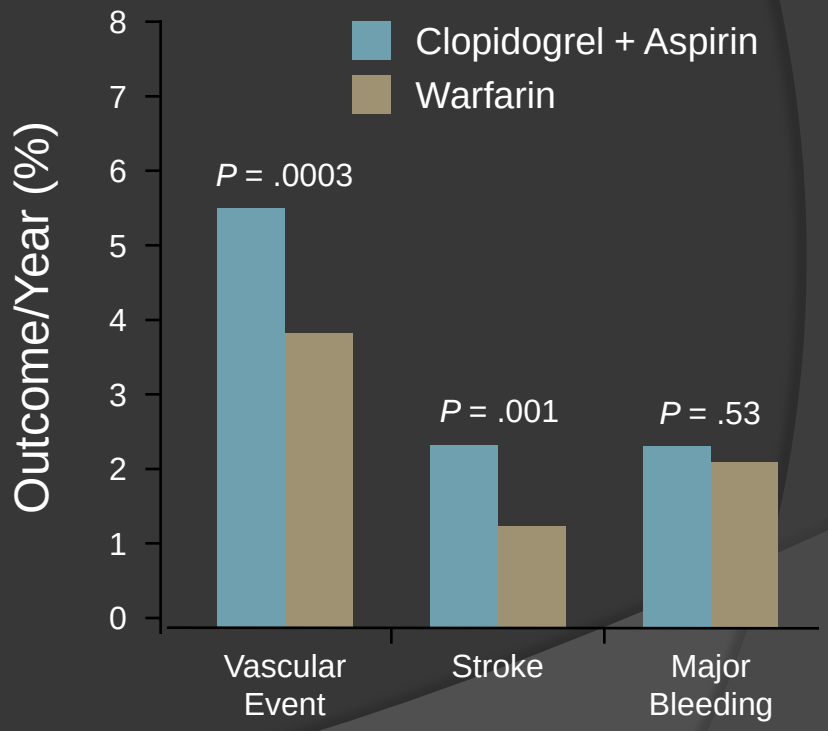
Adapted with permission from Hart et al. *Ann Intern Med.*1999.

Antiplatelet Therapy in AF

ACTIVE-A:
7554 randomized patients;
median follow-up of 3.6 years



ACTIVE-W:
6706 randomized patients;
trial stopped

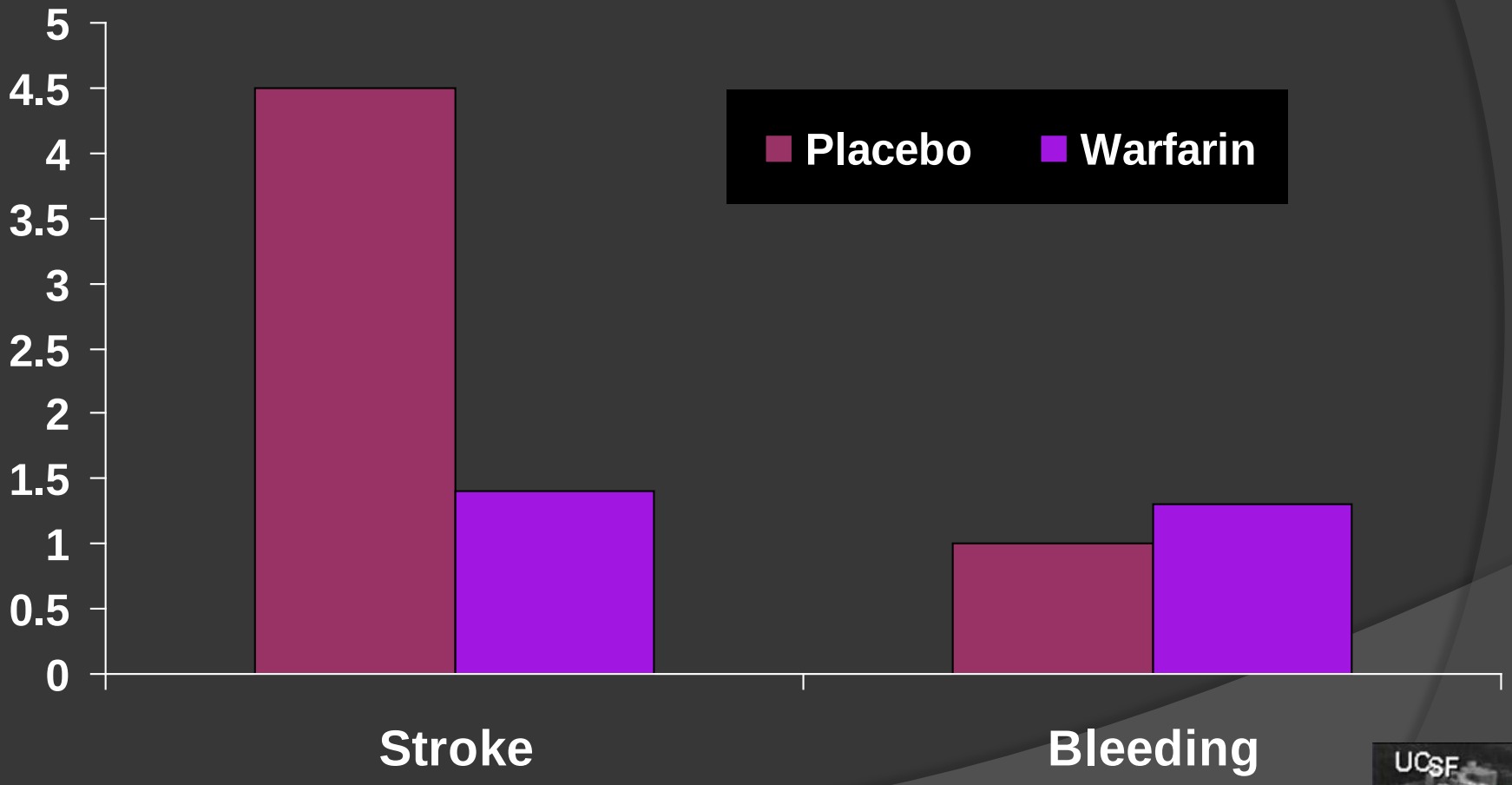


ACTIVE = Atrial Fibrillation Clopidogrel Trial with Irbesartan for Prevention of Vascular Events. Writing Group of the ACTIVE Investigators, et al. *Lancet.* 2006;367(9526):1903-1912. ACTIVE Investigators, et al. *N Engl J Med.* 2009;360(20):2066-2078.

Bottom Line: ASA for Stroke Prevention

- Aspirin can be considered for low risk AF patients
- Little role for aspirin in moderate to high risk AF patients

Risk of Stroke and Bleeding with Warfarin in Atrial Fibrillation



Atrial Fibrillation Investigators. Arch Intern Med. 1994;154:1449-1457.

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Annals of Internal Medicine
Established in 1927 by the American College of Physicians

From: Warfarin Use among Ambulatory Patients with Nonvalvular Atrial Fibrillation: The AnTicoagulation and Risk Factors in Atrial Fibrillation (ATRIA) Study

Ann Intern Med. 1999;131(12):927-934. doi:10.7326/0003-4819-131-12-199912210-00004

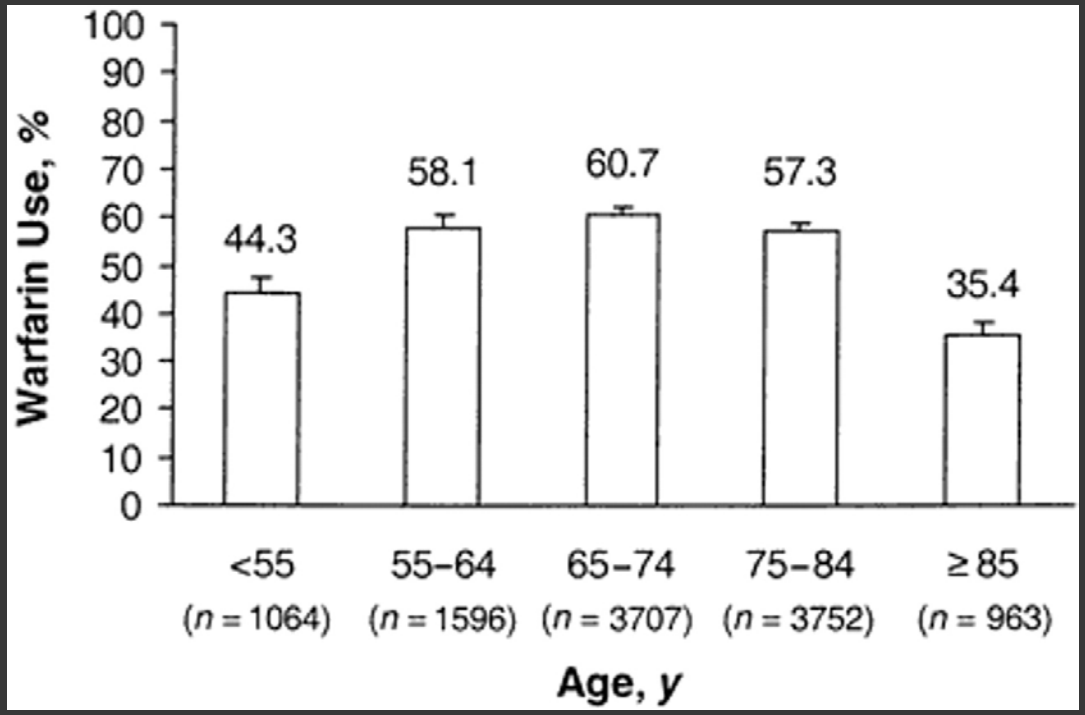

Figure Legend:

Prevalent warfarin use by age among 11 082 ambulatory patients with nonvalvular atrial fibrillation and no identified contraindications to warfarin therapy.Numbers in parentheses represent the number of patients in the denominator of each category. Error bars represent upper 95% confidence limits.

Date of download: 4/14/2015

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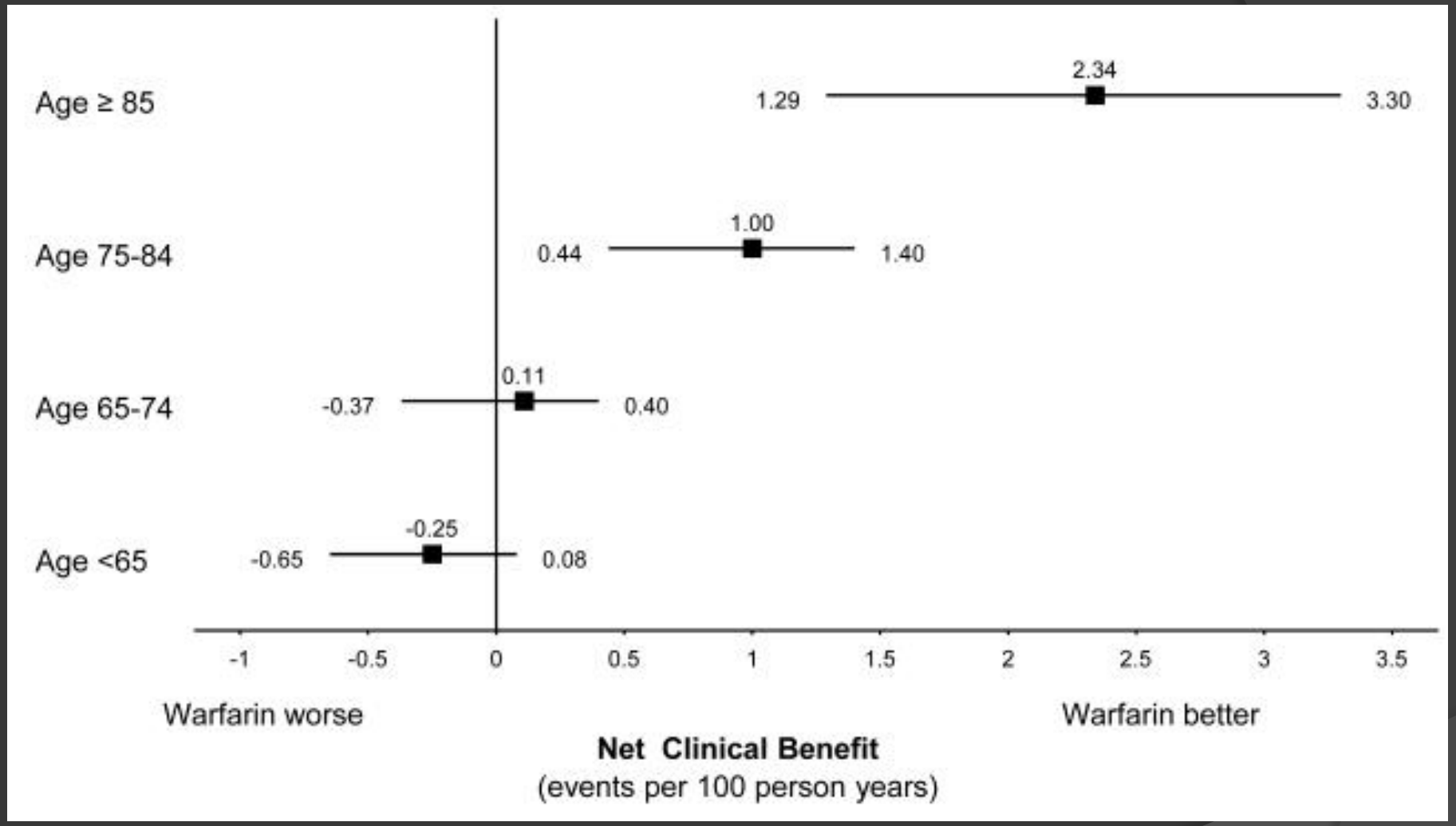

