

CSANZ Clinical Update: Atrial Fibrillation

Prof Prash Sanders MBBS, PhD, FRACP

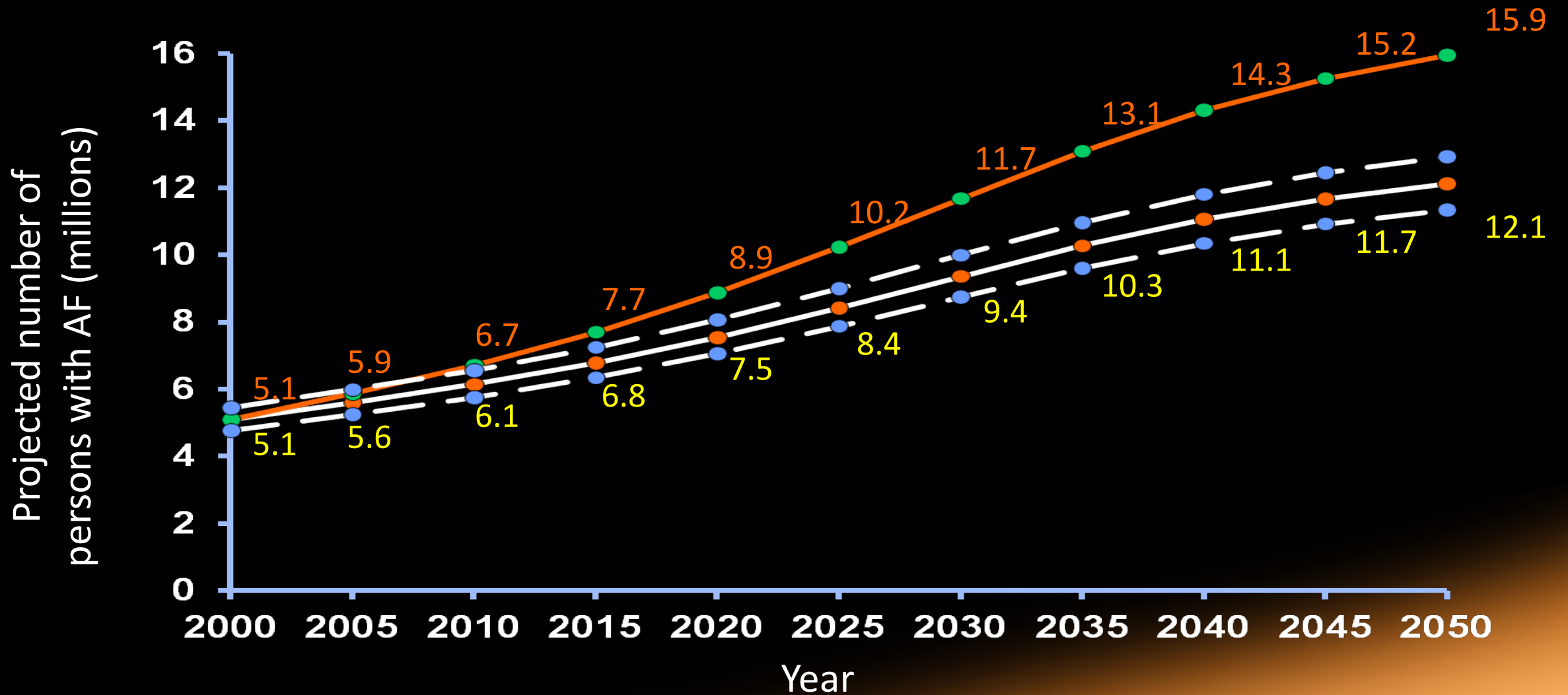
Director, Centre for Heart Rhythm Disorders, South Australian Health and Medical Research Institute (SAHMRI) & University of Adelaide;
Director, Cardiac Electrophysiology & Pacing, Royal Adelaide Hospital



Disclosures 2016

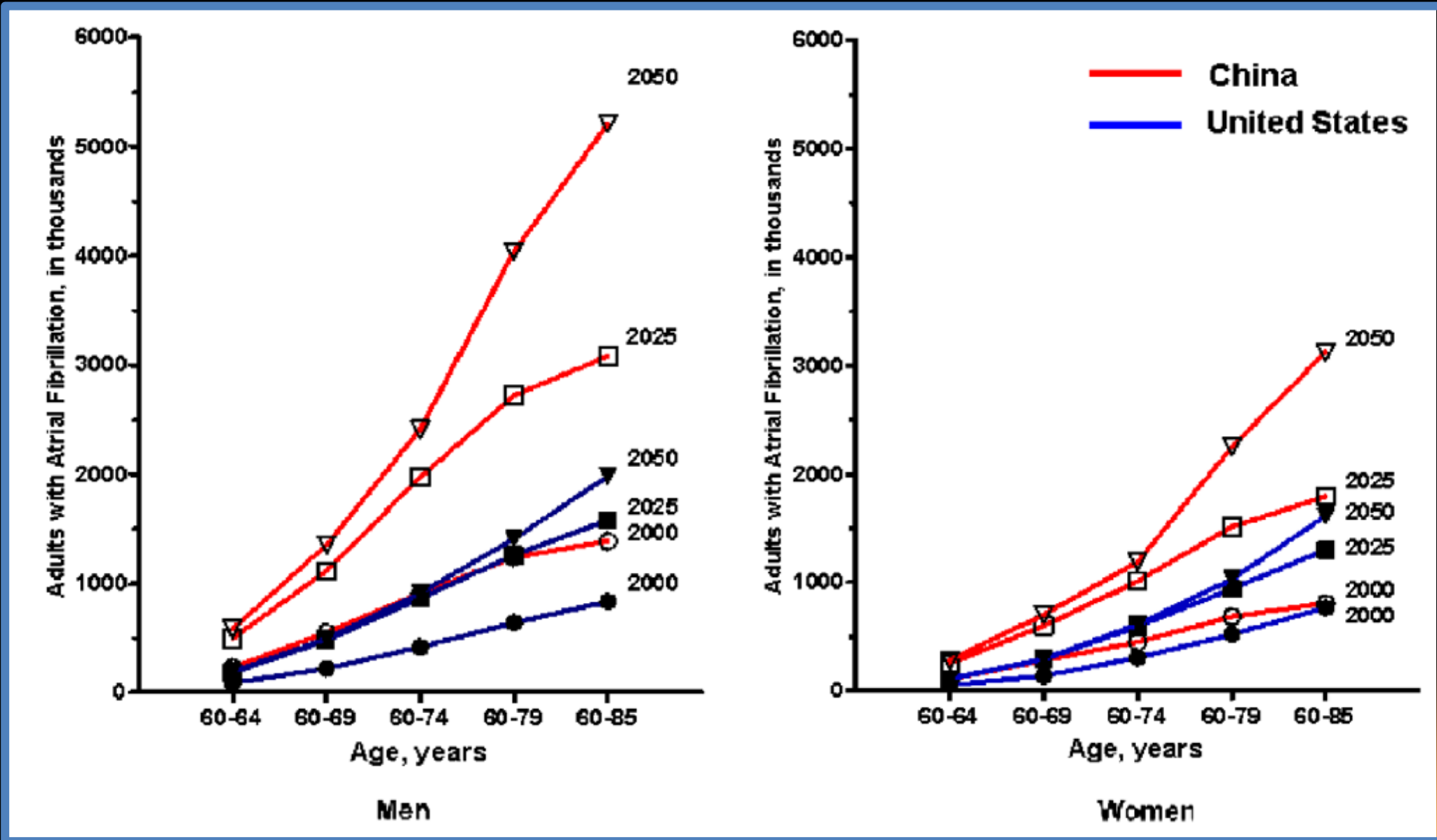
- **Advisory Board:** Biosense-Webster, Medtronic, St Jude Medical, Boston Scientific, CathRx
- **Lecture Fees and Research Funding:** Biosense-Webster, Medtronic, Boston Scientific, Biotronik, Sorin and St Jude Medical

Projected prevalence of AF

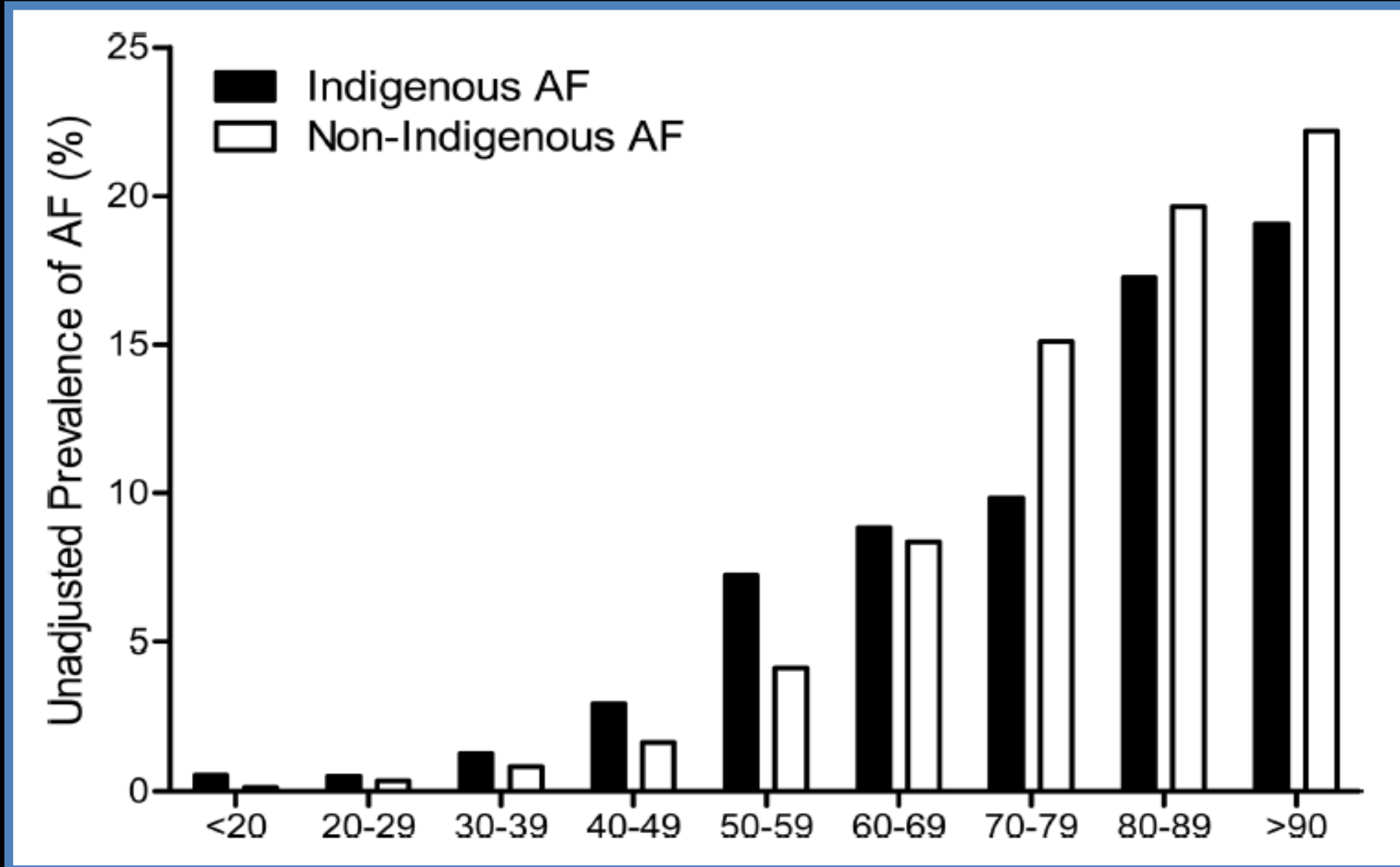


Miyasaka Y et al., Circulation 2006

Change in global prevalence of AF

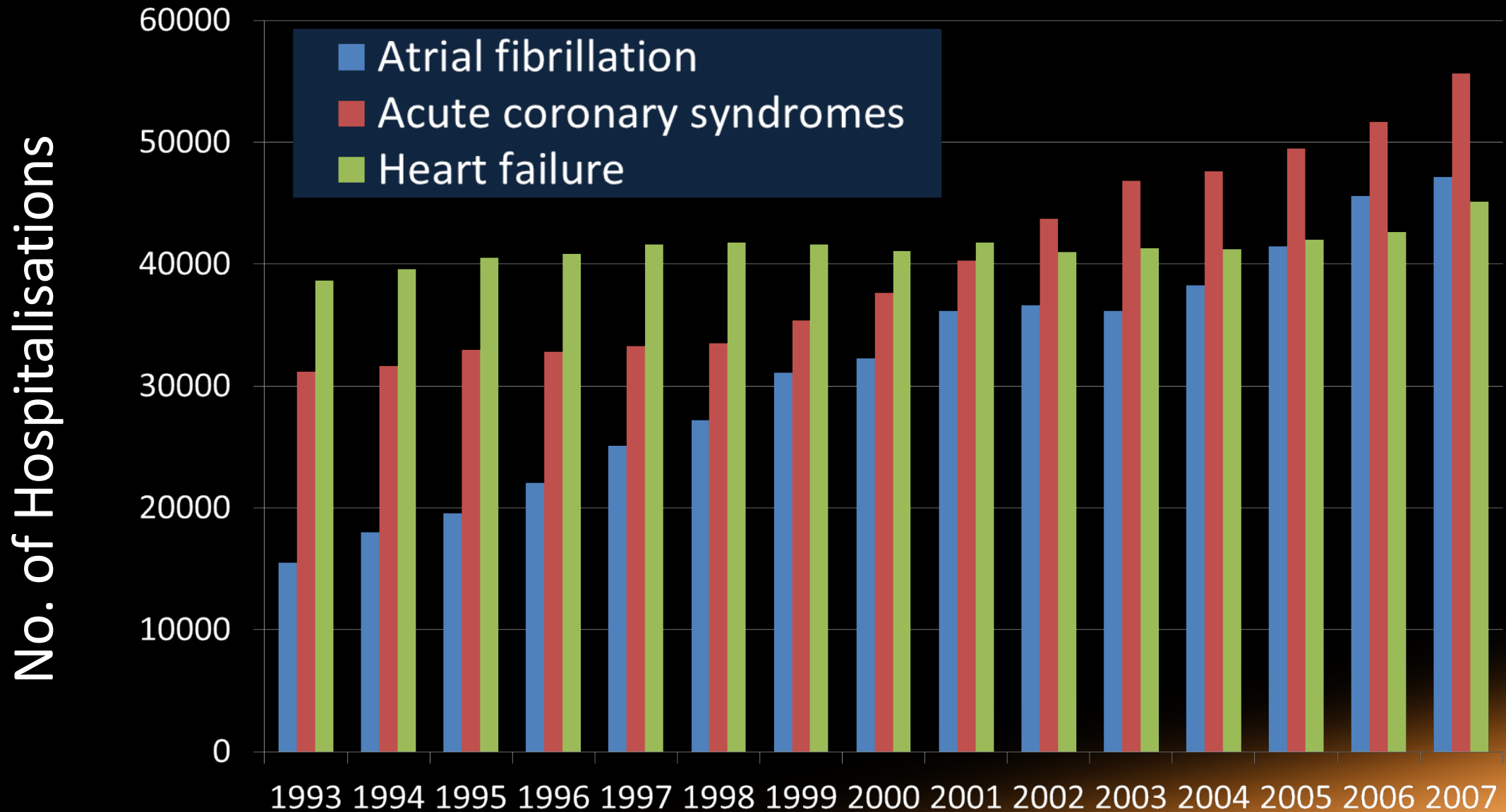


AF in the indigenous Australian population



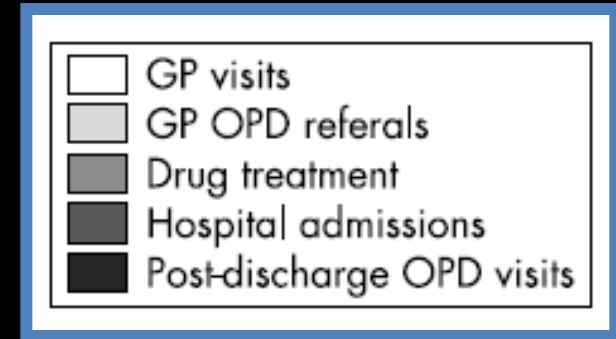
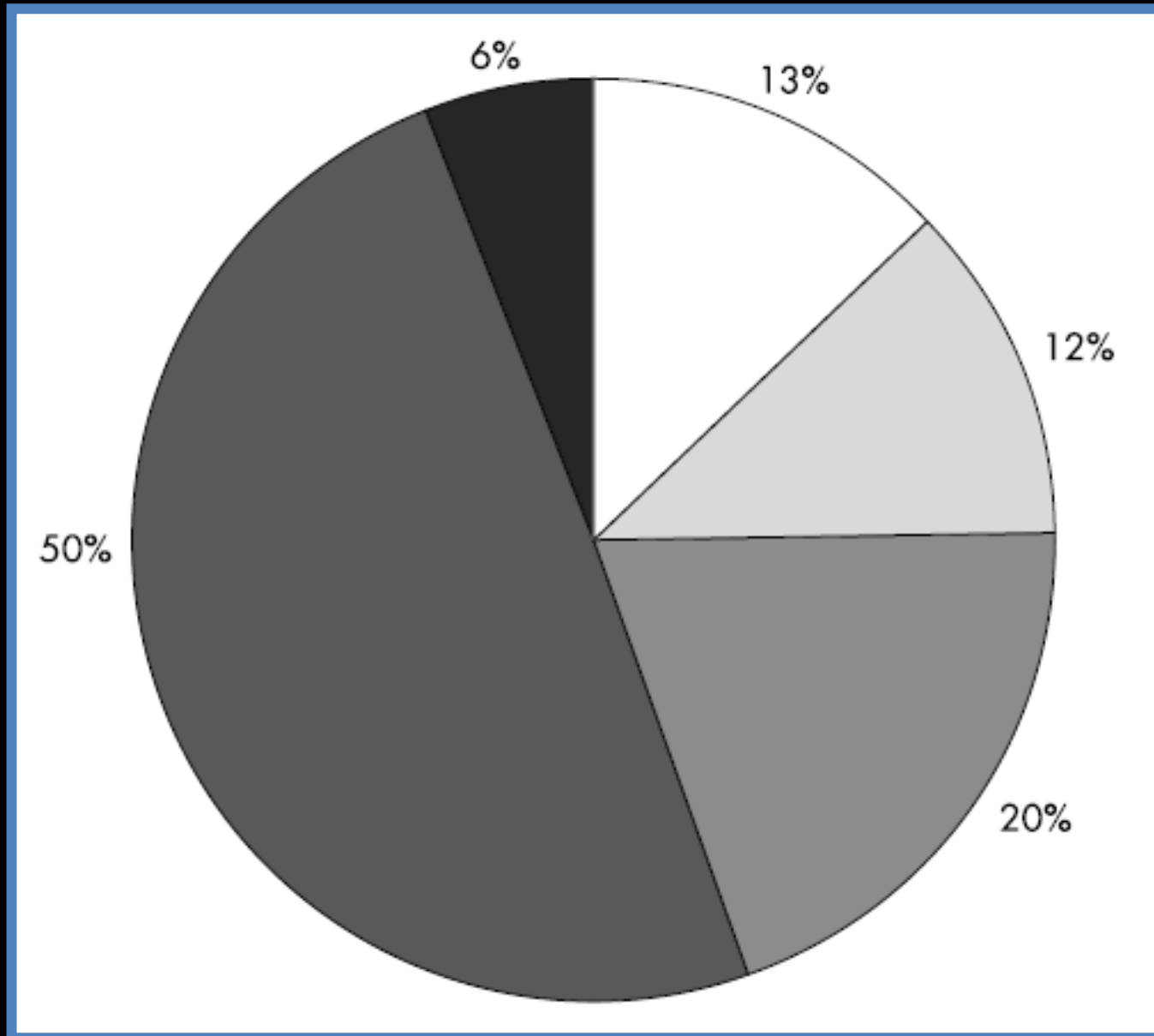
Wong CX et al., *BMJ Open* 2014

