ATRIAL FIBRILLATION

RAJA NAZIR, FACC

No disclosures

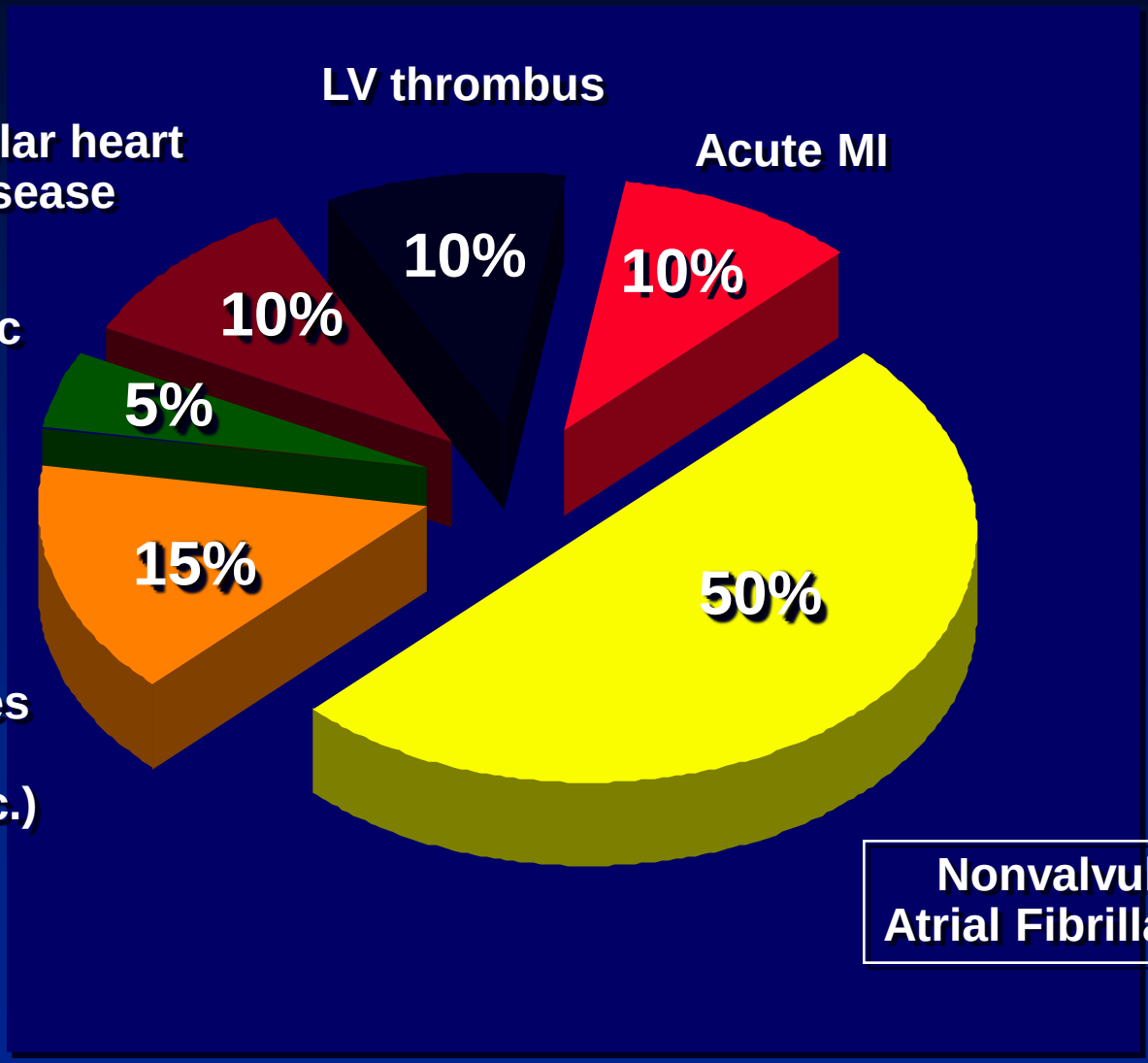
- 70 WF presented with slurred speech and right sided weakness, improved in 4 hours
- Past medical history
  - HTN,OBESITY (BMI 37)
- Physical exam
  - NORMAL WITH NEURODEFICIT THAT RESOLVED
- LABS
  - WNL
- CT
  - NEGATIVE
- CTA
  - MILD CAROTID DISEASE
- EKG
  - NSR, Tele no arrhythmia

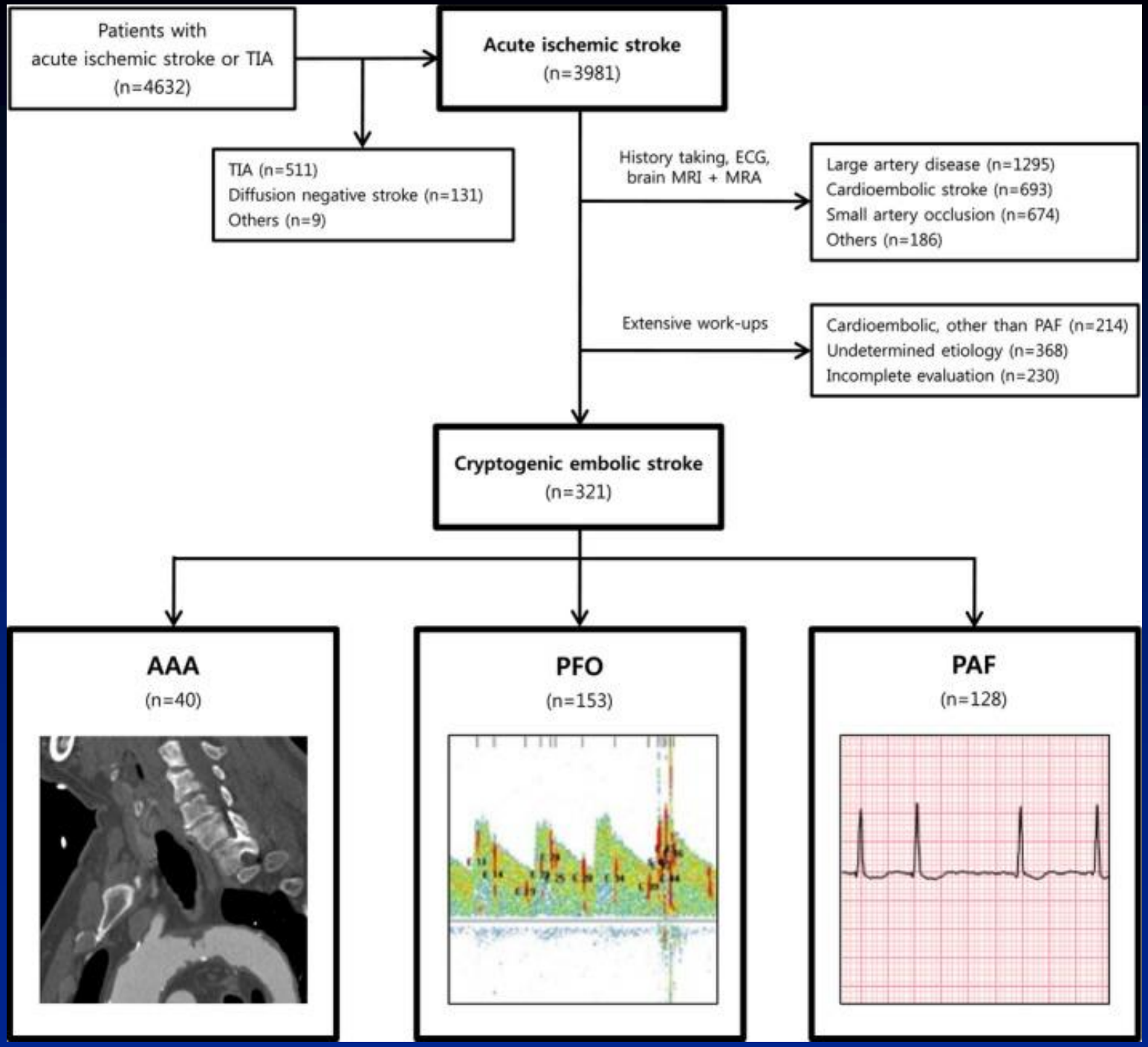
CARDIOLOGY CONSULT

- **TEE**
  - NO PFO, NO THROMBUS, NO AORTIC ATHEROMA
- **EVALUATE FOR A-FIB**
  - HOLTER
  - EVENT MONITOR
  - IMPLANTABLE LOOP

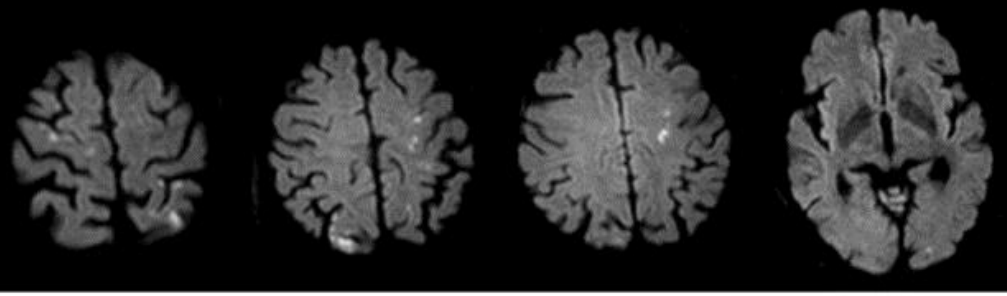
  - PATIENTS SENT HOME ON EVENT MONITOR
  - ON ASA
  - STATIN

CARDIOEMBOLIC SOURCES



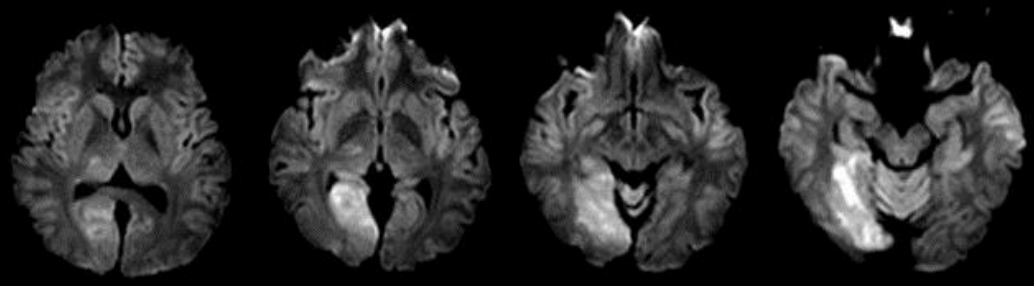

Patients with
acute ischemic stroke or TIA
(n=4632)
Acute ischemic stroke
(n=3981)
TIA (n=511)
Diffusion negative stroke (n=131)
Others (n=9)
History taking, ECG,
brain MRI + MRA
Large artery disease (n=1295)
Cardioembolic stroke (n=693)
Small artery occlusion (n=674)
Others (n=186)
Extensive work-ups
Cardioembolic, other than PAF (n=214)
Undetermined etiology (n=368)
Incomplete evaluation (n=230)
Cryptogenic embolic stroke
(n=321)
AAA
(n=40)
PFO
(n=153)
PAF
(n=128)

A



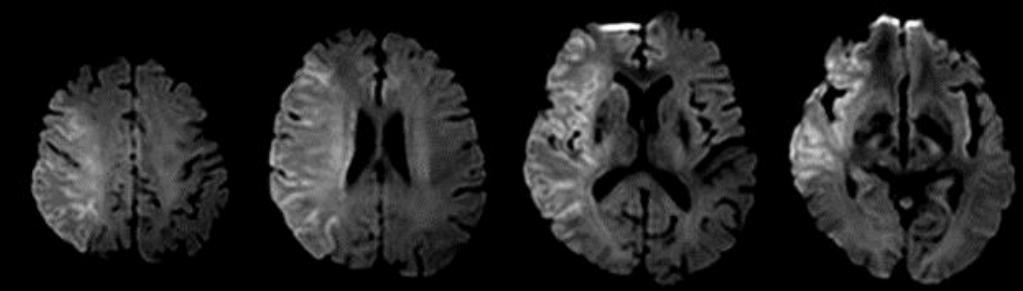
Age	NIHSS	Hypertension	Largest lesion (mm)	Lesion number	Posterior lesion	Multiple vascular territories	Probability		
							AAA	PFO	PAF
78	0	+	9.1	34	-	+	**0.94**	0.05	0.01

B

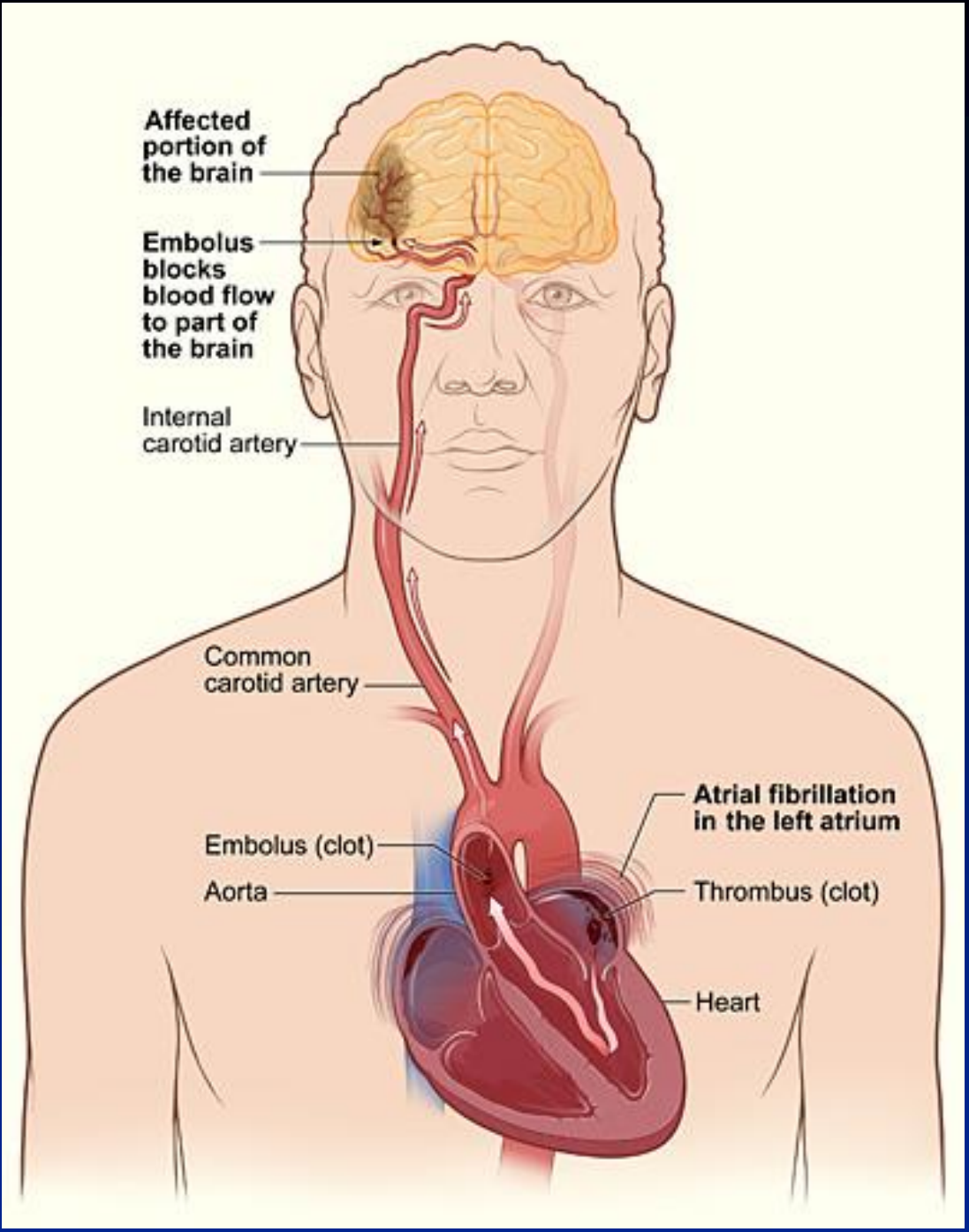


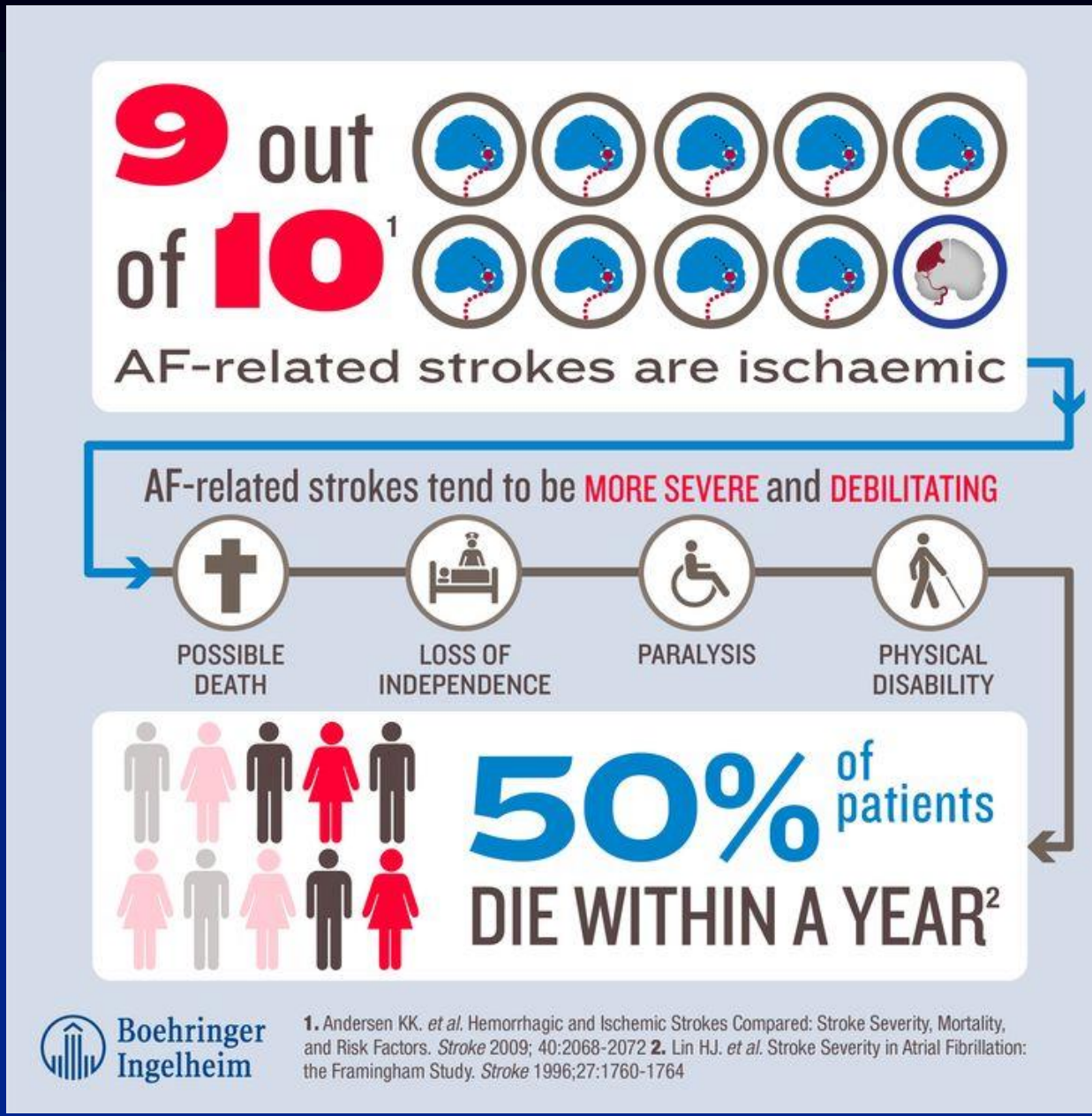
Age	NIHSS	Hypertension	Largest lesion (mm)	Lesion number	Posterior lesion	Multiple vascular territories	Probability		
							AAA	PFO	PAF
29	2	-	59.4	2	+	-	<0.01	**0.97**	0.03

C

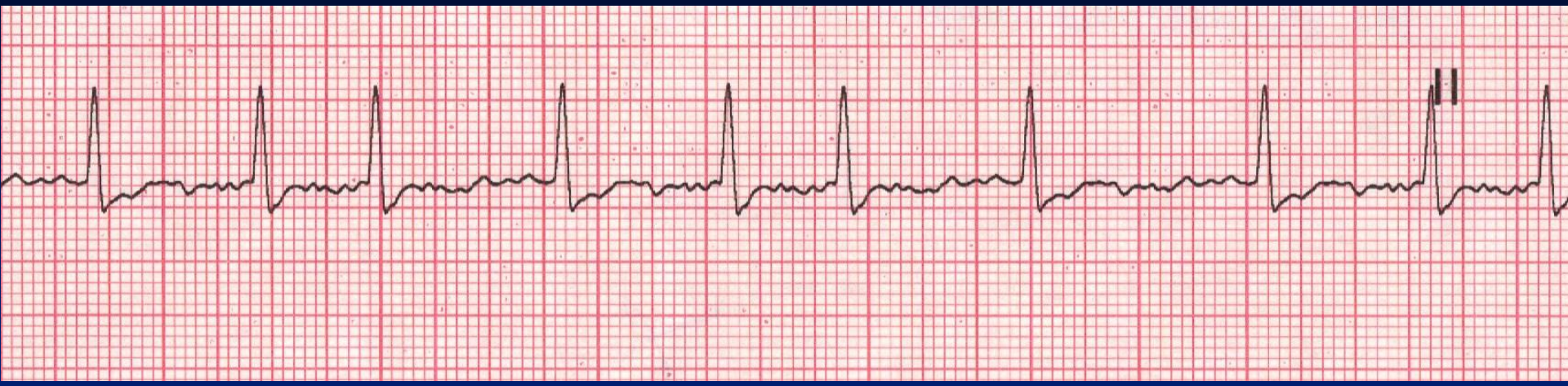


Age	NIHSS	Hypertension	Largest lesion (mm)	Lesion number	Posterior lesion	Multiple vascular territories	Probability		
							AAA	PFO	PAF
74	17	+	123.9	1	-	-	0.01	0.05	**0.94**

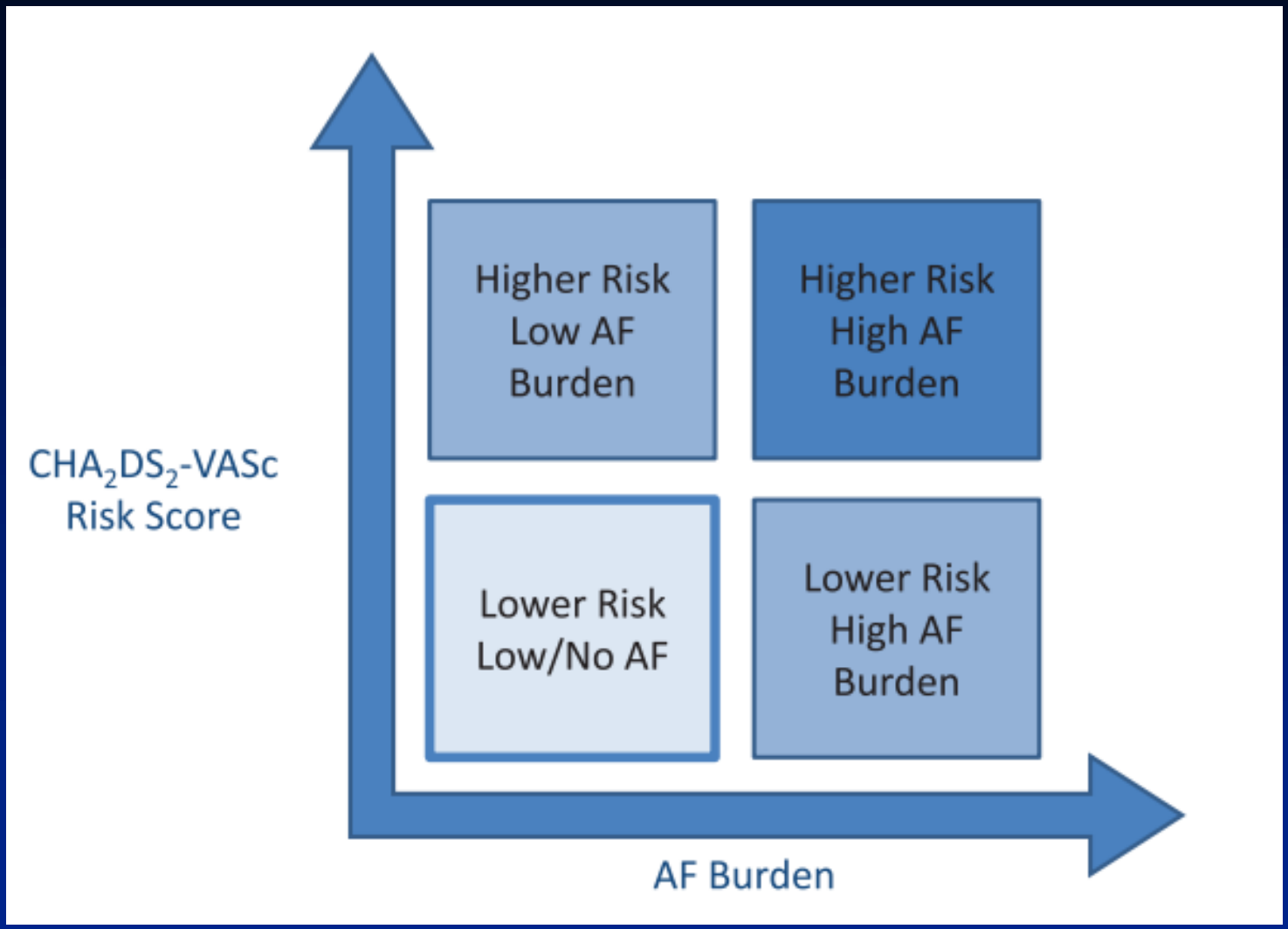

Affected portion of the brain
Embolus blocks blood flow to part of the brain
Internal carotid artery
Common carotid artery
Atrial fibrillation in the left atrium
Embolus (clot)
Aorta
Thrombus (clot)
Heart


