

# Atrial fibrillation and stroke



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# Content

- Stroke – what is the problem for patients with AF ?
- Does abolishing AF prevents stroke ?
- Is AF a mechanism or just a marker for stroke ?
- AF is progressive disease and AF progression is associated with stroke, heart failure and mortality



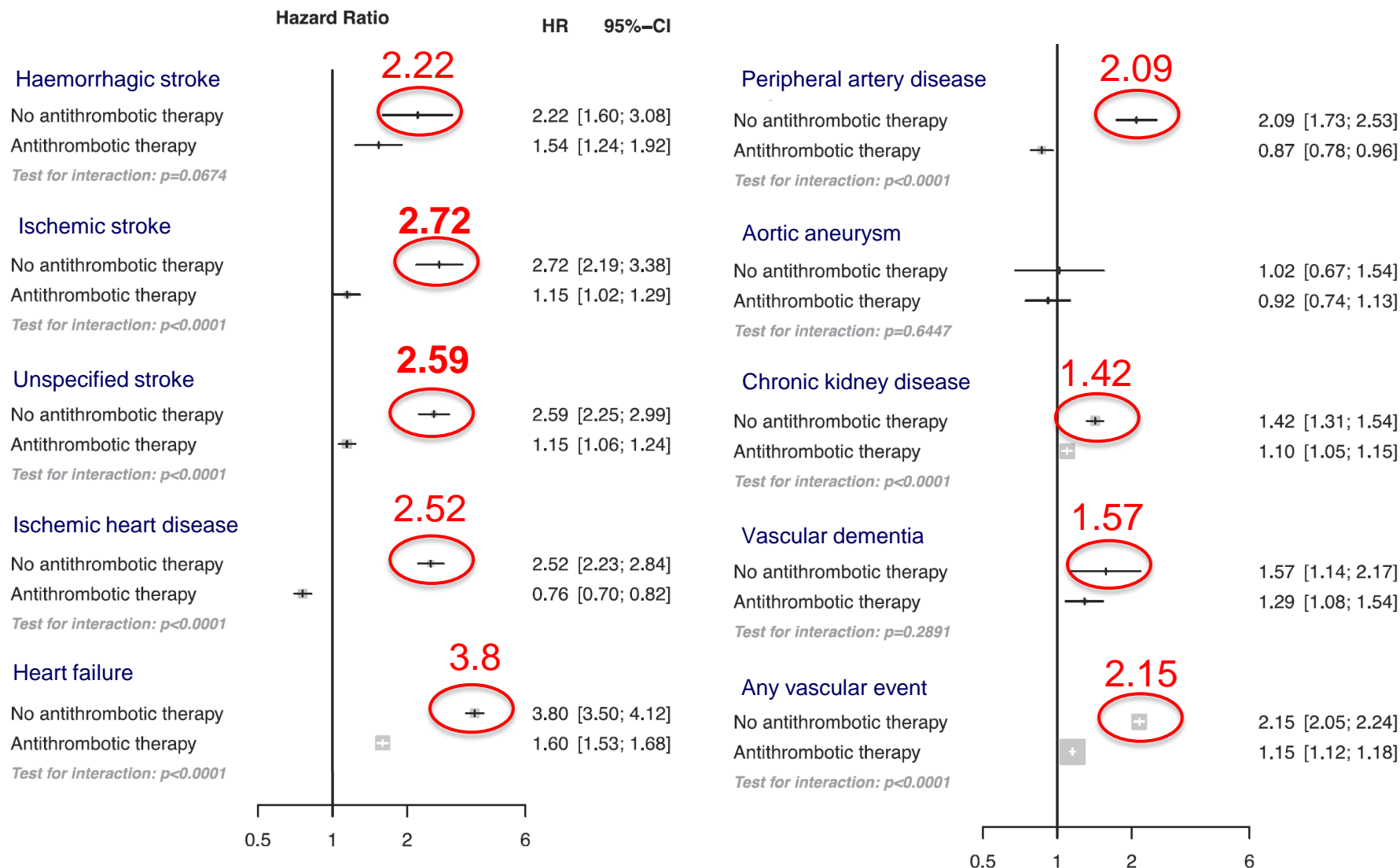
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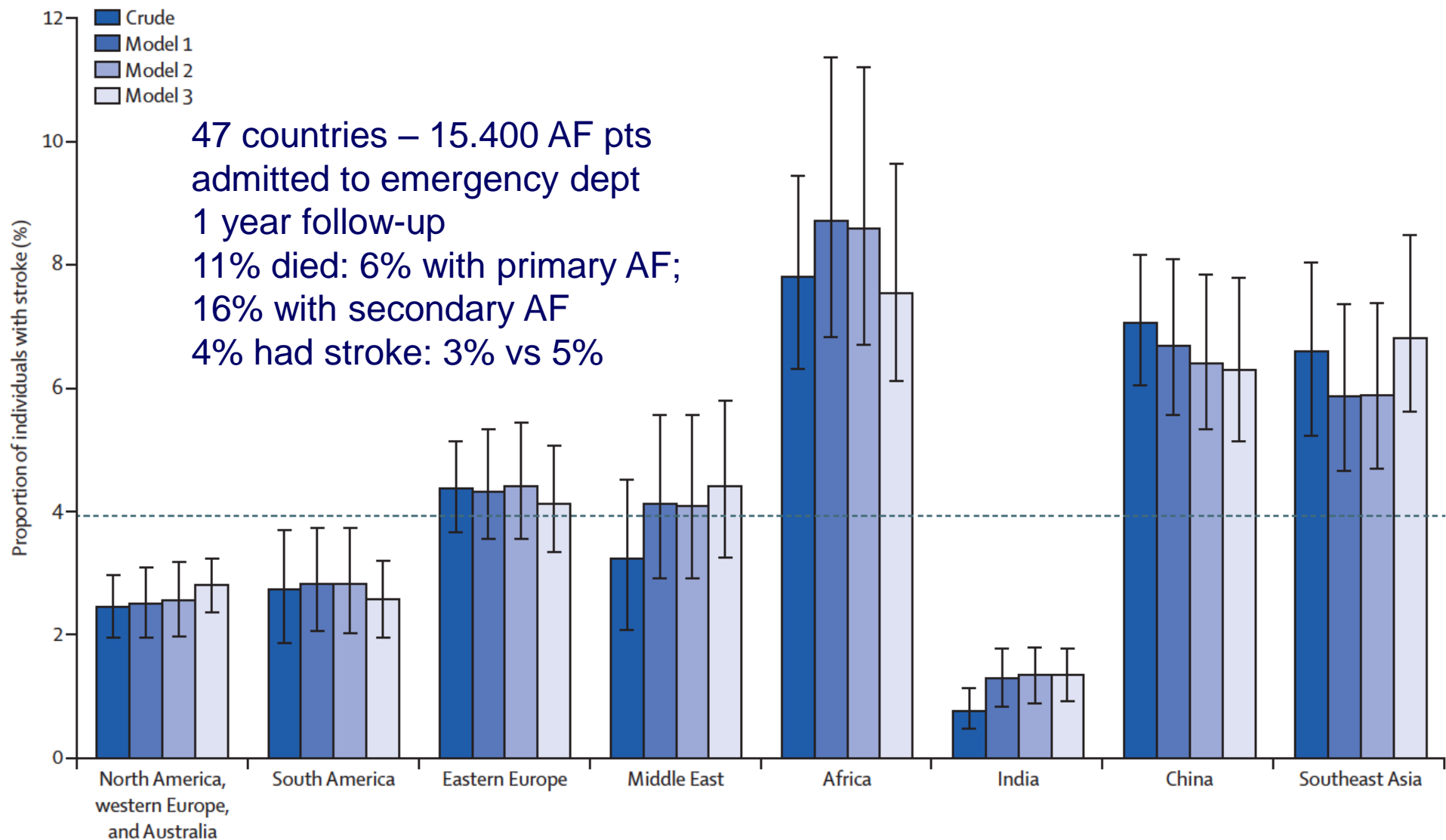