ATRIA Study Data ***Singer et al. Annals of Internal Medicine 2009***

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Choosing Antithrombotic Therapy for Elderly Patients With Atrial Fibrillation Who Are at Risk for Falls

Malcolm Man-Son-Hing, MD, MSc, FRCPC; Graham Nichol, MD, MPH, FRCPC; Anita Lau; Andreas Laupacis, MD, MSc, FRCPC

Objective: To determine whether the risk of falling (with a possible increased chance of subdural hematoma) should influence the choice of antithrombotic therapy in elderly patients with atrial fibrillation.

Design: A Markov decision analytic model was used to determine the preferred treatment strategy (no antithrombotic therapy, long-term aspirin use, or long-term warfarin use) for patients with atrial fibrillation who are 65 years of age and older, are at risk for falling, and have no other contraindications to antithrombotic therapy. Input data were obtained by systematic review of MEDLINE. Outcomes were expressed as quality-adjusted life-years.

Results: For patients with average risks of stroke and falling, warfarin therapy was associated with 12.90 quality-adjusted life-years per patient; aspirin therapy, 11.17 quality-adjusted life-years; and no antithrombotic therapy, 10.15 quality-adjusted life-years. Sensitivity analysis demonstrated that, regardless of the patients' age or baseline risk of stroke, the risk of falling was not an important factor in determining their optimal antithrombotic therapy.

Conclusions: For elderly patients with atrial fibrillation, the choice of optimal therapy to prevent stroke depends on many clinical factors, especially their baseline risk of stroke. However, patients' propensity to fall is not an important factor in this decision.

Arch Intern Med. 1999;159:677-685

- Estimated that a patient had to fall 295x per year for the risk of intracranial hemorrhage to outweigh the benefit of warfarin!

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The HAS-BLED bleeding risk score

Letter	Clinical characteristic*	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age > 65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

*Hypertension is defined as systolic blood pressure > 160 mmHg.

INR = international normalized ratio.

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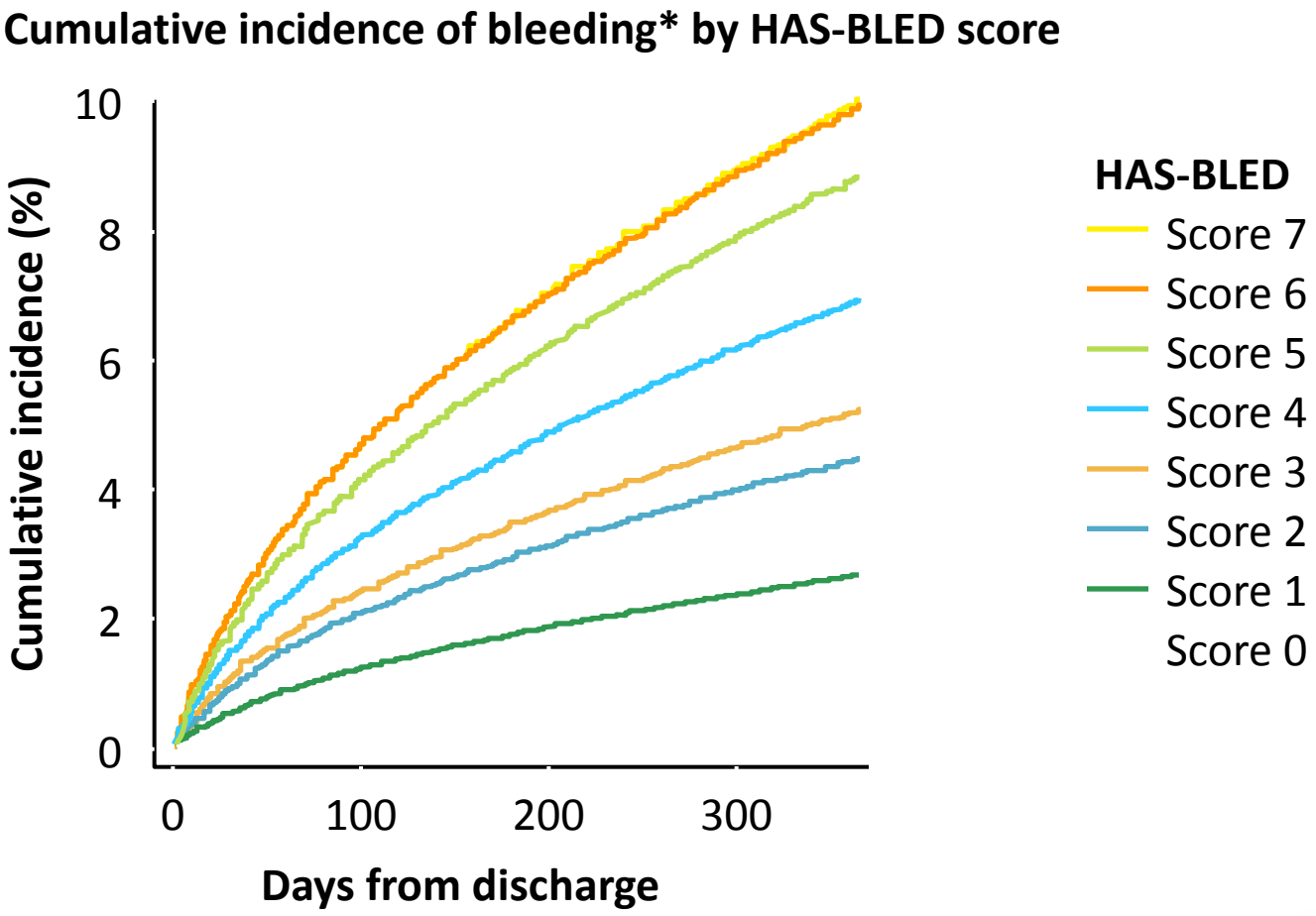
Higher bleeding rates seen with high HAS-BLED score (p-value for trend <0.001)



*Non-OAC cohort

Olesen JB. J Thromb Haemost 2011;9:1460-1467

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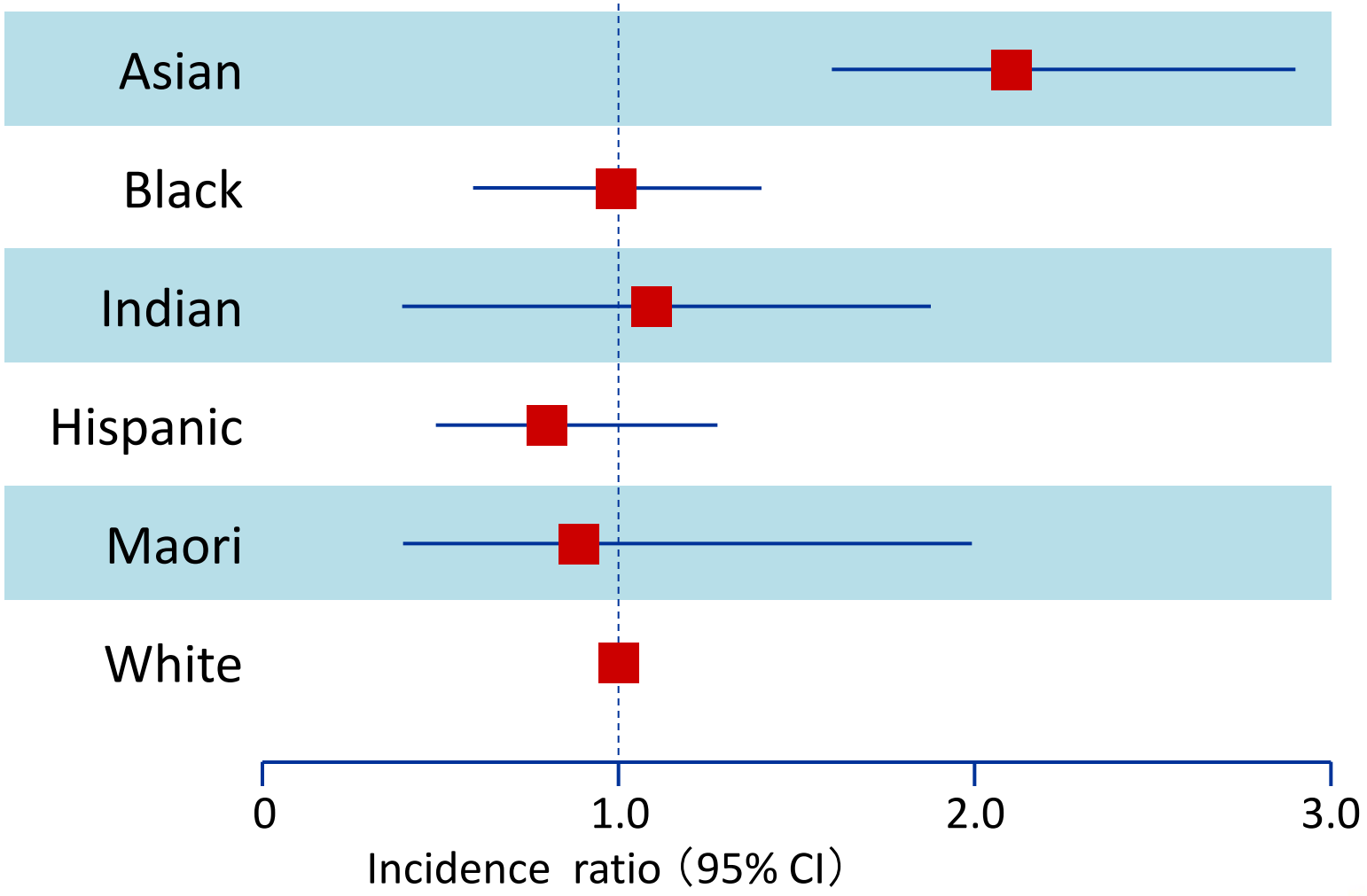
Incidence Ratios of Cerebral Hemorrhage in Different Ethnic Groups (Meta-analysis)



van Asch CJ, et al. *Lancet Neurol.* 2010;9(2):167-176.

