Atrial Fibrillation Update

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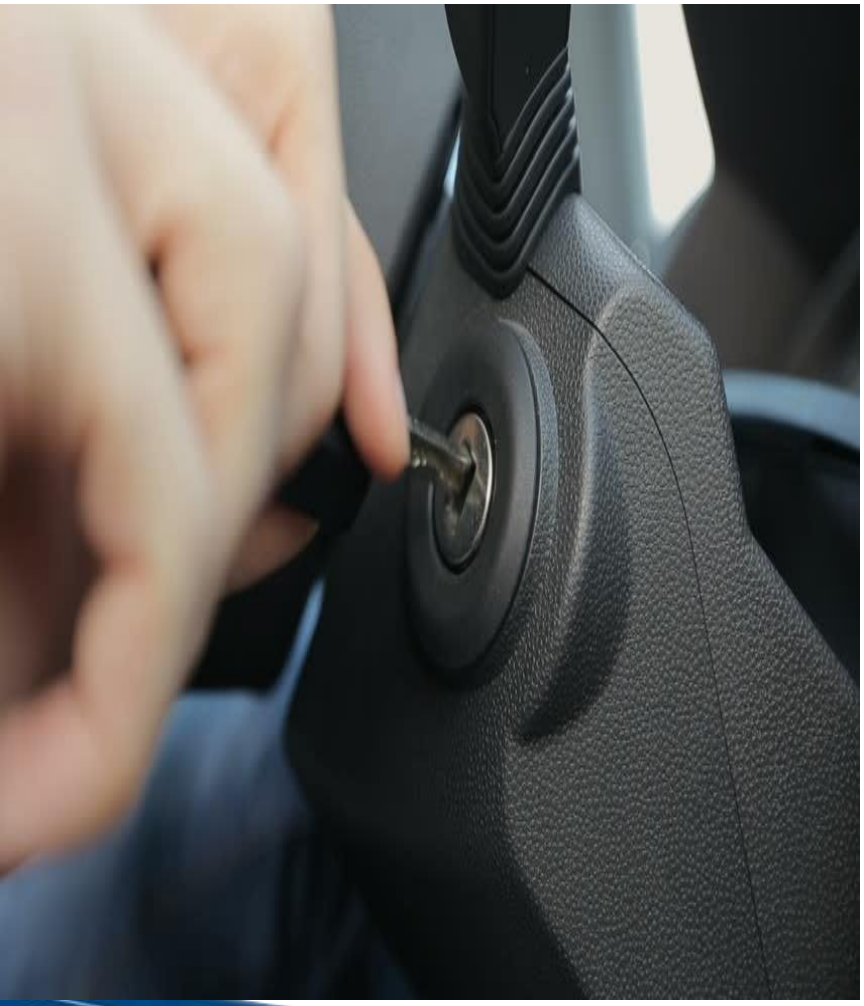
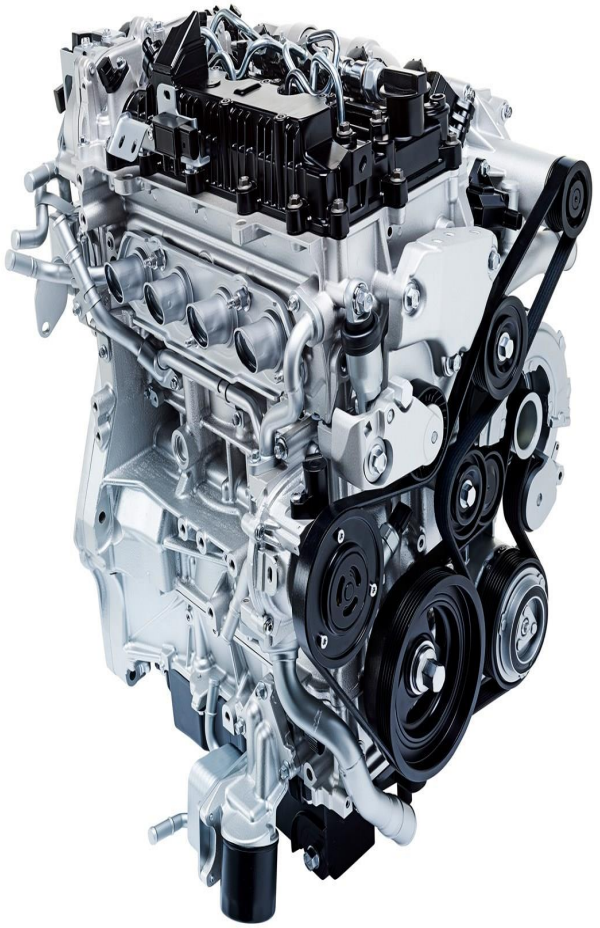
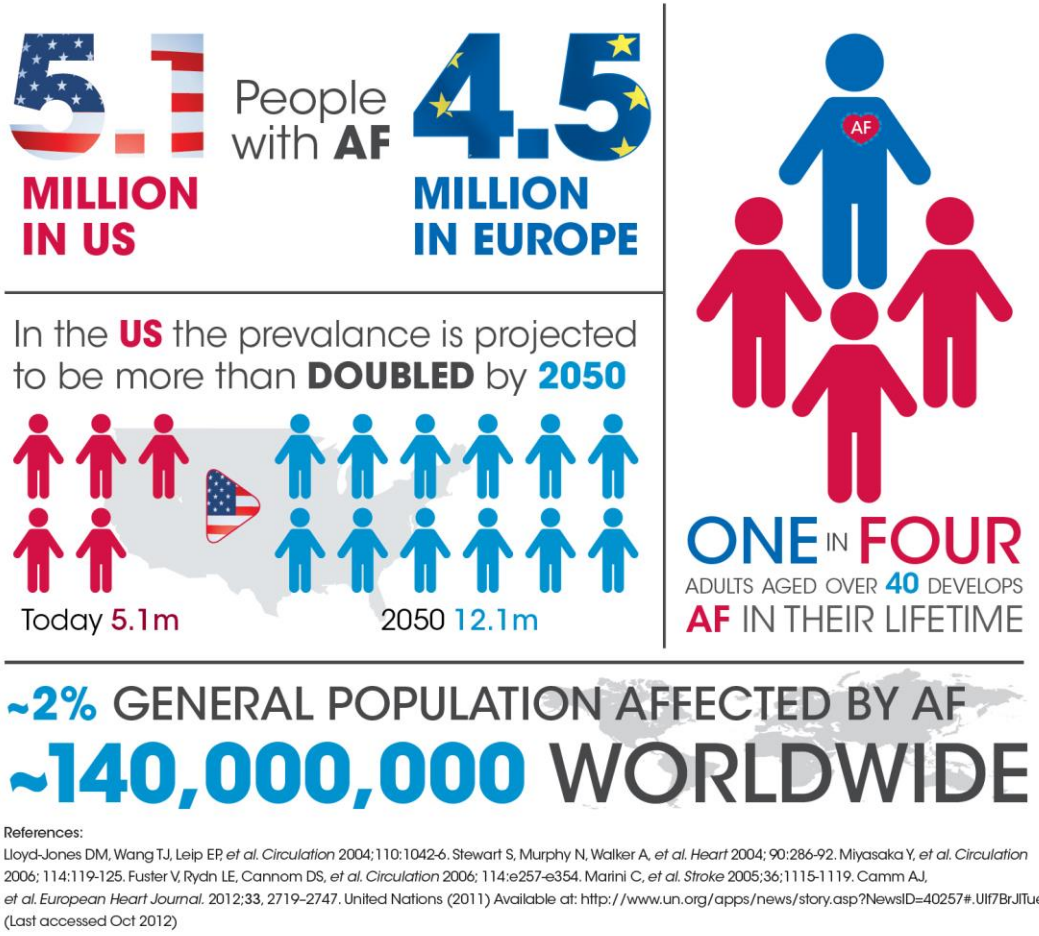
Atrial Fibrillation





Who, me ?



References:
Lloyd-Jones DM, Wang TJ, Leip EP, *et al. Circulation* 2004;110:1042-6. Stewart S, Murphy N, Walker A, *et al. Heart* 2004; 90:286-92. Miyasaka Y, *et al. Circulation* 2006; 114:119-125. Fuster V, Rydn LE, Cannom DS, *et al. Circulation* 2006; 114:e257-e354. Marini C, *et al. Stroke* 2005;36;1115-1119. Camm AJ, *et al. European Heart Journal.* 2012;33, 2719–2747. United Nations (2011) Available at: http://www.un.org/apps/news/story.asp?NewsID=40257#.Ulf7BrJITue (Last accessed Oct 2012)

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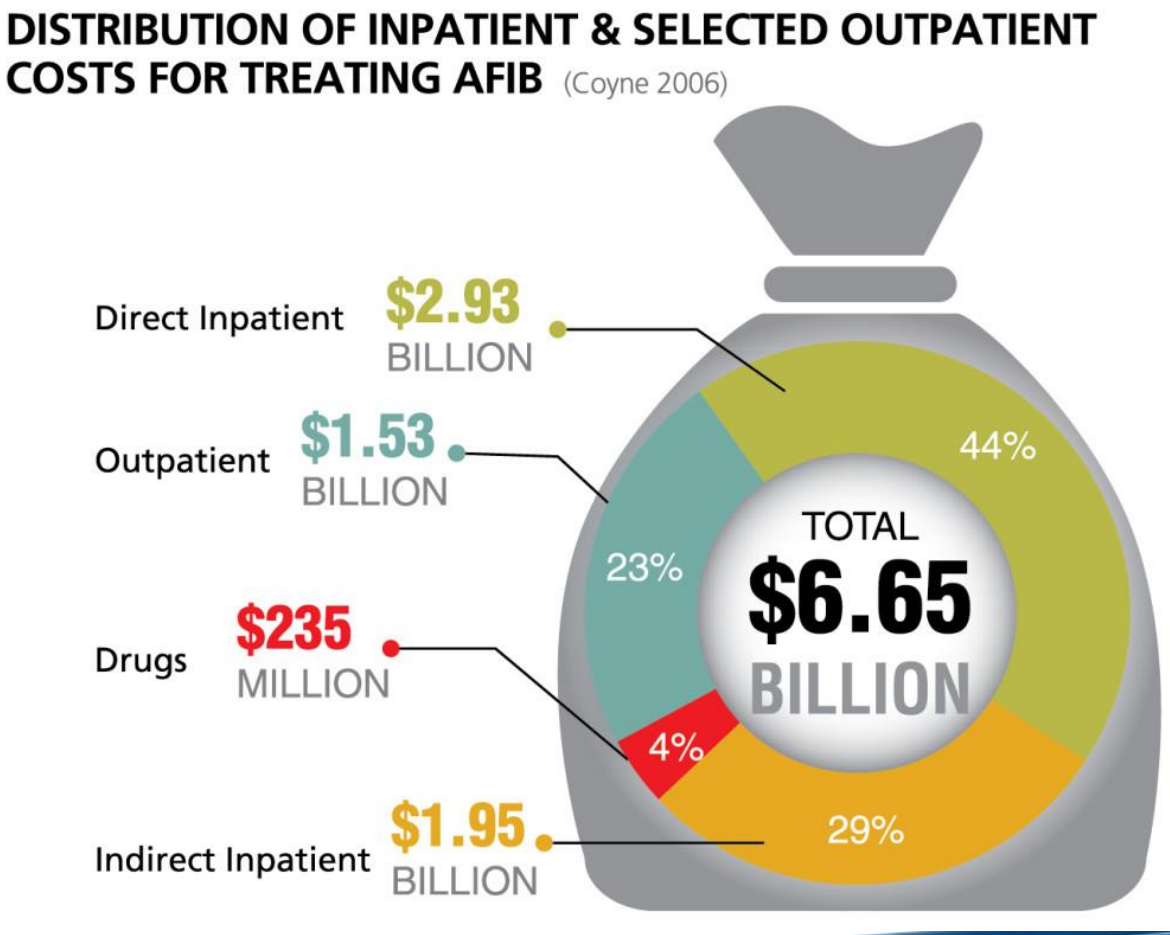
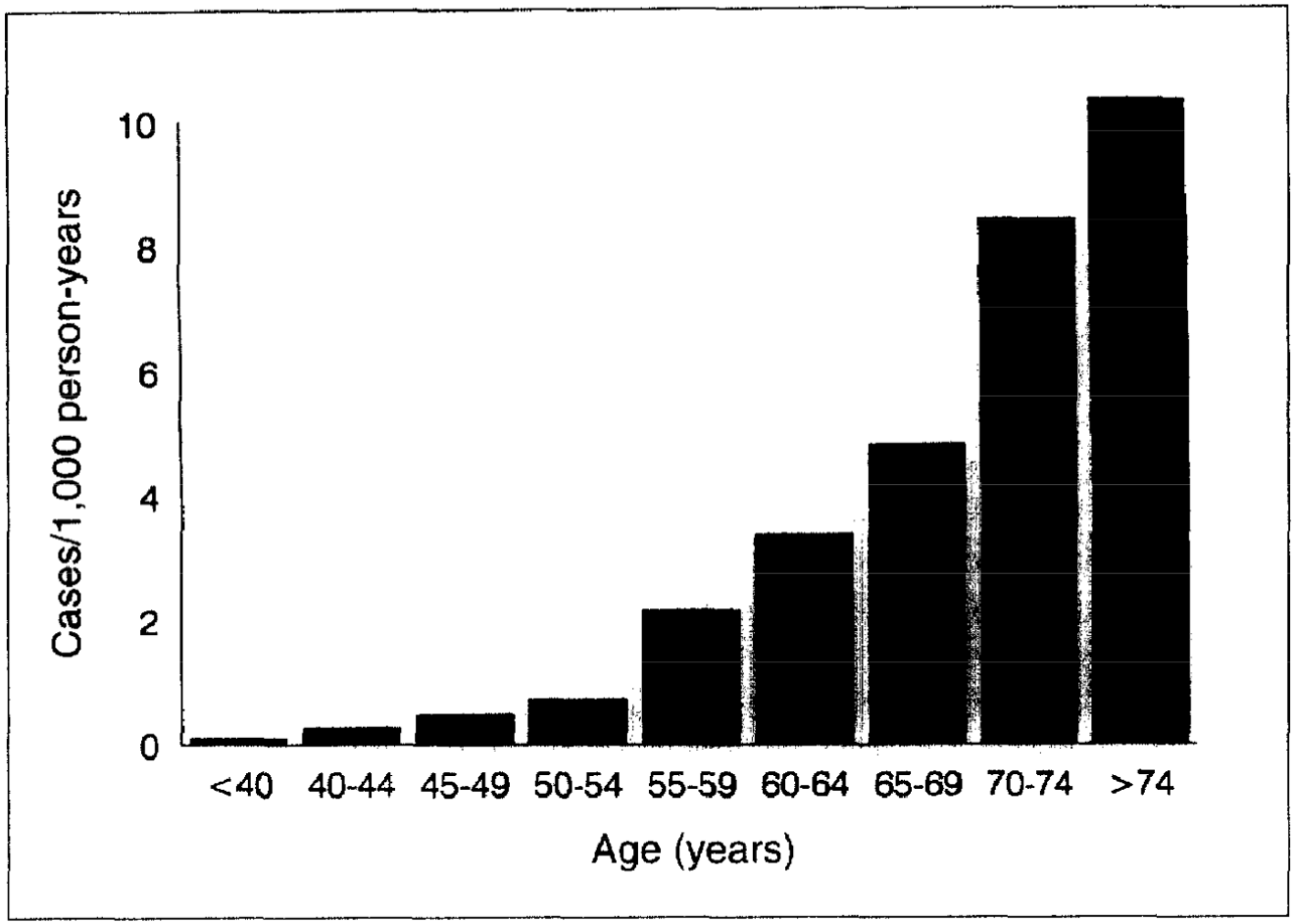
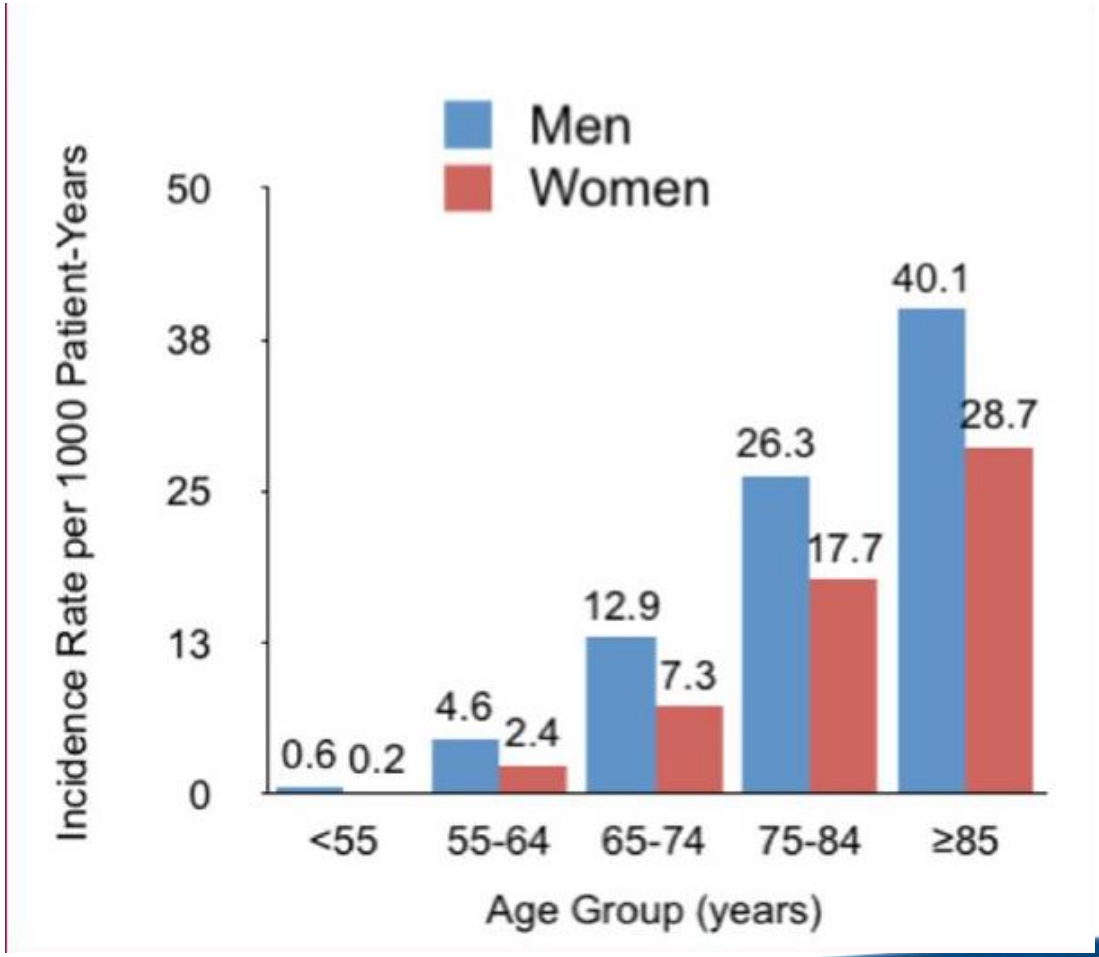
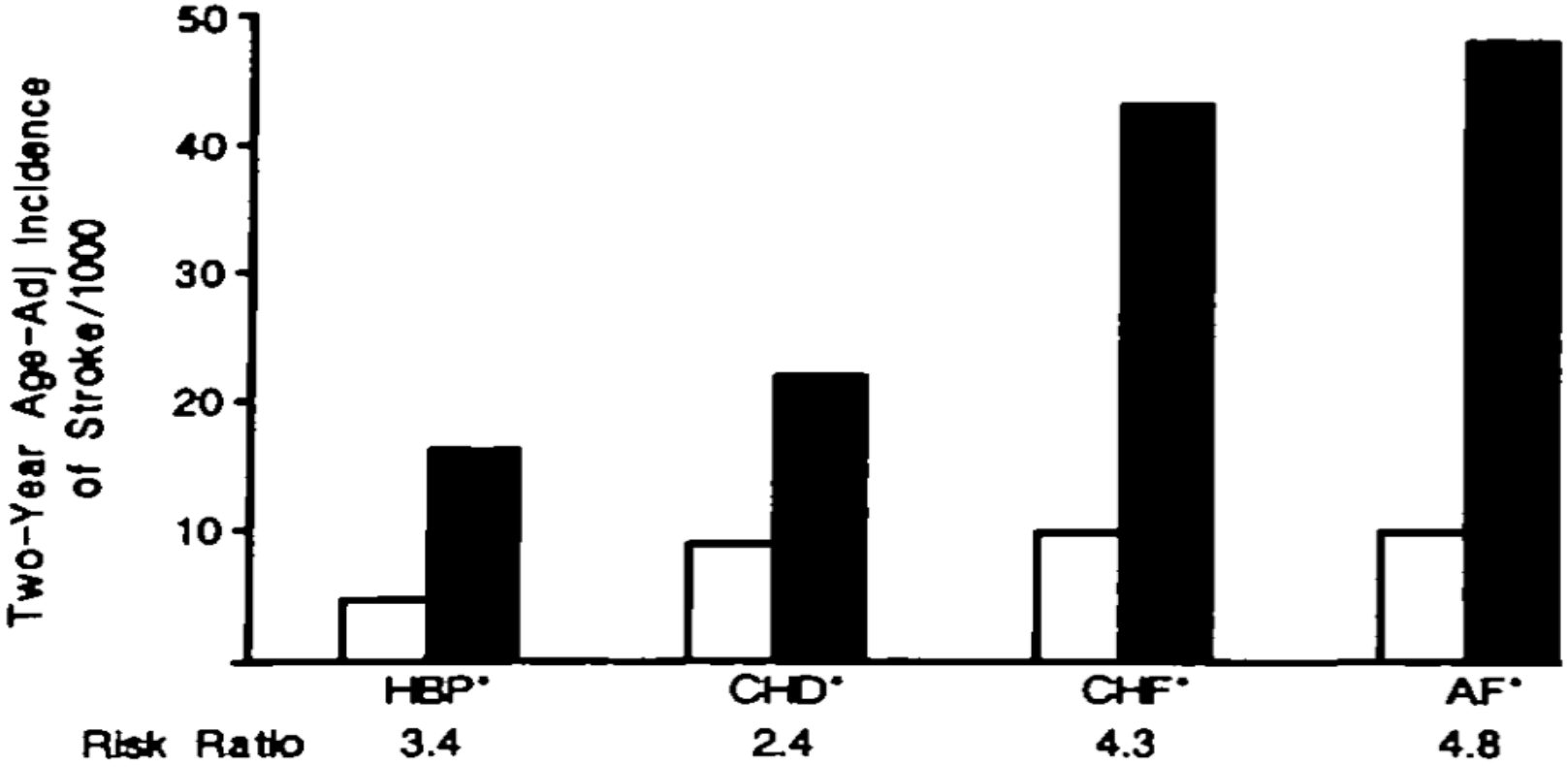