# AF and HRs for stroke and other vascular events

Primary care research database, UK population (87% white)  
Linked with secondary care data and cause-specific mortality data  
4.3 million adults, included at standard GP with 1 RR 1990-2013 FU 7 yrs



# Individuals with stroke

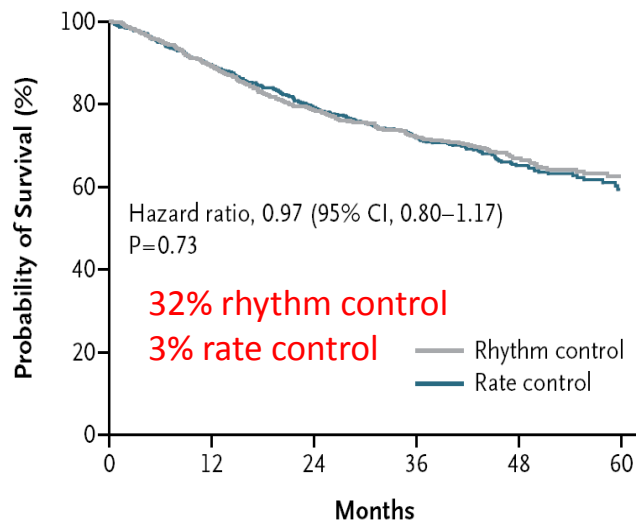


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- Does abolishing AF prevents stroke ?