Hospitalizations for AF



Wong CX et al. Archives of Internal Medicine 2012

Health care expenditure related to AF



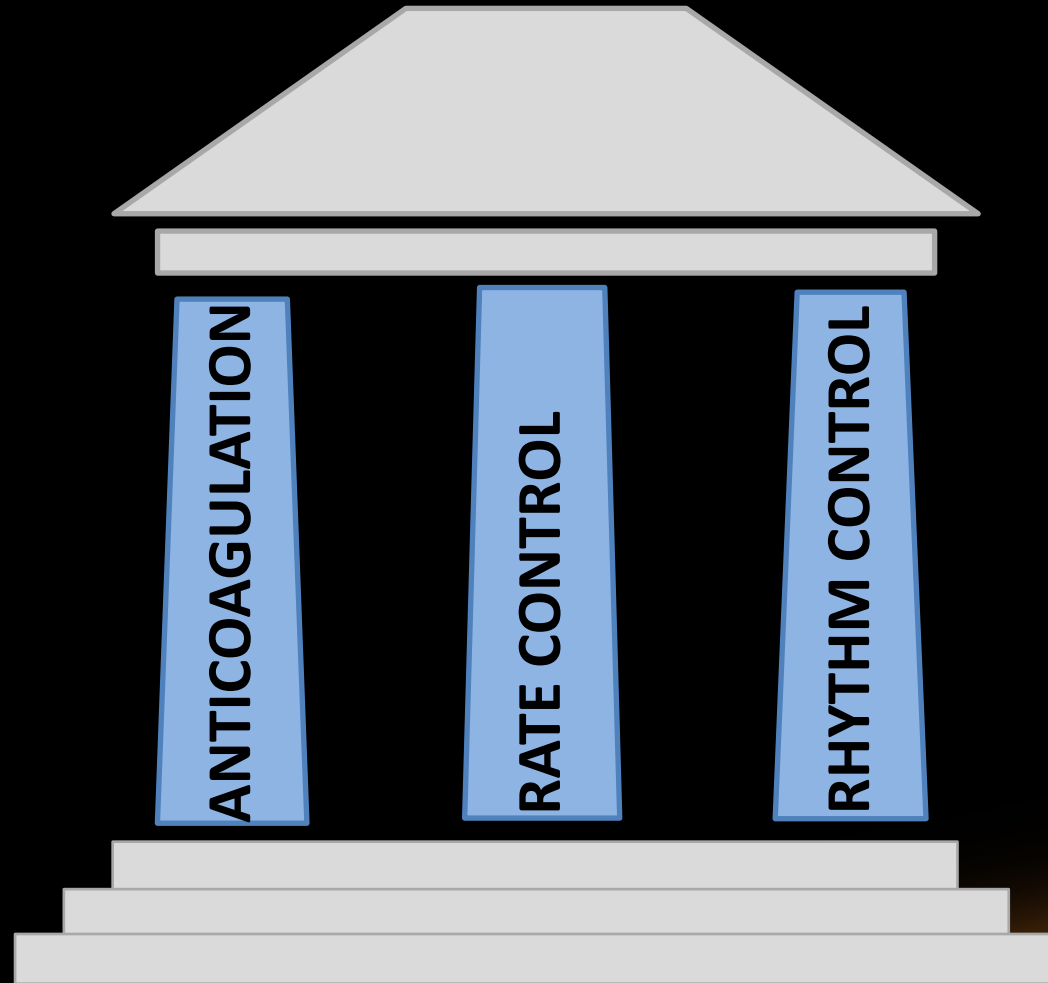
Almost 1% of the NHS expenditure per year (£460 million)

Stewart S, Heart 2004

AF in Australia

- Estimated prevalence 1.1%
- Contributes to 6,300 extra strokes per year
- > 45,000 hospitalizations
- Estimated cost: AUD 1.25 billion per year
 - Direct medical costs
 - Long term care
 - Lost productive output
 - 'Conservative' estimates

3 Pillars of AF management

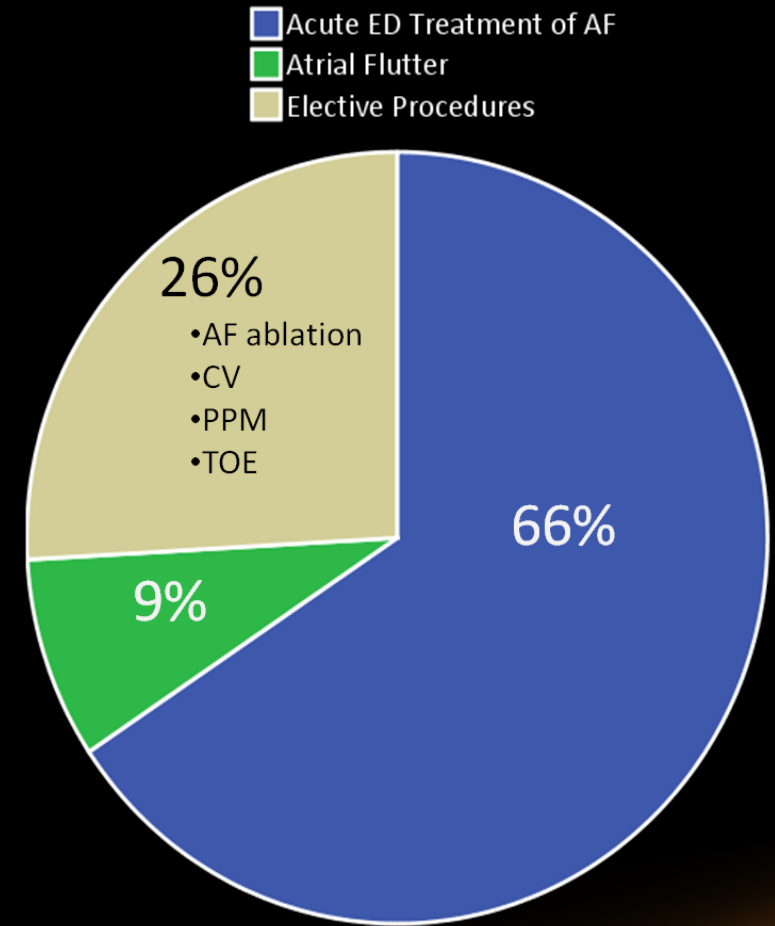


Stroke Prevention

AF presentations over 12 months

- All admitted/non-admitted ICD-10 code I48 over 12 months (n=858; 605 unique)
- Excluded
 - Atrial flutter (elective or acute treatment)
 - Elective procedures for AF (ablation, CV, TOE, PPM)
 - Renal failure requiring dialysis within the capture period
- Final sample (n=356) – pts presenting to the ED for acute treatment of AF

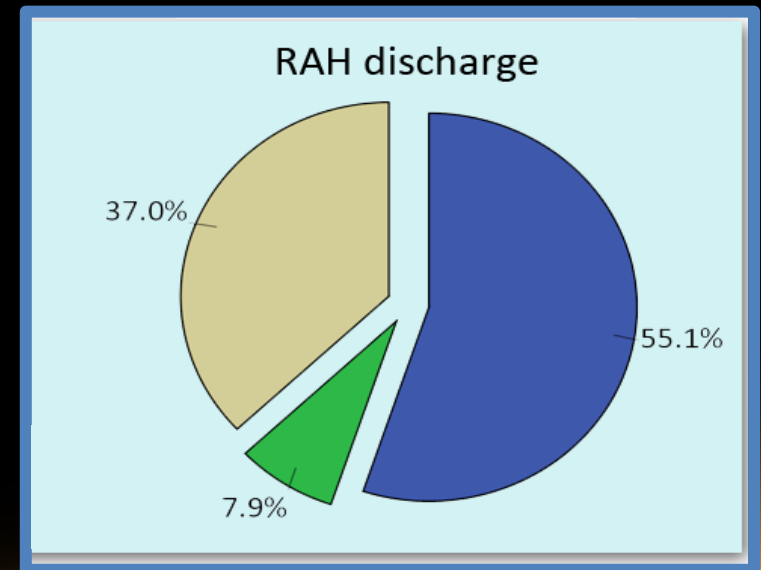
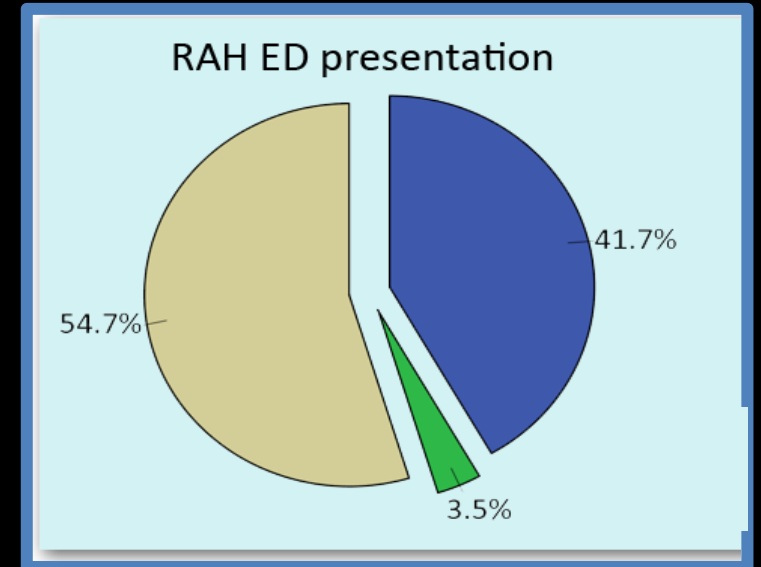
Rangnekar G, CSANZ 2012



**Followed for
1.4±0.3 years**

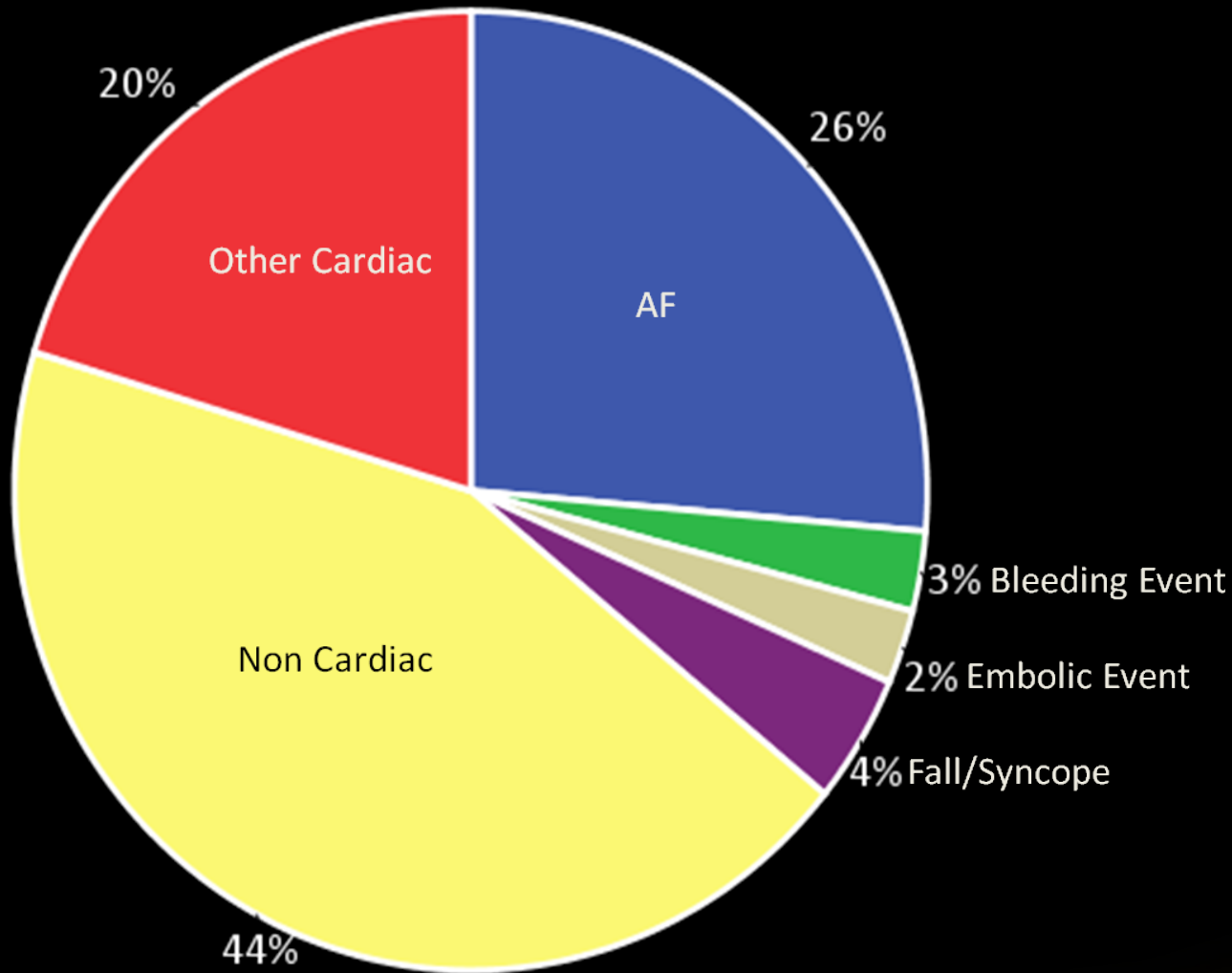
Anticoagulation

- 254 had complete drug and risk factor data
- Majority of AF pts are under-OAC, which was marginally improved upon hospital discharge
- ?reasons
 - Guideline non-adherence,
 - Lack of willingness to initiate chronic therapy in acute setting
 - Contra-indications to OAC



■ ADHERENT
■ OVERTREATED
■ UNDERTREATED

Readmission for AF within 12 months



- 356 index presentations for AF
- 482 all-cause re-admissions (in 177 pts) within 1.4 ± 0.3 yrs

26% of all-cause re-admissions were for AF

10.2% mortality

Prevention of thromboembolism

CHA₂DS₂-VASc Risk Score

| Risk factor | Score |
|---|----------|
| Congestive heart failure/LV dysfunction | 1 |
| Hypertension | 1 |
| Age ≥ 75 | 2 |
| Diabetes mellitus | 1 |
| Stroke/TIA/thrombo-embolism | 2 |
| Vascular disease ^a | 1 |
| Age 65–74 | 1 |
| Sex category (i.e. female sex) | 1 |
| Maximum score | 9 |

CHA₂DS₂-VASc risk score

| Risk category | CHA ₂ DS ₂ -VASc score | Recommended antithrombotic therapy |
|--|--|--|
| One 'major' risk factor or ≥ 2 'clinically relevant non-major' risk factors | ≥ 2 | OAC ^a |
| One 'clinically relevant non-major' risk factor | 1 | Either OAC ^a or aspirin 75–325 mg daily. Preferred: OAC rather than aspirin. |
| No risk factors | 0 | Either aspirin 75–325 mg daily or no antithrombotic therapy. Preferred: no antithrombotic therapy rather than aspirin. |

Risk of Thromboembolism on the basis of duration of AF

Ganesan AN et al. EHJ (In Press)

B

Stroke or Systemic Embolism (adjusted)

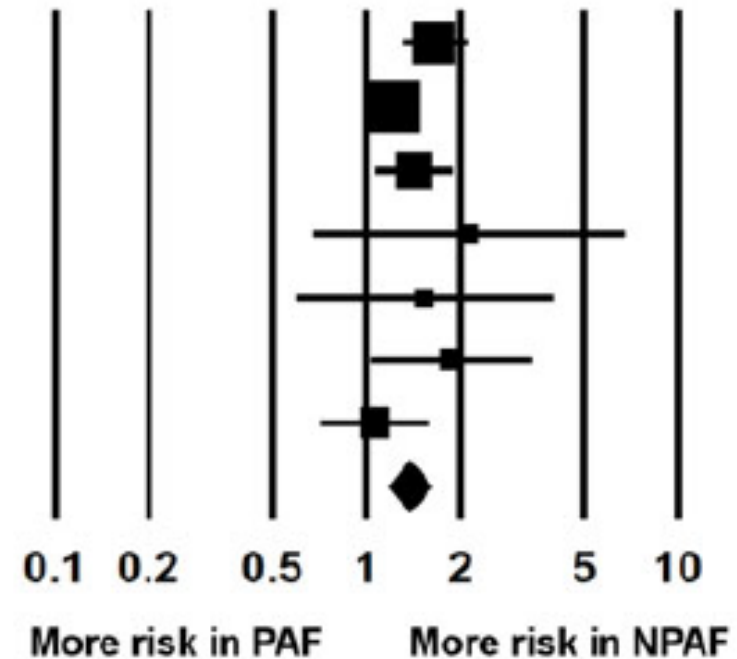
Study name

Statistics for each study

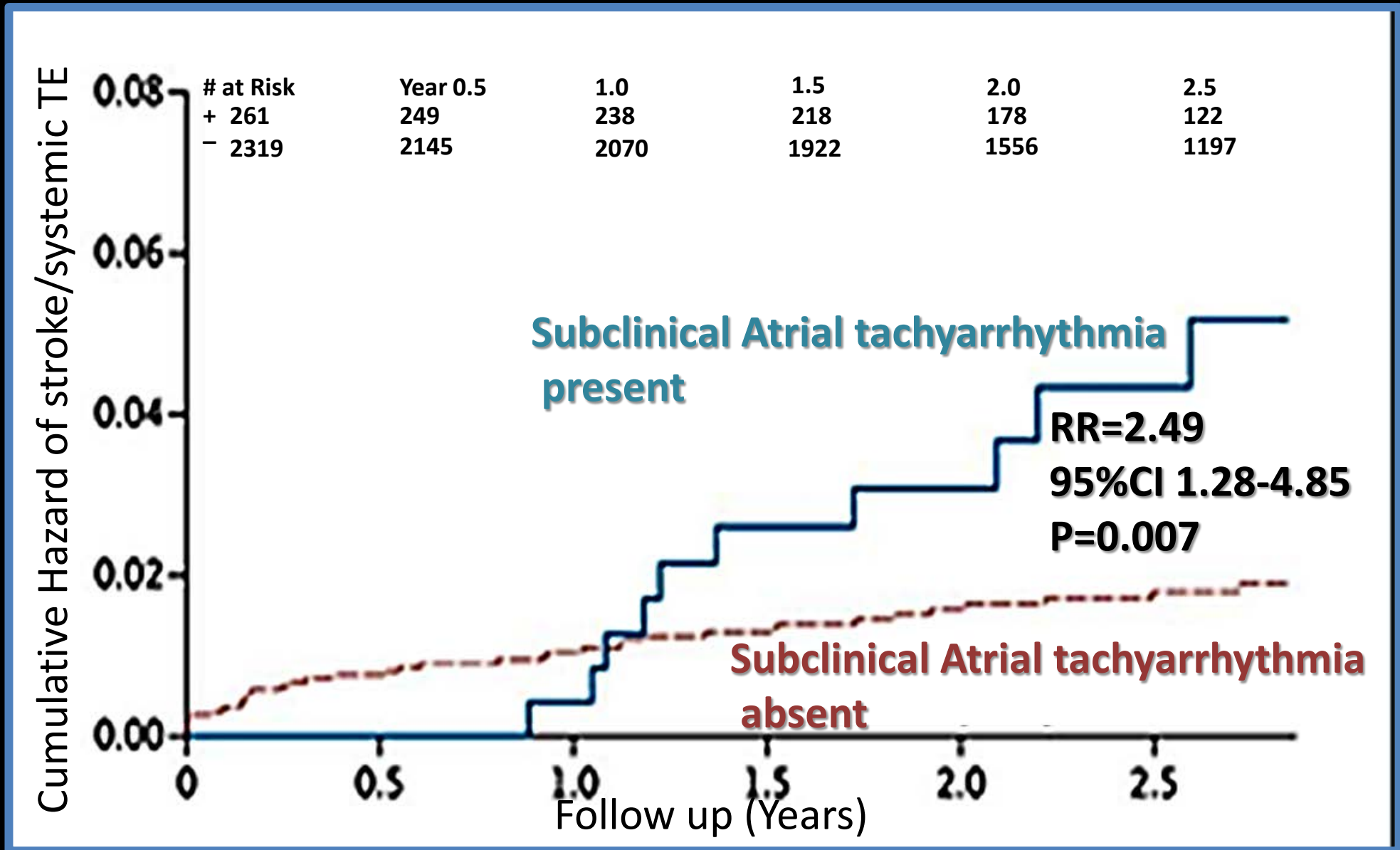
Hazard ratio and 95% CI

Hazard ratio Lower limit Upper limit p-Value

| | | | | |
|-------------------|--------------|--------------|--------------|--------------|
| ACTIVE A/AVERROES | 1.658 | 1.316 | 2.089 | 0.000 |
| ROCKET-AF | 1.220 | 1.060 | 1.403 | 0.006 |
| ARISTOTLE | 1.429 | 1.072 | 1.904 | 0.015 |
| GISSI-AF | 2.141 | 0.677 | 6.774 | 0.195 |
| Euro Heart Survey | 1.538 | 0.595 | 3.980 | 0.374 |
| SPORTIF | 1.870 | 1.041 | 3.359 | 0.036 |
| Active W | 1.064 | 0.714 | 1.586 | 0.761 |
| OVERALL | 1.384 | 1.191 | 1.608 | 0.000 |