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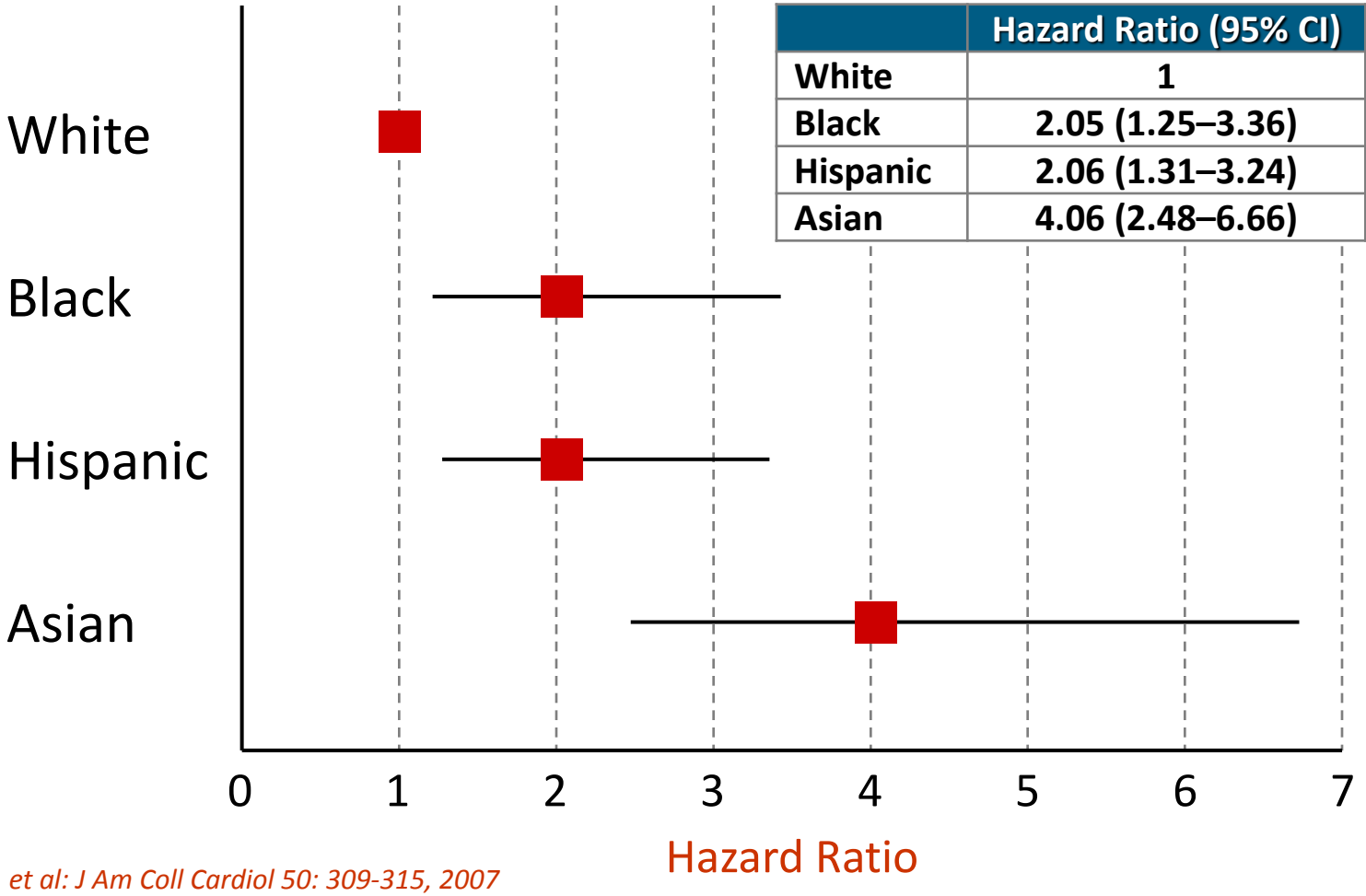
Adjusted Hazard Ratio for Intracranial Hemorrhage on Warfarin Treatment



	Hazard Ratio (95% CI)	p Value
White	1	-
Black	2.05 (1.25–3.36)	0.005
Hispanic	2.06 (1.31–3.24)	0.002
Asian	4.06 (2.48–6.66)	<0.0001

Shen AY, et al: J Am Coll Cardiol 50: 309-315, 2007

Multiethnic cohort of 18,867 patients hospitalized with first-time AF (January 1995 – December 2000)

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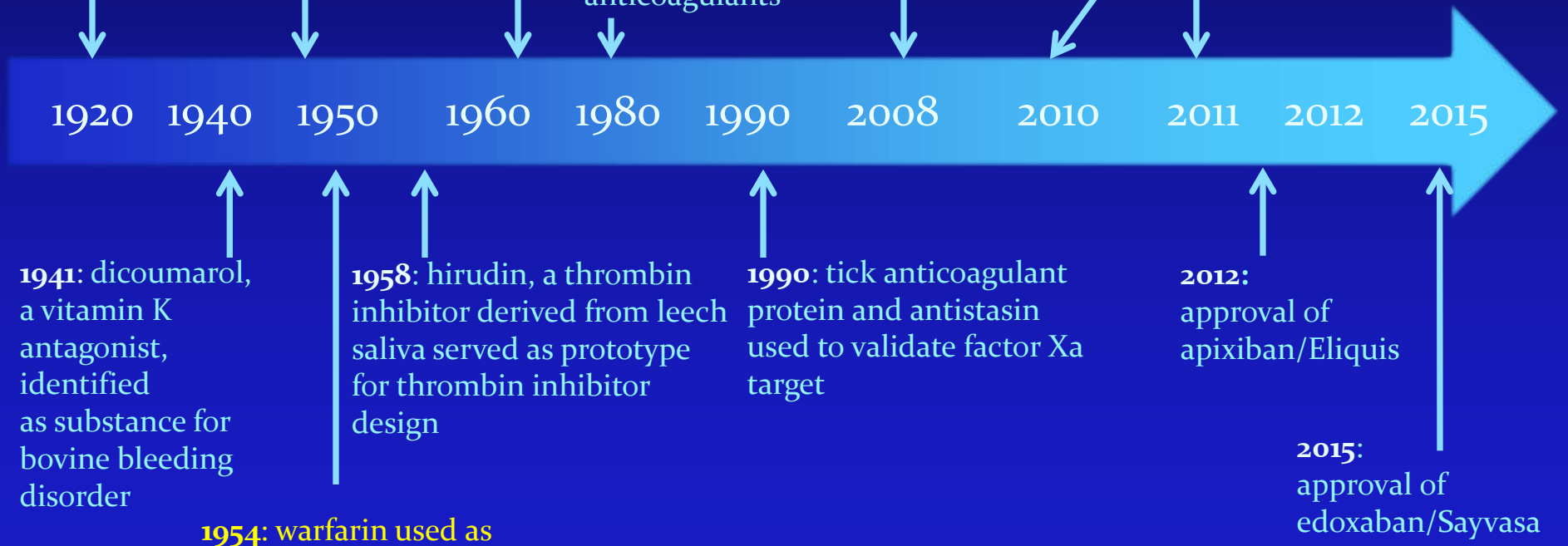
- Incidence and Disease Burden
- Indications for stroke prophylaxis
- Anticoagulant choice
- Novel devices to prevent stroke

Historical perspective of anticoagulation



1920: cattle eating spoiled sweet clover noted to have a bleeding disorder

1941: dicoumarol, a vitamin K antagonist, identified as substance for bovine bleeding disorder

1948: warfarin, a dicoumarol derivative, marketed as rodenticide

1954: warfarin used as anticoagulant in humans

1958: hirudin, a thrombin inhibitor derived from leech saliva served as prototype for thrombin inhibitor design

1960: first clinical trials of anticoagulants

1980: factor Xa identified as new target for anticoagulants

1990: tick anticoagulant protein and antistasin used to validate factor Xa target

2008: dabigatran and rivaroxiban approved as alternatives to LMWH for VTE prevention

2010: dabigatran approved as alternative to warfarin for SPAF

2011: approval of rivaroxiban/Xarelto

2012: approval of apixiban/Eliquis

2015: approval of edoxaban/Sayvasa

Courtesy of Gordon Leung MD

Table 2: Properties of Warfarin and the NOACs

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Molecular target	Vitamin K dependent clotting factors	Thrombin	Factor Xa	Factor Xa	Factor Xa
Dosing in AF	Once daily	Twice daily	Once daily	Twice daily	Once daily
Time to peak plasma concentration (mins)	240.00	85-150	30 -180	30-120	30-60
Time to peak effect (h)	96-120	2	2-3	1-2	1-2
Half life (h)	40.00	14-17	5-9 (increased to 11-13 in elderly)	8-15	9-11
Renal clearance	<1%	≈80%	≈30%	≈27%	0.35
Food and drug interactions	Foods rich in vitamin K, Substrates of CYP2C9, CYP3A4 and CYP1A2	Strong P-gp inhibitors and inducers	Strong CYP3A4 inducers, strong inhibitors of both CYP3A4 and P-gp	Strong inhibitors and inducers of CYP3A4 and P-gp	Strong P-gp inhibitors
Creatine clearance below which drug is contraindicated	n/a	<30mL/min	<15mL/min	<15mL/min	<30mL/min (Japan)

Lip et al. Journal of Internal Medicine 2015

Characteristics of New Oral Anticoagulants

Drug	Dabigatran	Rivaroxaban	Apixaban
Mechanism of action	Thrombin inhibitor	Factor Xa inhibitor	Factor Xa inhibitor
$T_{1/2}$	14-17 hours	5-11 hours	12 hours
Regimen	BID	QD, BID	BID
Peak to trough	2	12 (QD)	3-5
Renal excretion of absorbed drug	~80%	36%-45%	25%-30%
Potential for drug interactions	P-glycoprotein inhibitor	CYP3A4 substrate and P-glycopr inhibitor	CYP3A4 substrate and P-glycopr inhibitor

CYP3A4 = cytochrome P450 3A4.

Usman MH ….. Ezekowitz : *Curr Treat Cardiovasc Med.* 2008;10(5):388-397. Piccini JP, et al. *Curr Opin Cardiol*. 2010;25(4):312-320.