DISTRIBUTION OF INPATIENT & SELECTED OUTPATIENT COSTS FOR TREATING AFIB (Coyne 2006)
Direct Inpatient
$2.93 BILLION
Outpatient
$1.53 BILLION
Drugs
$235 MILLION
Indirect Inpatient
$1.95 BILLION
TOTAL
$6.65 BILLION
44%
23%
4%
29%



Krahn, A et al: The Natural History of Atrial Fibrillation: Incidence, Risk Factors, and Prognosis in the Manitoba Follow-up Study. Am J Med 1995; 98: 476-484

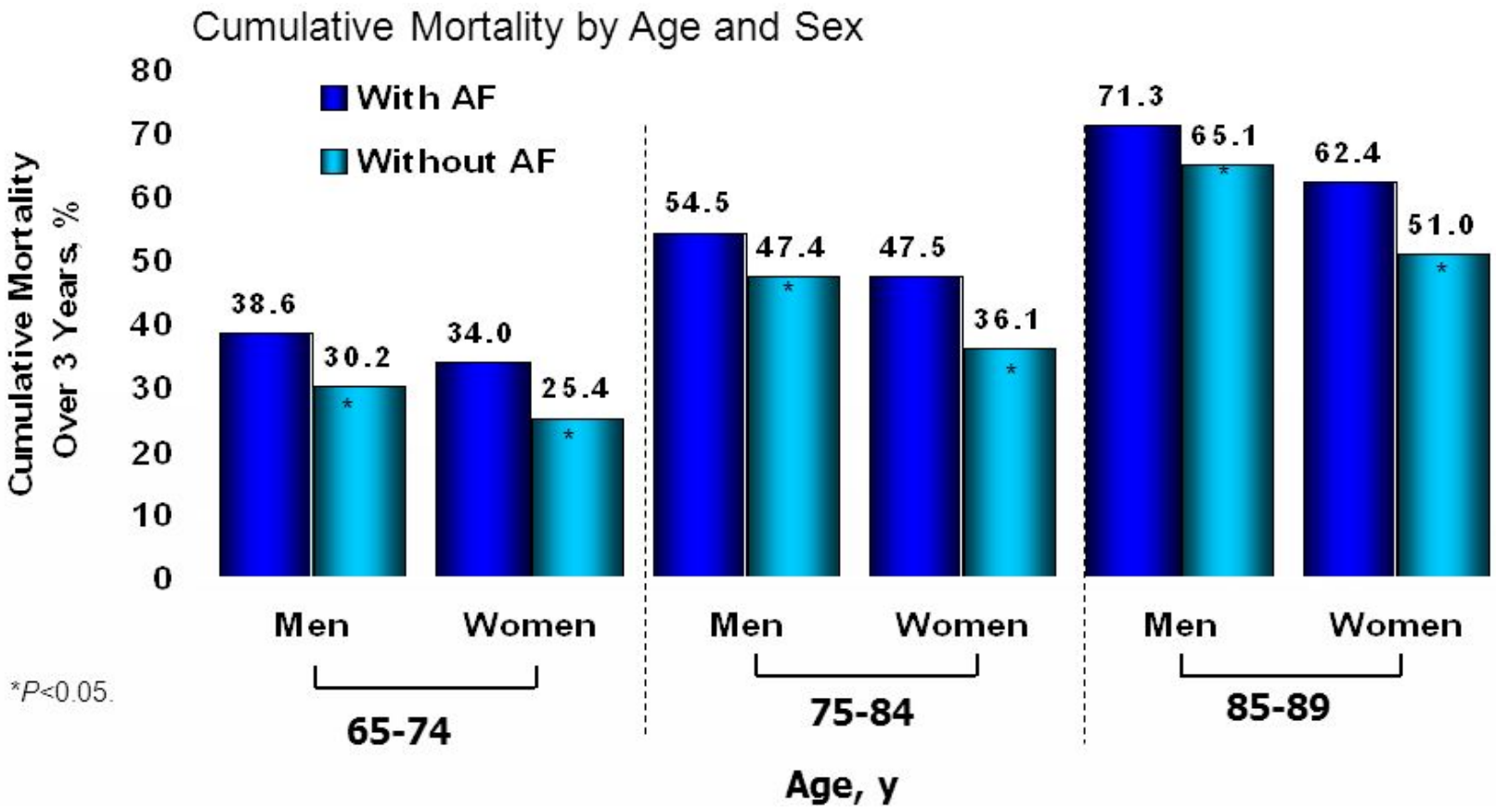
Age and Sex-Adjusted Incidence of AF 1995-2000





Wolf, et al. Atrial Fibrillation as a risk factor for stroke: The Framingham Study: Stroke 1991;22:983-988

Atrial Fibrillation is Associated with Increased Mortality

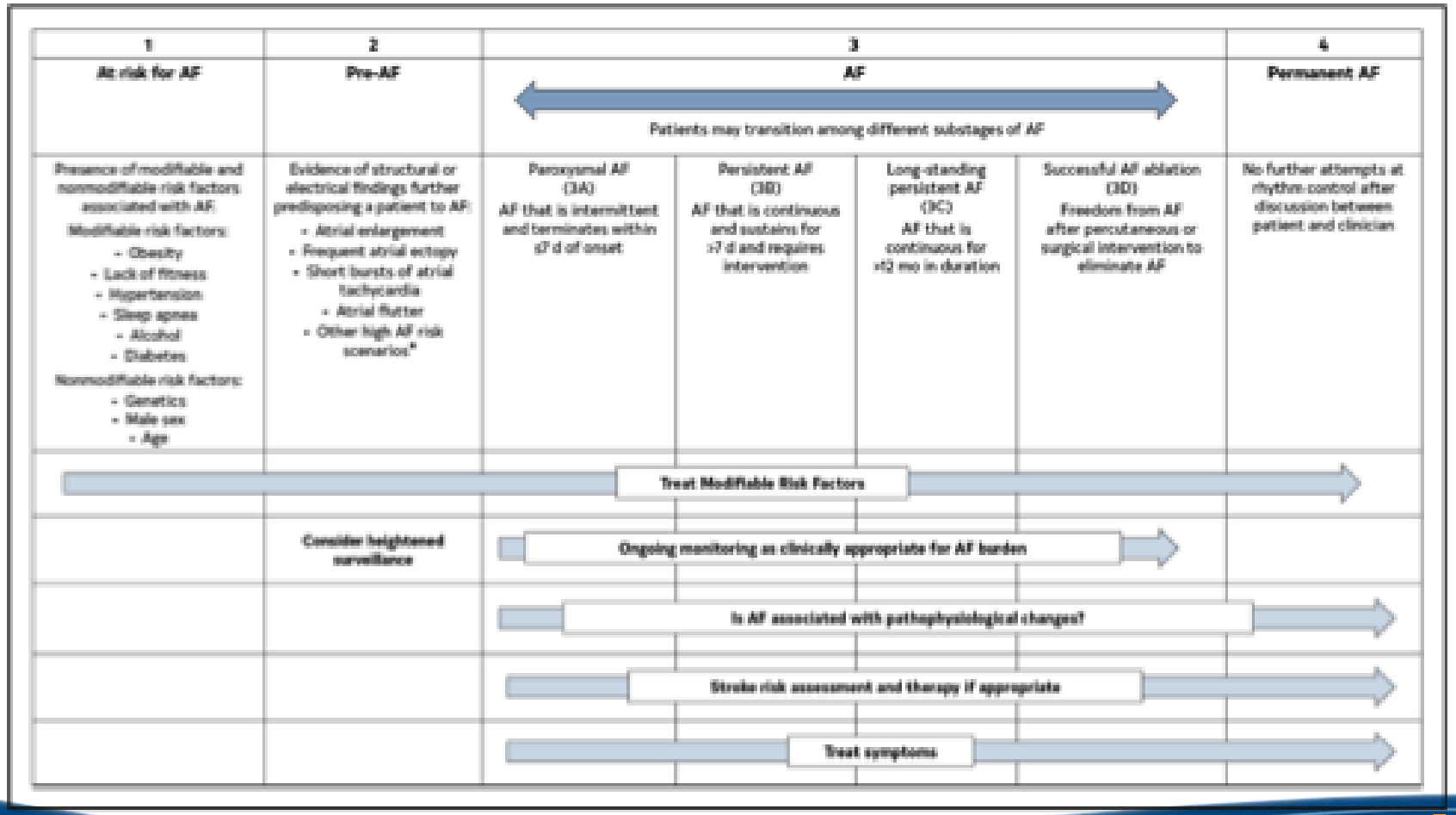


Wolf PA et al. Arch Intern Med.

How do you define Atrial Fibrillation?

Term	Definition
Paroxysmal AF	• AF that terminates spontaneously or with intervention within 7 d of onset. • Episodes may recur with variable frequency.
Persistent AF	• Continuous AF that is sustained >7 d.
Long-standing persistent AF	• Continuous AF >12 mo in duration.
Permanent AF	• The term "permanent AF" is used when the patient and clinician make a joint decision to stop further attempts to restore and/or maintain sinus rhythm. • Acceptance of AF represents a therapeutic attitude on the part of the patient and clinician rather than an inherent pathophysiological attribute of AF. • Acceptance of AF may change as symptoms, efficacy of therapeutic interventions, and patient and clinician preferences evolve.
Nonvalvular AF	• AF in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair.