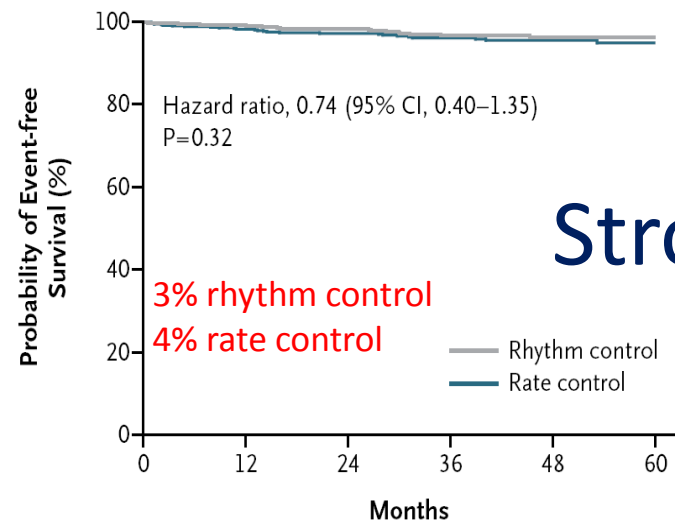
### A Death from Any Cause



#### No. at Risk

Rhythm control	593	514	378	228	82
Rate control	604	521	381	219	69

### B Stroke

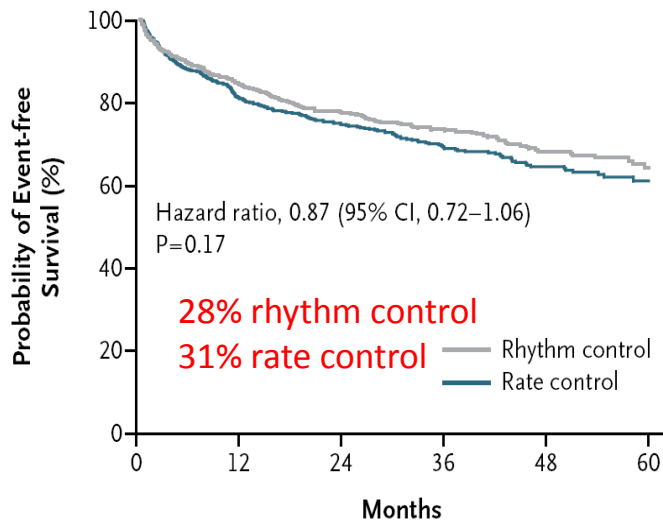


#### No. at Risk

Rhythm control	589	507	367	221	79
Rate control	596	512	373	216	68

## Stroke

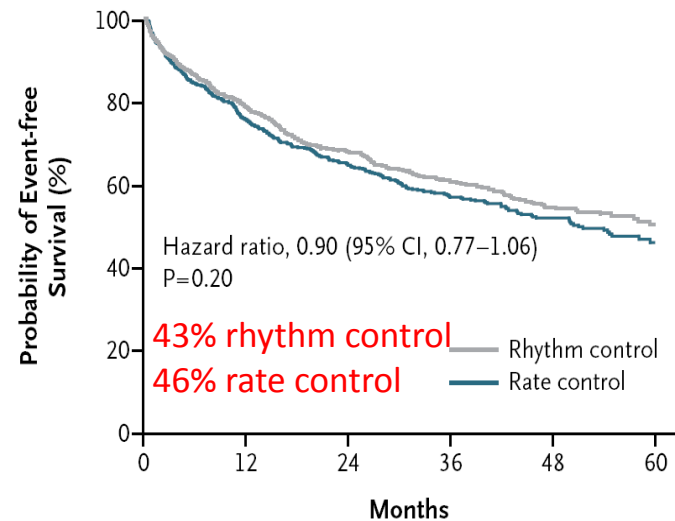
### C Worsening Heart Failure



#### No. at Risk

Rhythm control	523	436	311	174	63
Rate control	509	419	289	165	54

### D Composite Outcome CV death, stroke, worsening HF



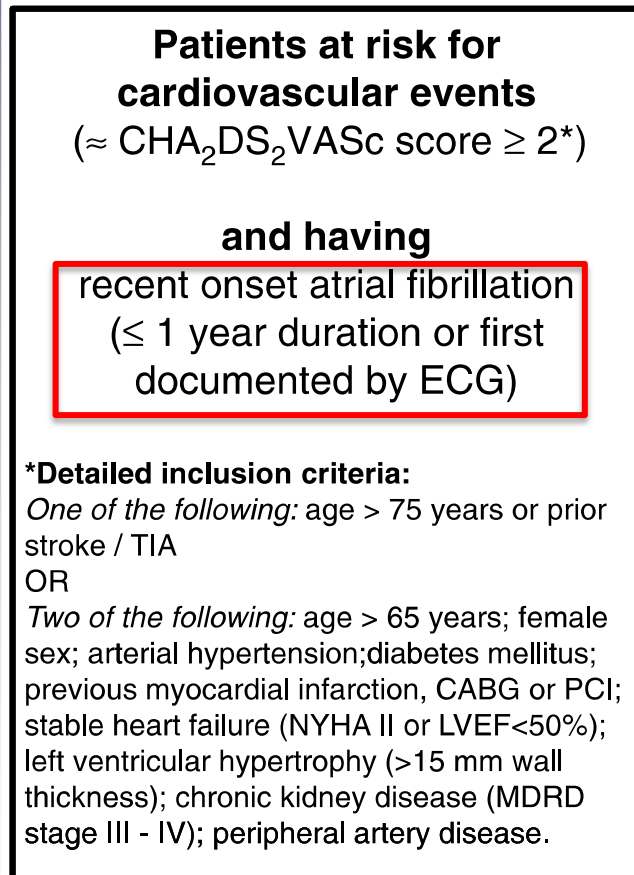
#### No. at Risk

Rhythm control	518	432	303	169	60
Rate control	502	412	281	162	53

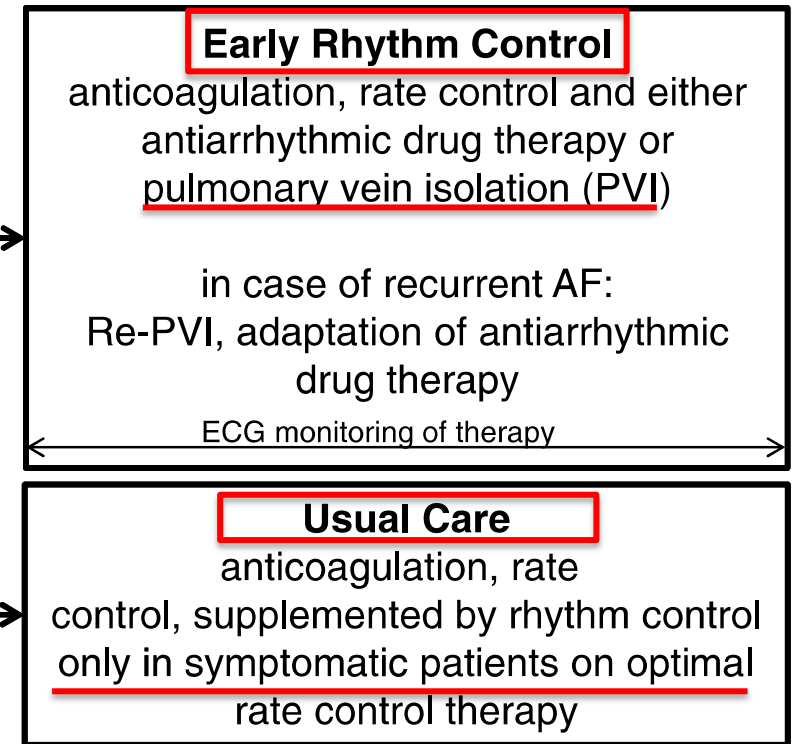


# Early treatment of AF for Stroke prevention Trial EAST

## Pre-Study Screening



## Study Procedures



outpatient FU at 12, 24, 36 months (both study groups)  
therapy of underlying heart disease (both study groups)  
blind assessment of primary outcomes (both study groups)



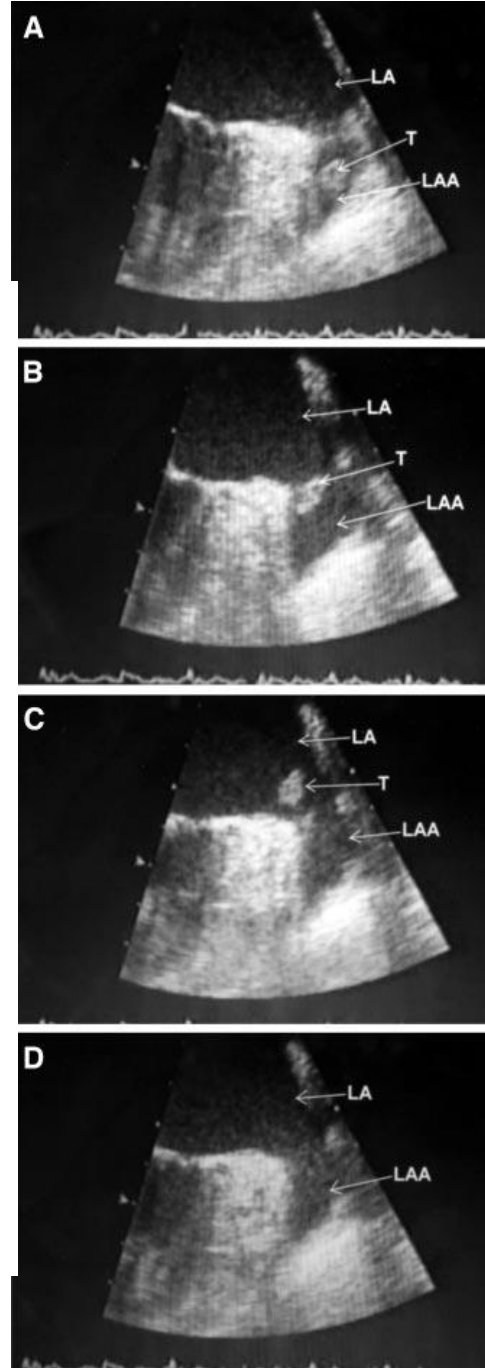
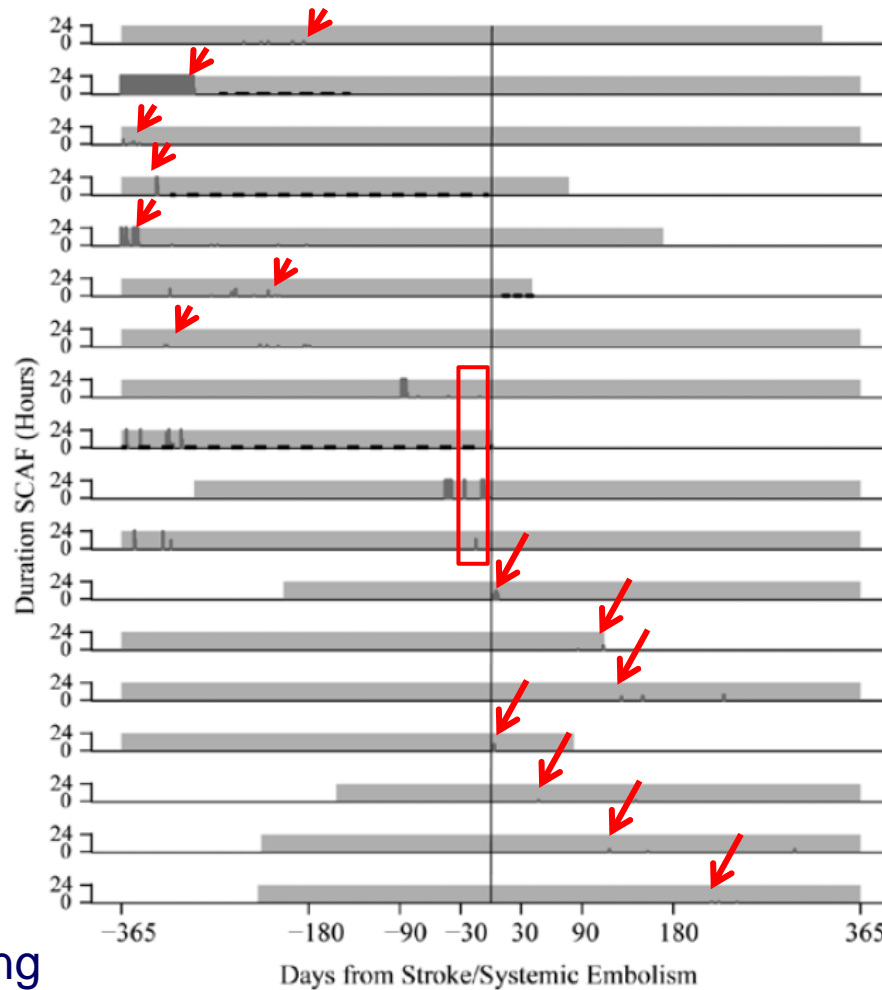


