# The 10 Most Important AF-Stroke Clinical Research Questions:

## CSPIN and More

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# Disclosures

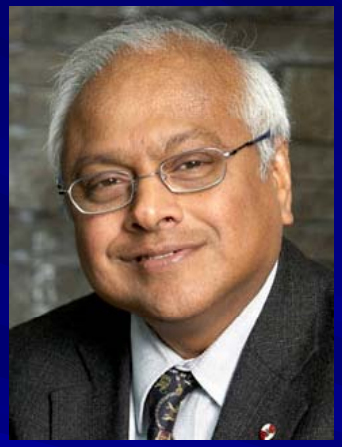
- Research grants and speaking fees
  - Boston Scientific, Medtronic, St. Jude Medical
  - Bayer, Bristol-Meyers-Squibb, Boehringer-Ingelheim

  - Mid-career investigator, Heart and Stroke Foundation of Ontario
  - Chair, CSPIN network

# Canadian AF-Stroke Research

C-SPIN
Canadian Stroke Prevention Intervention Network



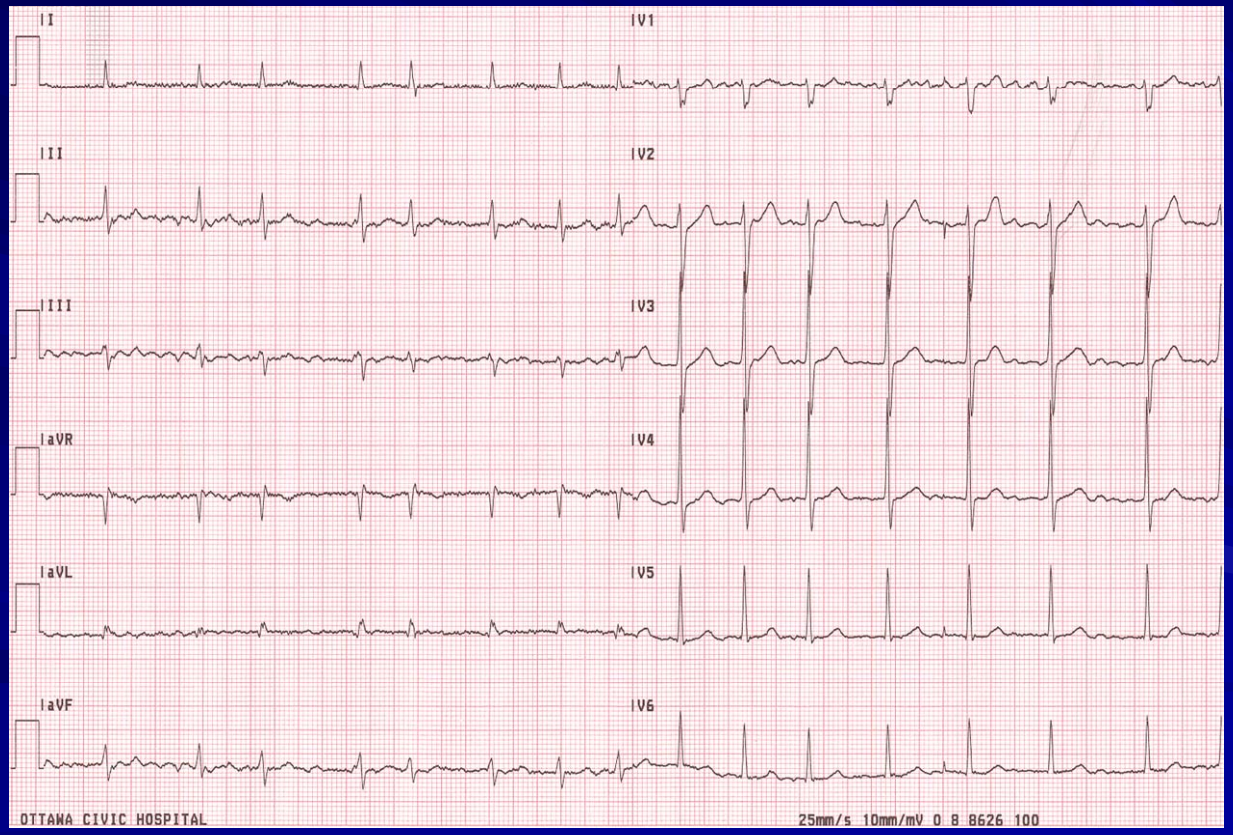




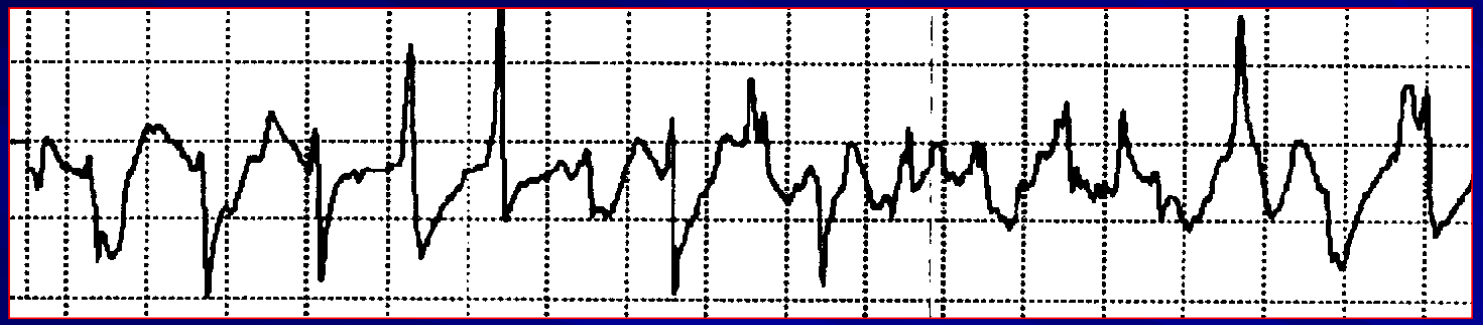

# The Big AF and Stroke Questions

- 1. What is atrial fibrillation?
- 2. What is stroke?
- 3. How does atrial fibrillation cause stroke?
- b. Does AF cause stroke, or is it simply a risk marker?
- 4. How does one prevent AF-related stroke?