AF Stages of Progression



Atrial Fibrillation

Triggers

- Ectopic focal triggers

Maintenance

- Multiple reentrant wavelets
- >1 firing foci
- >1 rotor

Atrial fibrillation: Risk factors

When to Intervene

- Symptoms of AF
- Palpitations, chest pain, SOB, fatigue
- No symptoms
- Stroke

Management of Atrial fibrillation

- Symptoms of AF
  - Medications
    - Anticoagulation
    - Atrioventricular Nodal Blocker
    - Antiarrhythmic medications
  - Ablation
- No symptoms
  - Anticoagulation

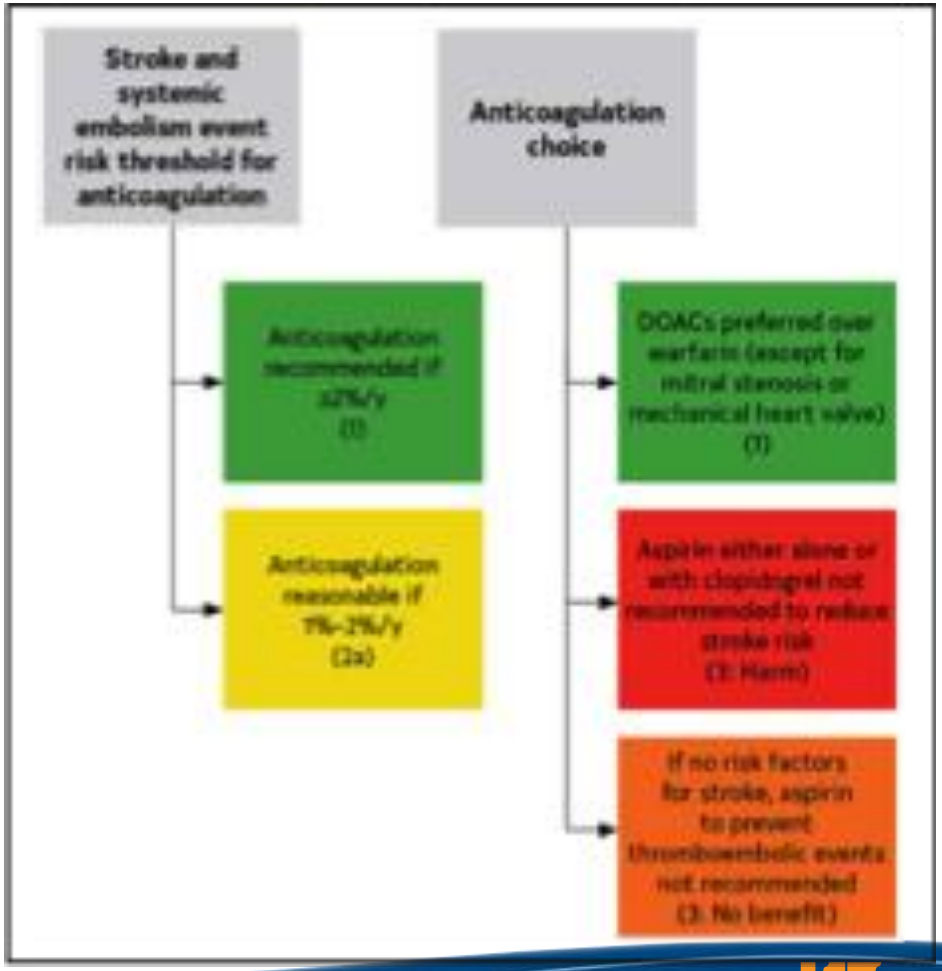
Risk Scoring to determine Anticoagulation

	Score		Adjusted Stroke Rate (% per y)
$CHADS_2$		$CHADS_2$*	
Congestive HF	1	0	1.9
Hypertension	1	1	2.8
Age ≥75 y	1	2	4.0
Diabetes mellitus	1	3	5.9
Stroke/TIA/TE	2	4	8.5
Maximum score	6	5	12.5
		6	18.2
CHA_2DS_2-VASc		CHA_2DS_2-VASc†	
Congestive HF	1	0	0
Hypertension	1	1	1.3
Age ≥75 y	2	2	2.2
Diabetes mellitus	1	3	3.2
Stroke/TIA/TE	2	4	4.0
Vascular disease (prior MI, PAD, or aortic plaque)	1	5	6.7
Age 65–74 y	1	6	9.8
Sex category (i.e., female sex)	1	7	9.6
Maximum score	9	8	6.7
		9	15.20

Anticoagulation

Recommendations for Antithrombotic Therapy
Referenced studies that support the recommendations are summarized in the Online Data Supplement.

COR	LOE	Recommendations
1	A	1. For patients with AF and an estimated annual thromboembolic risk of ≥2% per year (eg, CHA_2DS_2-VASc score of ≥2 in men and ≥3 in women), anticoagulation is recommended to prevent stroke and systemic thromboembolism.[1-7]
1	A	2. In patients with AF who do not have a history of moderate to severe rheumatic mitral stenosis or a mechanical heart valve, and who are candidates for anticoagulation, DOACs are recommended over warfarin to reduce the risk of mortality, stroke, systemic embolism, and ICH.[1-7]
2a	A	3. For patients with AF and an estimated annual thromboembolic risk of ≥1% but <2% per year (equivalent to CHA_2DS_2-VASc score of 1 in men and 2 in women), anticoagulation is reasonable to prevent stroke and systemic thromboembolism.[1,3]
3: Harm	B-R	4. In patients with AF who are candidates for anticoagulation and without an indication for antiplatelet therapy, aspirin either alone or in combination with clopidogrel as an alternative to anticoagulation is not recommended to reduce stroke risk.[8,9]
3: No Benefit	B-NR	5. In patients with AF without risk factors for stroke, aspirin monotherapy for prevention of thromboembolic events is of no benefit.[10,11]



Blood Thinners

DOAC	CrCl (mL/min)				
	>95	51-95	31-50	16-30	<15 or on dialysis
Apixaban	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*	5 or 2.5 mg twice daily*
Dabigatran	150 mg twice daily	150 mg twice daily	150 mg twice daily	75 mg twice daily	Contraindicated
Edoxaban	Contraindicated	60 mg once daily	30 mg once daily	30 mg once daily	Contraindicated
Rivaroxaban	20 mg once daily	20 mg once daily	15 mg once daily	15 mg once daily	15 mg once daily†

Blood Thinners

COR	LOE	Recommendations
1	B-NR	1. In patients with AF receiving dabigatran who develop life-threatening bleeding, treatment with idarucizumab is recommended to rapidly reverse dabigatran's anticoagulation effect.[1-4]
2a	C-LD	2. In patients with AF receiving dabigatran who develop life-threatening bleeding, treatment with activated prothrombin complex concentrate (PCC) is reasonable to reverse dabigatran's anticoagulation effect if idarucizumab is unavailable.[4,5]
1	B-NR*	3. In patients with AF receiving factor Xa inhibitors who develop life-threatening bleeding, treatment with either andexanet alfa (apixaban or rivaroxaban;* edoxaban†) or 4-factor prothrombin complex concentrate† is recommended to rapidly reverse factor Xa inhibitor's anticoagulation effect.[4,7]
	C-LD†	

COR	LOE	Recommendations
1	A	4. In patients with AF receiving warfarin who develop life-threatening bleeding, treatment with 4-factor prothrombin complex concentrate (if available) in addition to intravenous vitamin K is recommended to rapidly achieve INR correction over fresh frozen plasma and intravenous vitamin K treatment.[8-10]
2b	B-NR	5. In patients with AF who develop major gastrointestinal bleeding, resumption of oral anticoagulation therapy may be reasonable after correction of reversible causes of bleeding and reassessment of its long-term benefits and risks with a multidisciplinary team approach during SDM with patients.[11,12]

Percutaneous Stroke Prevention

Endocardial

- Watchman
- Amplatzer

Epicardial / Endocardial

- Lariat

The WATCHMAN™ Device is a catheter-delivered heart implant intended to reduce the risk of AFib-related stroke by closing the left atrial appendage.

The WATCHMAN™ Device in place, closing off the left atrial appendage in the heart.

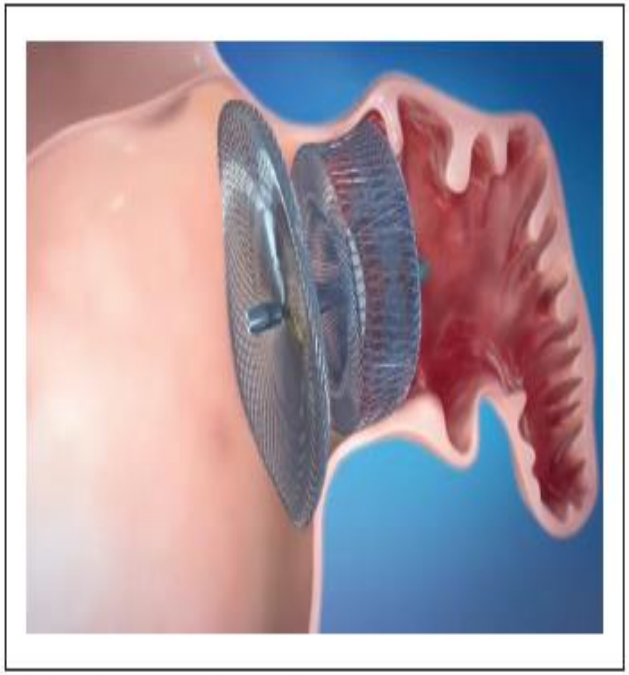
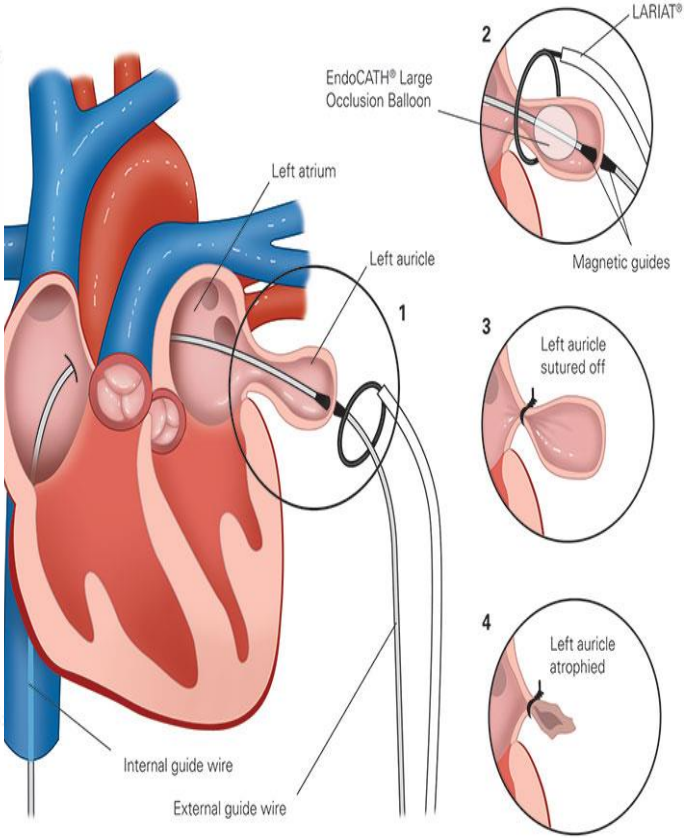


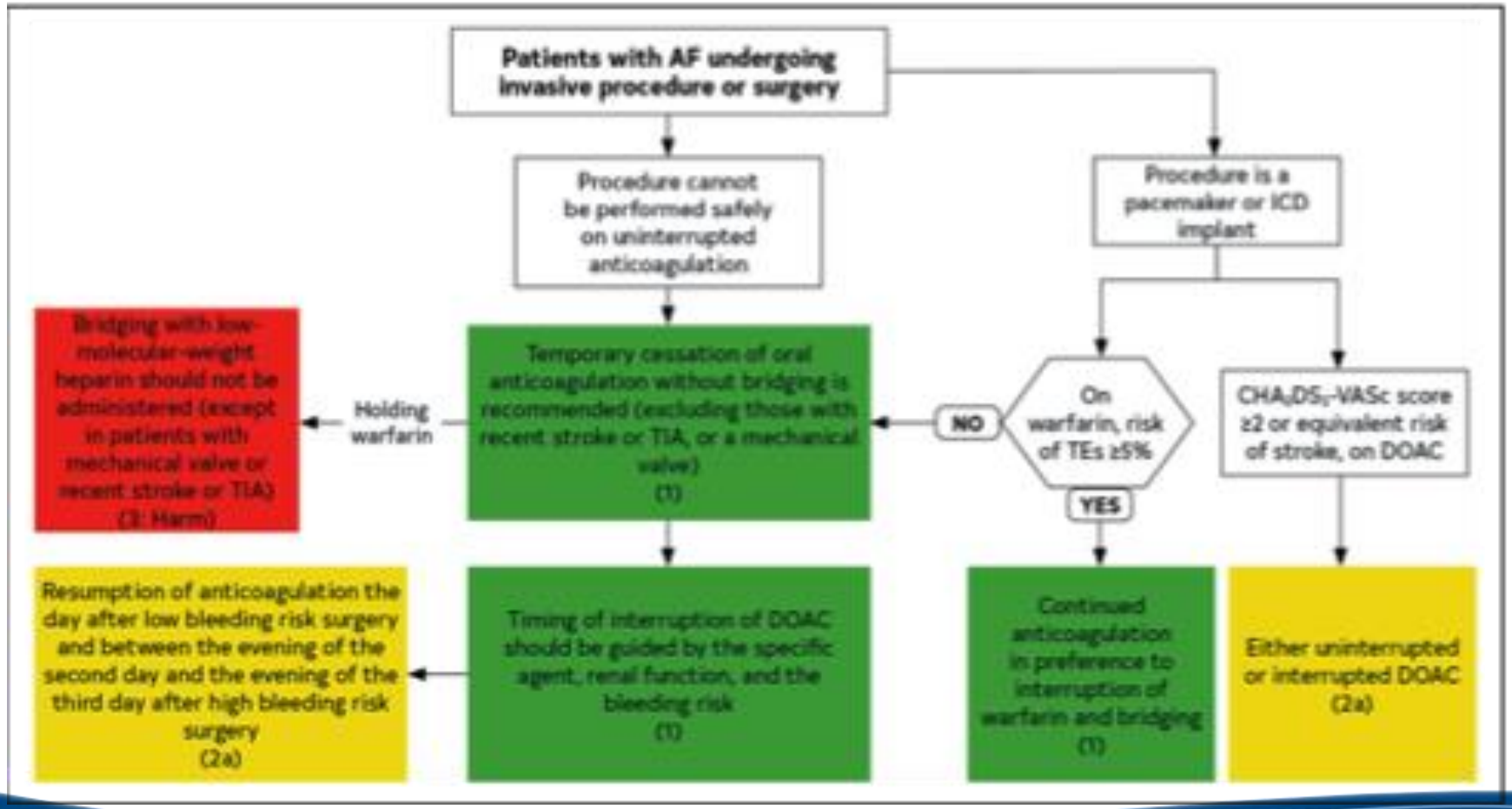
Figure 2 – *Disposition in "baby's pacifier" after implantation (Photos courtesy of St. Jude Medical Inc.).*



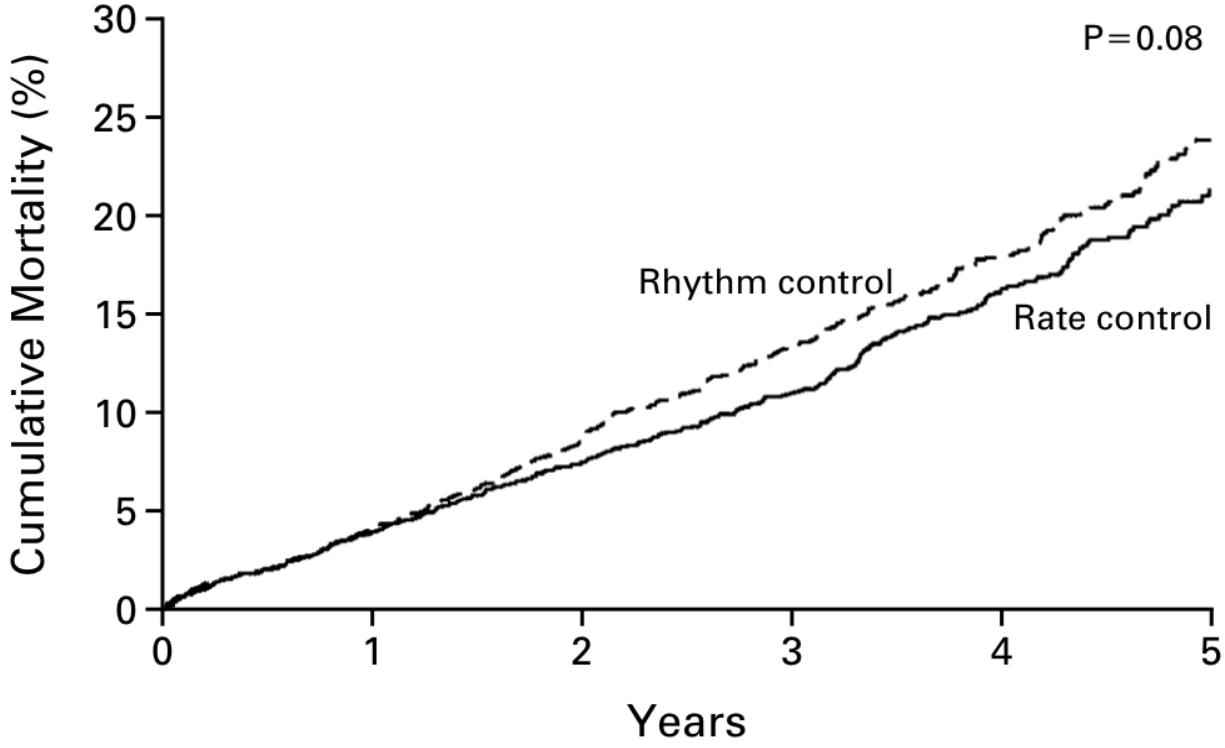
Surgical Excision of the LAA

- Concomitant AF: May be considered in those undergoing cardiac surgery
- Incomplete occlusion >50%
- Check for complete lack of flow and knub <1 cm