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# Temporal disconnect

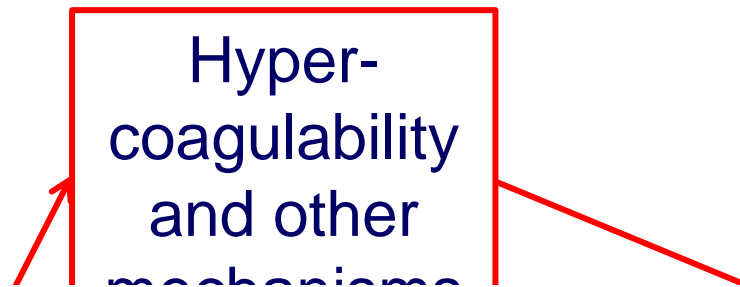


# AF: mechanism or marker for stroke ?

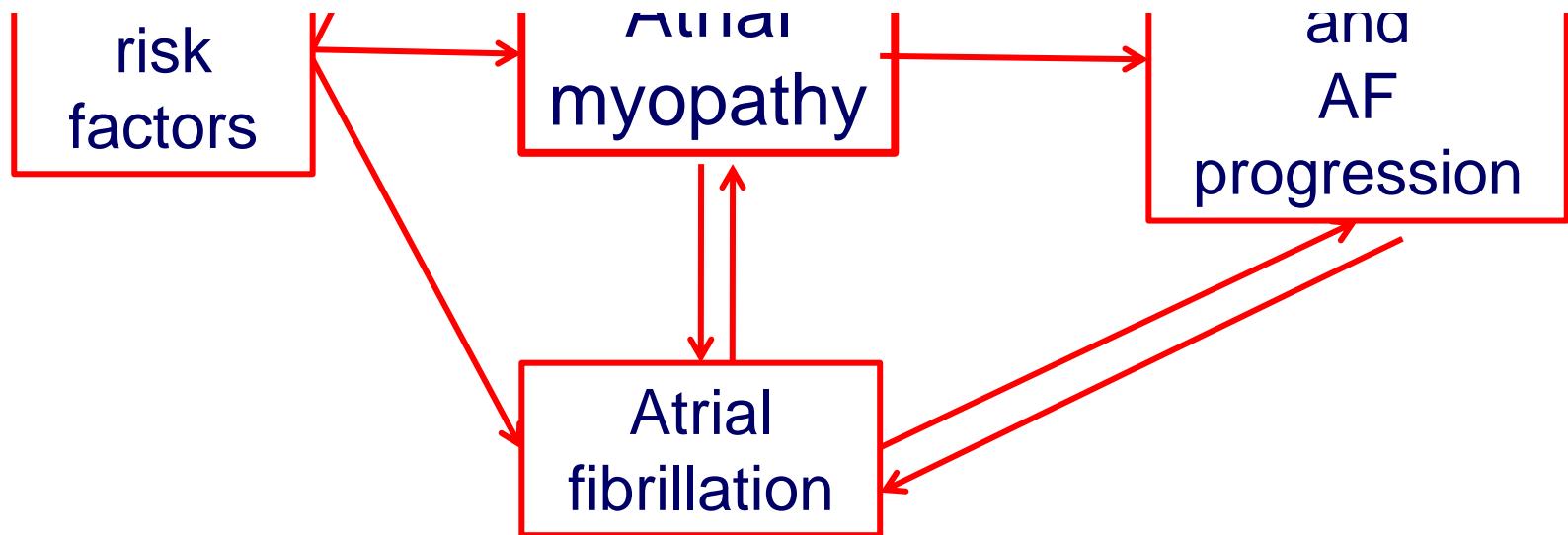
SCAF episodes are associated with AF but  
only a minority had SCAF in the month  
before their stroke



# AF and stroke – mechanism more complicated



AF: mechanism or marker for stroke ?



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# AF progression is associated with vascular risks

	n	FU, years	AF progression
Euro Heart Survey AF, 2010	1219	1	15%
Record-AF, 2012	2137	1	15%

De Vos, Crijns, Euro Heart Survey JACC 2010	AF progression	No AF progression	p value
CV admissions (%)	71 %	50 %	<0.001
Stroke	6 %	2 %	0.003
CV mortality	7 %	3 %	0.005

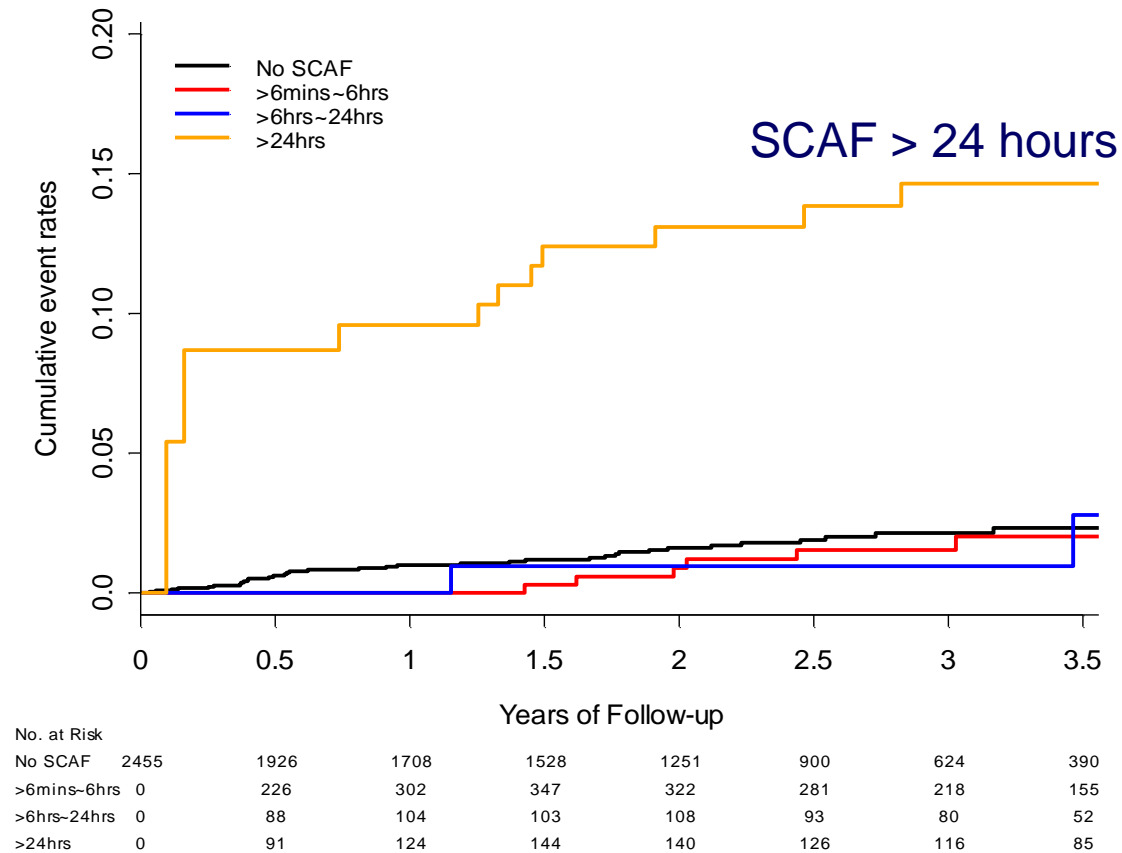


# Risk of ischemic stroke or embolism in SCAF

Clinical Outcome	Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months				Hazard Ratio with Subclinical Atrial Tachyarrhythmias (95% CI)	P Value
	Present (N=261)		Absent (N=2319)			
	no. of events	%/yr	no. of events	%/yr		
Ischemic stroke or systemic embolism*	11	1.69	40	0.69	2.49 (1.28–4.85)	0.007
Ischemic stroke	10	1.54	36	0.62	2.52 (1.25–5.08)	0.01
Systemic embolism	1	0.15	4	0.07	2.24 (0.25–20.10)	0.47



