

ATRIAL FIBRILLATION

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FINANCIAL DISCLOSURES

- Speaker's Bureau – Biosense Webster

OUTLINE

- Epidemiology and Risk Factors
- Anticoagulation
- Management Options

OUTLINE

- **Epidemiology and Risk Factors**
- Anticoagulation
- Management Options

DEFINITIONS

- Paroxysmal AF

- Persistent AF



Early Persistent



Long Standing Persistent

- Permanent AF

DEFINITIONS

- **Lone Atrial fibrillation**
- **Chronic Atrial fibrillation**

EPIDEMIOLOGY

Prevalence of atrial fibrillation and flutter (per 100,000) by region, 2010

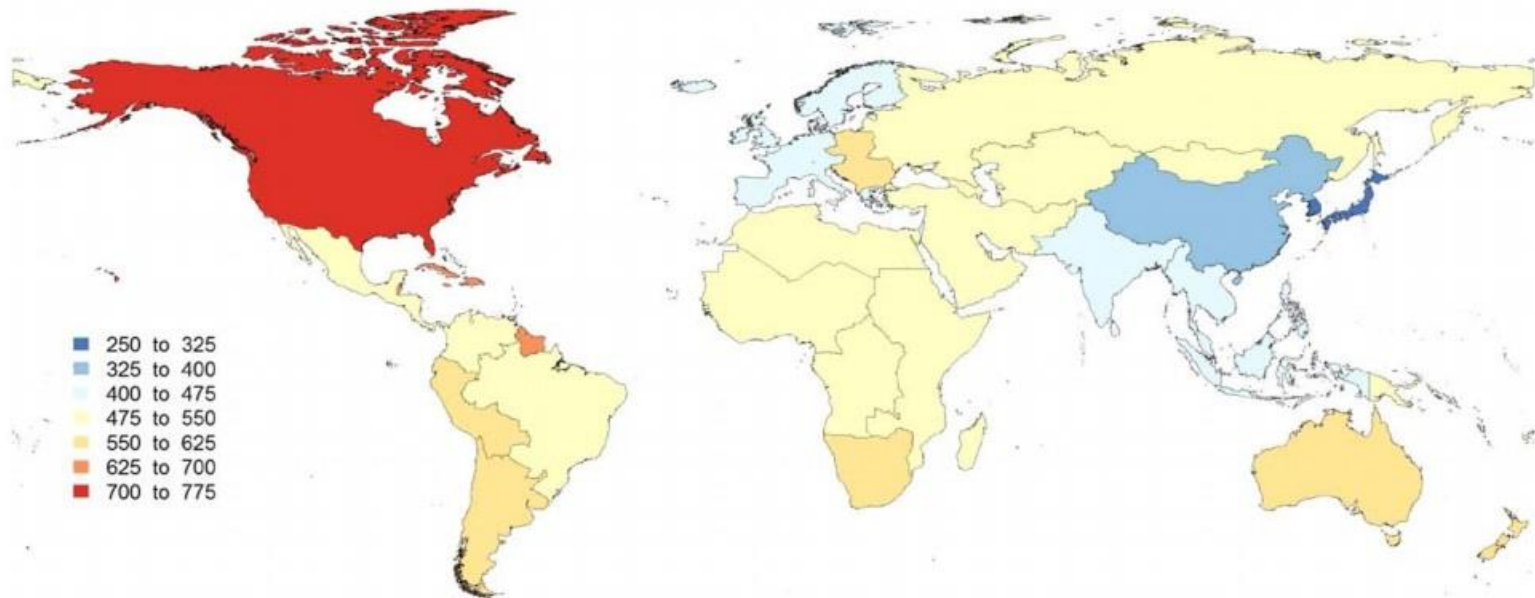


Figure World map showing the age-adjusted prevalence rates (per 100 000 population) of atrial fibrillation in the 21 Global Burden of Disease regions, 2010.

EPIDEMIOLOGY

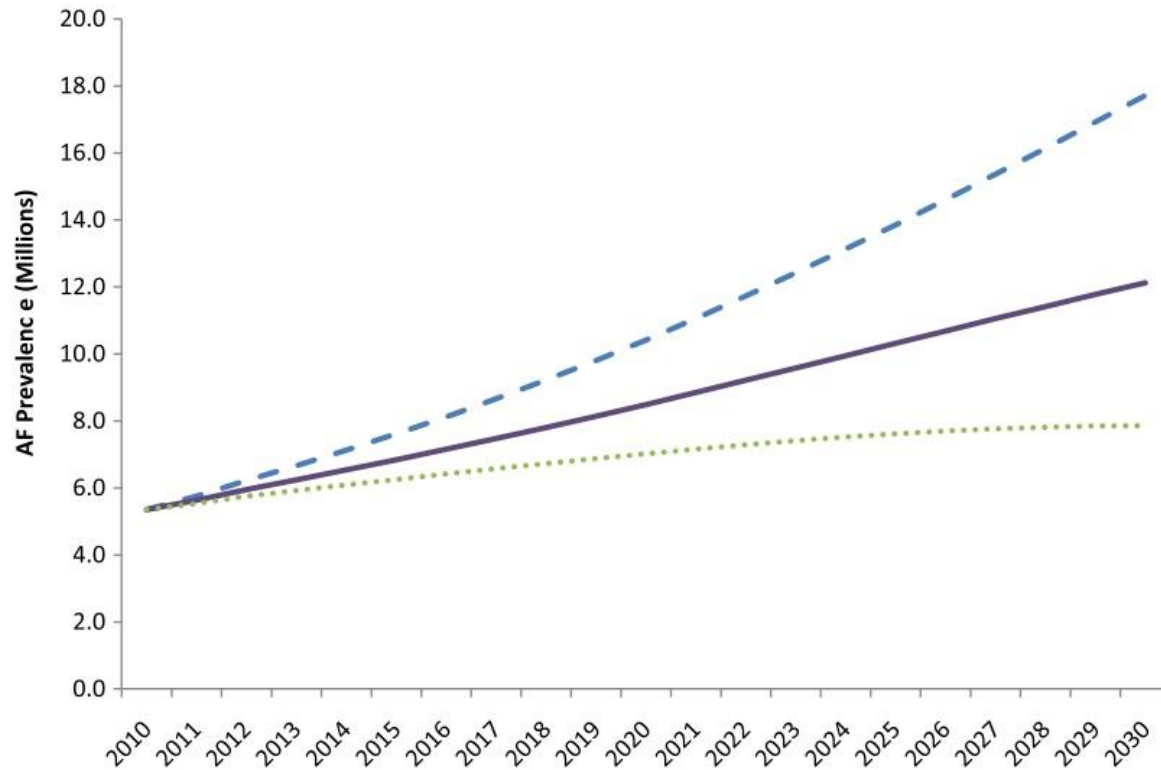


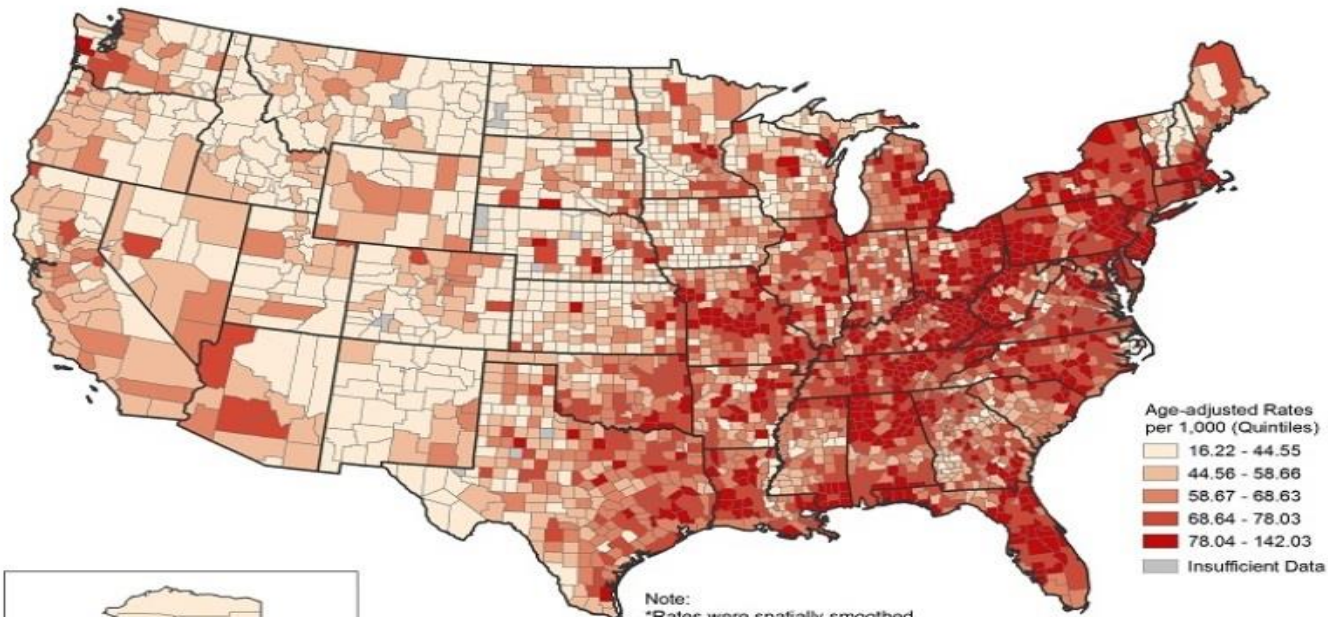
Figure Probabilistic range of uncertainty around the projected AF prevalence estimate for sensitivity analysis by simultaneously varying all the input parameters used in model. The probabilistic range of AF prevalence estimates is represented by the upper 10% likelihood (blue dashed line) and the lower 10% likelihood estimate (green dotted line) around the base AF prevalence estimate with logarithmic incidence growth rate projection (purple solid line).

Colilla S, et al. Estimates of current and future incidence and prevalence of atrial fibrillation in the U.S. adult population. Am J Cardiol 2013;112(8):1142–1147.

EPIDEMIOLOGY

Fee-For-Service Medicare Beneficiaries
Ages 65 Years and Older 2009-2014

Atrial Fibrillation Hospitalization Rates*
Total Population

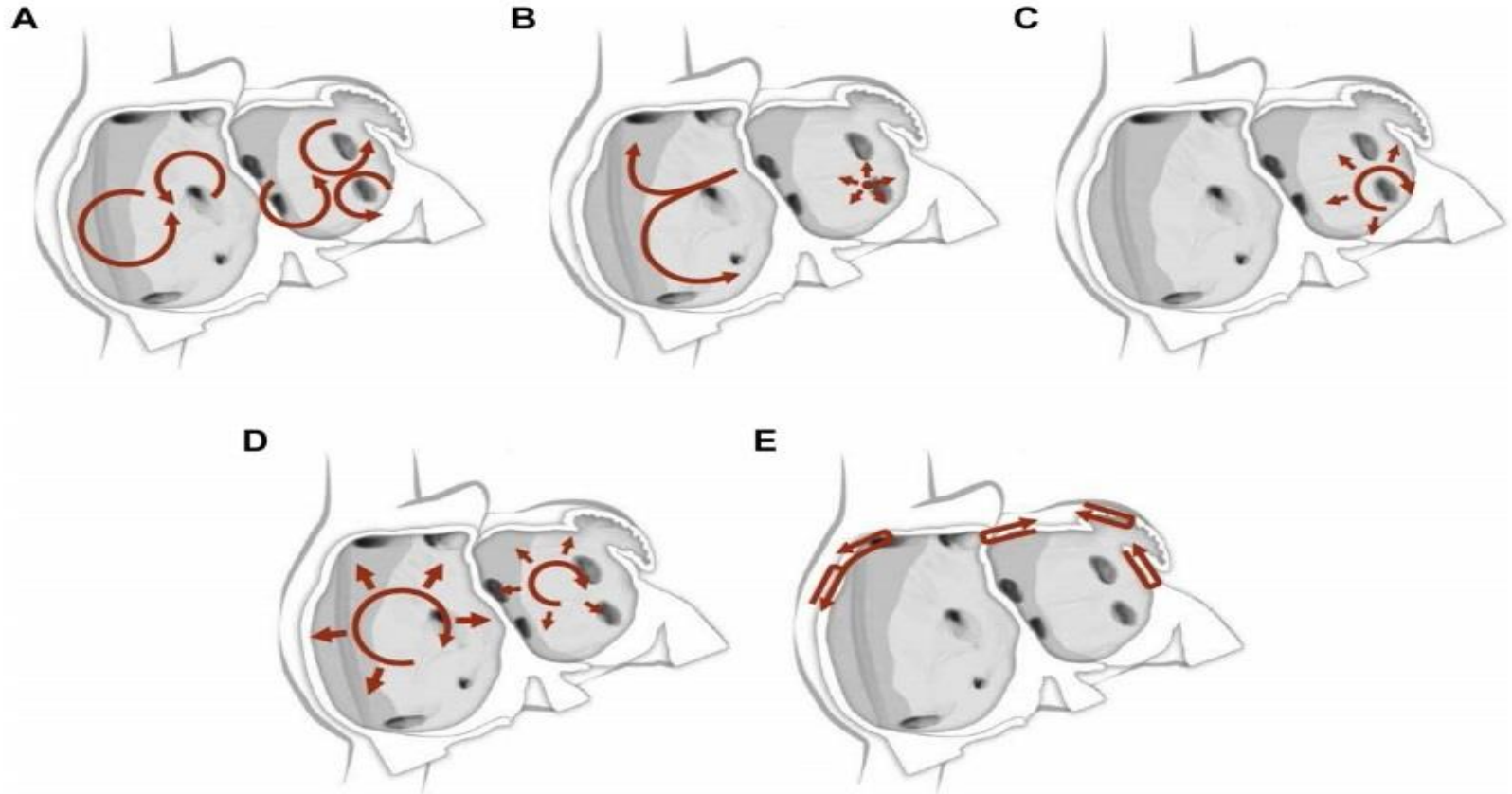


Note:
*Rates were spatially smoothed.
Data include any indication atrial fibrillation (ICD-9CM 427.3) on the discharge form.