Pre-Procedure Evaluation



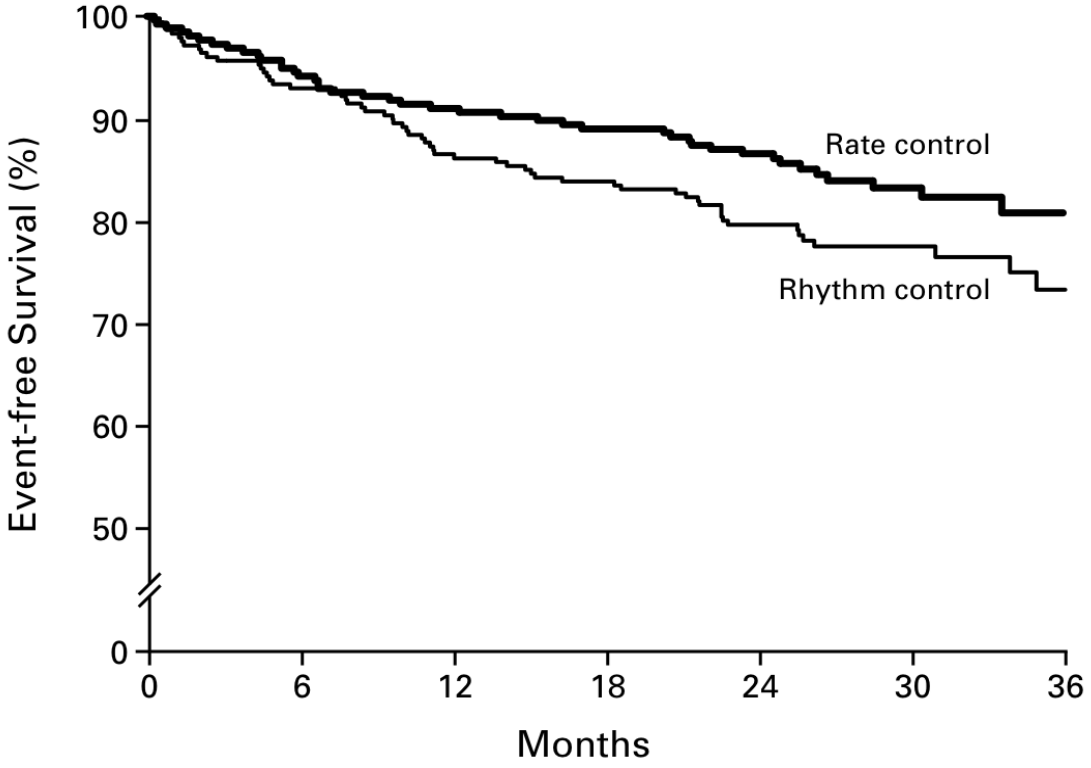
Management of Atrial fibrillation



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)

Wyse D.G., Waldo AL et al. A Comparison of Rate Control and Rhythm Control in Patients with Atrial Fibrillation AFFIRM NEJM 2002; 347:1825-33

Management of Atrial fibrillation

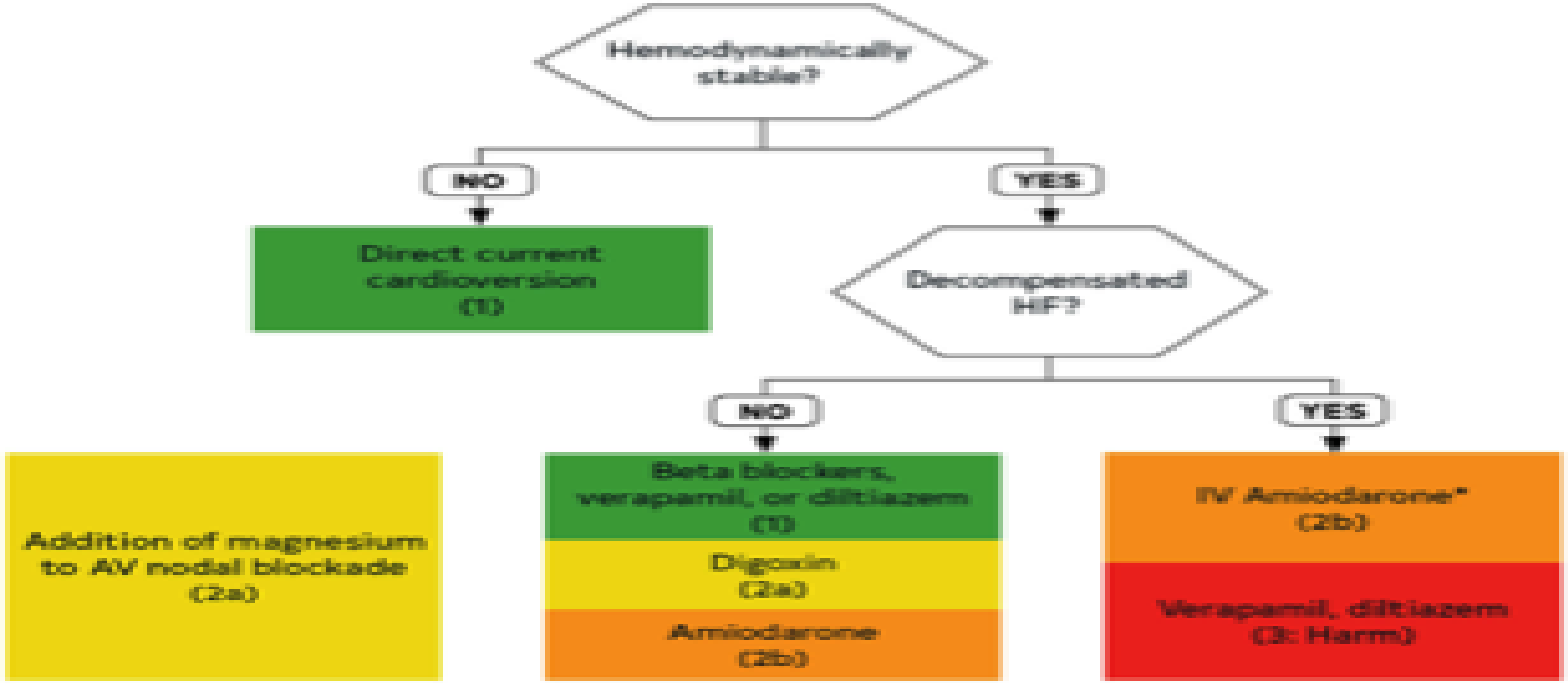


No. at Risk							
Rate control	256	239	232	222	212	99	25
Rhythm control	266	243	224	218	207	85	24

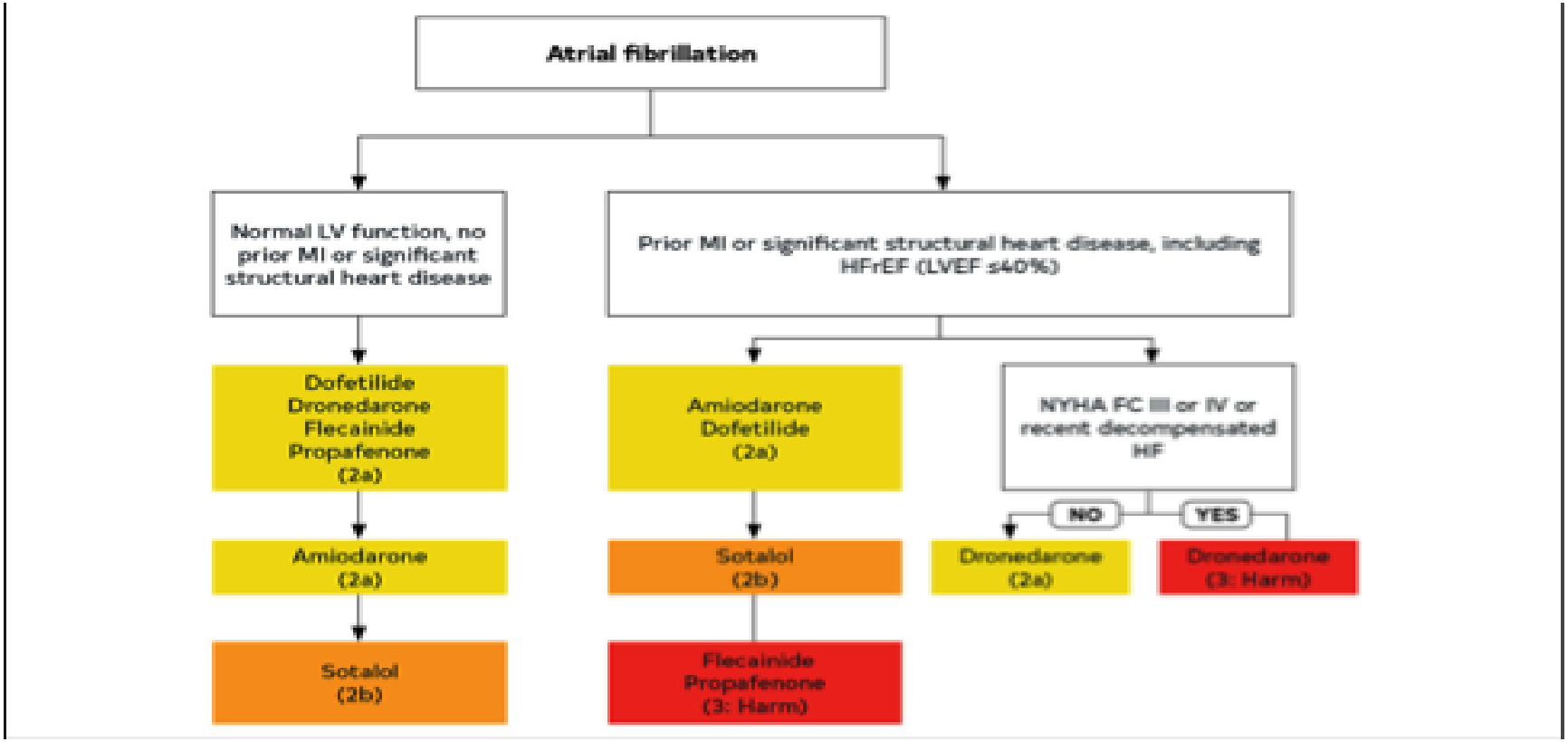
Figure 2. Kaplan–Meier Curves for Event-free Survival in the Rate-Control and Rhythm-Control Groups.

Gelde, I et al. RACE Investigators. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. NEJM 2002 347;23 1837-1840r

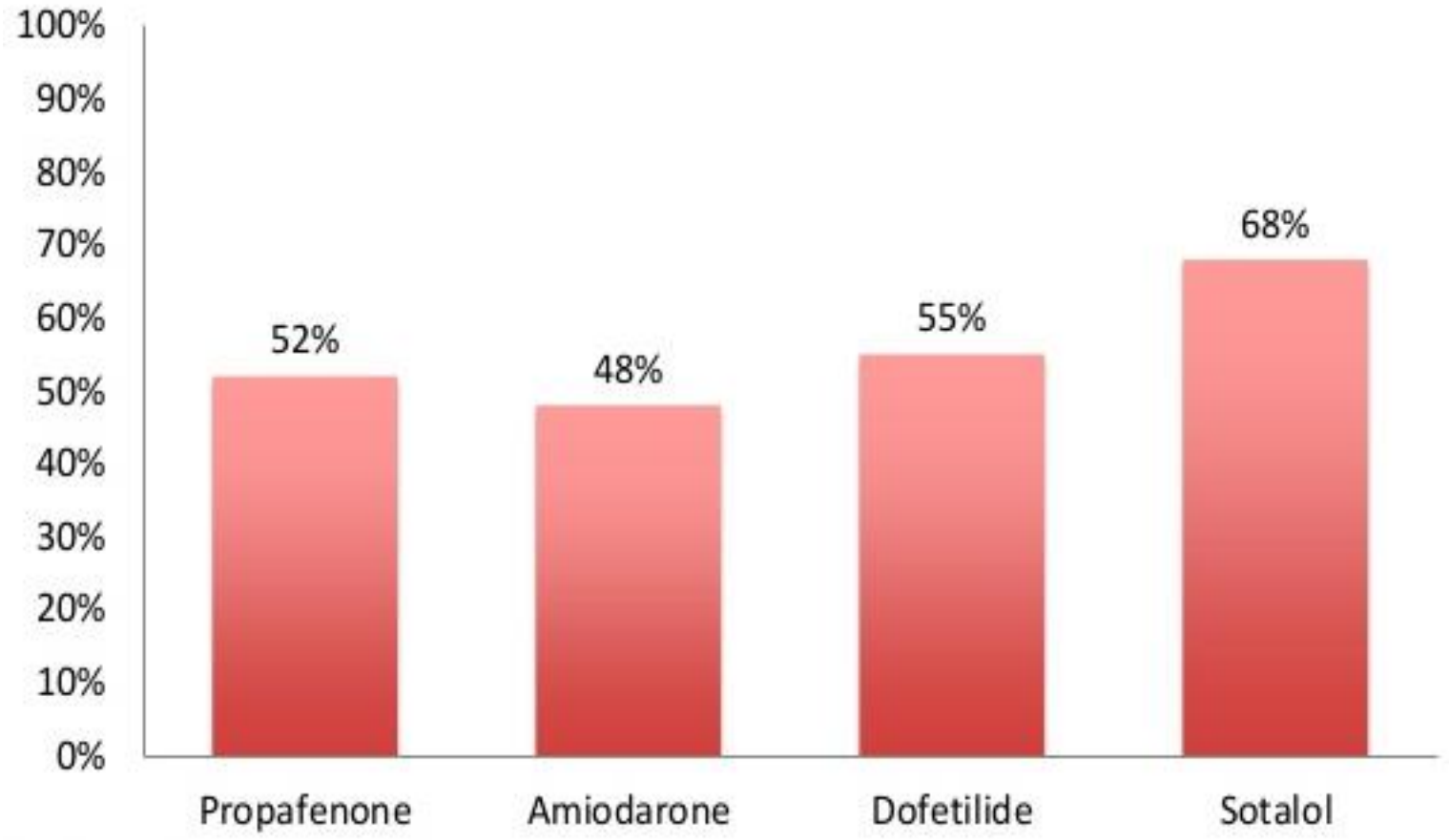
Management of Atrial fibrillation



Management of Atrial fibrillation



Failure rates of AAD



NEJM 205;352:1861-72; Circulation 2000;102:2385-2390;Arch Intern Med. 2006;166:719-728

TABLE 3. ADVERSE EVENTS.*

EVENT	OVERALL (N=4060)	RATE-CONTROL GROUP (N=2027)	RHYTHM-CONTROL GROUP (N=2033)	P VALUE
		no. of patients (%)		
Primary end point (death)	666 (26.3)	310 (25.9)	356 (26.7)	0.08†
Secondary end point (composite of death, disabling stroke, disabling anoxic encephalopathy, major bleeding, and cardiac arrest)	861 (32.3)	416 (32.7)	445 (32.0)	0.33
Torsade de pointes	14 (0.5)	2 (0.2)‡	12 (0.8)	0.007
Sustained ventricular tachycardia	15 (0.6)	9 (0.7)	6 (0.6)	0.44
Cardiac arrest followed by resuscitation				
Ventricular fibrillation or ventricular tachycardia	19 (0.6)	10 (0.7)	9 (0.5)	0.83
Pulseless electrical activity, bradycardia, or other rhythm	10 (0.3)	1 (<0.1)	9 (0.6)	0.01
Central nervous system event				
Total	211 (8.2)	105 (7.4)	106 (8.9)	0.93
Ischemic stroke§	157 (6.3)	77 (5.5)	80 (7.1)	0.79
After discontinuation of warfarin	69	25	44	
During warfarin but with INR <2.0	44	27	17	
Concurrent atrial fibrillation	67	42	25	
Primary intracerebral hemorrhage	34 (1.2)	18 (1.1)	16 (1.3)	0.73
Subdural or subarachnoid hemorrhage	24 (0.8)	11 (0.8)	13 (0.8)	0.68
Disabling anoxic encephalopathy	9 (0.3)	4 (0.2)	5 (0.4)	0.74
Myocardial infarction	140 (5.5)	67 (4.9)	73 (6.1)	0.60
Hemorrhage not involving the central nervous system	203 (7.3)	107 (7.7)	96 (6.9)	0.44
Systemic embolism	16 (0.5)	9 (0.5)	7 (0.4)	0.62
Pulmonary embolism	8 (0.3)	2 (0.1)	6 (0.5)	0.16
Hospitalization after base line	2594 (76.6)	1220 (73.0)	1374 (80.1)	<0.001