9 out of 10[1]
AF-related strokes are ischaemic
AF-related strokes tend to be MORE SEVERE and DEBILITATING
POSSIBLE DEATH
LOSS OF INDEPENDENCE
PARALYSIS
PHYSICAL DISABILITY
50% of patients
DIE WITHIN A YEAR[2]
Boehringer Ingelheim
1. Andersen KK. et al. Hemorrhagic and Ischemic Strokes Compared: Stroke Severity, Mortality, and Risk Factors. Stroke 2009; 40:2068-2072 2. Lin HJ. et al. Stroke Severity in Atrial Fibrillation: the Framingham Study. Stroke 1996;27:1760-1764

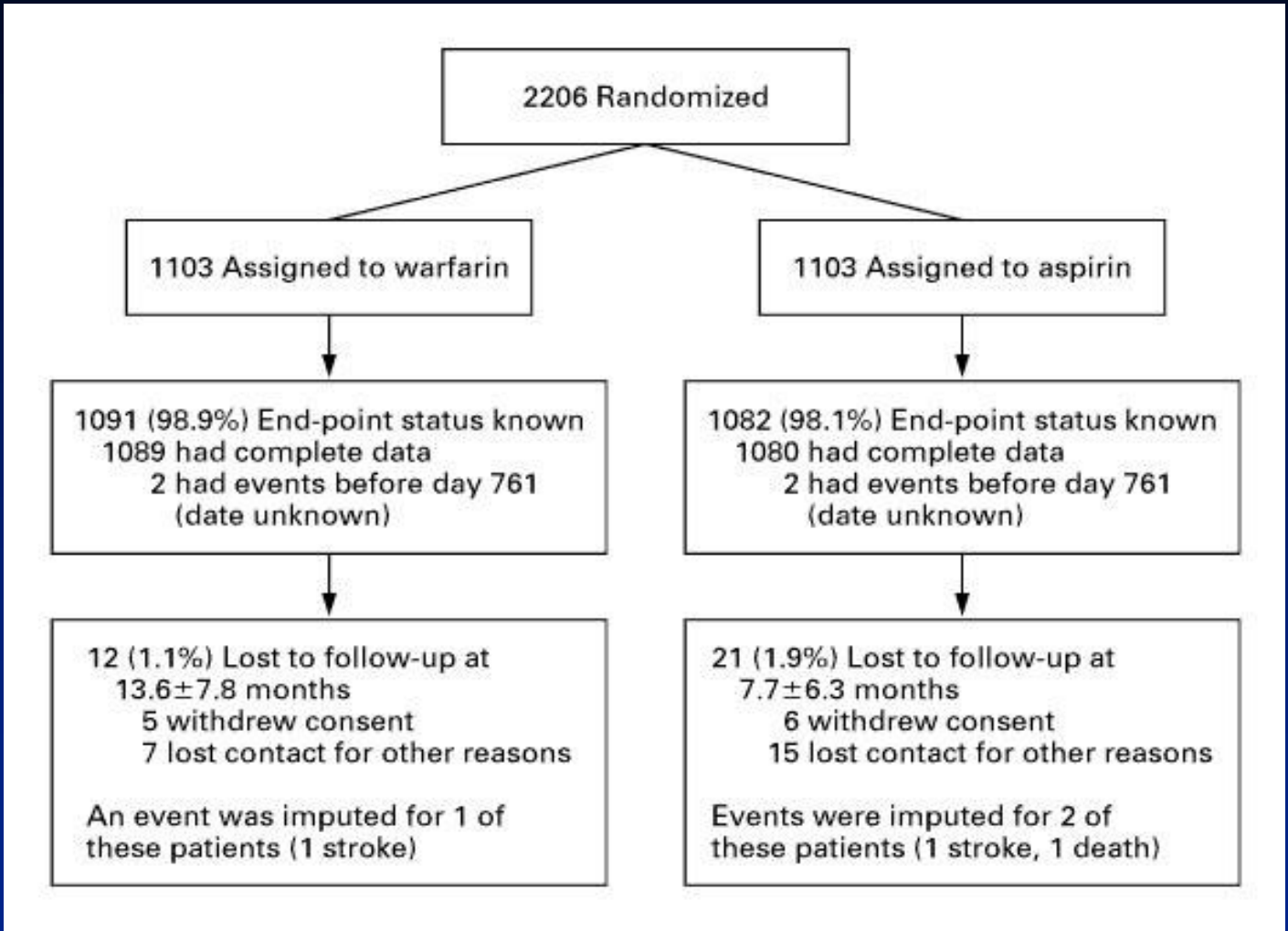
- **Event monitor**
  - **5 episodes of A-FIB longest episode 30 minutes**



A-FIB BURDEN
RISK OF THROMBOEMBOLISM
RISK OF BLEEDING


Higher Risk
Low AF
Burden
Higher Risk
High AF
Burden
Lower Risk
Low/No AF
Lower Risk
High AF
Burden
CHA2DS2-VASc
Risk Score
AF Burden

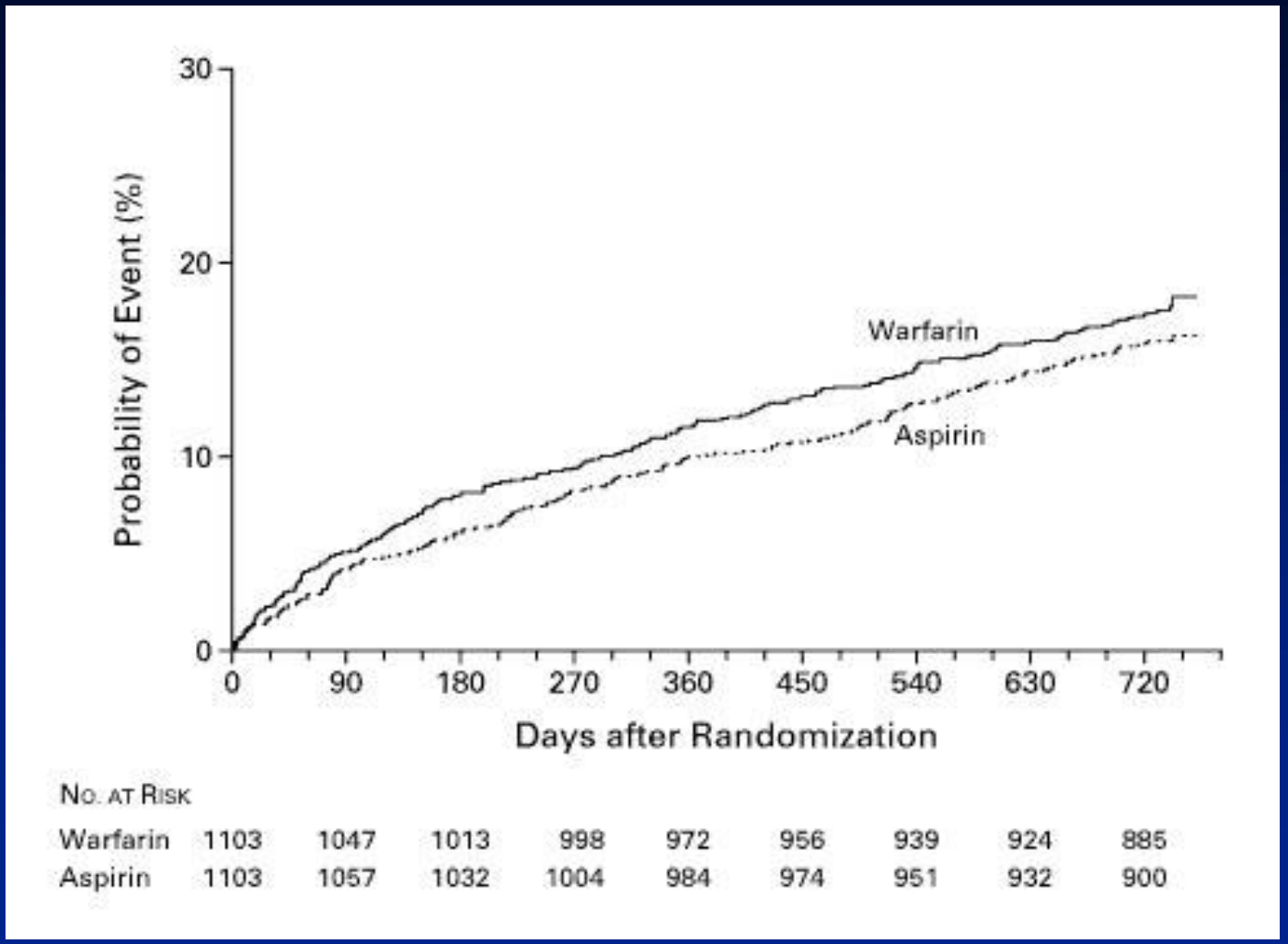
Follow-up of Patients and Imputation of Events



Mohr J et al. N Engl J Med 2001;345:1444-1451.

The NEW ENGLAND JOURNAL of MEDICINE

Kaplan–Meier Analyses of the Time to Recurrent Ischemic Stroke or Death According to Treatment Assignment



No. at Risk

Warfarin	1103	1047	1013	998	972	956	939	924	885
Aspirin	1103	1057	1032	1004	984	974	951	932	900

Mohr J et al. N Engl J Med 2001;345:1444-1451.

- How to look for subclinical A-Fib?
- Define A-Fib burden
- How much A-Fib is required for stroke?
- What is the temporal relationship of A-Fib with stroke?
- Who should be anticoagulated?
- When to ablate A-fib?
- What is the role of LAAC?

CHA_2DS_2-VASc Assessment of Thromboembolic Risk

CHF/ LV dysfunction	1
Hypertension	1
Age ≥ 75	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease	1
Age 65-74	1
Sex **c**ategory (female)	1

Score 0 – 9

Validated in 1084 NVAF patients not on OAC with known TE status at 1 year in Euro Heart Survey

Score	Annual stroke rate, %	
n	1084	73 538
0	0	0.78
1	1.3	2.01
2	2.2	3.71
3	3.2	5.92
4	4.0	9.27
5	6.7	15.26
6	9.8	19.78
7	9.6	21.50
8	6.7	22.38
9	15.2	23.64

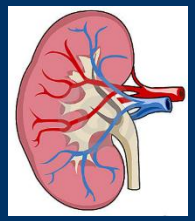
Lip GYH, et al. Chest 2009

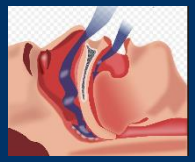
Olesen JB et al. BMJ 2011;342:124

Atrial Fibrillation Guidelines

Risk	Recommended Therapy	
	ESC 2016	AHA/ACC/HRS 2014
No risk factors CHA_2DS_2-VASc= 0	No antithrombotic therapy (III B)	No antithrombotic therapy (IIa)
CHA_2DS_2-VASc= 1	OAC (IIa B) (NOAC > VKA)	None or OAC or ASA (IIb)
CHA_2DS_2-VASc≥ 2	OAC (I) (NOAC > VKA (IA))	OAC (I) (NOAC or VKA)
Mechanical valve, mitral stenosis	VKA	

ESC Guidelines. Eur Heart J 2016
AHA/ACC/HRS Guidelines. Circulation 2014





Novel Clinical Risk Factors

- Chronic kidney disease
- Obstructive sleep apnea
- AF burden

Serum Biomarkers

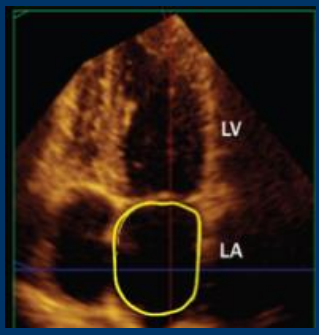
- Natriuretic peptides
- Troponin

Established Clinical Risk Factors (CHADS-VASc)

- Prior stroke/TIA
- Age
- Hypertension
- Diabetes
- Heart failure
- Female sex
- Vascular disease

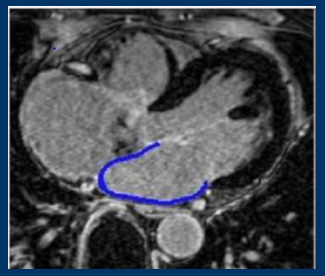
Echo Parameters

- LA volume
- LA and LAA Function



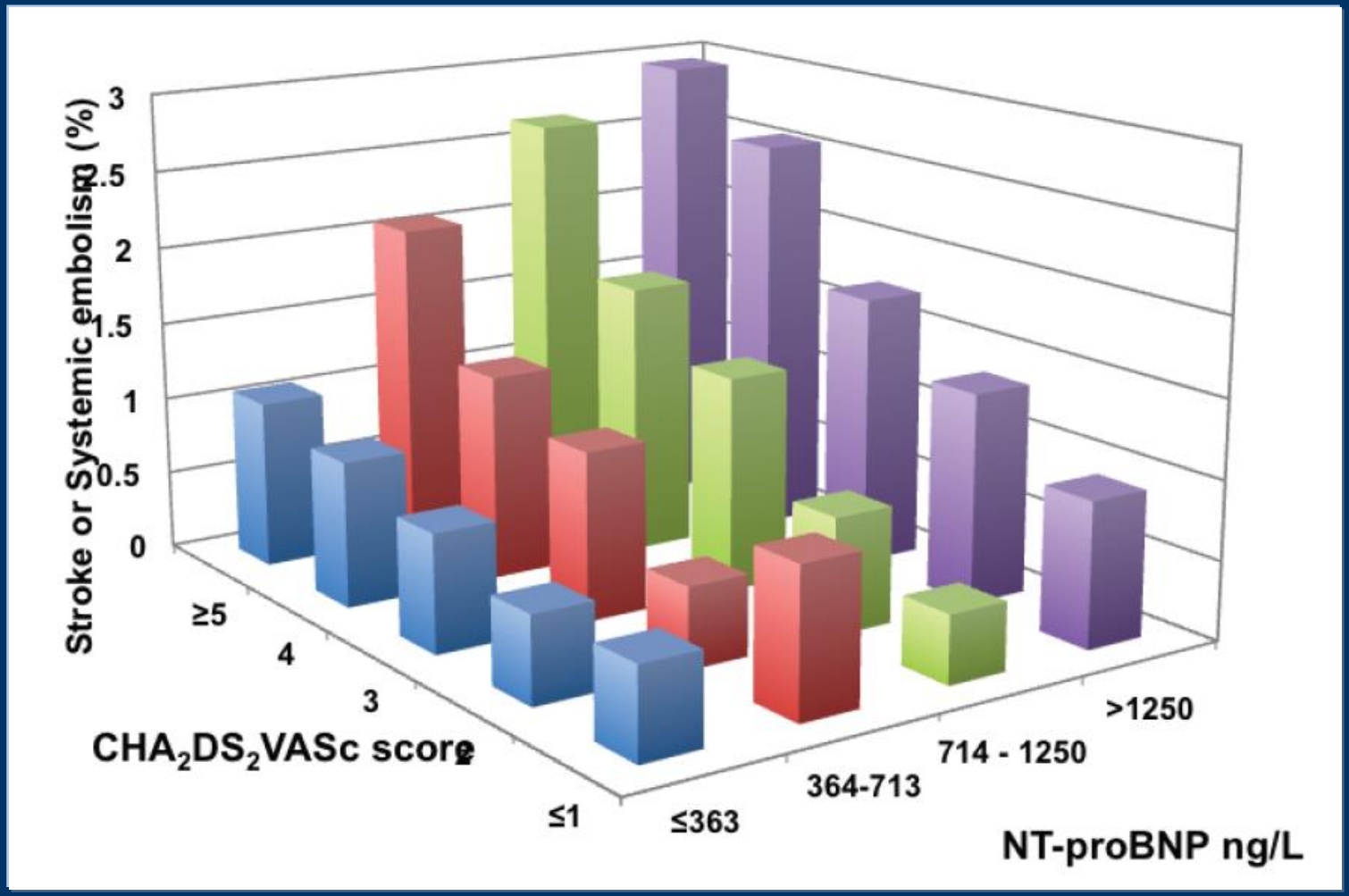
Advanced Imaging

- LA fibrosis
- LAA morphology



Calenda B et al. Nat Rev Cardiol. 2016 Sep;13(9):549-59

Biomarkers and Risk in A-Fib
By Quartiles of NT-proBNP and CHADS-VASc



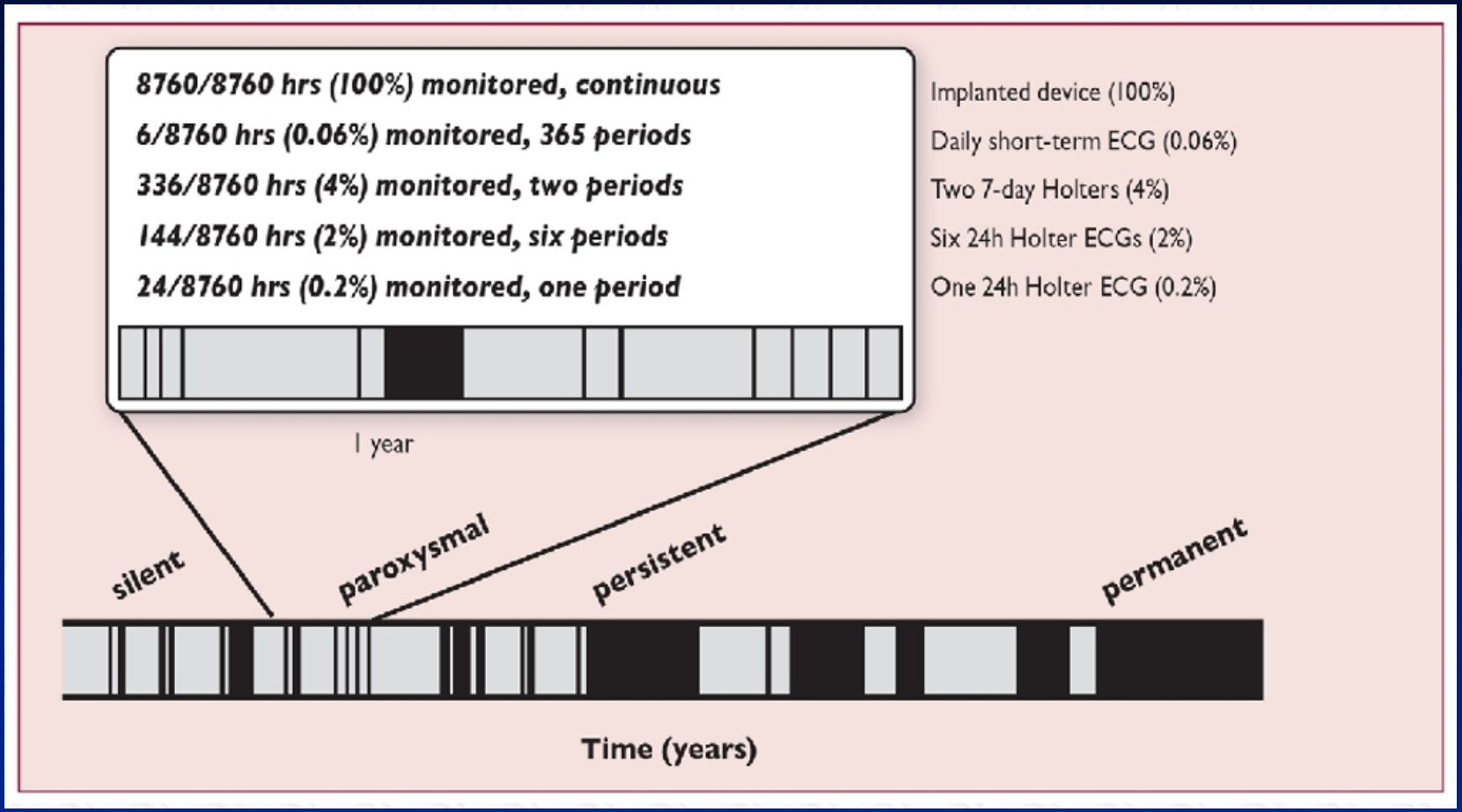
Hijazi Z. J Am Coll Cardiol 2013;61:2274-2284
Hijazi Z. Eur Heart J 2016;37:1582-1590

- **OUR PATIENTS CHADS2VASC SCORE**
  - **FEMALE 1**
  - **AGE 1**
  - **HTN 1**
  - **STROKE/TIA 2**

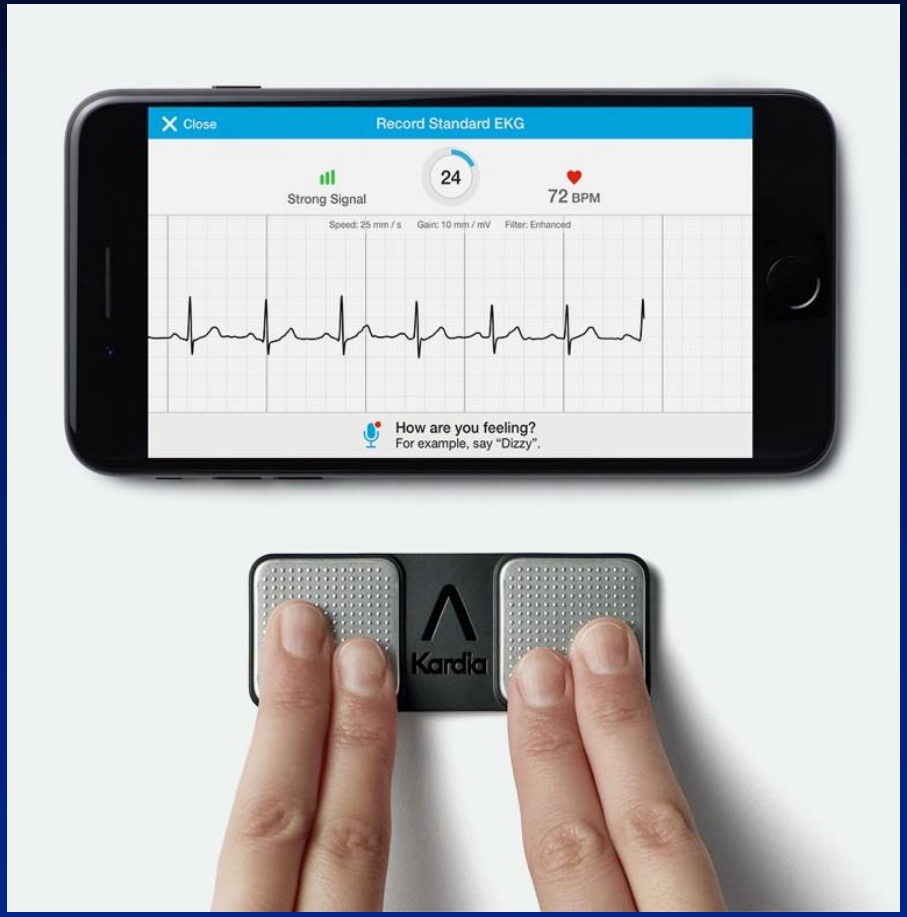
  - **SCORE 5**
  - **PATIENT STARTED ON DOACs**