Data Source:
Centers for Medicare & Medicaid Services
Medicare Provider Analysis and Review (MEDPAR) file, Part A



MECHANISMS



Schematic drawing showing various hypotheses and proposals concerning the mechanisms of atrial fibrillation. **A:** Multiple wavelets hypothesis. **B:** Rapidly discharging automatic foci. **C:** Single reentrant circuit with fibrillatory conduction. **D:** Functional reentry resulting from rotors or spiral waves. **E:** AF maintenance resulting from dissociation between epicardial and endocardial layers, with mutual interaction producing multiplying activity that maintains the arrhythmia.

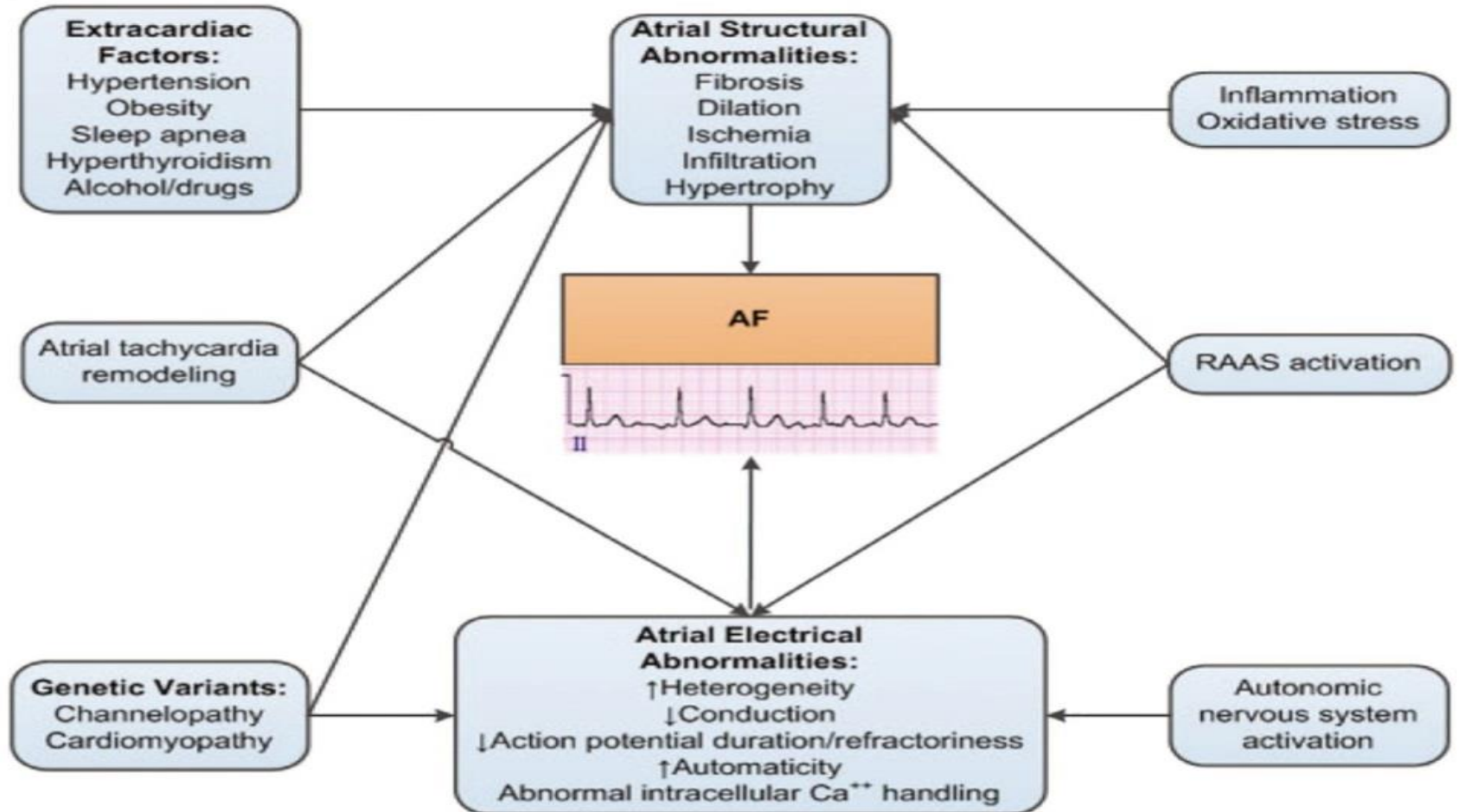
RISK FACTORS

- Approximately 2% of people younger than age 65 have atrial fibrillation, while about 9% of people aged 65 years or older have atrial fibrillation.¹
- African Americans are less likely than those of European descent to have atrial fibrillation.¹
- Among people of European descent, the lifetime risk of developing AF after age 40 is 26% for men and 23% for women.²

¹ https://www.cdc.gov/dhdsdp/data_statistics/fact_sheets/fs_atrial_fibrillation.htm

² Lloyd-Jones DM, et al. Lifetime risk for development of atrial fibrillation: the Framingham Heart Study. *Circulation* 2004;110(9):1042–1046.

RISK FACTORS



2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society

RISK FACTORS

- **Obesity**

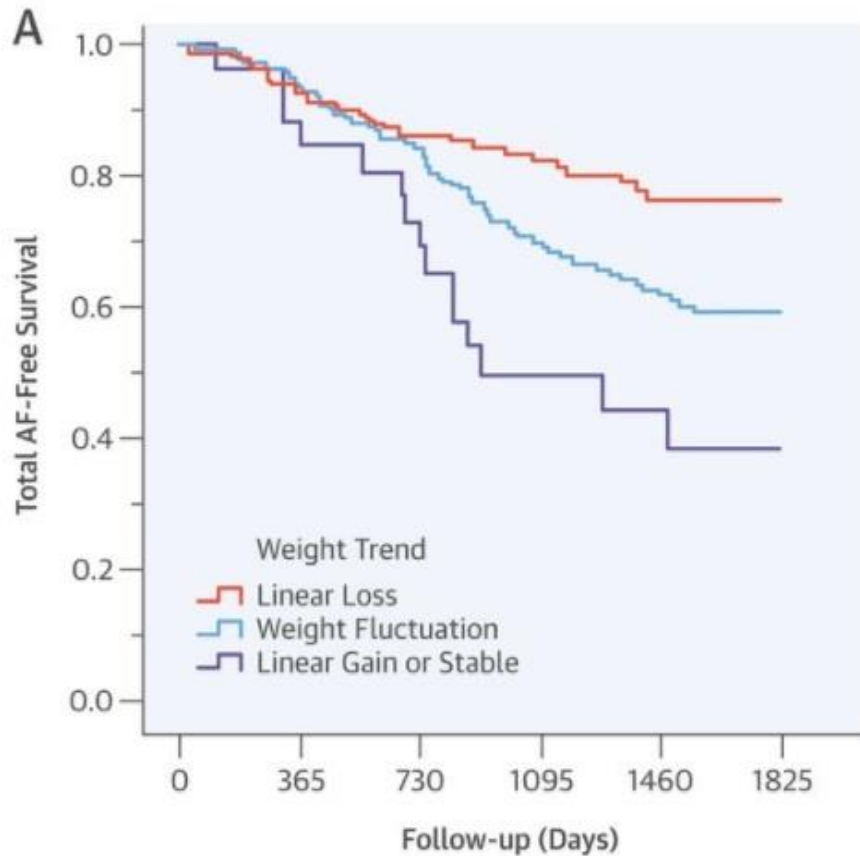
Risk of New-Onset Atrial Fibrillation According to BMI*

BMI Measure	Cases, No. (n = 425)	Controls, No. (n = 707)	OR (95% CI)	P Value
Categorical				.002 For trend
Normal (18.5-24.9)	100	147	1.00	
Overweight (25.0-29.9)	138	252	0.97 (0.68-1.38)	
Obese class 1 (30.0-34.9)	99	171	1.18 (0.80-1.73)	
Obese class 2 (35.0-39.9)	44	82	1.34 (0.82-2.18)	
Obese class 3 (≥ 40.0)	44	55	2.31 (1.36-3.91)	
Per-unit incremental	425	707	1.03 (1.01-1.05)	.001

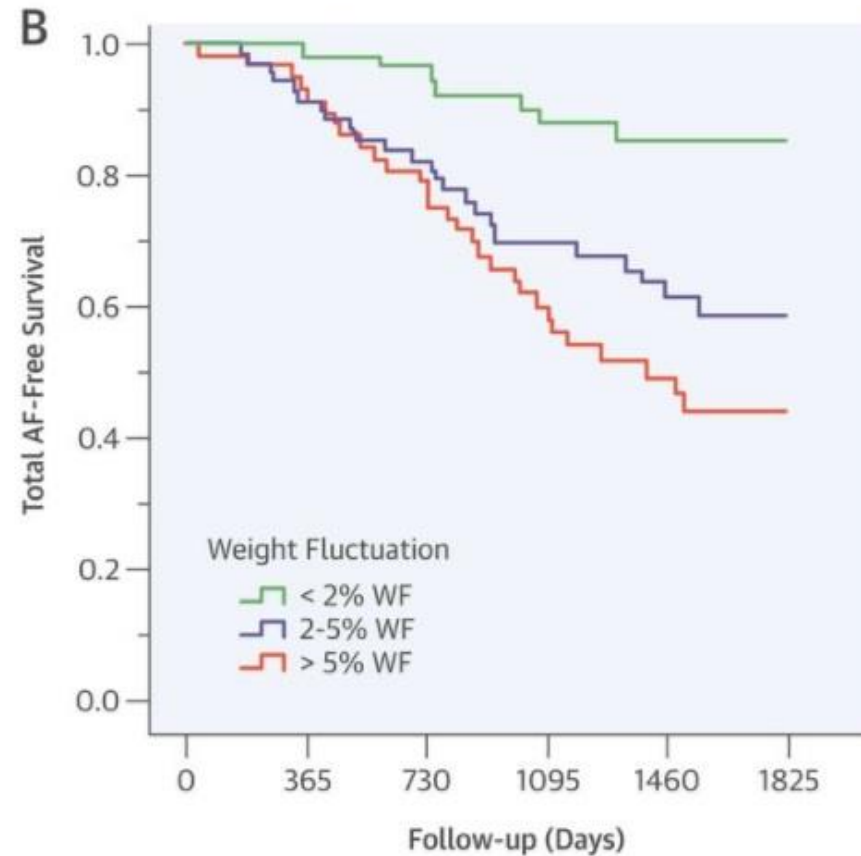
Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CI, confidence interval; OR, odds ratio.

*Models are adjusted for sex, treated hypertension, and age (cubic spline). Adjustment for additional potential confounding factors did not alter risk estimates substantially.

Dublin S, et al. Risk of new-onset atrial fibrillation in relation to body mass index. Arch Intern Med 2006;166(21):2322-2328.



Time (Days)	0	365	730	1095	1460	1825
Linear Loss	141	130	122	80	52	29
Fluctuation	179	165	140	99	71	44
Linear Gain	24	20	18	12	8	5



Time (Days)	0	365	730	1095	1460	1825
< 2% WF	54	52	49	39	33	19
2-5% WF	68	62	54	39	27	15
> 5% WF	57	53	45	31	19	14

Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort
 A Long-Term Follow-Up Study (LEGACY)

Rajeev K. Pathak et al Journal of the American College of Cardiology Volume 65, Issue 20, May 2015

Risk factors

Sleep Apnea

A variety of mechanisms have been implicated in the pathogenesis of OSA-associated AF.