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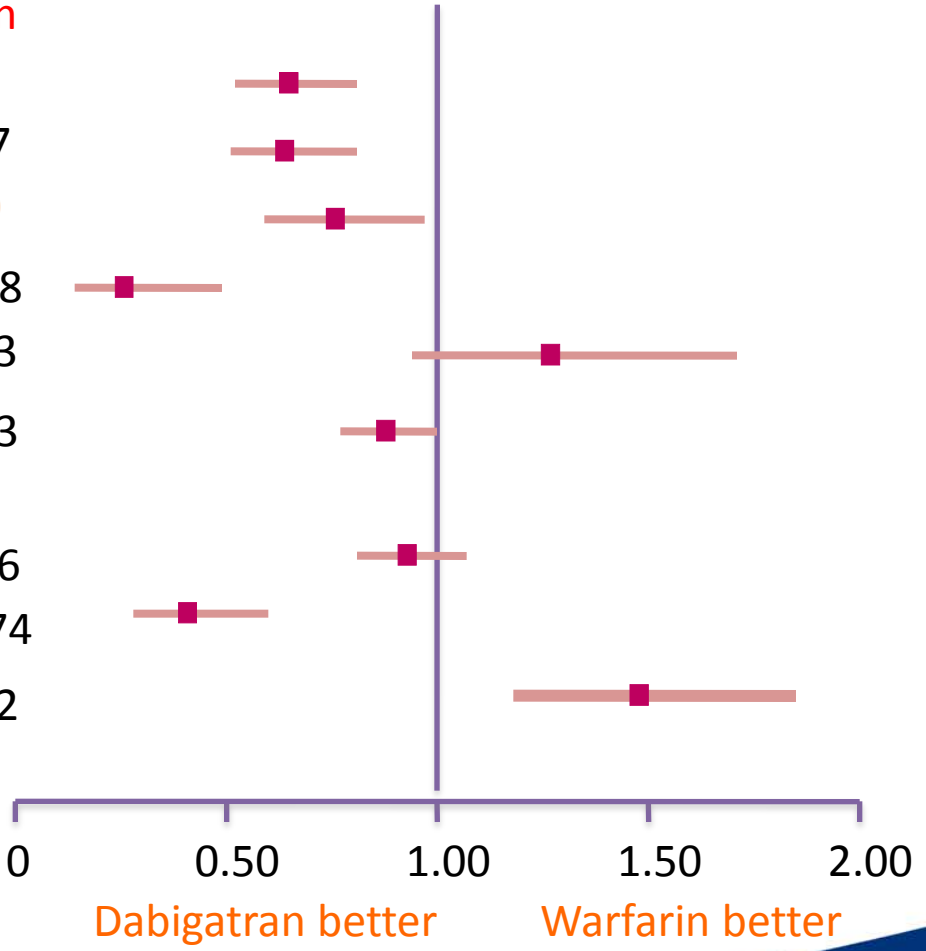
RELY - Dabigatran 150 mg vs Warfarin (TTR 66%) Chads2 Score 2.1 (Mean)

(Event Rate, %/year)

Efficacy Outcomes	Dabigatran	Warfarin
Stroke/Systemic Embolism	1.11	1.69
Stroke	1.01	1.57
Ischemic Stroke	0 .92	1.20
Hemorrhagic Stroke	0 .10	0 .38
MI	0 .74	0 .53
All-Cause Mortality	3.64	4.13
Safety Outcomes		
Major Bleeding	3.11	3.36
ICH	0 .30	0 .74
Major GI Bleeding	1.51	1.02



Connolly SJ,Ezekowitz MD et al. *N Engl J Med*. 2009;361(12):1139-1151.

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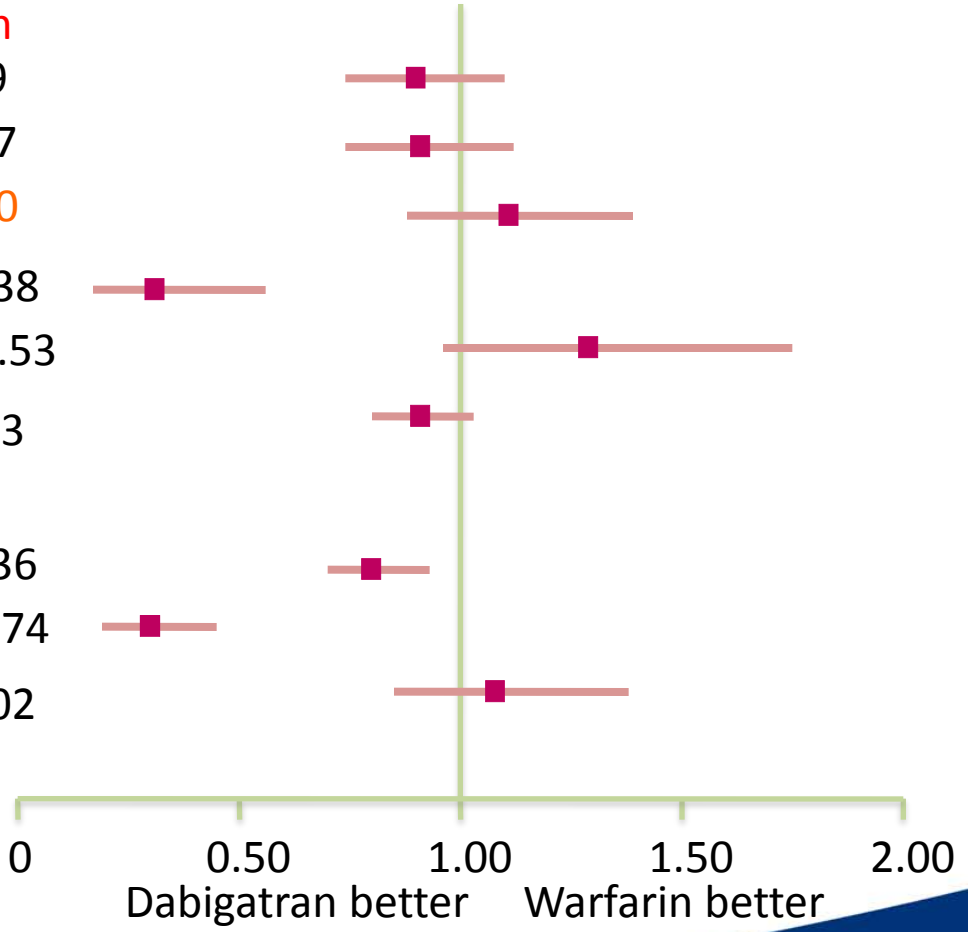
RELY – Dabigatran 110 mg vs. Warfarin

(Event Rate, %/year)		
Efficacy Outcomes	**Dabigatran**	**Warfarin**
Stroke/Systemic Embolism	1.53	1.69
Stroke	1.44	1.57
Ischemic Stroke	1.34	1.20
Hemorrhagic Stroke	0 .12	0 .38
MI	0 .72	0 .53
All-Cause Mortality	3.75	4.13
Safety Outcomes		
Major Bleeding	2.71	3.36
ICH	0 .23	0 .74
Major GI Bleeding	1.12	1.02



Connolly SJ,Ezekowitz MD et al. *N Engl J Med*. 2009;361(12):1139-1151.

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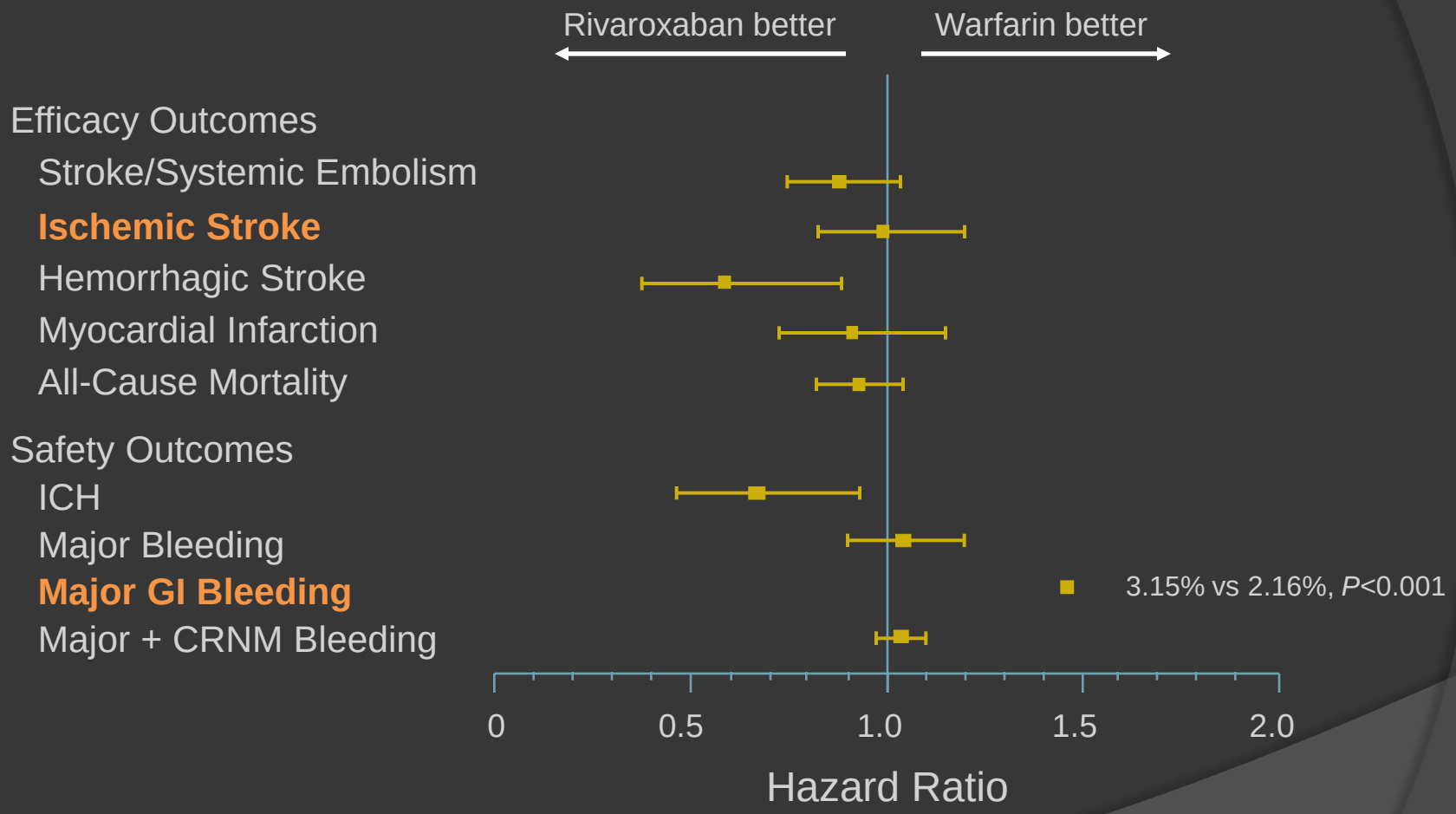
ROCKET AF: Rivaroxaban vs. Warfarin (TTR 55%)

Mean $CHADS_2$ score = 3.5



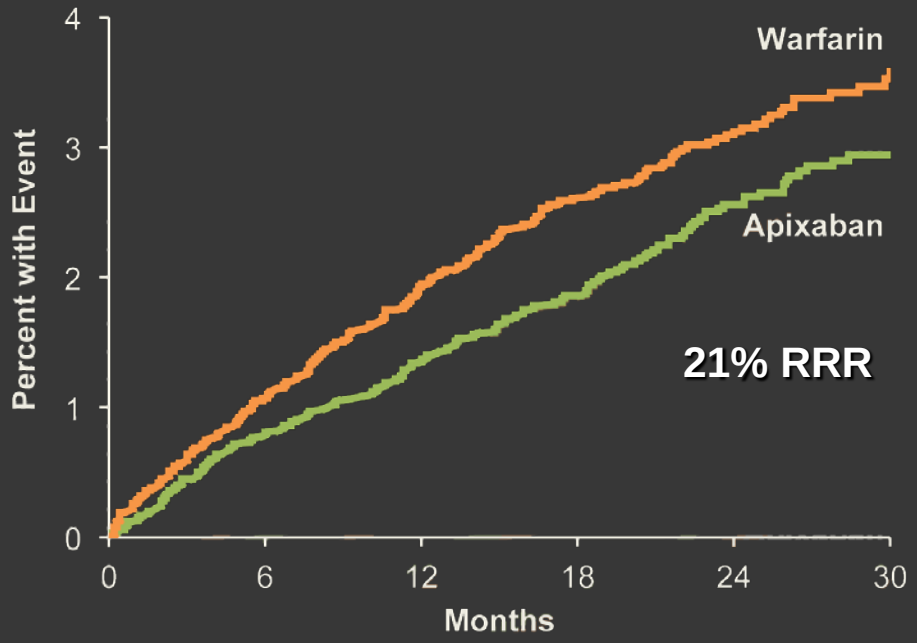
Courtesy of MD Ezekowitz.

Mahaffey KW. Presented at AHA, November 2010.

Patel M et al. *N Engl J Med.* 2011;365:883-891.