# Atrial Fibrillation in Framingham

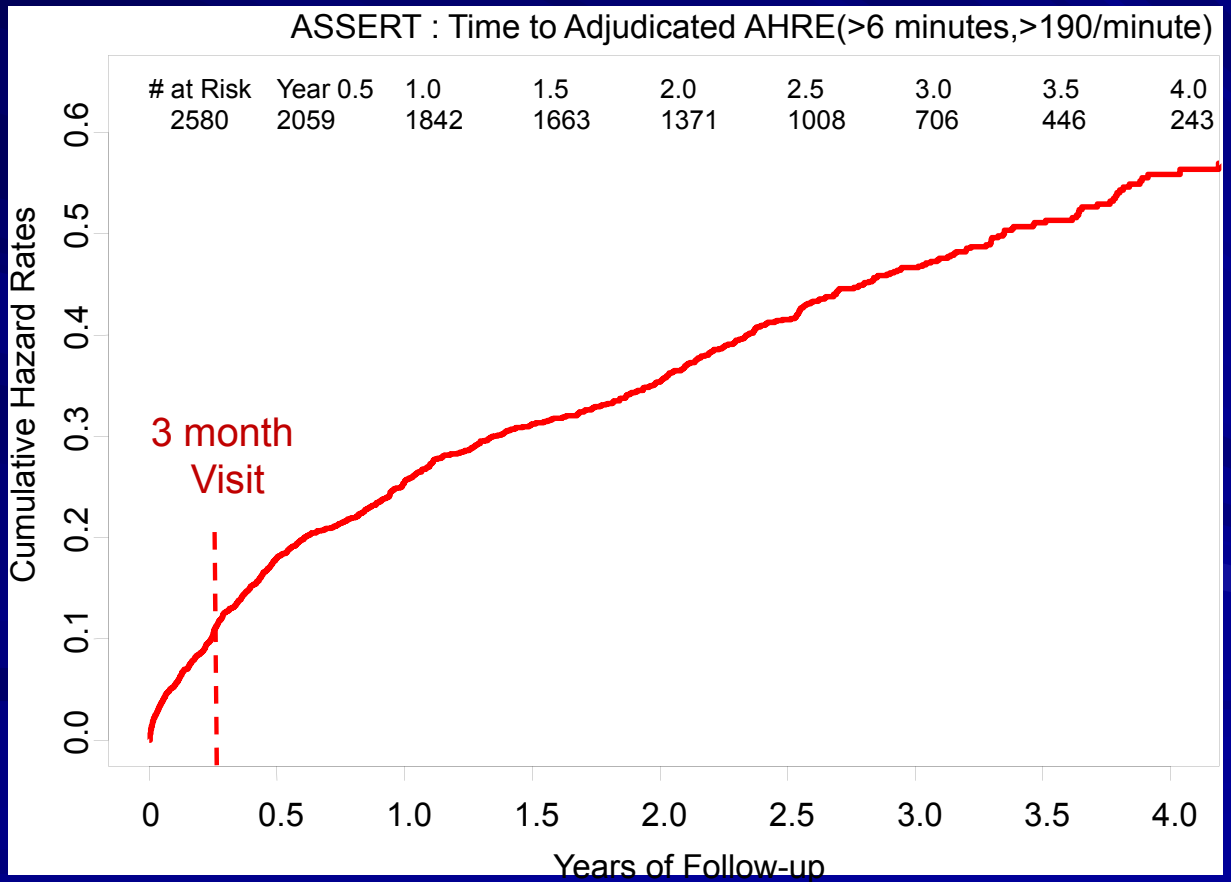


# Sub-Clinical AF Detected by Pacemakers



1. Mostly asymptomatic
2. Relatively short episodes detected only with long-term, continuous monitoring

# Time to First Device-Detected Atrial Tachyarrhythmia > 6 min, >190 bpm



# Are brief episodes of AF detected