- Autonomic Nervous System modulation
- Hypoxia
- LA dilatation
- Hypercapnia

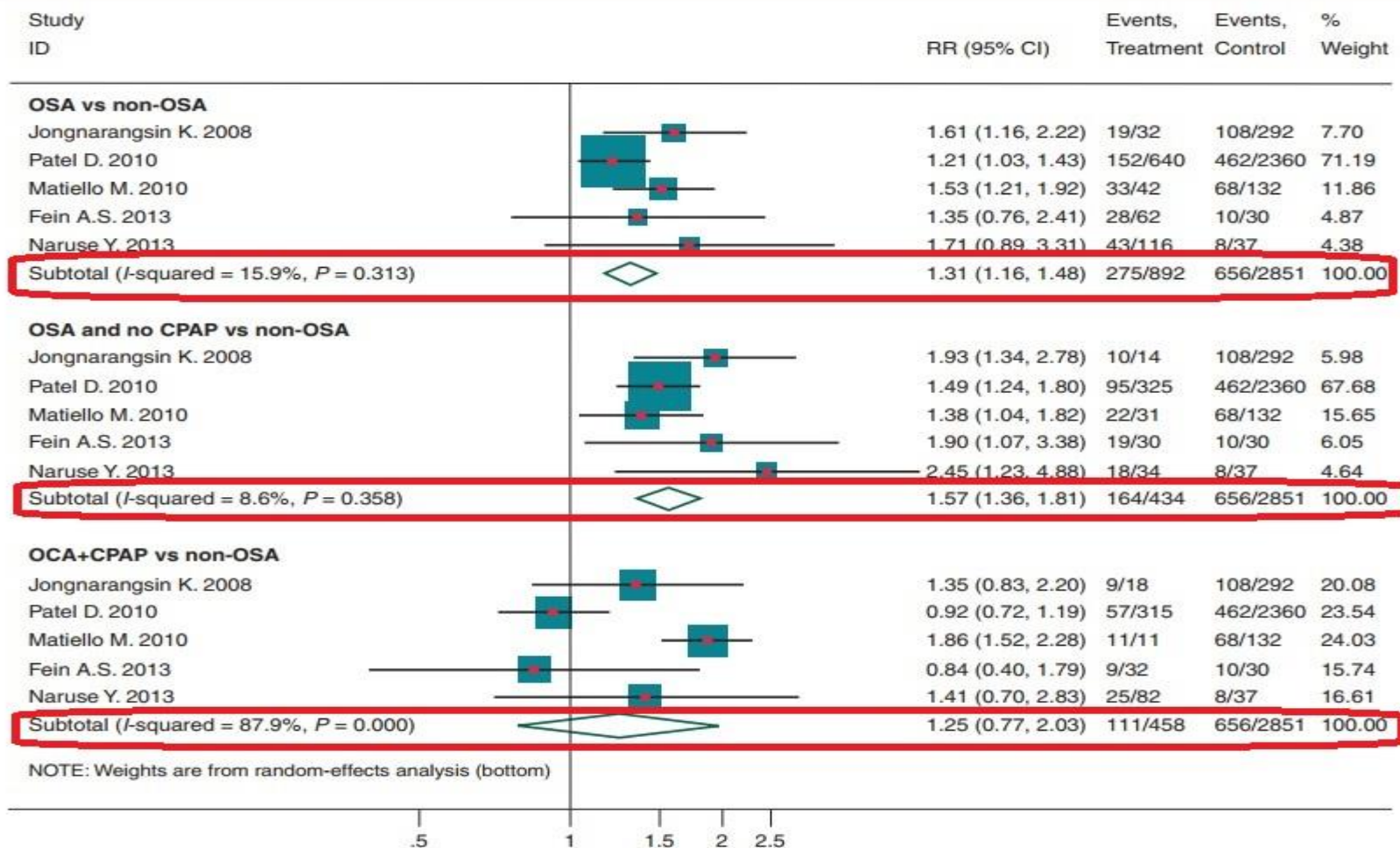
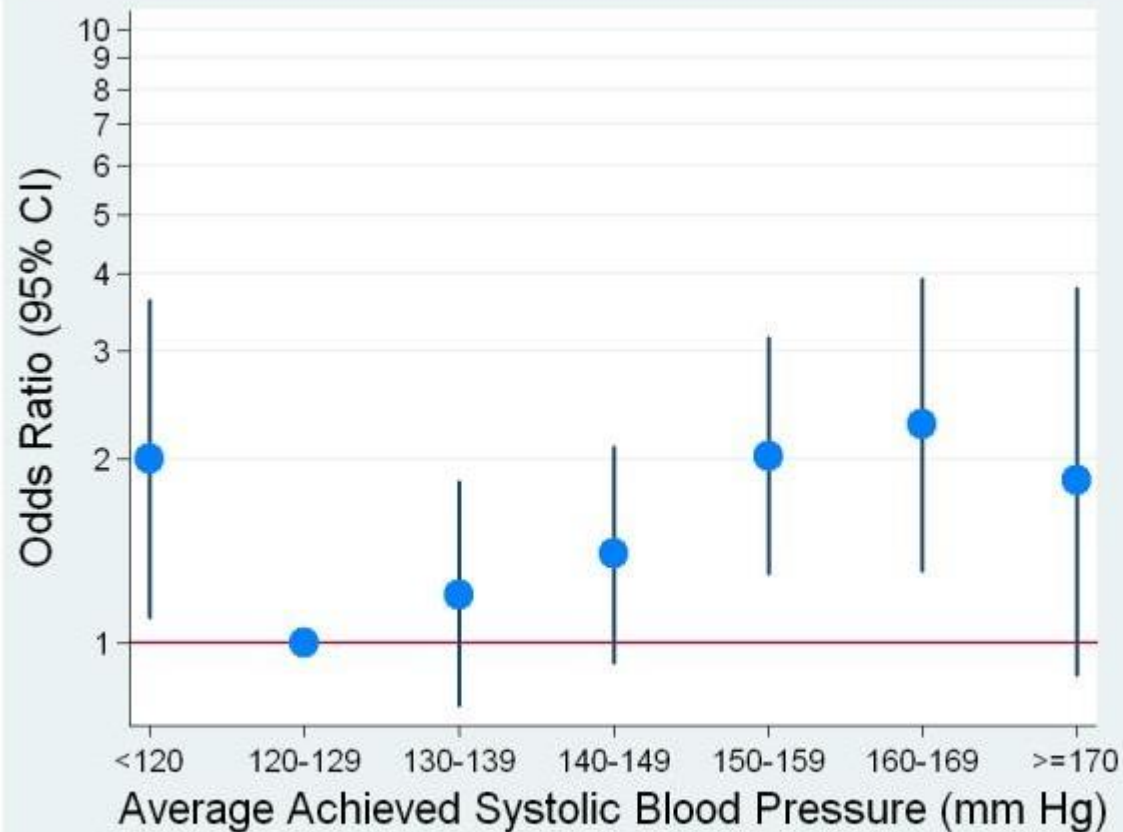


Figure 2 Forest plot in the comparison of AF recurrence after catheter ablation in patients with OSA and non-OSA (top), OSA and no CPAP vs non-OSA (middle), OSA + CPAP and non-OSA (bottom).

RISK FACTORS

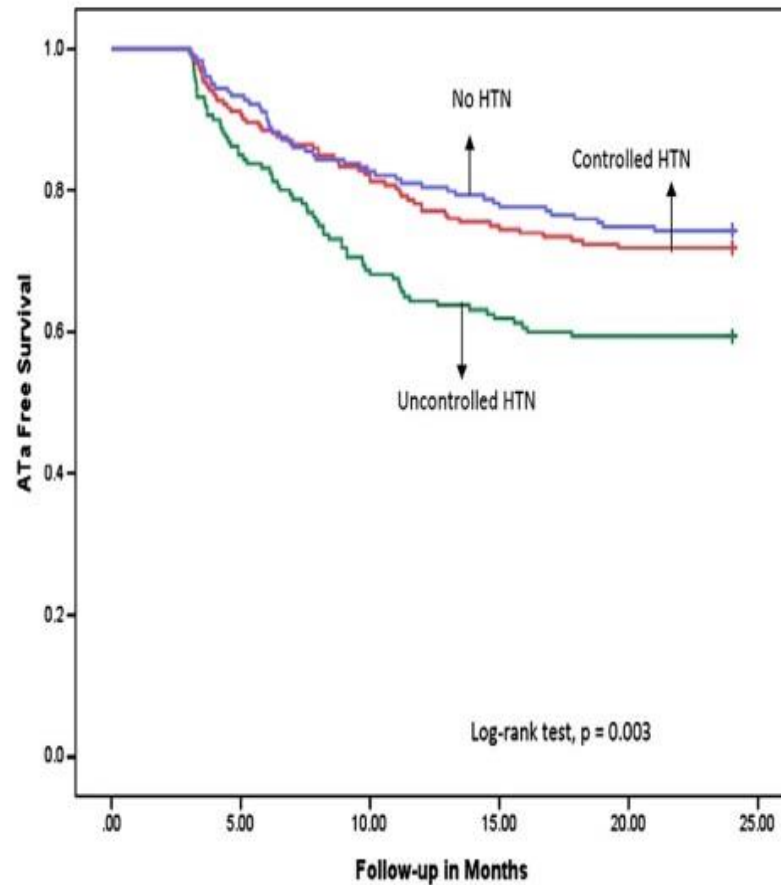


Odds ratios of incident atrial fibrillation associated with average achieved systolic blood pressure

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olic BP.

RISK FACTORS

FIGURE 1 Kaplan-Meier Curves of Freedom From Recurrent ATa for Different Groups After First Ablation



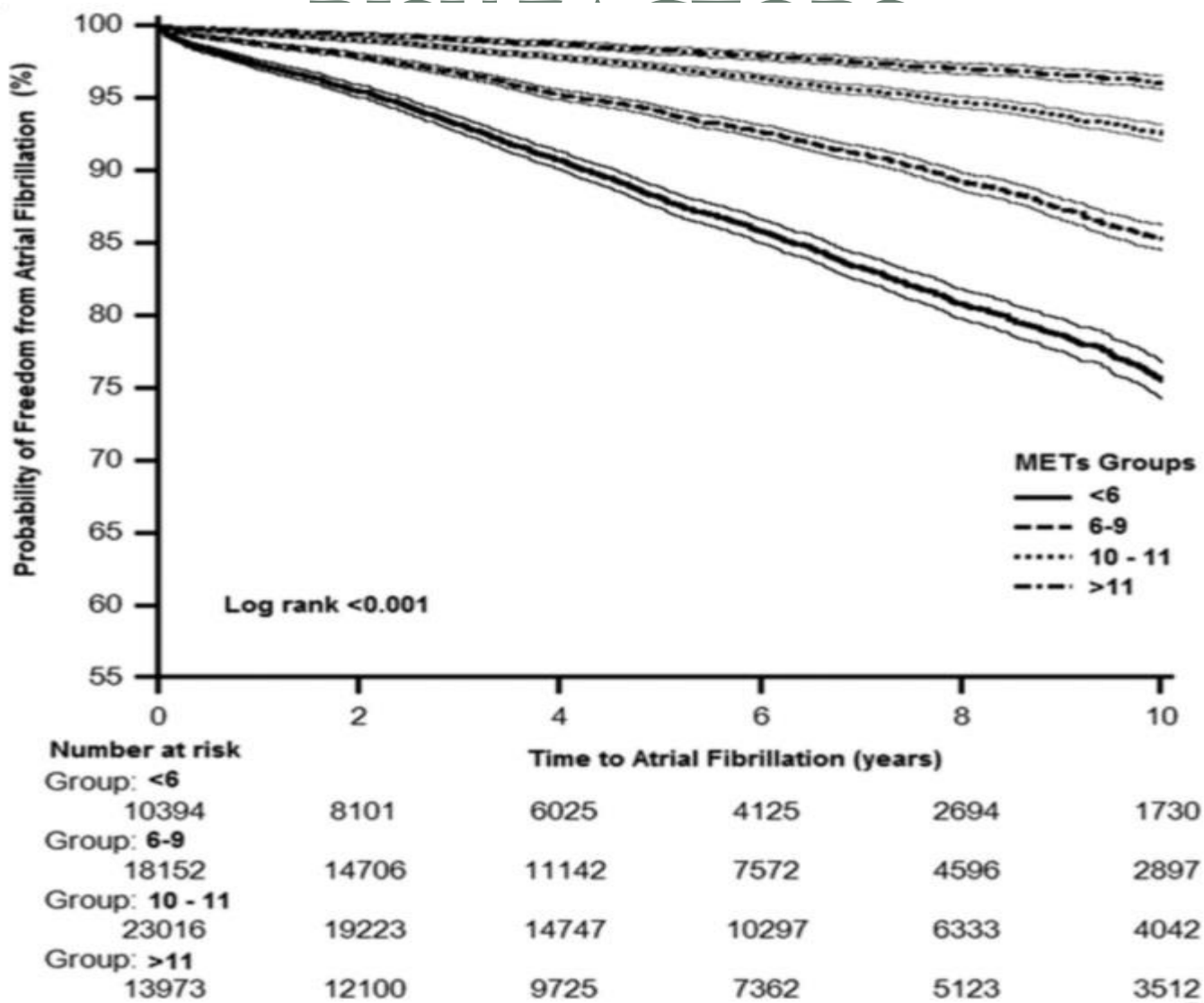
RISK FACTORS

Alcohol

- Alcohol consumption at varying degrees could increase the likelihood of incident AF and might also elevate the risk of thromboembolic events and post ablation recurrence in patients with AF.
- The ARREST-AF study demonstrated significant reduction in symptom severity, burden, and recurrence rate in patients with risk factor management that included lowering alcohol intake to 30 g per week.

Exer

- A study showing that higher cardiorespiratory fitness is associated with a lower risk of incident atrial fibrillation.



RISK FACTORS

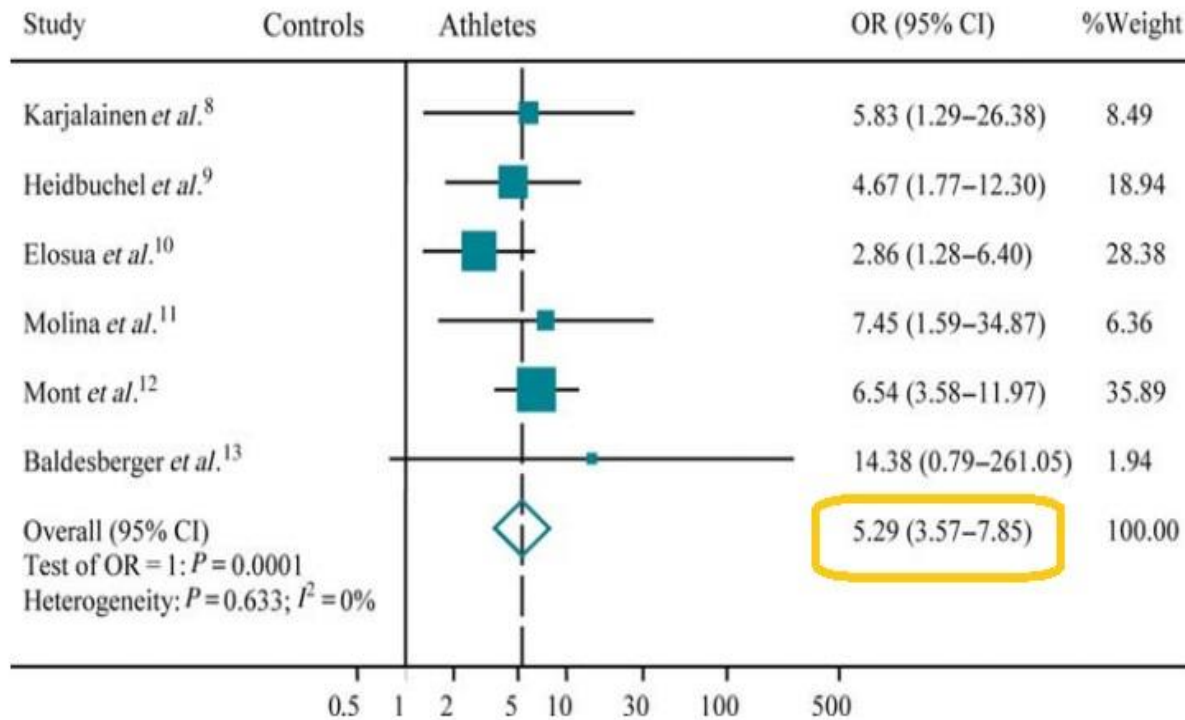


Figure 2 Meta-analysis of AF risk in athletes compared with controls.

