Atrial Fibrillation Around the World

North American Perspective and Specificities

Douglas L. Packer MD

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Heart House
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Disclosures

Dr. D. Packer in the past 12 months has provided consulting services for Biosense Webster, Inc., Boston Scientific, CyberHeart, Medtronic, Inc., nContact, Sanofi-Aventis, St. Jude Medical, and Toray Industries. Dr. Packer received no personal compensation for these consulting activities.

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Mayo Clinic and Drs. D. Packer and R. Robb have a financial interest in mapping technology that may have been used at some of the 10 centers participating in this pilot research. In accordance with the Bayh-Dole Act, this technology has been licensed to St. Jude Medical, and Mayo Clinic and Drs. Packer and Robb received annual royalties >$10,000, the federal threshold for significant financial interest.

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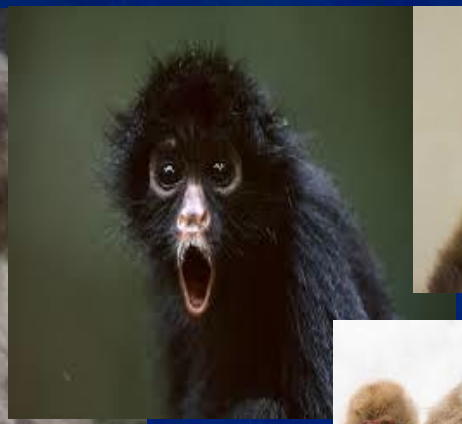
North American Risk Considerations












North American Perspective and Specificities

Contributors of AF occurrence

Prevalence of AF occurrence / risk

Stroke and other risks

Contributors of Obesity and OSA

Prevalence of unknown or cryptogenic AF and

Preventing risk of stroke in the absence of known AF

Role of monitoring in finding AF

Risk that AF isn’t a risk

Risks of dementia / cognitive impairment

Hospitalization, Cost, Quality of life risks

Risk of prevention of AF related stroke (NOACs / LAAO)

Risk of Drug and Ablative therapy

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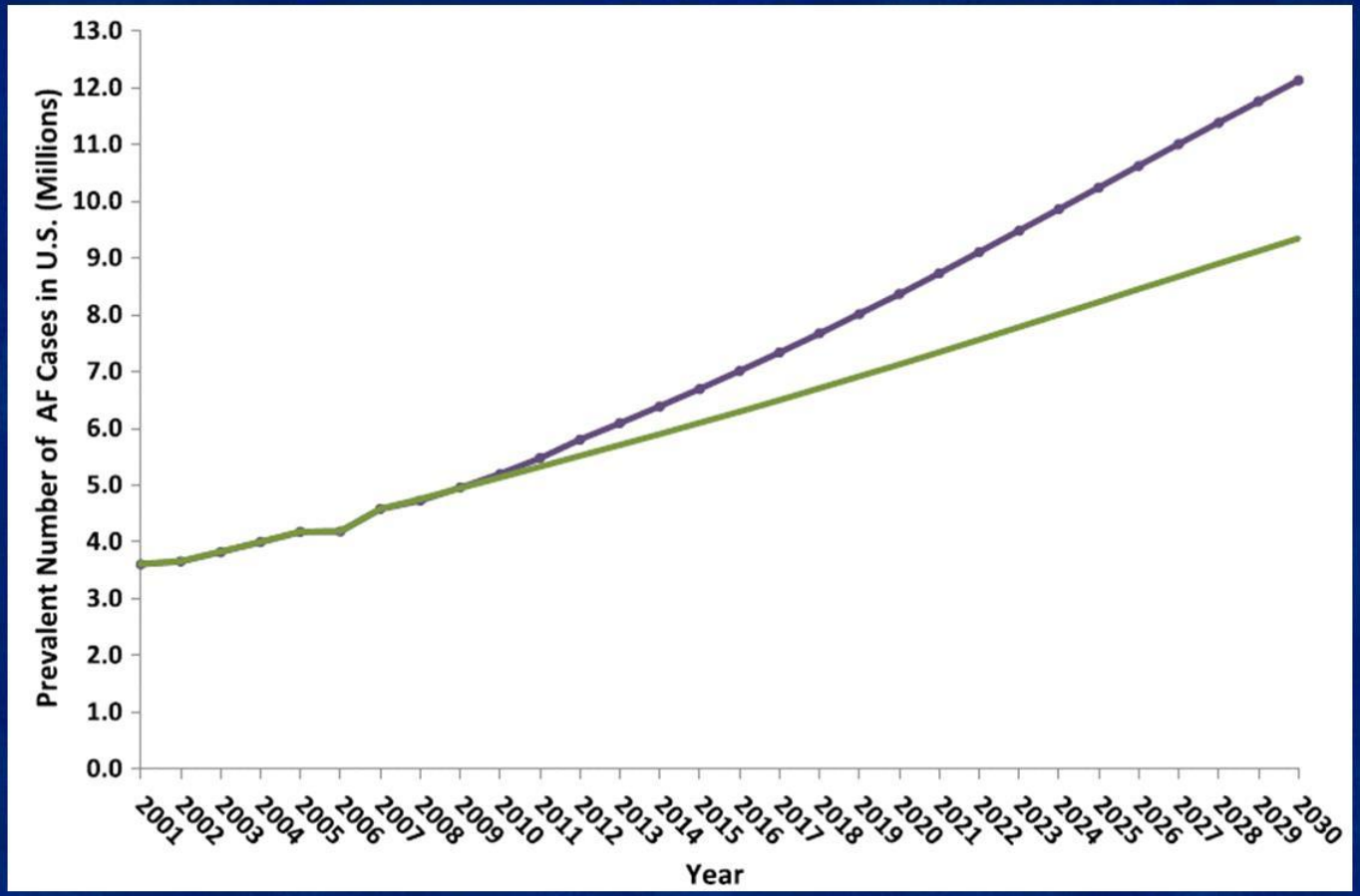
North American Perspective and Specificities

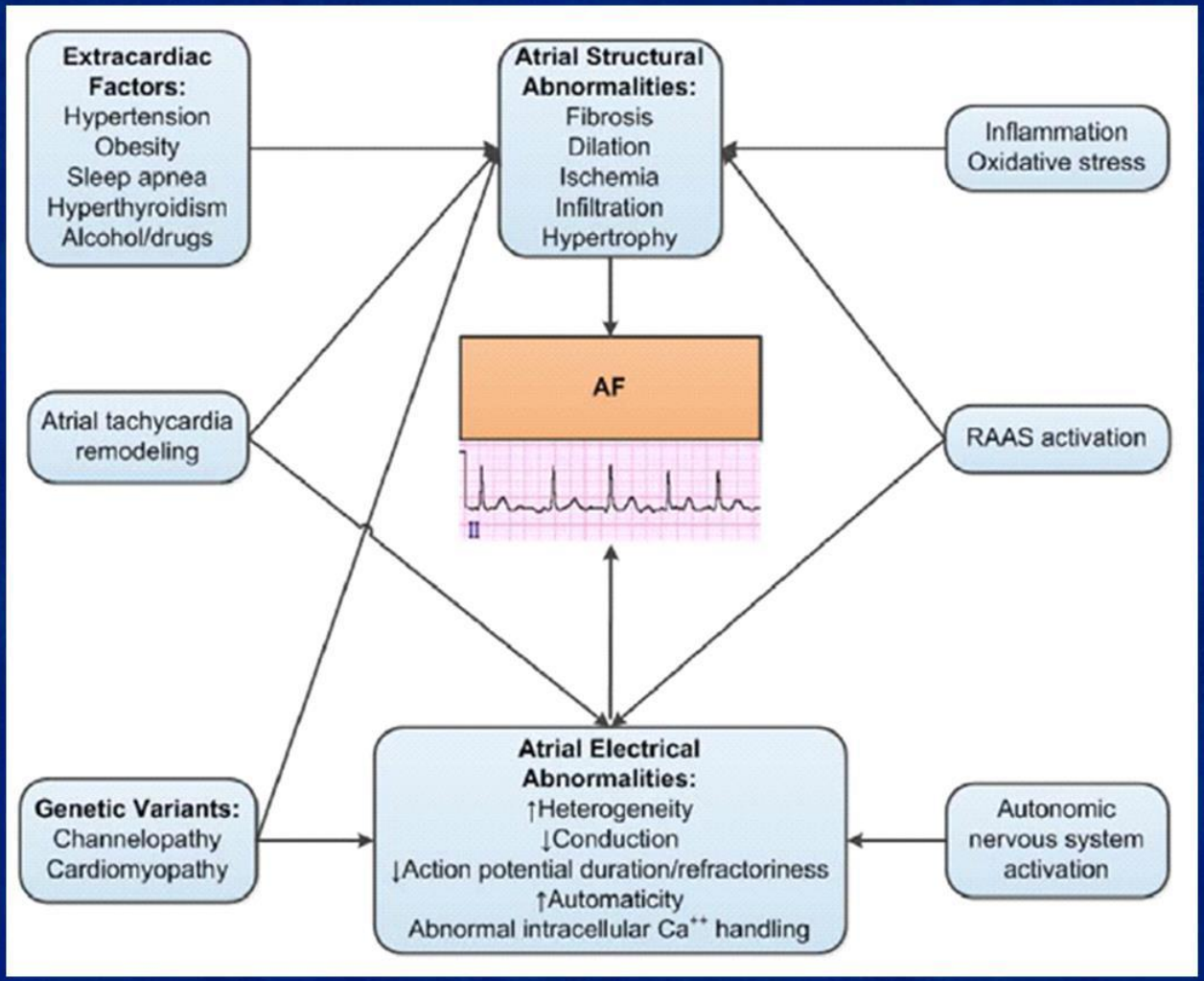
Contributors to AF Occurrence

Projected Prevalence of Diagnosed AF Cased in US from 2001 to 2030, Assuming No Increase in Incidence Rate After 2007 and a Logarithmic Growth in AF Incidence



Colilla, et al. Am J Cardiology 2013:1142

Mechanisms of AF



January et al. Circulation 2014:2071

CHEST Original Research

THROMBOEMBOLISM

Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach

The Euro Heart Survey on Atrial Fibrillation

Gregory Y. H. Lip, MD; Robby Nieuwlaat, PhD; Ron Pisters, MD; Deirdre A. Lane, PhD; and Harry J. G. M. Crijns, MD

Background: Contemporary clinical risk stratification schemata for predicting stroke and thromboembolism (TE) in patients with atrial fibrillation (AF) are largely derived from risk factors identified from trial cohorts. Thus, many potential risk factors have not been included.

Methods: We refined the 2006 Birmingham/National Institute for Health and Clinical Excellence (NICE) stroke risk stratification schema into a risk factor-based approach by reclassifying and/or incorporating additional new risk factors where relevant. This schema was then compared with existing stroke risk stratification schema in a real-world cohort of patients with AF (n = 1,084) from the Euro Heart Survey for AF.

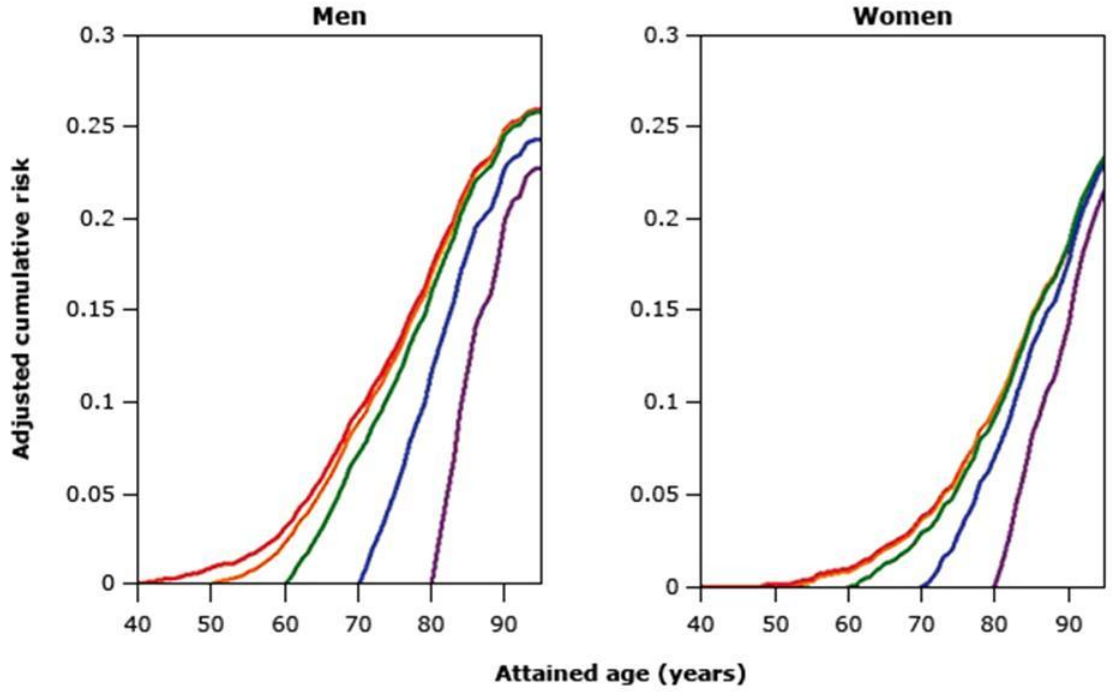
Results: Risk categorization differed widely between the different schemes compared. Patients classified as high risk ranged from 10.2% with the Framingham schema to 75.7% with the Birmingham 2009 schema. The classic $CHADS_2$ (Congestive heart failure, Hypertension, Age > 75, Diabetes, prior Stroke/transient ischemic attack) schema categorized the largest proportion (61.9%) into the intermediate-risk strata, whereas the Birmingham 2009 schema classified 15.1% into this category. The Birmingham 2009 schema classified only 9.2% as low risk, whereas the Framingham scheme categorized 48.3% as low risk. Calculated C-statistics suggested modest predictive value of all schema for TE. The Birmingham 2009 schema fared marginally better (C-statistic, 0.606) than $CHADS_2$. However, those classified as low risk by the Birmingham 2009 and NICE schema were truly low risk with no TE events recorded, whereas TE events occurred in 1.4% of low-risk $CHADS_2$ subjects. When expressed as a scoring system, the Birmingham 2009 schema (CHA_2DS_2-VASc acronym) showed an increase in TE rate with increasing scores (*P* value for trend = .003).

Conclusion: Our novel, simple stroke risk stratification schema, based on a risk factor approach, provides some improvement in predictive value for TE over the $CHADS_2$ schema, with low event rates in low-risk subjects and the classification of only a small proportion of subjects into the intermediate-risk category. This schema could improve our approach to stroke risk stratification in patients with AF.

CHEST 2010; 137(2):263–272

Lip, et al. Chest 2010:263

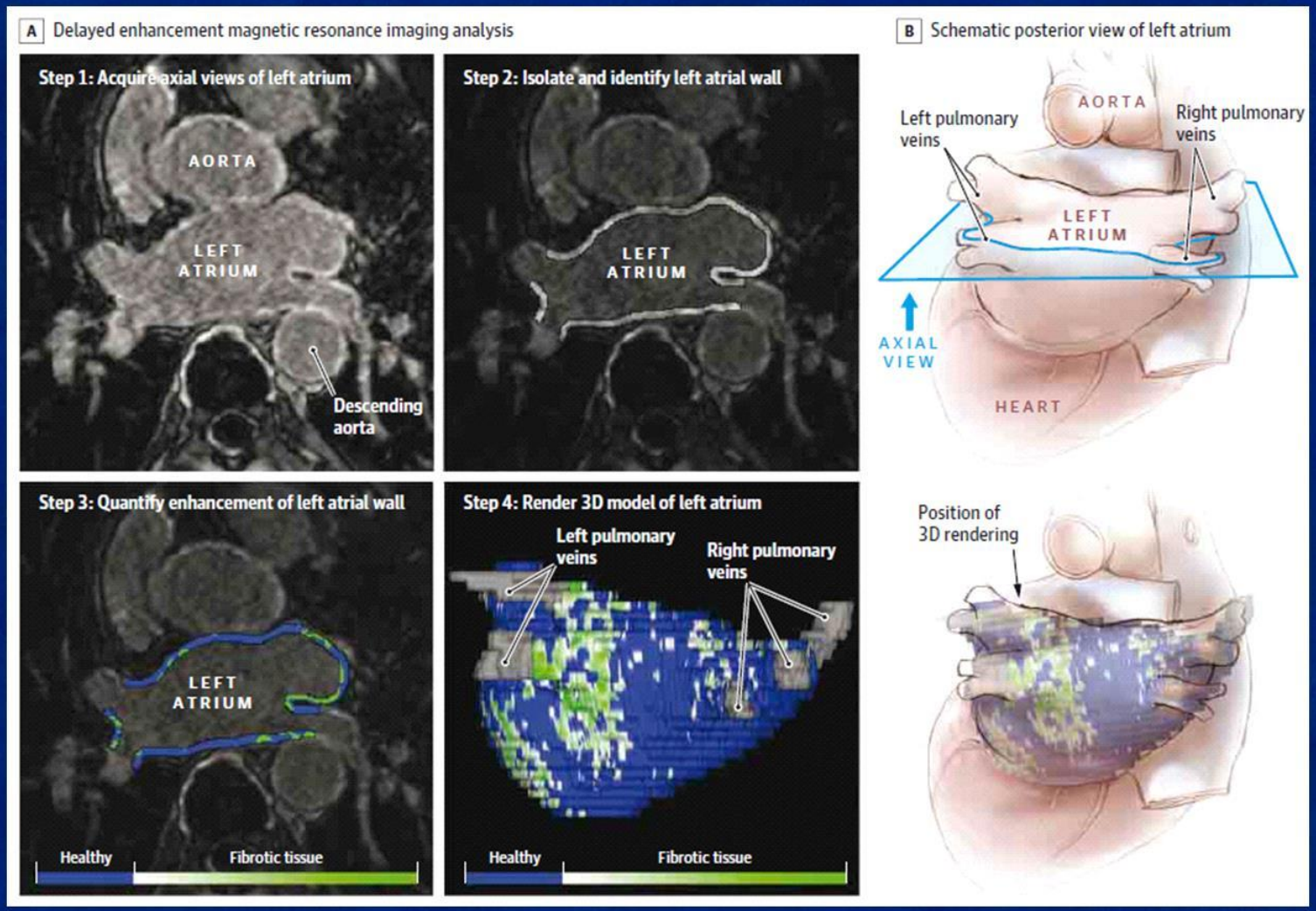
Prevalence of AF by Sex and Age



Lifetime risk for developing atrial fibrillation (AF) from the Framingham Heart Study. Men and women without AF at 40 years of age were determined to have a 26 and 23 percent likelihood of developing incident AF by 80 years of age.