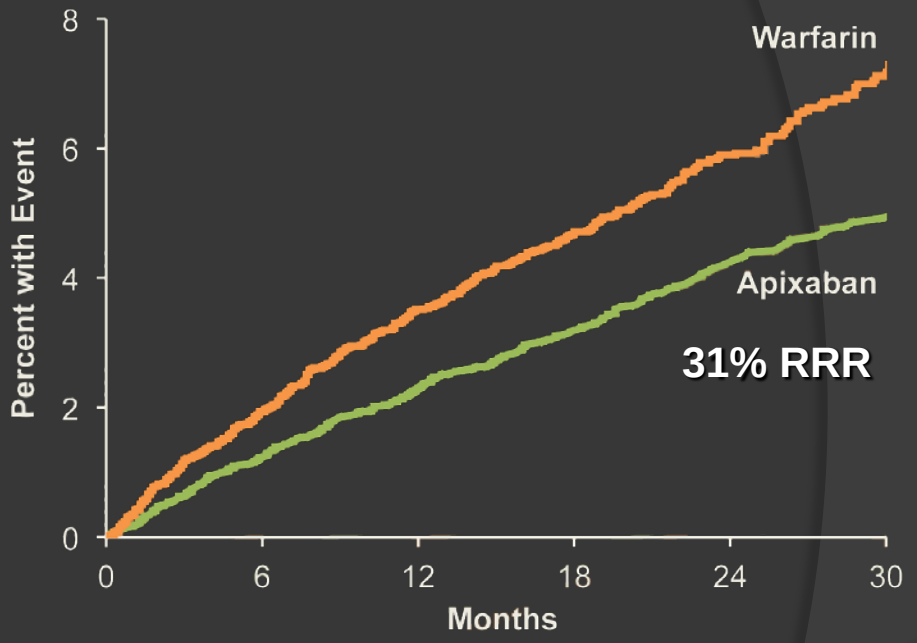
ARISTOTLE Main Trial Results

Stroke or systemic embolism



Apixaban 212 patients, 1.27% per year
Warfarin 265 patients, 1.60% per year
HR 0.79 (95% CI, 0.66–0.95); P=0.011

ISTH major bleeding

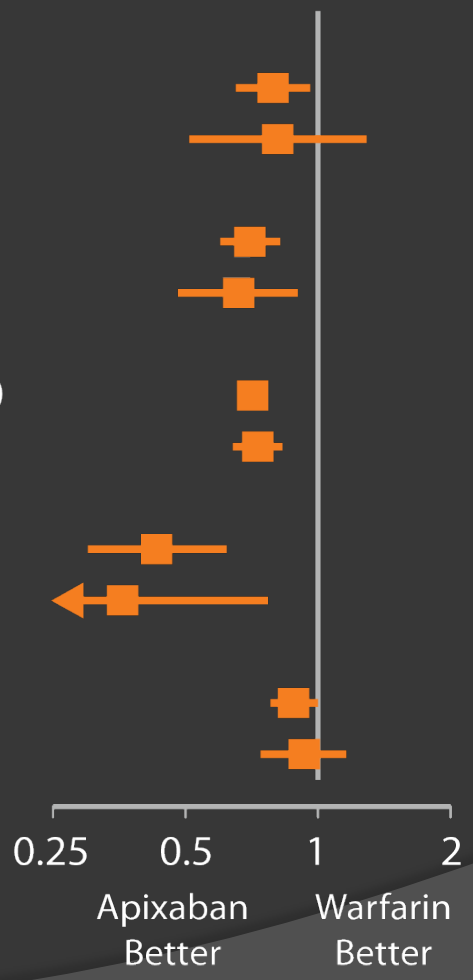


Apixaban 327 patients, 2.13% per year
Warfarin 462 patients, 3.09% per year
HR 0.69 (95% CI, 0.60–0.80); P<0.001

N Engl J Med 2011;365:981-92

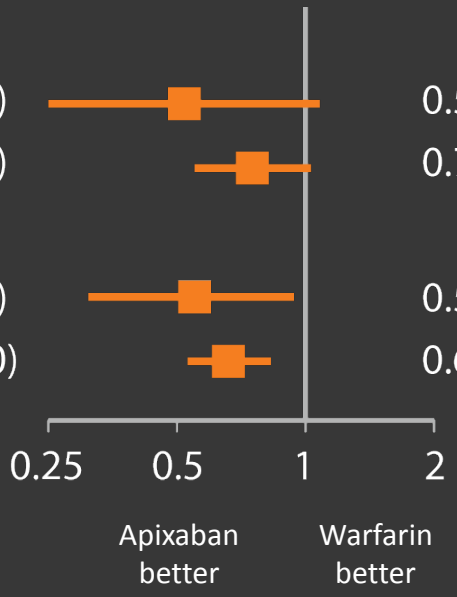
Apixaban vs Warfarin in Patients ≥ 80 vs < 80 Years

	Apixaban	Warfarin	HR (95% CI)	Interactio P-value
Stroke/Systemic Embolism	*Number of events (%/year)*			0.91
Age < 80	179(1.23)	225(1.55)	0.79 (0.65, 0.96)	
Age ≥ 80	33(1.53)	40(1.90)	0.81 (0.51, 1.29)	
Major Bleeding				0.74
Age < 80	260(1.93)	366(2.78)	0.70 (0.60, 0.82)	
Age ≥ 80	67(3.55)	96(5.41)	0.66 (0.48, 0.90)	
All Bleeding				0.83
Age < 80	1964(17.0)	2558(24.4)	0.71 (0.67, 0.76)	
Age ≥ 80	392(26.4)	502(37.4)	0.73 (0.64, 0.83)	
Intracranial Bleeding				0.67
Age < 80	43(0.32)	98(0.73)	0.43 (0.30, 0.62)	
Age ≥ 80	9(0.47)	24(1.32)	0.36 (0.17, 0.77)	
All-cause Mortality				0.73
Age < 80	452(3.03)	507(3.42)	0.88 (0.78, 1.00)	
Age ≥ 80	151(6.86)	162(7.44)	0.93 (0.74, 1.16)	



Stroke or Systemic Embolism and Major Bleeding in patients ≥75 years* in Relation to Apixaban dose

	No. of patients	Apixaban	Warfarin	Hazard Ratio (95 % CI)	Interaction P-value**
Stroke or systemic embolism (n=5678)					0.52
2.5 mg bid	790	11 (1.65)	20 (3.13)	0.52 (0.25, 1.08)	
5 mg bid	4888	68 (1.54)	89 (2.05)	0.75 (0.55, 1.03)	
Major bleeding (n=5655)					0.48
2.5 mg bid	786	20 (3.29)	35 (6.54)	0.55 (0.31, 0.94)	
5 mg bid	4869	131(3.21)	189 (5.00)	0.66 (0.53, 0.83)	



* A reduced dose of 2.5 mg twice daily or placebo were administered to a total of 831 patients; 790 of these patients were ≥75 years

** Interaction among treatment, dose, and age based on randomized or treated population

TSOA for stroke prevention in Asian patients with nonvalvular atrial fibrillation

Non–Vitamin K Antagonist Oral Anticoagulants for Stroke Prevention in Asian Patients With Nonvalvular Atrial Fibrillation

Meta-Analysis

Kang-Ling Wang, MD; Gregory Y.H. Lip, MD; Shing-Jong Lin, MD, PhD; Chern-En Chiang, MD, PhD

Background and Purpose—The use of vitamin K antagonists (VKAs), the cornerstone treatment for stroke prevention in patients with atrial fibrillation, is limited by the perceived risk of serious bleeding in Asia. Non-VKA oral anticoagulants (NOACs) are safer alternatives. Here, we evaluate performance differences of NOACs between Asians and non-Asians.

Methods—We compared efficacy and safety of NOACs between patients enrolled in Asian and non-Asian countries using aggregative data from phase III clinical trials. The odds ratios (ORs [95% confidence interval]) were calculated by a random effects model.

Results—Comparing with VKAs, standard-dose NOACs reduced stroke or systemic embolism (OR=0.65 [0.52–0.83] versus 0.85 [0.77–0.93], *P* interaction= 0.045) more in Asians than in non-Asians and were safer in Asians than in non-Asians about major bleeding (OR=0.57 [0.44–0.74] versus 0.89 [0.76–1.04], *P* interaction=0.004), hemorrhagic stroke (OR=0.32 [0.19–0.52] versus 0.56 [0.44–0.70], *P* interaction=0.046) in particular, whereas gastrointestinal bleeding was significantly increased in non-Asians (OR=0.79 [0.48–1.32] versus 1.44 [1.12–1.85], *P* interaction=0.041). Generally, low-dose NOACs were safer than VKAs without heterogeneity in efficacy and safety between Asians and non-Asians, except for ischemic stroke, major, and gastrointestinal bleeding.

Conclusions—Our findings suggest that standard-dose NOACs were more effective and safer in Asians than in non-Asians, whereas low-dose NOACs performed similarly in both populations. **(*Stroke*. 2015;46:2555-2561. DOI: 10.1161/STROKEAHA.115.009947.)**

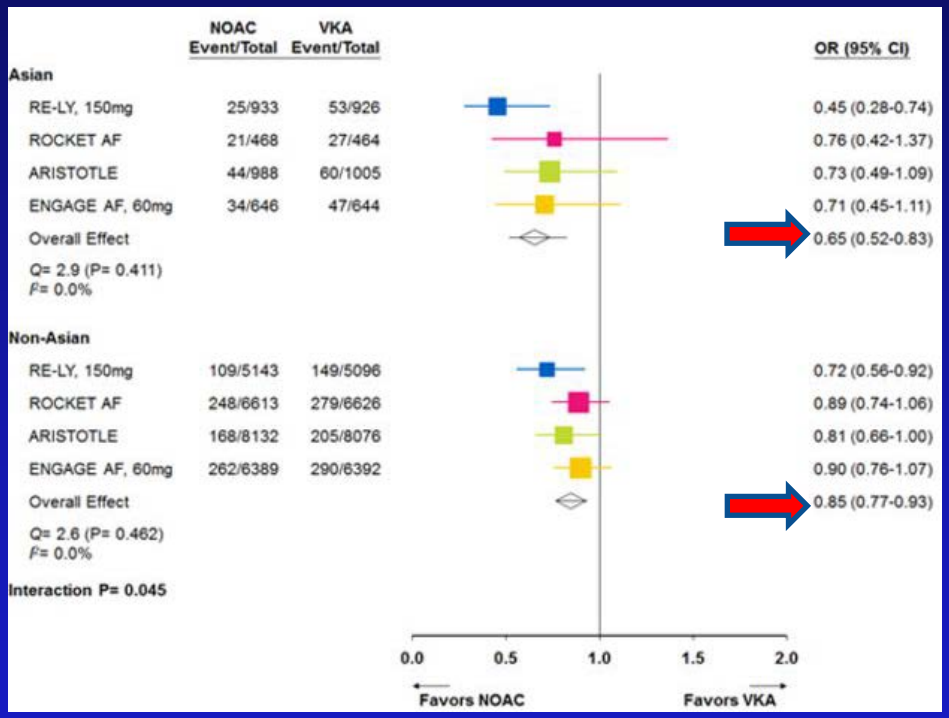
Key Words: anticoagulants ■ atrial fibrillation ■ hemorrhage ■ stroke