Subclinical AF and stroke

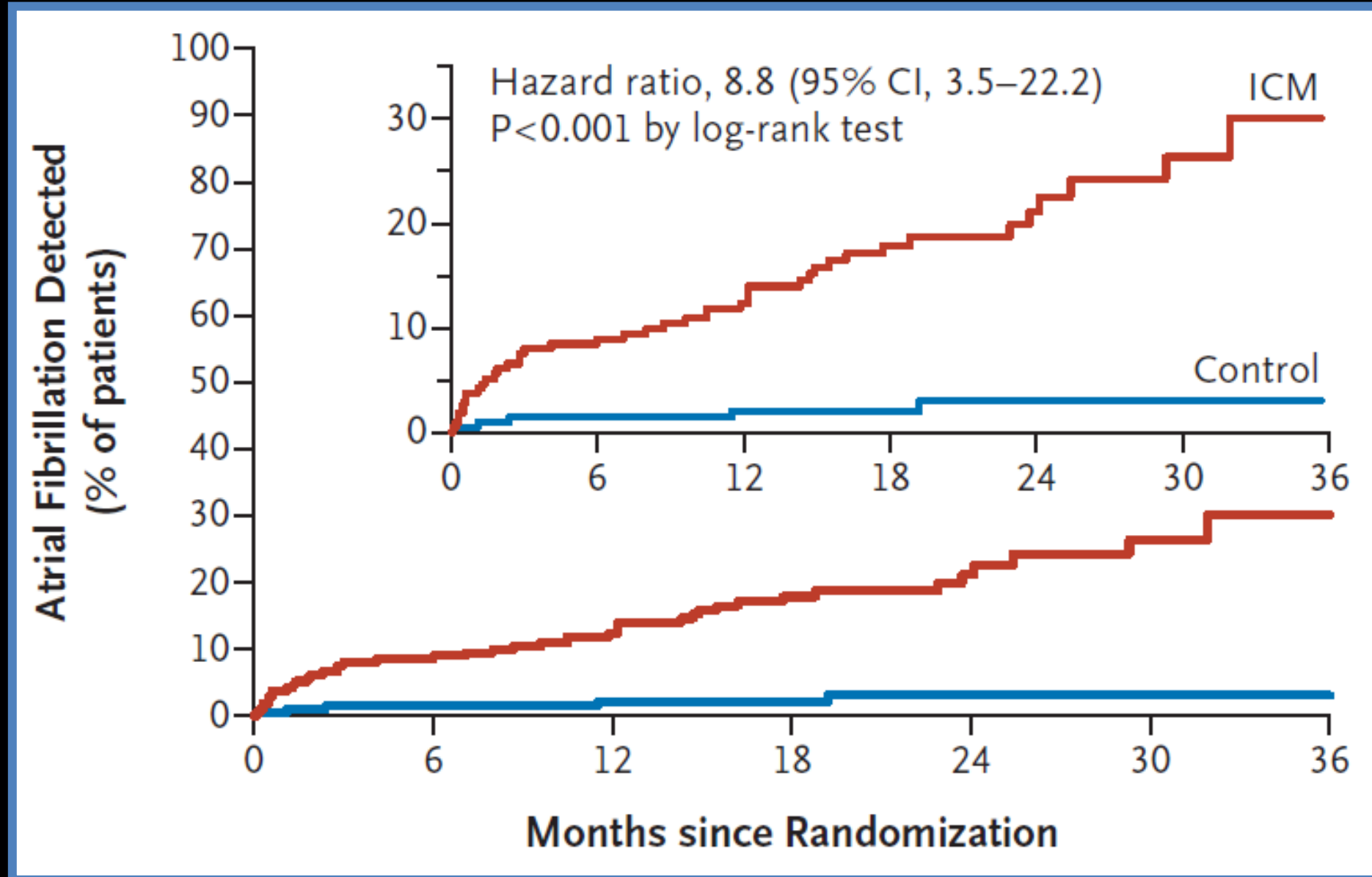


Healey JS, et al. N Engl J Med 2012

ASSERT analysis: CHADS2 score stratified stroke risk with subclinical AF

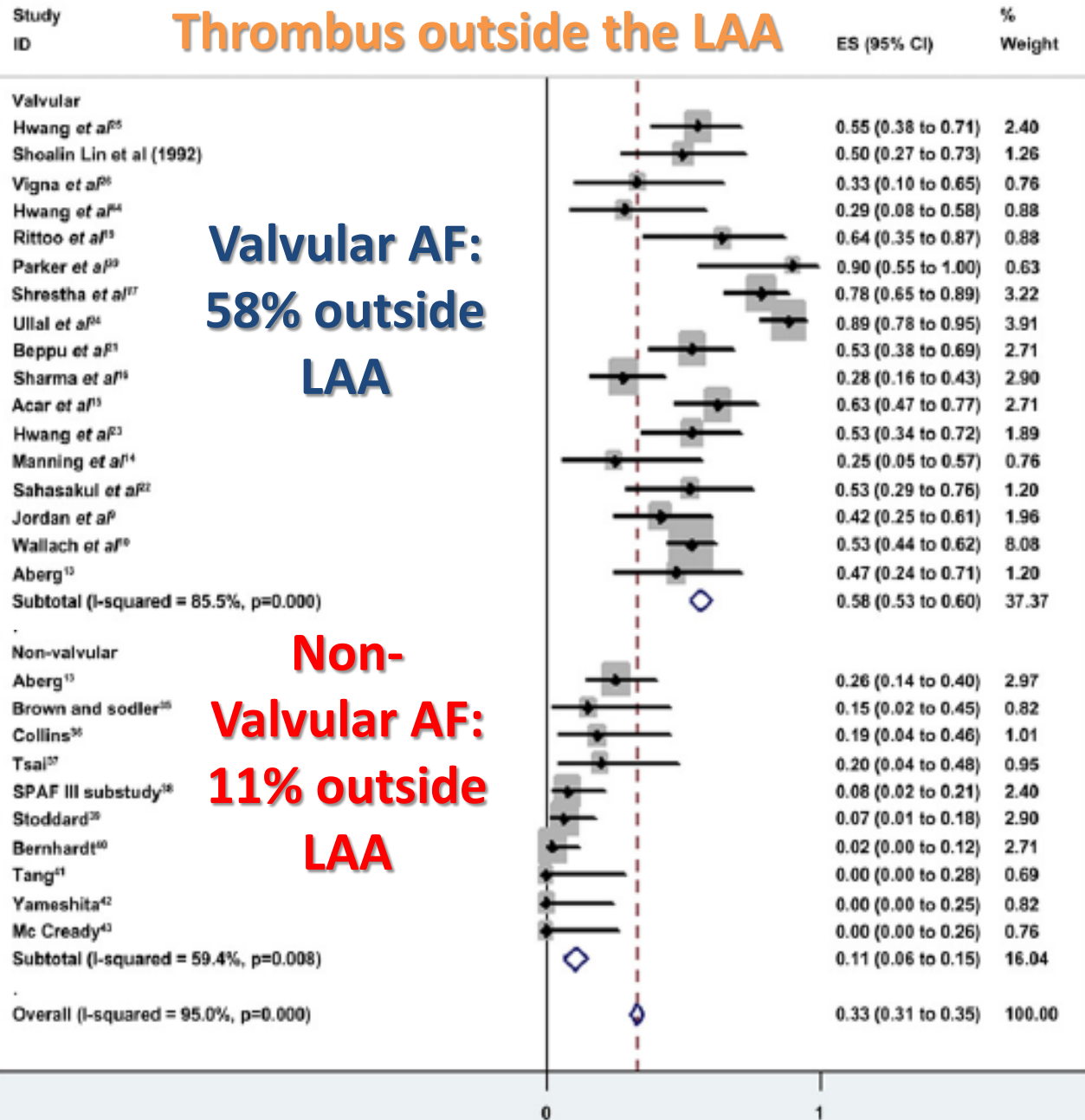
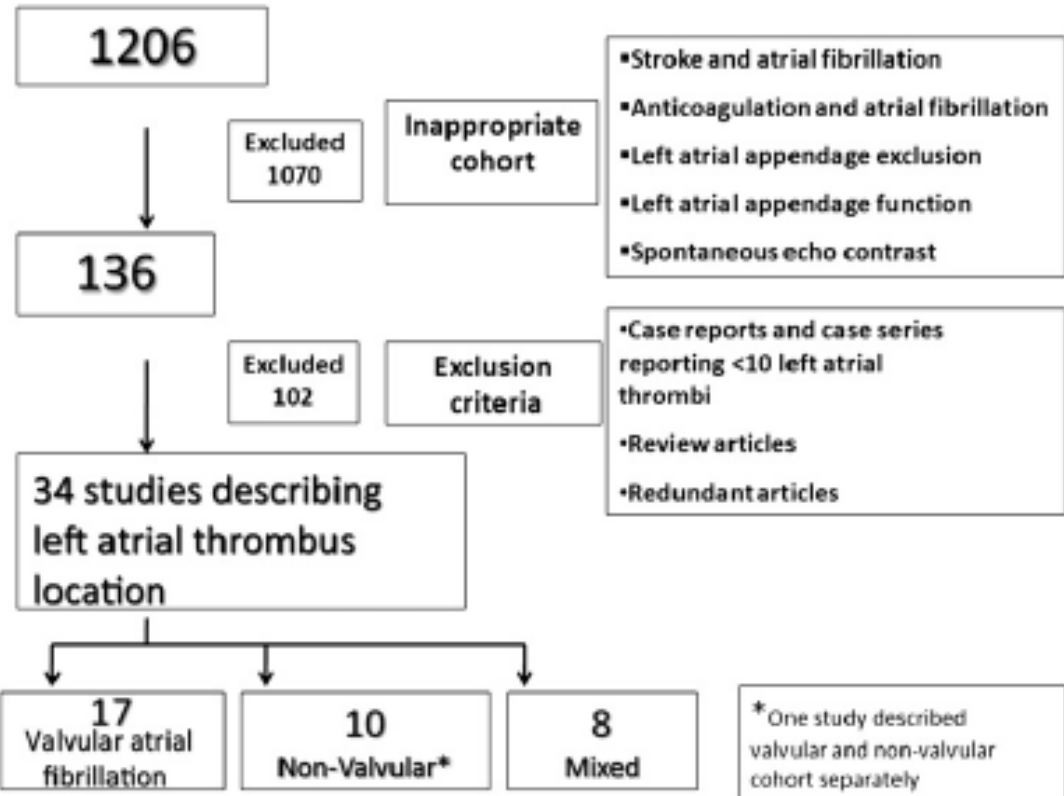
| CHADS ₂ Score | No. of Patients | Subclinical Atrial Tachyarrhythmias between Enrollment and 3 Months | | | | | | Hazard Ratio for Ischemic Stroke or Systemic Embolism with Subclinical Atrial Tachyarrhythmias (95% CI)* |
|--------------------------|-----------------|---|---------------|------|-----------------|---------------|------|--|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

Cryptogenic stroke - detection of AF



Location of thrombus in AF: role of LAA closure

Mahjan R et al. Heart 2012



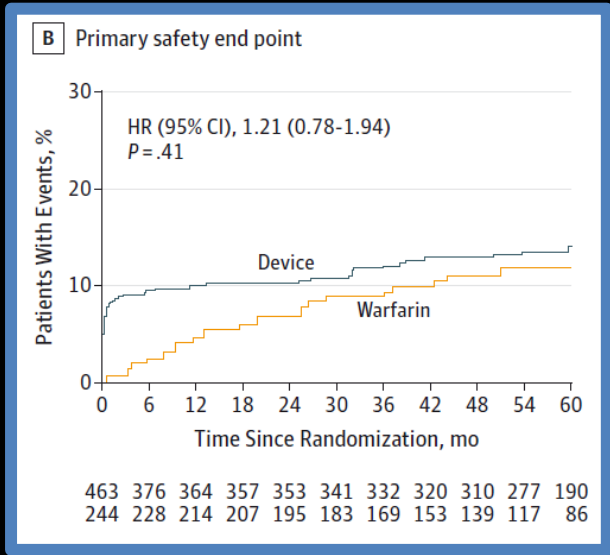
LAA occlusion: PROTECT-AF

- 700 non-valvular AF patients, 18 months f/up
- Randomized 2:1 design:
- Device group (WATCHMAN + 45 days warfarin) vs. Control group (long term warfarin)

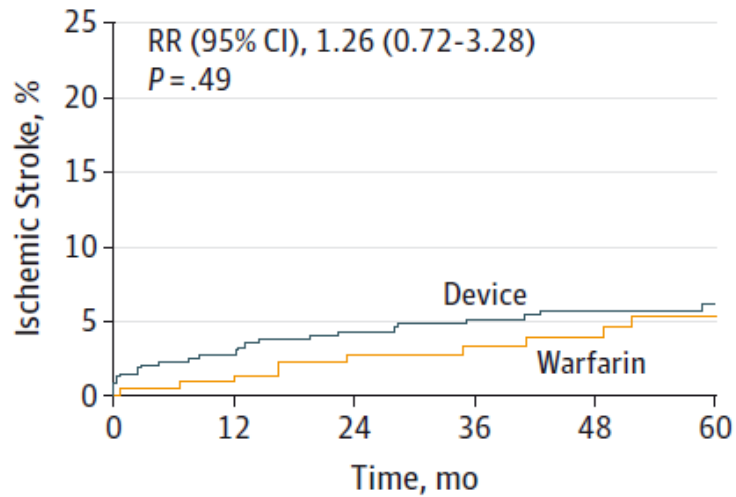


PROTECT AF: long-term results of LAA closure

Reddy VY et al. JAMA 2014

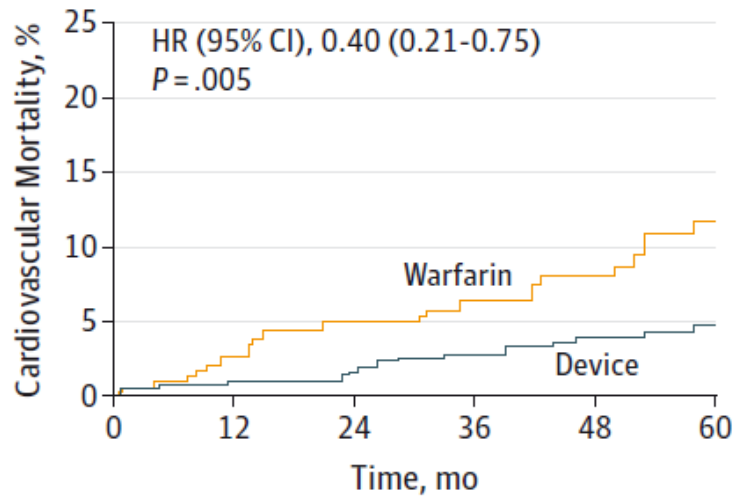


A Ischemic stroke



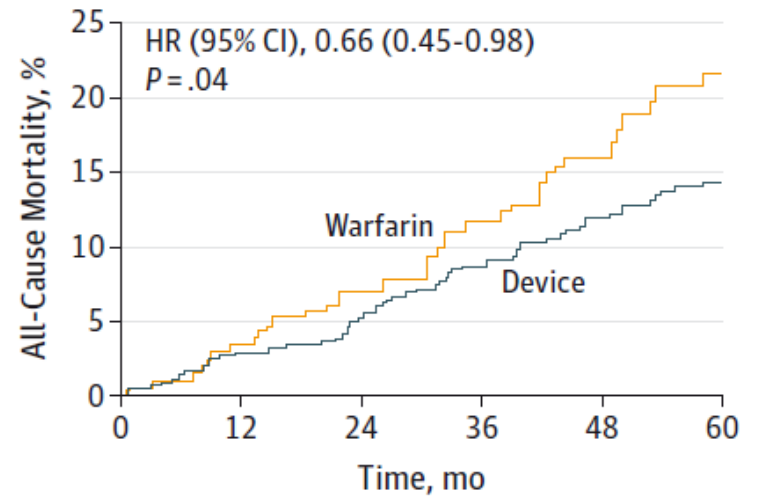
| No. of patients | 0 | 12 | 24 | 36 | 48 | 60 |
|-----------------|-----|-----|-----|-----|-----|-----|
| Device | 463 | 382 | 360 | 336 | 314 | 156 |
| Warfarin | 244 | 220 | 200 | 172 | 144 | 64 |

B Cardiovascular mortality



| No. of patients | 0 | 12 | 24 | 36 | 48 | 60 |
|-----------------|-----|-----|-----|-----|-----|-----|
| Device | 463 | 389 | 372 | 351 | 328 | 165 |
| Warfarin | 244 | 222 | 204 | 176 | 147 | 69 |