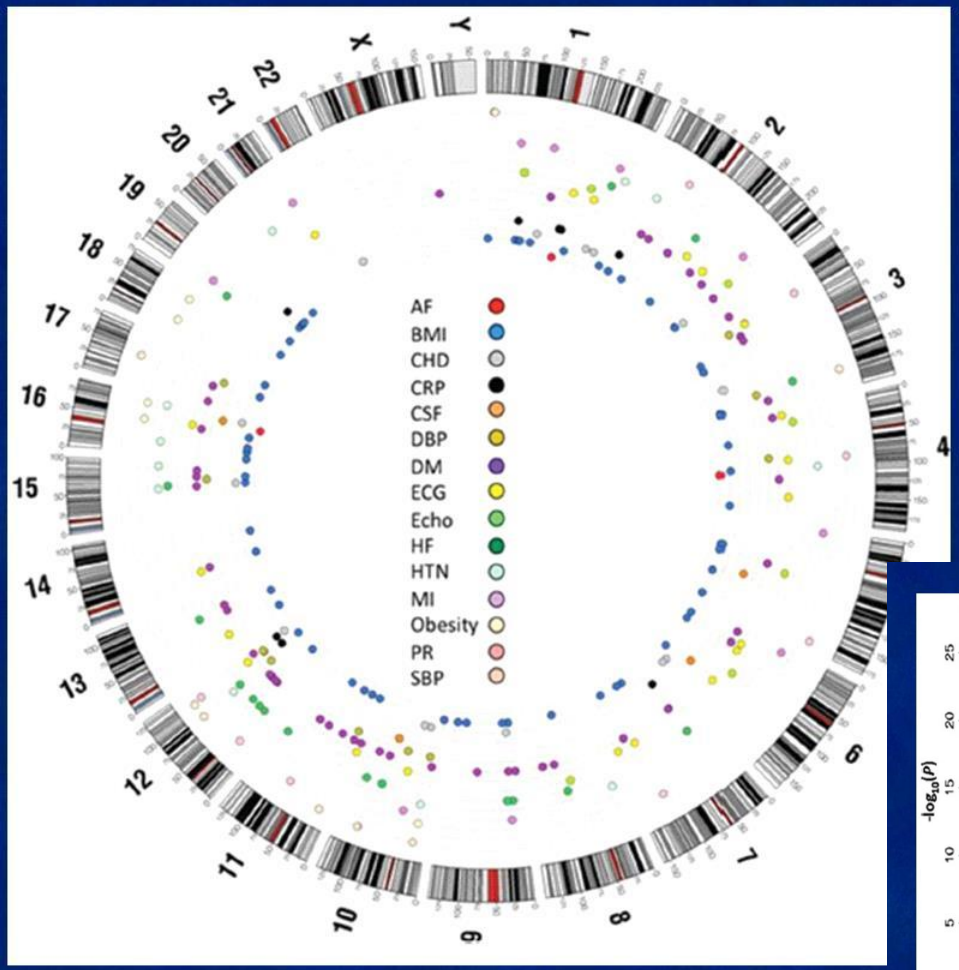
Genz, et al. UpToDate 2015

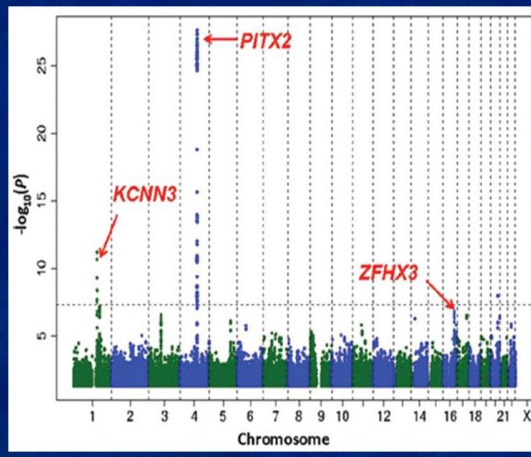
Process for Quantification of Left Atrial Wall Fibrosis



Marrouche, et al. JAMA 2014:498

Circos Plot Representing the Genetic Variants Found by Genome-wide Association Study for AF and AF Risk Factors





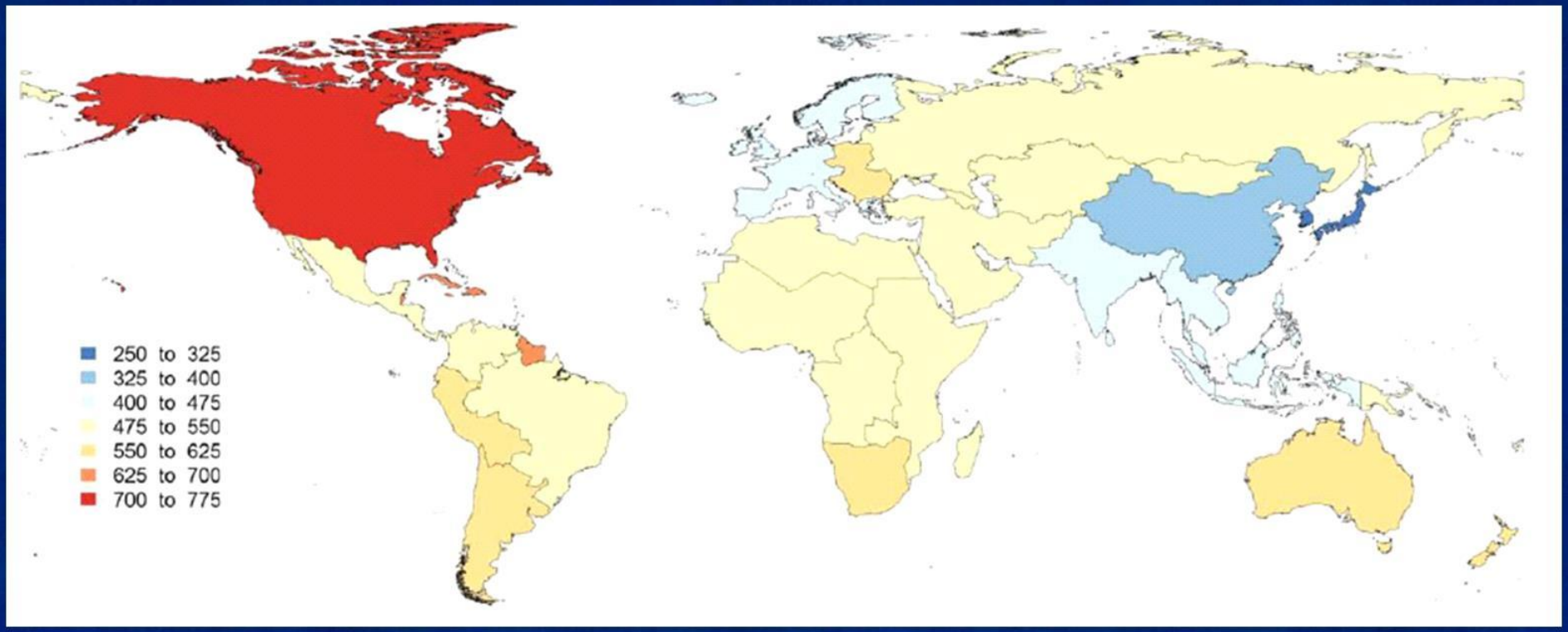
Magnani, et al. Circ 2011:1982

Atrial Fibrillation Around the World

North American Perspective and Specificities

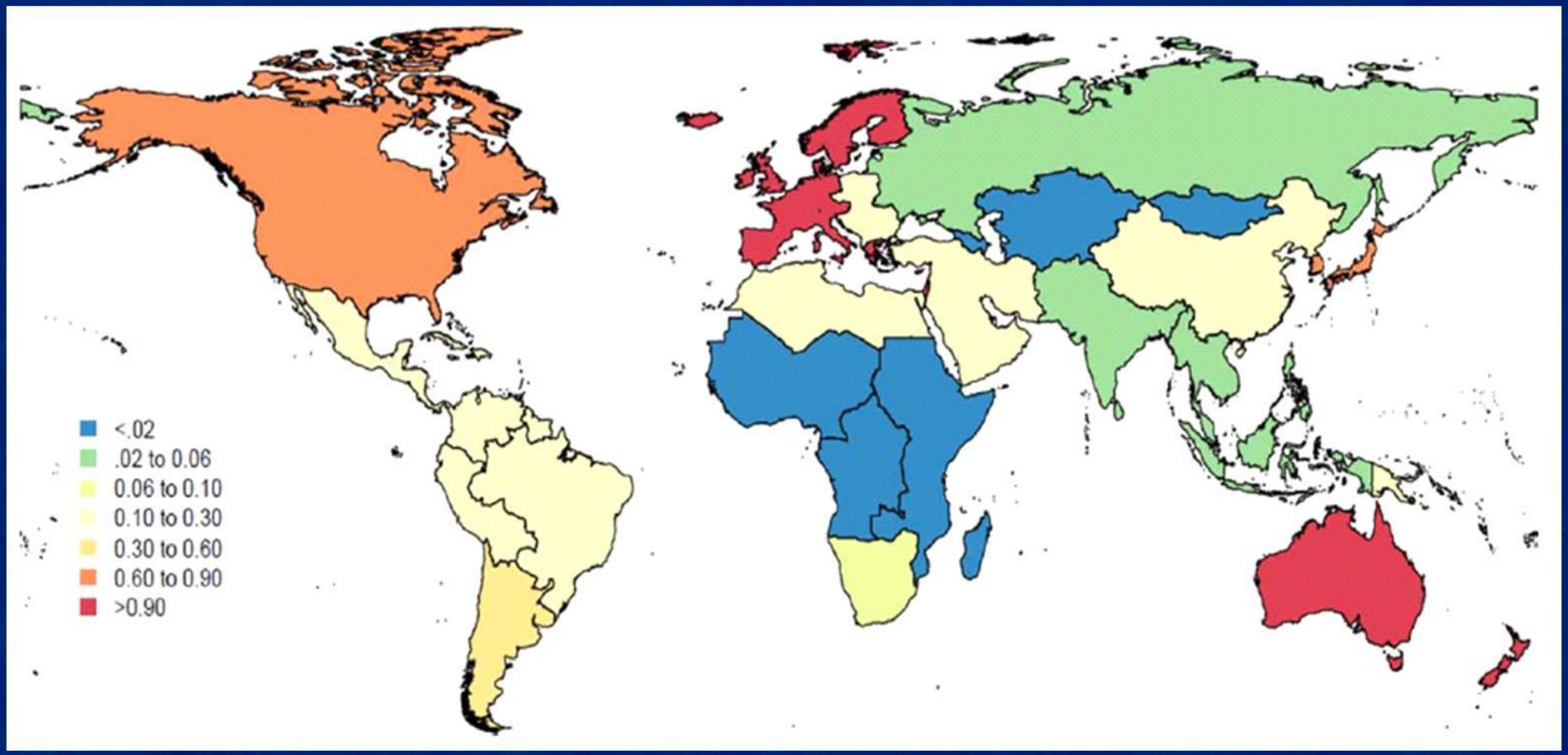
Obesity and OSA

Prevalence of AF and Aflutter by Region, 2010



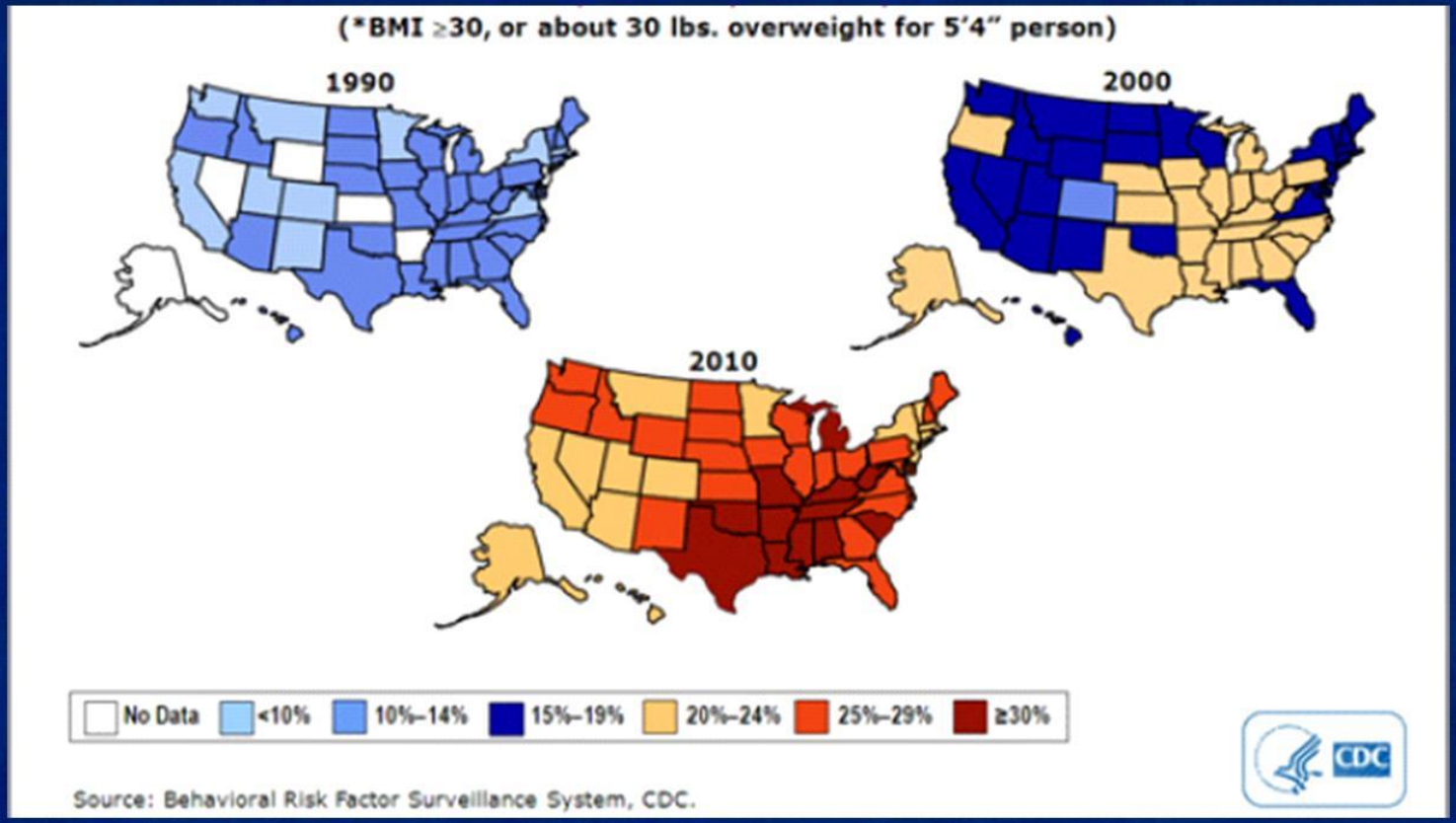
Chugh, et al. Circ 2014_837

Proportion of Global Deaths Associated with AF in 2010



Chugh, et al. Circ 2014_837

Obesity Trends Among US Adults BRFSS, 1990, 2000, 2010



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Risks of Stroke and Other Disasters

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CHEST 2010; 137(2):263–272

Lip, et al. Chest 2010:263

Risk Categorization, Incidence of TE, and Predictive Ability for Contemporary Risk Stratification Schema Among Euro Heart Survey Pts. Who Did not Receive Anticoagulation at Baseline

	Categorization of TE Risk			Predictive Ability	
	Low	Intermediate	High	C Statistic (95% CI)	*P* Value
AFI 1994					.209
% in risk category	16.7	12.2	71.1	0.573	
TE events, No. (%)	1 (0.6)	4 (3.0)	20 (2.6)	(0.470-0.676)	
SPAF 1999					.405
% in risk category	26.2	44.8	29.0	0.549	
TE events, No. (%)	5 (1.8)	11 (2.3)	9 (2.9)	(0.435-0.662)	
$CHADS_2$—classic					.296
% in risk category	20.4	61.9	17.7	0.561[b]	
TE events, No. (%)	3 (1.4)	16 (2.4)	6 (3.2)	(0.450-0.672)	
$CHADS_2$—revised					.140
% in risk category	20.4	34.9	44.7	0.586[b]	
TE events, No. (%)	3 (1.4)	7 (1.9)	15 (3.1)	(0.477-0.695)	
Framingham					.018
% in risk category	48.3	41.5	10.2	0.638[b]	
TE events, No. (%)	6 (1.2)	14 (3.2)	5 (4.6)	(0.532-0.744)	
NICE 2006					.094
% in risk category	13.1	39.2	47.7	0.598	
TE events, No. (%)	0 (0.0)	13 (3.1)	12 (2.3)	(0.498-0.698)	
ACC/AHA/ESC 2006					.228
% in risk category	19.6	32.6	47.8	0.571	
TE events, No. (%)	3 (1.4)	7 (2.0)	15 (2.9)	(0.461-0.680)	
ACCP 2008					.204
% in risk category	19.6	33.4	47.0	0.574	
TE events, No. (%)	3 (1.4)	7 (1.9)	15 (3.0)	(0.465-0.683)	
Birmingham 2009					.070
% in risk category	9.2	15.1	75.7	0.606	
TE events, No. (%)	0 (0.0)	1 (0.6)	24 (3.0)	(0.513-0.699)	