Courtesy of Gordon Leung MD

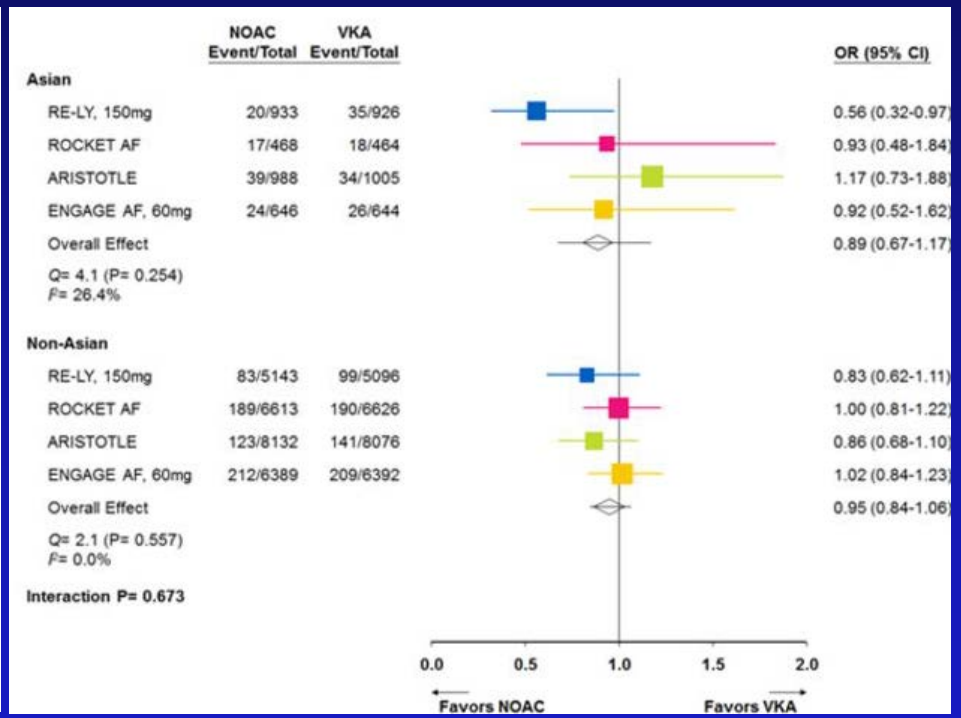
Stroke;46(9):2555-2561: August 24, 2015
American Heart Assn/American Stroke Assn

Efficacy outcomes of stroke/systemic embolism and ischemic stroke for TSOA vs VKA

Stroke or systemic embolism



Ischemic stroke

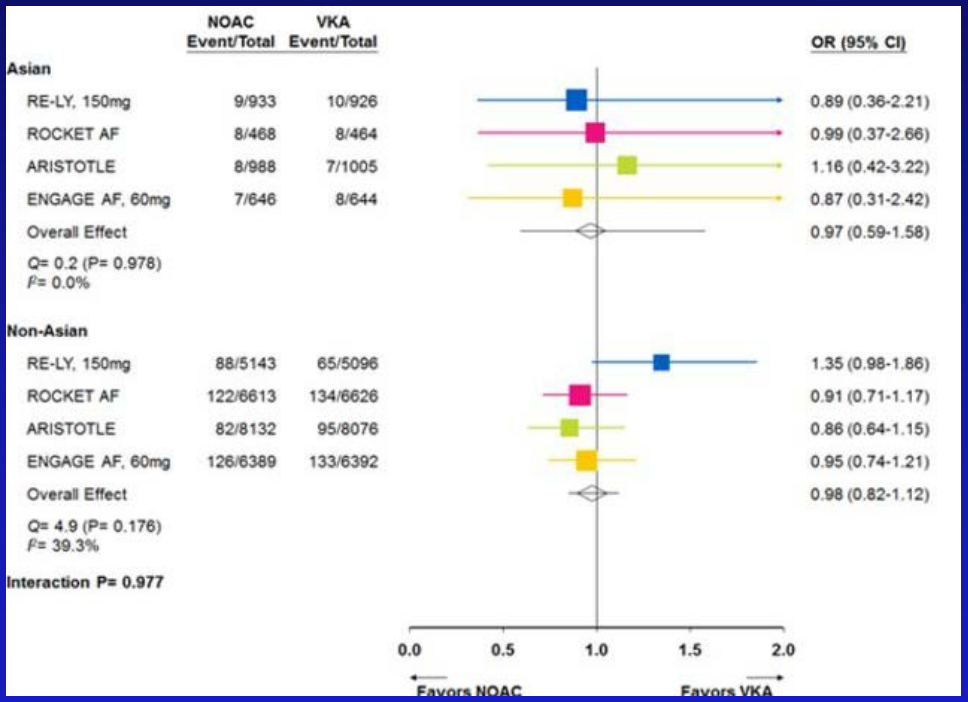


Courtesy of Gordon Leung MD

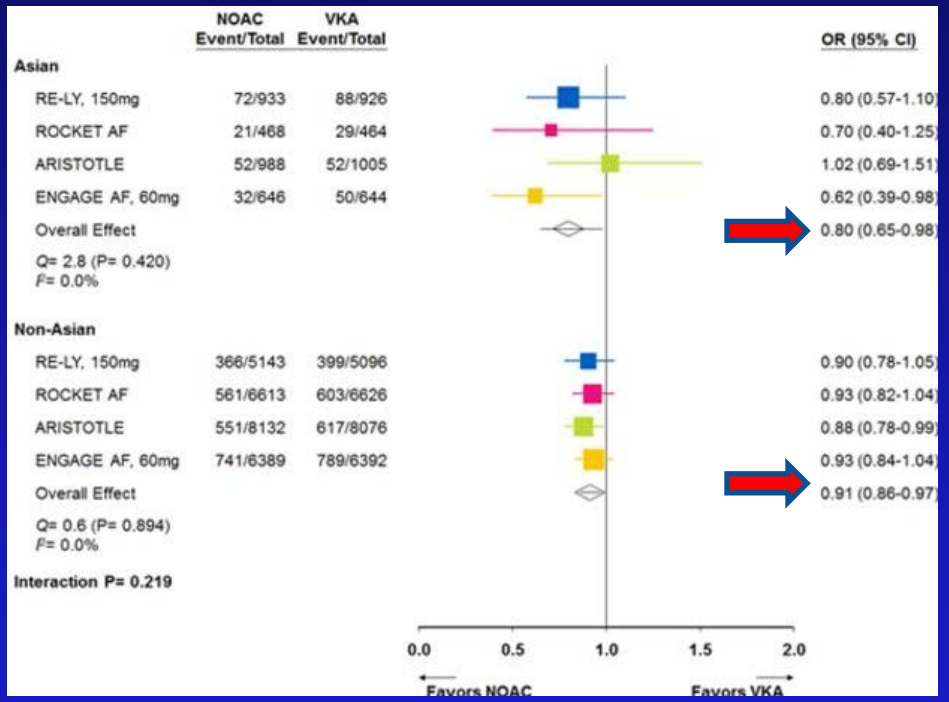
Kang-Ling Wang et al. Stroke. 2015;46:2555-2561

Efficacy outcomes of myocardial infarction and all cause mortality for NOAC vs VKA

Myocardial infarction



All cause mortality

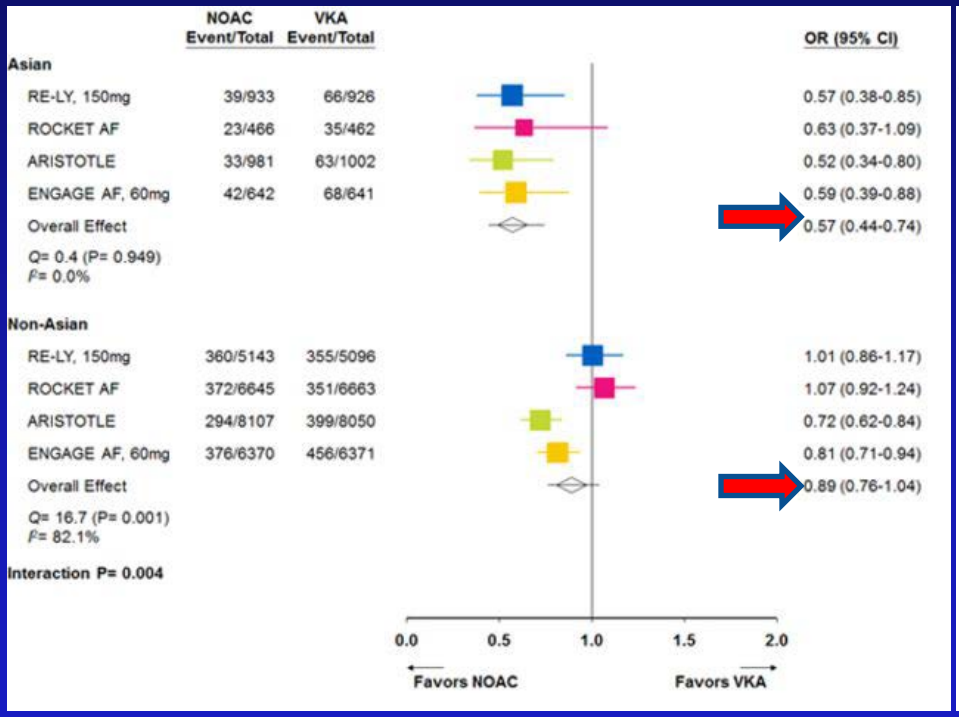


Courtesy of Gordon Leung MD

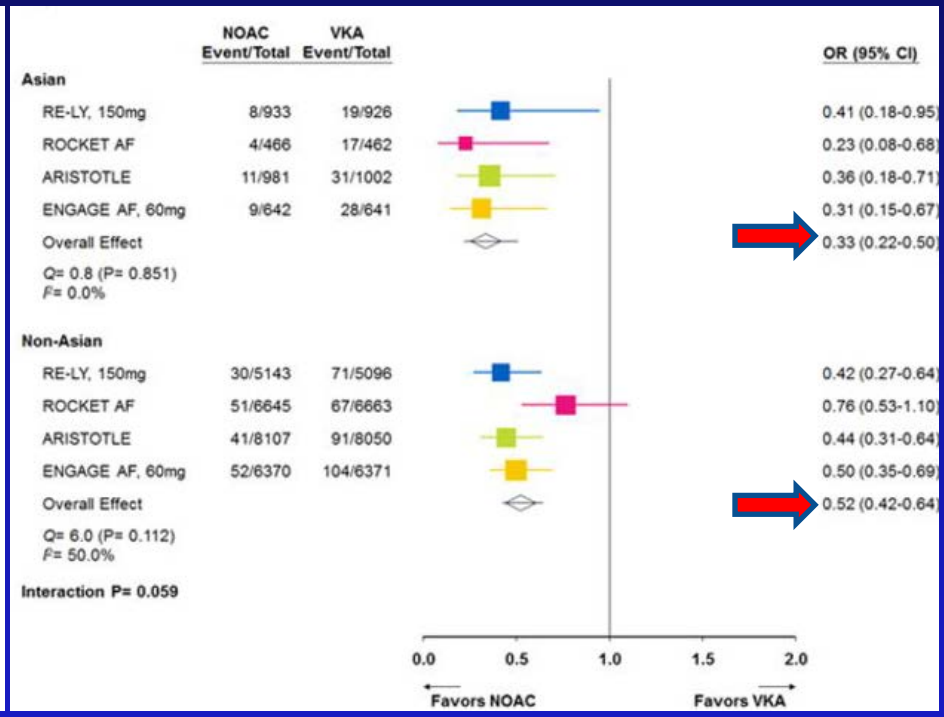
Kang-Ling Wang et al. Stroke. 2015;46:2555-2561

Safety outcomes of major bleeding and intracranial hemorrhage for TSOA vs VKA in Asians vs Non-Asians