SUBCLINICAL A-FIB

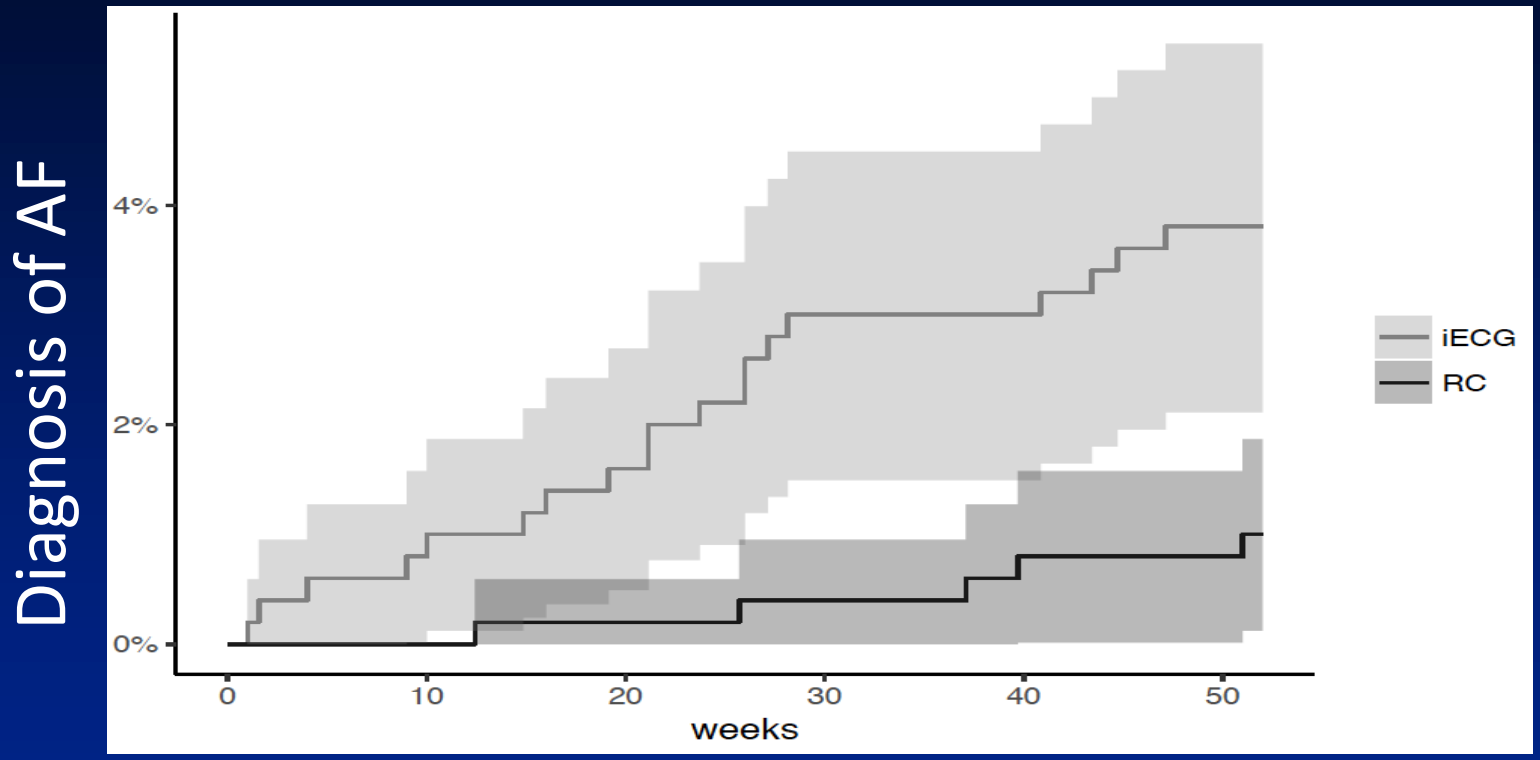
DIAGNOSTIC YIELD OF SCREENING TECHNIQUES



AliveCor Kardia Mobile



Diagnosis of AF

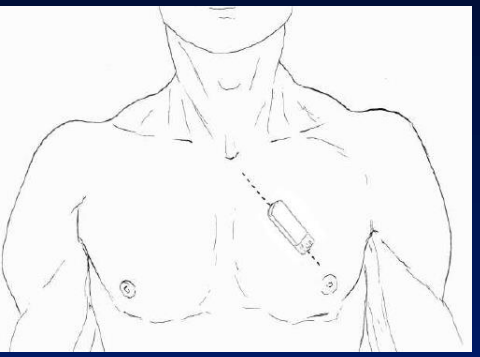


CRYSTAL-AF: Primary Objective

- **Assess whether a long-term cardiac monitoring strategy with an insertable cardiac monitor (ICM) is superior to standard monitoring for the detection of AF in patients with cryptogenic stroke**

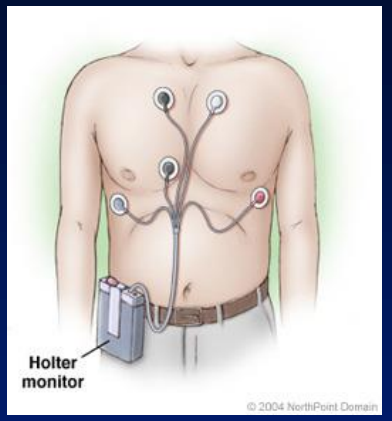
Comparison of Monitoring Strategies

Continuous Monitoring Arm: Insertion of REVEAL® XT

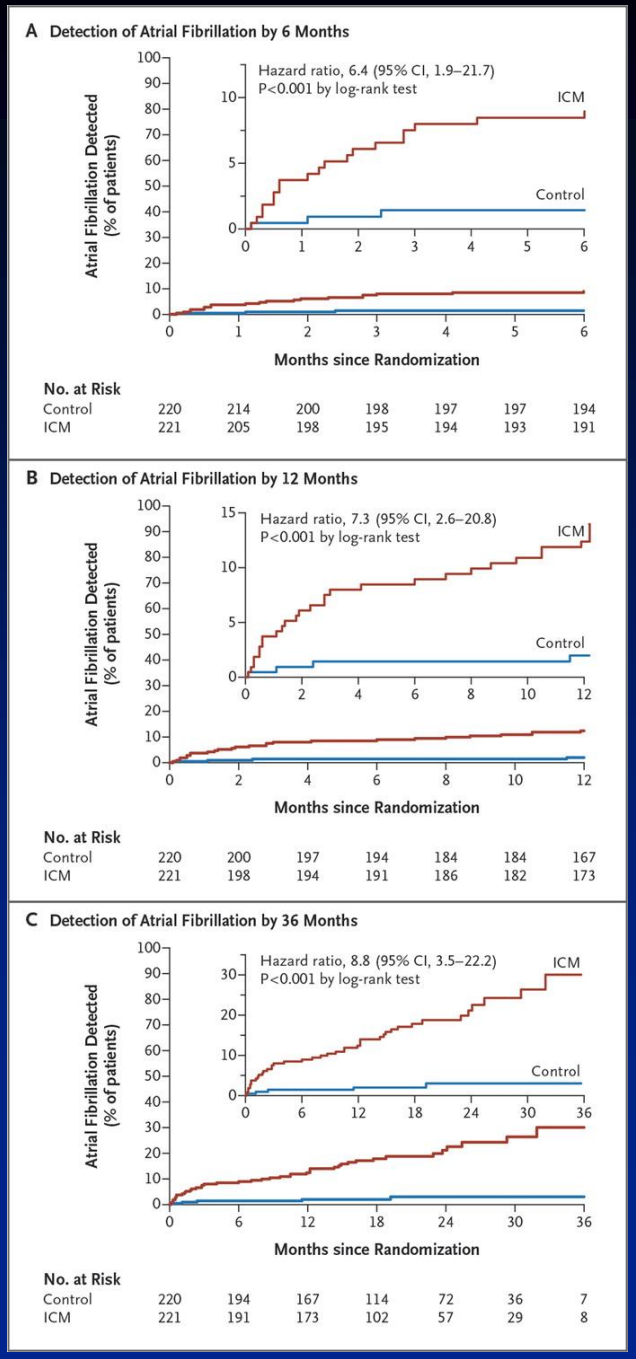


- Minimally invasive outpatient procedure
- Local anesthetic and no leads or fluoroscopy
- 15-30 minute procedure
- Device can be followed remotely
- MRI conditional
- 3 year device longevity
- Automatic AF detection algorithm

Standard Monitoring Arm



- Cardiac monitoring performed according to local standards, after mandated testing completed
- Symptoms consistent with AF were evaluated by study physicians


A Detection of Atrial Fibrillation by 6 Months
Hazard ratio, 6.4 (95% CI, 1.9–21.7)
P<0.001 by log-rank test
ICM
Control
Atrial Fibrillation Detected (% of patients)
Months since Randomization
No. at Risk
Control 220 214 200 198 197 197 194
ICM 221 205 198 195 194 193 191
B Detection of Atrial Fibrillation by 12 Months
Hazard ratio, 7.3 (95% CI, 2.6–20.8)
P<0.001 by log-rank test
ICM
Control
Atrial Fibrillation Detected (% of patients)
Months since Randomization
No. at Risk
Control 220 200 197 194 184 184 167
ICM 221 198 194 191 186 182 173
C Detection of Atrial Fibrillation by 36 Months
Hazard ratio, 8.8 (95% CI, 3.5–22.2)
P<0.001 by log-rank test
ICM
Control
Atrial Fibrillation Detected (% of patients)
Months since Randomization
No. at Risk
Control 220 194 167 114 72 36 7
ICM 221 191 173 102 57 29 8

Conclusions

- A-Fib detection of 30% in the ICM versus 3% in the control arm at 36 months
- Duration was more than 6 minutes on one or more days in > 94% of patients
- 89% of patients were prescribed OAC
- Majority of first AF episodes (75%) were asymptomatic
- 250 tests were required in order to find 5 patients with AF in the control arm
- Long-term continuous monitoring should be performed in patients with cryptogenic stroke

ASSERT STUDY

2580 PATIENTS WITH NO H/O A-FIB WITH ICD/PACEMAKER

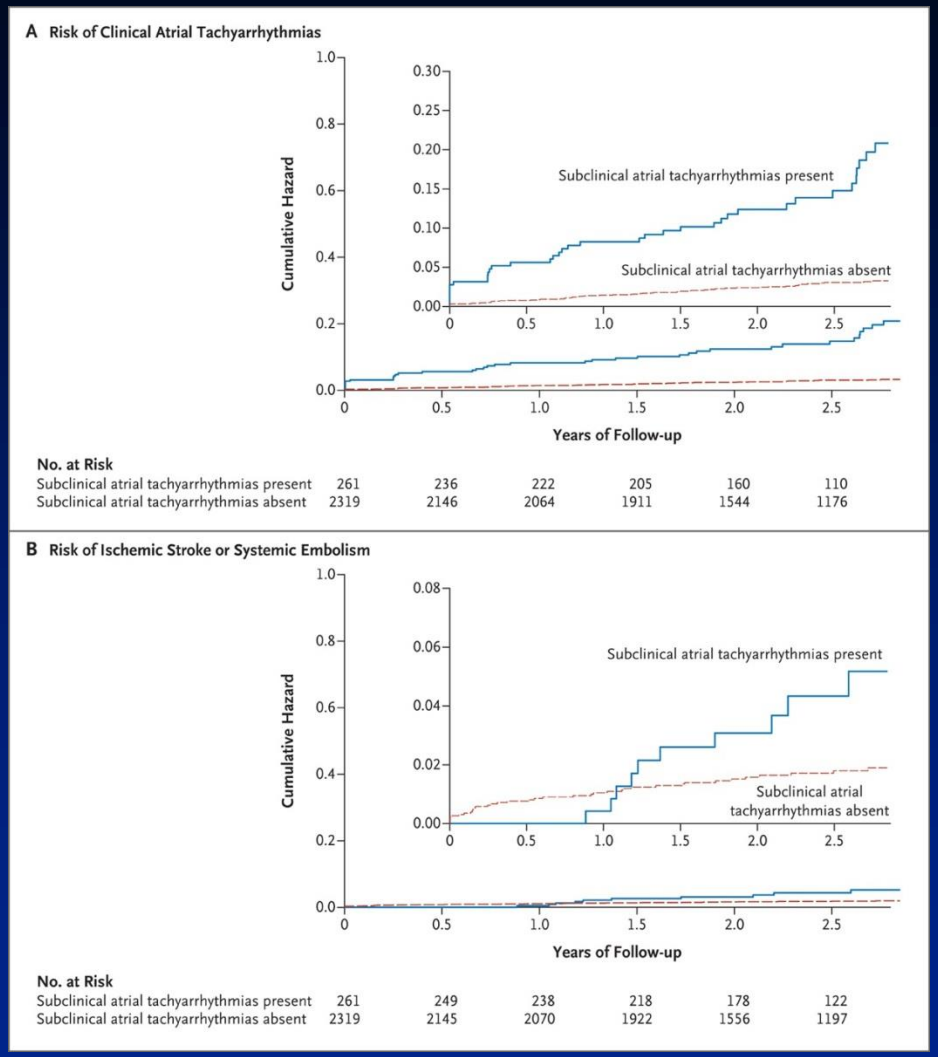
GROUP 1 N=261

ATRIAL FIBRILATION OF MORE THAN 6 MIN DURATION

GROUP 2 N=2319

NO ATRIAL FIBRILLATION NOTED

The Risk of Clinical Atrial Tachyarrhythmias and of Ischemic Stroke or Systemic Embolism, According to the Presence or Absence of Subclinical Atrial Tachyarrhythmias.

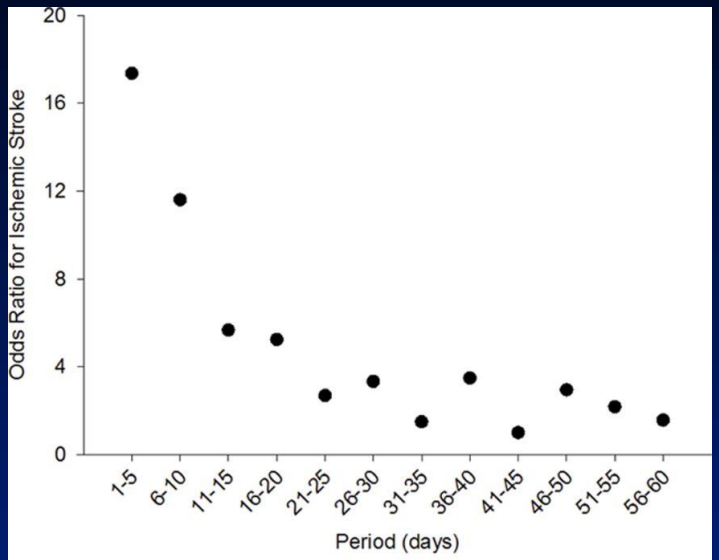


Healey JS et al. N Engl J Med 2012;366:120-129

TRENDS Study
A-FIB BURDEN AND RISK OF STROKE

AT/AF Burden Subset	Annualized TE Rate (95% CI), %	Annualized TE Rate Excluding TIAs (95% CI), %
Zero AT/AF burden	1.1 (0.8–1.6)	0.5 (0.3–0.9)
Low AT/AF burden (<5.5 h)	1.1 (0.4–2.8)	1.1 (0.4–2.8)
High AT/AF burden (5.5 h)	2.4 (1.2–4.5)	1.8 (0.9–3.8)

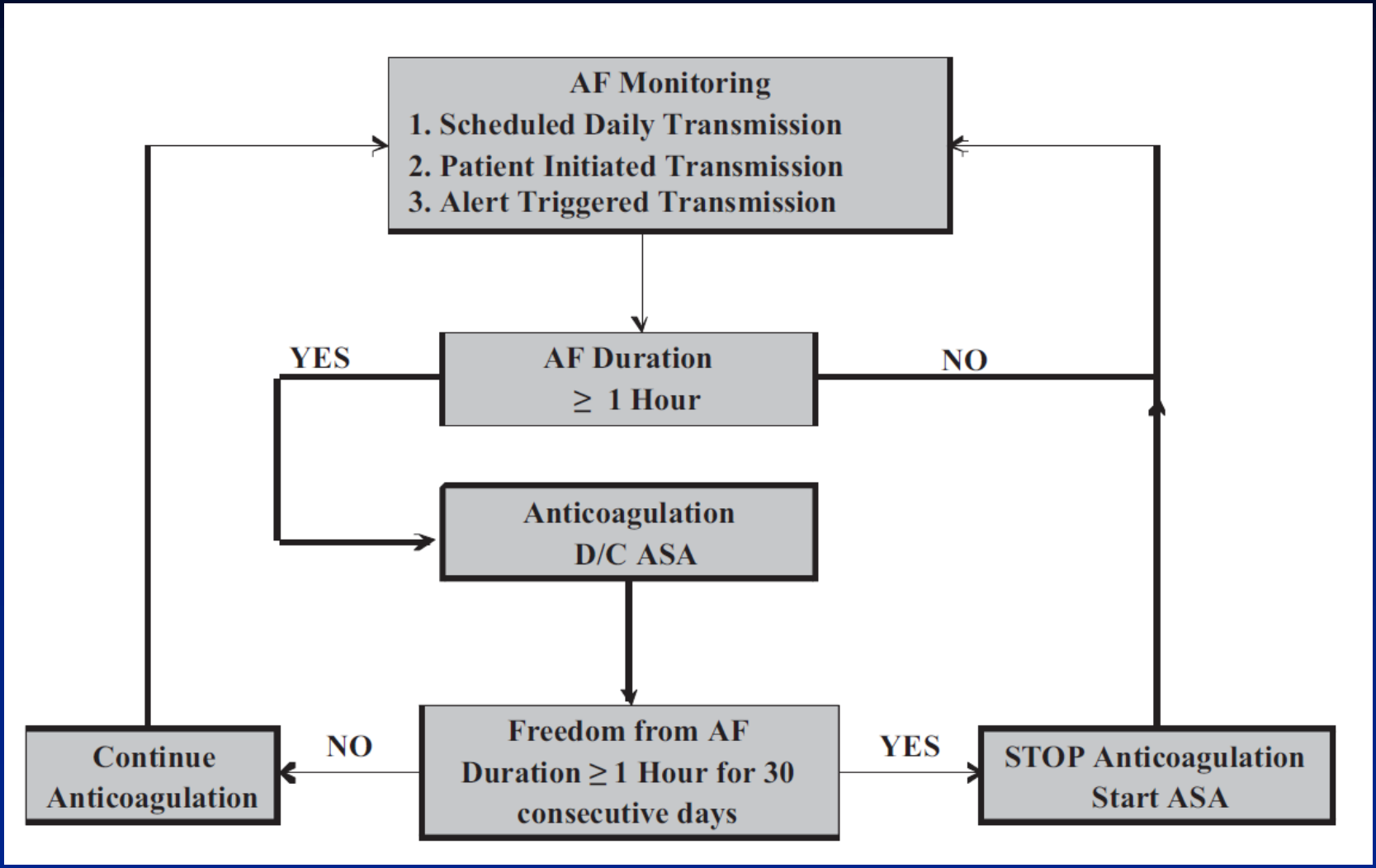
Crude odds ratios for ischemic stroke with positive atrial fibrillation (A-Fib) burden (≥5.5 h on any given day) for sequential nonoverlapping 5-d intervals from 1 to 5 days pre stroke (left-most point) to 56–60 days pre stroke (right-most point)



Period, days prior to stroke	Odds Ratio	95% Confidence Interval	P Value
1-5	17.4	5.39 - 73.1	<.0001
6-10	11.6	3.30 - 51.4	<.0001
11-15	5.66	1.65 - 20.5	0.0046
16-20	5.24	1.60 - 17.5	0.0053
21-25	2.68	0.689 - 9.63	0.1683
26-30	3.33	0.934 - 11.3	0.0647
31-35	1.49	0.296 - 6.06	0.7632
36-40	3.49	0.946 - 12.6	0.0615
41-45	1.00	0.160 - 4.68	1.0000
46-50	2.95	0.709 - 11.3	0.1476
51-55	2.18	0.470 - 8.52	0.3630
56-60	1.56	0.275 - 6.84	0.7445

Mintu P. Turakhia et al. Circ Arrhythm Electrophysiol. 2015;8:1040-1047

REACT.AF


AF Monitoring
1. Scheduled Daily Transmission
2. Patient Initiated Transmission
3. Alert Triggered Transmission
YES
AF Duration
≥ 1 Hour
NO
Anticoagulation
D/C ASA
Freedom from AF
Duration ≥ 1 Hour for 30
consecutive days
NO
YES
Continue
Anticoagulation
STOP Anticoagulation
Start ASA

AFTER ONE YEAR…

- PATIENT HAS DONE WELL ON ANTICOAGULATION
- SLEEP STUDY NEGATIVE
- BP UNDER CONTROL ON B-BLOCKERS AND ACE-I
- PRESENTS TO YOUR OFFICE WITH PALPITATIONS
- CLINICALLY NO SIGNS OF CHF
- ECG
  - A-FIB WITH HR 121

- RATE CONTROL AND CONTINUE ANTICOAGULATION
- CARDIOVERT AND START ANTIARRYTHMICS
- CARDIOVERT AND ABLATION

CARDIOVASCULAR MORBIDITY AND MORTALITY WITH A-FIB

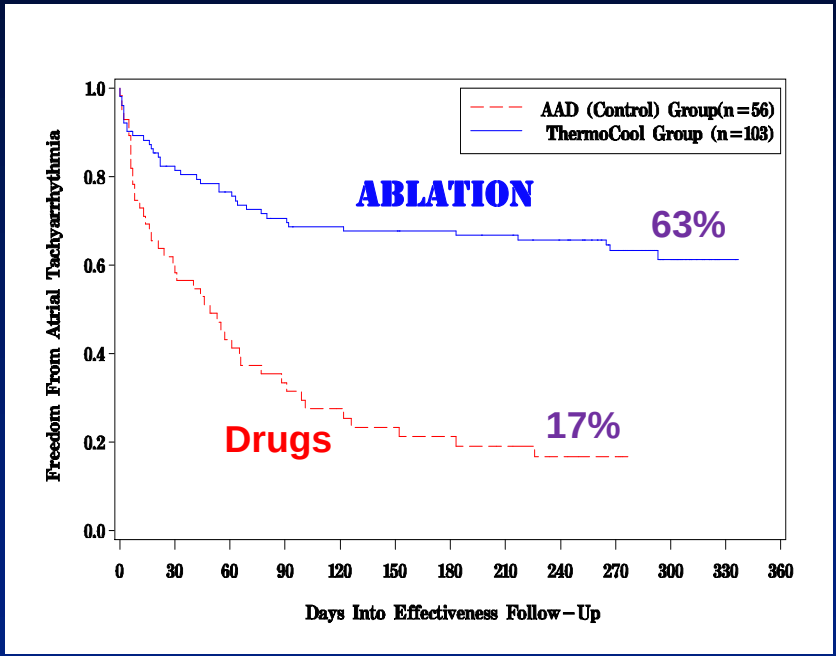
Event	Association with AF
Death	Increased mortality, especially cardiovascular mortality due to sudden death, heart failure or stroke.
Stroke	20–30% of all strokes are due to AF. A growing number of patients with stroke are diagnosed with 'silent', paroxysmal AF.
Hospitalizations	10–40% of AF patients are hospitalized every year.
Quality of life	Quality of life is impaired in AF patients independent of other cardiovascular conditions.
Left ventricular dysfunction and heart failure	Left ventricular dysfunction is found in 20–30% of all AF patients. AF causes or aggravates LV dysfunction in many AF patients, while others have completely preserved LV function despite long-standing AF.
Cognitive decline and vascular dementia	Cognitive decline and vascular dementia can develop even in anticoagulated AF patients. Brain white matter lesions are more common in AF patients than in patients without AF.