Lip, et al. Chest 2010:263

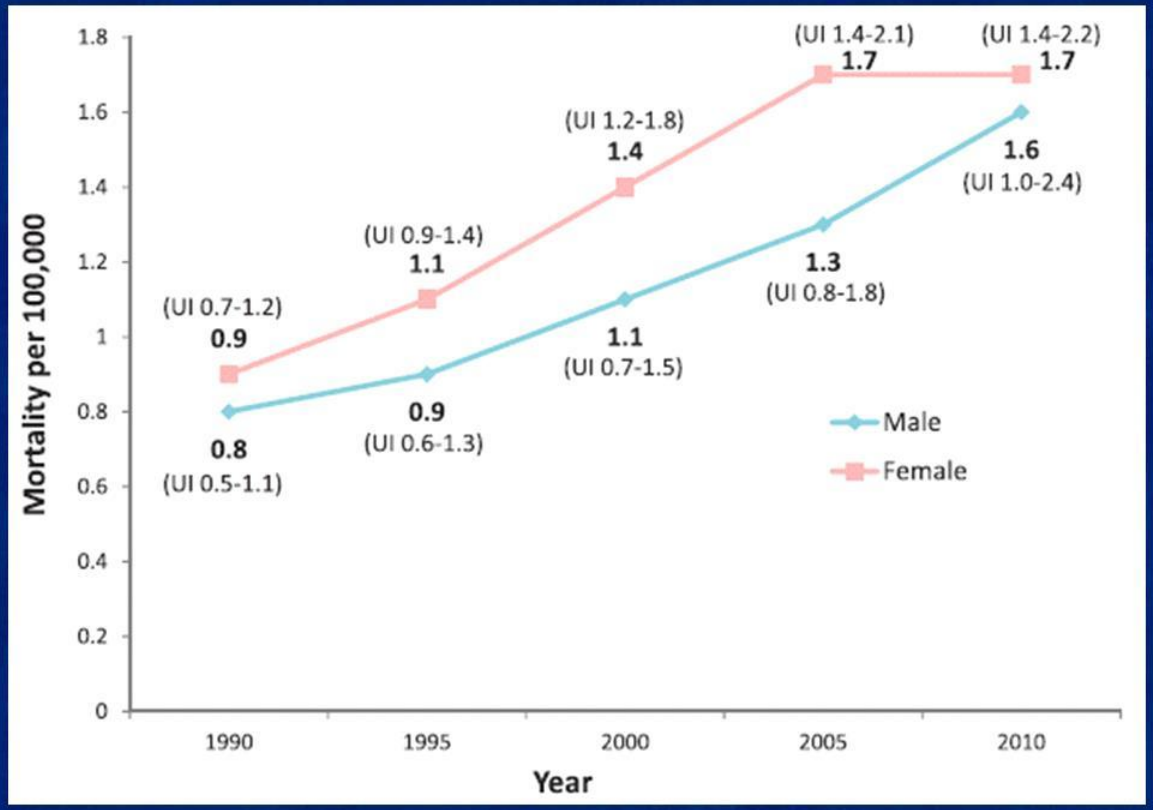
The 2009 Birmingham Schema Expressed as a Point-Based Scoring System, with the Acronym CHA_2DS_2-VASc

Risk Factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥ 75 y	2
Diabetes mellitus	1
Stroke/TIA/TE	2
Vascular disease (prior myocardial infarction, peripheral artery disease, or aortic plaque)	1
Age 65-74 y	1
Sex category (ie female gender)	1

LV = left ventricular; TE = thromboembolism. See Table 1 for expansion of other abbreviations.

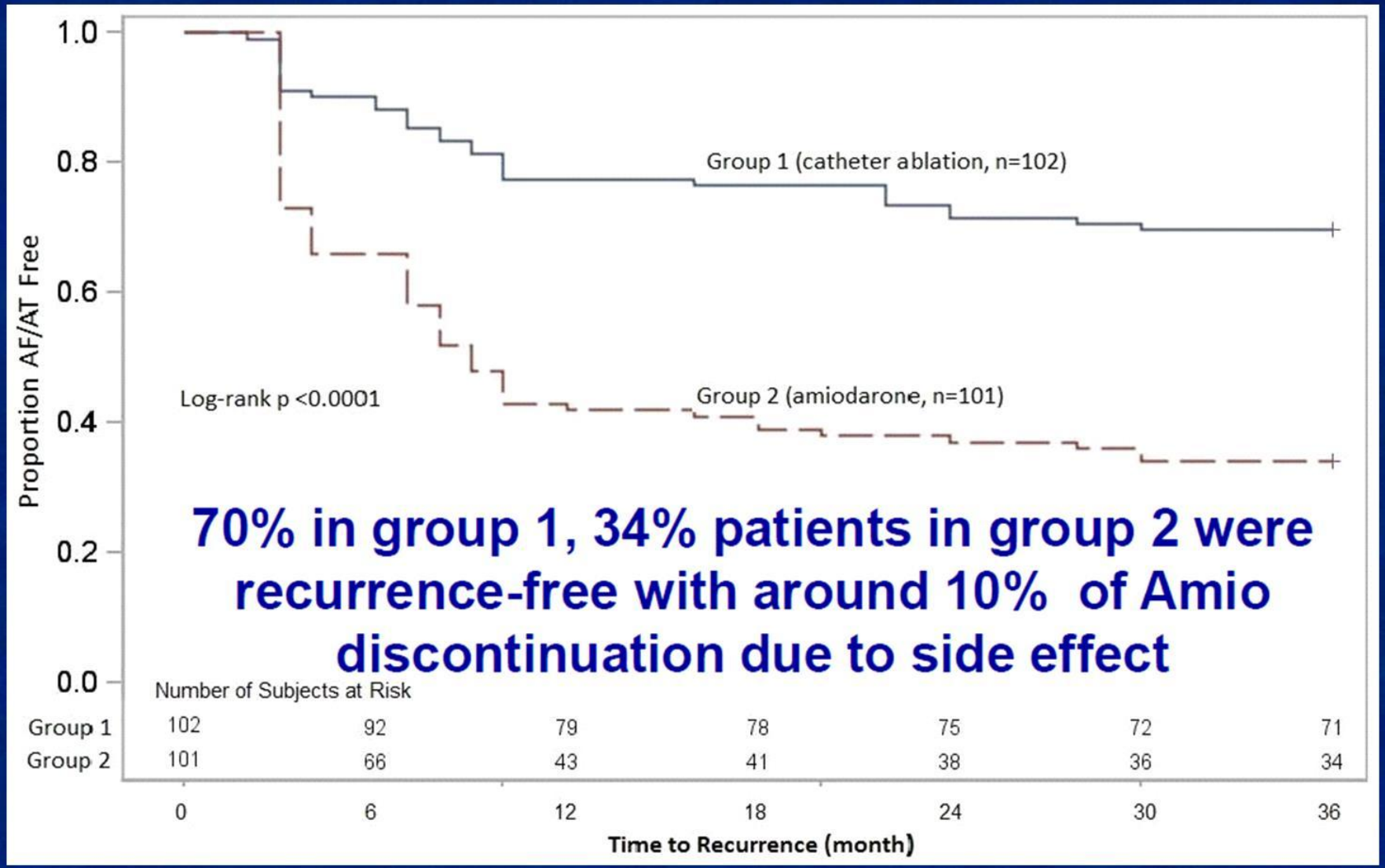
Lip, et al. Chest 2010:263

Mortality Associated with AF: 1990 - 2010



Chugh, et al. Circ 2014_837

KM Curves Comparing Success Rate



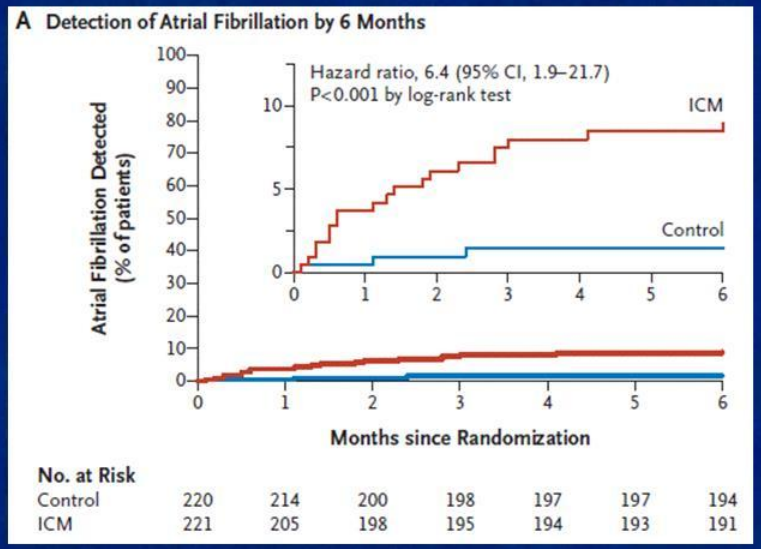
DiBiase L, et al. ACC 2015

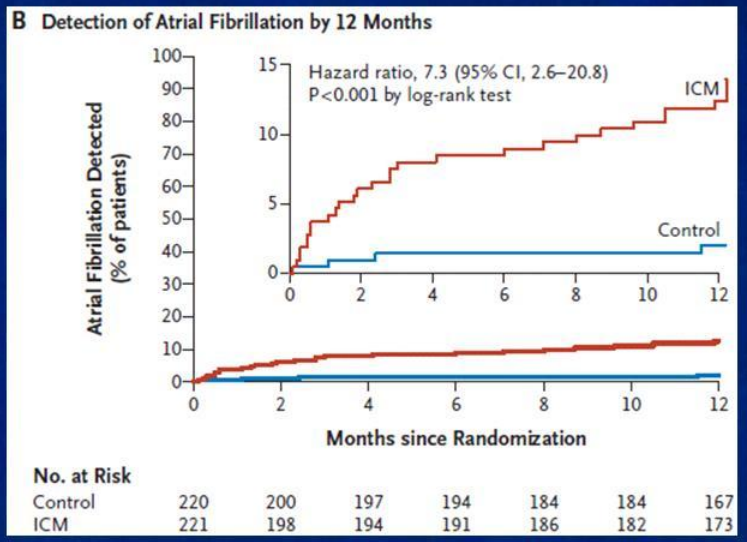
Atrial Fibrillation Around the World

North American Perspective and Specificities

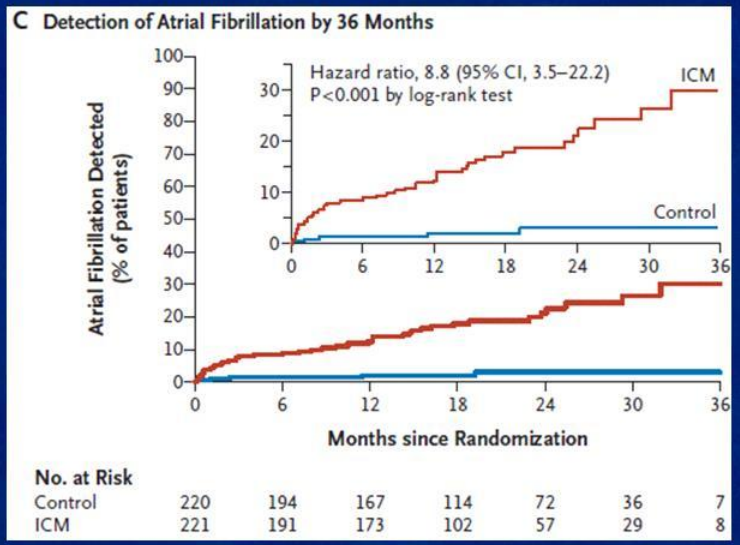
Prevalence of unknown or cryptogenic AF and

Time to First Detection of AF





In Crystal AF

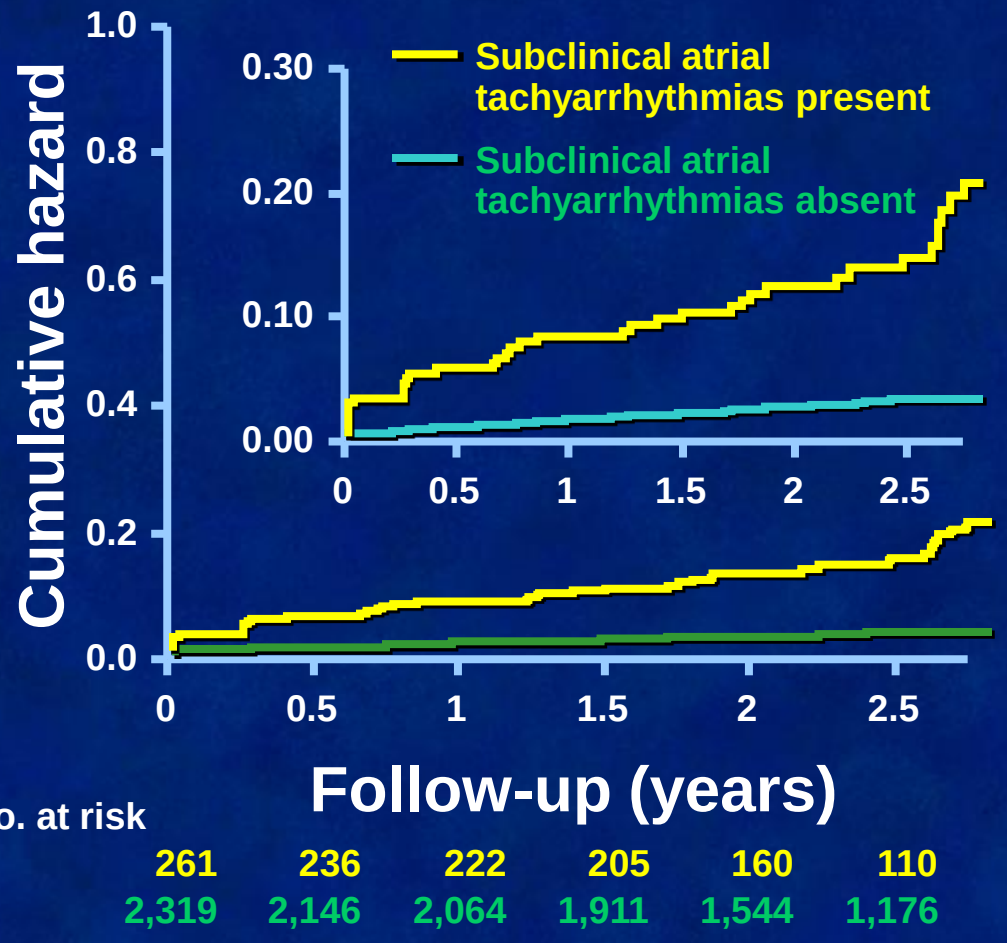


Sanna, et al. NEJM 2014:2478

ASSERT: Risk of subclinical and clinical atrial arrhythmia

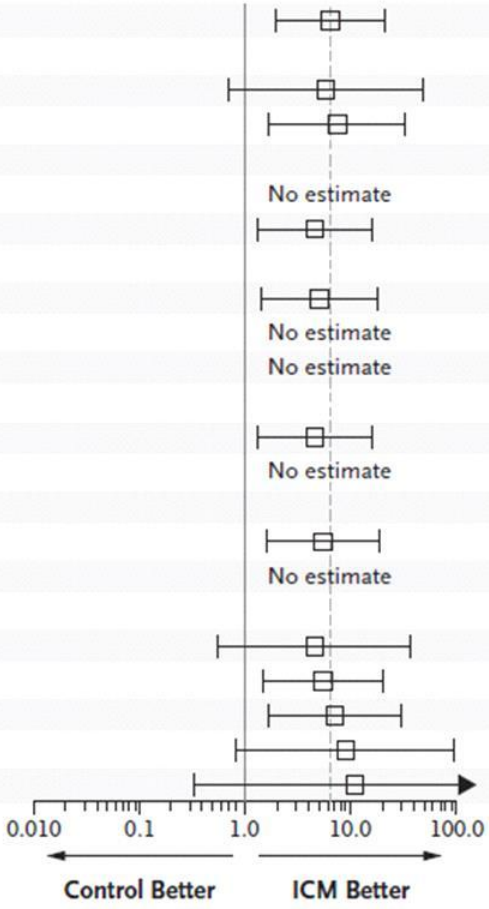
35% of patients had atrial high rate episodes during the study

Risk of clinical atrial arrhythmia during follow up



Subgroup Analysis of Time to First Detection of AF by 6 Mos.