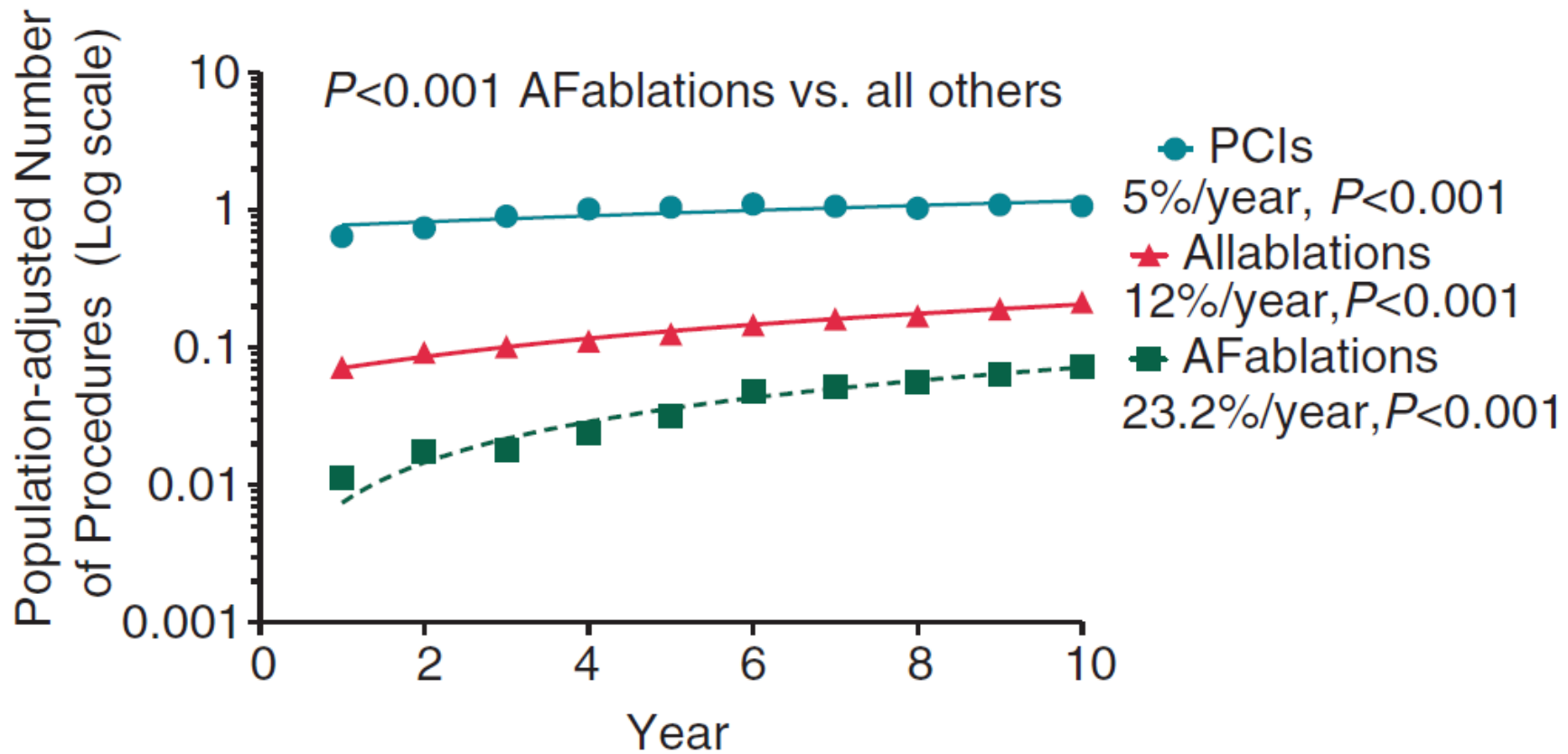
C All-cause mortality



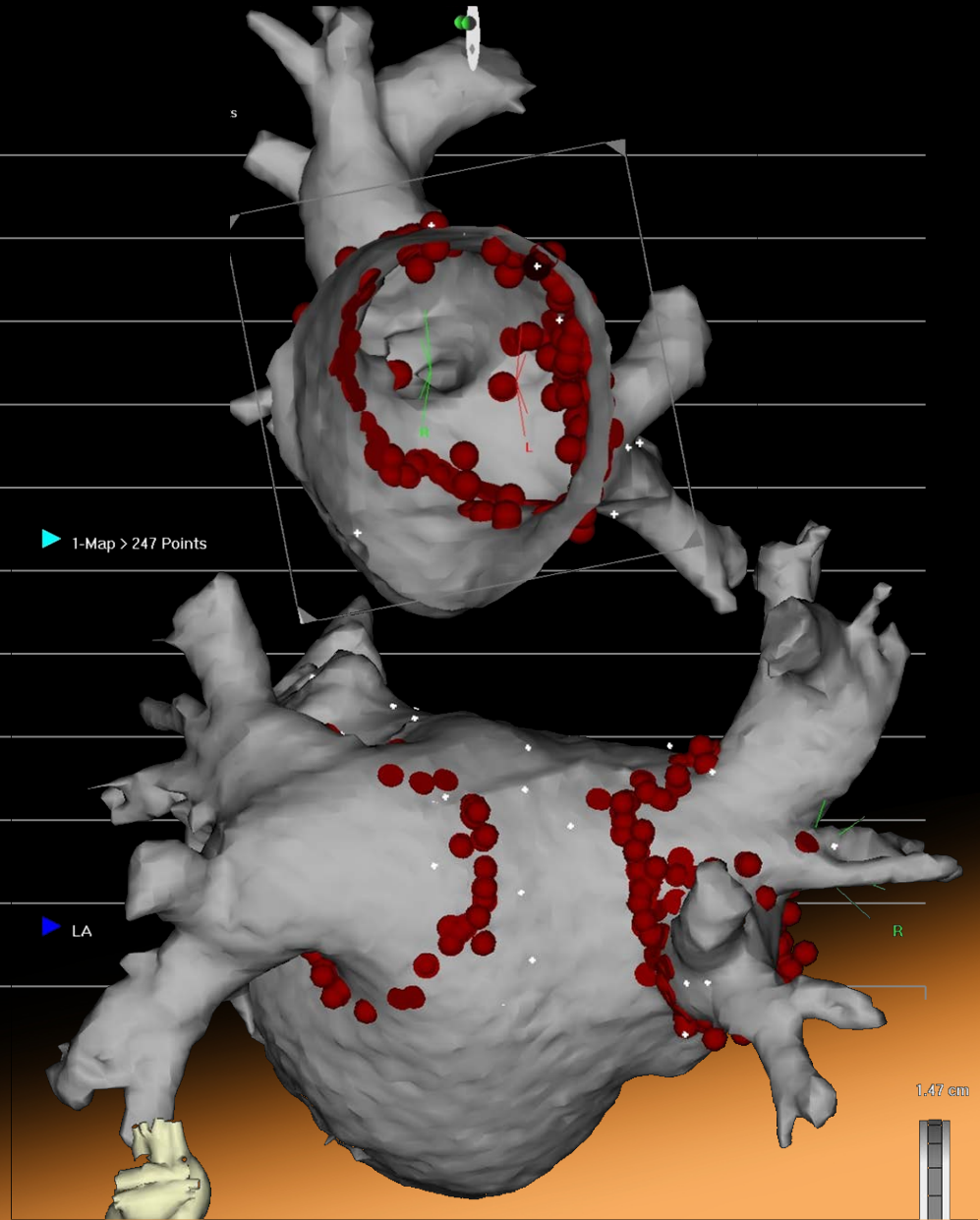
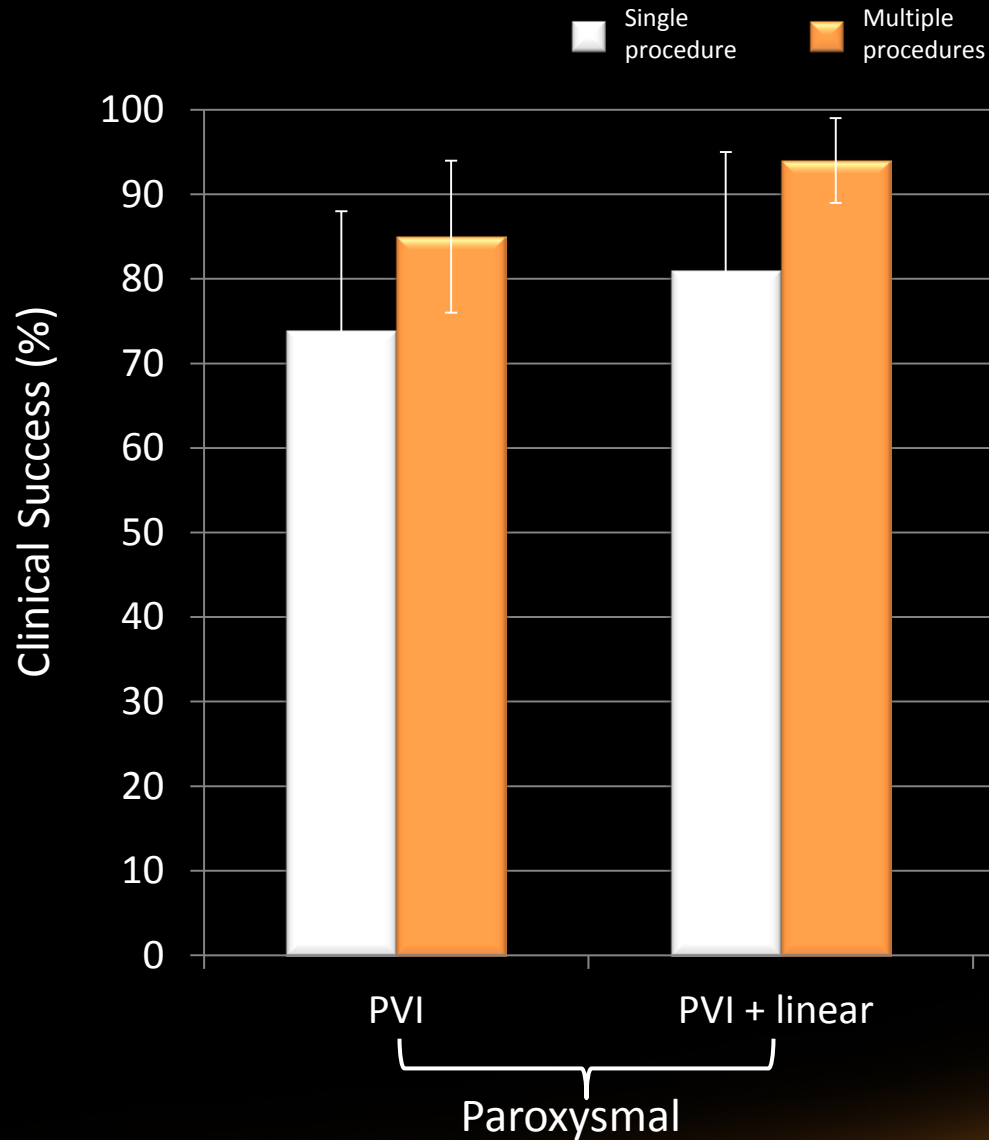
| No. of patients | 0 | 12 | 24 | 36 | 48 | 60 |
|-----------------|-----|-----|-----|-----|-----|-----|
| Device | 463 | 389 | 373 | 352 | 330 | 202 |
| Warfarin | 244 | 222 | 204 | 177 | 150 | 92 |

Rhythm control: AF Ablation

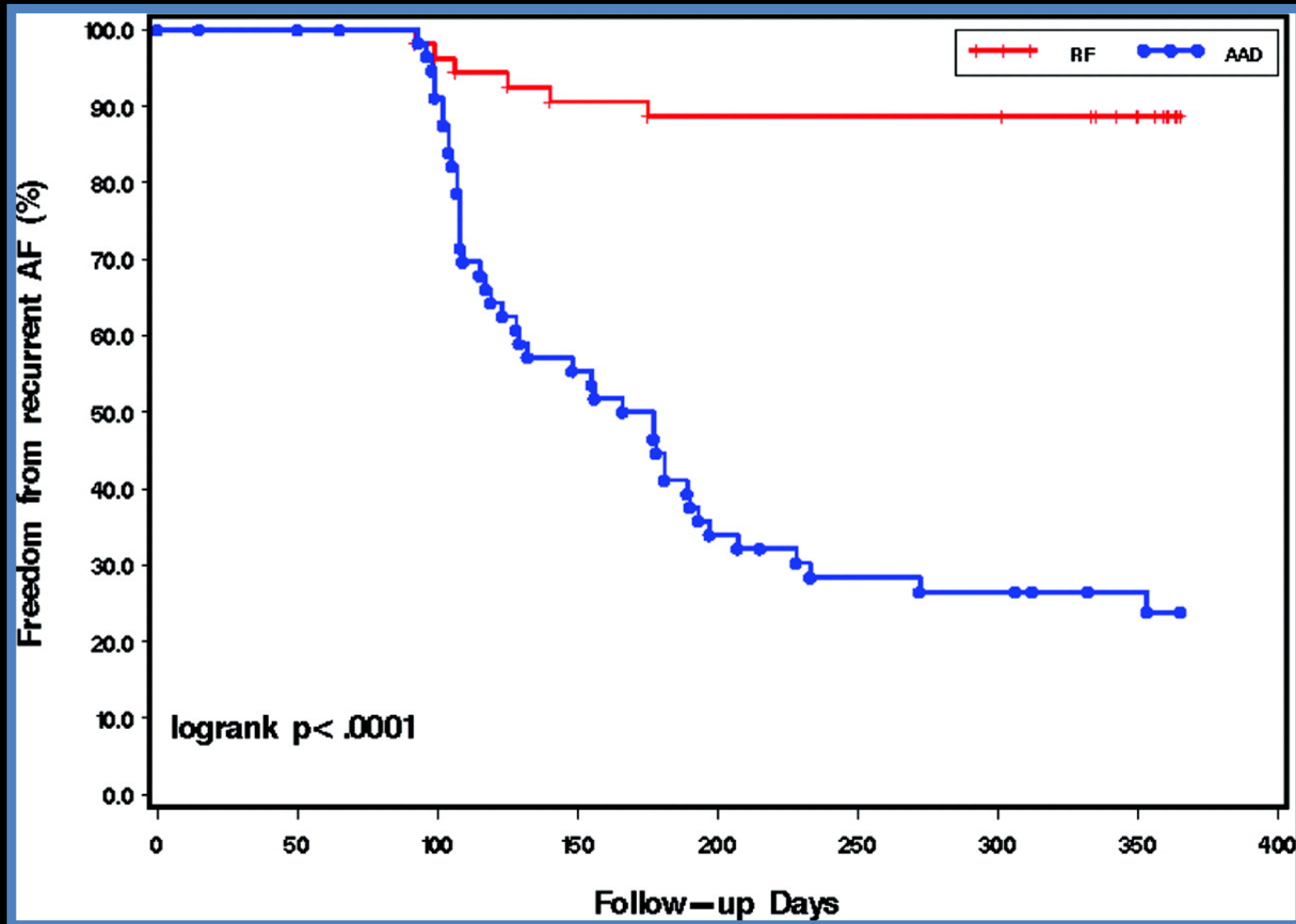
Exponential use of AF ablation



Clinical success in paroxysmal AF

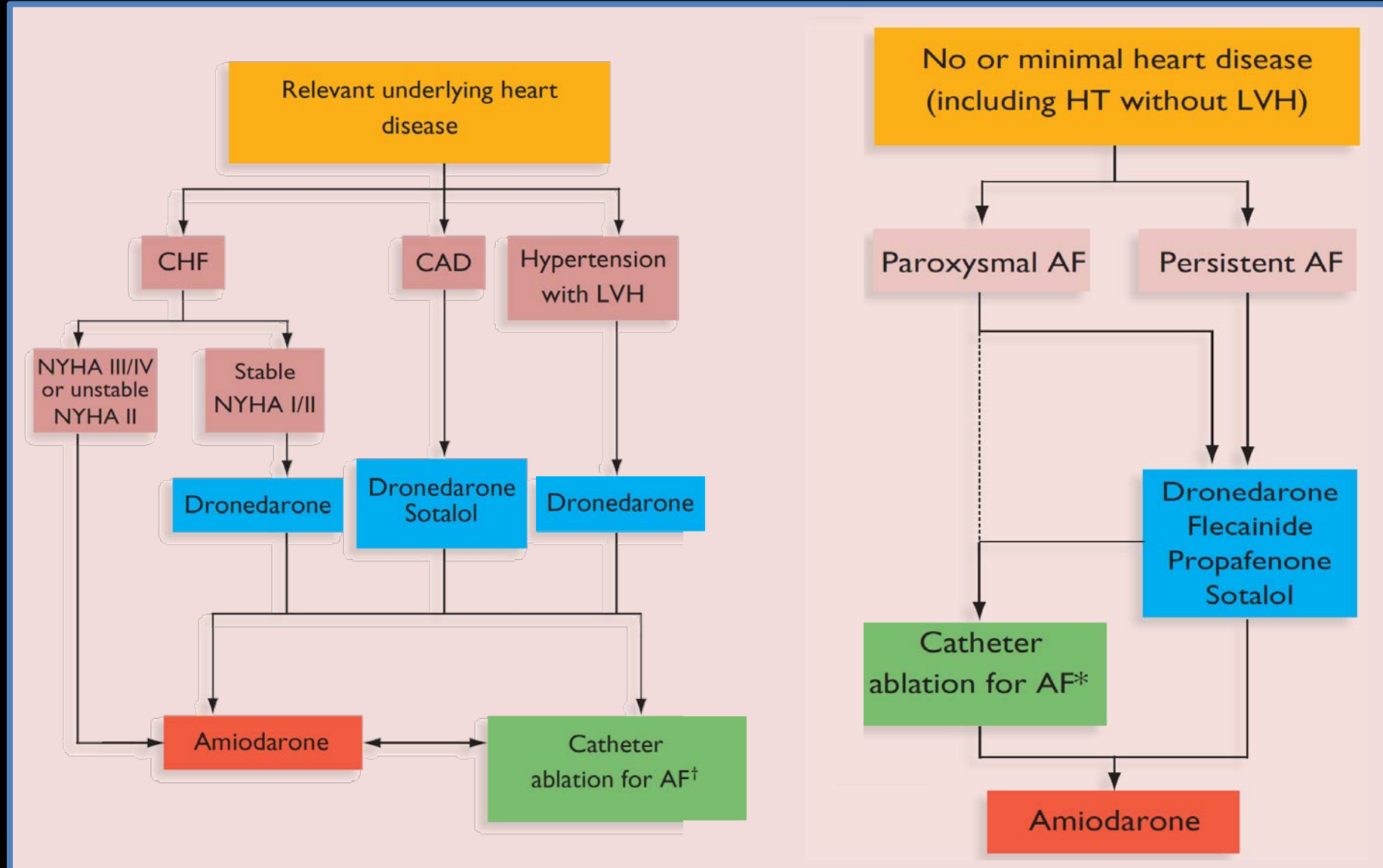


AAD vs ablation: maintenance of SR

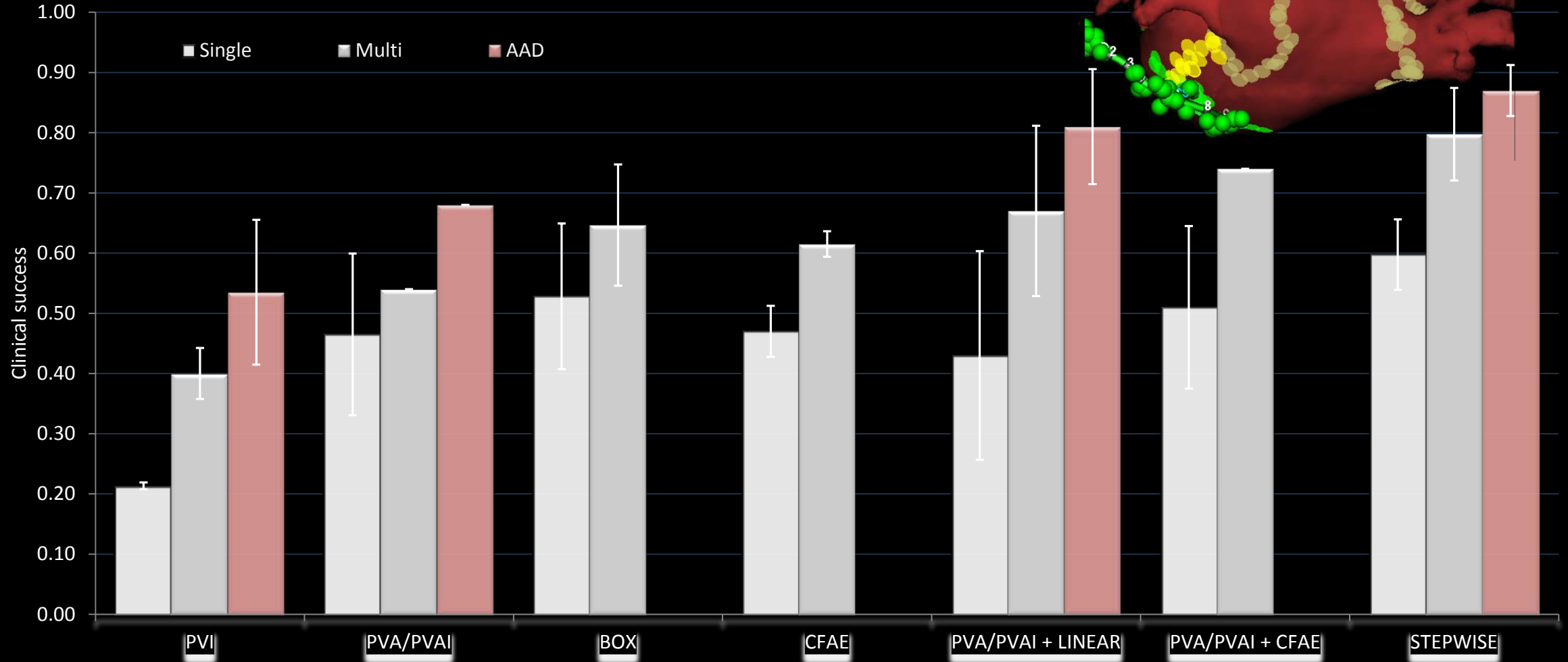
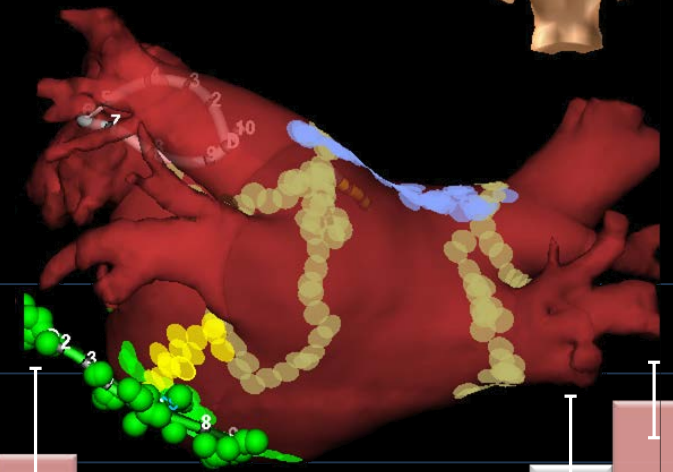