OUTLINE

- Epidemiology and Risk Factors
- **Anticoagulation**
- Management Options

ANTICOAGULATION



ANTICOAGULATION

CHA₂DS₂-VASc score

Risk Factor	Score
C - Congestive heart failure	1
H - Hypertension	1
A - Age ≥ 75 yrs	2
D - Diabetes mellitus	1
S₂ - Prior stroke or TIA	2
V - Vascular disease	1
A - Age 65-74 years old	1
Sc - Sex category (female)	1

HAS-BLED score

Condition	Points	HAS-BLED score	Bleeds per 100 patient-years
H - Hypertension	1	0	1.13
A - Abnormal renal or liver function (1 point each)	1 or 2	1	1.02
S - Stroke	1	2	1.88
B - Bleeding	1	3	3.74
L - Labile INRs	1	4	8.70
E - Elderly (> 65 years)	1	5	12.5
D - Drugs or alcohol (1 point each)	1 or 2		

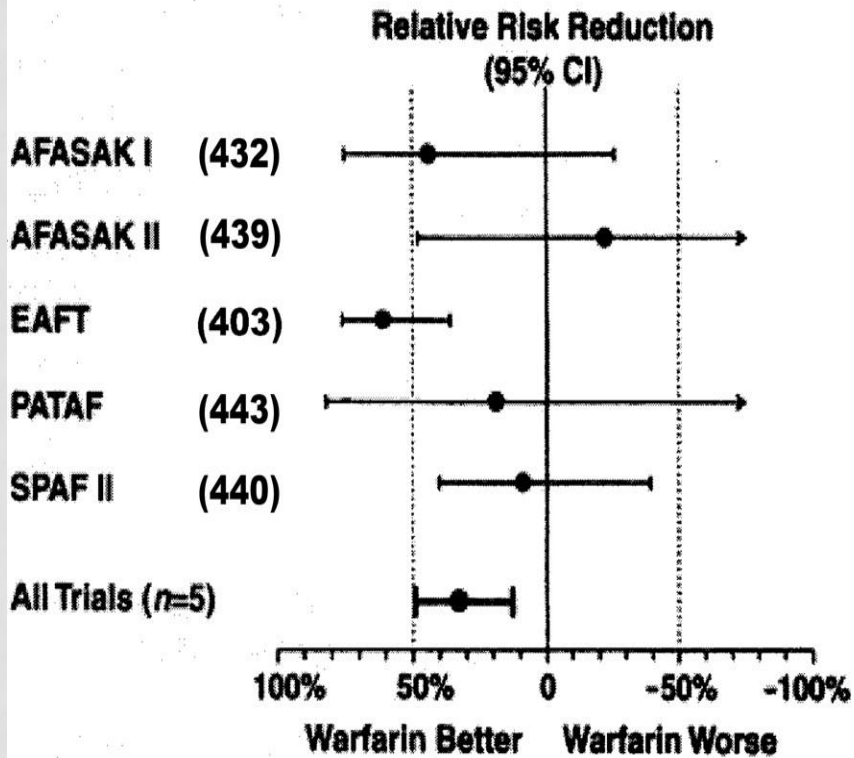
Note: HAS-BLED has been validated for warfarin, but not for the new anticoagulants.

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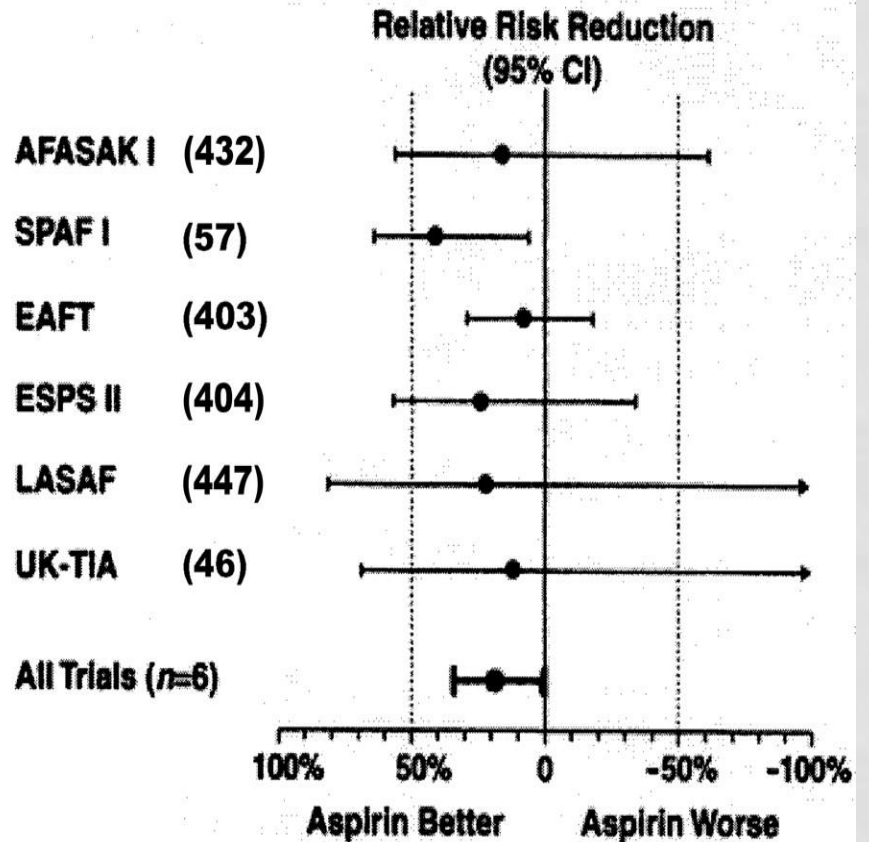
- Aspirin
- Warfarin
- Dabigatran (Pradaxa®)
- Rivaroxaban (Xarelto®)
- Apixiban (Eliquis®)
- Edoxoban (Savaysa®)

ANTICOAGULATION

Warfarin Compared with Aspirin



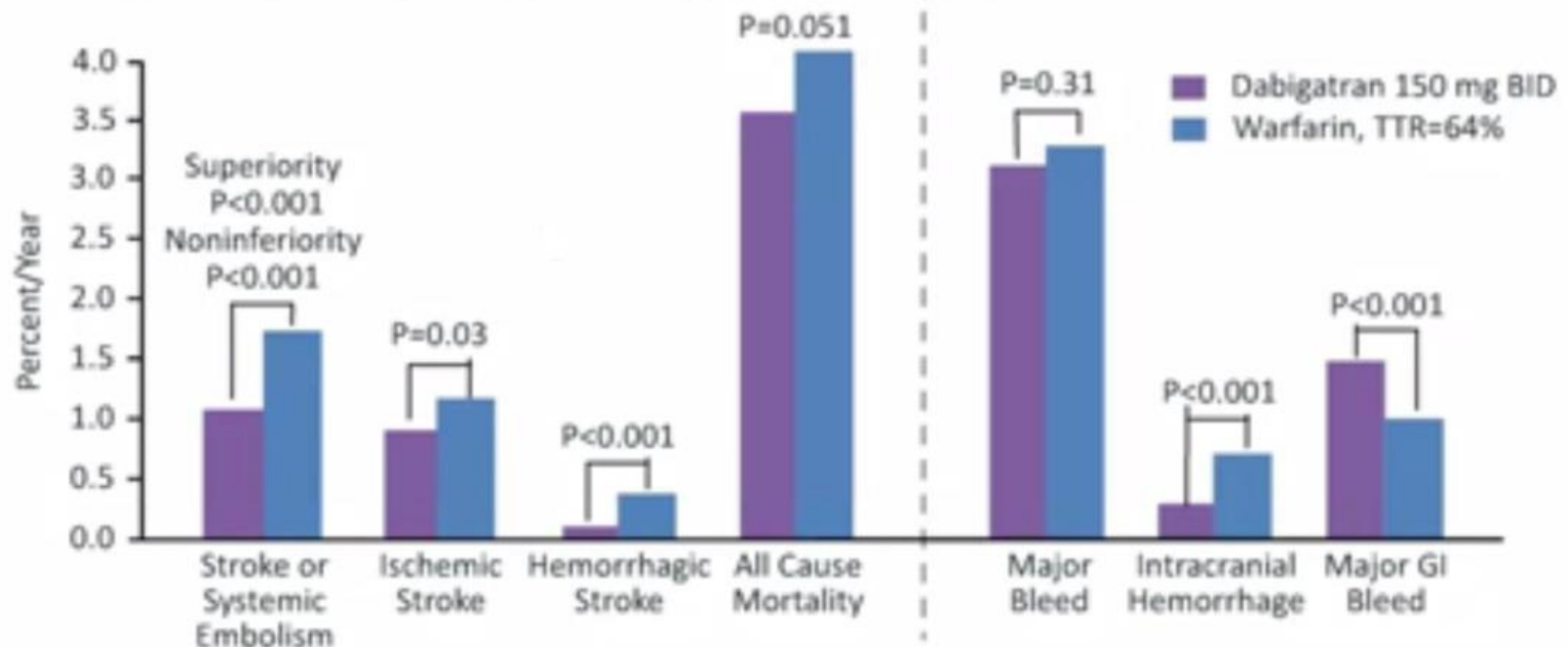
Aspirin Compared with Placebo



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Dabigatran versus Warfarin in NVAf—RE-LY Trial

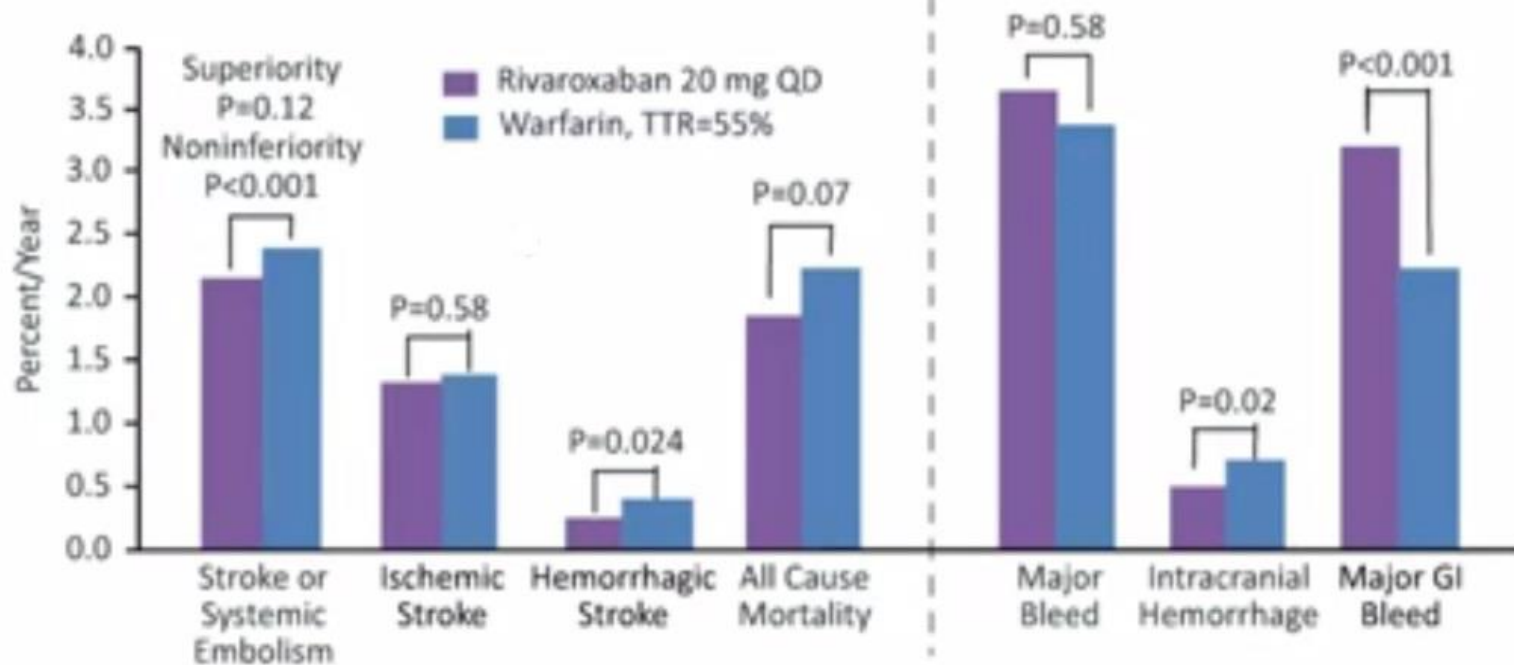
18,113 patients with NVAf randomized to warfarin (INR of 2-3), dabigatran (150 mg BID), or dabigatran (110 mg BID) for a median of 2 years



ANTICOAGULATION

Rivaroxaban versus Warfarin in NVAf—ROCKET AF Trial

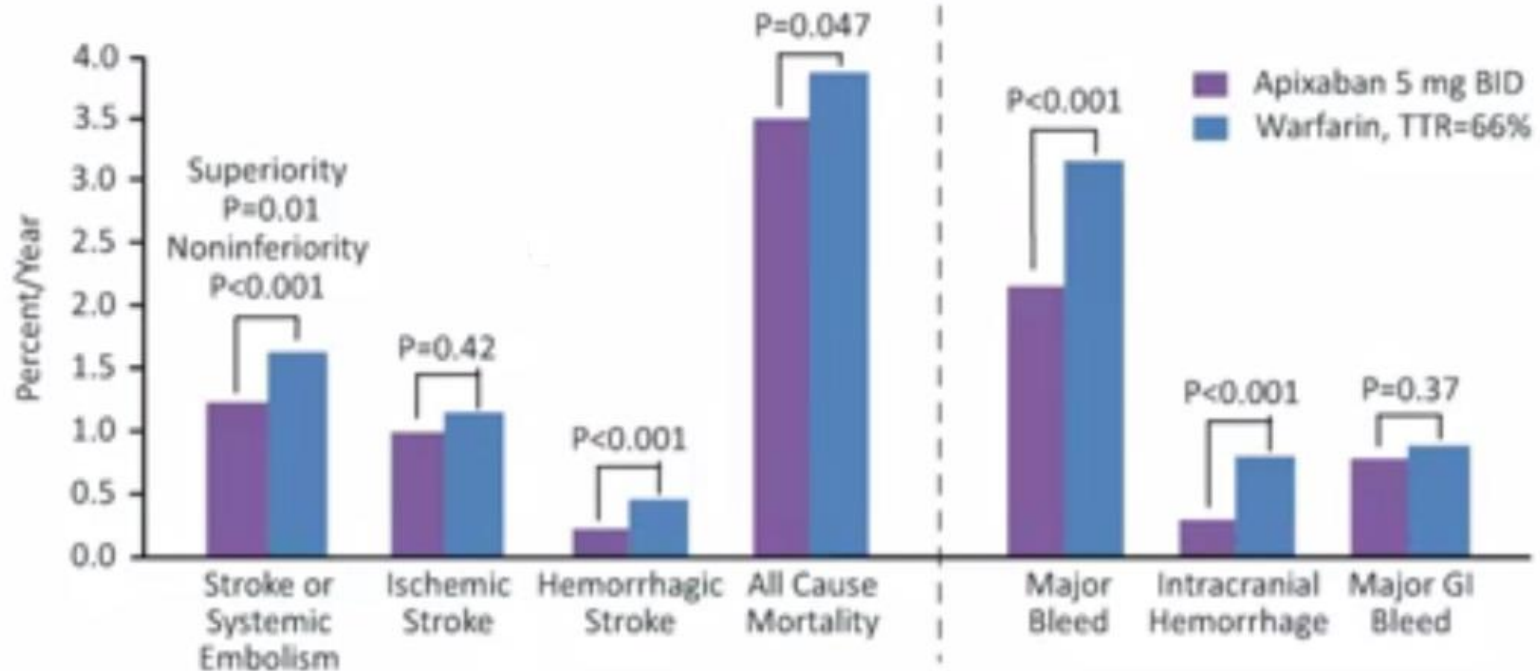
14,264 patients with NVAf randomized to warfarin (INR of 2-3) or rivaroxaban (15-20 mg QD) for 1.6 years