Subgroup	No. of Patients (%)	Atrial Fibrillation Detected by 6 Mo (% of patients)		P Value for Interaction
		ICM	Control	
Overall	441 (100.0)	8.9	1.4	
Age				0.85
≤65 yr	276 (62.6)	4.4	0.8	
>65 yr	165 (37.4)	17.0	2.5	
Sex				0.99
Female	161 (36.5)	6.7	0.0	
Male	280 (63.5)	10.1	2.3	
Race or ethnic group				1.00
White	385 (87.3)	8.0	1.6	
Other	29 (6.6)	9.1	0.0	
Not available	27 (6.1)	20.0	0.0	
Patent foramen ovale				0.99
No	343 (77.8)	8.0	1.8	
Yes	98 (22.2)	11.8	0.0	
Index event				0.99
Stroke	401 (90.9)	8.3	1.6	
TIA	40 (9.1)	15.0	0.0	
$CHADS_2$ score				0.73
2	150 (34.0)	3.0	0.0	
3	183 (41.5)	7.8	2.2	
4	84 (19.0)	15.4	3.2	
5	23 (5.2)	33.3	0.0	
6	1 (0.2)	0.0	NA	



Sanna, et al. NEJM 2014:2478

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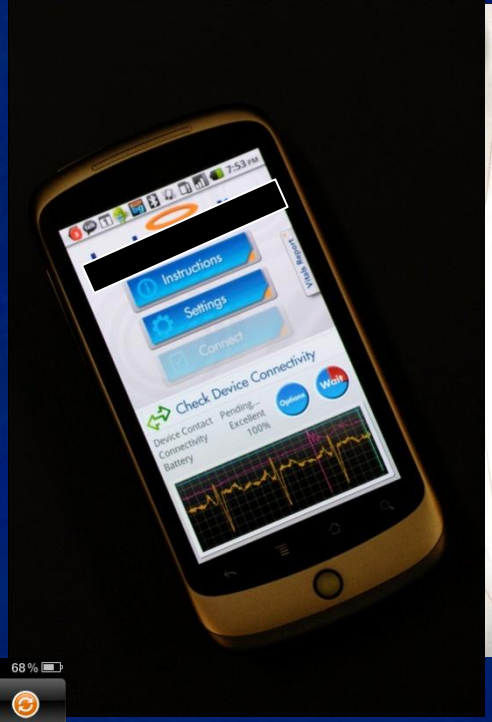
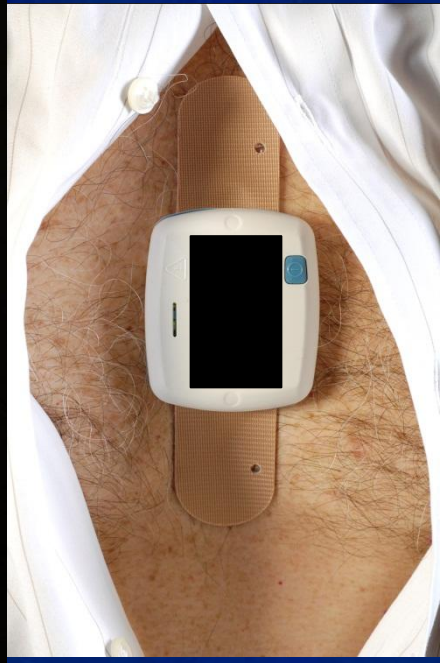
Role of monitoring in finding AF

Remote Patient Monitoring

- ECG
- Respiration
- Body position
- Physical activity





Studies of Prolonged Ambulatory Cardiac Rhythm Monitoring in Pts. with Stroke/TIA

Study	No. of Patients	Study Design	Patient Selection	Interval From CV Event	Definition of PAF	Type of Monitor	Duration	Diagnostic Yield
Higgins et al[18]	100	Randomized trial	Any TIA or stroke without known AF	≤7 d	20 s for sustained <20 s but 6 VC for nonsustained*	50 SP 50 aELR	7 d	4% SP 44% ELRa for PAF of any duration
Rabinstein et al[19]	132	Case control	66 CS 66 SKC	≤90 d (28±20 d)	Any duration*	MCOT (all)	21 d	25% in CS 14% in SKC
Ritter et al[20]	60	Prospective cohort, comparative	CS	13 d (IQR, 10–65)	30 s (2 min required for ILR detection)*	ILR plus initial 7-d Holter	ILR 382 d (IQR, 89–670)	17% ILR 1.7% 7-d Holter
Etgen et al[21]	22	Prospective cohort	CS	Mostly within 10 d	6 min	ILR	365 d	27%
Cotter et al[22]	51	Prospective, cohort	CS	174±134 d	2 min*	ILR	Until detection (≤229±116 d)	25.5%
Kamel et al[17]	40	Randomized trial	CS or CTIA	≤60 d (22±12 d)	30 s*	20 MCOT 20 routine follow-up	21 d	0% (36% had MCOT noncompliance)
Miller et al[23]	156	Retrospective cohort	Mostly CS or CTIA (24% were not cryptogenic)	≤180 d (33±36 d)	Any duration	MCOT	≤30 d	17.3%
Flint et al[24]	239	Prospective cohort	CS	29 d (17–50 d)	5 s*	aELR	≤30 d (24.5±9 d)	12.1%
Manina et al[25]	114	Prospective cohort	CS or CTIA	Up to 30 d	Any duration*	Holter	4 d	24.3%
Doliwa et al[26]	249	Prospective cohort	Any TIA or stroke without known AF	≤14 d	10 s*	Serial ECG, patient activated	30 d	6%
Bhatt et al[27]	62	Retrospective cohort	CS or CTIA	29 d (16–48) after hospital discharge	30 s*	MCOT	≤28 d	24%
Stahrenberg et al[28]	224	Prospective cohort	Any TIA or stroke without known AF	9.5 h (IQR, 6–16 h)	Any duration*	Holter	7 d	12.5%
Gaillard et al[29]	98	Retrospective cohort	Mostly CS or CTIA (16% were not cryptogenic)	≤180 d	32 s*	TTM with serial ECG (patient activated)	≤30–90 d	9.2%
Dion et al[30]	24	Prospective cohort	CS, age <75 (mean age, 49±14 y)	Up 120 d	Any duration*	ILR	14.5 mo	4.2%
Elijovich et al[31]	20	Retrospective cohort	CS or CTIA	NA	30 s*	aELR	≤30 d	20%
Tayal et al[32]	56	Retrospective cohort	CS or CTIA	≤90 d	Any duration	MCOT	≤21 d	23%
Jabaudon et al[33]	88	Prospective cohort	Any TIA or stroke (patients with remote PAF were not excluded)	Mean 55 d	NA	aELR	7 d	5.7%
Barthélémy et al[34]	60	Prospective cohort	Any TIA or stroke (including 28 with CS or CTIA)	10±2 d	30 s	aELR	4 d (70±31 h)	20% whole cohort 14.3% CS/CTIA
Schuchert et al[35]	82	Retrospective cohort	CS	≤14–21 d	1 min	Holter	3 d	4.9%

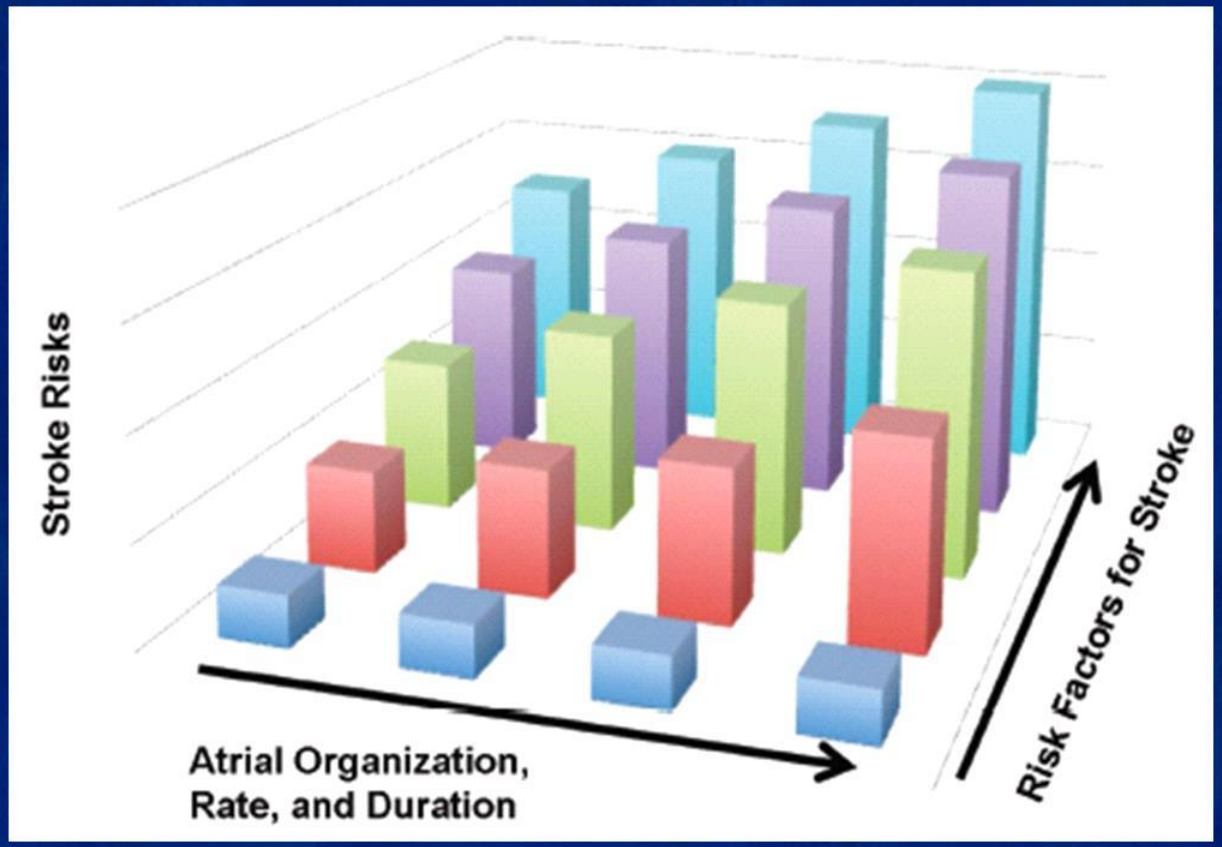
Rabinstein AA. Stroke 2014:1208

AF Detected by Insertable Cardiac Monitors in Pts. with Cryptogenic Stroke

Study (year)	No. of patients	AF definition	Monitoring duration	AF detection yield	Notes
Cotter et al[25] (2013)	51	2 minutes	Mean 229 (116) days	25.5%	Median time from ICM implant to first new AF episode: 48 days (range 0–154 days) Median duration of first new AF episode: 6 minutes (range 1– 4320 minutes)
Ritter et al[26] (2013)	60	2 minutes	1 year	16.7%	Mean time from ICM implant to first new AF episode: 64 days (1-556). 7-day Holter detected AF in only 1.7%
Etgen et al[27] (2013)	22	6 minutes	1 year	27.3%	Mean time from stroke to first new AF episode: 5 months
Rojo-Martinez et al[28] (2013)	101	2 minutes	281 ± 212 days	33.7%	
SURPRISE[29] (2014)	85	2 minutes	569 ± 310 days	16.1 %	Mean time from stroke to first new AF episode 109 ± 48 days
CRYSTAL AF[11] (2014)	221	>30 seconds*	Minimum 6 months	8.9% at 6 months 12.4% at 12 months 30.0% at 36 months	

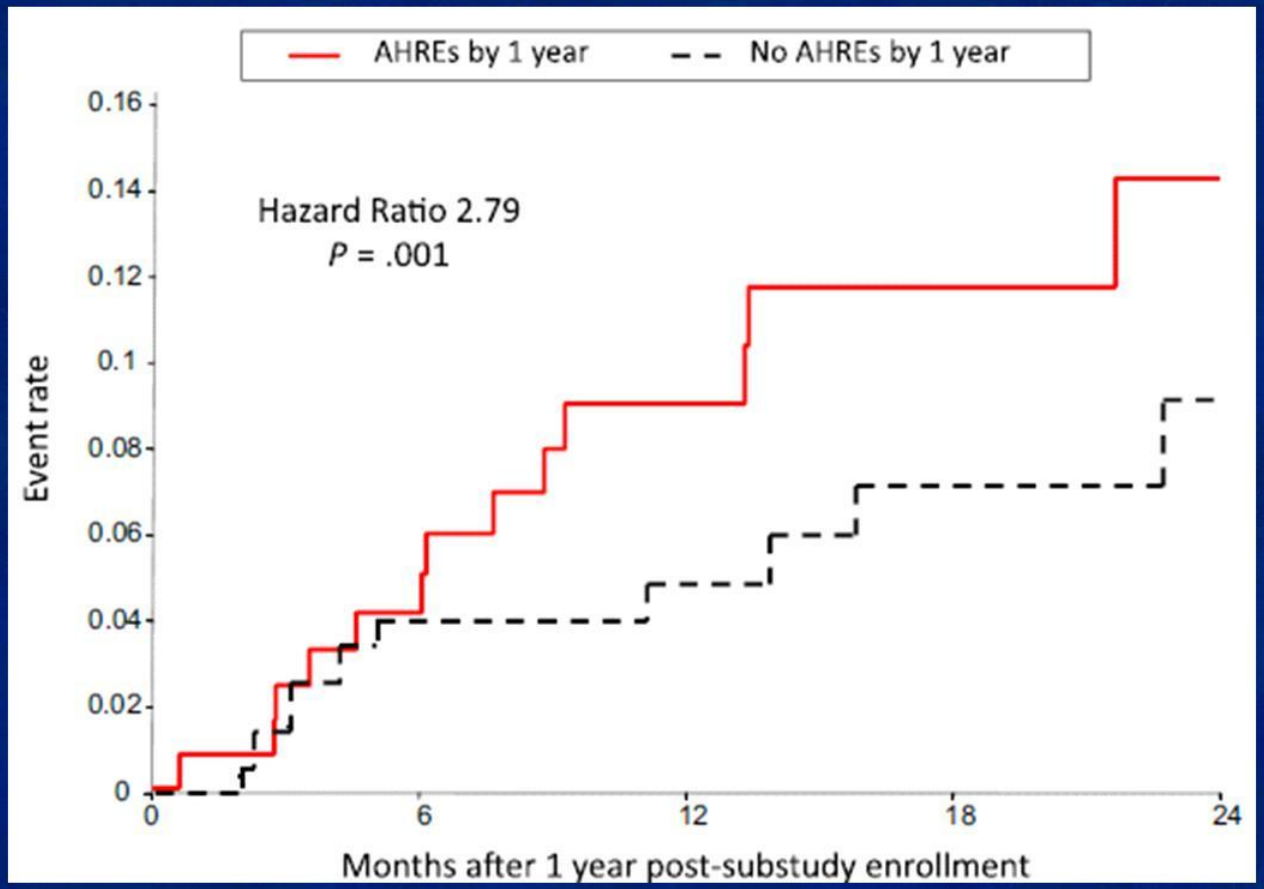
Glotzner/Ziegler. Heart Rhythm 2015:234

Hypothsized Interplay Between Atrial Arrhythmia Type and Stroke Risks



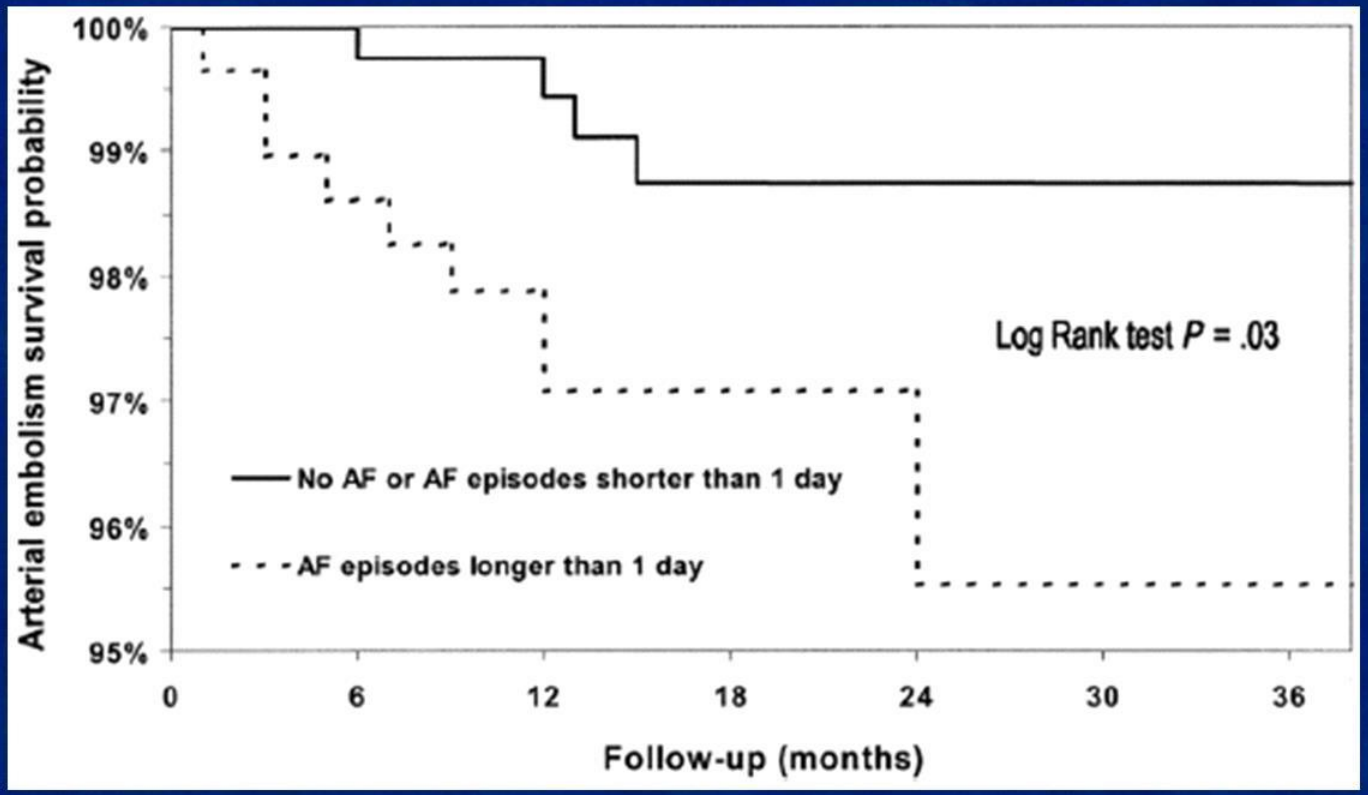
Seet, et al. Circulation 2011:477

MOST Ancillary Study: KM Plot of Death or Nonfatal Stroke after 1 Yr. of F/up in Pts. with AHREs vs. Those without AHREs