Category	Intervention	Follow-up aspects	Performance indicator (examples)
Prognostic	Comorbidity control (relevant examples given)	Obesity Arterial hypertension Heart failure Coronary artery disease Diabetes Valvular heart disease	Weight loss Blood pressure control Heart failure therapy and hospitalizations Statin and antiplatelet therapy; revascularization Glycaemic control Valve repair or replacement
Prognostic	Anticoagulation	Indication (risk profile; timing, e.g. post-cardioversion). Adherence (NOAC or VKA) and INR (if VKA). NOAC dosing (co-medications; age; weight; renal function).	Stroke Bleeding Mortality
Mainly symptomatic Partly prognostic	Rate control	Symptoms Average resting heart rate <110 bpm	Modified EHRA score Heart failure status LV function Exercise capacity Hospitalization Therapy complications
Symptomatic at present	Rhythm control	Symptoms vs. side effects Exclusion of pro-arrhythmia (PR; QRS; QTc interval)	
Relevant for implementation of therapy and adherence	Patient education and self-care capabilities	Knowledge (about disease; about treatment; about management goals) Capabilities (what to do if...)	Adherence to therapy Directed evaluation, preferably based on systematic checklists
Relevant for chronic care management	Caregiver involvement	Who? (spouse; GP; home nurse; pharmacist) Clearly spelling out participation roles Knowledge and capabilities	Directed evaluation of task performance (e.g. via patient card) Dispensed medication Log of follow-up visits

Success of Catheter Ablation

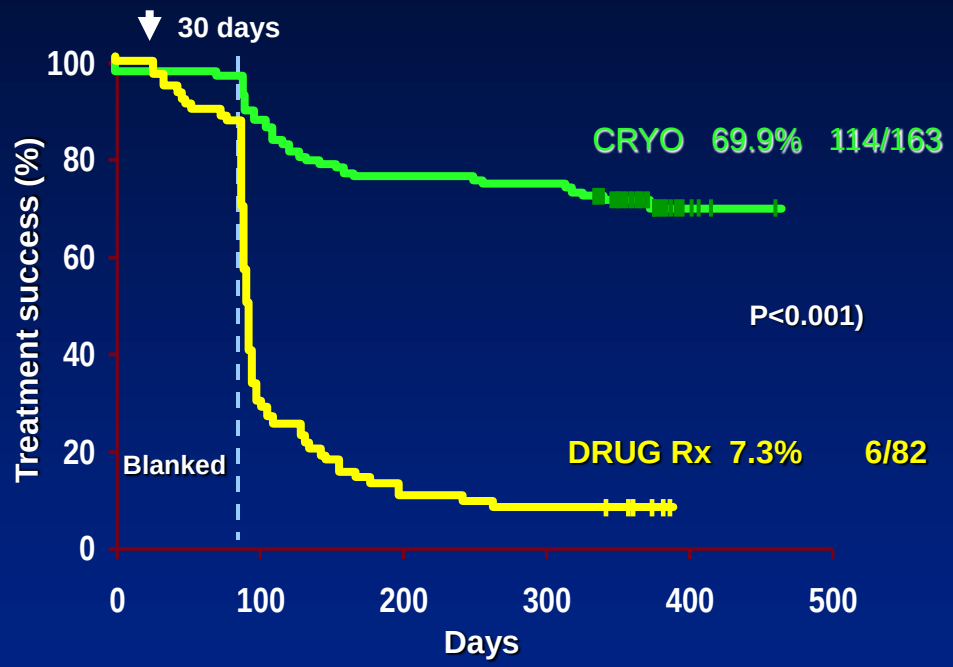
Multicenter RCTs: Ablation *vs* Medications

Thermocool IDE: RF Ablation



Wilber et al, *JAMA*, 2010

STOP-AF: Cryoballoon

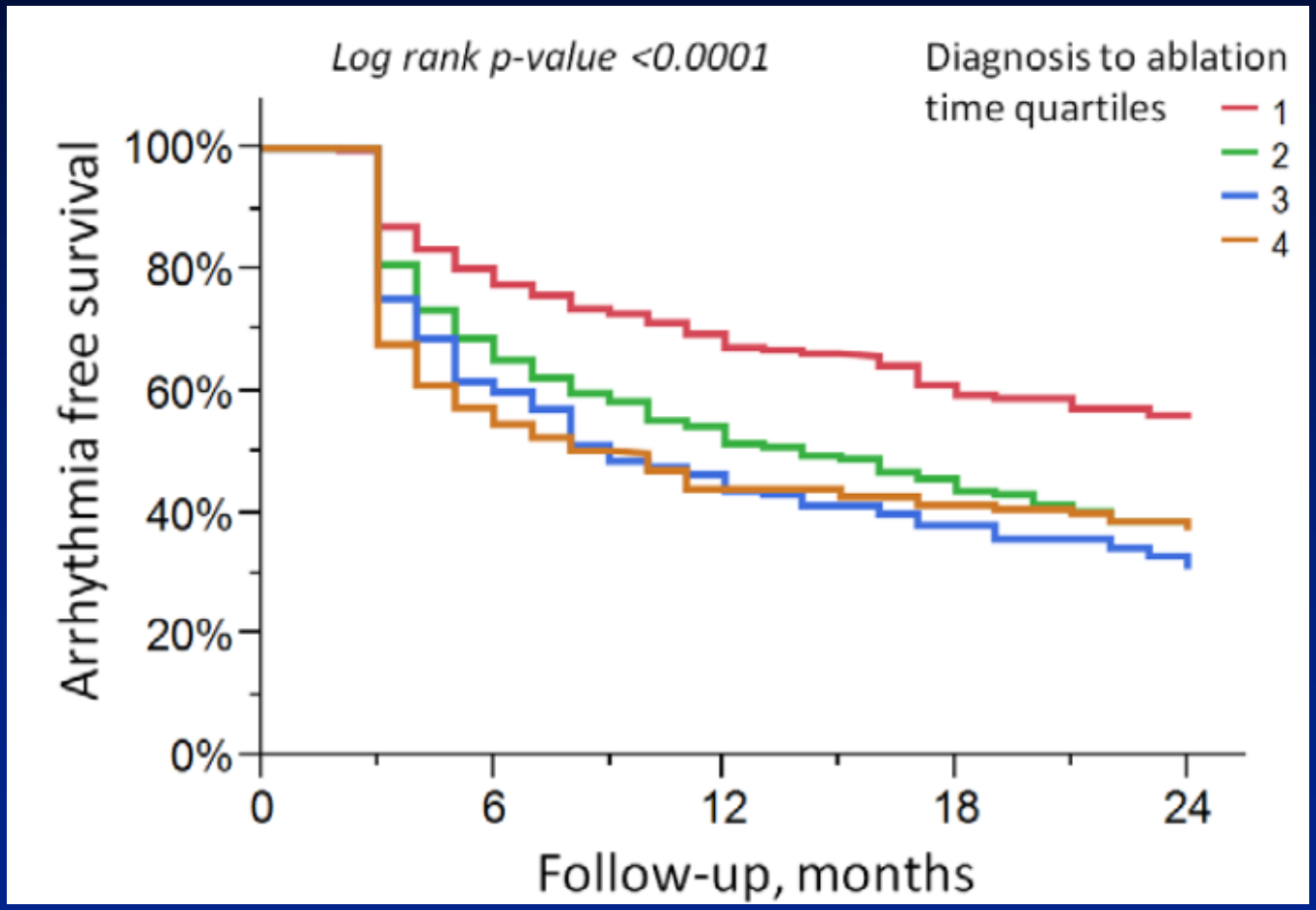


Packer et al, *JACC*, 2013

Outcome of Persistent AF Ablation

Effect of Time Between Diagnosis and Ablation

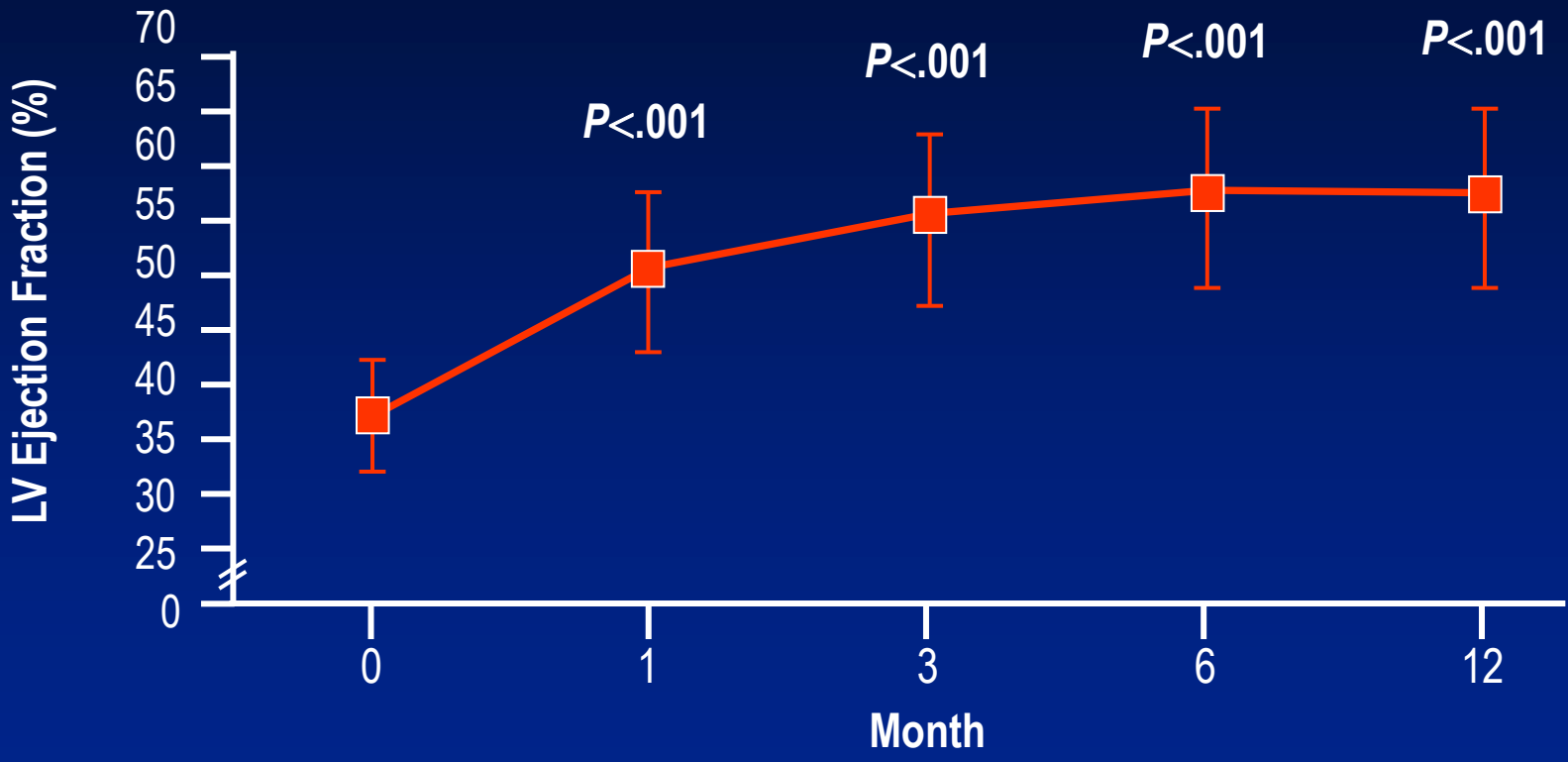
Time Interval Between the 1st Diagnosis of Persistent A-Fib and the Ablation Procedure



AA.Hussein et al, *Circ Arry* (2016) doi:10.1161/CIRCEP.115.003669

A-Fib Ablation in LV Dysfunction Patients

Improvement in LV Function

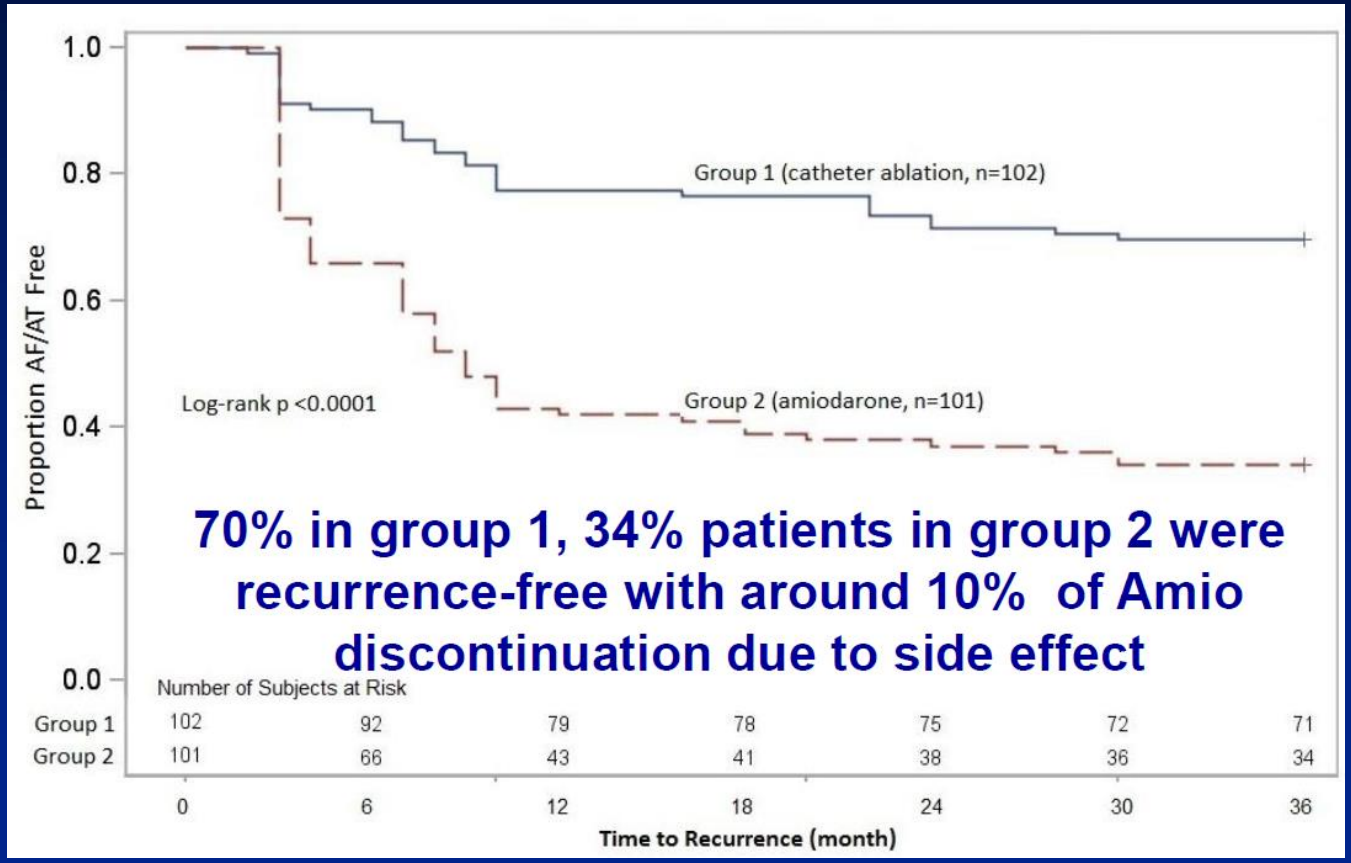


Hsu et al. *N Engl J Med*. 2004;351:2373-2383

AATAC-AF

Ablation *vs* Amiodarone in CHF-AF Patients

- ICD/CRTD patients with LVEF≤40%, NYHA II-III, Persistent AF
- Randomized 203 patients (1:1)
- Primary Endpoint: Freedom from AF/AFL/AT of >30sec off AAD



L.DiBiase, P.Mohanty, S.Mohanty, et al. *Circulation* (2016)

AATAC-AF: Secondary Endpoints Cardiovascular Hospitalization & Mortality

	Group 1 Ablation	Group 2 Amio	p value
CV Hospitalization	32 (31%)	58 (57%)	< 0.001
All-Cause Mortality	8 (8%)	18 (18%)	0.037

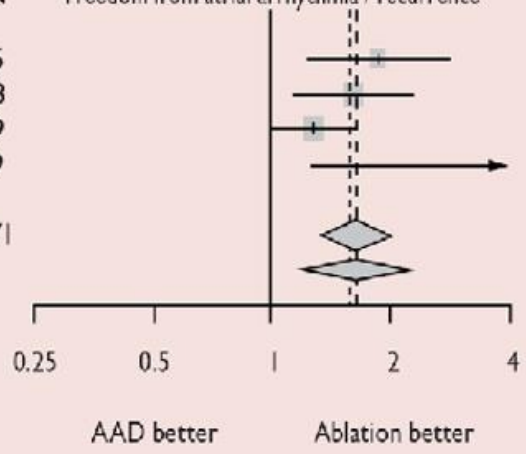
L.DiBiase, P.Mohanty, S.Mohanty, et al. *Circulation* (2016)

ABLATION VS CVN+AAD

Freedom from recurrence of atrial fibrillation or atrial arrhythmias, comparing catheter ablation with antiarrhythmic drug therapy in patients with persistent or long-standing persistent atrial fibrillation

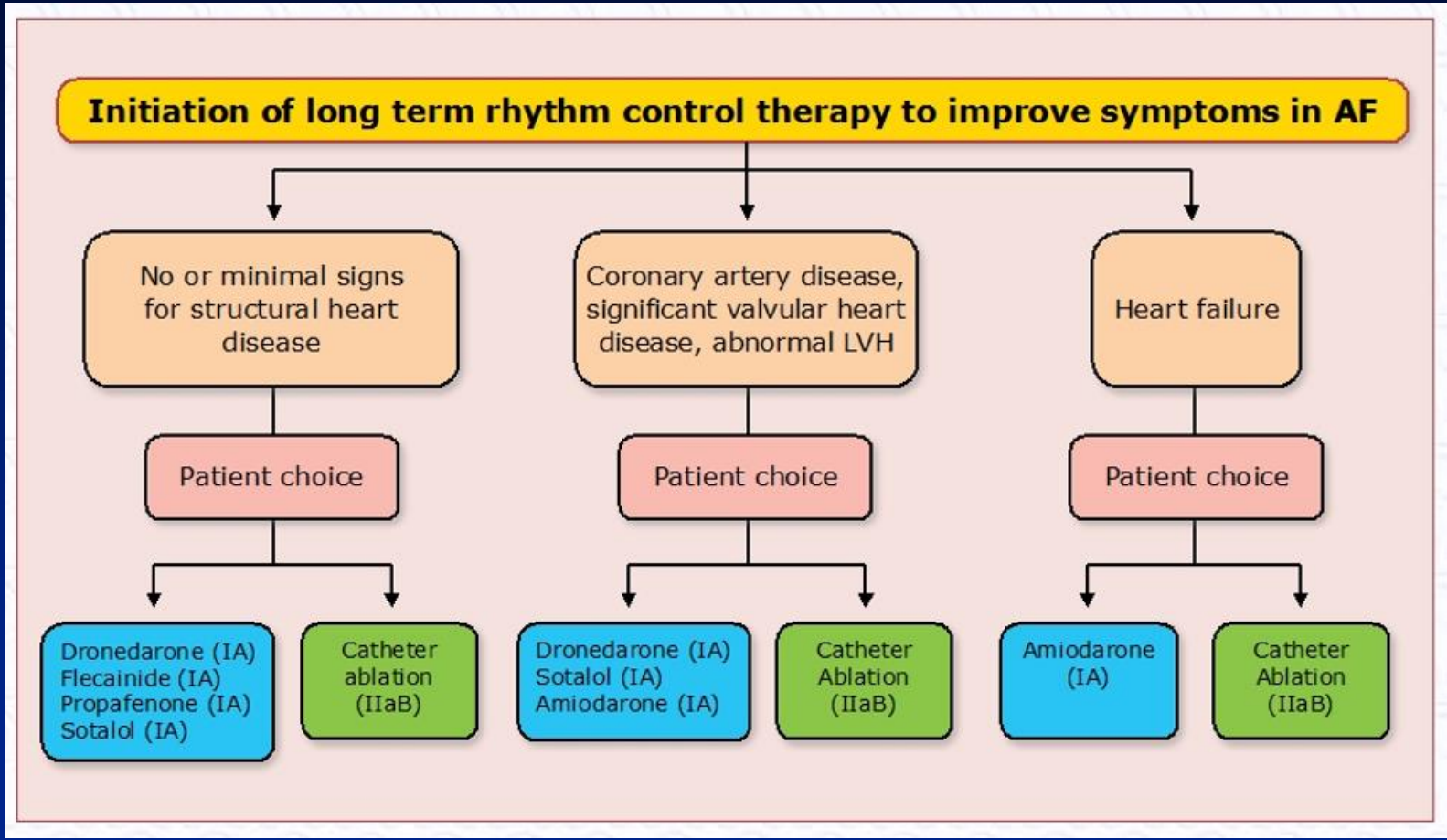
Study	Ablation Events	Ablation N	AAD Events	AAD N	RR	95% CI	W(fixed)	W(random)
Forleo	28	35	15	35	1.87	[1.23; 2.83]	17.5%	27.7%
Mont 2009	69	98	21	48	1.61	[1.14; 2.27]	32.8%	32.0%
Oral 2006	57	77	40	69	1.28	[1.00; 1.62]	49.1%	38.9%
Stabile 2006	13	26	0	19	20.00	[1.26; 319.89]	0.7%	1.4%
Fixed effects model		236		171	1.61	[1.34; 1.94]	100%	-
Random effects model					1.59	[1.14; 2.22]	-	100%

Heterogeneity: I-squared = 58,9%, p= 0.063



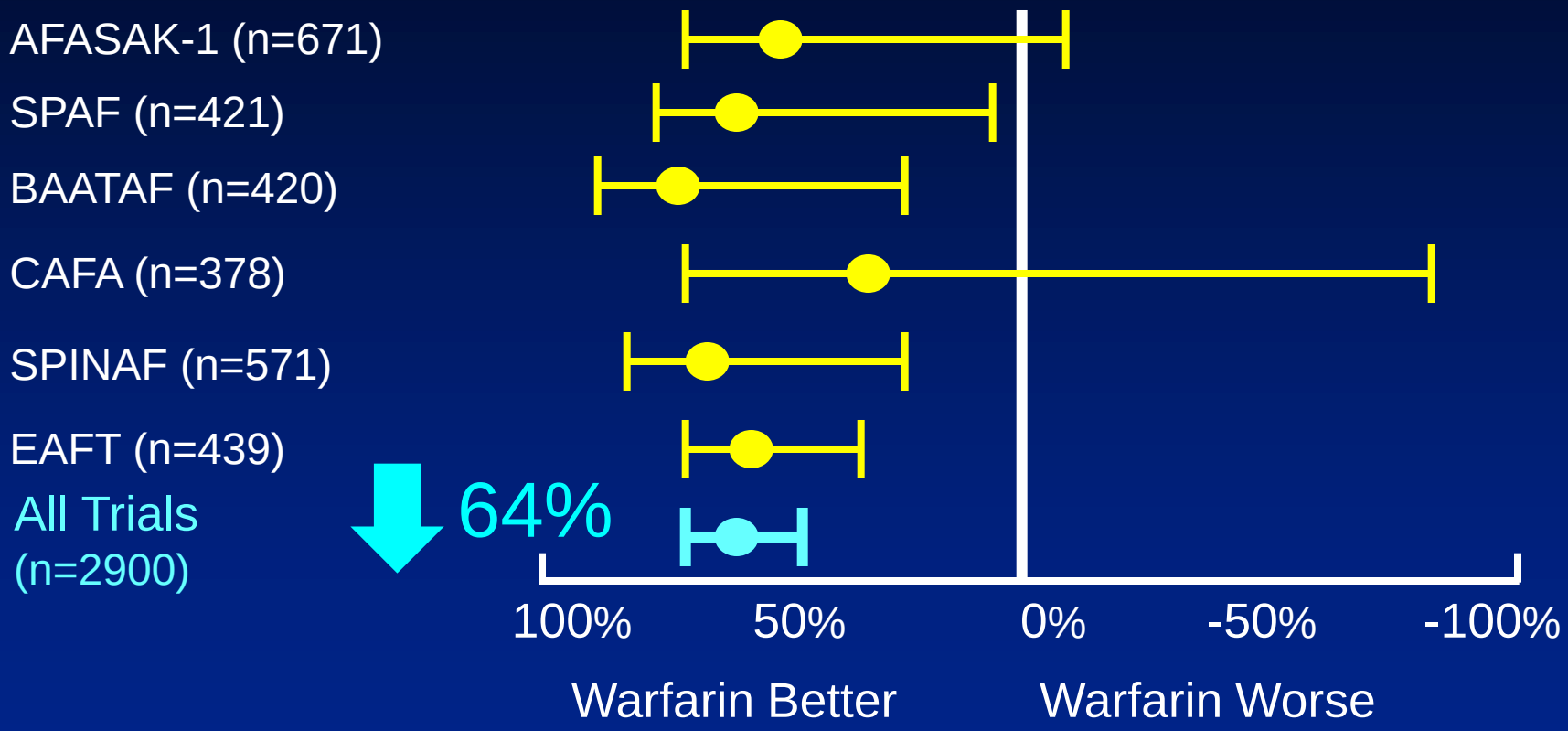
AAD = antiarrhythmic drug therapy; CI = confidence interval; N = number of patients; RR = risk ratio; W = study weighting.