ANTICOAGULATION

Apixaban versus Warfarin in NVAF—ARISTOTLE Trial

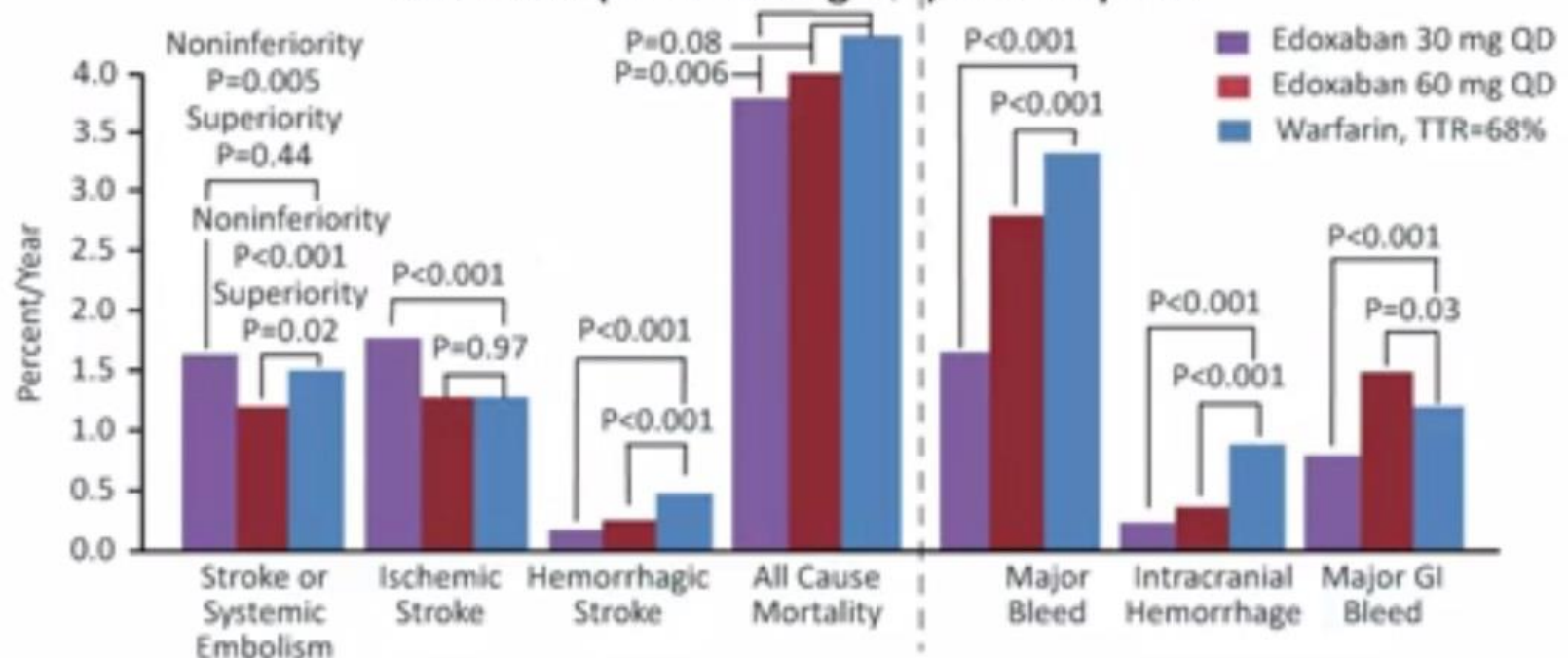
18,201 patients with NVAF randomized to warfarin (INR of 2-3) or apixaban (5 mg BID) for 1.8 years



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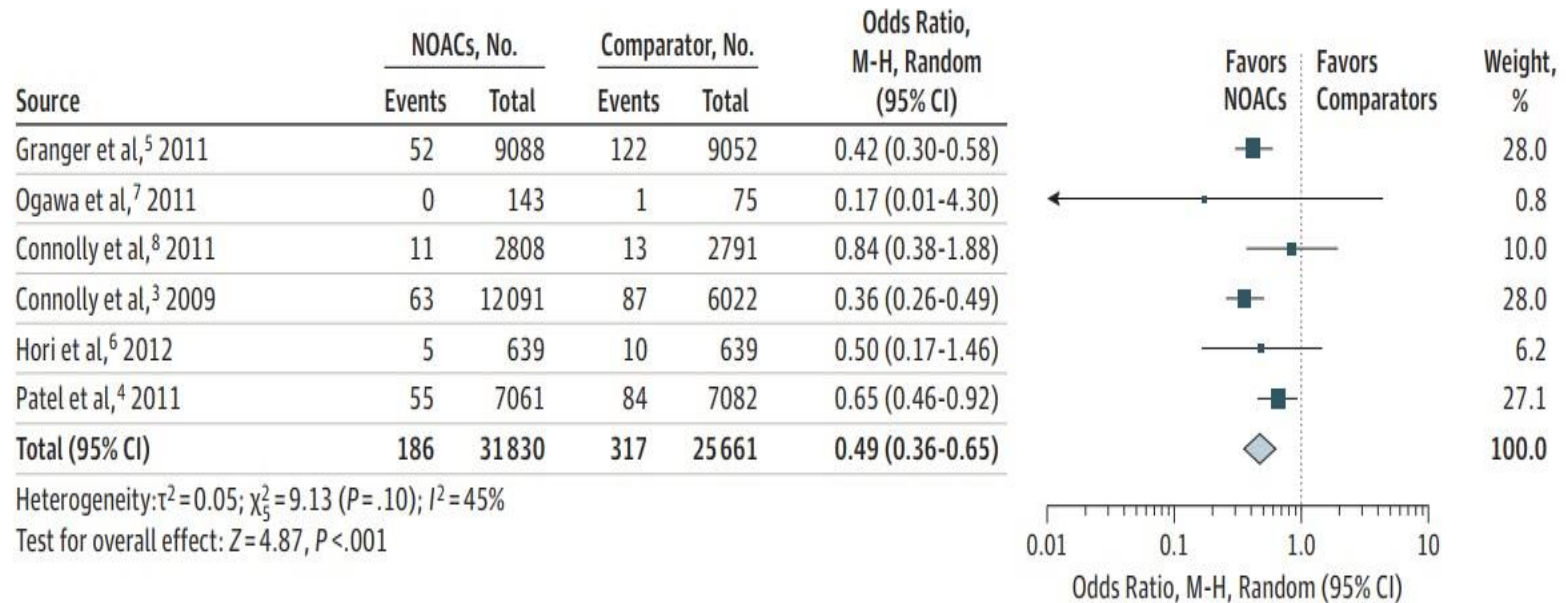
Edoxaban versus Warfarin in NVAF—ENGAGE AF Trial

21,105 patients with NVAF randomized to warfarin (INR of 2-3) or edoxaban (30 or 60 mg QD) for 2.8 years



ANTICOAGULATION

Figure. Odds Ratios of Intracranial Hemorrhage With Use of Novel Oral Anticoagulants



M-H indicates Mantel-Haenszel; NOACs, novel oral anticoagulants.

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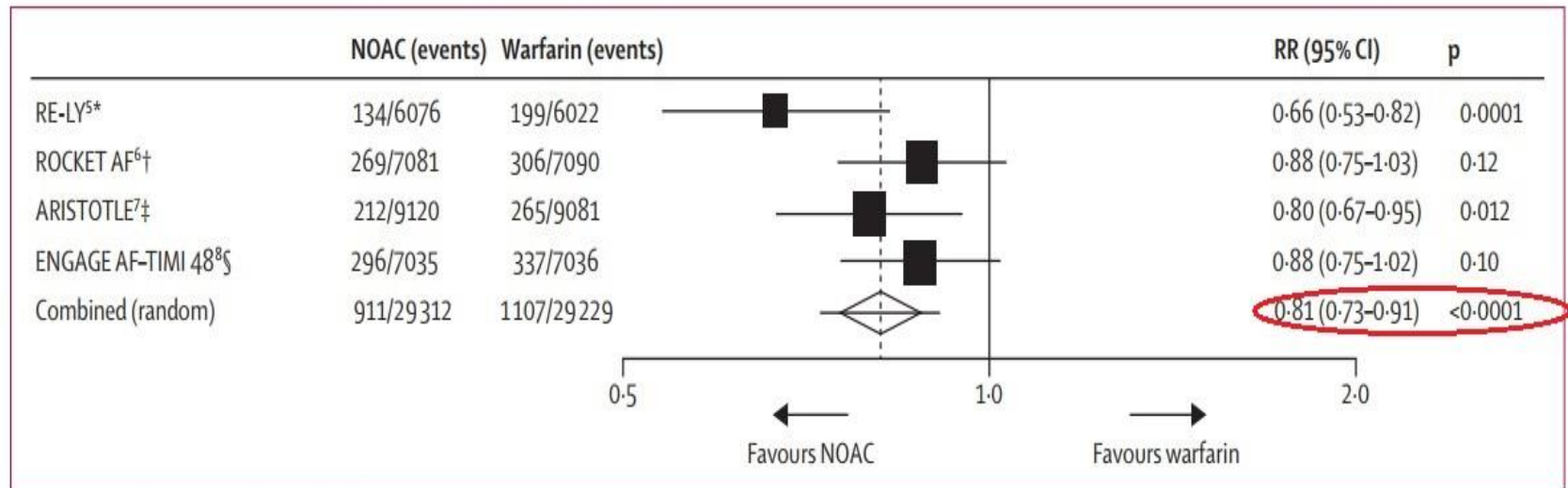


Figure 1: Stroke or systemic embolic events

Data are n/N, unless otherwise indicated. Heterogeneity: $I^2=47\%$; $p=0.13$. NOAC=new oral anticoagulant. RR=risk ratio. *Dabigatran 150 mg twice daily. †Rivaroxaban 20 mg once daily. ‡Apixaban 5 mg twice daily. §Edoxaban 60 mg once daily.

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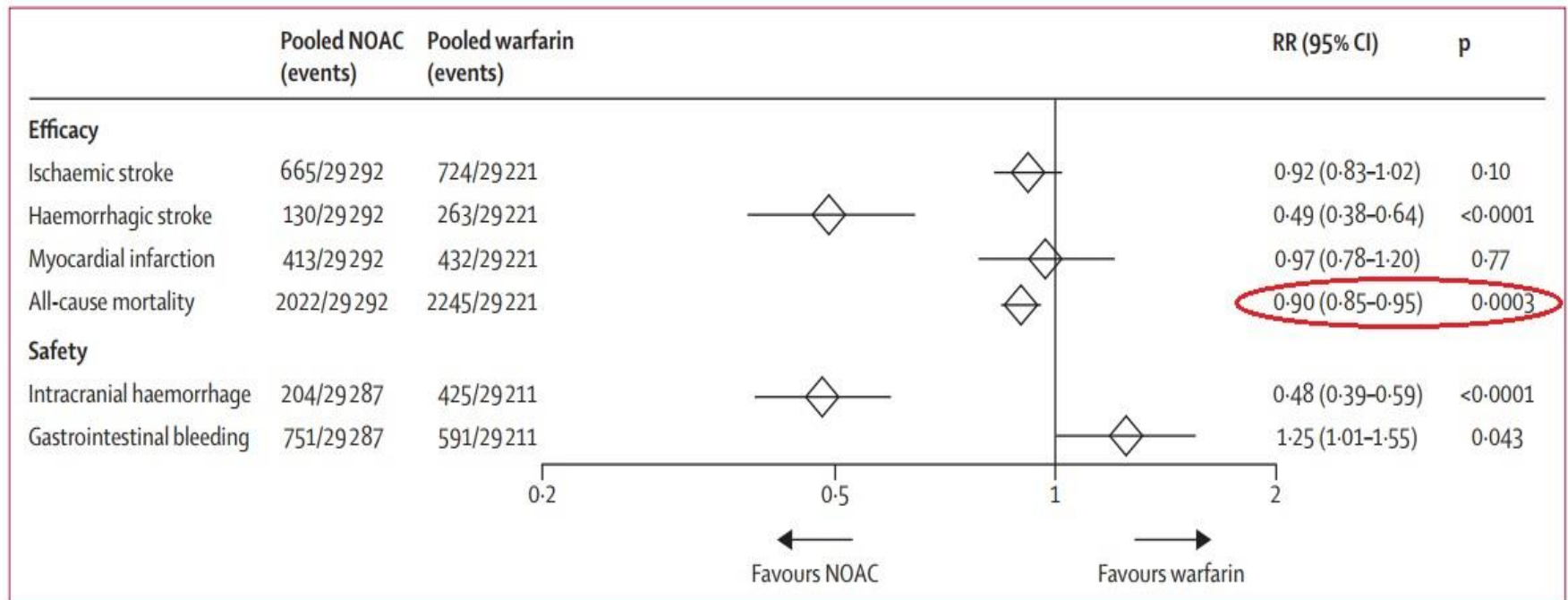


Figure 2: Secondary efficacy and safety outcomes

Data are n/N, unless otherwise indicated. Heterogeneity: ischaemic stroke $I^2=32\%$, $p=0.22$; haemorrhagic stroke $I^2=34\%$, $p=0.21$; myocardial infarction $I^2=48\%$, $p=0.13$; all-cause mortality $I^2=0\%$, $p=0.81$; intracranial haemorrhage $I^2=32\%$, $p=0.22$; gastrointestinal bleeding $I^2=74\%$, $p=0.009$. NOAC=new oral anticoagulant. RR=risk ratio.