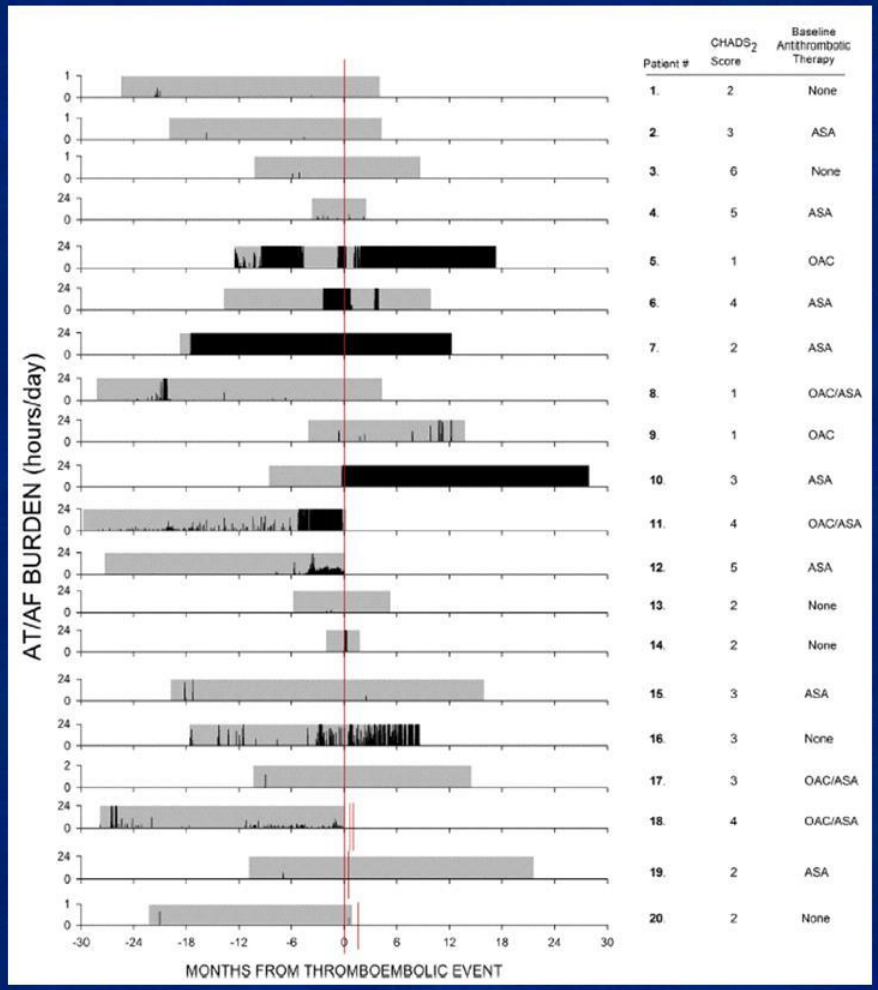
Glotzer/Ziegler. Cardiol Clin 2014:271

Italian AT500 Registry: KM Cumulative Survival from Embolic Events for Pts with AF Episodes Longer than 1 Day and of Pts. without AF Recurrences or with AF Episodes Shorter than 1 day



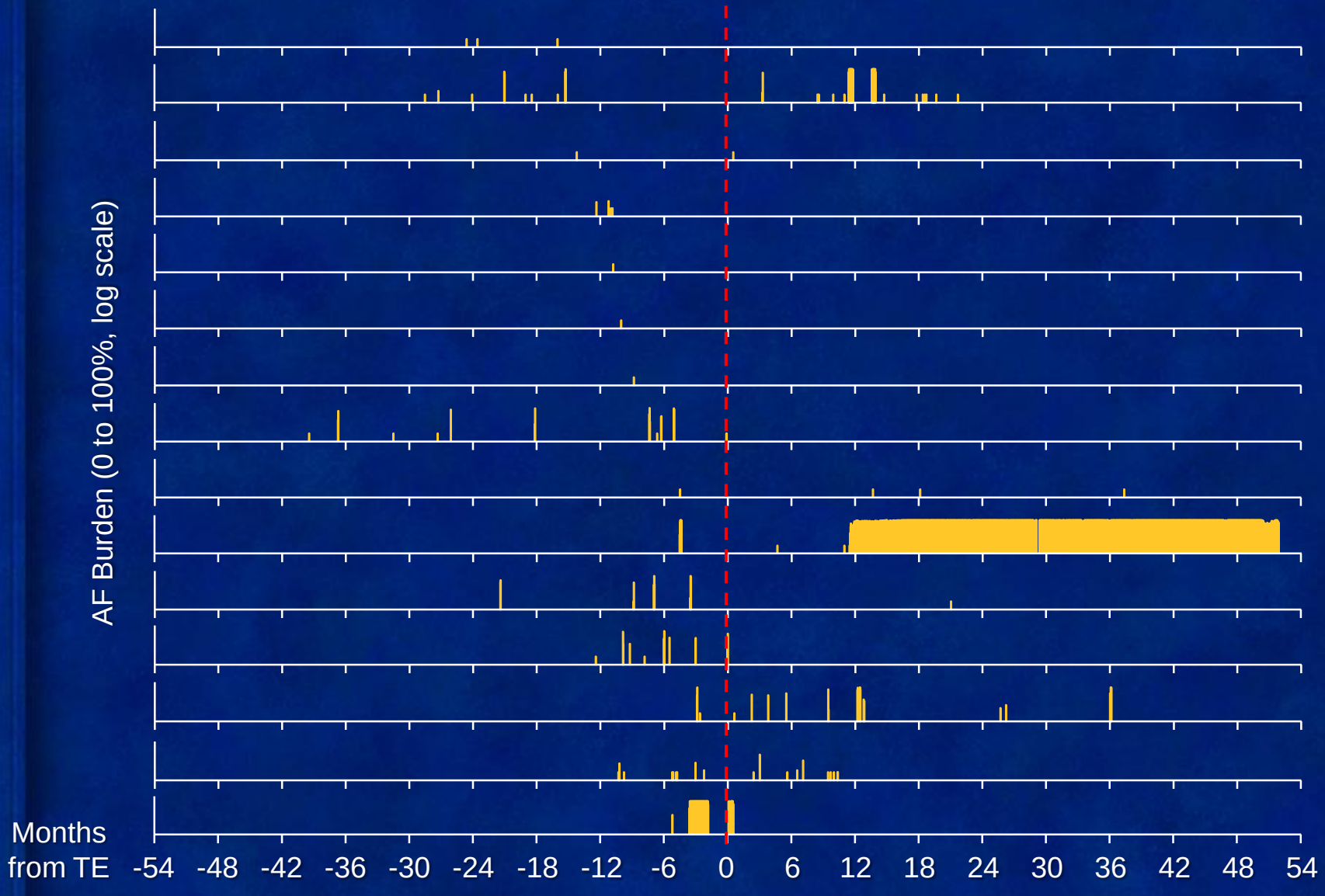
Glotzer/Ziegler. Cardiol Clin 2014:271

TRENDS Trial: Summary of AT/AF Burden Per Day Relative to Onset of Cerebrovascular Events/Systemic Emboli

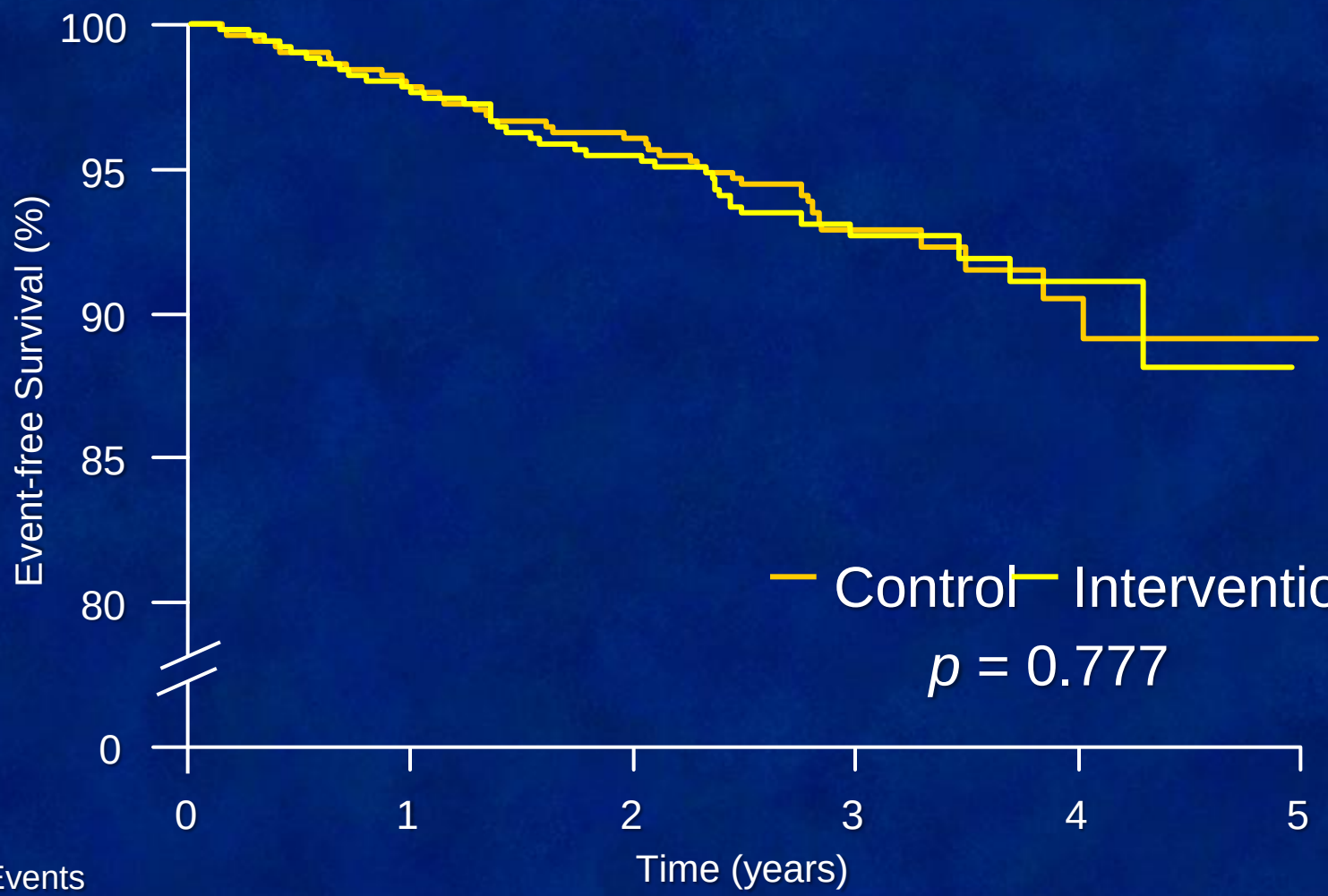


Glotzer/Ziegler. Cardiol Clin 2014:271

Temporal Dissociation between Atrial Fibrillation & Thromboembolism



Primary Outcome Events



N, Events						
Control	1361, 0	928, 27	543, 43	228, 57	75, 60	2, 61
Intervention	1357, 0	906, 28	538, 49	214, 59	66, 62	3, 63

My question

What does this all mean??

ATRIAL FIBRILLATION

Cryptogenic stroke—can we abandon this apologetic diagnosis?

A. John Camm

Cryptogenic stroke is an apology for ignorance about the cause of ischaemic stroke. Now, in two new studies involving long-term electrocardiogram monitoring, investigators from the EMBRACE and CRYSTAL-AF trials suggest that many instances of cryptogenic stroke might be caused by undetected atrial fibrillation.

Camm, A. J. *Nat. Rev. Cardiol.* **11**, 504–505 (2014); published online 29 July 2014; doi:10.1038/nrcardio.2014.111

Sudden occlusion of an artery supplying the brain can lead to embolic stroke or transient ischaemic attack (TIA). However, many embolic strokes remain unexplained and are described as 'cryptogenic', one of many words (such as essential, primary, lone, and idiopathic) that we use to disguise our ignorance of the underlying cause. In two new studies, in which the potential causes of cryptogenic stroke were investigated, the researchers of the EMBRACE[1] and CRYSTAL-AF[2] trials unequivocally demonstrate that prolonged electrocardiogram (ECG) monitoring reveals more atrial fibrillation than standard 12-lead ECG or 24-h or 48-h Holter ECG protocol, and conclude that these arrhythmias were a likely cause of embolic stroke or TIA.

Ischaemic events might result from a number of different mechanisms, such as a dislodged thrombus, or rarely a tumour, from the atrium or ventricle, or a detachment of atheromatous debris from the aorta or arterial vessels that lead to the brain. Similarly, embolism of a venous thrombus or air through an atrial septal defect or patent foramen ovale into the arterial circulation can also lead to an ischaemic event. However, the most-commonly diagnosed cause of ischaemic stroke is atrial fibrillation, which can lead to the formation of a blood clot and its subsequent embolization, commonly in the left atrial appendage. Many investigators have suspected that atrial fibrillation, which is often undetected and an intermittent arrhythmia, might cause many unexplained ischaemic strokes.[3,4] In some studies, repeated 12-lead ECGs and additional ambulatory ECG monitoring for ≥24 h can reveal atrial fibrillation in a substantial proportion of patients within hours or days of the embolic event.[5] Physicians have, therefore, been easily satisfied that this atrial fibrillation was relevant to the pathophysiology of stroke, and consequently initiated anticoagulant rather than antiplatelet therapy to prevent a recurrence.

However, about one-quarter of embolic strokes remain unexplained, and other studies have shown that atrial fibrillation can be highly transient, ephemeral, and silent.[6,7] Physicians have struggled with the diagnostic inadequacy of momentary ECG recordings. Continuous and sustained ECG readings might, therefore, be needed to uncover the arrhythmia. When new and robust ECG-monitoring techniques became available, trials were initiated with these new technologies to explore the possibility that the left atrium was the source of a greater proportion of embolic strokes that previously recognised.

The investigators in both the EMBRACE and CRYSTAL-AF studies used the standard definition of atrial fibrillation, which was developed specifically to reveal whether the arrhythmia can occur after an ablation procedure. However, whether a 30 s episode of atrial fibrillation has any mechanistic influence on thrombus formation is unclear.[8] Gladstone and colleagues (EMBRACE)[1] used continuous surface ECG monitoring for 30 days, whereas Sanna *et al.* (CRYSTAL-AF)[2] implanted miniature ECG monitors beneath the skin and monitored heart rhythm for up to 3 years after the initial stroke. The monitoring periods in both trials took place on average well after the stroke had occurred (Table 1). Can one realistically infer from an episode of atrial fibrillation occurring at some interval after the embolic event that this arrhythmia explained its occurrence? My opinion is that one should be reasonably sceptical. Nonetheless, many of the recorded episodes were not remote from the index event and might, therefore, provide at least a clue about events that precipitated the stroke. In the EMBRACE trial,[1] Gladstone and colleagues report that only half of the cases of atrial fibrillation were detected in the first week after the stroke, and the remainder occurred over the next 3 weeks. Whereas in the CRYSTAL-AF study,[2] which was conducted over 3 years, cases arose throughout the recording period. Moreover, neither trial included a control group of patients who had not sustained an ischaemic stroke or TIA against which to judge the relevance of the recorded arrhythmia. The studies were not configured to investigate the prognostic importance of the atrial fibrillation in terms of subsequent stroke or TIA recurrence because physicians were free to act on the ECG diagnosis, and their interventions would have compromised any possible conclusion.