Jais, P. et al. Circulation 2008

ESC Guidelines



Outcomes of persistent AF ablation

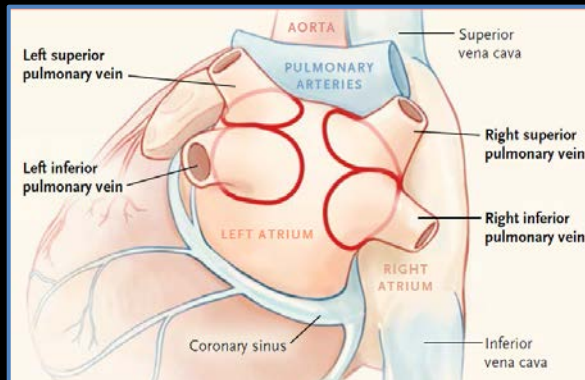


Brooks AG et al. Heart Rhythm 2010

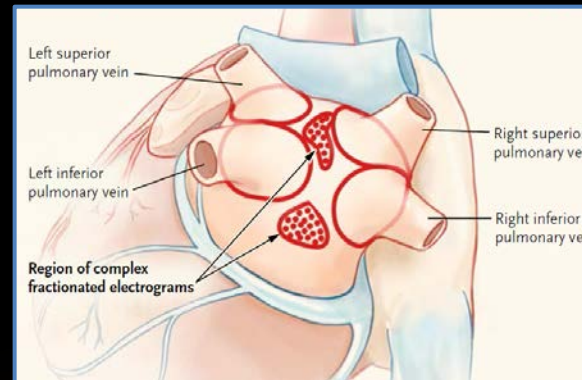
Approaches to Catheter Ablation for Persistent Atrial Fibrillation

Atul Verma, M.D., Chen-yang Jiang, M.D., Timothy R. Betts, M.D., M.B., Ch.B., Jian Chen, M.D., Isabel Deisenhofer, M.D., Roberto Mantovan, M.D., Ph.D., Laurent Macle, M.D., Carlos A. Morillo, M.D., Wilhelm Haverkamp, M.D., Ph.D., Rukshen Weerasooriya, M.D., Jean-Paul Albenque, M.D., Stefano Nardi, M.D., Endrj Menardi, M.D., Paul Novak, M.D., and Prashanthan Sanders, M.B., B.S., Ph.D., for the STAR AF II Investigators*

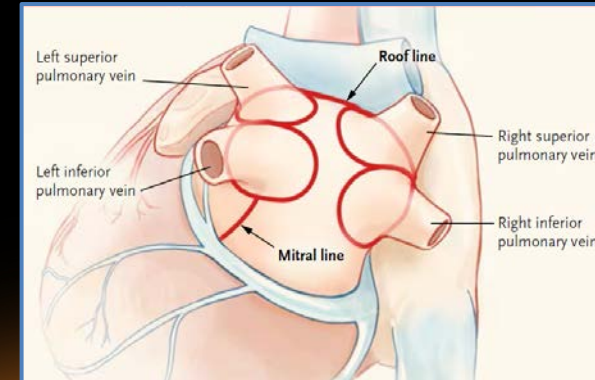
Pulmonary vein isolation



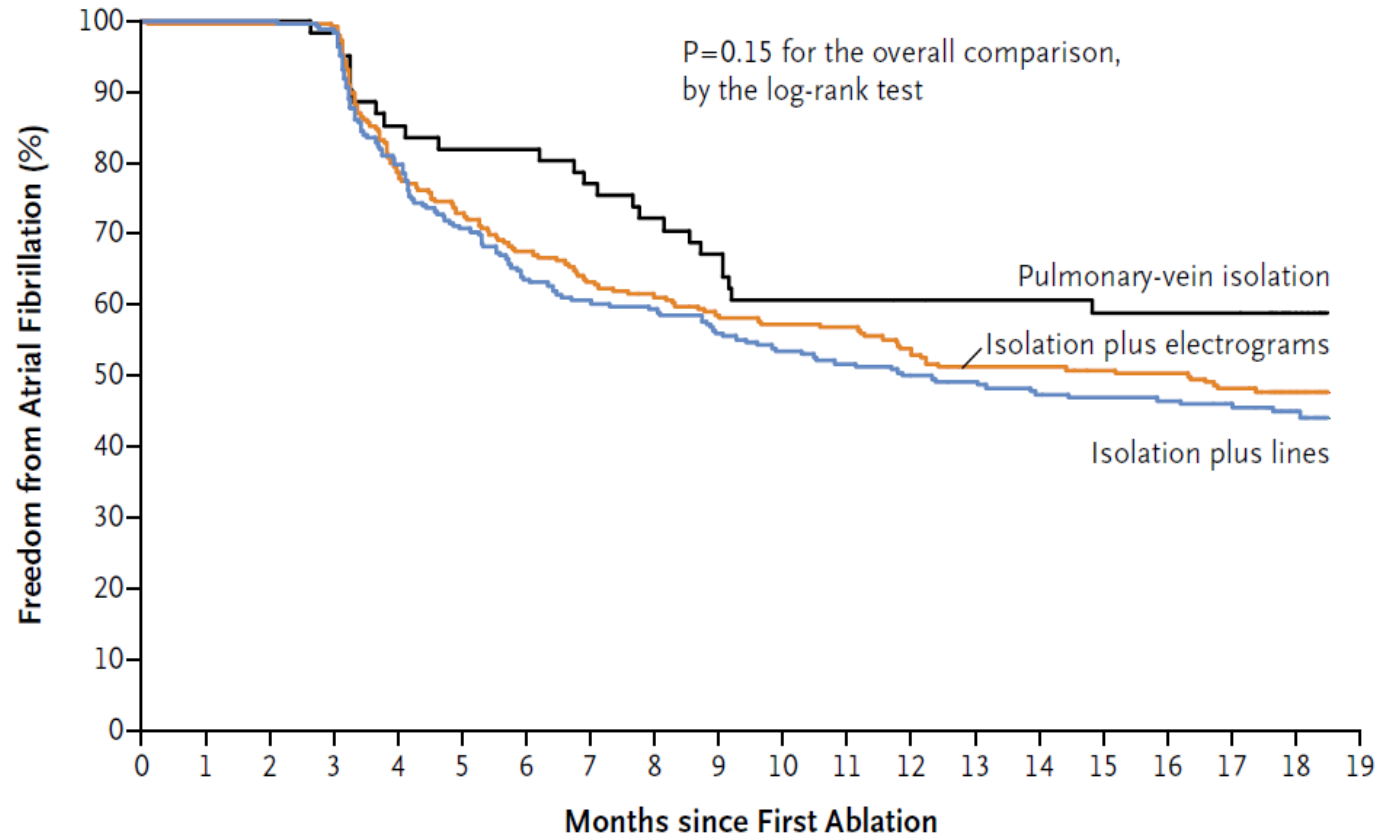
Pulmonary vein isolation and CFAE ablation



Pulmonary vein isolation and linear ablation



Persistent AF: no difference between strategies



No. at Risk

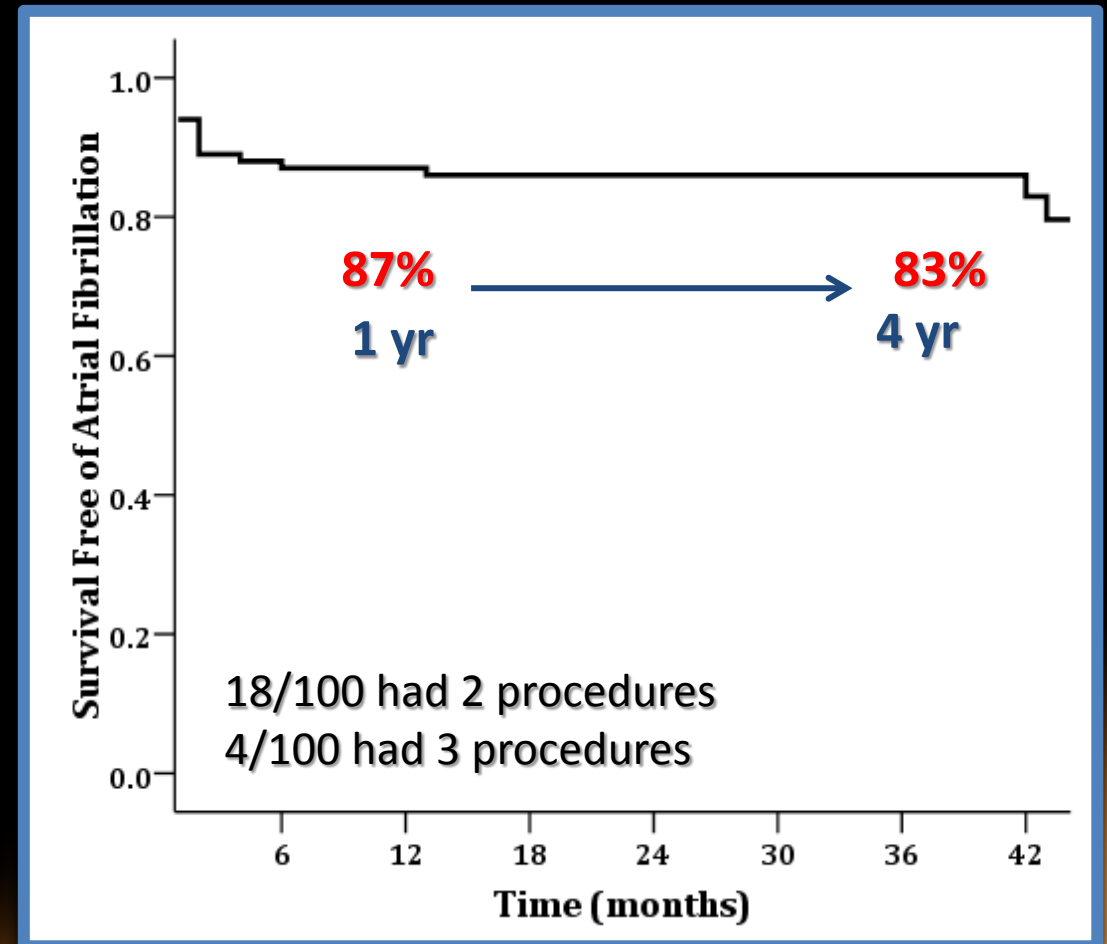
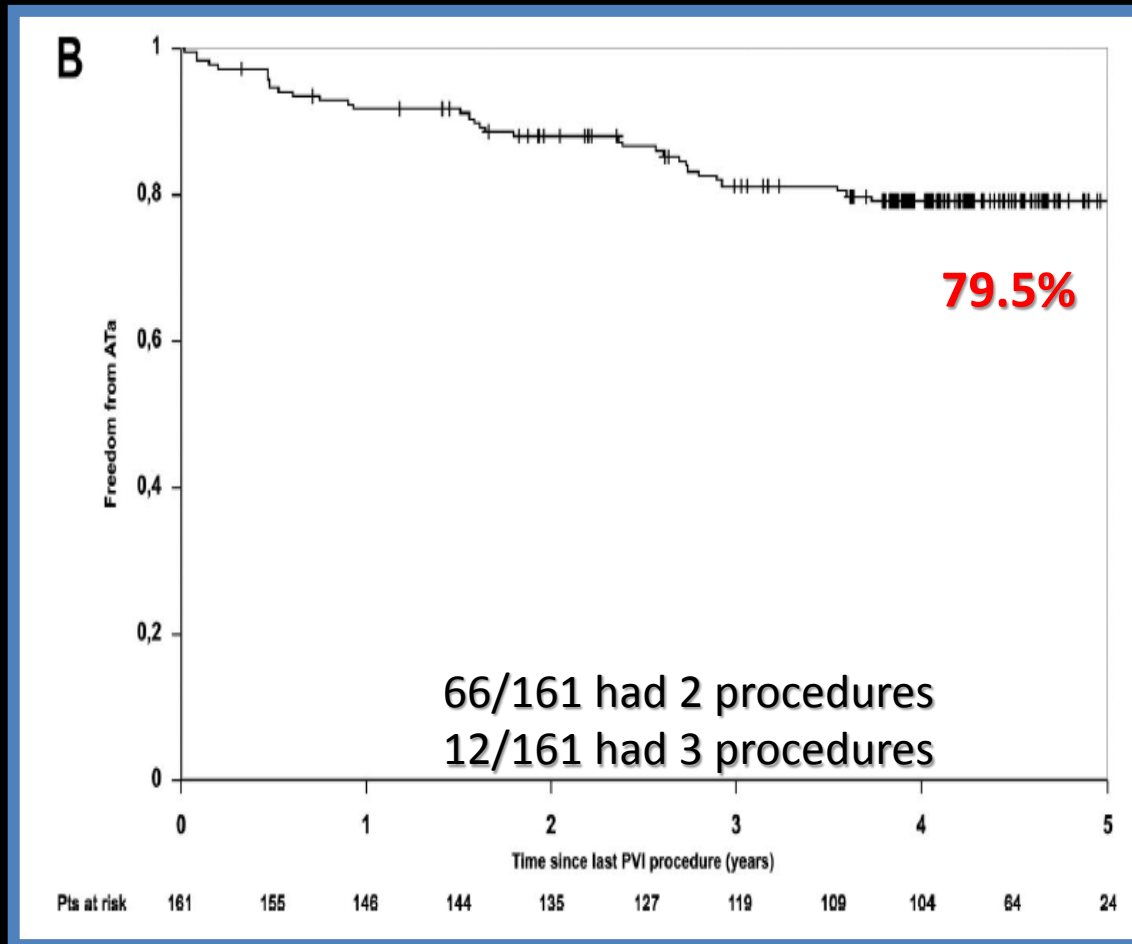
| | | | | | | |
|-----------------------------|-----|-----|-----|-----|-----|----|
| Pulmonary-vein isolation | 61 | 60 | 50 | 41 | 36 | 23 |
| Isolation plus electrograms | 244 | 242 | 161 | 137 | 124 | 72 |
| Isolation plus lines | 244 | 240 | 152 | 133 | 115 | 57 |