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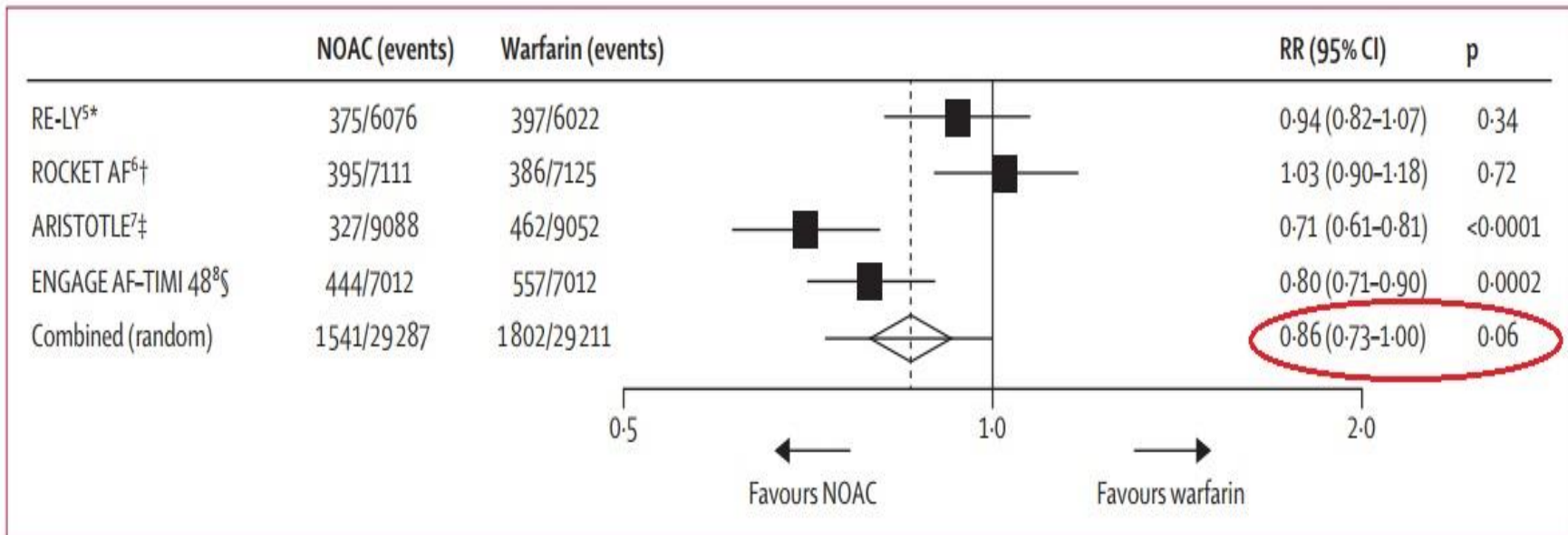


Figure 3: Major bleeding

Data are n/N, unless otherwise indicated. Heterogeneity: $I^2=83\%$; $p=0.001$. NOAC=new oral anticoagulant. RR=risk ratio. *Dabigatran 150 mg twice daily.

†Rivaroxaban 20 mg once daily. ‡Apixaban 5 mg twice daily. §Edoxaban 60 mg once daily.

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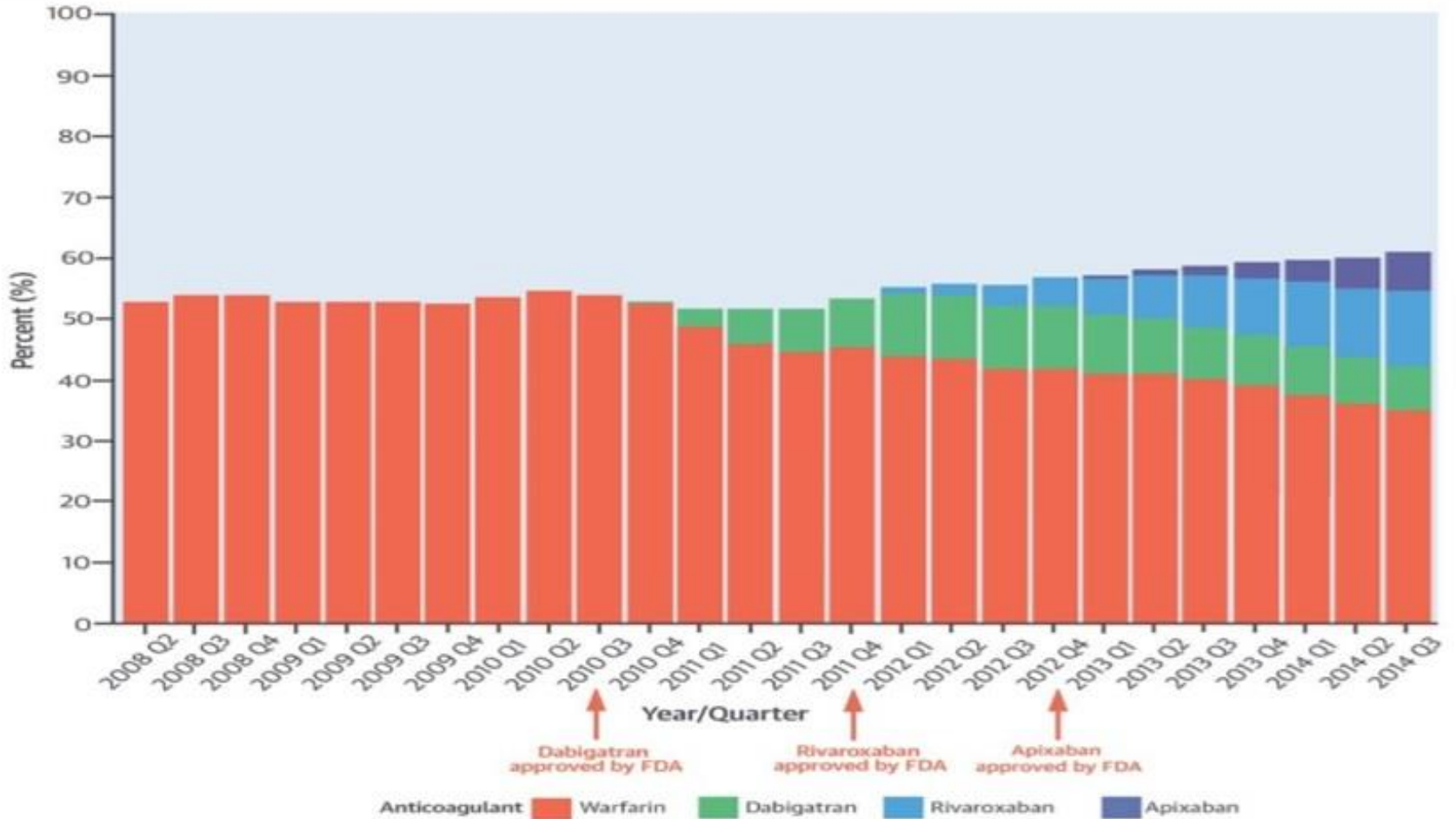
Advantages of DOACs

- Superior or comparable efficacy in reducing stroke/systemic embolism.
- Reduced rate of intra-cranial hemorrhage.
- No need for monitoring of levels.
- Rapid onset and offset.
- Minimal interaction with food.

Disadvantages of DOACs

- High cost.
- Lack of a reversal agent (except dabigatran).
- Higher risk of major GI bleed with some.

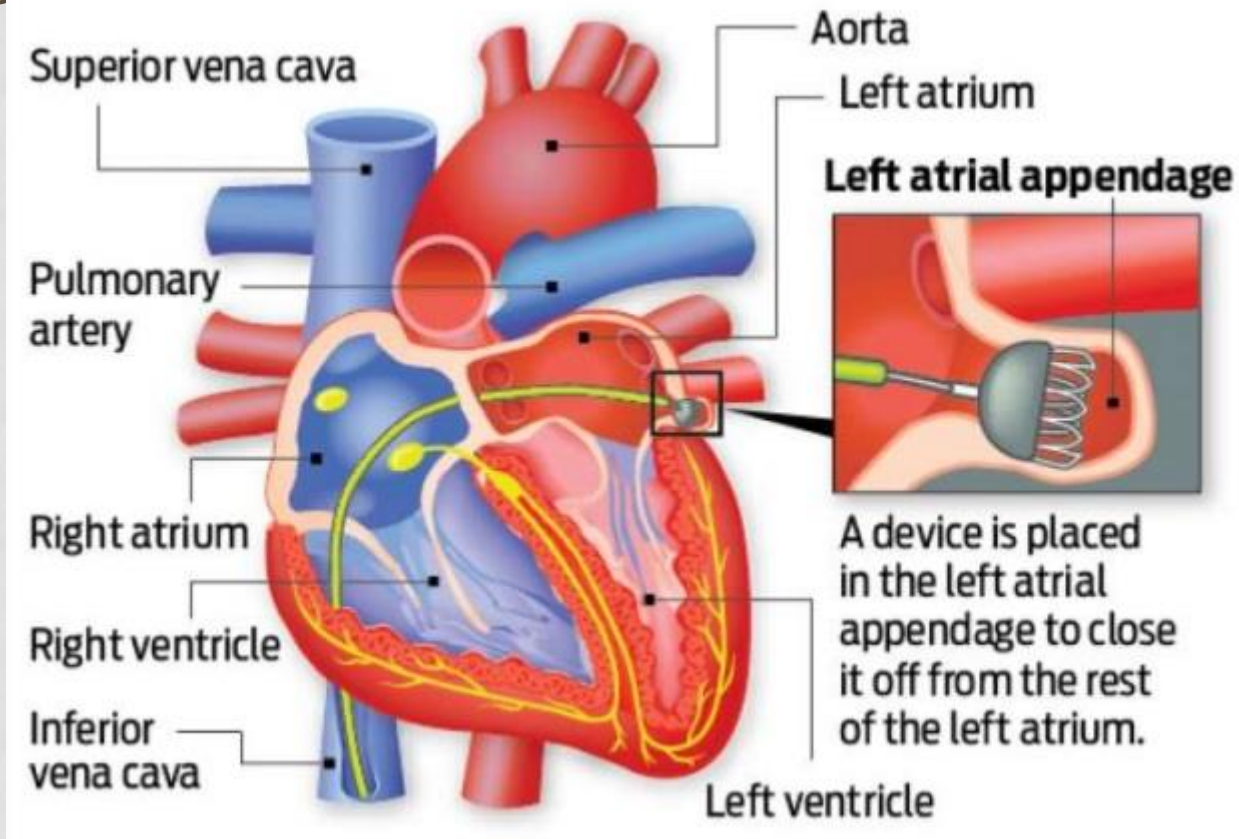
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Anticoagulation



Minimally Invasive, Local Solution

- Available sizes: 21, 24, 27, 30, 33 mm diameter

Intra-LAA design

- Avoids contact with left atrial wall to help prevent complications

Nitinol Frame

- Conforms to unique anatomy of the LAA to reduce embolization risk
- 10 active fixation anchors - designed to engage tissue for stability

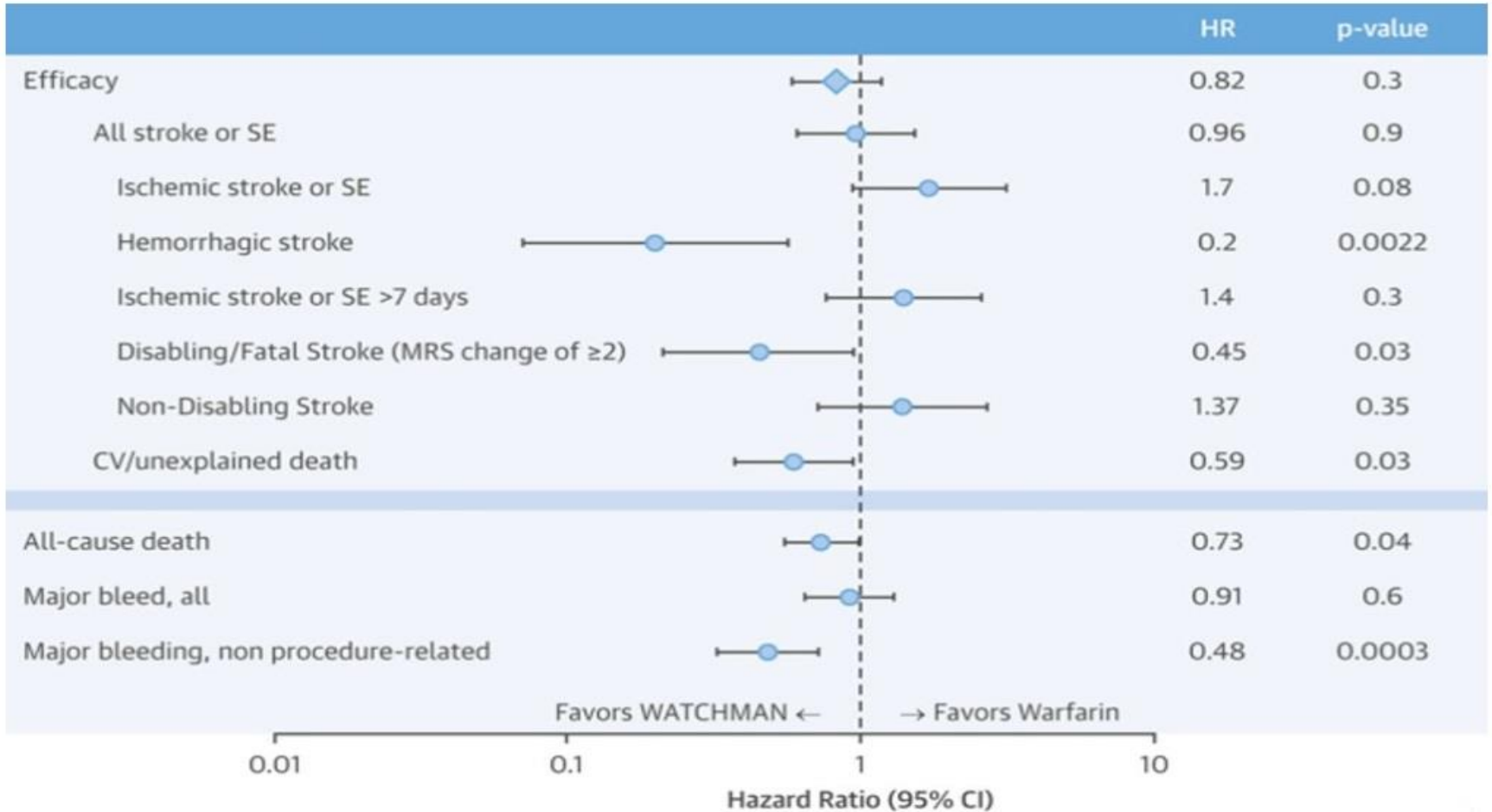
Proximal Face

- Minimizes surface area facing the left atrium to reduce post-implant thrombus formation
- 160 micron membrane PET cap designed to block emboli and promote healing