No-one would disagree with the conclusions made by both teams of investigators that atrial fibrillation was the underlying cause of the observed cryptogenic stoke

Table 1 | Comparison of the EMBRACE[1] and CRYSTAL-AF[2] trials

Study	Investigation group	*n*	Onset of monitoring after stroke (days)	Duration of monitoring (days)	Proportion with AF (%)
EMBRACE[1]	Usual*	285	75.1±38.6	90	3.2
	Intensive‡	286			16.1
CRYSTAL-AF[2]	Usual*	220	38.1±27.6	~180	1.4
	Intensive§	221			8.9

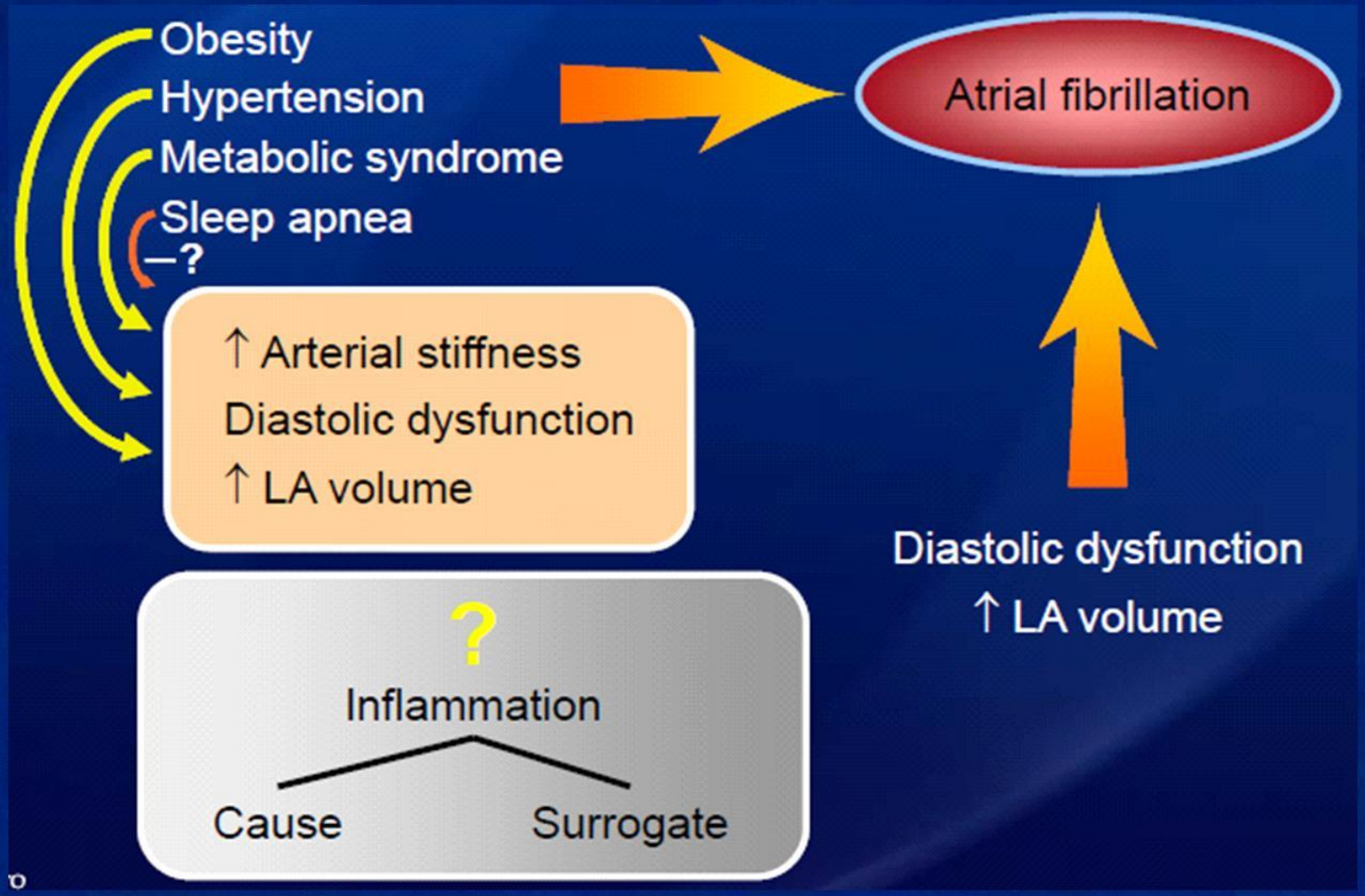
*12-lead ECG and Holter ECG monitoring for 24–48 h. ‡Continuous surface ECG for 4 weeks. §Subcutaneous ECG monitoring with an implanted device for up to 3 years. Abbreviations: AF, atrial fibrillation; ECG, electrocardiogram.

Atrial Fibrillation Around the World

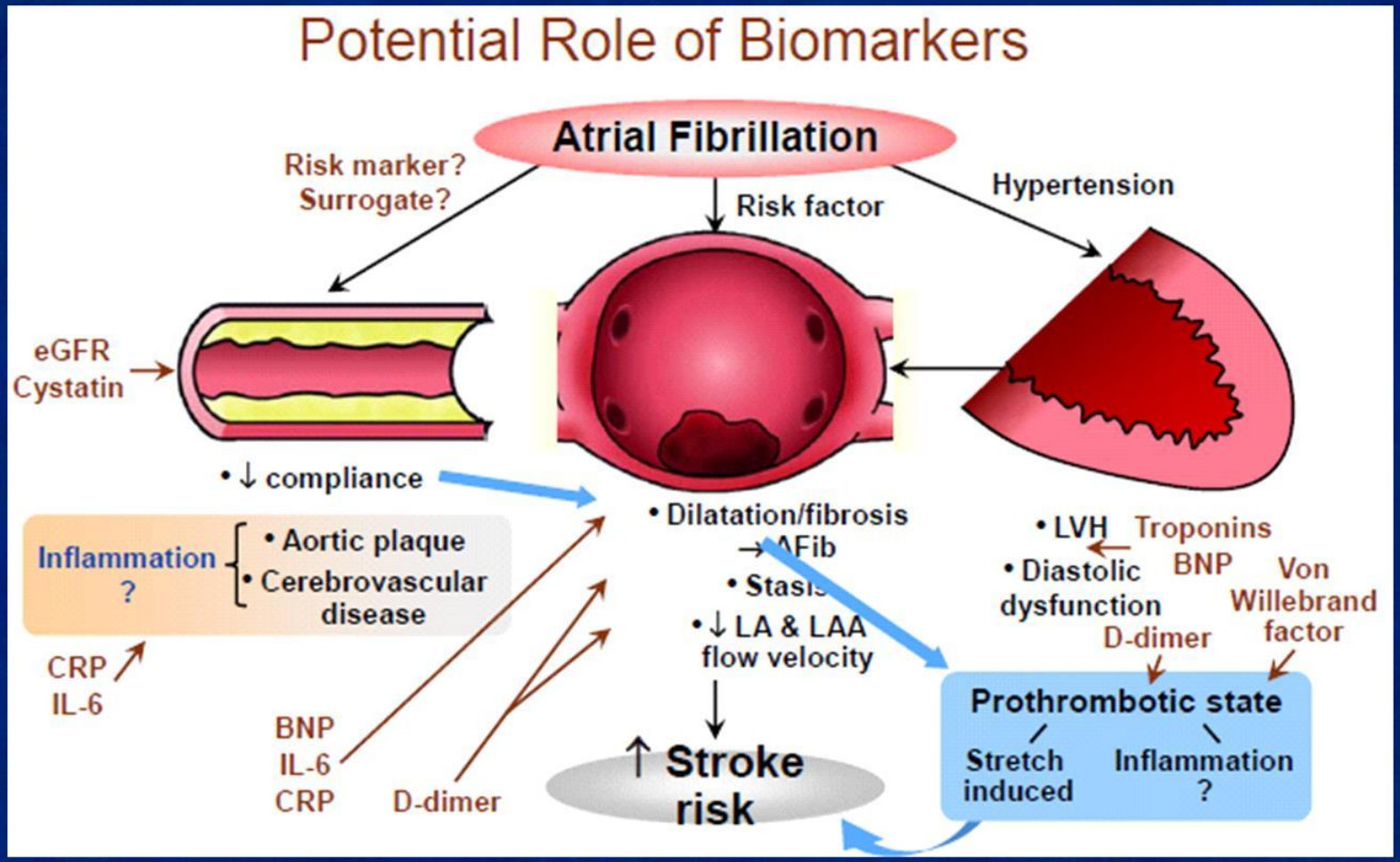
North American Perspective and Specificities

Risk that AF isn't a risk

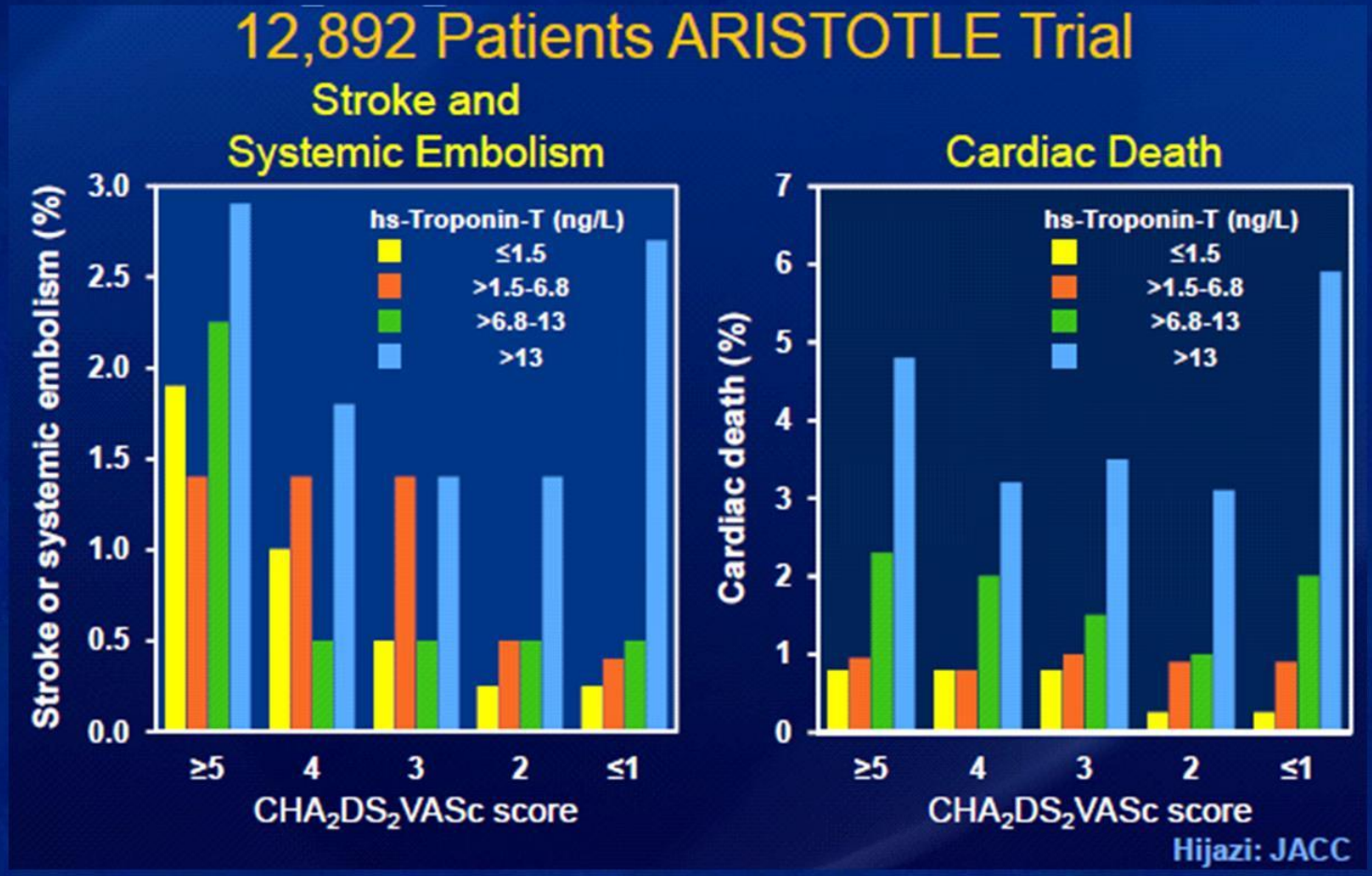
Afib as a Vascular Disease – Suggestive Evidence



AF and the Risk of Stroke



Outcomes in Patients with AF Stratified by CHA_2DS_2-VASc Score and hs-TnT



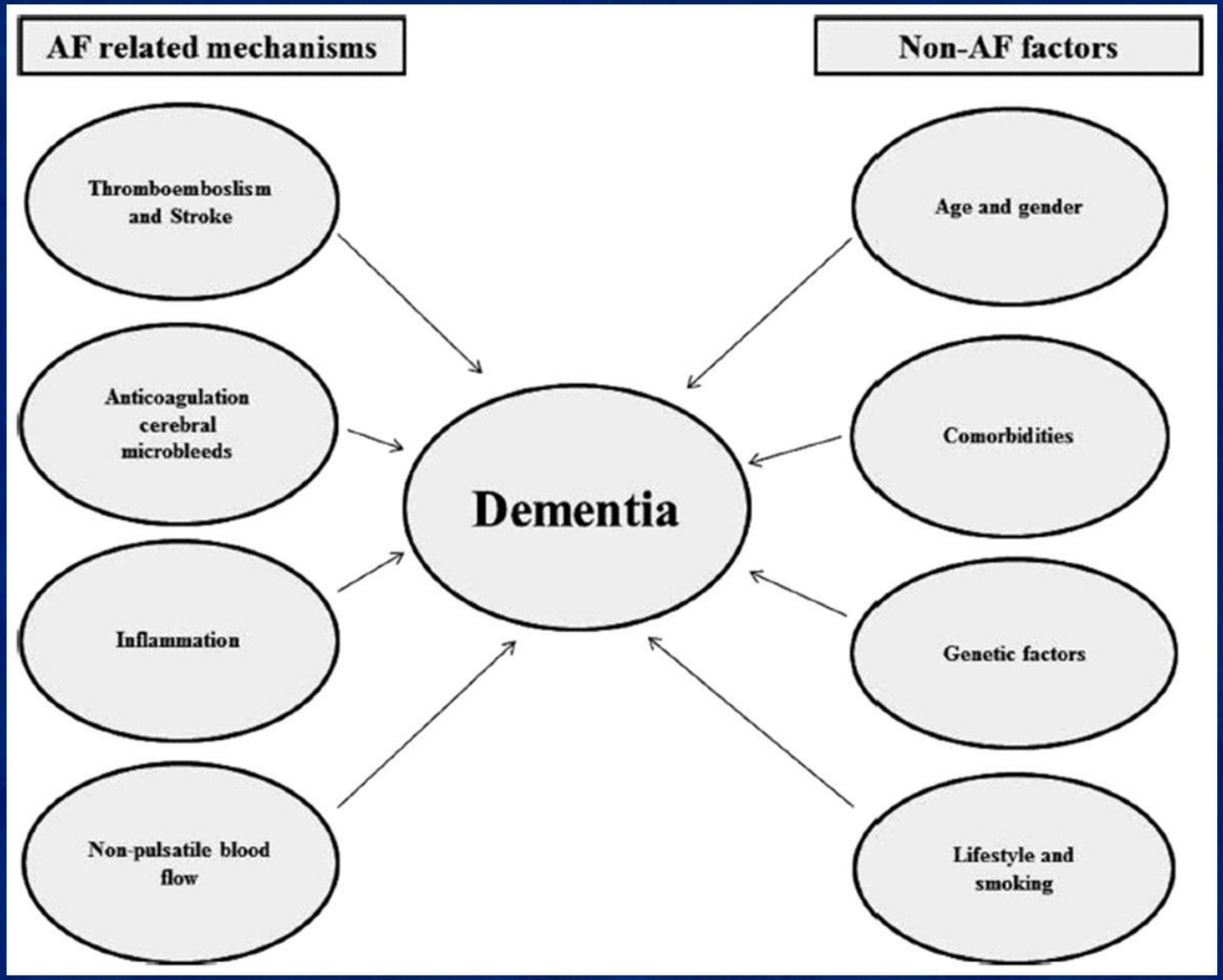
Just When I Knew All of Life's Answers, They Changed All the Questions

Atrial Fibrillation Around the World

North American Perspective and Specificities

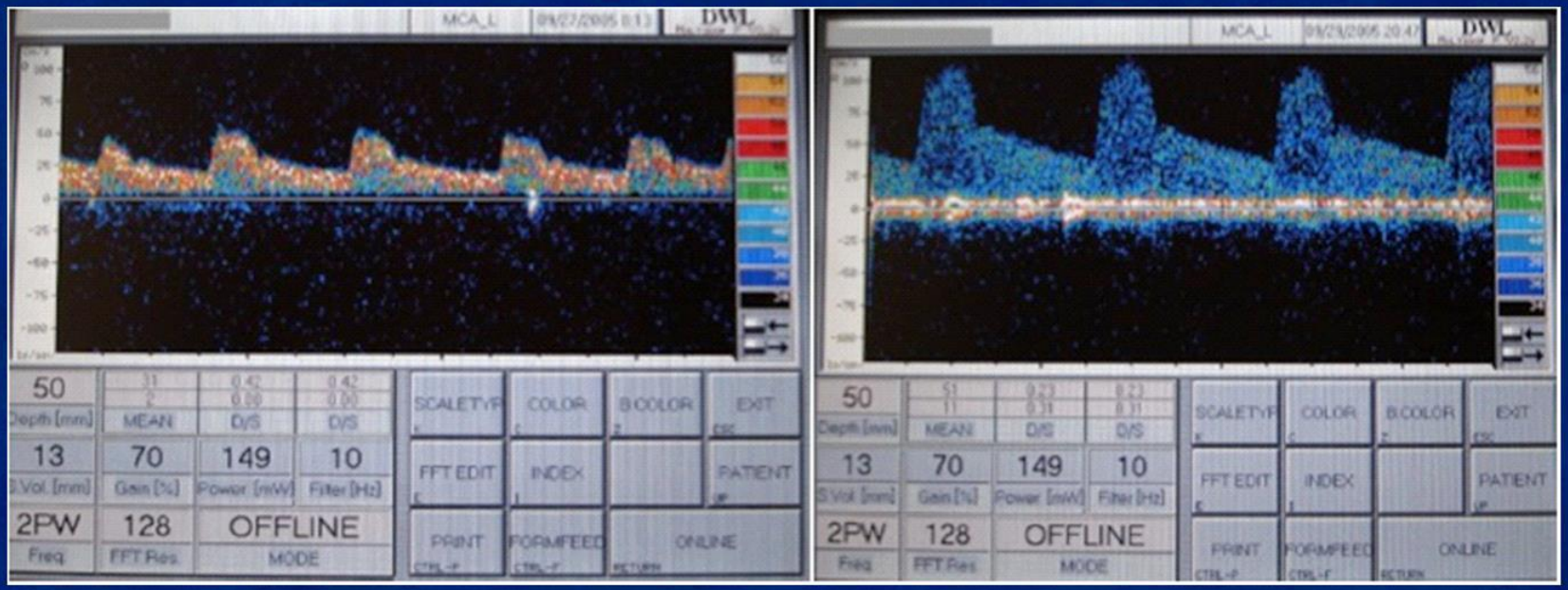
Demnetia and CNS Misadventures

Mechanisms of Pathology of Dementia in AF



Kanmanthareddy, et al. Curr Cardiol Rep 2014:519

Waveforms Depicting Blood Flow in Left MCA in Pt. in AF (L), Waveform in the Same Pt. After Cardioversion (R)