# Longer subclinical AF: higher risk of stroke



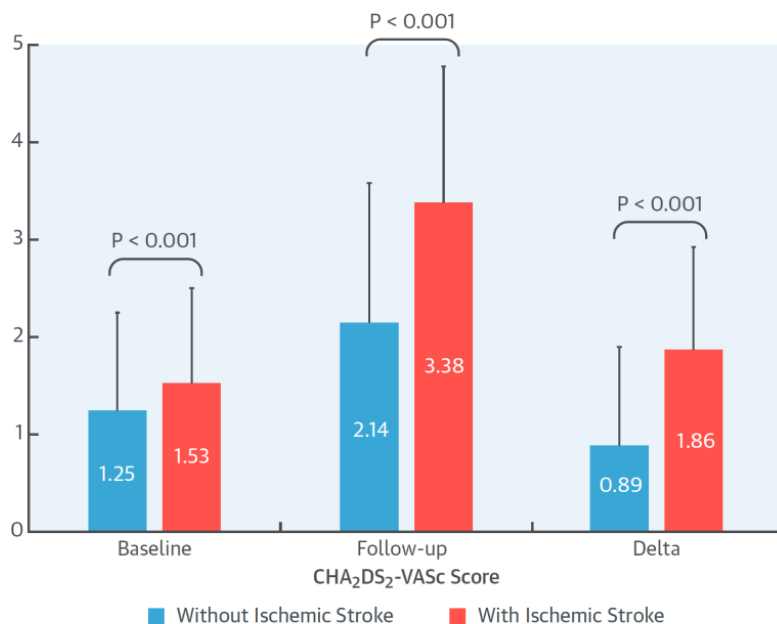


# Conclusions

- Stroke is still a significant problem in AF, next to heart failure
- Mechanism of stroke in AF still not completely known
- AF mechanism or bystander of stroke, anyway AF often increases risk of stroke



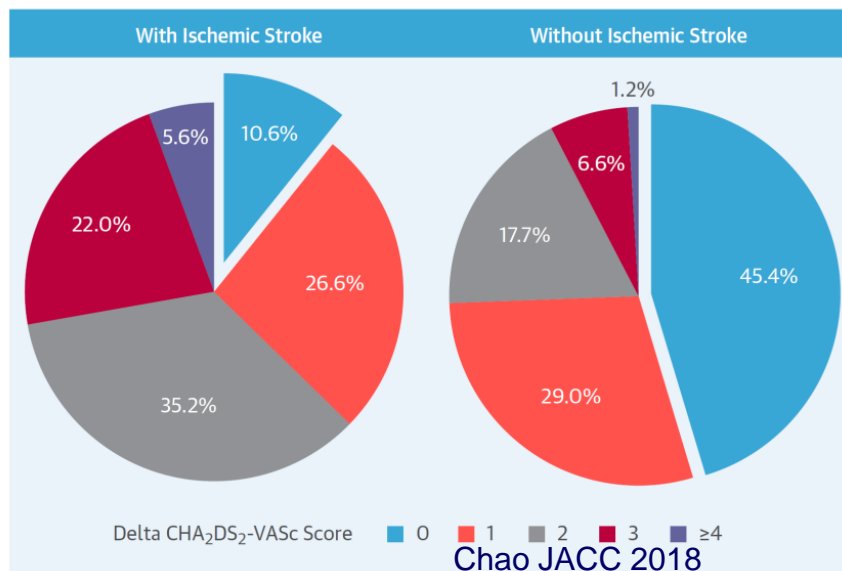
# CHA<sub>2</sub>DS<sub>2</sub>-VASc score is not static !



CHA<sub>2</sub>DS<sub>2</sub>-VASc score:

- Not static

- Most pts with ischemic stroke developed ≥1 new stroke risk factor

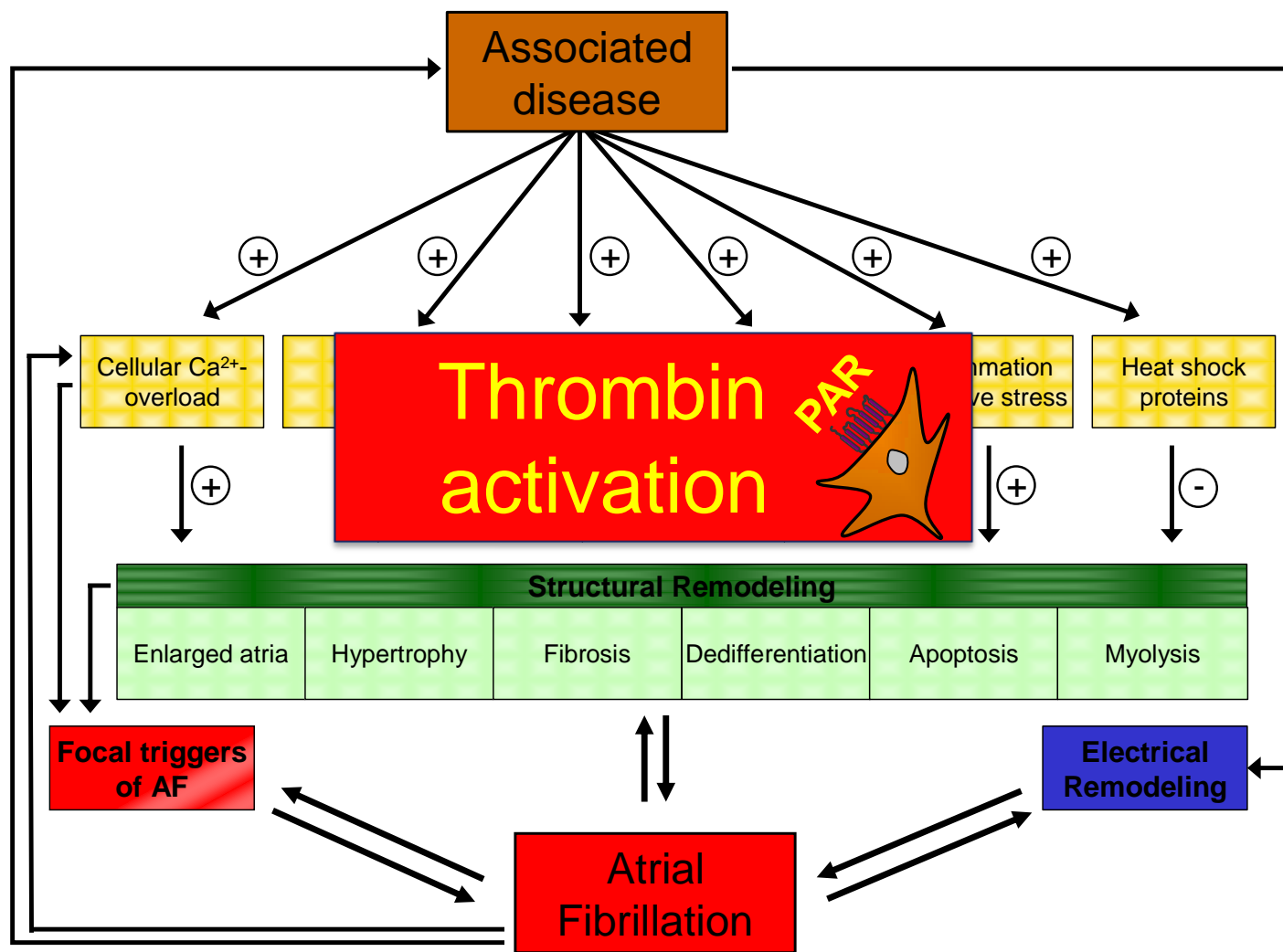


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- Stroke – what is the problem for patients with AF ?
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- AF is progressive disease and AF progression is associated with stroke, heart failure and mortality
- Hypercoagulability not only mechanism of stroke but also of AF progression ?