Major bleeding



Intracranial hemorrhage

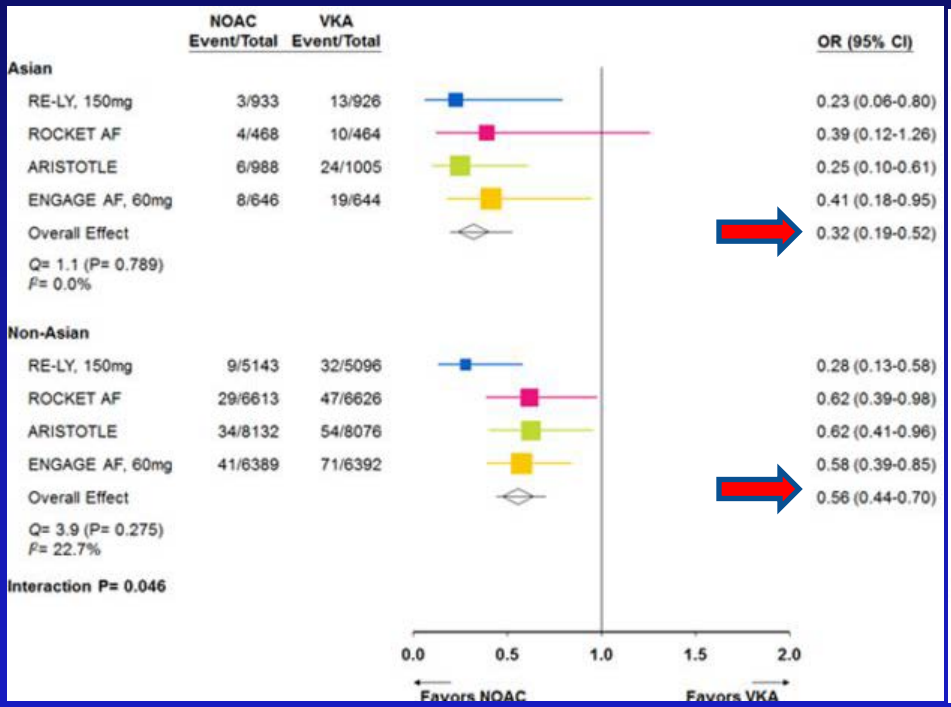


Courtesy of Gordon Leung MD

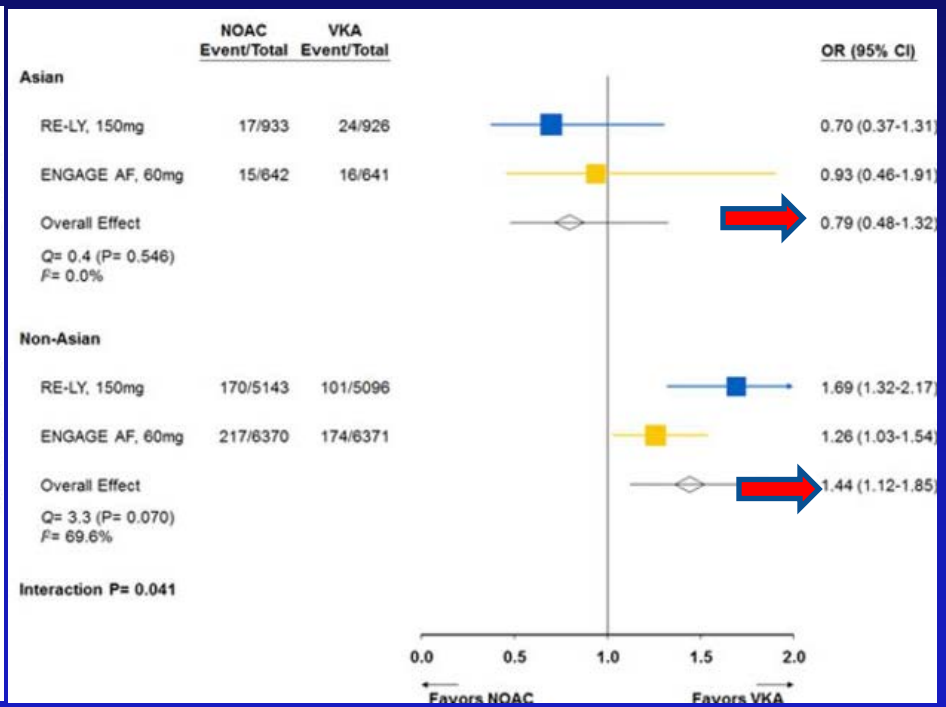
Kang-Ling Wang et al. Stroke. 2015;46:2555-2561

Safety outcomes of hemorrhagic stroke and GI bleeding for TSOA vs VKA in Asians vs Non-Asians

Hemorrhagic stroke



GI bleeding



Courtesy of Gordon Leung MD

Kang-Ling Wang et al. Stroke. 2015;46:2555-2561

82 year old Chinese woman with AF detected by cardiac device, HTN, CRI.

Anticoagulant therapy:

a) Do nothing
b) Increase aspirin 325mg daily
c) Adjusted dose warfarin INR 2-3
d) Dabigatran 150mg bid
e) Rivaroxaban 20mg daily
f) Apixaban 2.5 mg twice daily

82 year old Chinese woman with AF detected by cardiac device, HTN, CRI.

CHA_2DS_2-VASc score = 4 for HTN,Age2,Sex → 9.2%/year risk of stroke

HASBLED score = 3 for HTN, CRI, Age → 5.0 %/year risk of major bleed

Anticoagulant therapy:

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b) Increase aspirin 325mg daily
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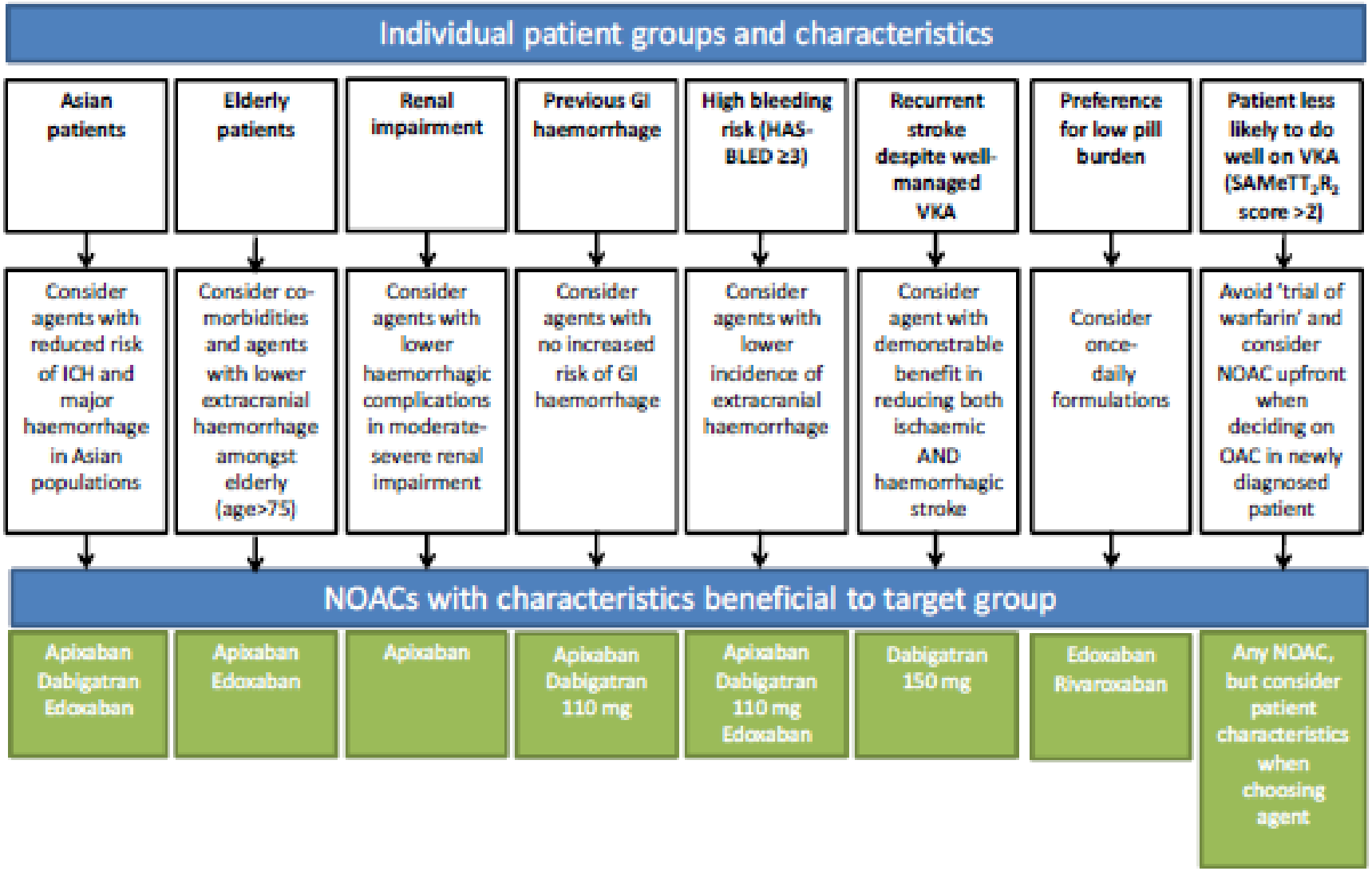
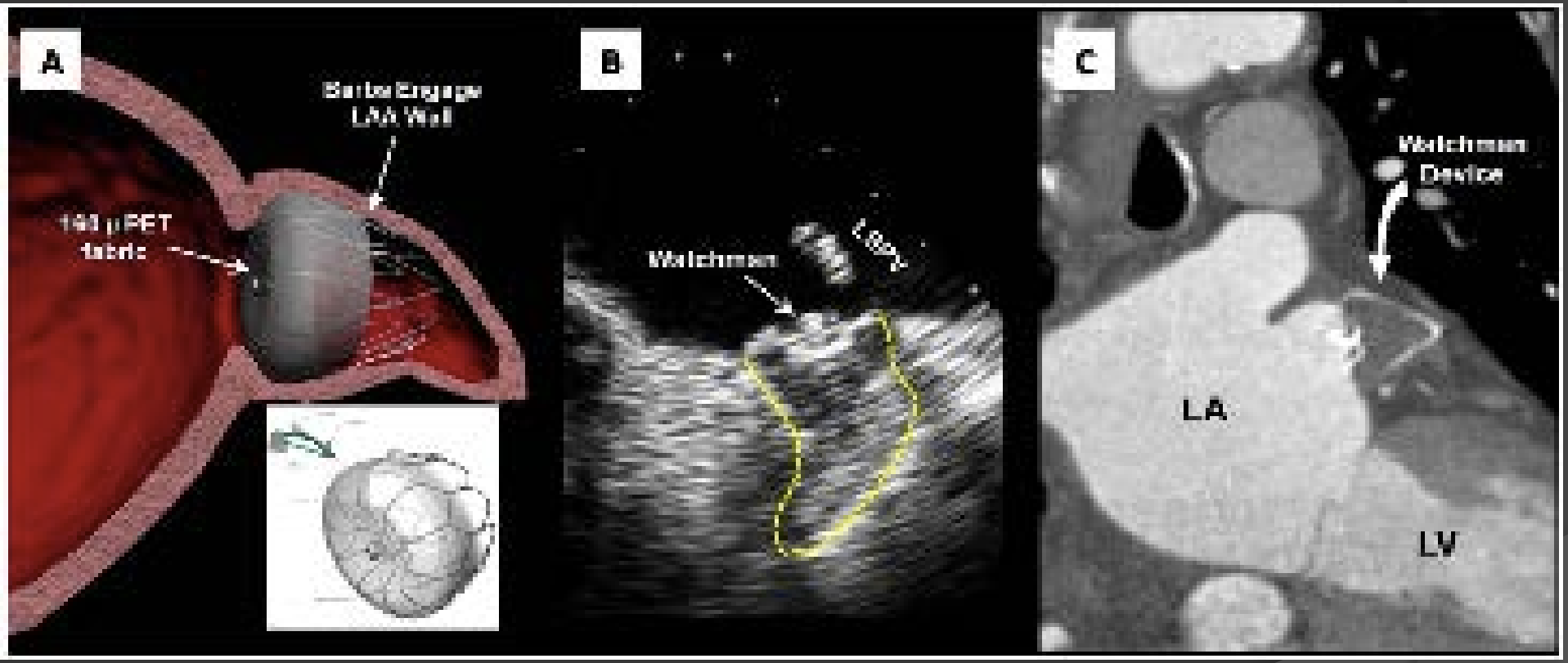


Lip et al. Journal of Internal Medicine 2015

- Incidence and Disease Burden
- Indications for stroke prophylaxis
- Anticoagulant choice
- Novel devices to prevent stroke