Kanmanthareddy, et al. Curr Cardiol Rep 2014:519

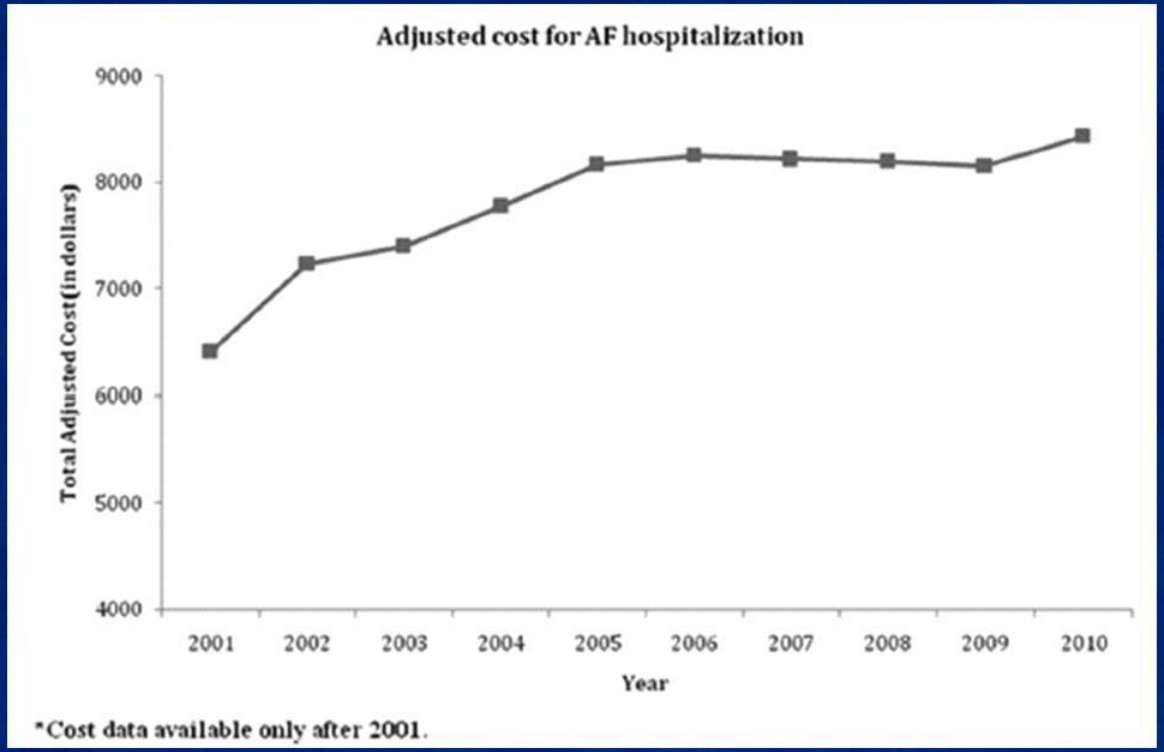
Atrial Fibrillation Around the World

North American Perspective and Specificities

Hospitalization

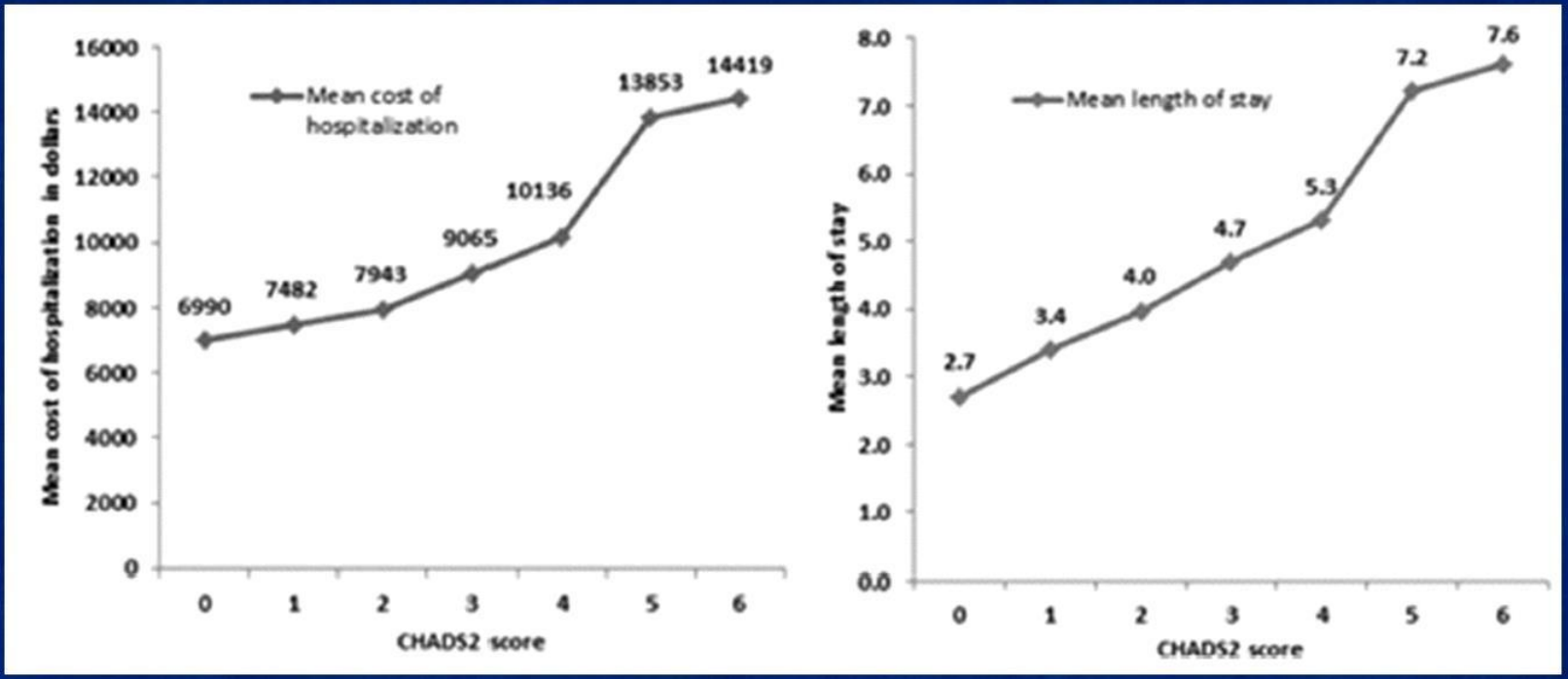
And Cost

Trend in Cost of Care for AF Hospitalizations



Patel, et al. Cirulation 2014:2371

Mean Length of Stay and Cost of AF Hospitalization According to $CHAD_s$ Score



Patel, et al. Cirulation 2014:2371

What Is The Art That We Are Stating?









Atrial Fibrillation Around the World

North American Perspective and Specificities

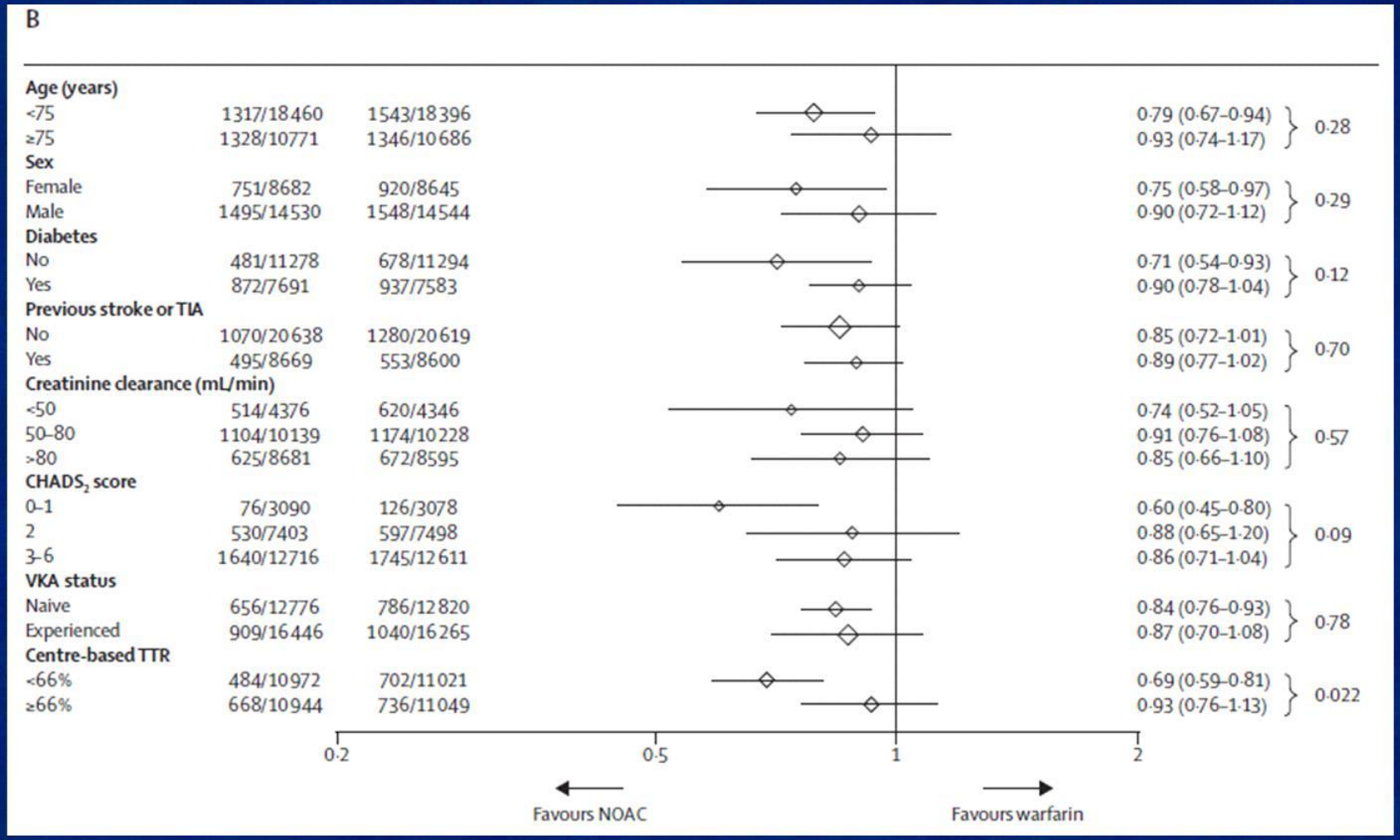
NOACs

Baseline Characteristics of Intention-to-Treat Population

	RE-LY[5]			ROCKET-AF[6]		ARISTOTLE[7]		ENGAGE AF-TIMI 48[8]			Combined	
	Dabigatran 150 mg (n=6076)	Dabigatran 110 mg (n=6015)	Warfarin (n=6022)	Rivaroxaban (n=7131)	Warfarin (n=7133)	Apixaban (n=9120)	Warfarin (n=9081)	Edoxaban 60 mg (n=7035)	Edoxaban 30 mg (n=7034)	Warfarin (n=7036)	NOAC (n=42 411)	Warfarin (n=29 272)
Age (years)	71·5 (8·8)	71·4 (8·6)	71·6 (8·6)	73 (65–78)	73 (65–78)	70 (63–76)	70 (63–76)	72 (64–68)	72 (64–78)	72 (64–78)	71·6	71·5
≥75 years	40%	38%	39%	43%	43%	31%	31%	41%	40%	40%	38%	38%
Women	37%	36%	37%	40%	40%	36%	35%	39%	39%	38%	38%	37%
Atrial fibrillation type												
Persistent or permanent	67%	68%	66%	81%	81%	85%	84%	75%	74%	75%	76%	77%
Paroxysmal	33%	32%	34%	18%	18%	15%	16%	25%	26%	25%	24%	22%
CHADS2*	2·2 (1·2)	2·1 (1·1)	2·1 (1·1)	3·5 (0·94)	3·5 (0·95)	2·1 (1·1)	2·1 (1·1)	2·8 (0·97)	2·8 (0·97)	2·8 (0·98)	2·6 (1·0)	2·6 (1·0)
0–1	32%	33%	31%	0	0	34%	34%	<1%	<1%	<1%	17%	17%
2	35%	35%	37%	13%	13%	36%	36%	46%	47%	47%	35%	33%
3–6	33%	33%	32%	87%	87%	30%	30%	54%	53%	53%	48%	50%
Previous stroke or TIA*	20%	20%	20%	55%	55%	19%	18%	28%	29%	28%	29%	30%
Heart failure†	32%	32%	32%	63%	62%	36%	35%	58%	57%	58%	46%	47%
Diabetes	23%	23%	23%	40%	40%	25%	25%	36%	36%	36%	31%	31%
Hypertension	79%	79%	79%	90%	91%	87%	88%	94%	94%	94%	88%	88%
Prior myocardial infarction	17%	17%	16%	17%	18%	15%	14%	11%	12%	12%	15%	15%
Creatinine clearance‡												
<50 mL/min	19%	19%	19%	21%	21%	17%	17%	20%	19%	19%	19%	19%
50–80 mL/min	48%	49%	49%	47%	48%	42%	42%	43%	44%	44%	45%	45%
>80 mL/min	32%	32%	32%	32%	31%	41%	41%	38%	38%	37%	36%	36%
Previous VKA use§	50%	50%	49%	62%	63%	57%	57%	59%	59%	59%	57%	57%
Aspirin at baseline	39%	40%	41%	36%	37%	31%	31%	29%	29%	30%	34%	34%
Median follow-up (years)¶	2·0	2·0	2·0	1·9	1·9	1·8	1·8	2·8	2·8	2·8	2·2	2·2
Individual median TTR	NA	NA	67 (54–78)	NA	58 (43–71)	NA	66 (52–77)	NA	NA	68 (57–77)	NA	65 (51–76)