Long-term results of antral isolation for paroxysmal AF

Paroxysmal AF with antral isolation

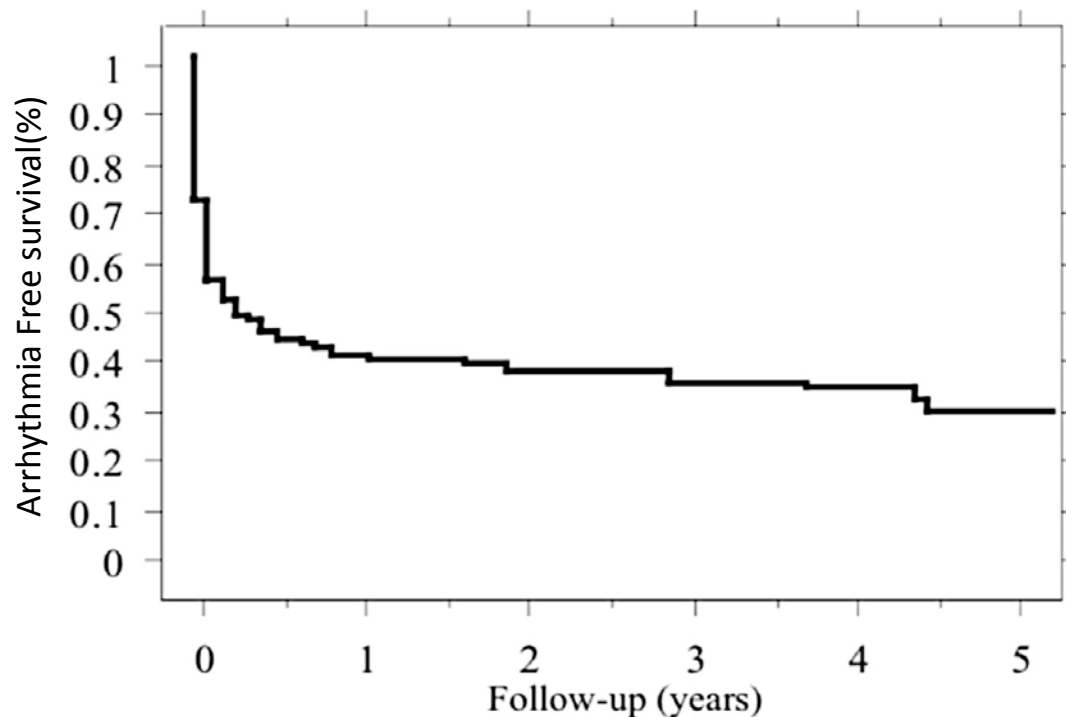
Ouyang et al, Circulation 2010

Medi et al, JCE 2011

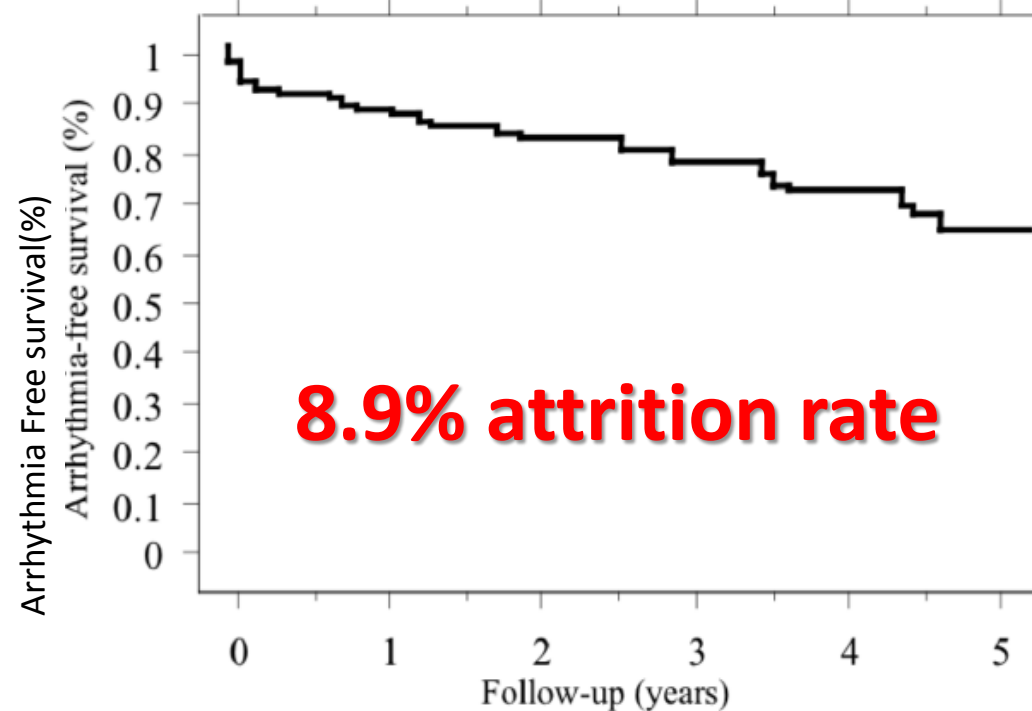


Long-term outcomes of AF ablation in mixed cohorts

Single Procedure



Multiple Procedure

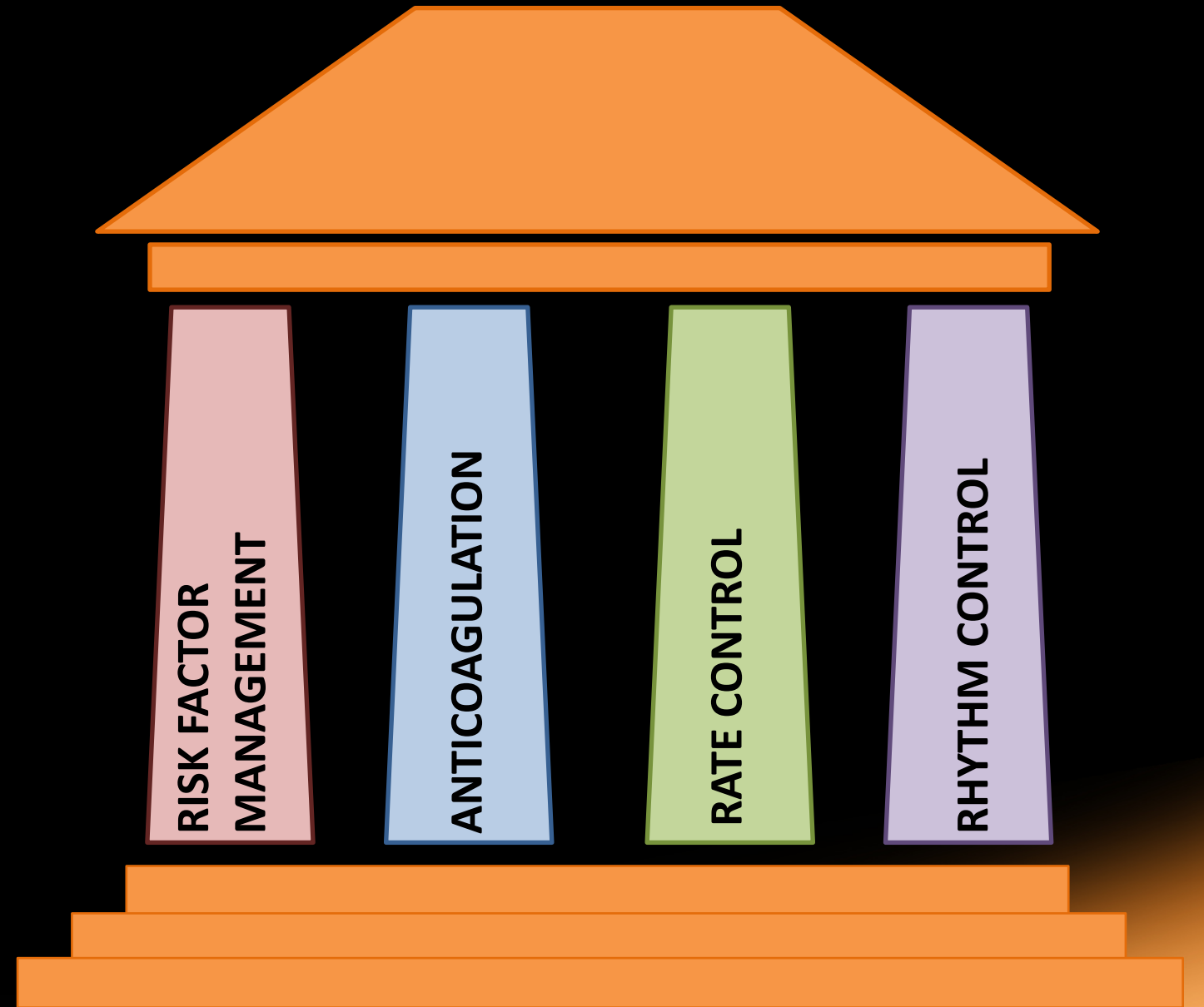


Predictors of recurrence after AF ablation

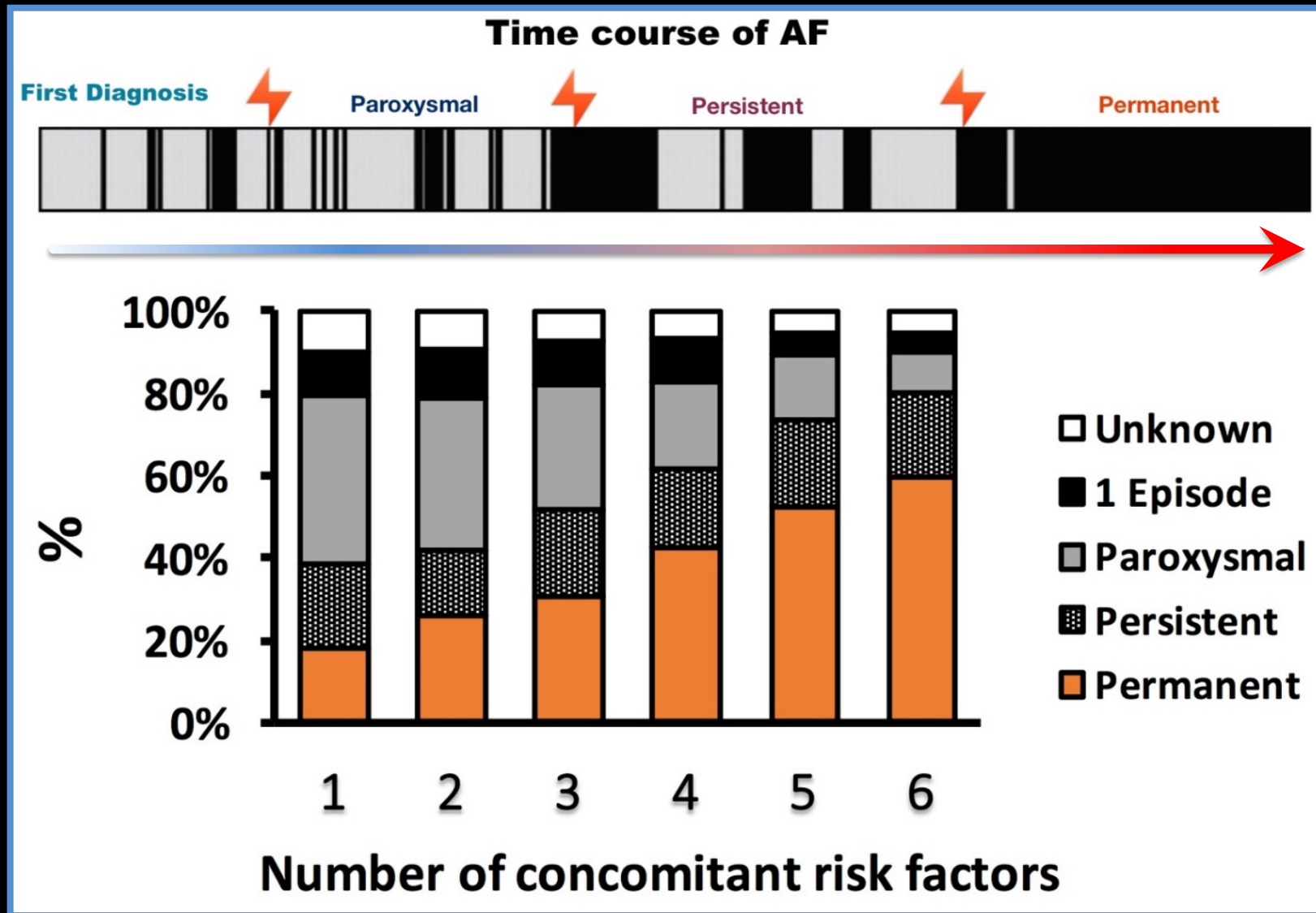
| AF Characteristics | |
|--------------------|--|
| Persistent AF | Tzou Circ 10, Cheema JICE 06 |
| Risk Factors | |
| Hypertension | Shah JCE 08, Sawhney AJC 09 |
| Diabetes | Wokhlu JCE 09 |
| OSA | Jongnarangsin JCE 08, Naruse HR 13, Fein JACC 13 |
| Hyperlipidemia | Shah JCE 08 |
| Obesity | Mainigi JCE 07 |
| Metabolic Syndrome | Berkowitsch PACE 12, Mohanty JACC 12 |
| Other Markers | |
| Left atrial size | Jiang JICE 06, Wokhlu JCE 09 |
| Aortic stiffness | Lau PLoS 13 |
| Pericardial Fat | Wong JACC 11 |

4th Pillar of AF management

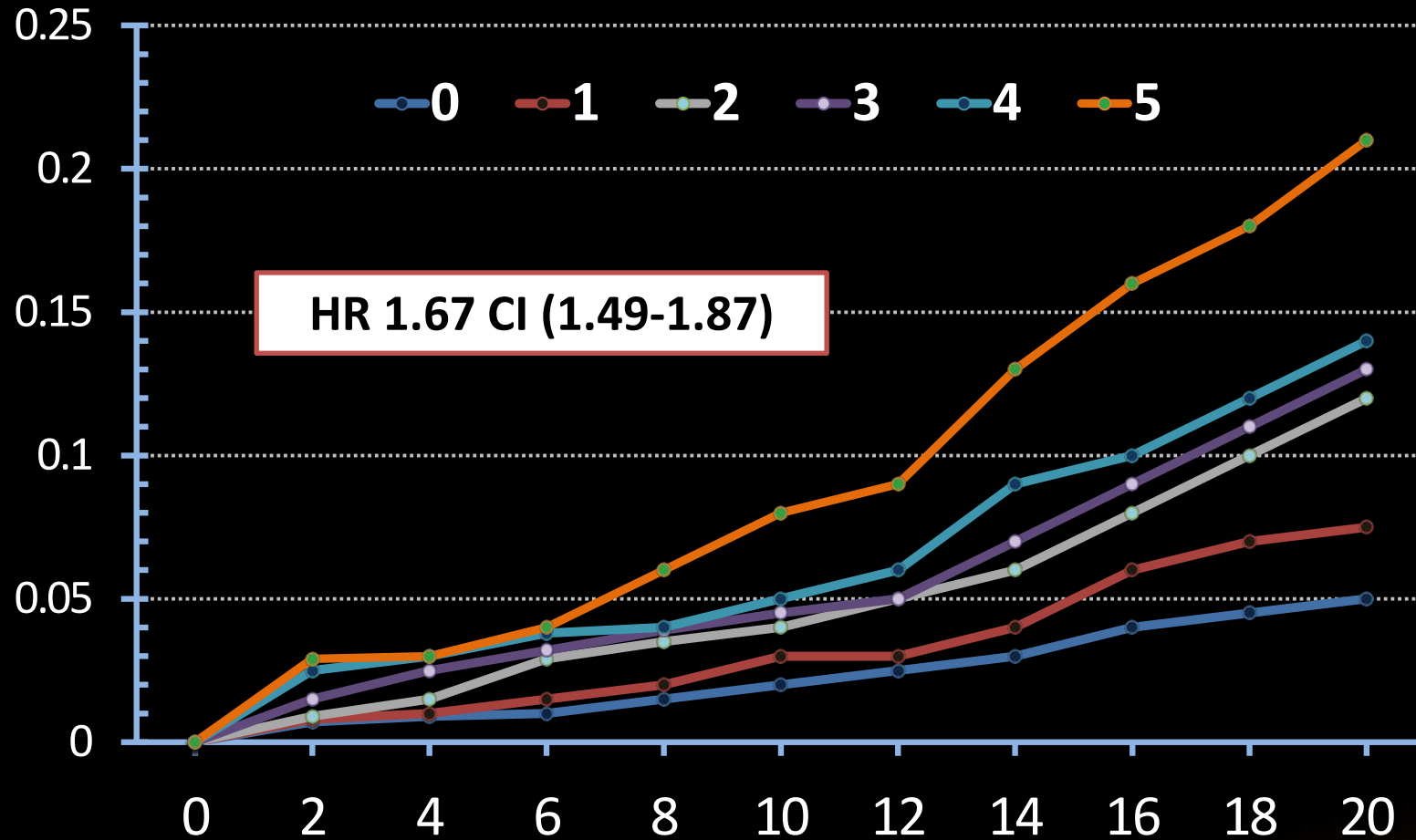
Risk Factor management



AF: A Progressive Disease



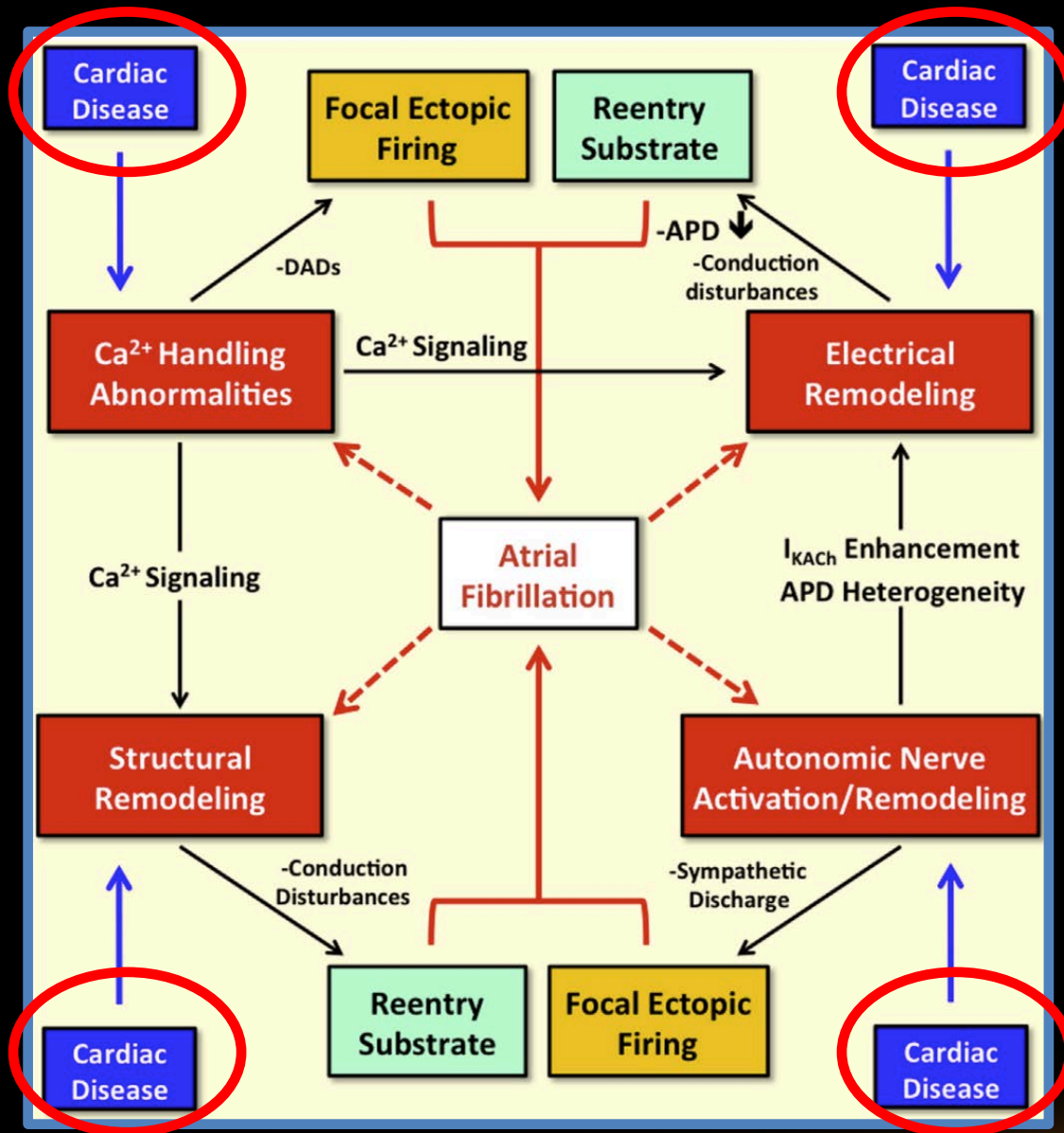
Probability of AF in Metabolic Syndrome



| HR (CI) | |
|------------------------------|----------------------------|
| Metabolic Syndrome Component | |
| Elevated waist circumference | 1.40 (1.23-1.59) |
| Elevated blood pressure | 1.95 (1.72-2.21) |
| Elevated triglycerides | 0.95 (0.84-1.09) |
| Low HDL cholesterol | 1.20 (1.06-1.37) |
| Impaired fasting glucose | 1.16 (1.03-1.31) |

Chamberlain et al, ARIC Study, AHJ 2010

Treat the causes of AF

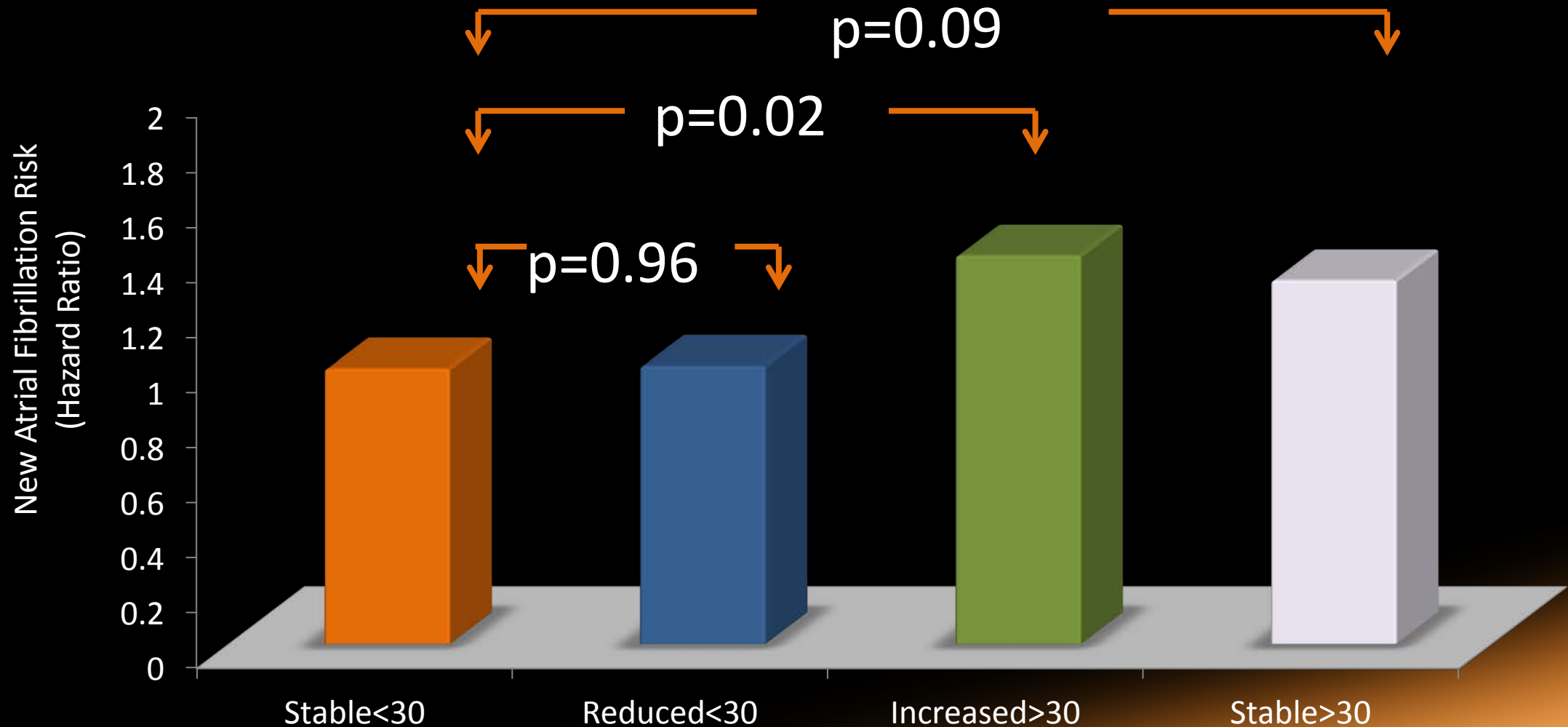


Nattel et al, JACC 2014

Risk Factors

Aging
Hypertension
Diabetes
Heart Failure
Alcohol Excess
Ischemic heart disease
Valvular heart disease
Obesity
Physical Inactivity
Obstructive Sleep Apnea
Pre-hypertension
Aortic Stiffness
Familial AF