SYMPTOMATIC PATIENTS RHYTHM CONTROL STRATEGY



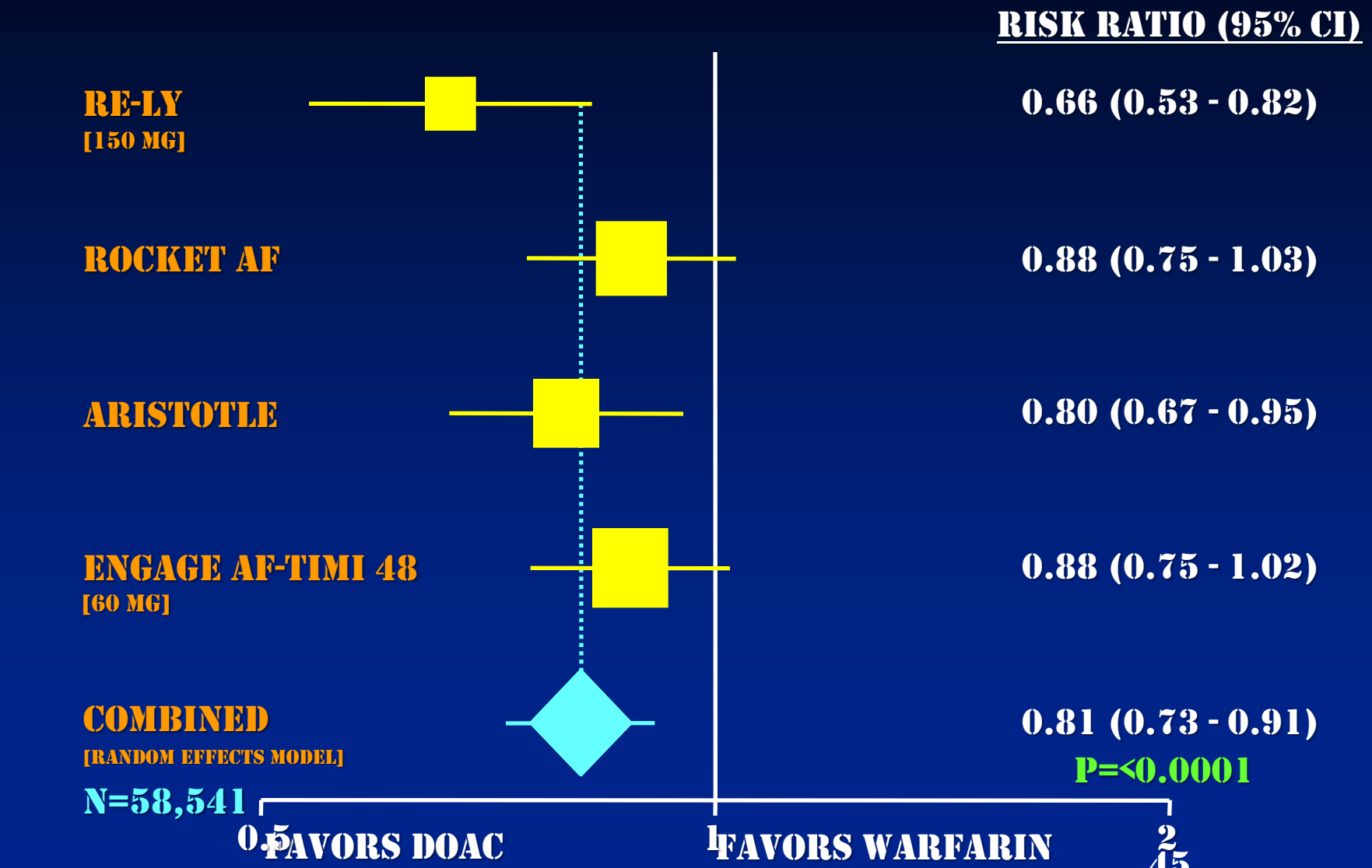
- PATIENT UNDERWENT ABLATION
- MAINTAINED IN SINUS RHYTHM ON DOACs
- 2 YEARS LATER
- COMES TO ER WITH GI BLEED HB 8 g/dL
- EGD NL
- COLON DIVERTICULOSIS
- NSR
- DOACs held for 2 weeks
  - Restart anticoagulation
  - Consider LAAC

Stroke Prevention in AF
6 Trials of Warfarin vs. Placebo



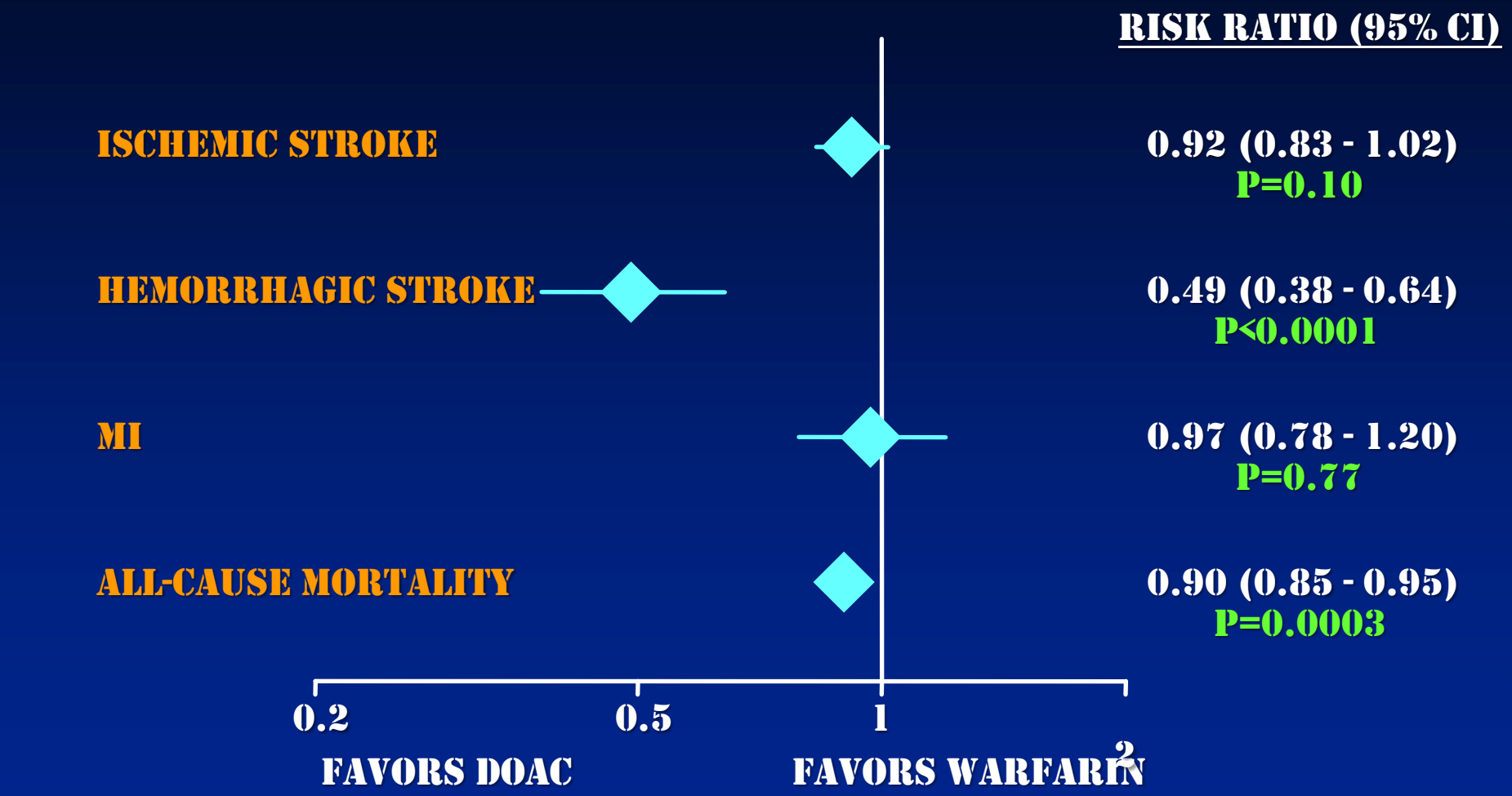
HART RG. ANN INTERN MED 2007;146:857-867.

All DOACS: Stroke or SEE



RUFF CT, ET AL. LANCET 2014;383:955-962

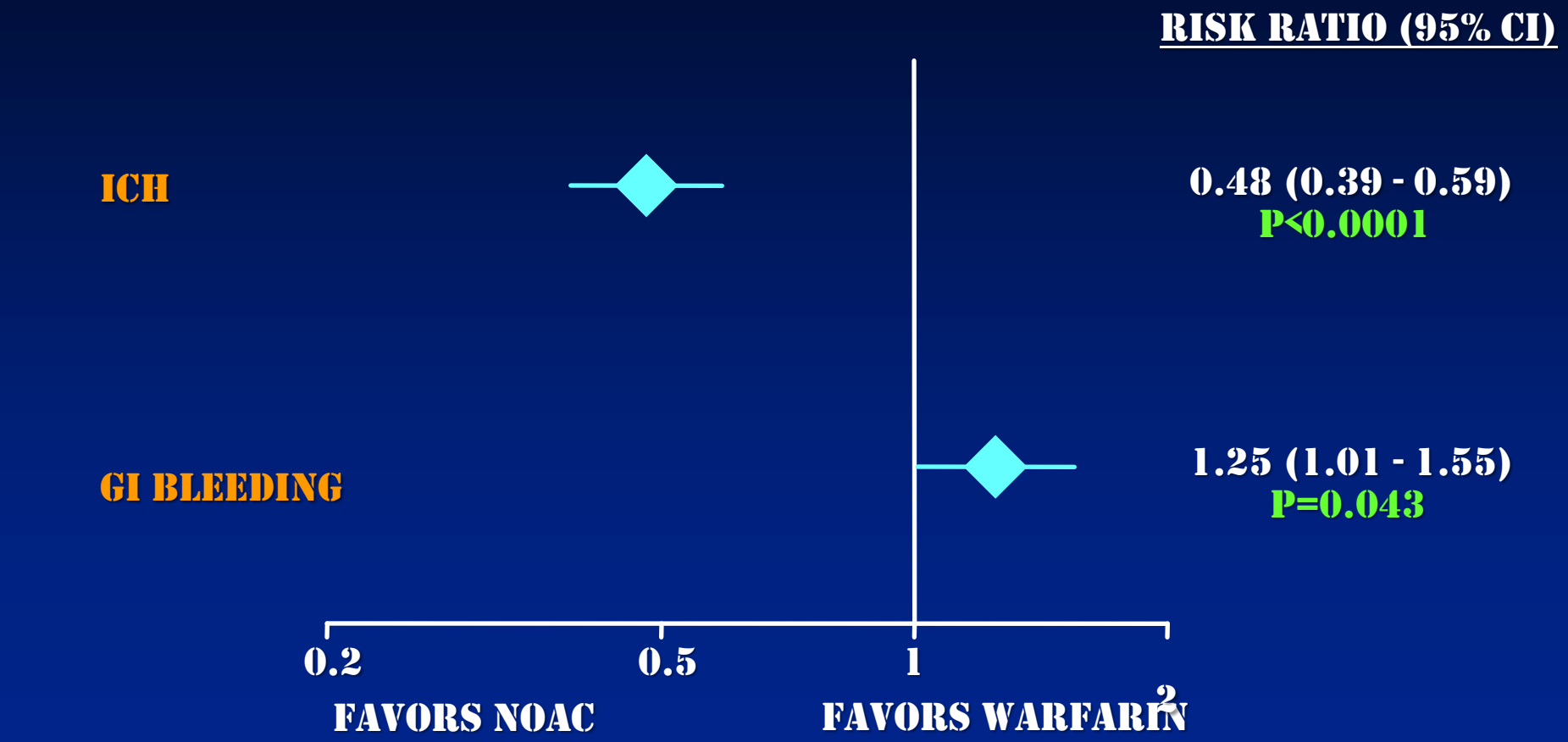
Secondary Efficacy Outcomes



HETEROGENEITY P=NS FOR ALL OUTCOMES

RUFF CT, ET AL. LANCET 2014;383:955-962

Secondary Safety Outcomes



HETEROGENEITY
ICH, P=0.22
GI BLEEDING, P=0.009

RUFF CT, ET AL. LANCET 2014;383:955-962

HAS-BLED Score

Letter	Clinical Characteristic	Points Awarded
H	Hypertension	1
A	Abnormal renal &/or liver function (1 point each)	1 or 2
S	Stroke history	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (age ≥ 65)	1
D	Drugs or alcohol (1 point each)	1 or 2
	Maximum score	**9**

Hypertension = systolic BP≥160 mmHg; Abnormal renal function = presence of chronic dialysis or renal transplantation or serum creatinine≥200μmol/L; Abnormal liver function = chronic hepatitis disease (e.g., cirrhosis) or biochemical evidence of significant hepatic derangement (e.g., bilirubin>2x upper limit of normal, in association with AST/ALP/ALP>3x upper limit normal, etc.); Bleeding = previous bleeding history or predisposition to bleeding (e.g., bleeding diathesis, anemia, etc.); Labile INRs = unstable/high INRs or poor time in therapeutic range (e.g., <60%); Drugs or alcohol = concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatories, or alcohol abuse, etc.; INR = international normalized ratio

Annual Adjusted Bleeding Rate

0 points = 1.13%
1 point = 1.02%
2 points = 1.88%
3 points = 3.74%
4 points = 8.70%
5 points = 12.50%
Any score = 1.56%

ATRIA Score

	Clinical Characteristic	Points Awarded
	Anemia	3
	Severe renal disease	3
	Age ≥ 75	2
	Bleeding history	1
	Hypertension	1
	Maximum score	**10**

Severe renal disease = glomerular filtration rate <30ml/min or dialysis-dependent
ATRIA = Anticoagulation and Risk Factors in Atrial Fibrillation
0 – 3 points = low risk
4 points = intermediate risk
5 – 10 points = high risk
Annual Adjusted Bleeding Rate
0 – 3 points = 0.8%
4 points = 2.6%
≥ 5 points = 5.8%

HEMORR2HAGES Score

	Clinical Characteristic	Points Awarded
H	Hepatic or renal disease	1
E	Ethanol abuse	1
M	Malignancy	1
O	Older (age >75)	1
R	Reduced platelet count or fxn	1
R_2	Rebleeding risk	2
H	Hypertension (uncontrolled)	1
A	Anemia	1
G	Genetic factors	1
E	Excessive fall risk*	1
S	Stroke	1
	Maximum score	**12**

*Including neuropsychiatric disease
0 – 1 points = low risk
2 – 3 points = intermediate risk
≥4 points = high risk

Annual Adjusted Bleeding Rate
0 points = 1.9%
1 point = 2.5%
2 points = 5.3%
3 points = 8.4%
4 points = 10.4%
≥ 5 points = 12.3%

Outpatient Bleeding Risk Index (OBRI)

	Clinical Characteristic	Points Awarded
	Age ≥ 65 years	1
	History of GI bleeding	1
	History of stroke	1
	One or more comorbid conditions	1
	Maximum score	**4**

Comorbid conditions = recent MI, anemia (hematocrit <30%), renal impairment (creatinine level >1.5mg/dL), or diabetes mellitus
0 points = low risk
1 – 2 points = intermediate risk
≥3 points = high risk

Modifiable bleeding risk factors:
Hypertension (especially when systolic blood pressure is >160 mmHg)
Labile INR or time in therapeutic range <60% in patients on vitamin K antagonists
Medication predisposing to bleeding, such as antiplatelet drugs and non-steroidal anti-inflammatory drugs
Excess alcohol (≥8 drinks/week)
Potentially modifiable bleeding risk factors:
Anaemia
Impaired renal function
Impaired liver function
Reduced platelet count or function

Non-modifiable bleeding risk factors:
Age (>65 years) (≥75 years)
History of major bleeding
Previous stroke
Dialysis-dependent kidney disease or renal transplant
Cirrhotic liver disease
Malignancy
Genetic factors
Biomarker-based bleeding risk factors:
High-sensitivity troponin
Growth differentiation factor-15
Serum creatinine/estimated CrCl

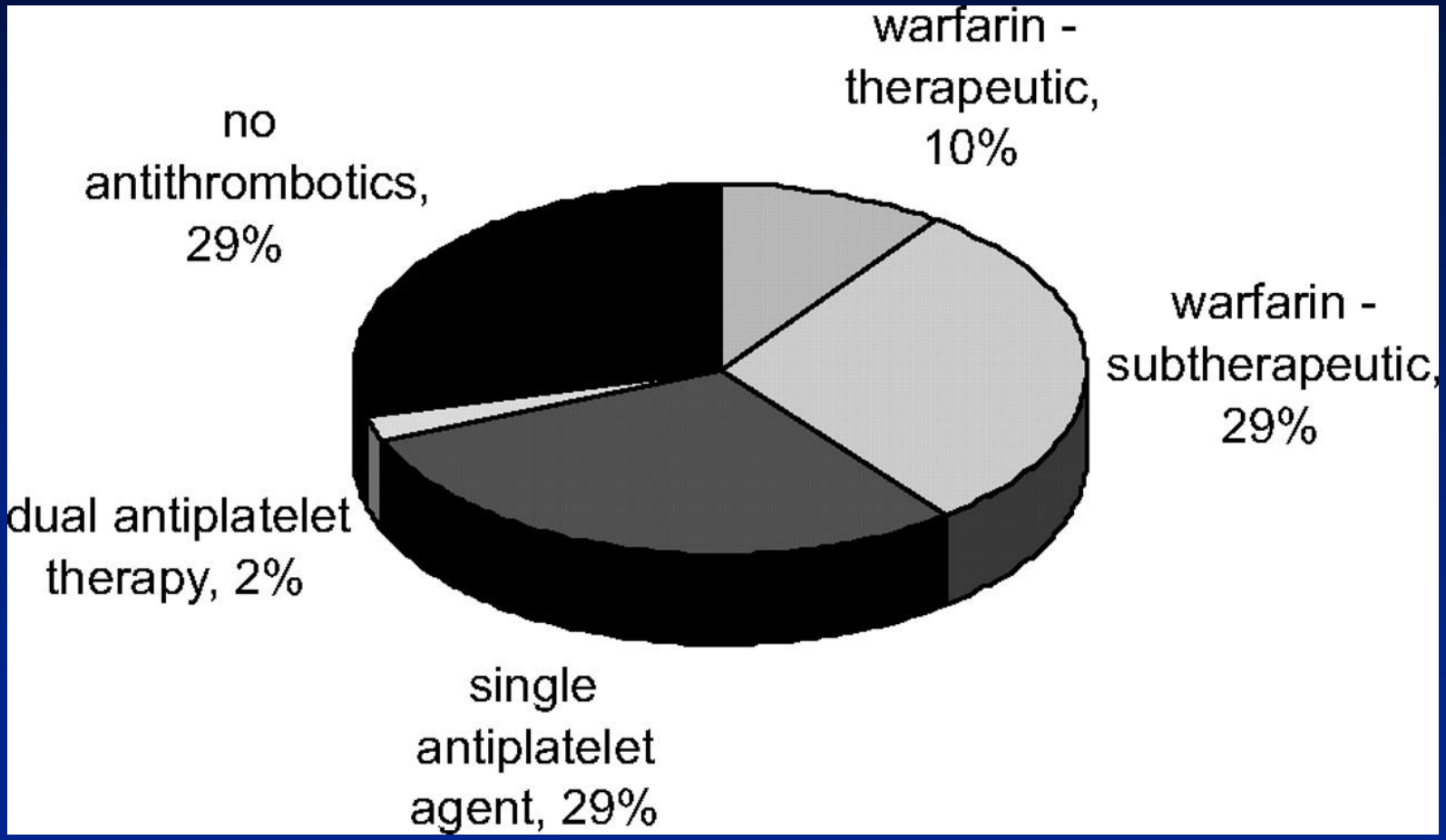
When to close LAA?

Non valvular A-Fib, high risk of stroke

- Contraindication to OAC
- High risk of bleeding with OAC
- Difficult to maintain INR within the therapeutic range
- Poor compliance/intolerance to DOACs
- Recurrence on anticoagulation

Preadmission medications in patients with known A-Fib who were admitted with acute ischemic stroke

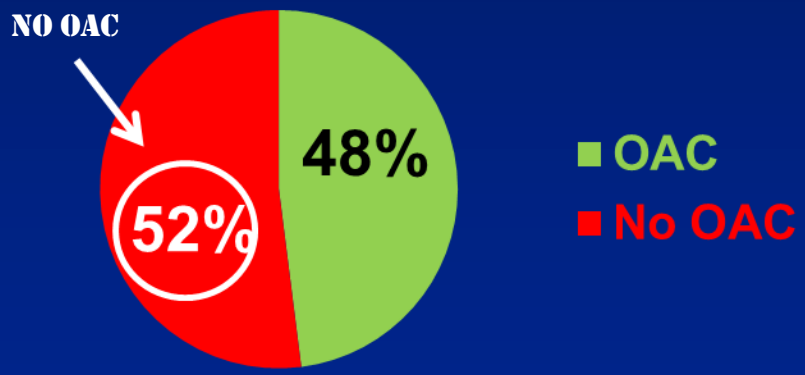
GLADSTONE ET AL STROKE 2009



"Shocking Level" of OAC Undertreatment in A-Fib Patients at High Risk for Stroke

PINNACLE Registry
(N=429,417 outpatients with AF[a])

Most AF Patients at High Risk of Stroke Do Not Receive OAC Therapy!



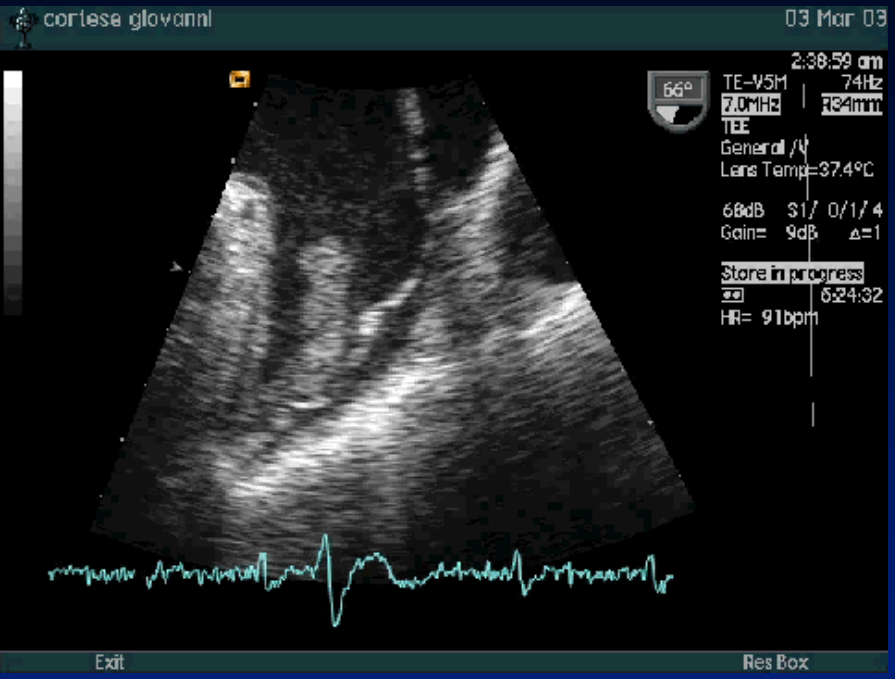
Why???