Warfarin Cessation

- 92% after 45 days, >99% after 12 months¹
- 95% implant success rate¹

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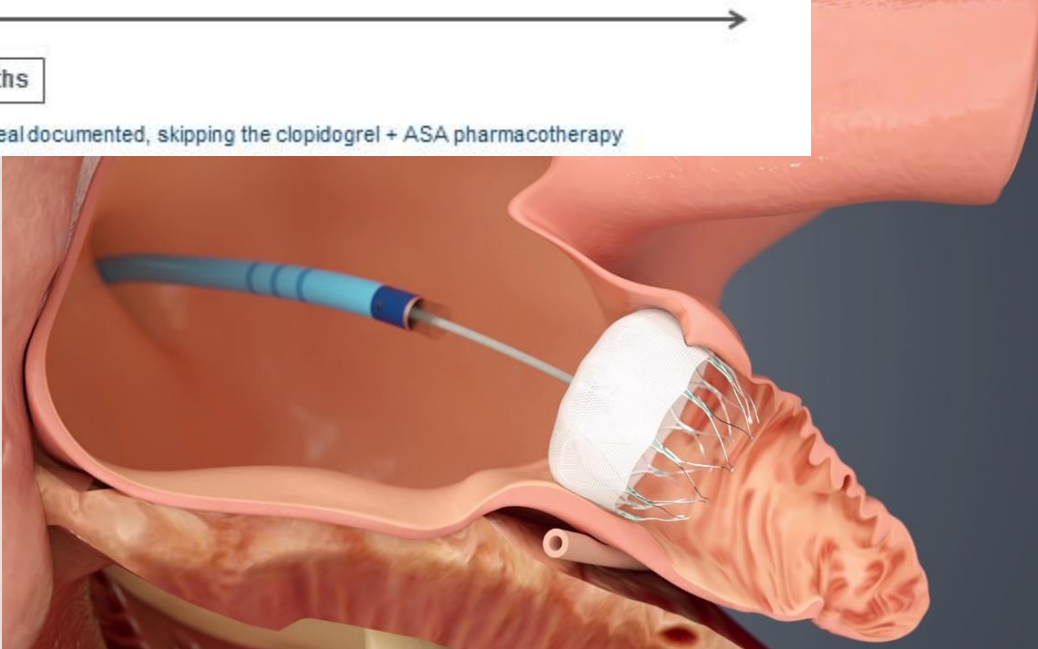


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- One-time implant that does not need to be replaced
- Performed in a cardiac cath lab/EP suite, does not need hybrid OR
- Performed by a Heart Team



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- 1 hour procedure*
- 1-2 day hospital stay*



* Typical to patient treatment in U.S. clinical trials

OUTLINE

- Epidemiology and Risk Factors
- Anticoagulation
- **Management Options**

MANAGEMENT OPTIONS

Recommended Therapies for Heart Rate and Rhythm Control in Patients with Atrial Fibrillation

Whether a rate control or rhythm control strategy is chosen is very specific to each individual patient. Factors to consider are: ability to tolerate medications, degree of symptoms, degree of functional limitation, occupation, age, and other co-morbidities. While many practitioners may have preferences for a particular strategy, the ACC recommends following the guidelines referenced below¹ and considering referral to a cardiologist with experience managing heart rhythm disorders.

Table 1: Recommended Drug Doses for Heart Rate Control in Patients with Atrial Fibrillation

Drug*	Dose Form	Loading or Starting Dose [†]	Maintenance Dose [†]	Potential Adverse Effects**
Amiodarone ^{6,1}	IV	150 mg over 10 min	0.5-1 mg/min	hypotension, heart block, sinus bradycardia, bronchospasm, HF, pulmonary toxicity, skin discoloration, hypothyroidism, hyperthyroidism, corneal deposits, optic neuropathy, warfarin interaction See black box warnings for this drug
	Oral	800 mg PO daily x 1 week, then 600 mg PO daily x 1 week, then 400 mg PO daily x 4 to 6 weeks, then 200 mg daily	Individual to patient	
Atenolol ²	Oral	25-100 mg daily	Same as starting dose	hypotension, heart block, bradycardia, bronchospasm, HF
Carvedilol ²	Oral	3.125-25 mg every 12 hrs (up to 50mg every 12 hrs for patients >85 kg). May use carvedilol sustained release 10-80 mg daily	Same as starting dose	hypotension, heart block, bradycardia, bronchospasm, HF See black box warnings for this drug
Digoxin ^{1,4}	IV	0.25 mg every 4-6 hrs up to 1 mg	0.125-0.25 mg daily (or orally)	life threatening arrhythmia, perceived color change, heart block, bronchospasm
Diltiazem ^{1,2}	IV	0.25 mg/kg over 2 min. 2 nd bolus can be given if HR > 100 bpm.	5-15 mg/hr	hypotension, heart block, HF
	Oral	Start with a non-sustained release dose 120-480 mg daily. Can switch to a slow-release/extended release dose, which is available and preferred	Same as starting dose	
Esmolol ¹	IV	500 mcg/kg over 1 min	50-200 mcg/kg/min	hypotension, heart block, bradycardia, bronchospasm, HF See black box warnings for this drug
Metoprolol ^{1,2}	IV	2.5-5 mg bolus over 2 min, up to 3 doses	N/A	hypotension, heart block, bradycardia, bronchospasm, HF See black box warnings for this drug
	Oral	25-100 mg twice daily. May use metoprolol succinate ER 25-200 mg daily	Same as starting dose	
Verapamil ^{1,2,4}	IV	0.075-0.15 mg/kg over 2 mins. 2 nd bolus can be given in 15-30 mins if needed	N/A	hypotension, heart block, HF
	Oral	Start with a non-sustained release dose 120-480 mg daily. Can switch to a slow-release/extended release dose, which is available and preferred	Same as starting dose	

*Drugs are listed alphabetically.

[†]Dosages given in the table may differ from those recommended by the manufacturers. **Refer to prescribing information for more complete information.

⁶Amiodarone can be useful to control heart rate in patients with atrial fibrillation when other measures are unsuccessful or contraindicated

Notes: AF = atrial fibrillation; BID = twice a day; GI = gastrointestinal; IV = intravenous; HR = heart rate; HF = heart failure; N/A = not applicable.

MANAGEMENT OPTIONS

Rhythm control



**Anti-arrhythmic
Medications**



Ablation

MANAGEMENT OPTIONS

Rhythm control



***Anti-arrhythmic
Medications***



Ablation

MANAGEMENT OPTIONS

Table 2: Recommended Drug Doses for Heart Rhythm Control in Patients with Atrial Fibrillation

Drug*	Dose Form	Loading or Starting Dose†	Maintenance Dose‡	Potential Adverse Effects**
Amiodarone ¹	Oral	Inpatient: 1.2 to 1.8 g per day in divided dose until 10 g total or 30 mg/kg as single dose Outpatient: 600 to 800 mg per day divided dose until 10 g total While 10 g desired to see max efficacy, does not have to be completed as an inpatient before fully loaded. ⁴	200-400 mg per day	hypotension, bradycardia, QT prolongation, torsades de pointes (rare), GI upset, constipation, phlebitis (IV), photosensitivity, pulmonary toxicity, polyneuropathy, hepatic toxicity, thyroid dysfunction, eye complications See black box warnings for this drug
Dofetilide ¹	Oral	Creatinine Clearance > 60 mL/min = 500 mcg BID 40-60 mL/min = 250 mcg BID 20 to 40 mL/min = 125 mcg BID < 20 mL/min = Contraindicated	125-500 mcg every 12 hrs, based on renal function. Must be initiated in hospital and patient must be registered to receive this drug. Adjust dose for renal function, body size and age.	QT prolongation, torsades de pointes See black box warnings for this drug
Dronedarone ²	Oral	400 mg twice daily, with meals	Same as starting dose	bradycardia, heart block, HF, hepatic toxicity, pulmonary toxicity, diarrhea, nausea, abdominal pain, vomiting, asthenia, stroke, death See black box warnings for this drug
Flecainide ^{1,2}	Oral	200-300 mg ^{1,‡} When starting a patient on flecainide, it is prudent to do a treadmill stress test after the patient is fully loaded. ³	50 to 150 mg every 12 hrs ²	hypotension, atrial flutter with high ventricular rate, ventricular tachycardia, HF Close monitoring of this drug is required. See black box warnings for this drug
Ibutilide ^{1,2}	IV	1 mg over 10 min; repeat 1 mg when necessary (but risk of proarrhythmia increases)	N/A	QT prolongation, torsades de pointes See black box warnings for this drug
Propafenone ^{1,2}	Oral	600 mg	150-300 mg every 8 hrs, or sustained release 225-425 mg every 12 hrs	hypotension, atrial flutter with high ventricular rate See black box warnings for this drug
Sotalol ^{1,2}	Oral	80-160 mg, to a max of 320 mg every 12 hrs, based on renal function Creatinine clearance should be calculated prior to dosing.	Same as starting dose	torsades de pointes, HF, bradycardia, exacerbation of chronic obstructive or bronchospastic lung disease See black box warnings for this drug

*Drugs are listed alphabetically. **Refer to prescribing information for more complete information.

† Dosages given in the table may differ from those recommended by the manufacturers.

‡ Insufficient data are available on which to base specific recommendations for the use of one loading regimen over another for patients with ischemic heart disease or impaired left ventricular function.

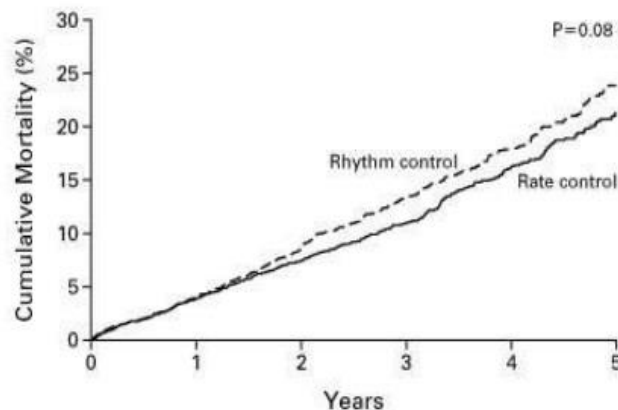
Notes: AF = atrial fibrillation; BID = twice a day; GI = gastrointestinal; IV = intravenous; HR = heart rate; HF = heart failure; N/A = not applicable.

Click on drug names in table for more detailed usage information for each drug.

MANAGEMENT OPTIONS

The AFFIRM trial

- 4,060 patients randomized
- Rate control vs. rhythm control
- Endpoint = All cause mortality



No. OF DEATHS		number (percent)				
Rhythm control	0	80 (4)	175 (9)	257 (13)	314 (18)	352 (24)
Rate control	0	78 (4)	148 (7)	210 (11)	275 (16)	306 (21)