Ruff CT, et al. The Lancet 2014:955

Major Bleeding subgroups



Ruff CT, et al. The Lancet 2014:955

Atrial Fibrillation Around the World

North American Perspective and Specificities

LAAO

EHRA New Slides
AF Risk

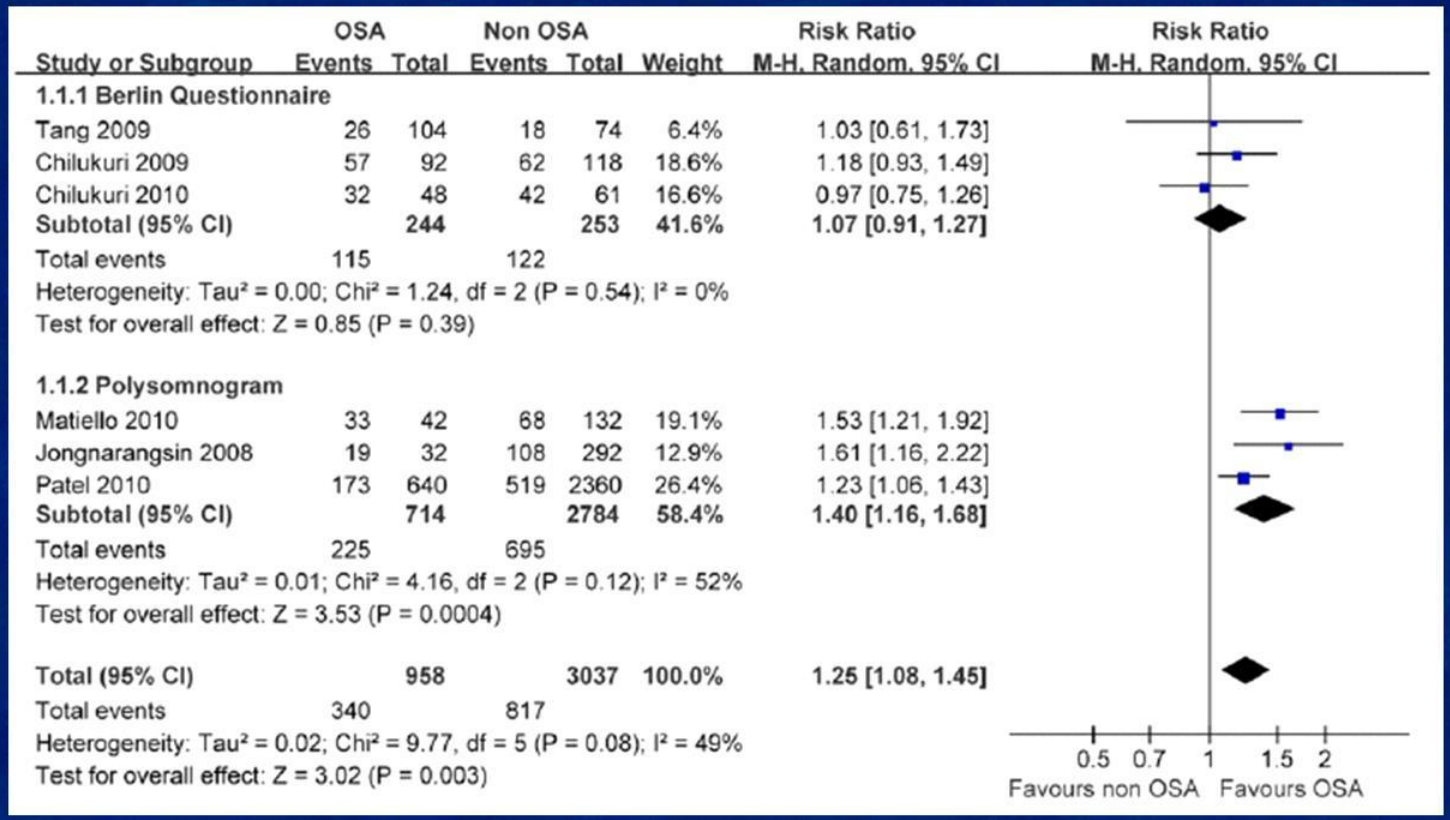
Drug and Ablative Therapies

Summary of Recommendations for Risk-Based Antithrombotic Therapy

Recommendations	COR	LOE	References
Antithrombotic therapy based on shared decision making, discussion of risks of stroke and bleeding, and patient's preferences	I	C	N/A
Selection of antithrombotic therapy based on risk of thromboembolism	I	B	64–67
CHA_2DS_2-VASc score recommended to assess stroke risk	I	B	68–70
Warfarin recommended for mechanical heart valves and target INR intensity based on type and location of prosthesis	I	B	71–73
With prior stroke, TIA, or CHA_2DS_2-VASc score ≥2, oral anticoagulants recommended. Options include:			
Warfarin	I	A	68–70
Dabigatran, rivaroxaban, or apixaban	I	B	74–76
With warfarin, determine INR at least weekly during initiation of therapy and monthly when stable	I	A	77–79
Direct thrombin or factor Xa inhibitor recommended if unable to maintain therapeutic INR	I	C	N/A
Reevaluate the need for anticoagulation at periodic intervals	I	C	N/A
Bridging therapy with UFH or LMWH recommended with a mechanical heart valve if warfarin is interrupted. Bridging therapy should balance risks of stroke and bleeding	I	C	N/A
For patients without mechanical heart valves, bridging therapy decisions should balance stroke and bleeding risks against duration of time patient will not be anticoagulated	I	C	N/A
Evaluate renal function before initiation of direct thrombin or factor Xa inhibitors, and reevaluate when clinically indicated and at least annually	I	B	80–82
For atrial flutter, antithrombotic therapy is recommended as for AF	I	C	N/A
With nonvalvular AF and CHA_2DS_2-VASc score of 0, it is reasonable to omit antithrombotic therapy	IIa	B	80,81
With CHA_2DS_2-VASc score ≥2 and end-stage CKD (CrCl <15 mL/min) or on hemodialysis, it is reasonable to prescribe warfarin for oral anticoagulation	IIa	B	82
With nonvalvular AF and a CHA_2DS_2-VASc score of 1, no antithrombotic therapy or treatment with oral anticoagulant or aspirin may be considered	IIb	C	N/A
With moderate-to-severe CKD and CHA_2DS_2-VASc scores ≥2, reduced doses of direct thrombin or factor Xa inhibitors may be considered	IIb	C	N/A
For PCI,* BMS may be considered to minimize duration of DAPT	IIb	C	N/A
After coronary revascularization in patients with CHA_2DS_2-VASc score ≥2, it may be reasonable to use clopidogrel concurrently with oral anticoagulants but without aspirin	IIb	B	83
Direct thrombin dabigatran and factor Xa inhibitor rivaroxaban are not recommended in patients with AF and end-stage CKD or on dialysis because of a lack of evidence from clinical trials regarding the balance of risks and benefits	III: No Benefit	C	74–76, 84–86
Direct thrombin inhibitor dabigatran should not be used with a mechanical heart valve	III: Harm	B	87

January et al. Circulation 2014:2071

Comparison of AF Recurrence after Catheter Ablation in Pts. with OSA and non-OSA Controls in Forest Plot



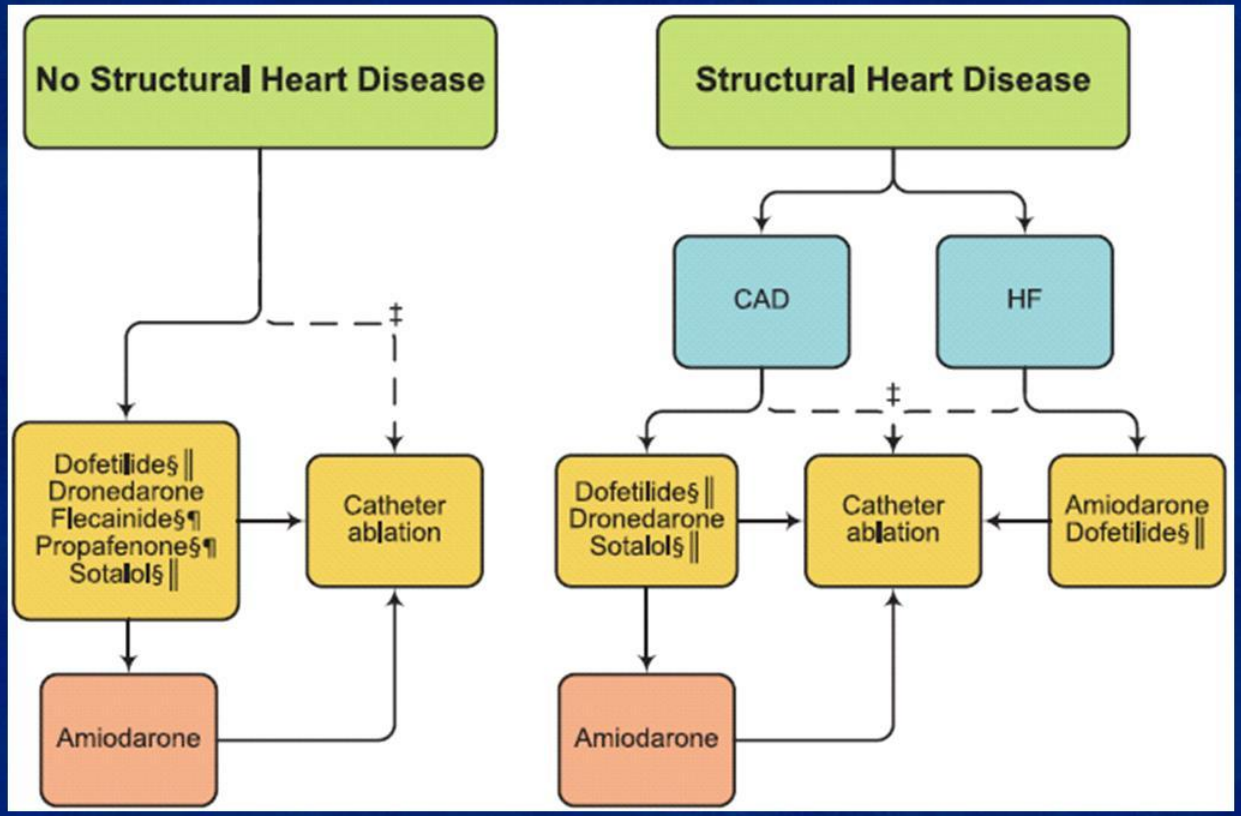
Ng CY, et al. Am J Cardiol 2011:47

Atrial Fibrillation Around the World

North American Perspective and Specificities

Ablation

Strategies for Rhythm Control in Pts with Paroxysmal and Persistent AF

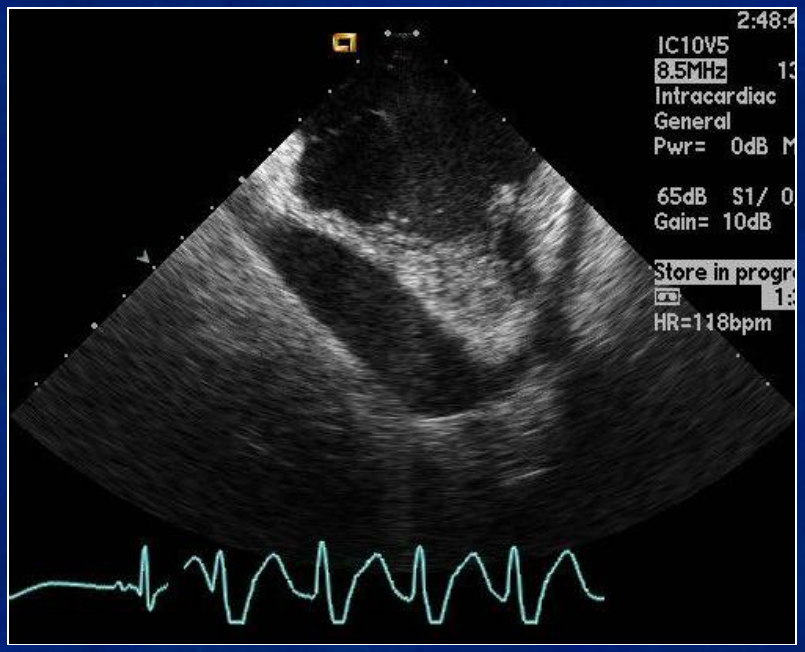


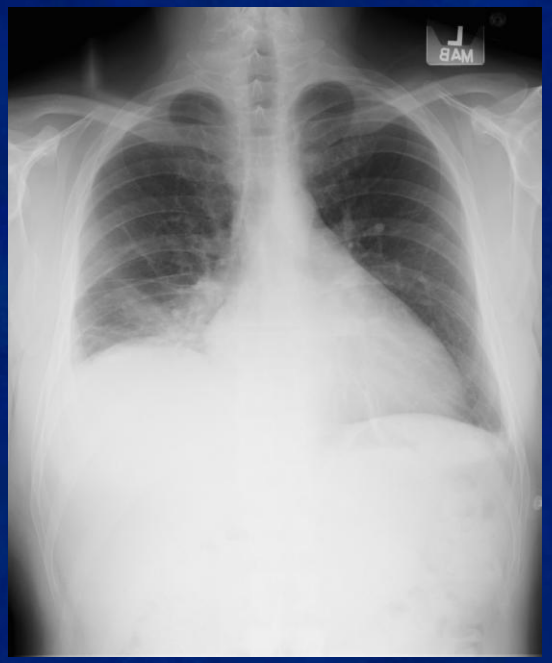
January et al. Circulation 2014:2071

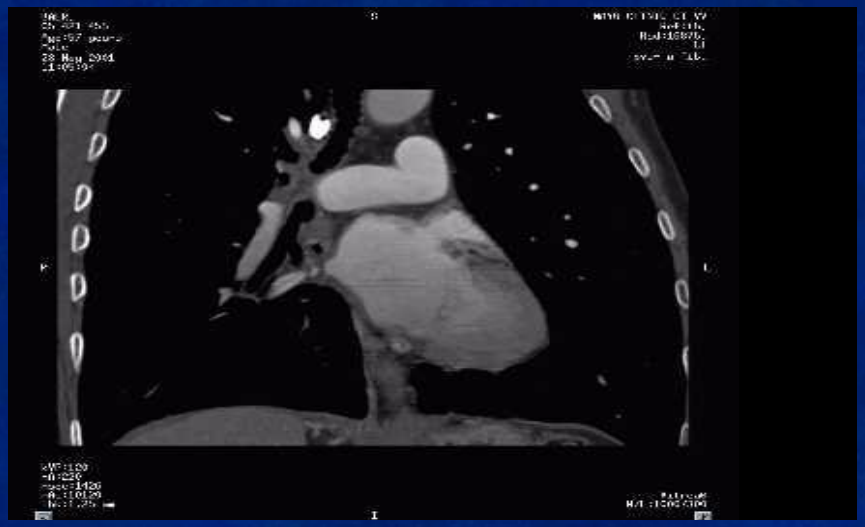
Risks of AF Ablation: The Second International AF Ablation Registry

Type of Complication	No of Pts	Rate,%
Death	25	0.15
Tamponade	213	1.31
Pneumo/ Hemo thorax	19	0.11
Sepsis, abscesses or endocarditis	2	0.01
Permanent diaphragmatic paralysis	28	0.17
Femoral pseudoaneurysm / A-V Fisula	152/88	.93/0.54
Valve damage/requiring surgery	11/7	0.07
Atrium-esophageal fistulae	3	0.02
Stroke / TIA	37 /115	0.23 / 0.71
Pulmonary veins stenoses requiring intervention	48	0.29
TOTAL	741	4.54

Causes for Dyspnea After Ablation



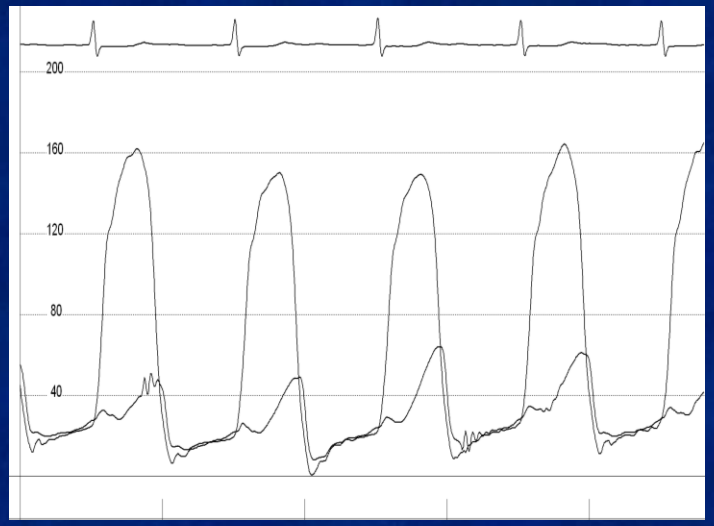




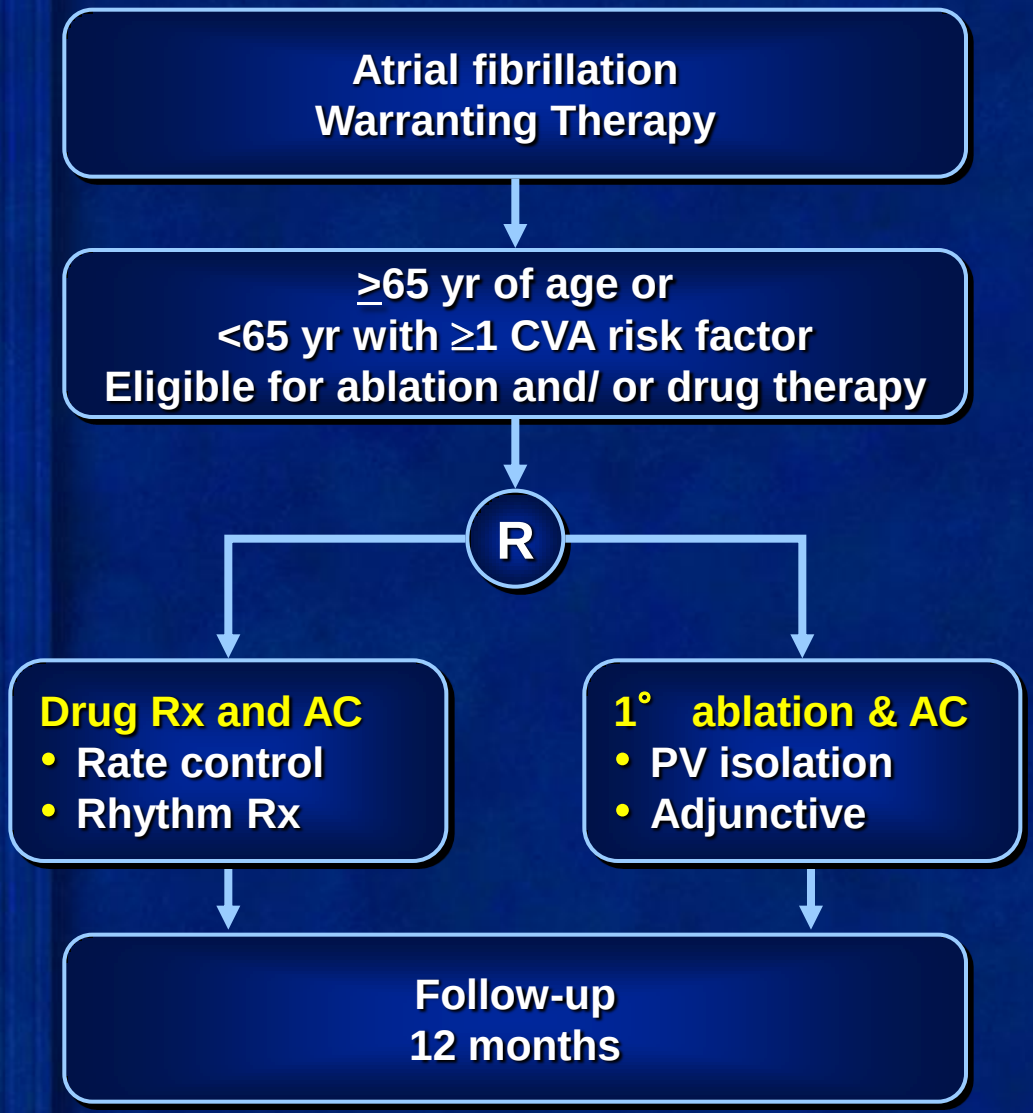
PT

LV

LA



Design of the CABANA Study



Inclusion Criteria

- ≥2 paroxysmal AF episodes (≥1 hour) over 4 mos or ≥1 persistent AF episode (>1 week)
- ≥65 yr of age, or <65 yr with ≥1 risk factors
  - Hypertension
  - Diabetes
  - Heart failure
  - Prior CVA or TIA
  - LA size >5.0 cm (Vol In ≥40 cc/m^2)
  - EF ≤35 %
- Eligible for ablation and ≥2 rhythm control and/or ≥3 rate control drugs

CABANA Pilot Study; ACC 2010