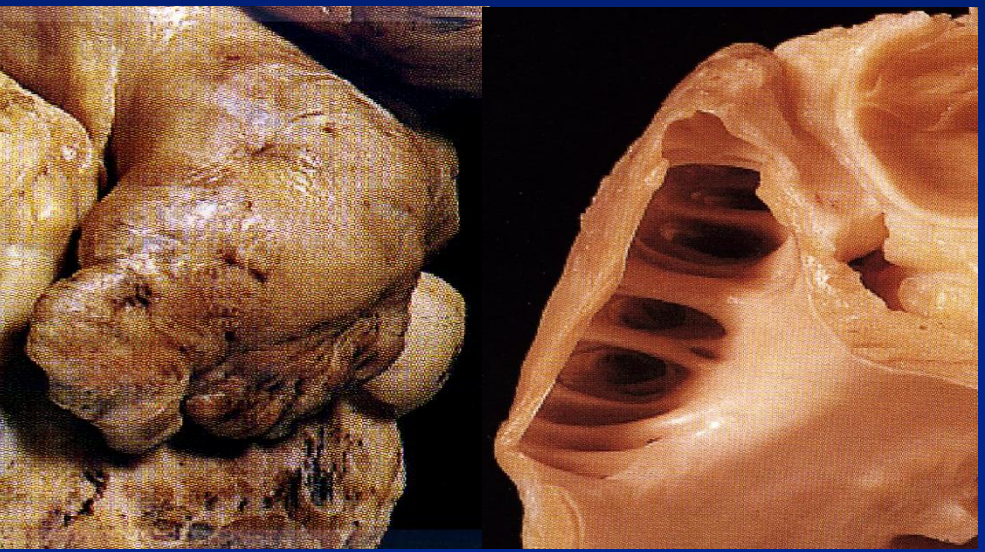
- *"HCPs may be more reluctant to prescribe anticoagulation in sicker patients due to concerns regarding bleeding risk."*
  - >2000 strokes/y could have been prevented if OAC therapy was used

A TREATED BY CARDIOVASCULAR SPECIALISTS

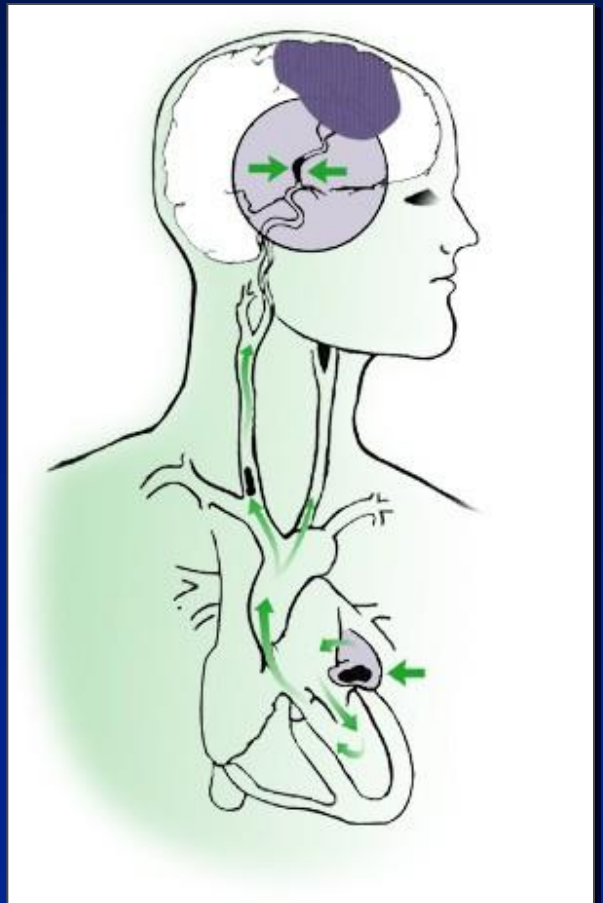
HSU JC ET AL. JAMA CARDIOL. 2016 MAR 16. [EPUB AHEAD OF PRINT]

STROKE IN A-FIB

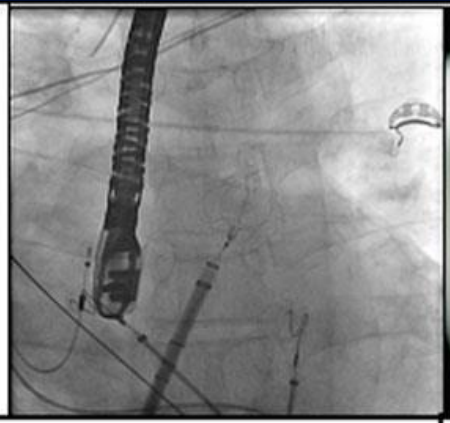




- Stroke in patients with A-Fib is largely due to the LAA as a thromboembolic source

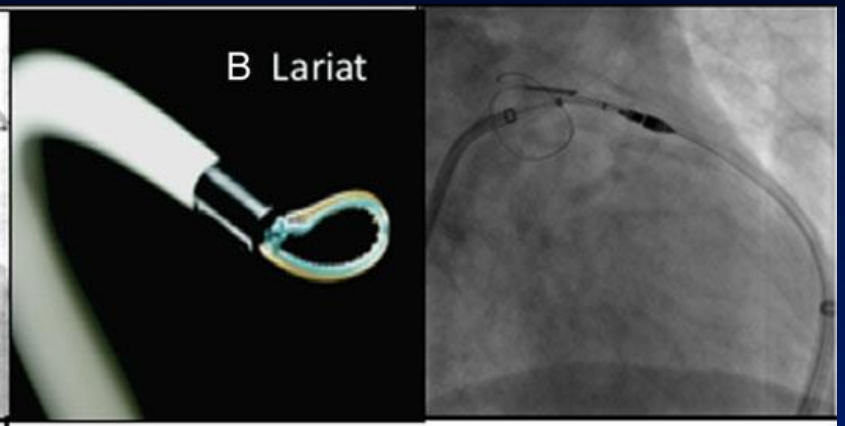


A Watchman



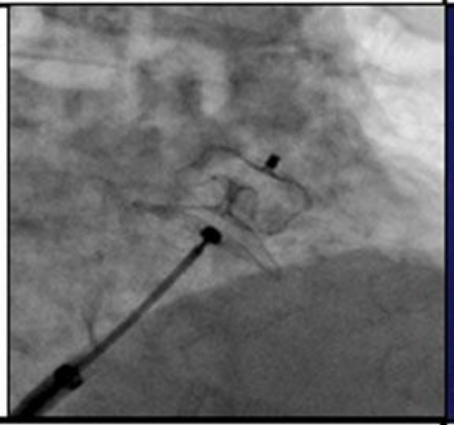
Requirements: LAA length > width, LAA diameter 17-31 mm, able to tolerate OAC x 45 days

B Lariat



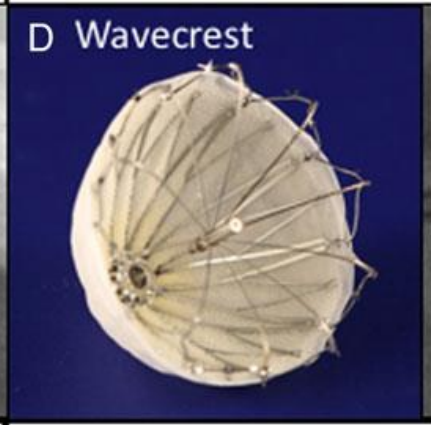
Requirements: No prior cardiac surgery, maximal LAA diameter <40 mm

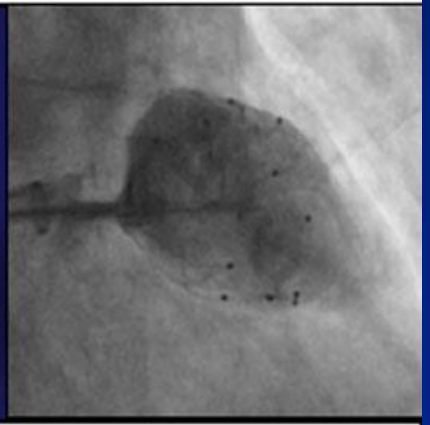
C Amulet



Requirements: Landing zone < 31 mm, LAA length <7.5 mm

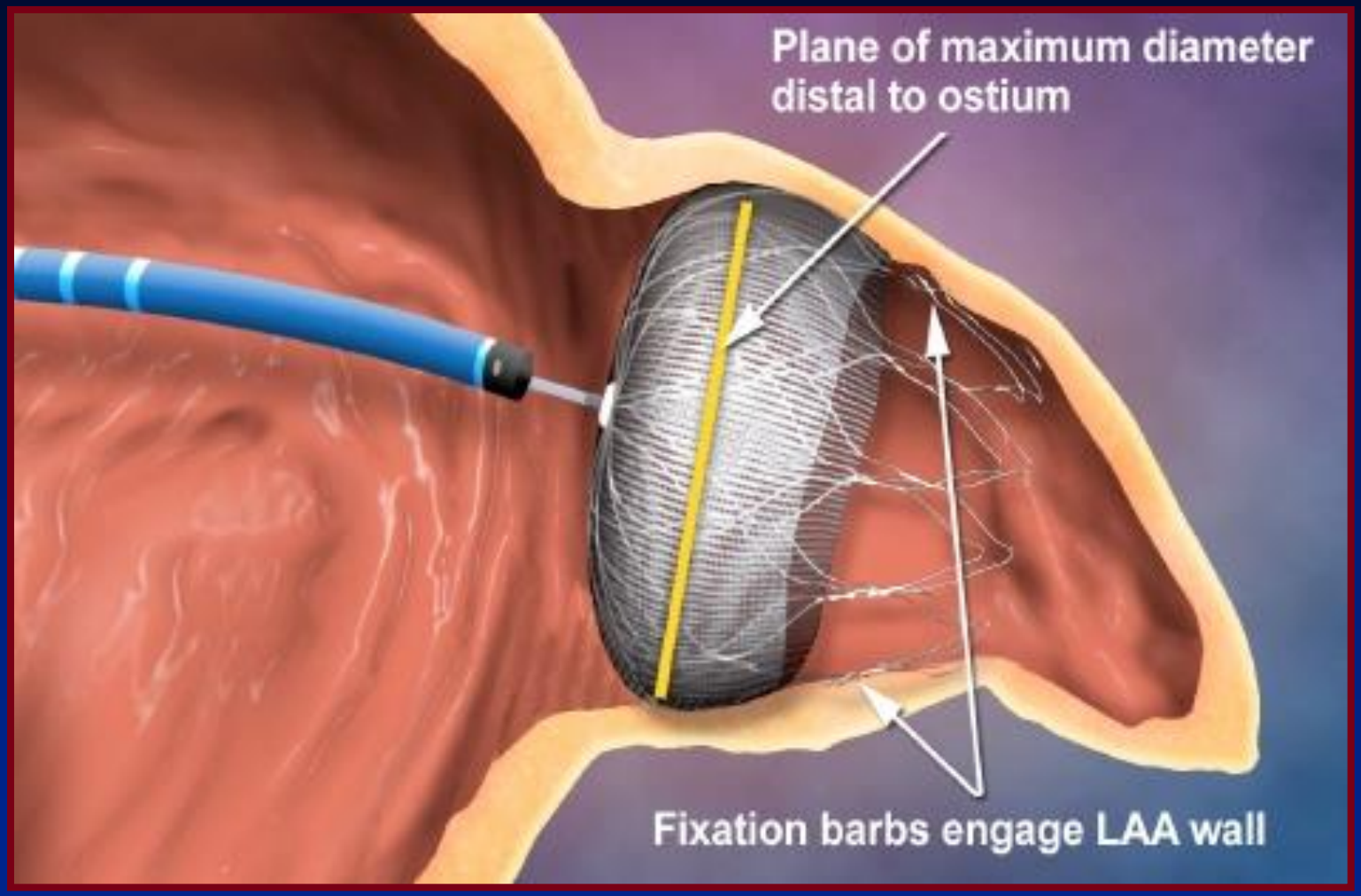
D Wavecrest





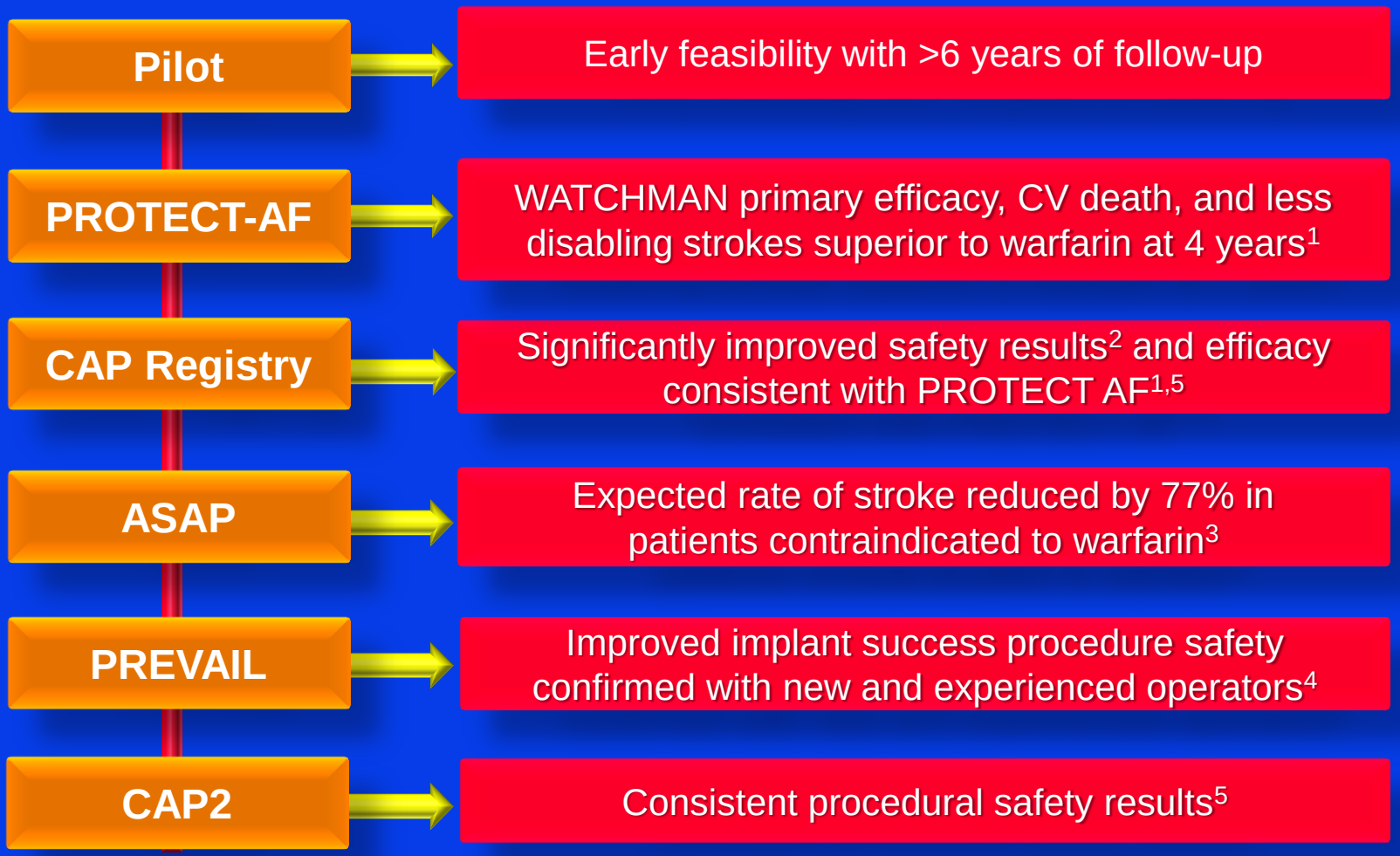
Requirements: Landing zone between 18-30 mm

WATCHMAN LAA Closure Device



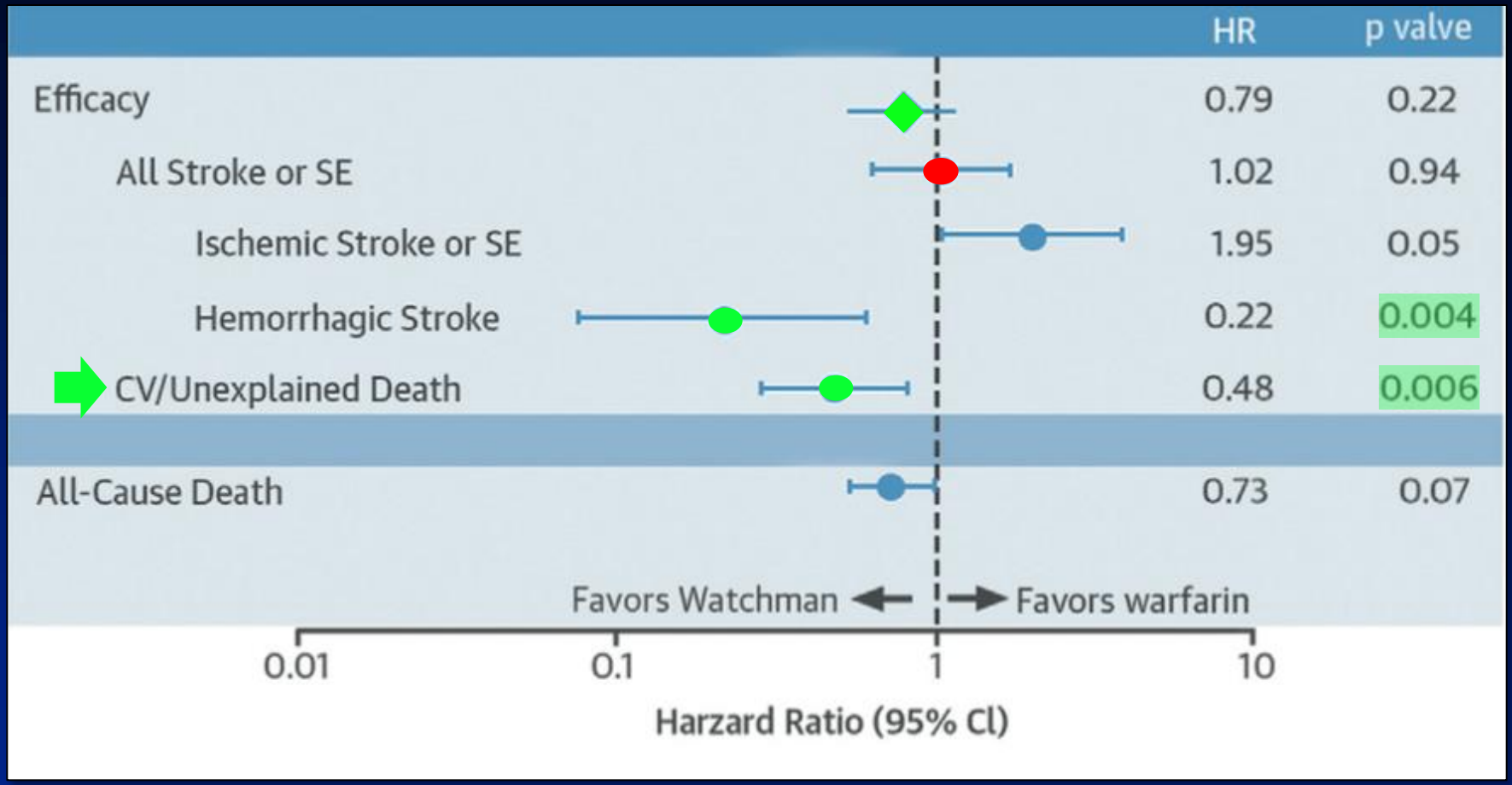
WATCHMAN™ Trials

>2,500 patients with >6,000 patient years follow-up



1 Reddy, VY et al. JAMA. 2014; 312(19):1988-1998. 2 Reddy, VY et al. Circ. 2011;123:417-424; 3 Reddy, et al. JACC 2013; 61(25):2551–6. 4 ***HOLMES, DR ET AL. JACC. 2014; 64(1):1-12. 5 FDA PANEL OCTOBER 2014.***

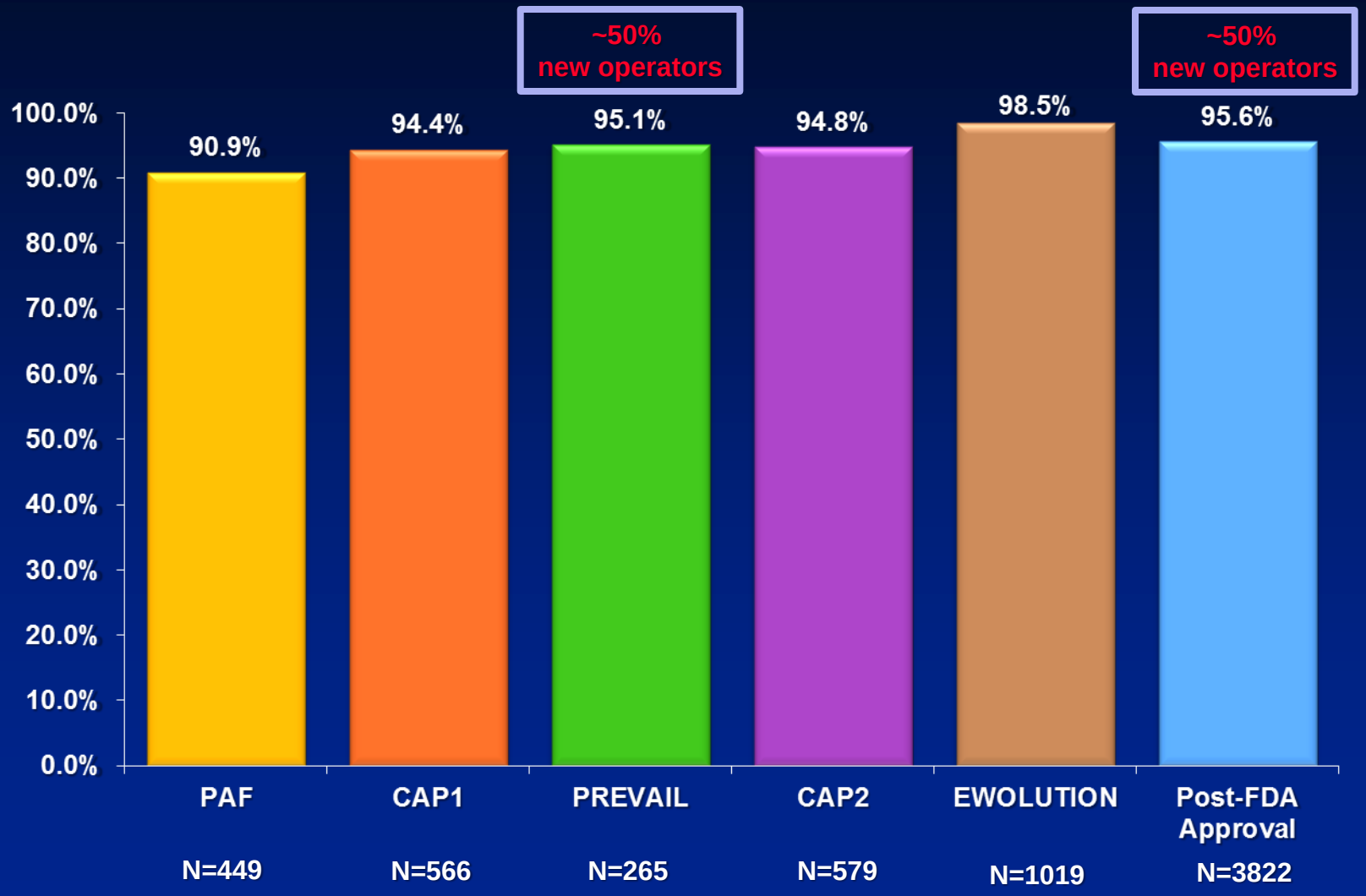
Left Atrial Appendage Closure vs Warfarin in AF
A Patient-Level Meta-Analysis



COMBINATION OF PROTECT AF AND PREVAIL PATIENTS RECEIVING THE WATCHMAN DEVICE, VS WARFARIN FOR OVERALL STROKE, ISCHEMIC STROKE, AND ALL-CAUSE DEATH.