# Hypercoagulability and remodeling



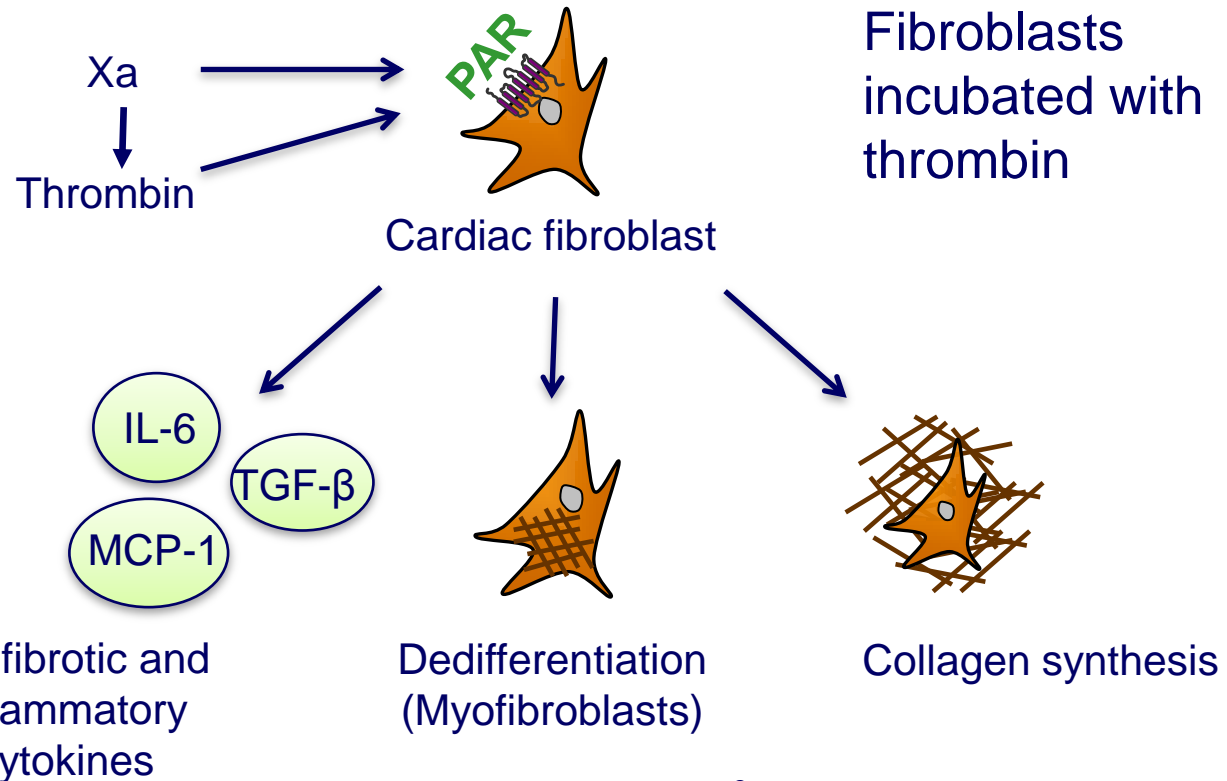
# Hypercoagulability and remodeling

- Hypercoagulability represents a so far unrecognized key mechanism in atrial remodeling and AF progression



# Hypercoagulability associated with atrial remodeling

Hyper-coagulability

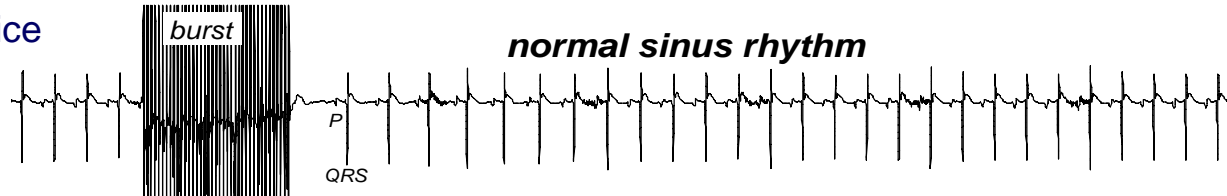


	MCP-1	$\alpha$ -SMA	$^3\text{H}$ -proline incorporation
Thrombin (0.01U/ml)	+72%	+200%	+120%
Thrombin + Dabigatran	ns	ns	ns

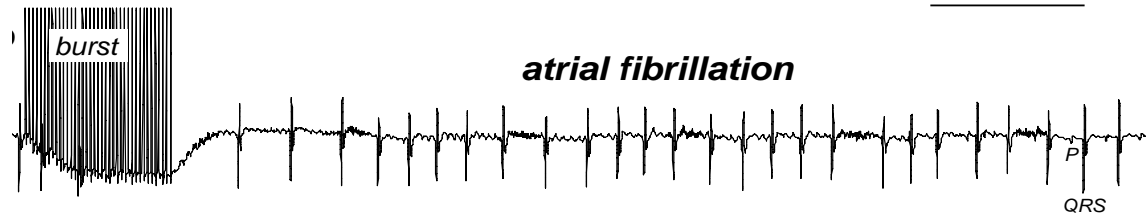


# Thrombin promotes AF

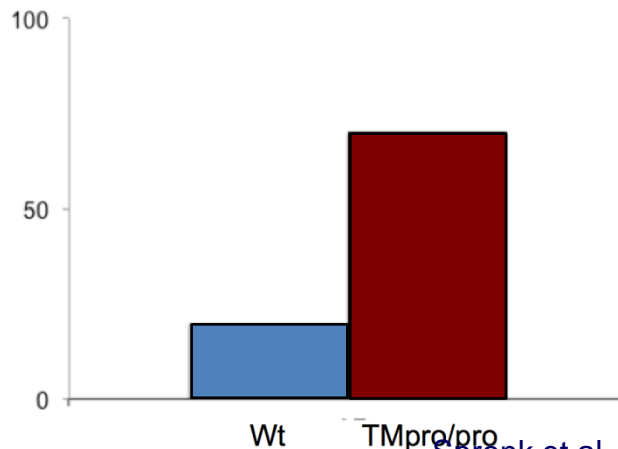
Wildtype mice



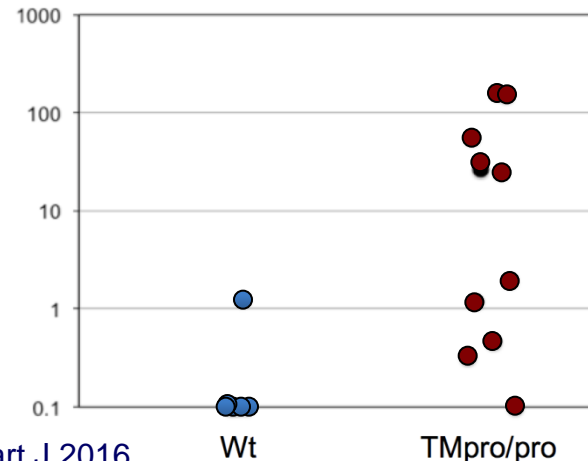
TM pro/pro  
transgenic mice  
with enhanced  
thrombin activity  
(hypercoagulable  
phenotype)