Weight change and AF risk



WHS JACC 2010

Original Investigation

Effect of Weight Reduction and Cardiometabolic Risk Factor Management on Symptom Burden and Severity in Patients With Atrial Fibrillation

A Randomized Clinical Trial

Hany S. Abed, BPharm, MBBS; Gary A. Wittert, MBBch, MD; Darryl P. Leong, MBBS, MPH, PhD;
Masoumeh G. Shirazi, MD; Bobak Bahrami, MBBS; Melissa E. Middeldorp; Michelle F. Lorimer, BSc;
Dennis H. Lau, MBBS, PhD; Nicholas A. Antic, MBBS, PhD; Anthony G. Brooks, PhD;
Walter P. Abhayaratna, MBBS, PhD; Jonathan M. Kalman, MBBS, PhD; Prashanthan Sanders, MBBS, PhD

JAMA 2013

248 highly symptomatic AF patients with BMI>27 & WC >100 (male) or >90 (female)

Exclusions: Serious medical/psychiatric disorder; Recent weight loss program; Malabsorption disorder; Unstable INR; LVEF≤35%; DM – on insulin; Valvular disease; Endocrinopathy

150 Randomised

75 Control

75 Intervention

Aggressive Risk Factor Management

Weight Management and Exercise

- Initial target: >10% weight loss
 - Final target: BMI <27 kg/m²
 - Avoid weight fluctuation
 - Exercise: 30 minutes for 3-4x per week
- Increase up to 250 minutes per week

Hyperlipidaemia

- Initial lifestyle measures
- At 3 months: Start statins if LDL >2.6 mmol/L
- Add fibrates if TG >2.6 mmol/L
- Start fibrates if TG >5.6 mmol/L

Obstructive Sleep Apnoea

- Overnight sleep study
- CPAP if AHI ≥30; or ≥20/h with resistant HT or daytime somnolence
- Check adherence: regular CPAP machine data download

Hypertension

- Home BP diary: 2-3x daily
- Reduce salt
- Start ACEI or ARB
- Target: <130/80 mmHg (at rest)
<200/100 mmHg (at peak exercise)

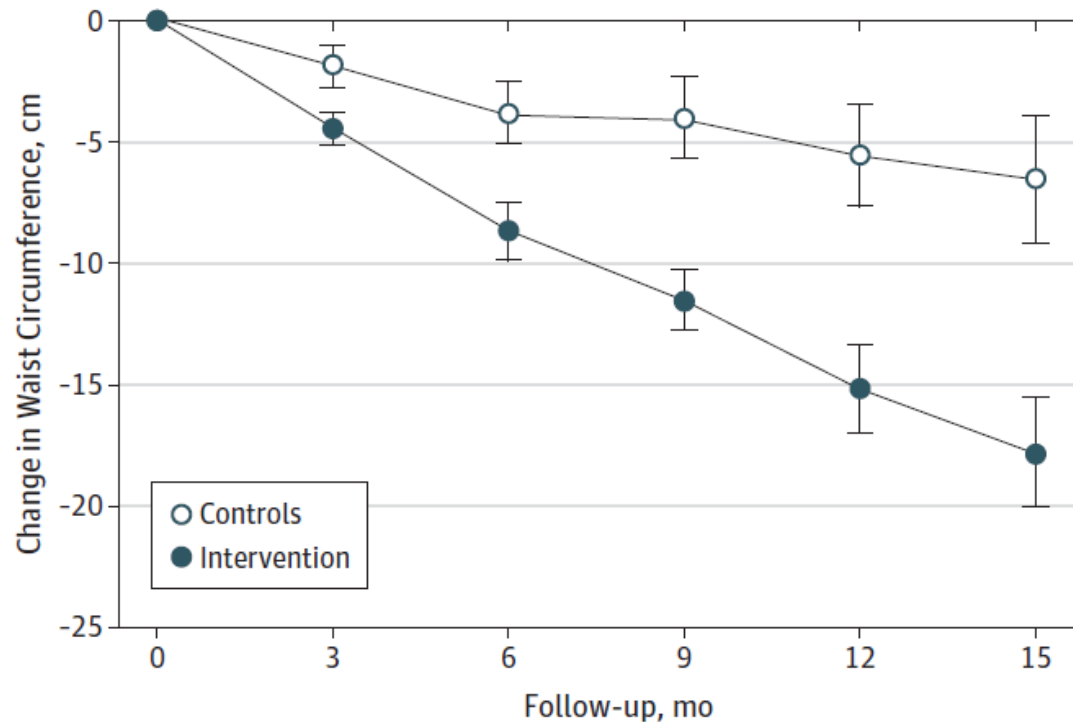
Diabetes

- Glucose tolerance test
- Lifestyle measures
- At 3 months: Metformin if HbA1c >6.5%
- Diabetes clinic or endocrine review

Smoking Cessation & Alcohol Abstinence (or reduction to 30g per week)

Changes in anthropometric measurements

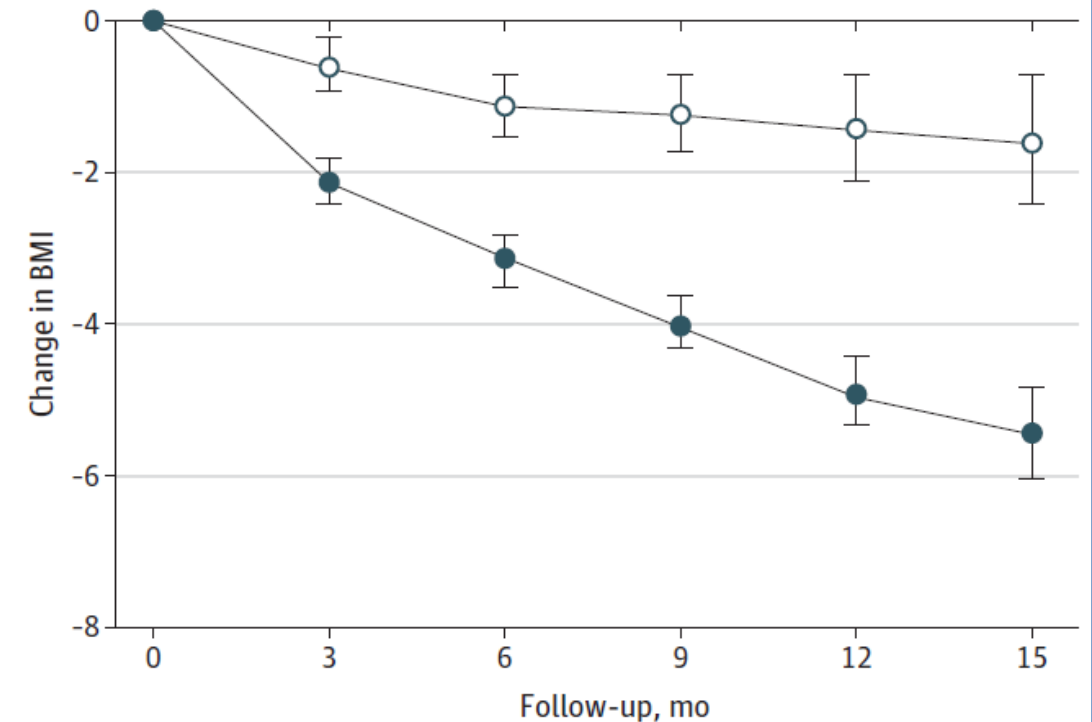
Waist Circumference



No. of patients

| | | | | | | |
|--------------|----|----|----|----|----|----|
| Controls | 75 | 75 | 72 | 61 | 52 | 39 |
| Intervention | 75 | 75 | 75 | 73 | 57 | 42 |

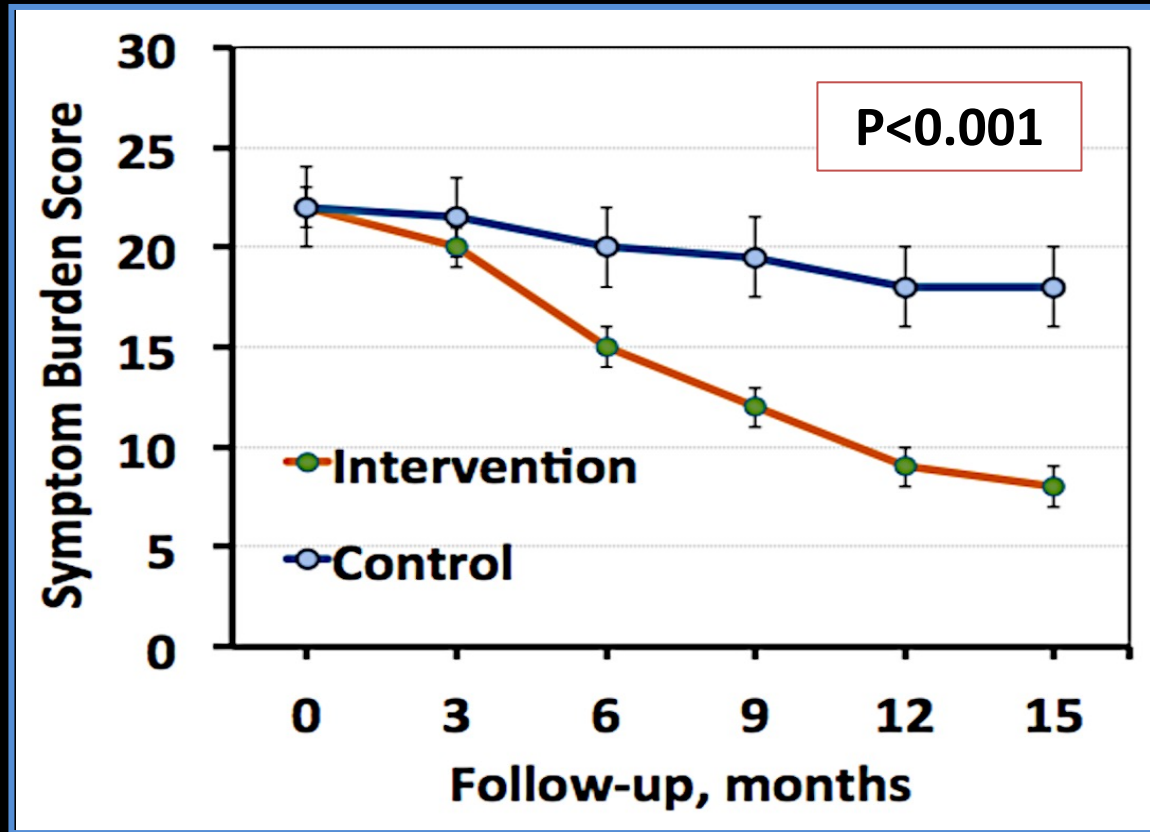
Body Mass Index



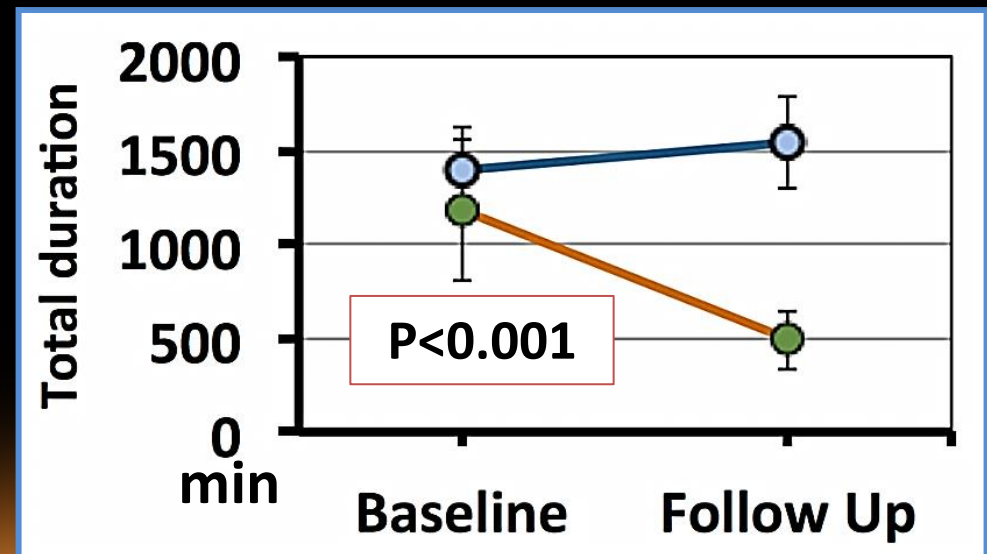
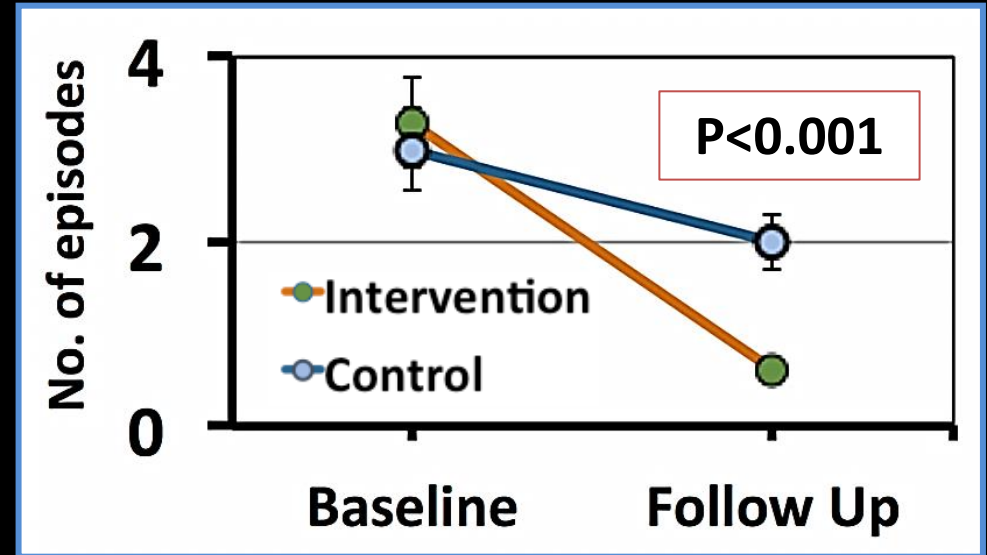
| | | | | | | |
|--------------|----|----|----|----|----|----|
| Controls | 75 | 75 | 72 | 61 | 52 | 39 |
| Intervention | 75 | 75 | 75 | 73 | 57 | 42 |

Effect of Short-Term Weight Loss

Symptom Burden Score



Continuous Monitoring



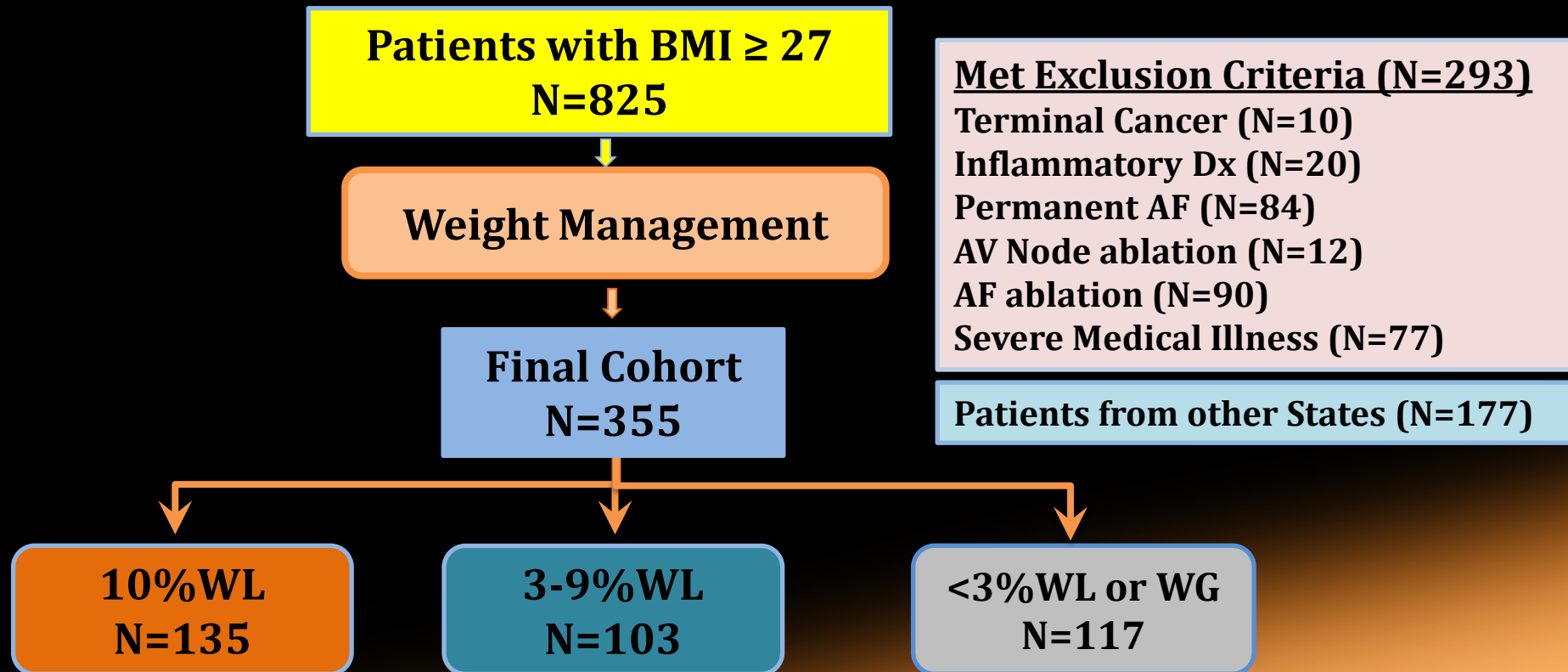
Long-Term Effect of Goal-Directed Weight Management in an Atrial Fibrillation Cohort



A Long-Term Follow-Up Study (LEGACY)

Rajeev K. Pathak, MBBS,* Melissa E. Middeldorp,* Megan Meredith,* Abhinav B. Mehta, MAcST,†
Rajiv Mahajan, MD, PhD,* Christopher X. Wong, MBBS, PhD,*‡ Darragh Twomey, MBBS,* Adrian D. Elliott, PhD,*§
Jonathan M. Kalman, MBBS, PhD,¶ Walter P. Abhayaratna, MBBS, PhD,# Dennis H. Lau, MBBS, PhD,*
Prashanthan Sanders, MBBS, PhD*