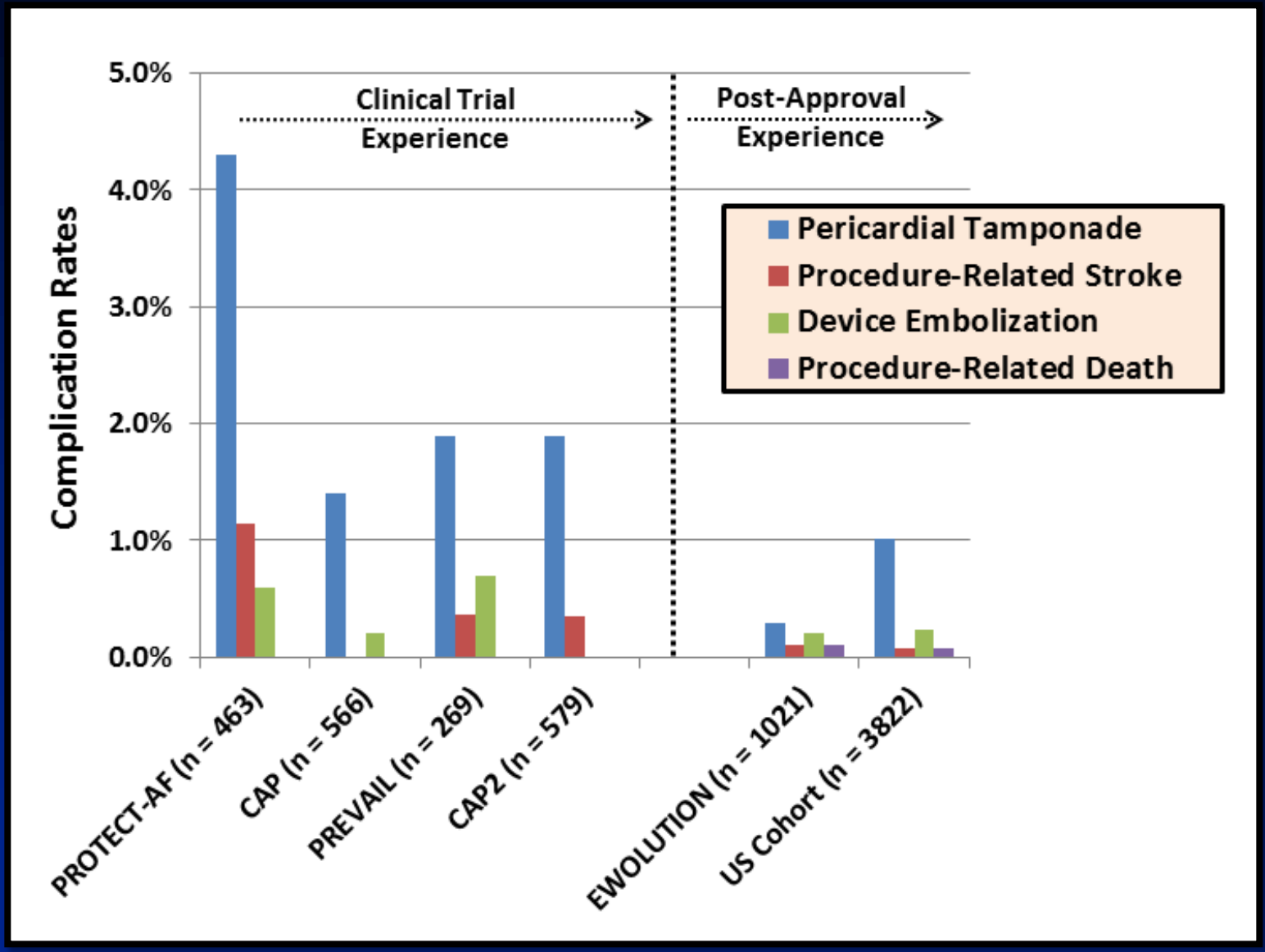
J AM COLL CARDIOL 2015;65:2614–

Procedural Success

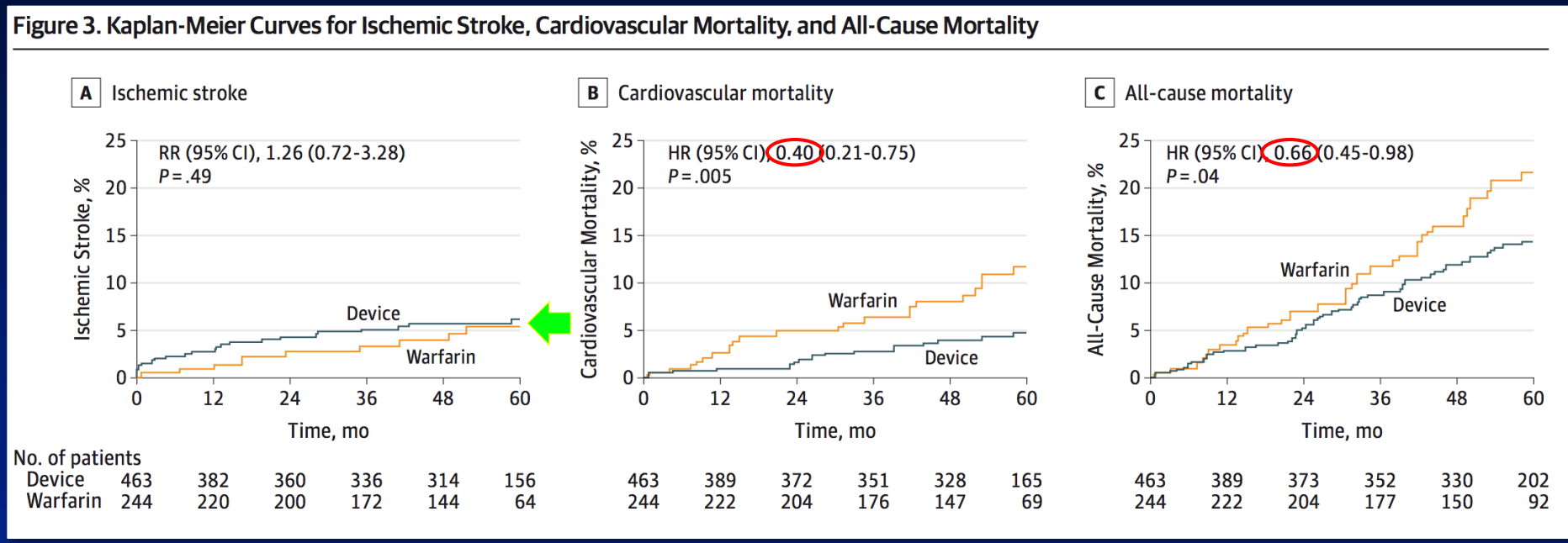


Implant success defined as deployment and release of the device into the LAA; no leak ≥ 5 mm

Comparison of Procedural Complications Across Watchman Studies



WATCHMAN vs Warfarin
4 Year Follow-up

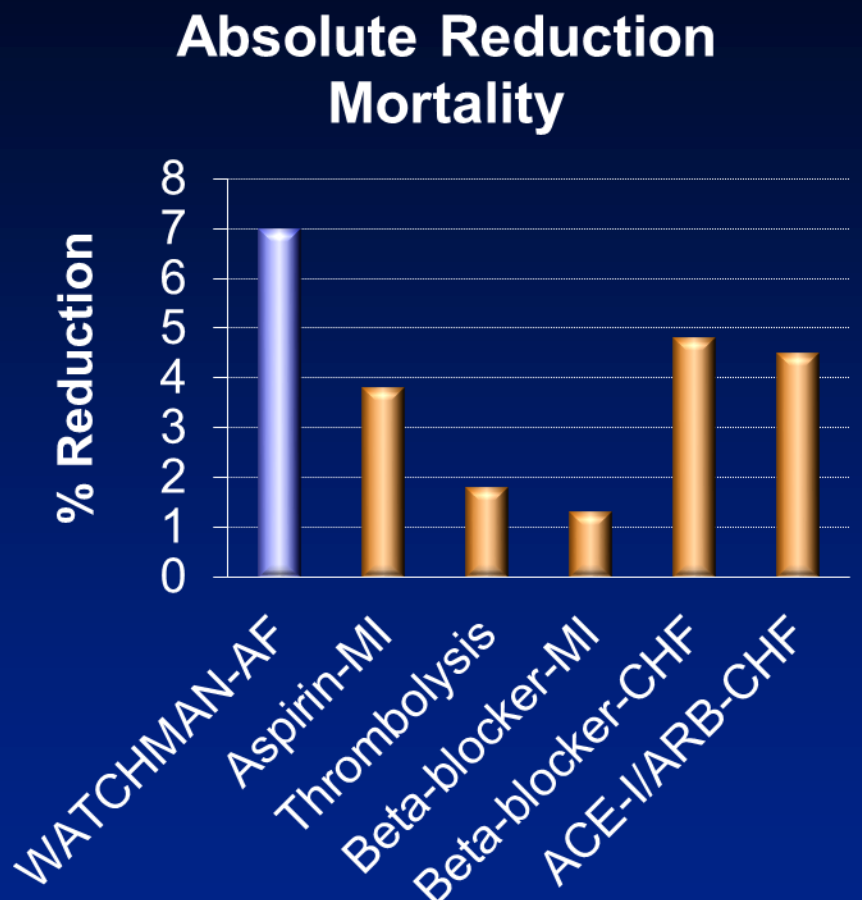


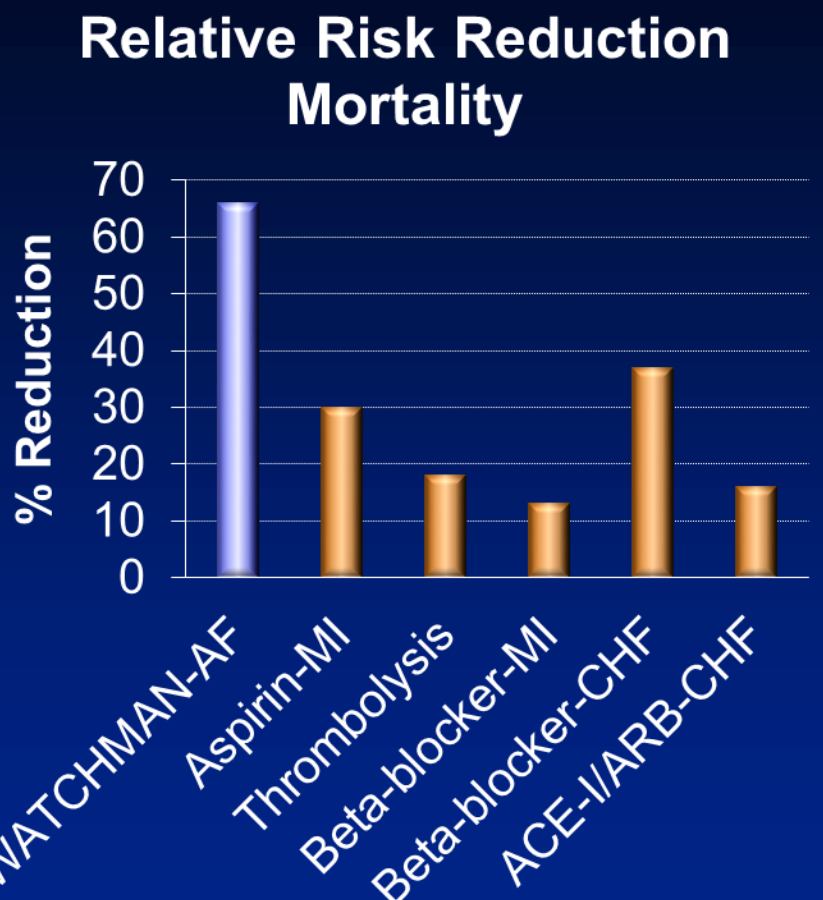
NO DIFFERENCE VS WARFARIN FOR ISCHEMIC STROKE

LOWER MORTALITY VS WARFARIN

JAMA. 2014;312(19):1988-1998.

Magnitude of Therapeutic Effect



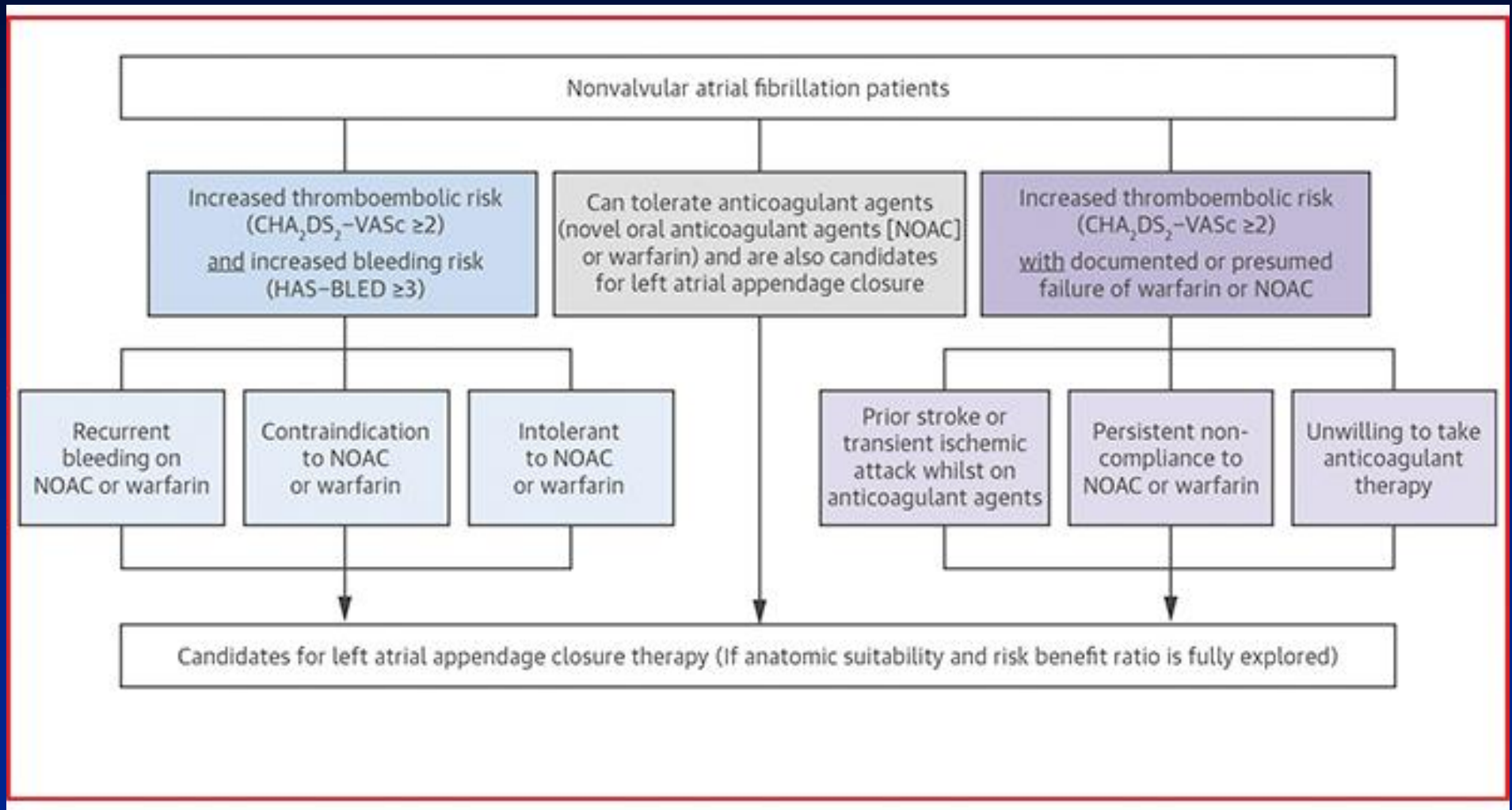


RESULTS FROM DIFFERENT CLINICAL TRIALS:

J AM COLL CARDIOL. 2006 AUG 1;48(3):434-7.

JAMA. 2014;312(19):1988-1998. DOI:10.1001/JAMA.2014.15192

LAAC


Nonvalvular atrial fibrillation patients
Increased thromboembolic risk (CHA_2DS_2–VASc ≥2) and increased bleeding risk (HAS–BLED ≥3)
Can tolerate anticoagulant agents (novel oral anticoagulant agents [NOAC] or warfarin) and are also candidates for left atrial appendage closure
Increased thromboembolic risk (CHA_2DS_2–VASc ≥2) with documented or presumed failure of warfarin or NOAC
Recurrent bleeding on NOAC or warfarin
Contraindication to NOAC or warfarin
Intolerant to NOAC or warfarin
Prior stroke or transient ischemic attack whilst on anticoagulant agents
Persistent non-compliance to NOAC or warfarin
Unwilling to take anticoagulant therapy
Candidates for left atrial appendage closure therapy (If anatomic suitability and risk benefit ratio is fully explored)

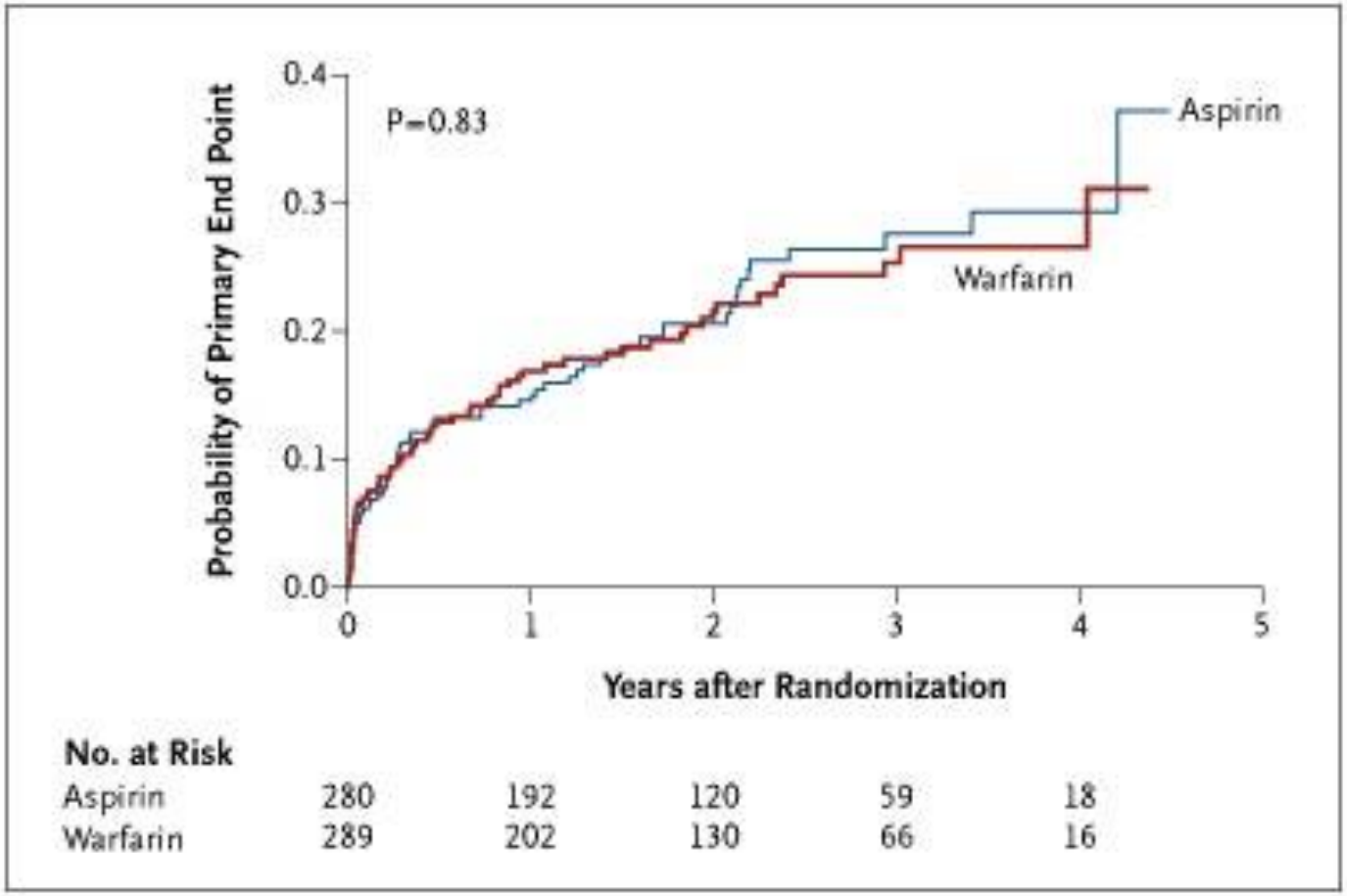
Stroke risk stratification in non valvular AF

Definition and Scores for $CHADS_2$ and CHA_2DS_2-VASc	Score
$CHADS_2$	
Congestive HF	1
Hypertension	1
Age ≥75 y	1
Diabetes mellitus	1
Stroke/TIA/TE	2
Maximum score	6
CHA_2DS_2-VASc	
Congestive HF	1
Hypertension	1
Age ≥75 y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior MI, PAD, or aortic plaque)	1
Age 65–74 y	1
Sex category (i.e., female sex)	1
Maximum score	9

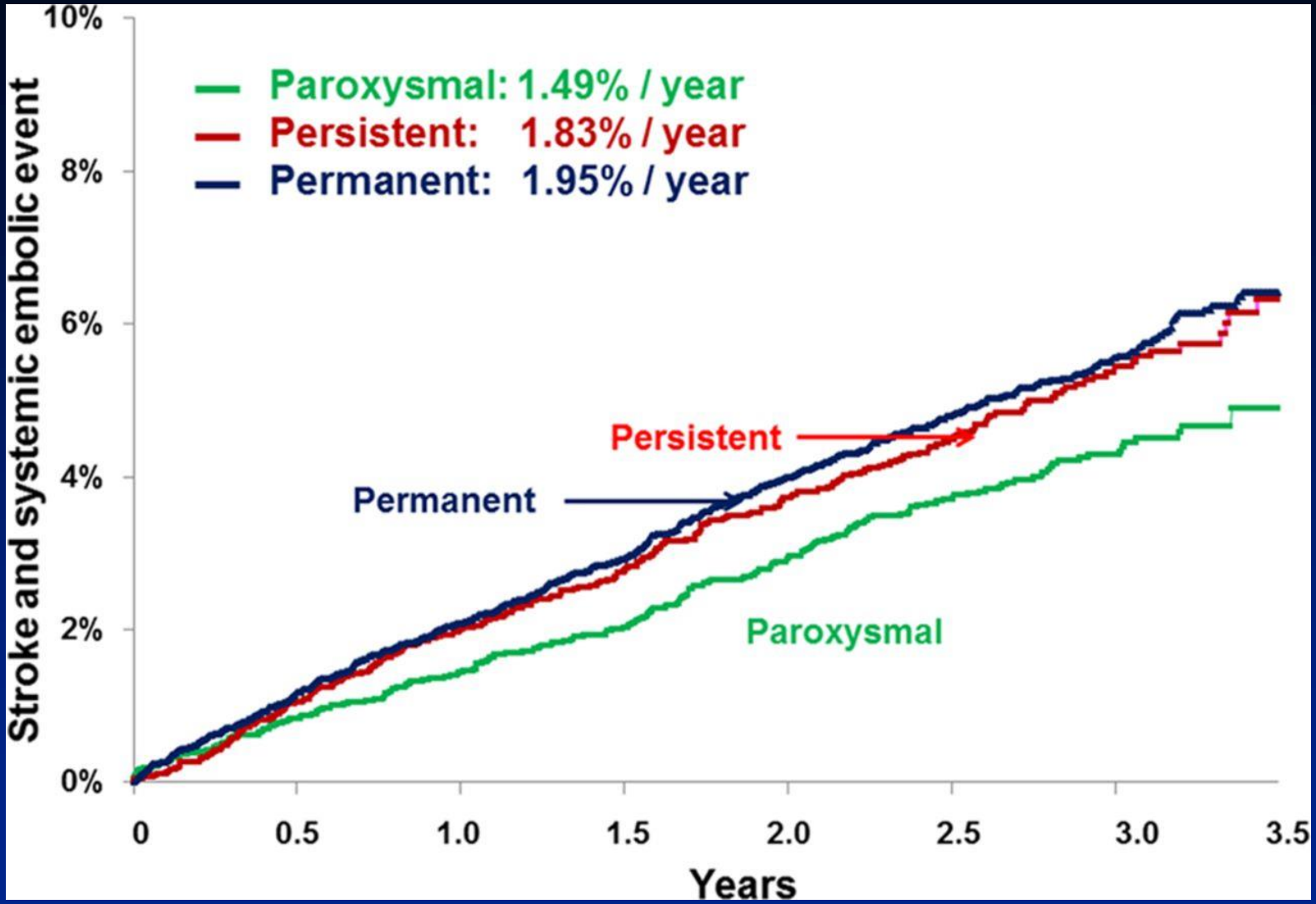
Annual Stroke Risk

CHA_2DS_2-VASc Score	Stroke Risk %	
0	0	
1	1.3	
2	2.2	
3	3.2	
4	4.0	
5	6.7	
6	9.8	
7	9.6	
8	12.5	
9	15.2	

Cumulative Incidence of the Primary End Point after Randomization, According to Treatment Assignment



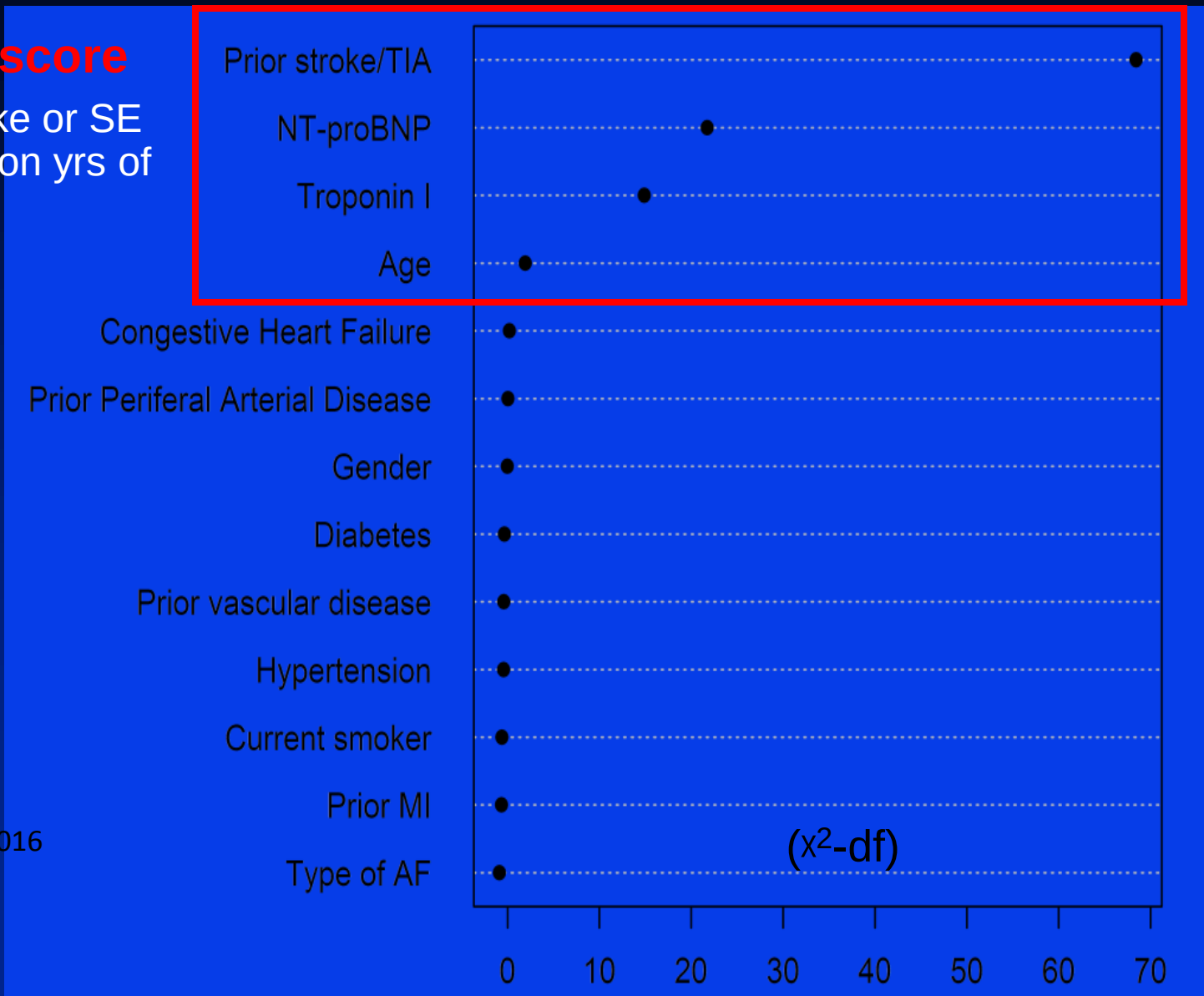
Chimowitz, M. et al. N Engl J Med 2005;352:1305-1316


Paroxysmal: 1.49% / year
Persistent: 1.83% / year
Permanent: 1.95% / year
Stroke and systemic embolic event
10%
8%
6%
4%
2%
0%
Persistent
Permanent
Paroxysmal
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Years

ABC (Age, Biomarker, Clinical factor) risk scores

ABC-stroke score

Based on 391 stroke or SE during 27,929 person yrs of follow-up from the ARISTOTLE trial



Hijazi Z et al. *Eur Heart J* 2016

Risk of Ischemic Stroke or Systemic Embolism after the 3-Month Visit, According to Baseline $CHADS_2$ Score and According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

Table 3. Risk of Ischemic Stroke or Systemic Embolism after the 3-Month Visit, According to Baseline $CHADS_2$ Score and According to Whether Subclinical Atrial Tachyarrhythmias Were or Were Not Detected between Enrollment and the 3-Month Visit.