No survival advantage with DC cardioversions and anti-arrhythmic drugs

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MANAGEMENT OPTIONS

Rhythm control



Anti-arrhythmic
Medications



ABLATION

ABLATION

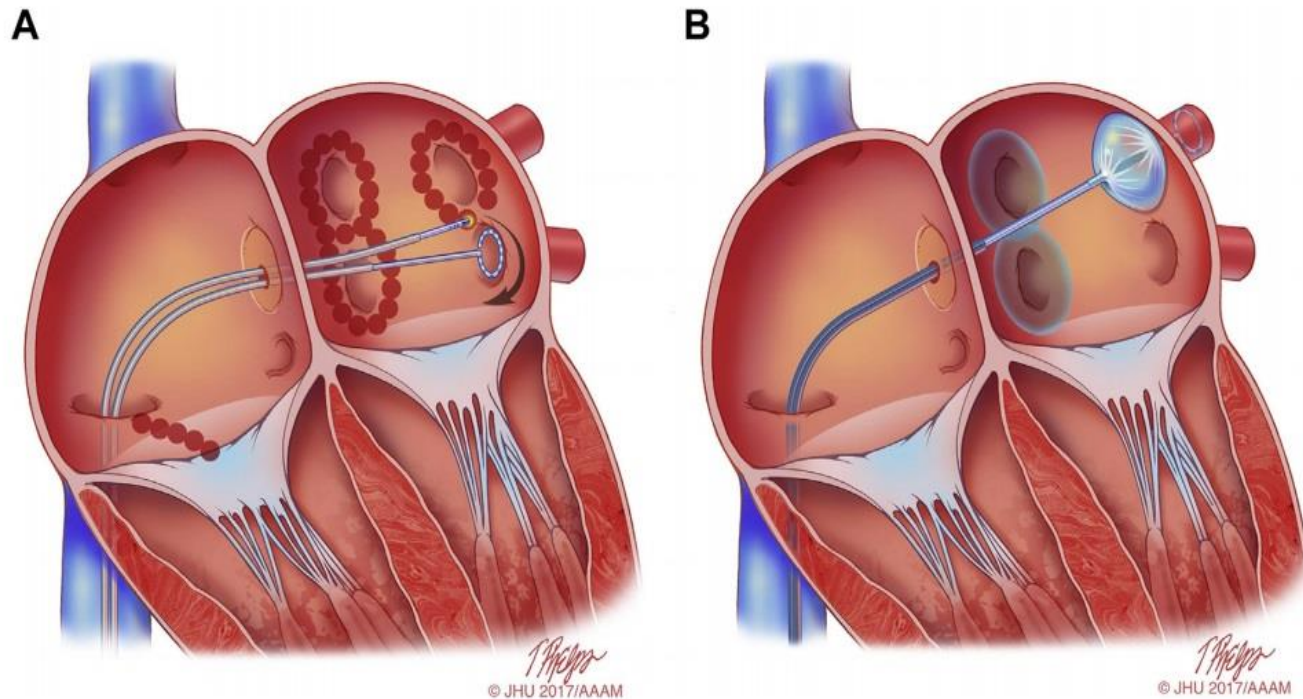
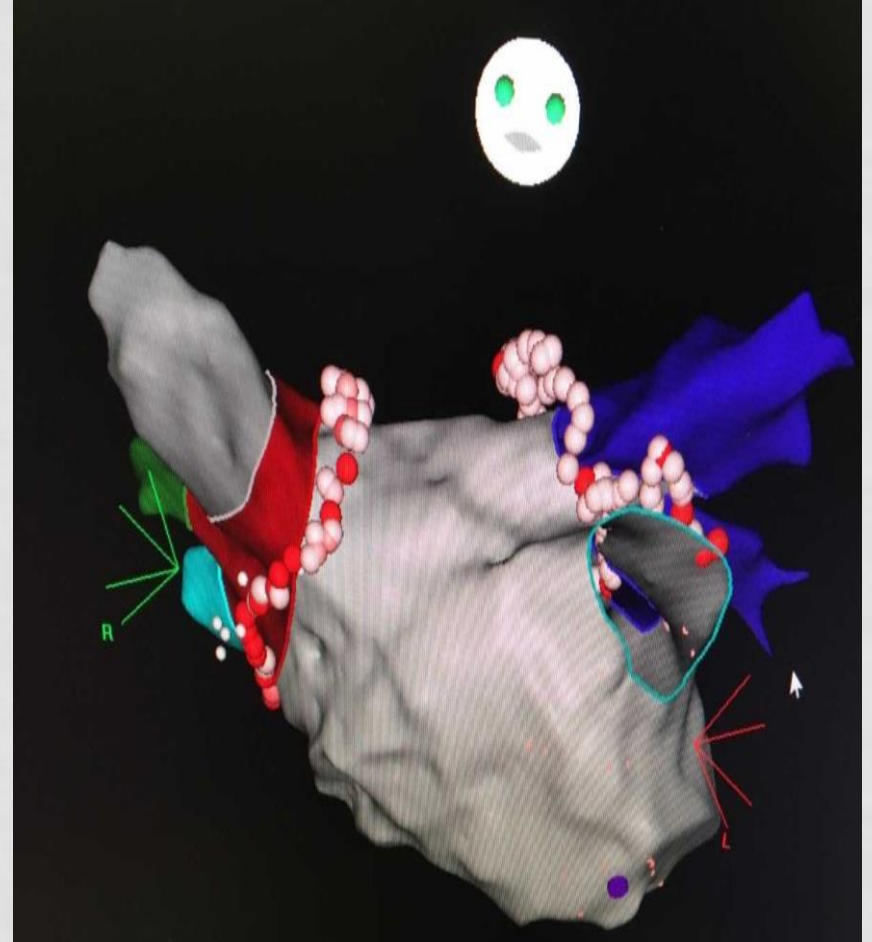
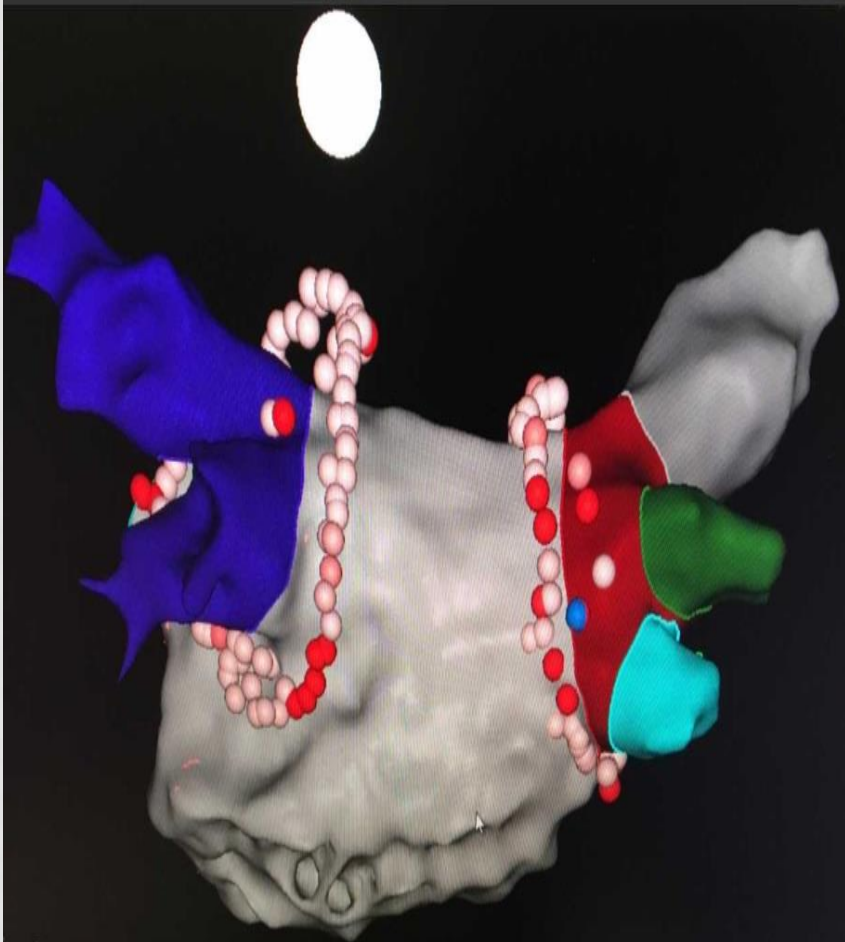


Figure 9 Schematic drawing showing catheter ablation of atrial fibrillation using either RF energy or cryoballoon AF ablation. **A:** Shows a typical wide area lesion set created using RF energy. Ablation lesions are delivered in a figure of eight pattern around the left and right PV veins. Also shown is a linear cavotricuspid isthmus lesion created for ablation of typical atrial flutter in a patient with a prior history of typical atrial flutter or inducible isthmus-dependent typical atrial flutter at the time of ablation. A multielectrode circular mapping catheter is positioned in the left inferior PV. **B:** Shows an ablation procedure using the cryoballoon system. Ablation lesions have been created surrounding the right PVs, and the cryoballoon ablation catheter is positioned in the left superior PV. A through the lumen multielectrode circular mapping catheter is positioned in the left superior PV. *Illustration: Tim Phelps © 2017 Johns Hopkins University, AAM.*

ABLATION



MANAGEMENT OPTIONS

Indications for Catheter Ablation of Symptomatic Atrial Fibrillation

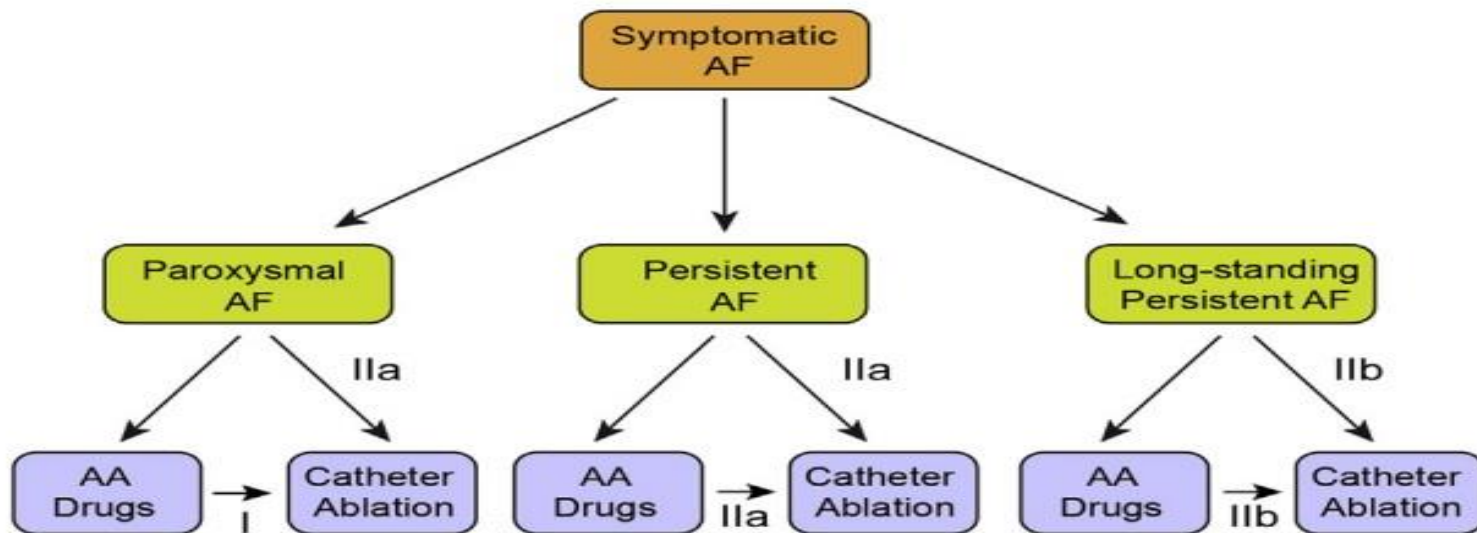
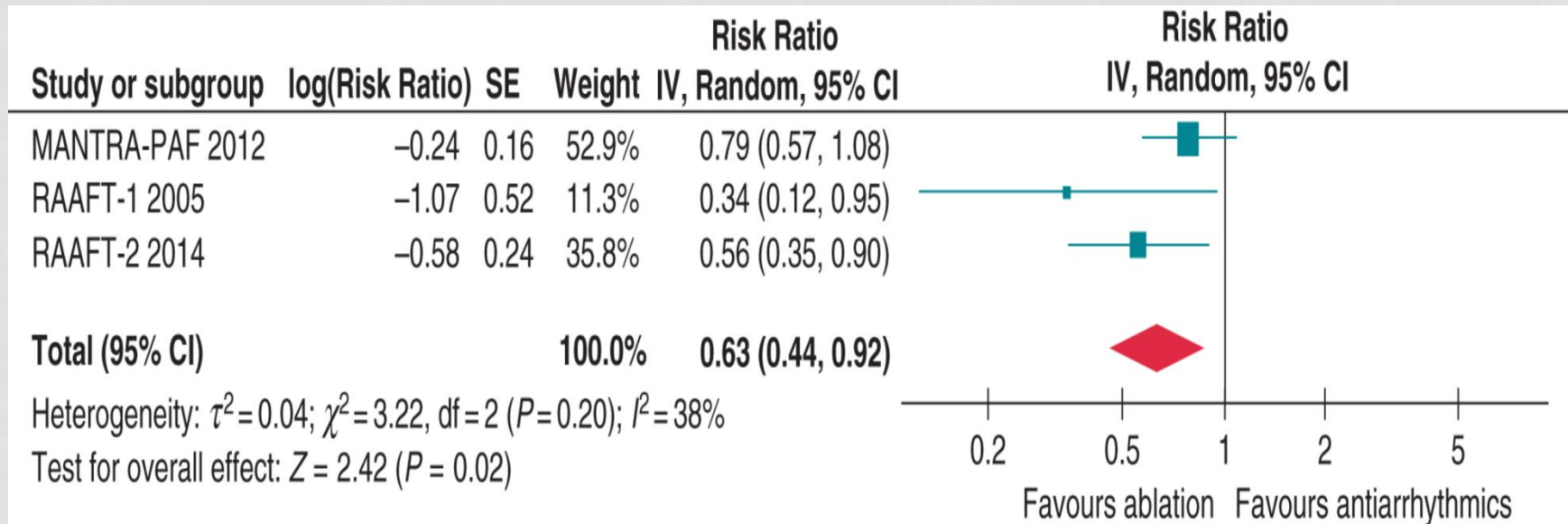


Figure Indications for catheter ablation of symptomatic atrial fibrillation. Shown in this figure are the indications for catheter ablation of symptomatic paroxysmal, persistent, and long-standing persistent AF. The Class for each indication based on whether ablation is performed after failure of antiarrhythmic drug therapy or as first-line therapy is shown.

CATHETER ABLATION OF AF AS FIRST-LINE THERAPY

- Patients with paroxysmal atrial fibrillation who have symptomatic pauses (tachy-brady syndrome).
- High-level competitive athletes with paroxysmal or persistent AF who want to avoid medications which could potentially reduce their peak heart rate and/or impair cardiac function.
- Patients with symptomatic paroxysmal or persistent AF and a left ventricular ejection fraction (LVEF) of ≤ 35 percent.

MANAGEMENT OPTIONS



Pillars of management of atrial fibrillation


- Risk Factor Modification
- Risk Factor Modification
- Risk Factor Modification
- Anticoagulation
- Rate Vs. Rhythm control

A word cloud of question words (Who, What, When, Where, Why, How) arranged around a large blue question mark on a chalkboard background. The words are written in white, uppercase letters of varying sizes and orientations, creating a circular pattern around the central question mark. The background is a dark, textured surface resembling a chalkboard.

HOW WHY HOW
WHERE WHEN WHERE WHO
WHERE WHY
WHAT WHO
WHAT WHO WHEN
WHAT WHAT
WHAT WHEN
WHO WHERE HOW
WHY



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Atrial Fibrillation (AF or AFib)



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What is Atrial Fibrillation?

AFib is an irregular heartbeat that can lead to stroke and other heart-related complications.



Symptoms of AFib

Sometimes people with AFib have no symptoms; others may experience one or more of the following symptoms.

Atrial Fibrillation

• Introduction

• What is Atrial Fibrillation?

• Why AFib Matters

High Blood Pressure, AFib and Stroke

• Understand your Risk for AFib

Children

• Symptoms of AFib

• Treatment & Prevention of AFib

Treatment Guidelines of AFib

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