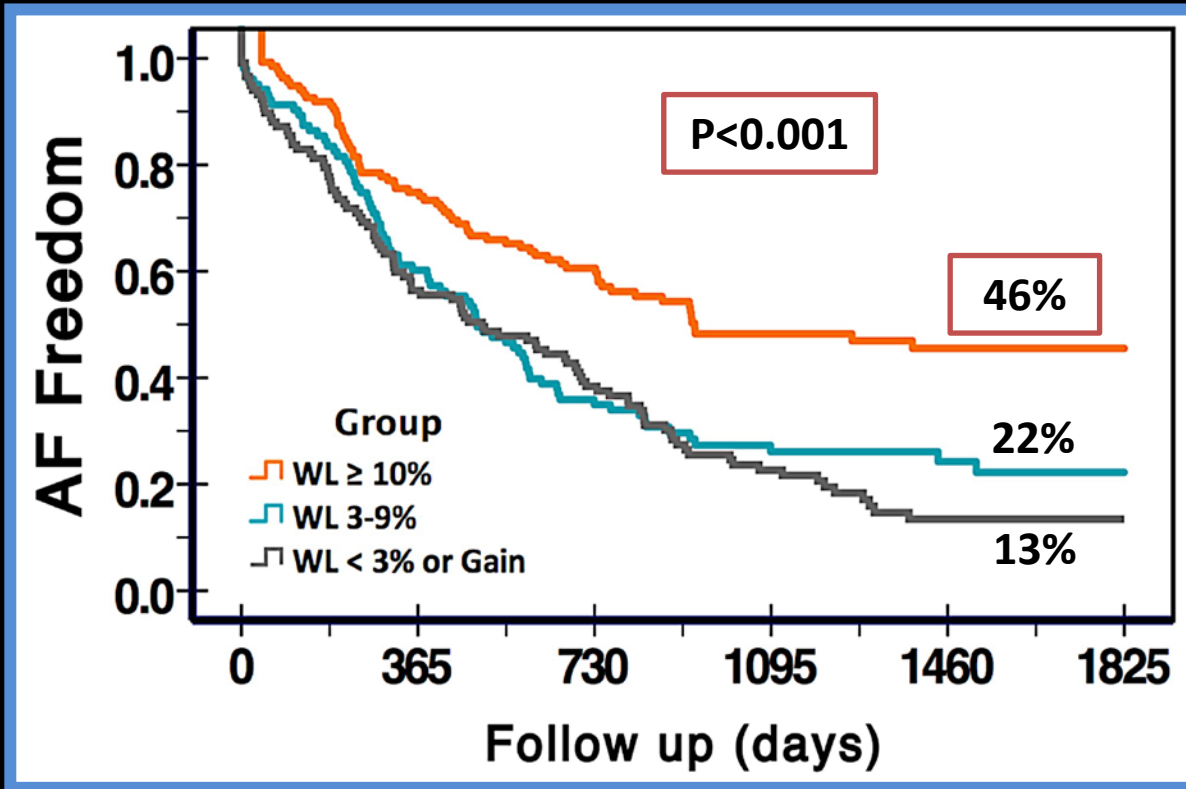
JACC 2015



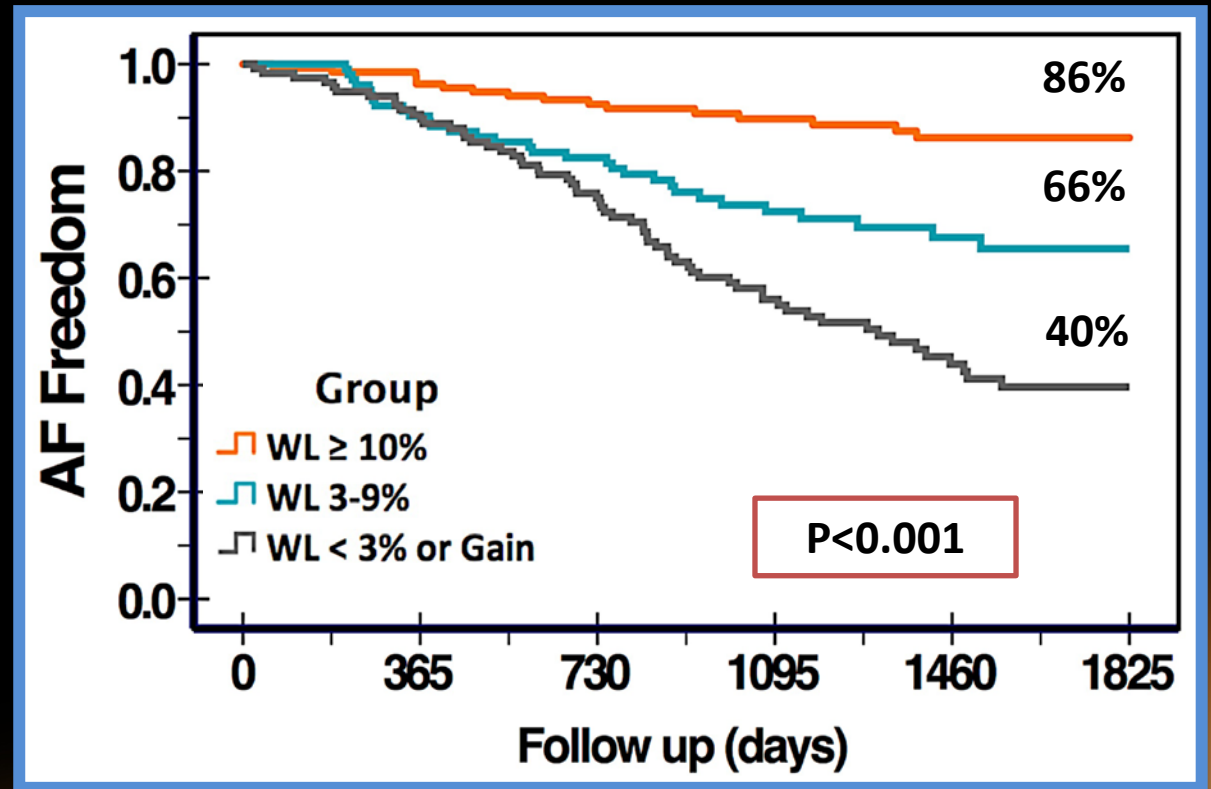
AF freedom: drug & ablation free

$\geq 10\%$ weight loss was associated with AF free survival: HR 5.7 [95% CI: 3.3-10.1] (P<0.001)

Without ablation or AAD



With ablation and/or AAD

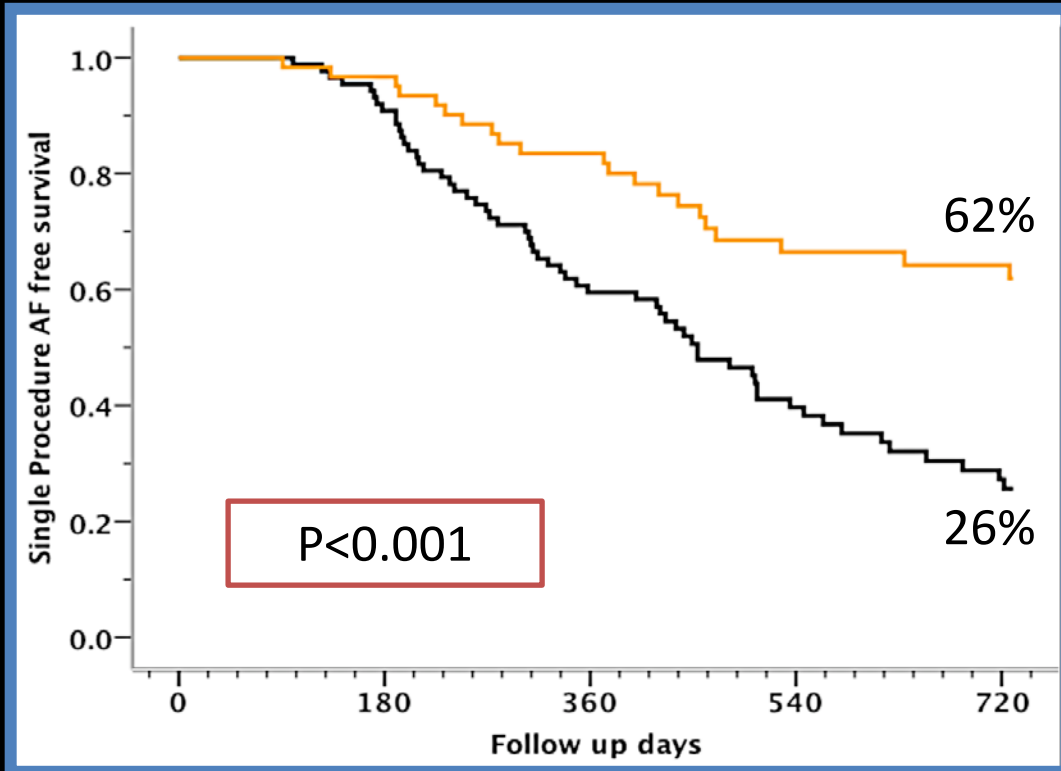


Aggressive Risk Factor Reduction Study for Atrial Fibrillation and Implications for the Outcome of Ablation

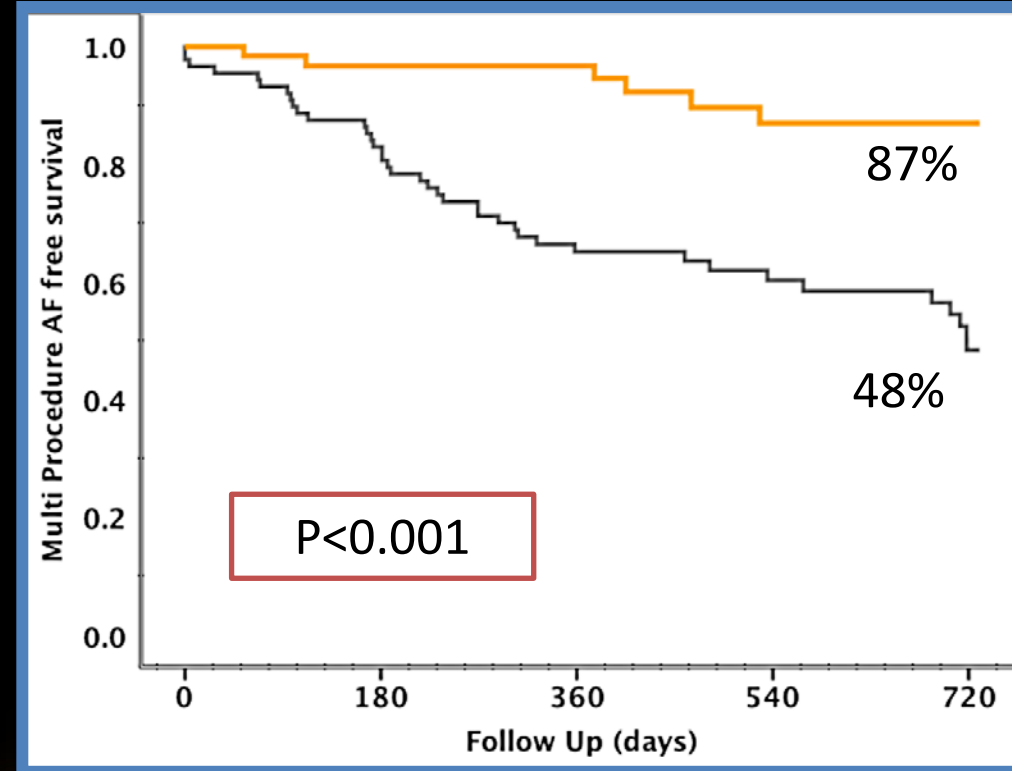
The ARREST-AF Cohort Study

RFM was associated with AF-free survival: HR 4.8 [95% CI: 2.04-11.4] (P<0.001)

Single procedure success



Multiple procedure success



RFM
Control

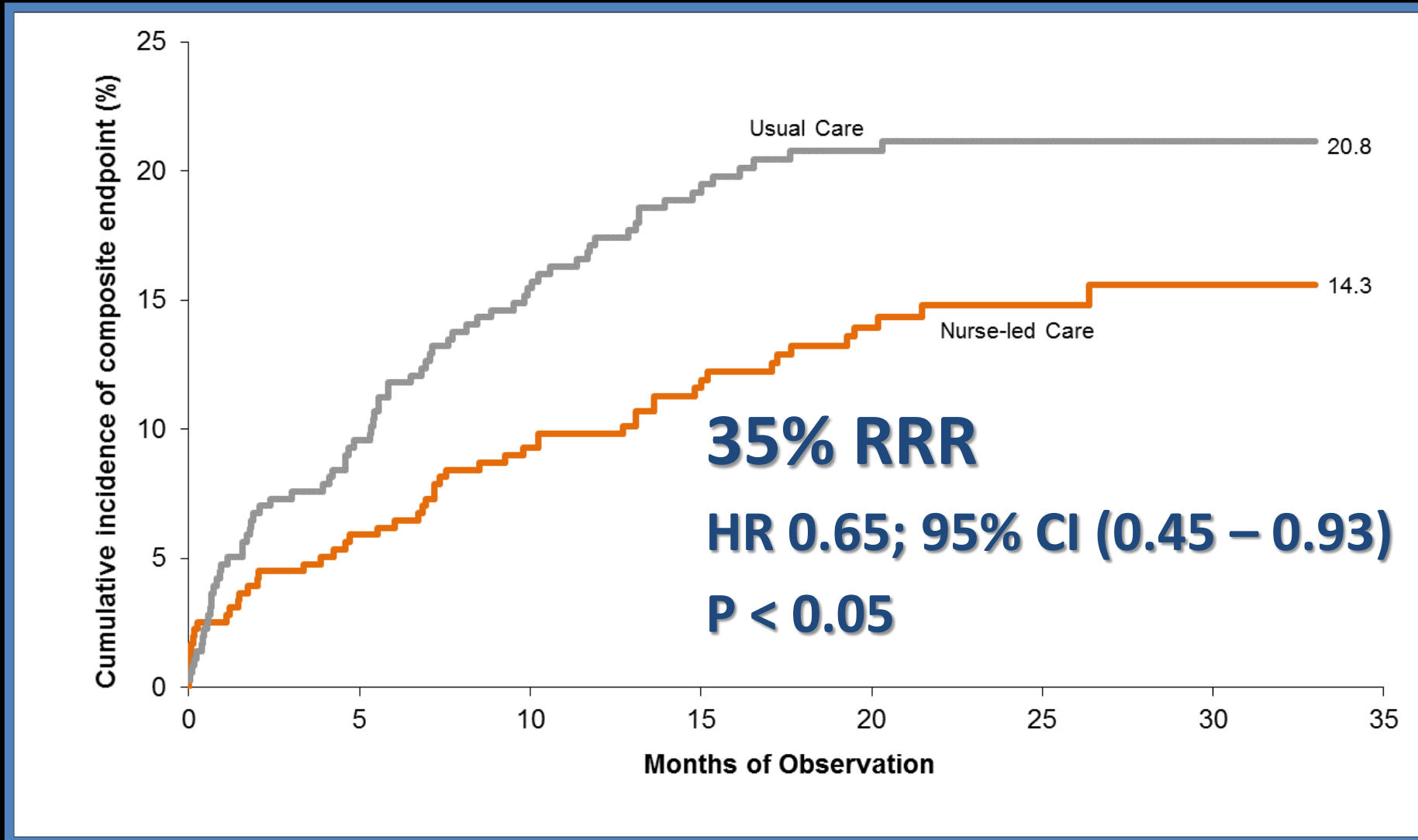
AF Care Delivery

Nurse-led care vs. usual care for patients with atrial fibrillation: results of a randomized trial of integrated chronic care vs. routine clinical care in ambulatory patients with atrial fibrillation

**Jeroen M.L. Hendriks^{1,2*}, Rianne de Wit², Harry J.G.M. Crijns¹,
Hubertus J.M. Vrijhoef⁴, Martin H. Prins³, Ron Pisters¹,
Laurent A.F.G. Pison¹, Yuri Blaauw¹, and Robert G. Tieleman⁵**

Integrated Care Management in AF would improve care and patient outcomes in patients with AF

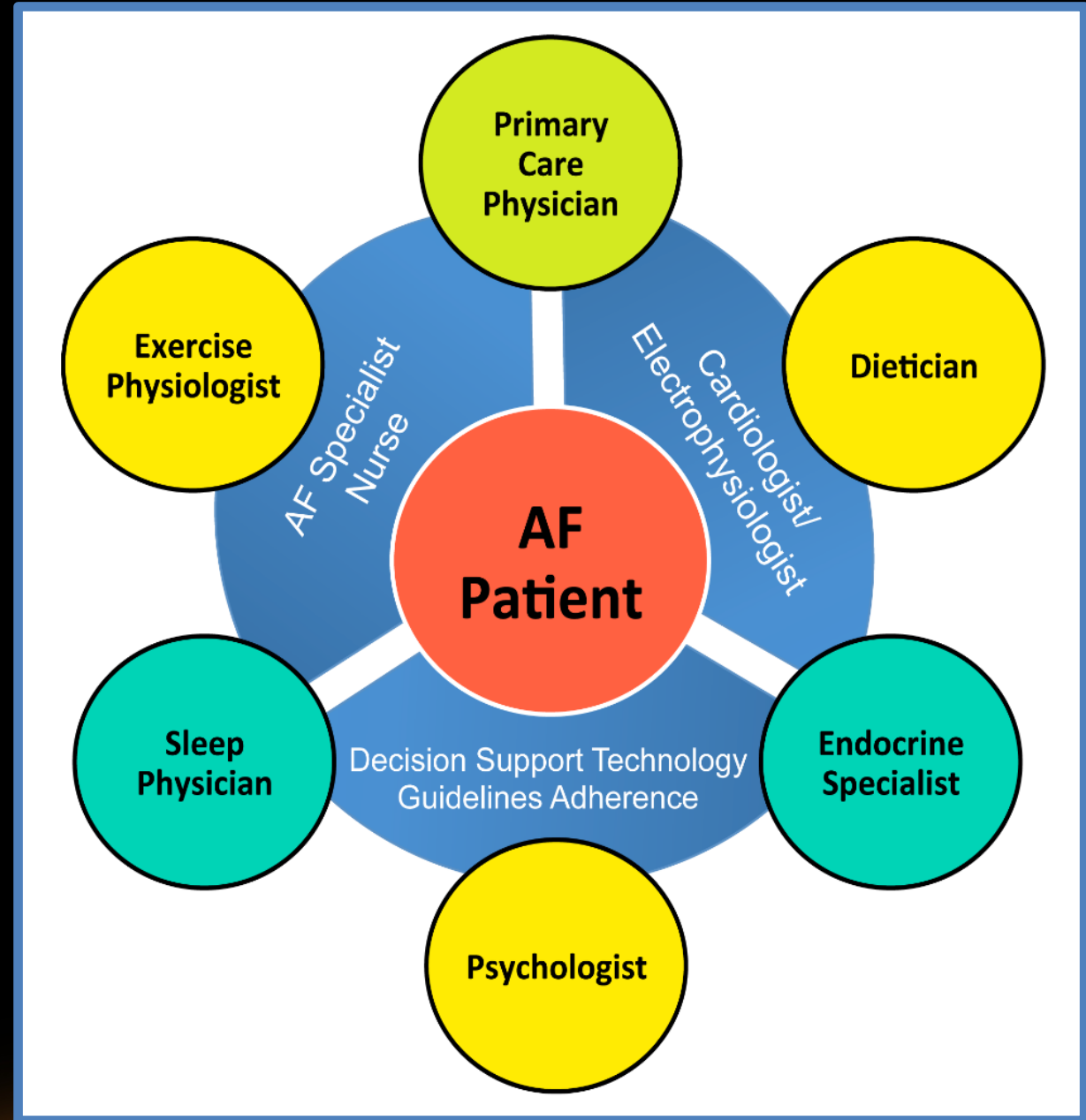
Composite Endpoint: Cardiovascular Hospitalisation or Death



Hendriks JM et al. Eur Heart J 2012

A new approach to manage AF: Integrated Care

Lau DH et al, Eur Heart J (In Press)



Management of AF

- Stroke prevention is essential
- Evolving role of catheter ablation (outside of symptomatic AF)
- Treating risk factors is an essential component of AF Mx
- Appropriate strategies needed to engage and educate