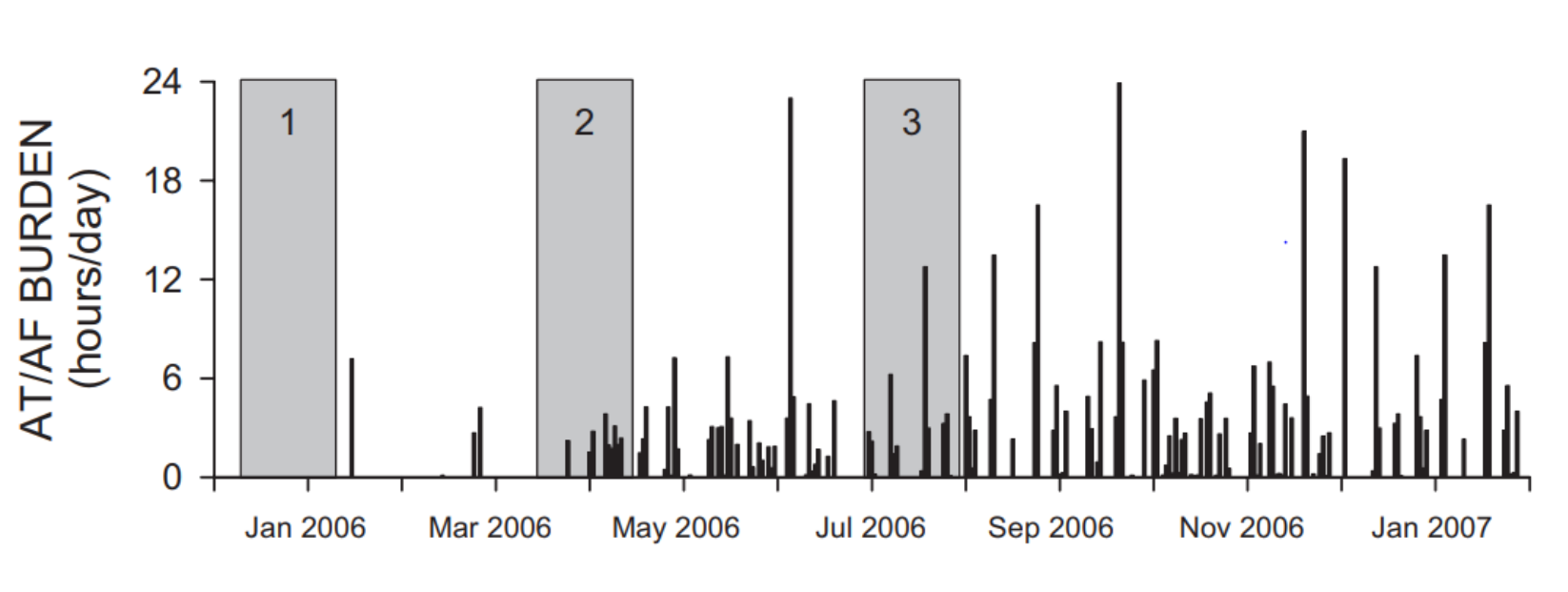
$CHADS_2$ Score	No. of Patients	Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months						Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)*
		Present			Absent			
		no. of patients	*no. of events*	*%/yr*	*no. of patients*	*no. of events*	*%/yr*	
1	600	68	1	0.56	532	4	0.28	2.11 (0.23–18.9)
2	1129	119	4	1.29	1010	18	0.70	1.83 (0.62–5.40)
>2	848	72	6	3.78	776	18	0.97	3.93 (1.55–9.95)

* The P value for trend is 0.35.

Healey JS et al. N Engl J Med 2012;366:120-129

TRENDS STUDY

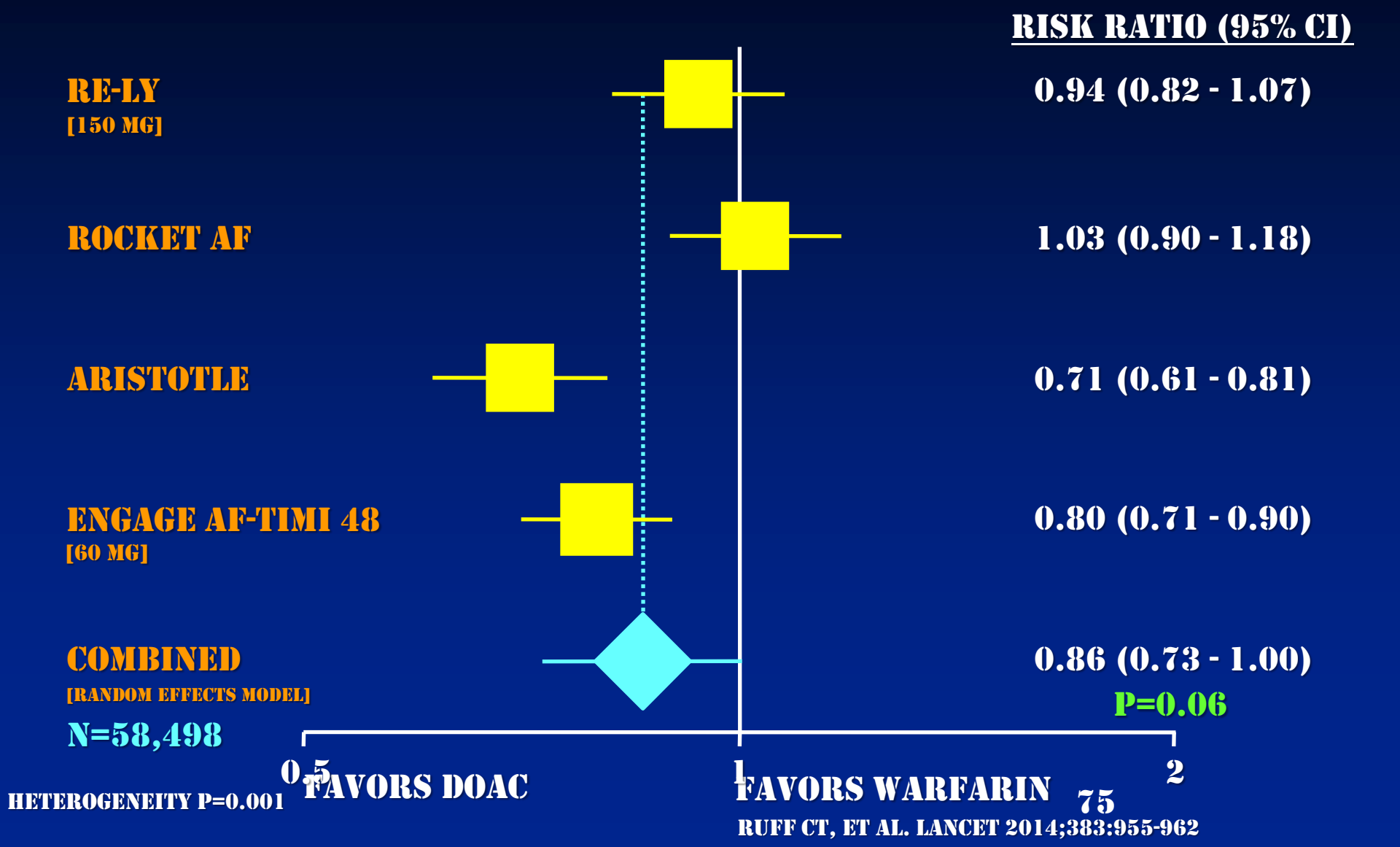
2486 PATIENTS WITH ICD/PACEMAKERS
30 DAYS OF DEVICE DATA
MEAN FOLLOW UP 1.4 YEARS
STUDY A-FIB BURDEN AND RISK OF STROKE



Characteristic/comorbidity	Association with AF
Genetic predisposition (based on multiple common gene variants associated with AF)	HR range 0.4–3.2
Older age 50-59 years 60-69 years 70-79 years 80-89 years	HR: 1.00 (reference) 4.98 (95% CI 3.49–7.10) 7.35 (95% CI 5.28–10.2) 9.33 (95% CI 6.68–13.0)
Hypertension (treated) vs. none	HR 1.32 (95% CI 1.08–1.60)
Heart failure vs. none	HR 1.43 (95% CI 0.85–2.40)
Valvular heart disease vs. none	RR 2.42 (95% CI 1.62–3.60)
Myocardial infarction vs. none	HR 1.46 (95% CI 1.07–1.98)
Thyroid dysfunction Hypothyroidism Subclinical hyperthyroidism Overt hyperthyroidism	(reference: euthyroid) HR 1.23 (95% CI 0.77–1.97) RR 1.31 (95% CI 1.19–1.44) RR 1.42 (95% CI 1.22–1.63)
Obesity (body mass index) None (<25 kg/m²) Overweight (25–30 kg/m²) Obese (≥31 kg/m²)	HR: 1.00 (reference) 1.13 (95% CI 0.87–1.46) 1.37 (95% CI 1.05–1.78)
Diabetes mellitus vs. none	HR 1.25 (95% CI 0.98–1.60)

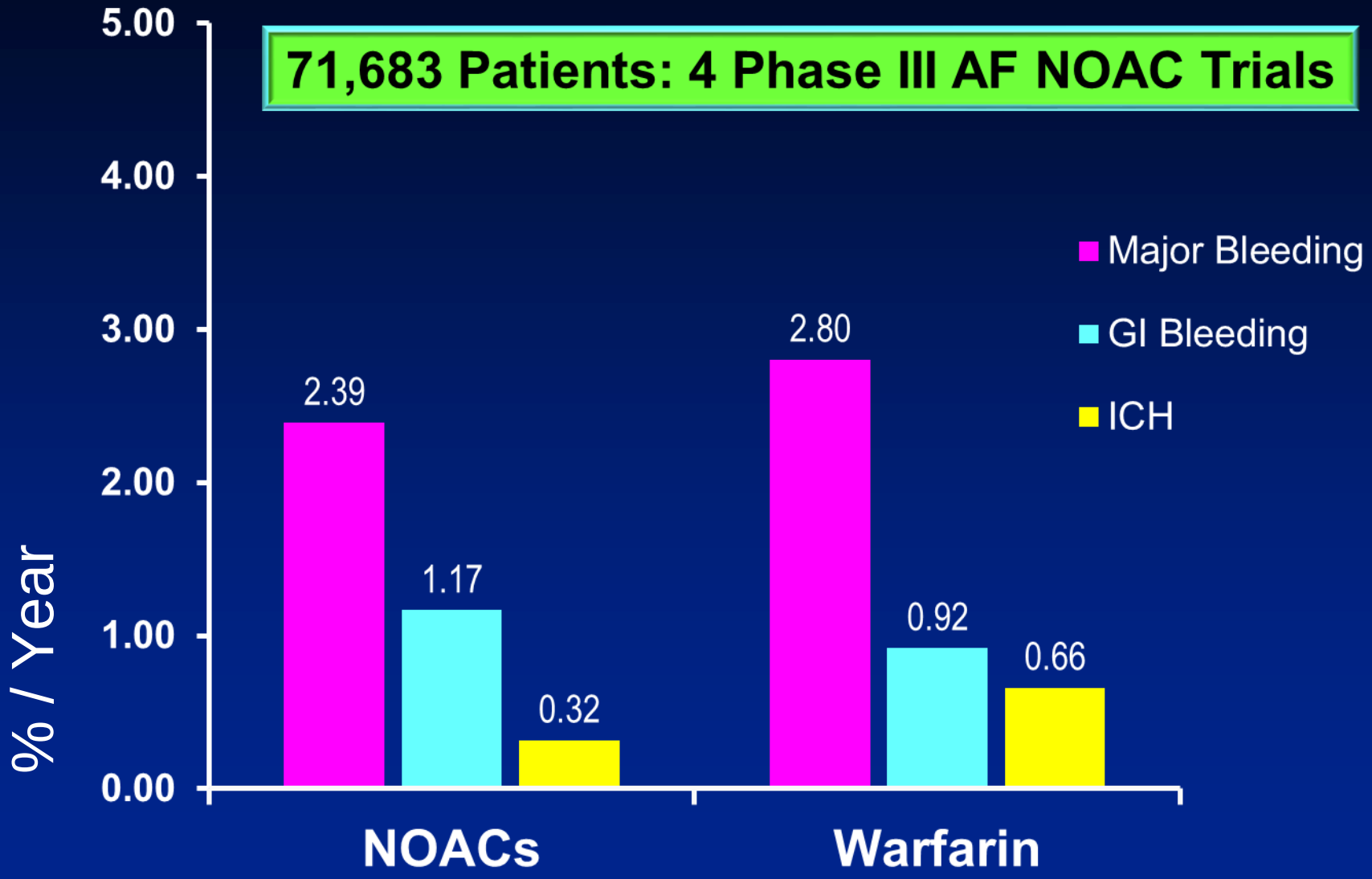
Characteristic/comorbidity	Association with AF
Chronic obstructive pulmonary disease FEV1 ≥80% FEV1 60–80% FEV1 <60%	RR: 1.00 (reference) 1.28 (95% CI 0.79–2.06) 2.53 (95% CI 1.45–4.42)
Obstructive sleep apnoea vs. none	HR 2.18 (95% CI 1.34–3.54)
Chronic kidney disease None Stage 1 or 2 Stage 3 Stage 4 or 5	OR: 1.00 (reference) 2.67 (95% CI 2.04–3.48) 1.68 (95% CI 1.26–2.24) 3.52 (95% CI 1.73–7.15)
Smoking Never Former Current	HR: 1.00 (reference) 1.32 (95% CI 1.10–1.57) 2.05 (95% CI 1.71–2.47)
Alcohol consumption None 1– 6 drinks/week 7–14 drinks/week 15–21 drinks/week >21 drinks/week	RR: 1.00 (reference) 1.01 (95% CI 0.94–1.09) 1.07 (95% CI 0.98–1.17) 1.14 (95% CI 1.01–1.28) 1.39 (95% CI 1.22–1.58)
Habitual vigorous exercise Non-exercisers <1 day/week 1–2 days/week 3–4 days/week 5–7 days/week	RR: 1.00 (reference) 0.90 (95% CI 0.68–1.20) 1.09 (95% CI 0.95–1.26) 1.04 (95% CI 0.91–1.19) 1.20 (95% CI 1.02–1.41)

All DOACS: Major Bleeding



RUFF CT, ET AL. LANCET 2014;383:955-962

HOW FREQUENT IS BLEEDING WITH DOACS?



RUFF CT, ET AL. LANCET. 2014; 383:955-962

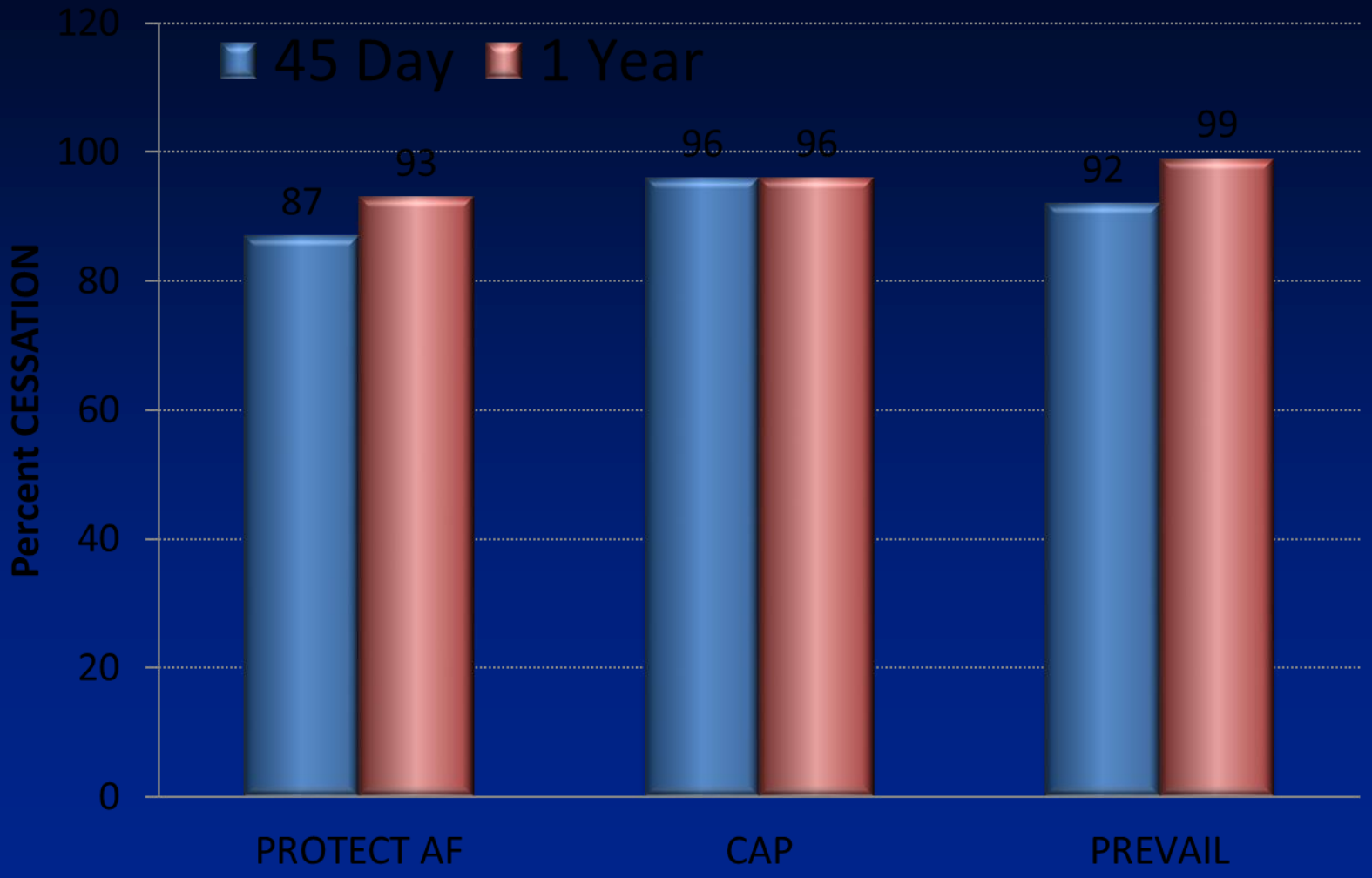
PATIENTS WHO SHOULD NOT BE ON NOACs

- Mechanical heart valve[1,2]
- Moderate or severe mitral stenosis[1,2]
- Severe renal* or hepatic impairment[2]
- Extremes of weight (>150 kg or <50 kg)[3]
- Pregnant or lactating women[2]
- Children[2]
- Poor adherence[3]

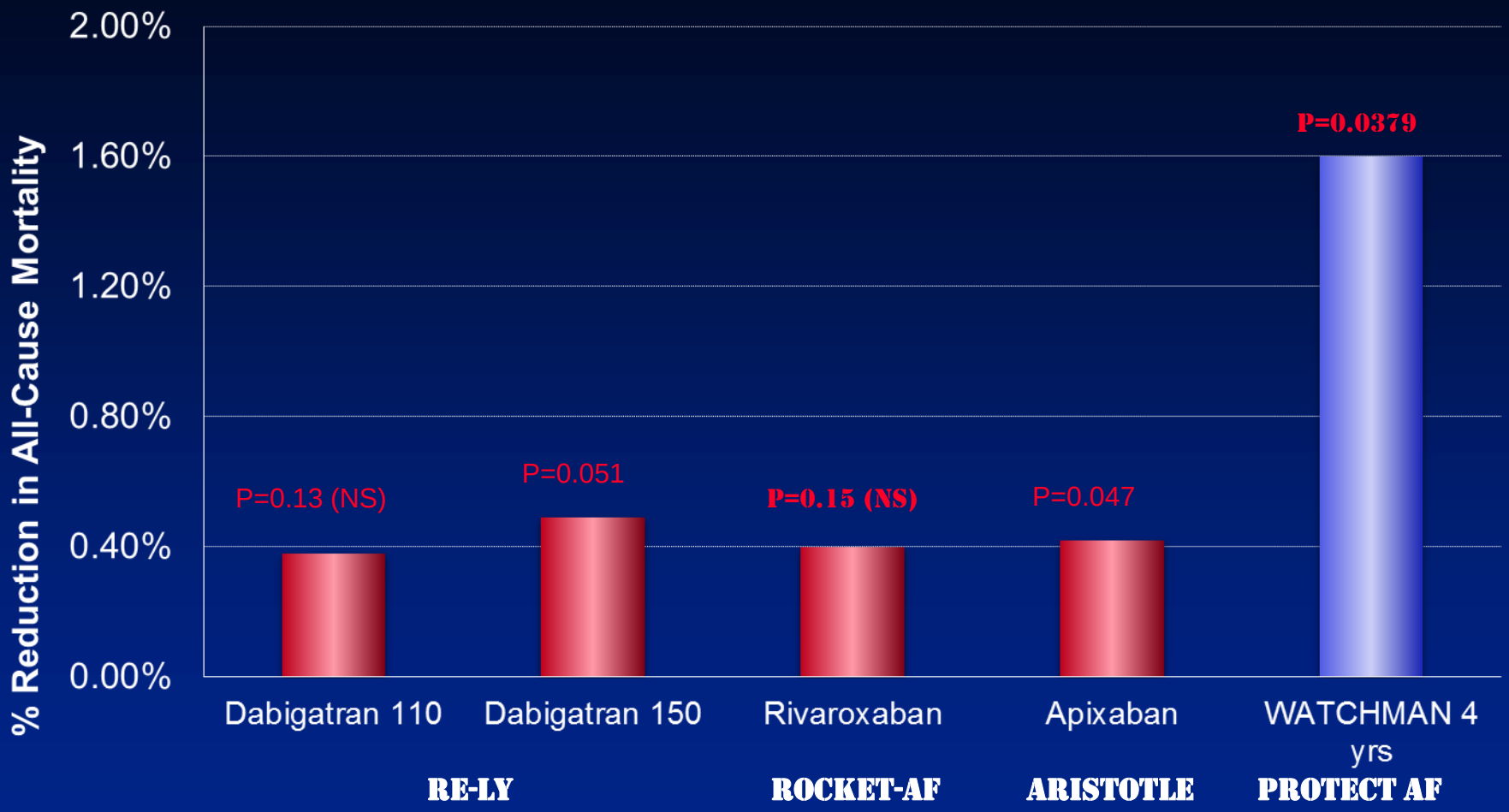
*Only apixaban may be used in stable patients on hemodialysis; avoid all other NOAC if CrCl < 15 ml/min

1. Heidbuchel H et al. Europace. 2015;17(10):1467-1507. 2. January CT et al. J Am Coll Cardiol. 2014;64(21):e1-e76. 3. Streiff MB et al. J Thromb Thrombolysis. 2016;41:32-67.

Warfarin Cessation after WATCHMAN



Mortality Reduction (vs Warfarin)



RESULTS FROM DIFFERENT CLINICAL TRIALS:

[1]CONNOLLY, S. NEJM 2009; 361:1139-1151 – 2 YRS F-UP
[2]PATEL, M. NEJM 2011; 365:883-891 – 1.9 YRS F-UP, ITT
[3]GRANGER, C NEJM 2011; 365:981-992 – 1.8 YRS F-UP
[4]REDDY, V. LBCT HRS 2013 – 4 YRS F-UP.