Wyse D.G., Waldo AL et al. A Comparison of Rate Control and Rhythm Control in Patients with Atrial Fibrillation AFFIRM NEJM 2002; 347:1825-33

TABLE 2. Covariates Significantly Associated With Survival Results With Echocardiographic Data Included

Covariate	*P*	HR	HR: 99% Confidence Limits Lower	Upper
Age at enrollment*	<0.0001	1.06	1.05	1.08
Coronary artery disease	<0.0001	1.56	1.20	2.04
Congestive heart failure	<0.0001	1.57	1.18	2.09
Diabetes	<0.0001	1.56	1.17	2.07
Stroke or transient ischemic attack	<0.0001	1.70	1.24	2.33
Smoking	<0.0001	1.78	1.25	2.53
Left ventricular dysfunction	0.0065	1.36	1.02	1.81
Mitral regurgitation	0.0043	1.36	1.03	1.80
Sinus rhythm	<0.0001	0.53	0.39	0.72
Warfarin use	<0.0001	0.50	0.37	0.69
Digoxin use	0.0007	1.42	1.09	1.86
Rhythm-control drug use	0.0005	1.49	1.11	2.01

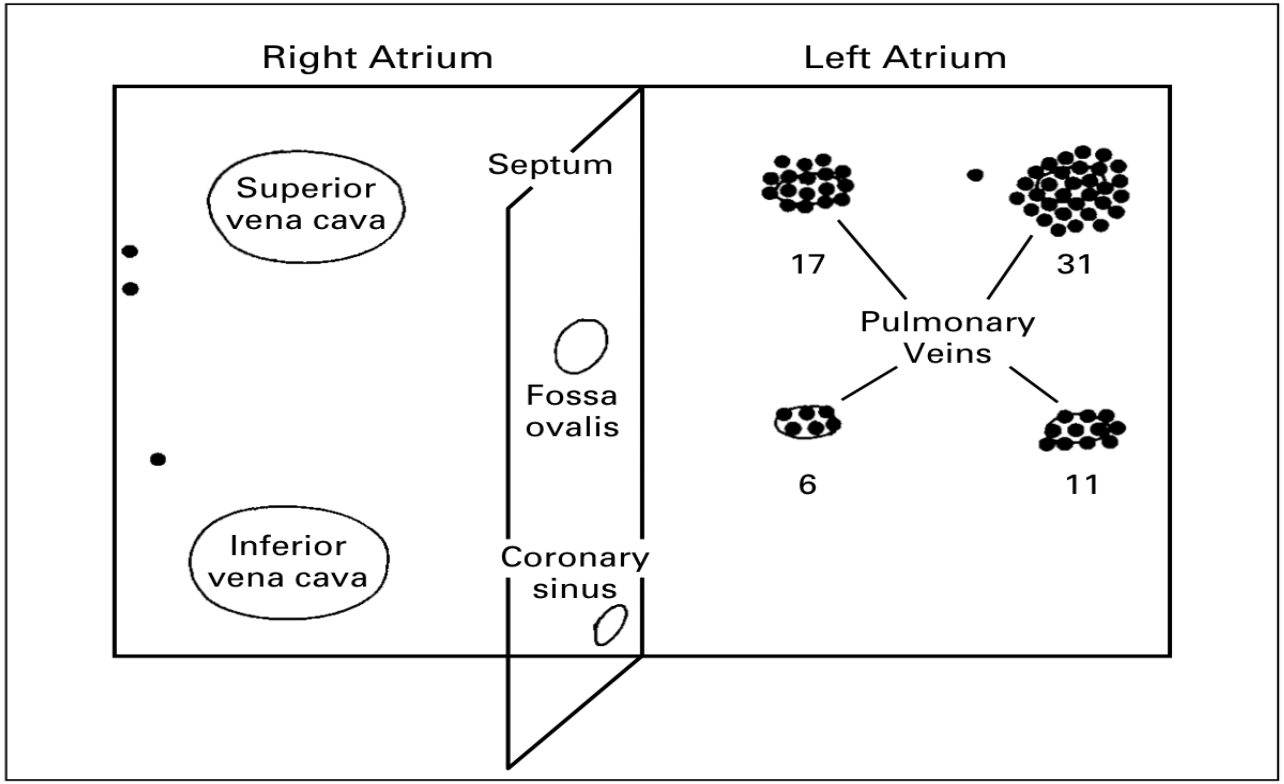
*Per year of age.

AFFIRM investigators: Relationships Between Sinus Rhythm, Treatment and Survival in the Atrial Fibrillation Follow-Up Investigation of Rhythm Management. Circ 2004; 109:1509-1513

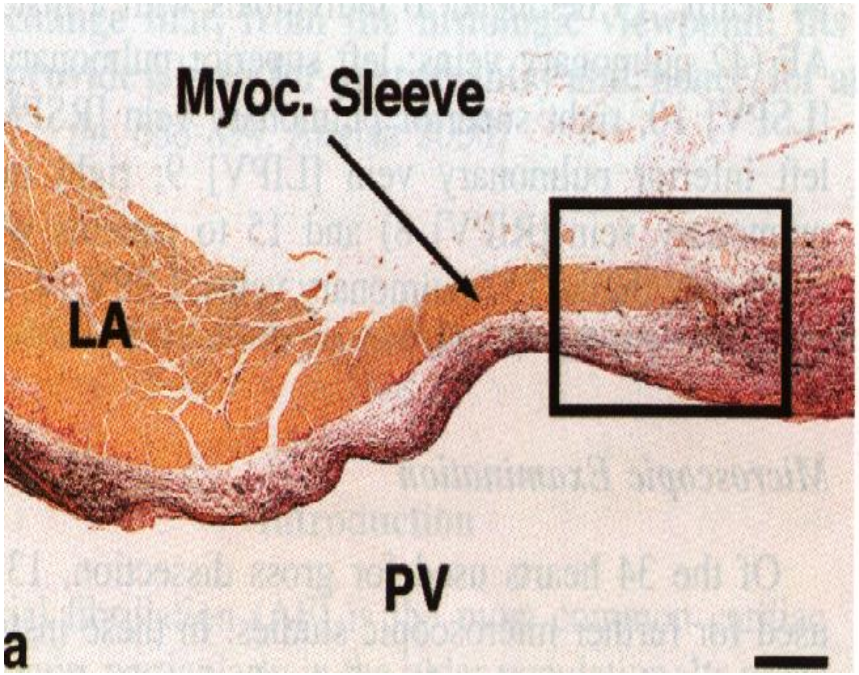
Ablation

COR	LOE	Recommendations
1	A	1. In patients with symptomatic AF in whom antiarrhythmic drugs have been ineffective, contraindicated, not tolerated or not preferred, and continued rhythm control is desired, catheter ablation is useful to improve symptoms.[1-15]
1	A	2. In selected patients (generally younger with few comorbidities) with symptomatic paroxysmal AF in whom rhythm control is desired, catheter ablation is useful as first-line therapy to improve symptoms and reduce progression to persistent AF.[1-15]
1	A	3. In patients with symptomatic or clinically significant AFL, catheter ablation is useful for improving symptoms.[15-18]

Management of Atrial fibrillation



Haissaguerre, M, et al. Spontaneous Initiation of Atrial Fibrillation by Ectopic Beats Originating in the Pulmonary Veins. NEJM 1998;339:659-66


Myoc. Sleeve
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PV
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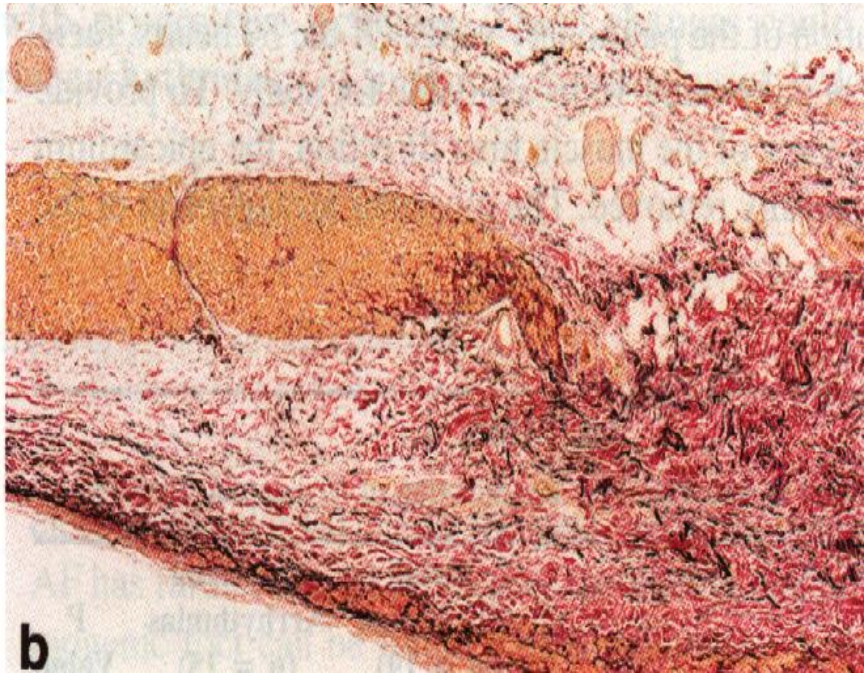
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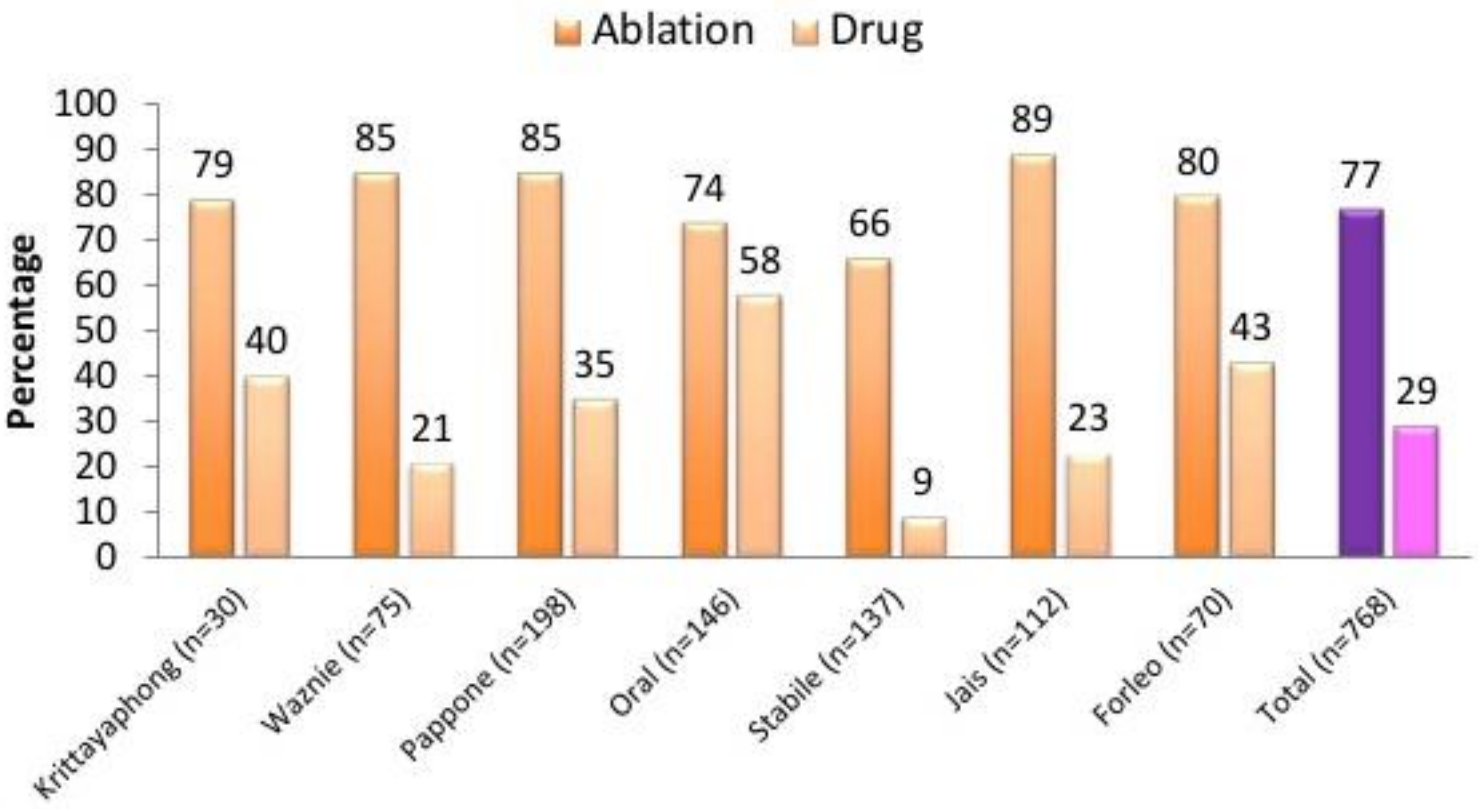
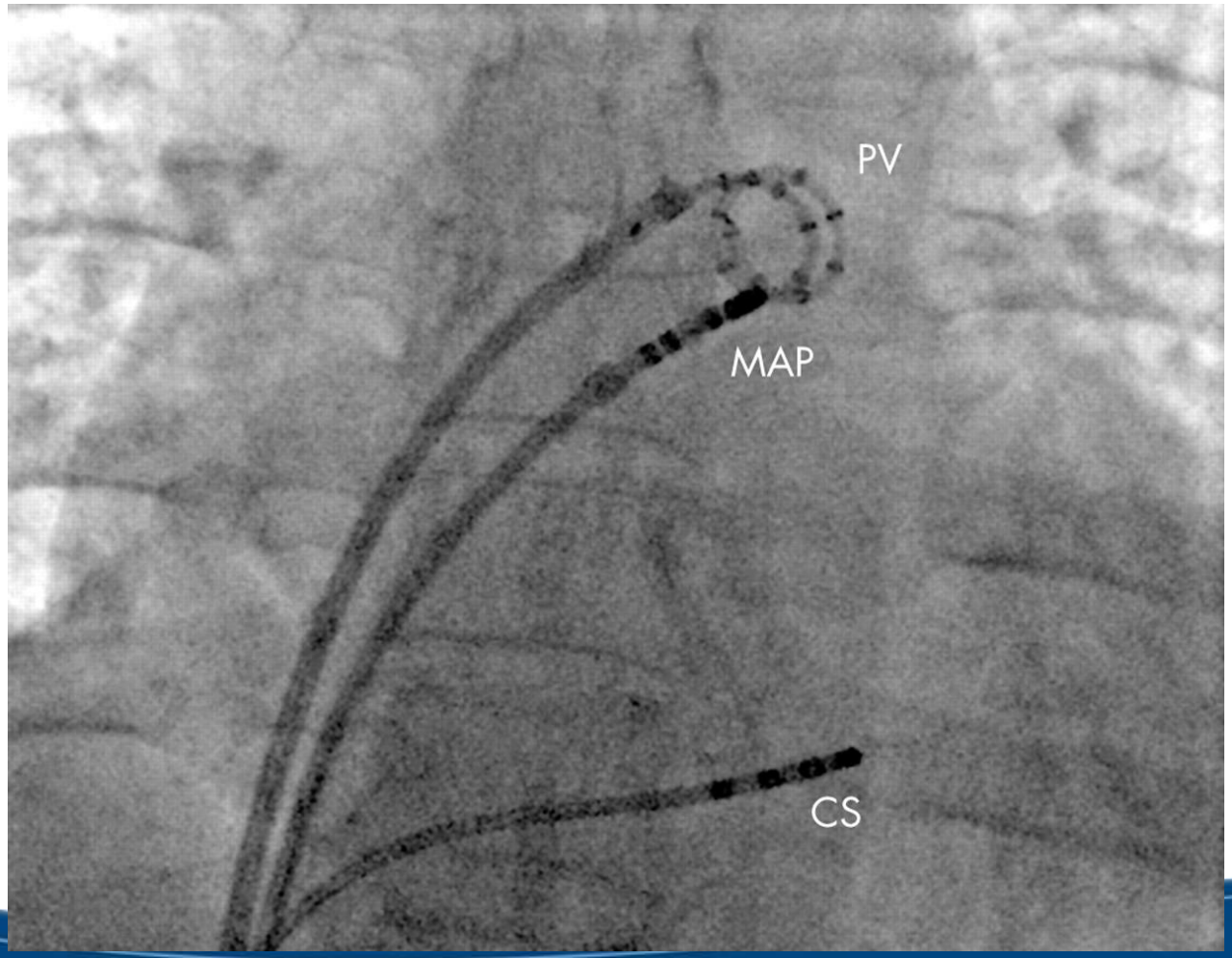
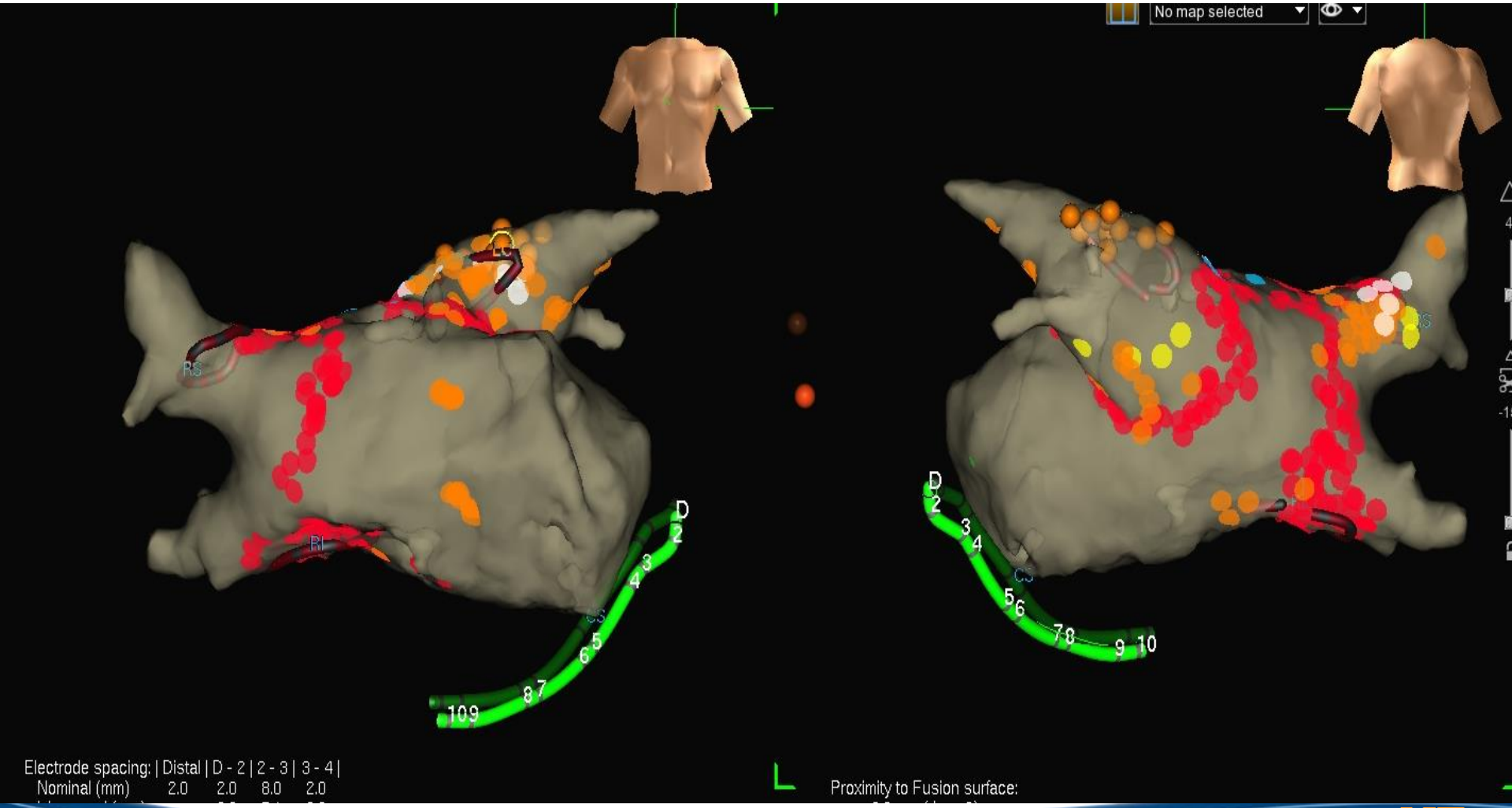
Ablation vs Drug