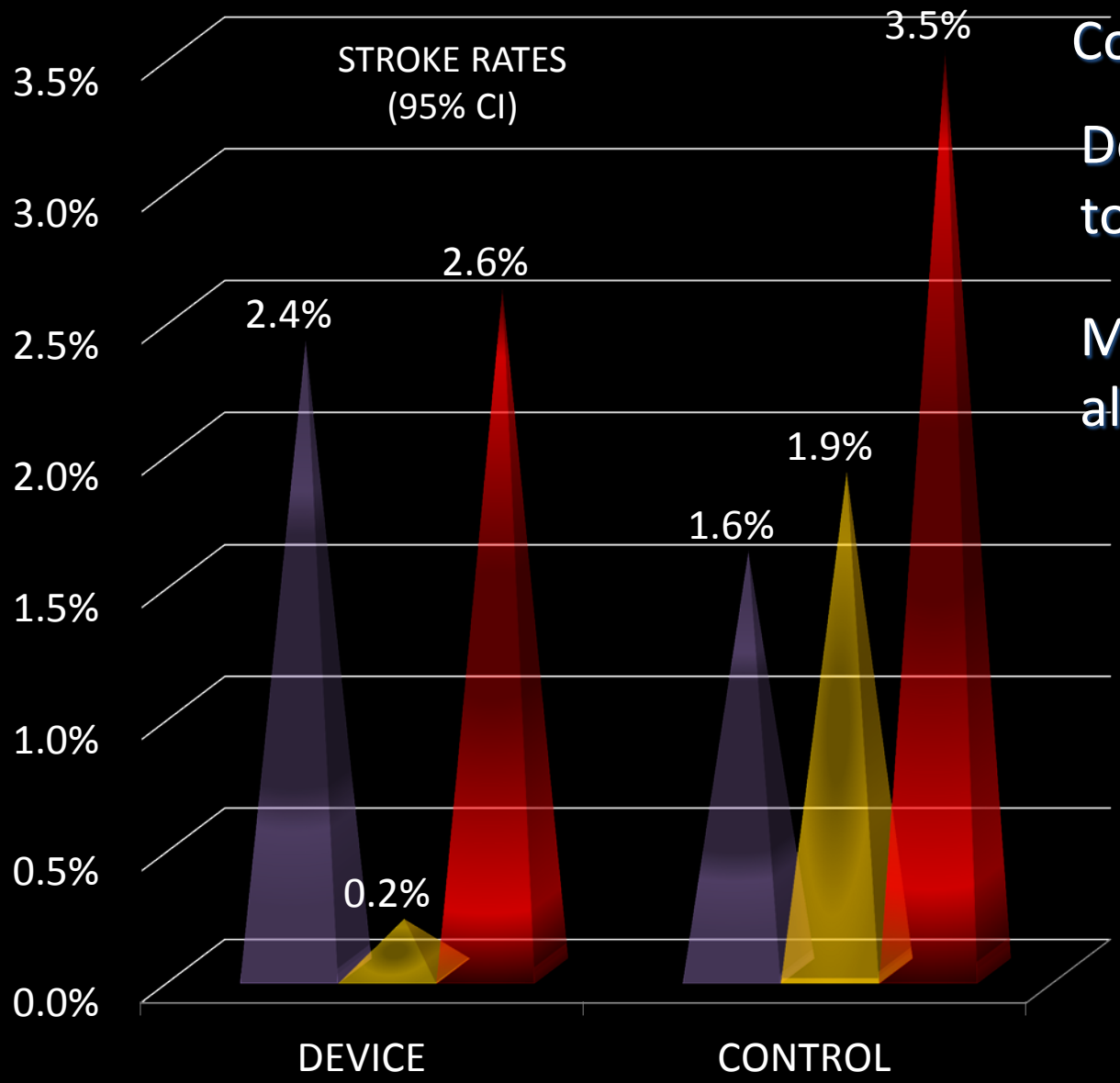
Watchman Device to occlude Left Atrial Appendage



Holmes et al. PROTECT AF. Lancet 2009

UCSF
Cardiac Electrophysiology

PROTECT AF STUDY

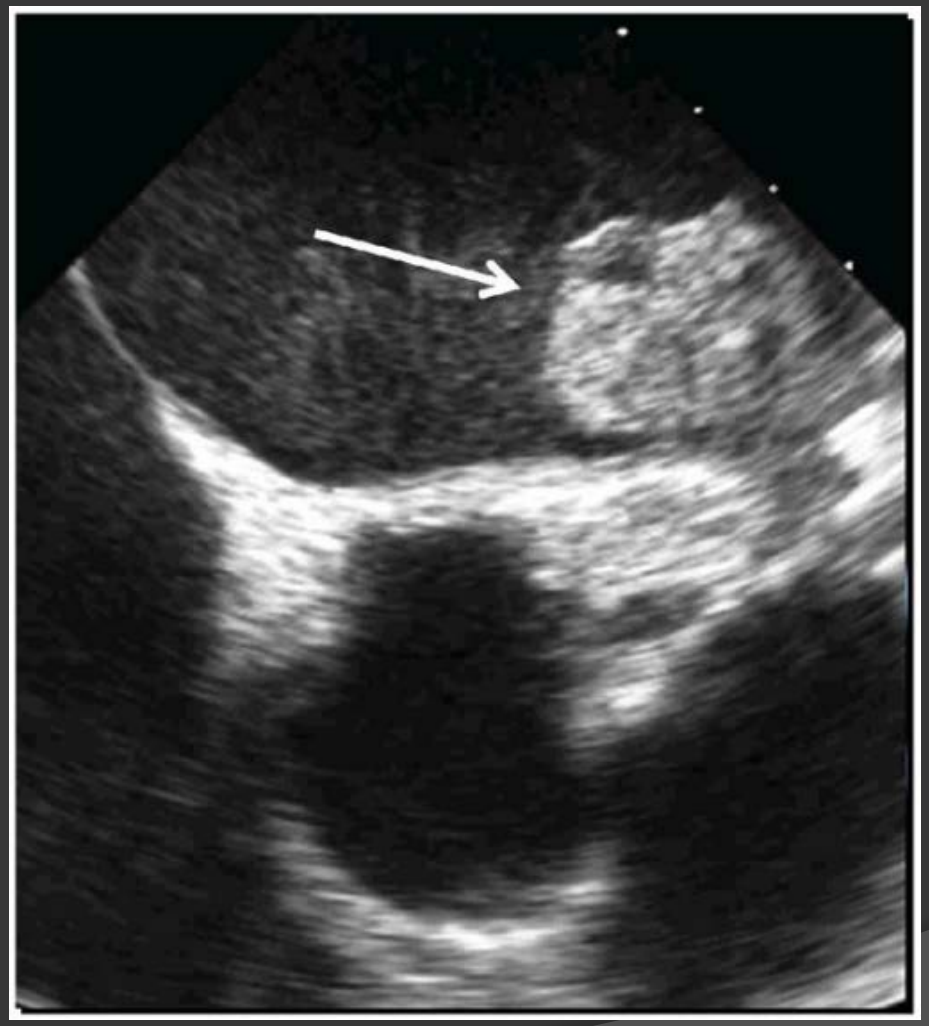


Conclusions:

Device is non-inferior to warfarin in stroke

May provide an alternative to warfarin

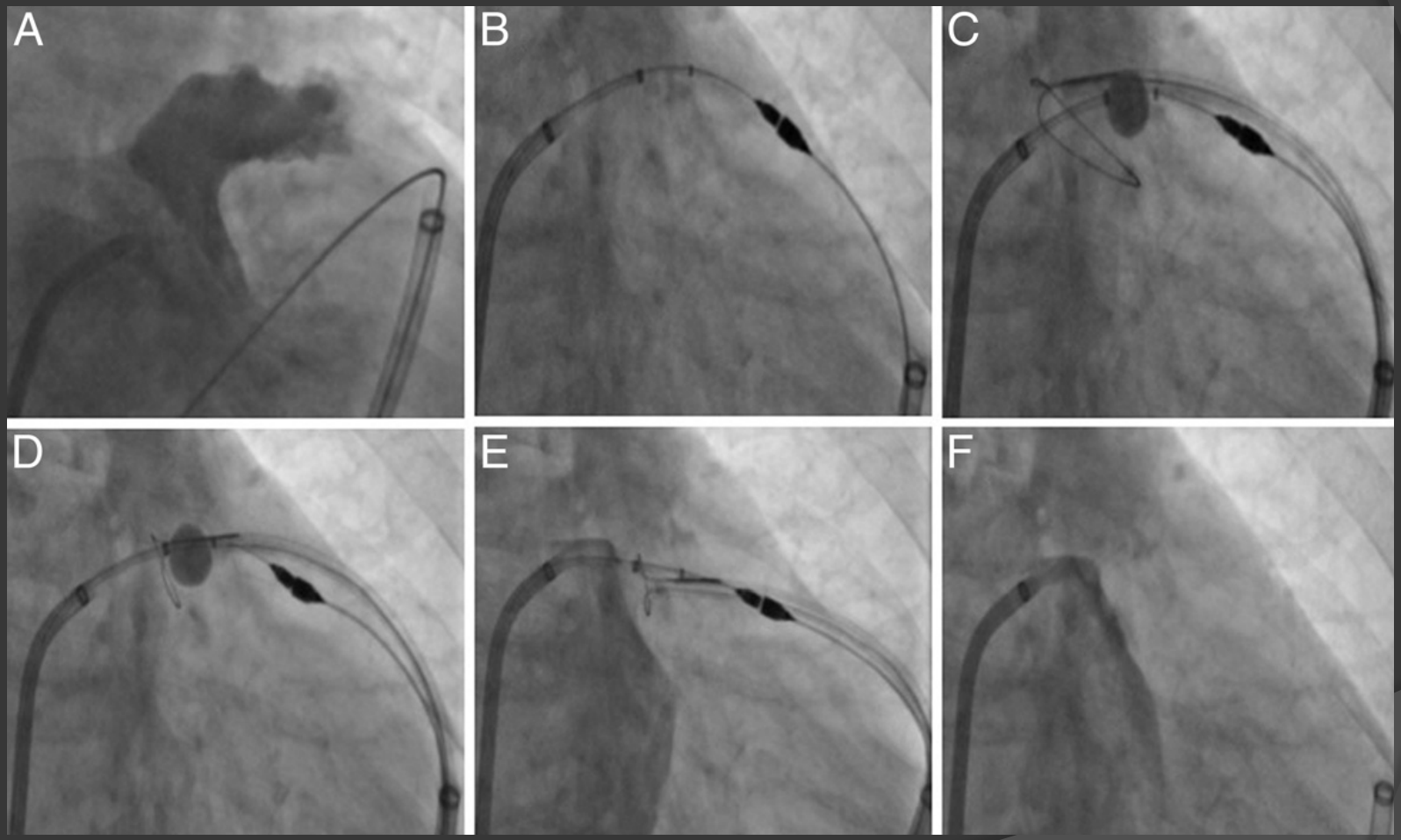
Thrombus after Watchman Implant



Patel et al. Cardiol Resid Pract 2012

UCSF
Cardiac Electrophysiology

Percutaneous Epicardial Left Atrial Appendage Ligation



Bartus, et al. JACC 2013;62:108-18.

Summary

- AF is common and increasing in prevalence
- Asymptomatic AF found lasting over 1 hour should prompt consideration of stroke prophylaxis
- CHA2DS2-VASc should replace CHADS2
- Neither aspirin nor aspirin/clopidogrel is enough for moderate to high risk AF patients
- Older age should make clinicians want to anticoagulate their patients more
- Falls are not good reasons to withhold anticoagulation
- Use HAS-BLED score to weigh risk of bleeding against risk of stroke
- NOACs have lower risk of bleeding and ICH when compared to coumadin, and appear to be particularly safe in Asians
- Novel devices may someday replace oral anticoagulants