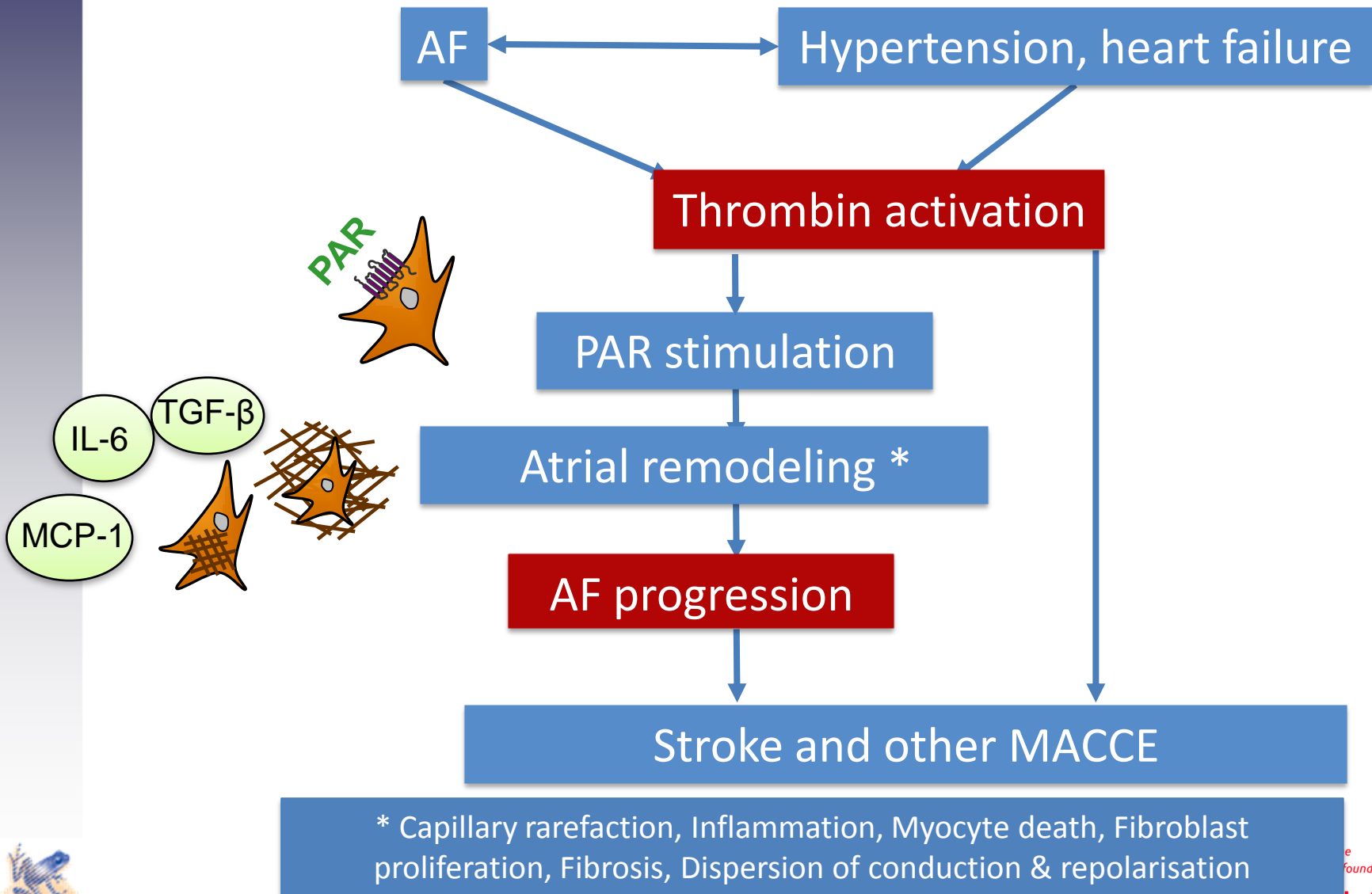
AF inducible (%)



AF Duration (s)



# Hypercoagulability and remodeling





# Hypothesis RACE V

- Hypercoagulability is one of the key mechanisms in AF progression (permanent AF and CV morbidity and mortality)
- Hypercoagulability varies depending on duration of AF and severity of the underlying vascular diseases
- Thrombin inhibitors, Factor Xa inhibitors and vitamin K antagonists differ with respect to prevention of AF progression



# Study design RACE V

- Multicenter, prospective, observational study
- 750 patients with self-terminating AF
  - Extensive phenotyping and characterization
  - Continuous rhythm monitoring
- Total inclusion duration 2 years
- Total follow-up 2.5 years
- Main study endpoint AF progression
- Expected AF progression rate 10%/ year → 187 AF progression events