Piccini J. Circ Arrhythm Electrophysiol 2009;2;626-633

Catheter Ablation for Atrial fibrillation

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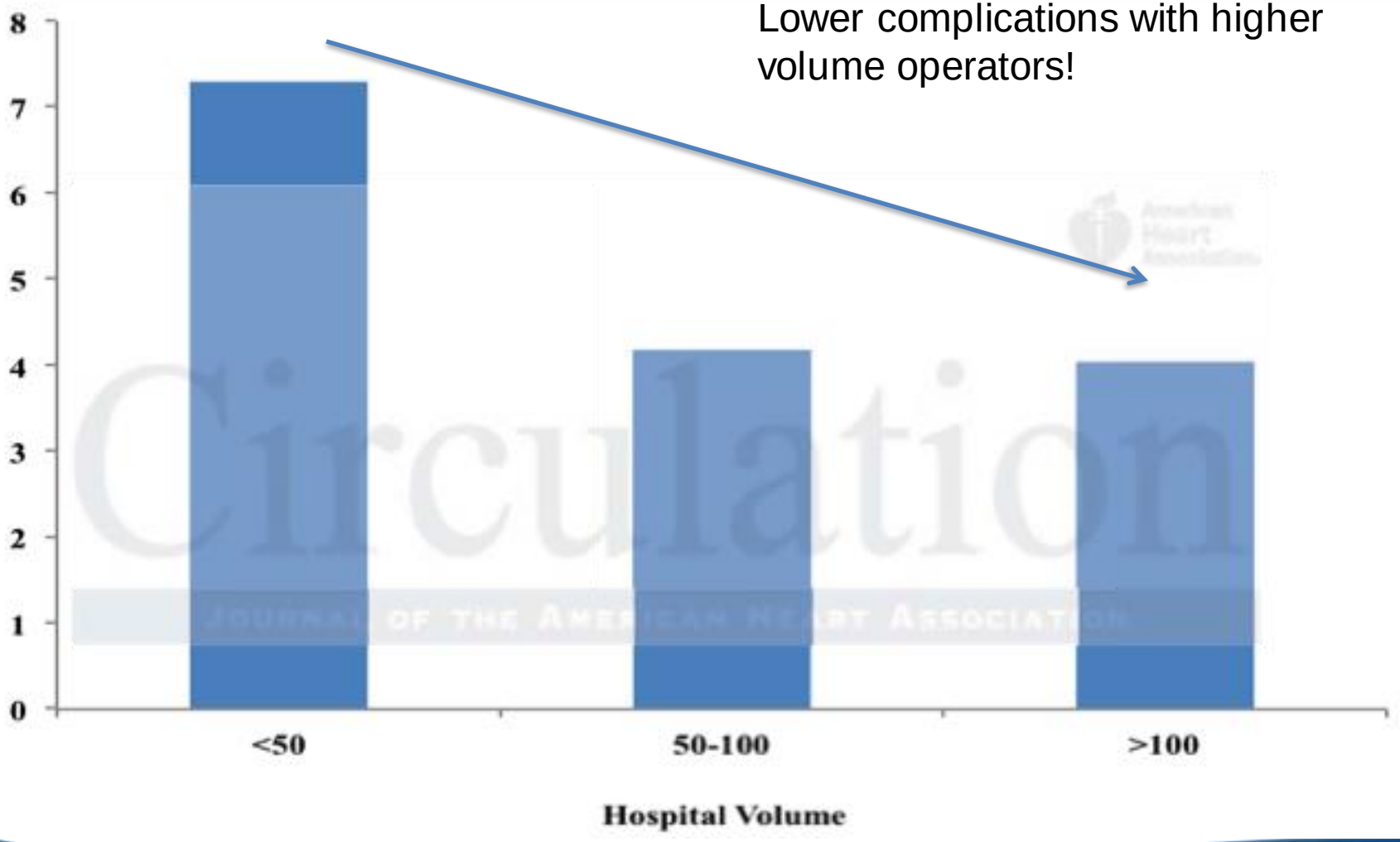
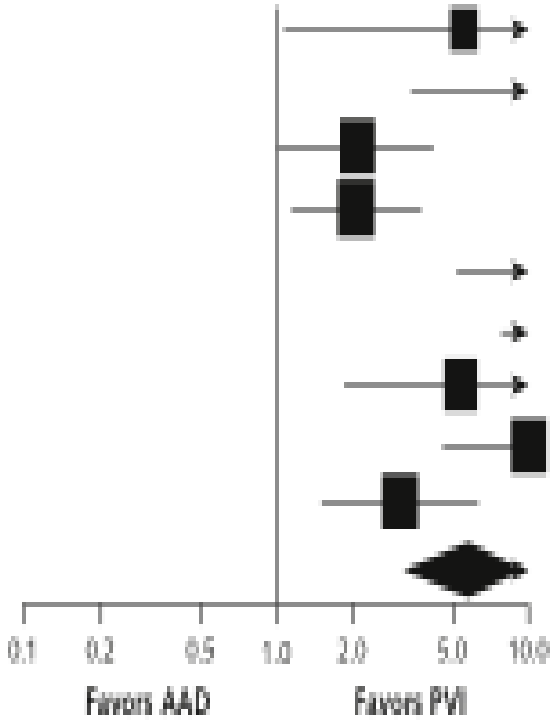
Electrode spacing: | Distal | D - 2 | 2 - 3 | 3 - 4 |
Nominal (mm) 2.0 2.0 8.0 2.0
Proximity to Fusion surface:

Risks


Lower complications with higher volume operators!
8
7
6
5
4
3
2
1
0
<50
50-100
>100
Hospital Volume

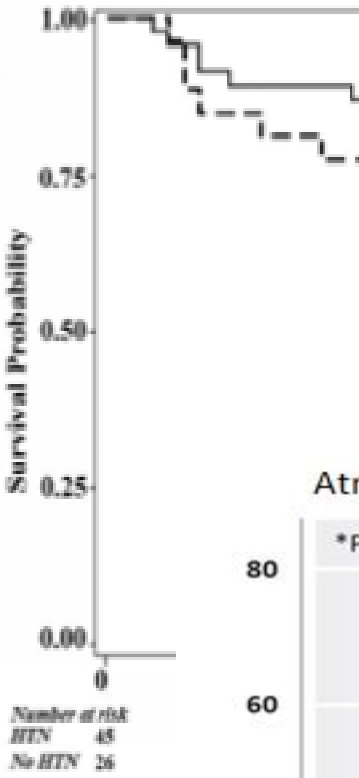
Drugs vs Ablation

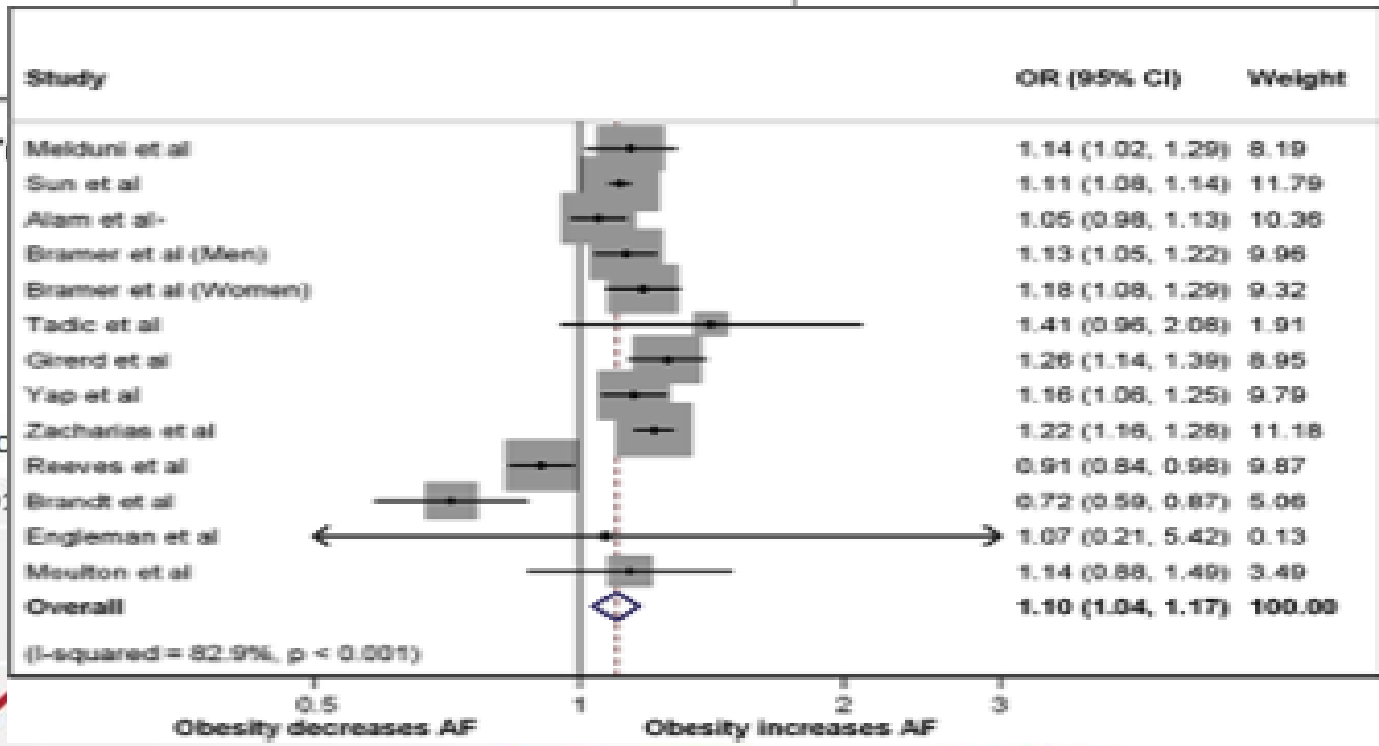
Study, Year (Reference)	Odds Ratio (95% CI)	Maintenance of Sinus Rhythm/Total, n/N	
		PVI	AAD
Krittayaphong et al, 2003 (147)	5.500 (1.065–28.416)	11/14	6/15
Wazni et al, 2005 (157)	11.846 (3.387–41.433)	28/32	13/35
Oral et al, 2006 (114)	2.066 (1.028–4.155)	57/77	40/69
Pappone et al, 2006 (115)	2.048 (1.130–3.711)	72/99	56/99
Stabile et al, 2006 (119)	13.300 (5.069–34.894)	38/68	6/69
Jais et al, 2008 (143)	24.769 (8.634–71.059)	46/52	13/55
Forleo et al, 2009 (112)	5.333 (1.839–15.471)	28/35	15/35
Wilber et al, 2010 (126)	9.917 (4.509–21.808)	70/106	10/61
Mont et al, 2014 (132)	3.059 (1.494–6.263)	69/98	21/48
Overall	5.874 (3.180–10.849)		

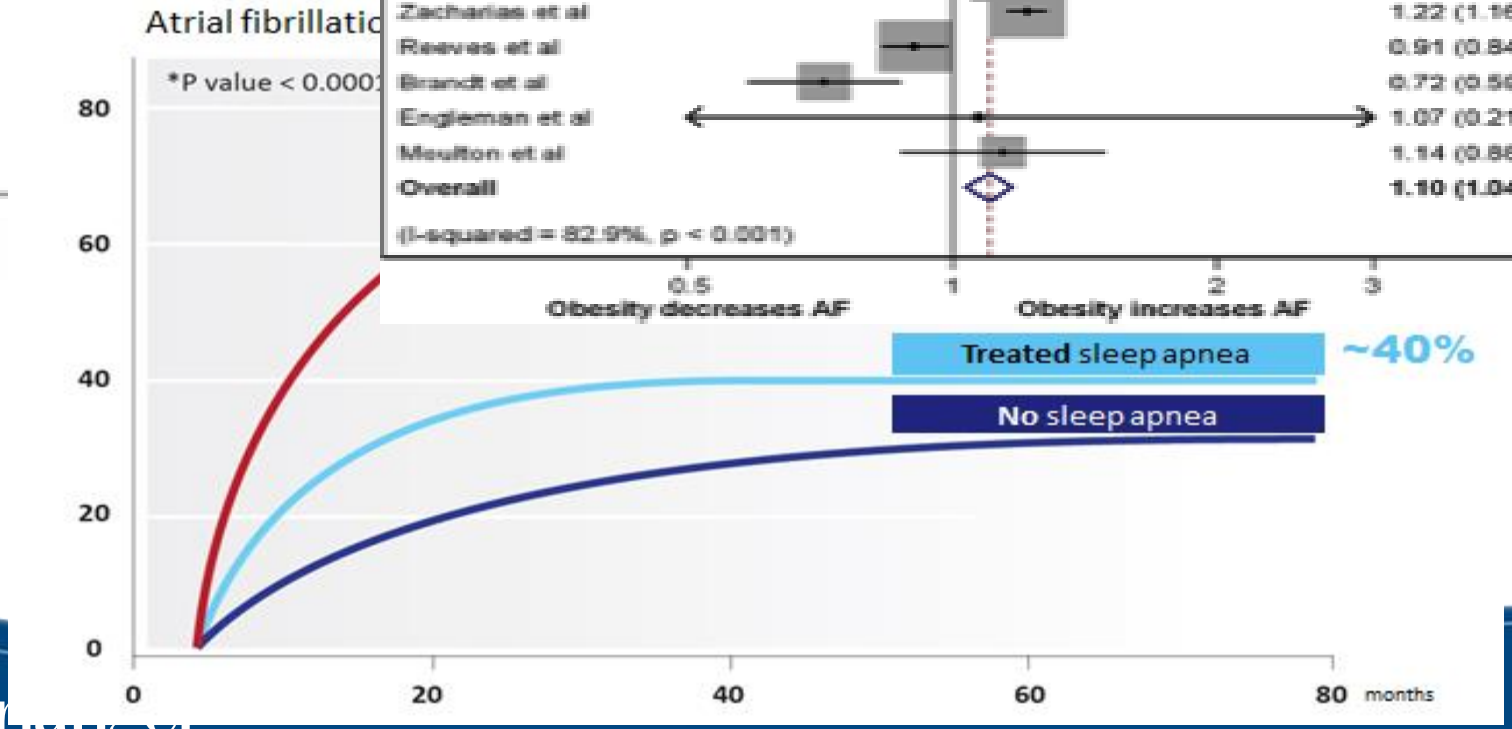


Al-Khatib, et al. Ann Intern Med. 2014:16;760-773

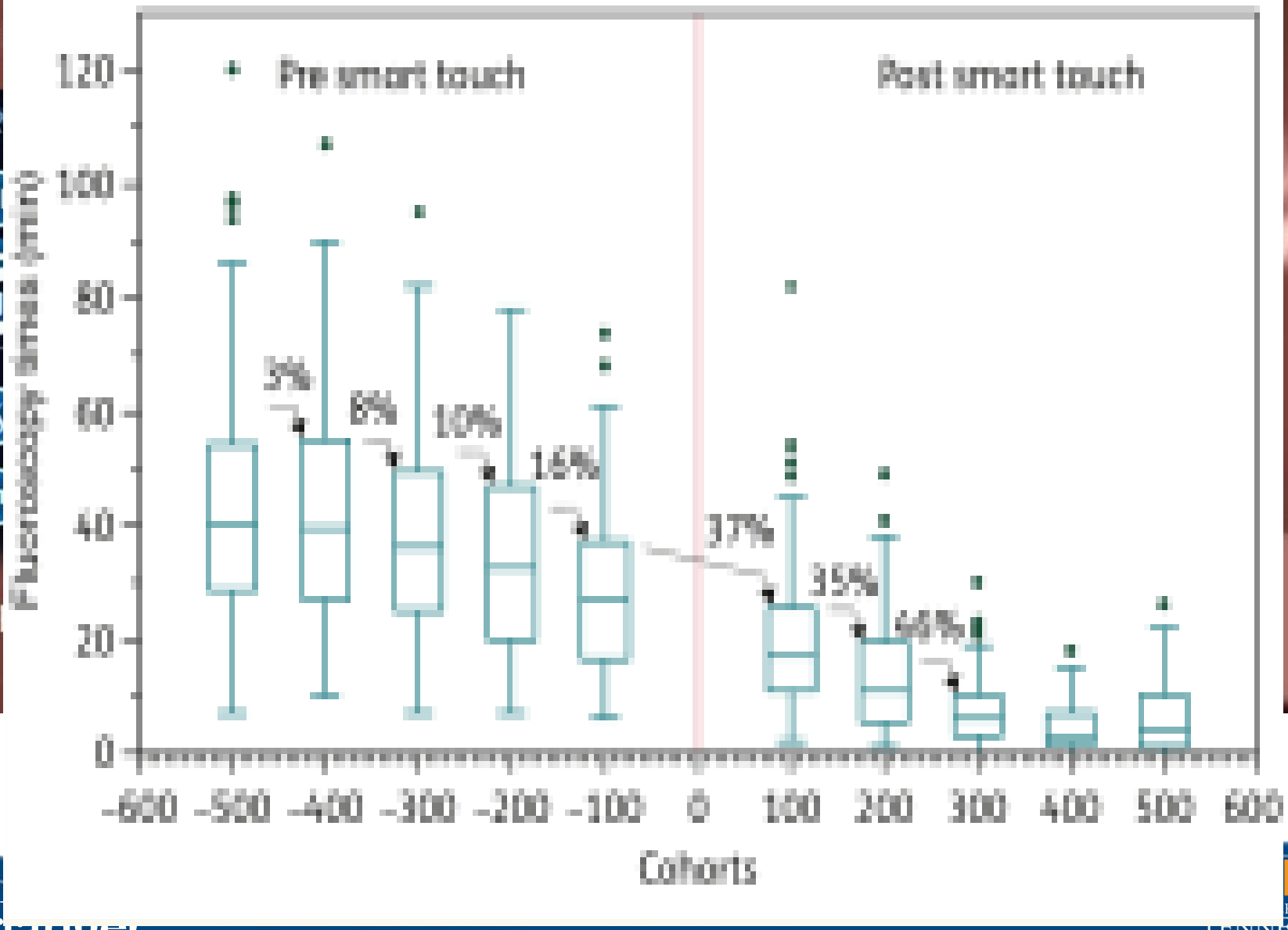
Control of Comorbidities





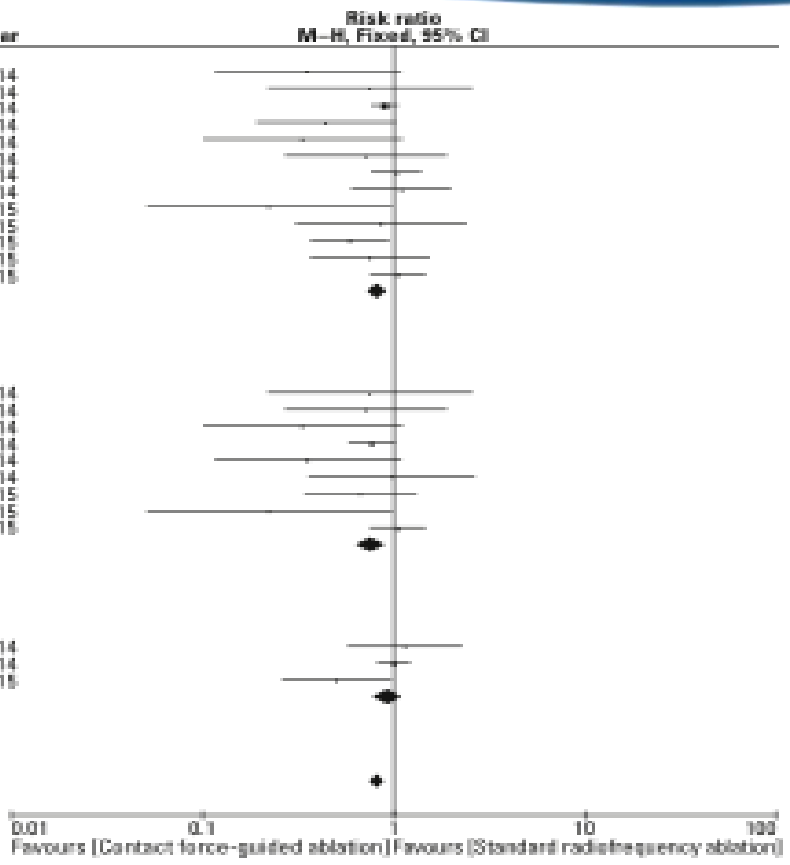


Catheter Ablation for Atrial



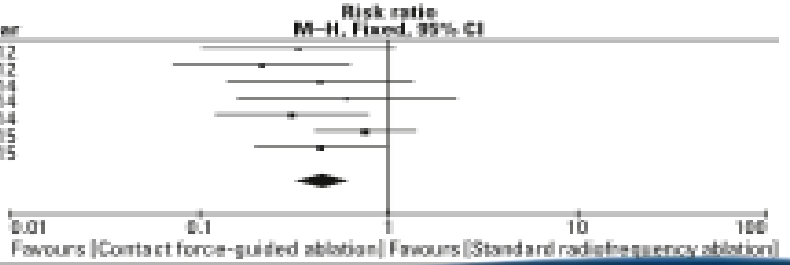
a

Study or subgroup	Contact force-guided ablation Events	Total	Standard radiofrequency ablation Events	Total	Weight	Risk ratio M–H, Fixed, 95% CI	Year
1.1.1. AF							
Andrade 2014	3	25	17	50	1.1%	0.35 [0.11, 1.09]	2014
Casella 2014	3	20	7	35	0.8%	0.75 [0.22, 2.58]	2014
Jarman 2014	190	280	223	400	23.5%	0.90 [0.76, 1.06]	2014
Wutzler 2014	5	31	41	112	2.8%	0.44 [0.19, 1.02]	2014
Marijon 2014	3	30	9	30	1.4%	0.33 [0.10, 1.11]	2014
Sciarra 2014	3	21	7	21	1.1%	0.71 [0.27, 1.89]	2014
Ullah 2014	32	50	31	50	4.9%	1.03 [0.76, 1.39]	2014
Wakili 2014	13	32	13	35	2.0%	1.09 [0.60, 1.99]	2014
Itoh 2015	2	50	9	50	1.4%	0.22 [0.05, 0.98]	2015
Nakamura 2015	6	60	7	60	1.1%	0.86 [0.31, 2.40]	2015
Sigmund 2015	20	89	34	89	5.4%	0.59 [0.37, 0.95]	2015
Makimoto 2015	9	25	12	35	1.9%	0.75 [0.36, 1.55]	2015
Reddy 2015	49	152	44	143	7.2%	1.05 [0.75, 1.47]	2015
Subtotal (95% CI)		**885**		**1120**	**55.3%**	**0.82 [0.73, 0.93]**	
Total events	250		454				
Heterogeneity: Chi²=17.88, df=12 (P=0.13); I²=32%							
Test for overall effect: Z=3.18 (P=0.001)							
1.1.2. Paroxysmal AF							
Casella 2014	3	20	7	35	0.8%	0.75 [0.22, 2.58]	2014
Sciarra 2014	3	21	7	21	1.1%	0.71 [0.27, 1.89]	2014
Marijon 2014	3	30	9	30	1.4%	0.33 [0.10, 1.11]	2014
Jarman 2014	35	80	38	184	10.4%	0.77 [0.56, 1.06]	2014
Andrade 2014	3	25	17	50	1.8%	0.35 [0.11, 1.09]	2014
Wakili 2014	5	18	6	21	0.9%	0.97 [0.36, 2.66]	2014
Sigmund 2015	11	62	17	64	2.6%	0.67 [0.34, 1.31]	2015
Itoh 2015	2	50	9	50	1.4%	0.22 [0.05, 0.98]	2015
Reddy 2015	49	152	44	143	7.2%	1.05 [0.75, 1.47]	2015
Subtotal (95% CI)		**438**		**598**	**27.7%**	**0.76 [0.63, 0.91]**	
Total events	119		215				
Heterogeneity: Chi²=10.13, df=8 (P=0.26); I²=21%							
Test for overall effect: Z=2.99 (P=0.003)							
1.1.3. Persistent AF							
Wakili 2014	8	14	7	14	1.1%	1.14 [0.57, 2.29]	2014
Jarman 2014	62	108	124	216	13.1%	1.00 [0.82, 1.22]	2014
Sigmund 2015	9	37	17	35	2.8%	0.50 [0.26, 0.97]	2015
Subtotal (95% CI)		**159**		**265**	**17.0%**	**0.93 [0.77, 1.12]**	
Total events	79		148				
Heterogeneity: Chi²=4.22, df=2 (P=0.12); I²=53%							
Test for overall effect: Z=0.78 (P=0.43)							
Total (95% CI)		**1434**		**1983**	**100.0%**	**0.82 [0.75, 0.90]**	
Total events	448		817				
Heterogeneity: Chi²=34.52, df=24 (P=0.08); I²=30%							
Test for overall effect: Z=4.28 (P<0.0001)							
Test for subgroup differences: Chi²=2.34, df=2 (P=0.31); I²=14.6%							

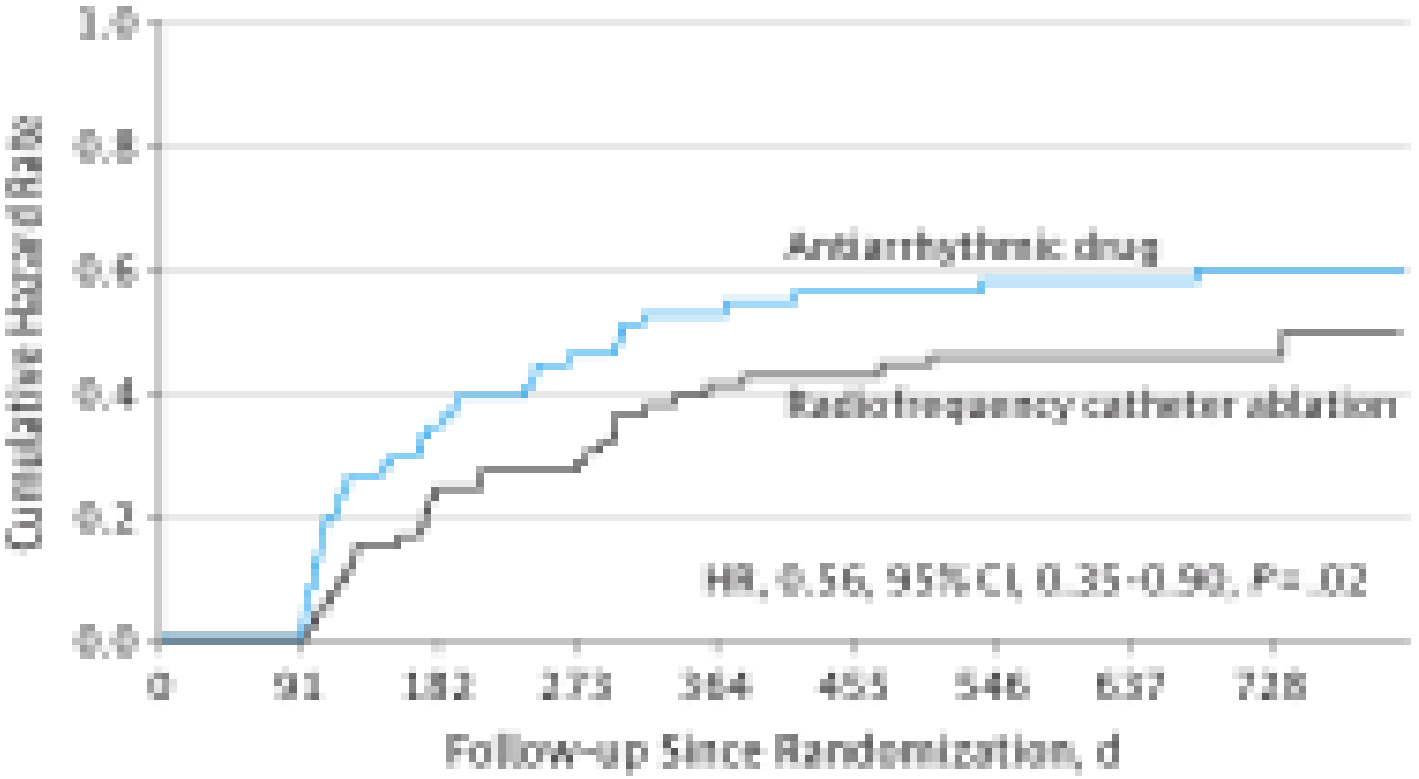


b

Study or subgroup	Contact force-guided ablation Events	Total	Standard radiofrequency ablation Events	Total	Weight	Risk ratio M–H, Fixed, 95% CI	Year
Martinek 2012	3	25	9	25	8.9%	0.33 [0.10, 1.09]	2012
Haldar 2012	3	20	14	20	15.4%	0.21 [0.07, 0.63]	2012
Sciarra 2014	4	83	9	81	19.0%	0.43 [0.14, 1.26]	2014
Marijon 2014	3	55	5	56	12.5%	0.60 [0.16, 2.25]	2014
Andrade 2014	4	25	26	50	19.0%	0.31 [0.12, 0.79]	2014
Reddy 2015	16	152	20	143	22.6%	0.75 [0.41, 1.39]	2015
Nakamura 2015	7	60	16	60	17.6%	0.44 [0.19, 0.99]	2015
Total (95% CI)		**395**		**485**	**100.0%**	**0.45 [0.32, 0.63]**	
Total events	40		99				
Heterogeneity: Chi²=5.55, df=6 (P=0.48); I²=0%							
Test for overall effect: Z=4.58 (P<0.00001)							