# Continuous rhythm monitoring RACE V

Medtronic Advisa Pacemaker



Medtronic Reveal LINQ

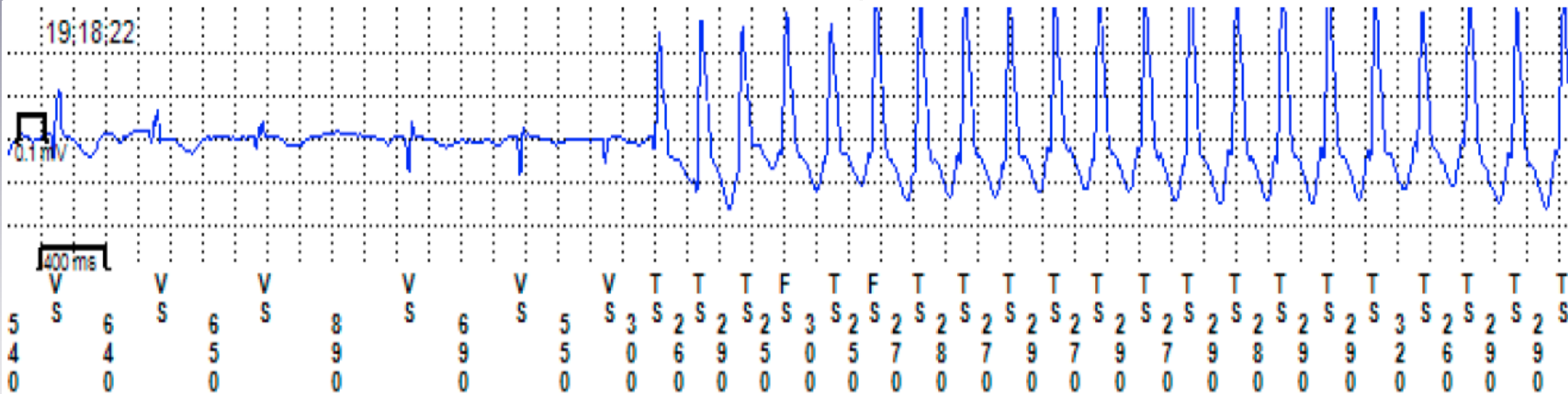


CareLink system



FOCUSON™

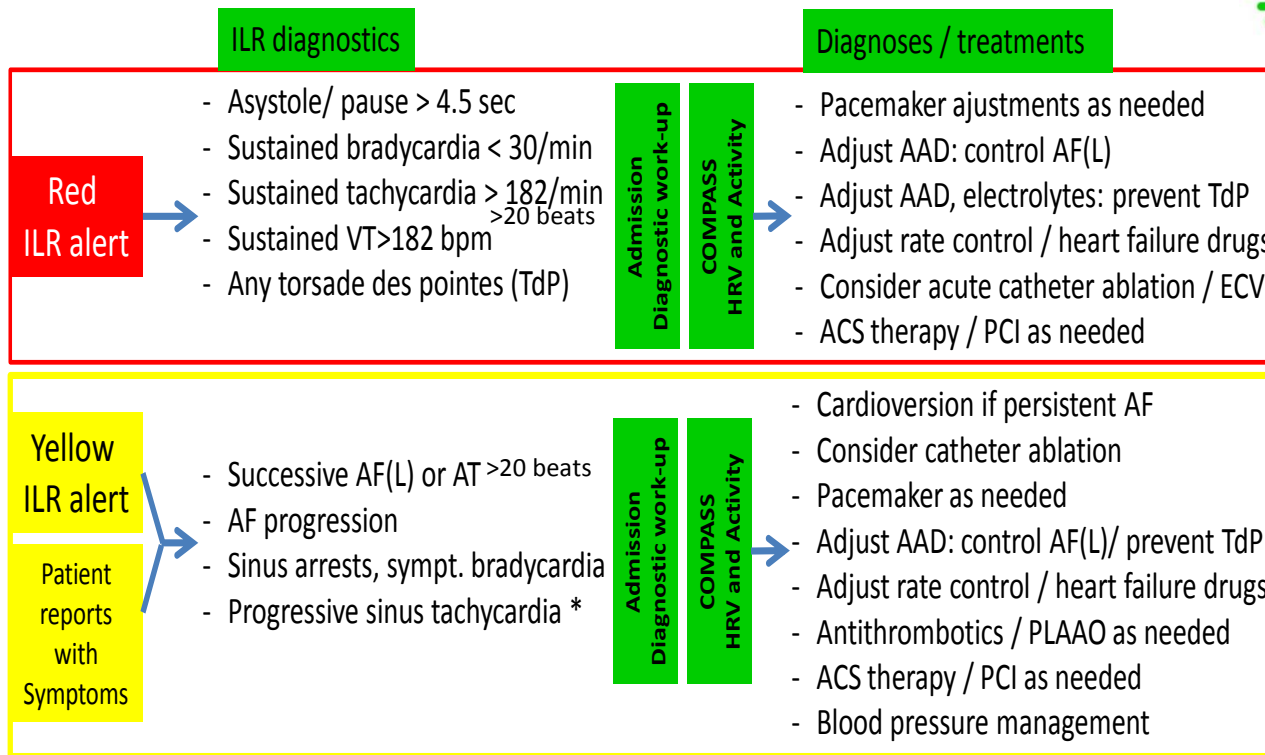




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### Red alert

- should be dealt with **within one working day**, subject to care by in-house 24/7 care service

### Yellow alert or symptomatic patient

- Should be dealt with **within 1 week**

### COMPASS guided diagnosis

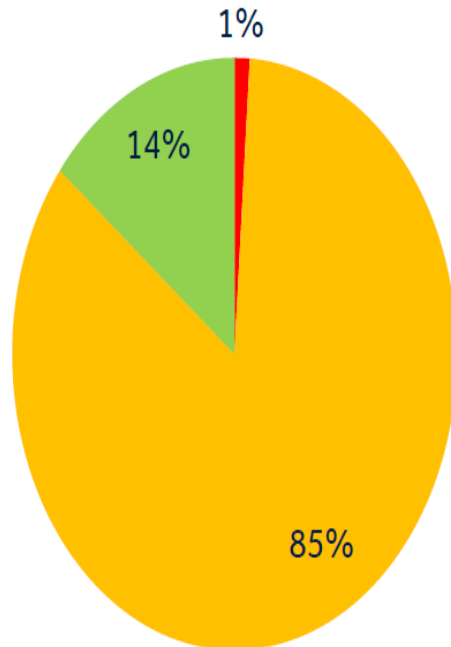
- Decreased HRV and/or activity support heart failure, uncontrolled hypertension, or points to impact of AF w/o tachycardia if any episodes
- Increased HRV supports SSS

\*) COMPASS current heart rate being > 1 week more than 25% or > 20 bpm higher than initial or set point heart rate; may indicate heart failure

# 1 month – 53 patients

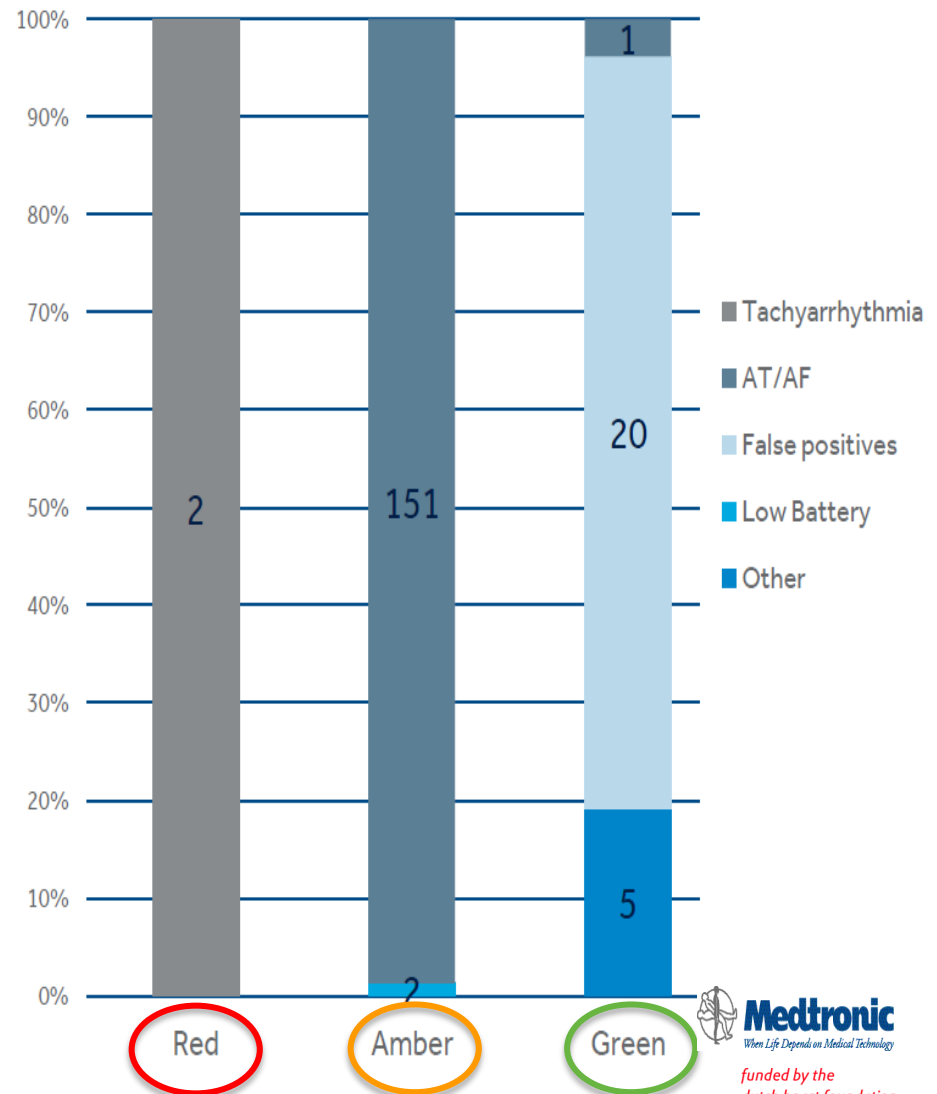
Event Types

## Transmissions Classification



■ Red ■ Amber ■ Green

- 338** Transmissions reviewed
- 181** Transmissions with events (in charts)
- 155** Transmissions with red or amber events in 17 patients



Transmission Classification



# FOCUSON™

SUBJECT TACHY

All,

Episode ID#	Episode Date and Time	Report type	Comment
7 - 16	maart 2017	Full 8 maart 2017 15:43	CareAlert AF, alle episoden tonen AF/PAF met snelle kamerrespons. Tevens zijn er een aantal breed complex tachycardieën zichtbaar max duur 20 seconden (#9) mogelijk VT, SVT/AT aberrante geleiding niet uitgesloten.





ECG rhythm strip showing a regular sinus rhythm. The rhythm is regular with a rate of approximately 75 bpm. The P waves are upright and the QRS complexes are narrow. A scale bar indicates 0.1 mV and 400 ms.

# Conclusions

- Remote monitoring of patients with implantable cardiac devices has benefits both for patients and physicians
  - Earlier detection of clinically relevant events not limited to SCAF
  - Probable a reduction of health care costs and consumption
- However, an issue is how to handle all those data efficiently
- The FOCUSON™ monitoring and triaging center may help to manage an adequate handling of all transmitted ECG data
- And it may potentially help to improve cardiovascular outcome



Thank you for your attention

# AF is progressive disease

- AF is the most frequent arrhythmia: > 1 million will have AF by 2040
- AF is not benign being associated with MACCE
- AF is a growing health care problem

## Atrial Fibrillation is a progressive disease

- ... often progresses from self-terminating to non-selfterminating AF

	n	FU, years	AF progression
Euro Heart Survey AF, 2010	1219	1	15%
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