Catheter Ablation for Atrial fibrillation

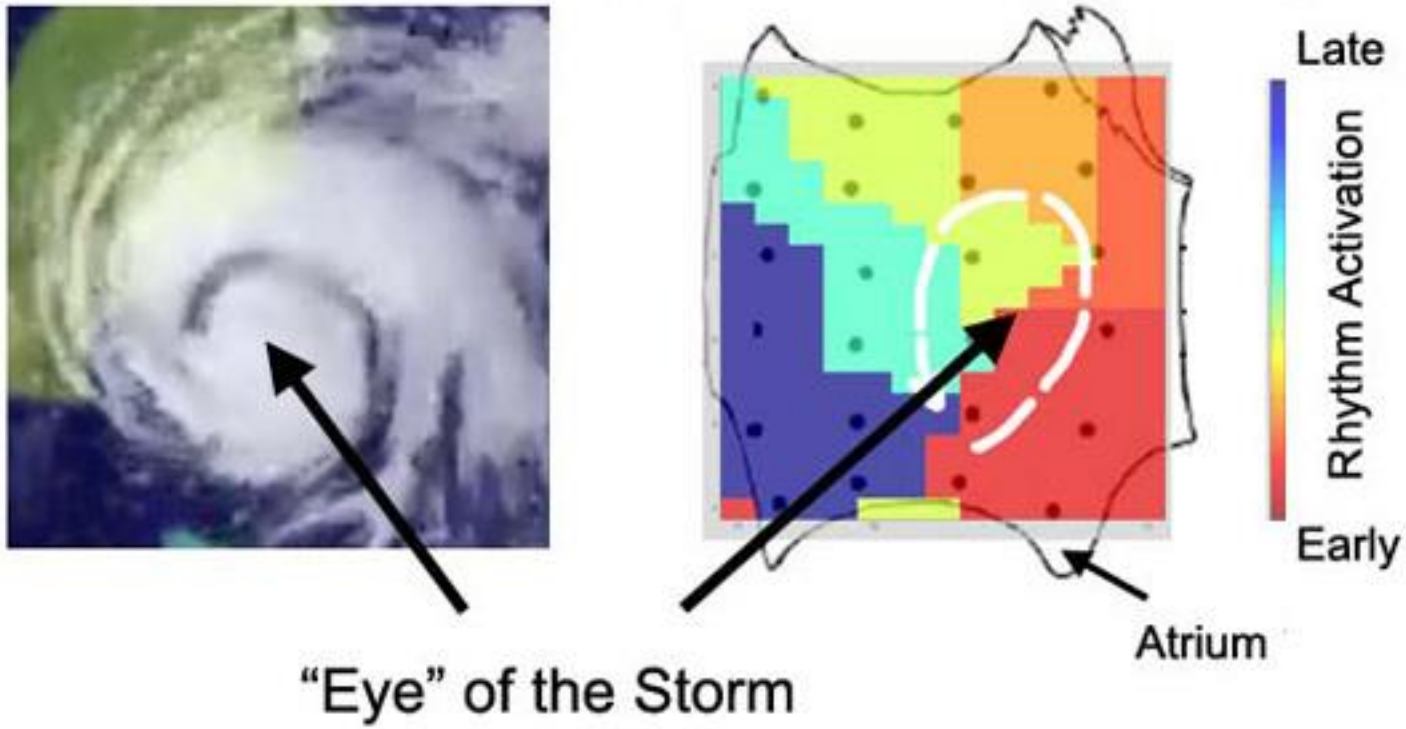


Morillo C, et al RAAFT2. JAMA 2014;311(7):692-699

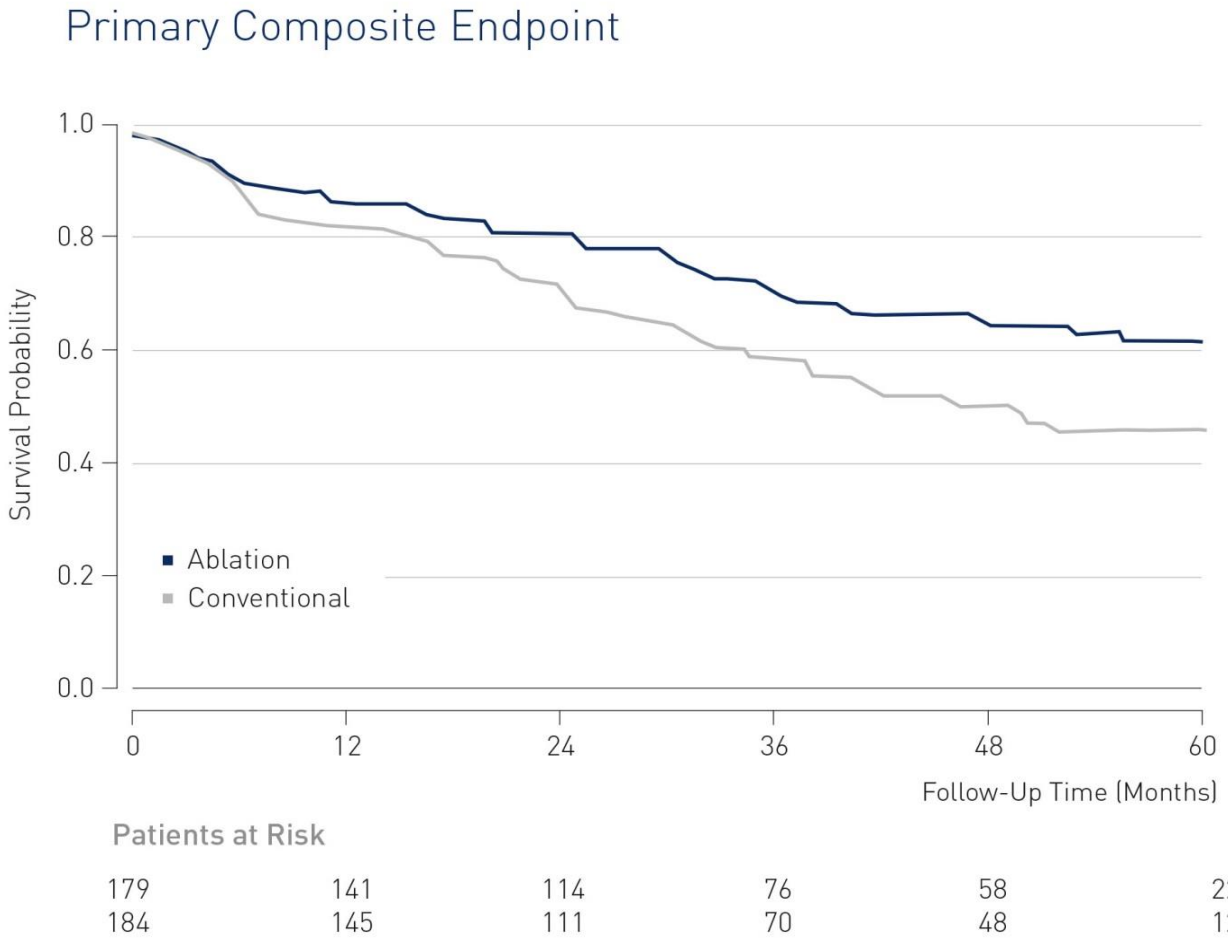
Substrate Mapping

Hurricane

Atrial Fibrillation
(actual San Diego patient)



Heart Failure

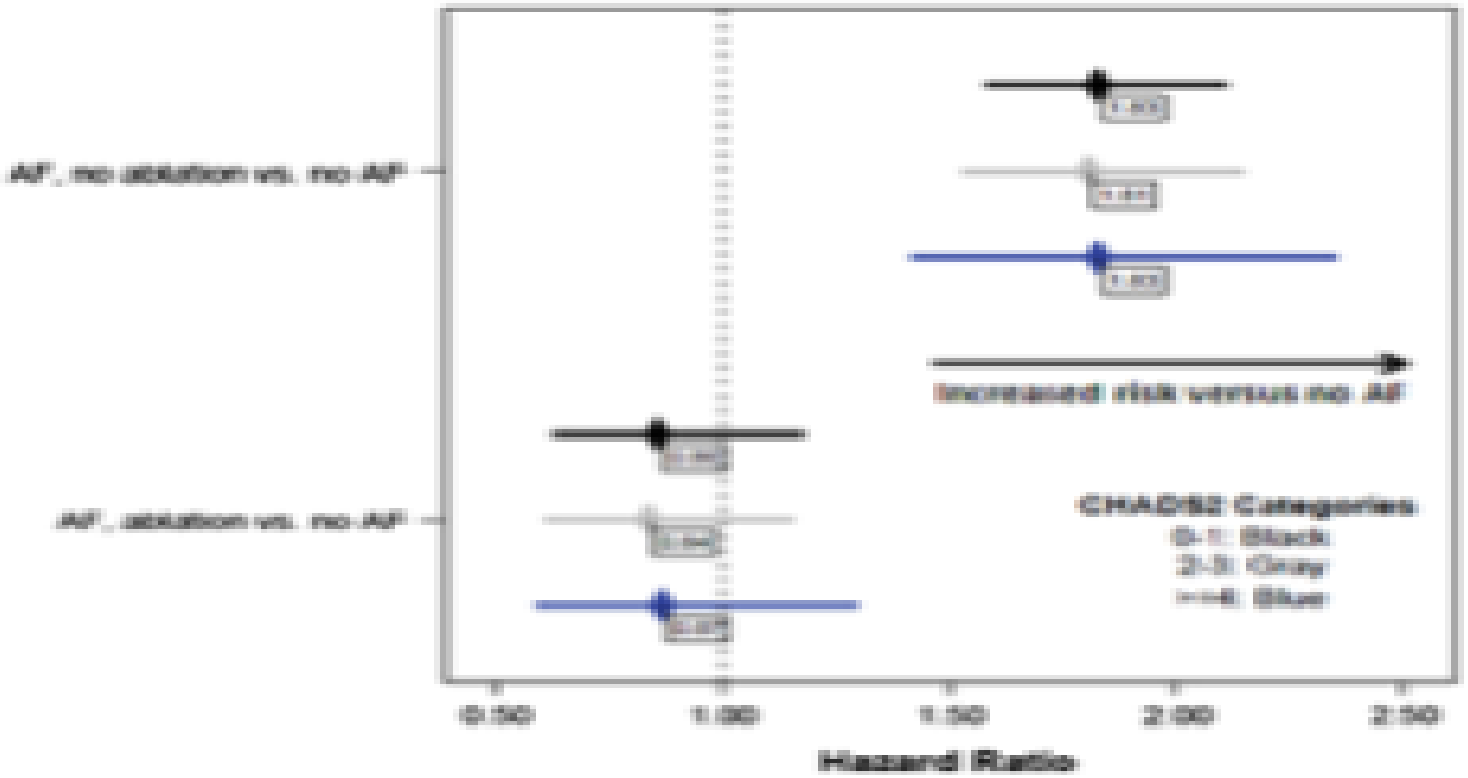


38% reduction of relative risk for **all-cause death** or **hospitalization** for heart failure

HR, 0.62 (95% CI, 0.43– 0.87); P=0.007
Log-rank test: P=0.006

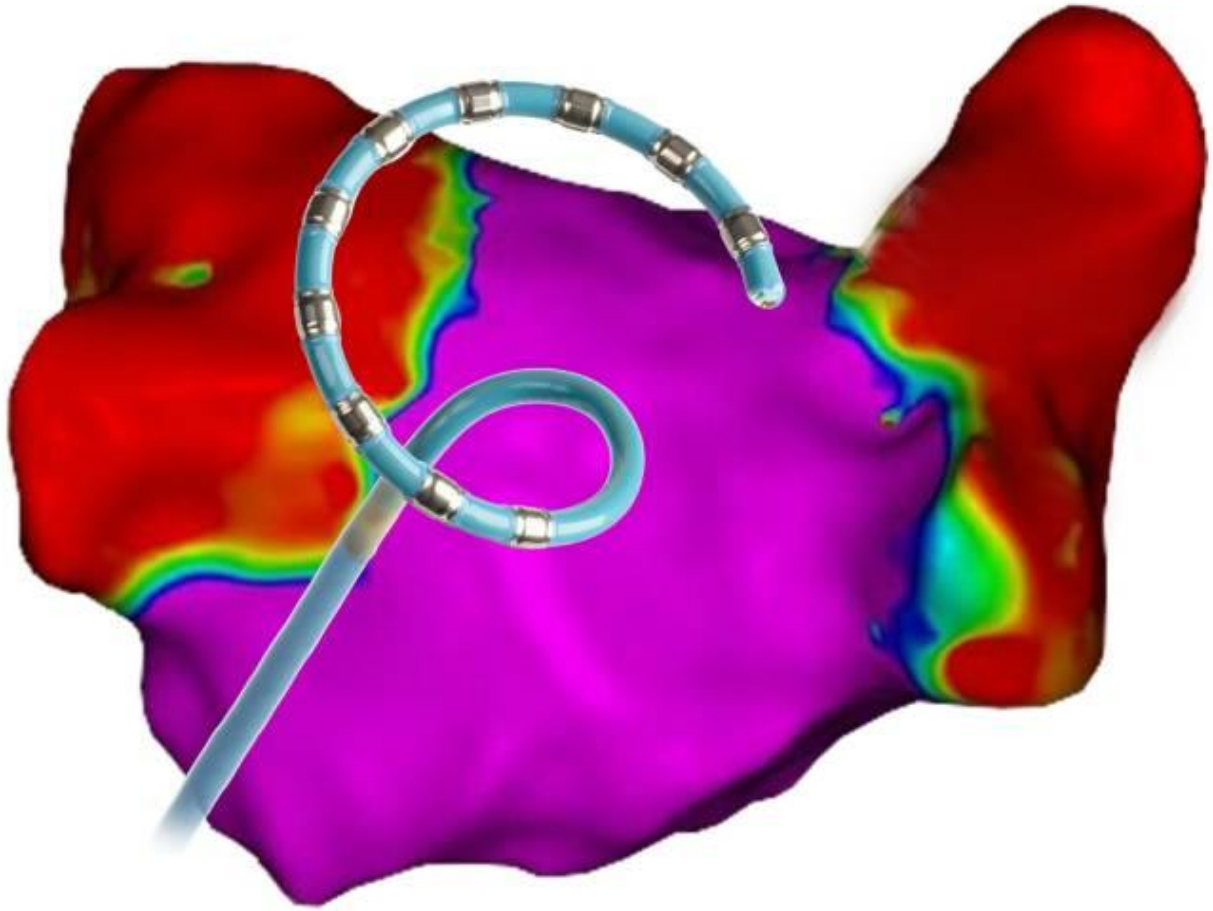
Marrouce N, et al. CASTLE-AF. NEJM 2018, 378(5)

Stroke Risk?



Bunch T, et al. Atrial fibrillation ablation patients have long-term stroke rates similar to patients without atrial fibrillation regardless of CHADS2 score. Heart Rhythm Journal V10, No9 Sept 2013

New Frontiers in Ablation



Atrial fibrillation Management

- Anticoagulate first
- Rate control second
- Atrial fibrillation ablation may be the right therapy for all symptomatic patients
- Technology continues to evolve and make our success rates continue to get better
- DOAC over coumadin