with long-term continuous monitoring associated with stroke?

How are they related?
How long must they be to increase stroke risk?

# ASSERT: Clinical Outcomes

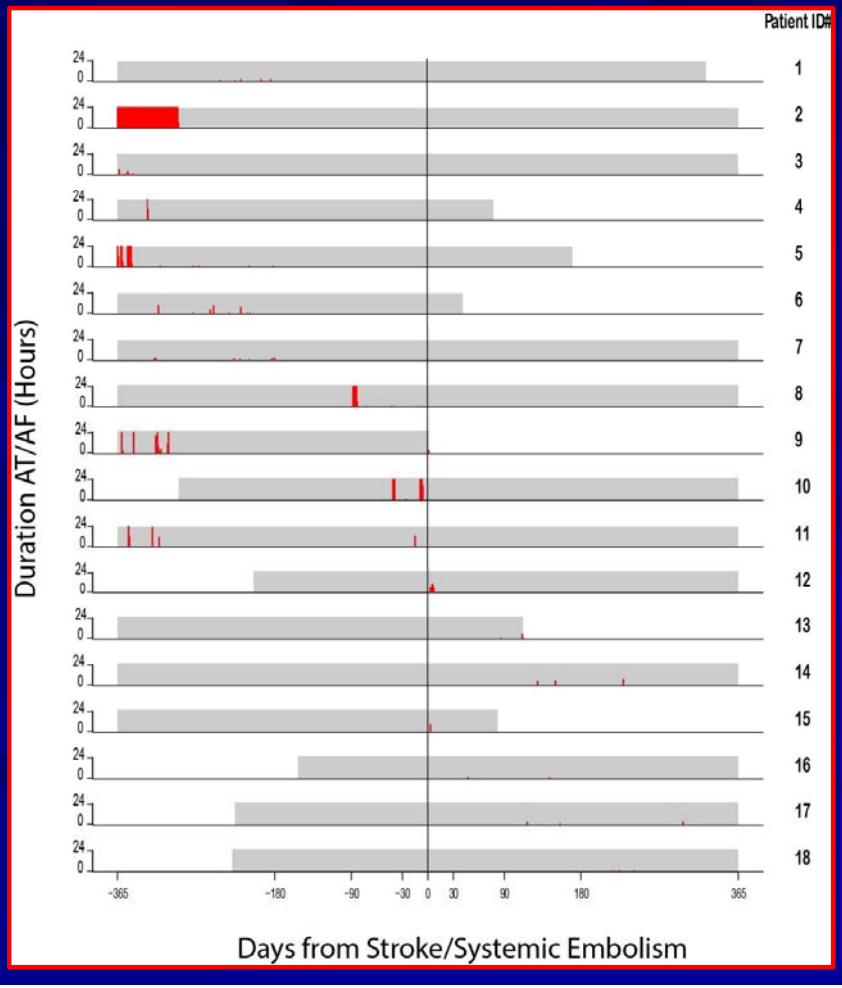
Healey JS, NEJM 2012

| Event | Device-Detected Atrial Tachyarrhythmia | | | | Device-Detected Atrial Tachyarrhythmia Present vs. absent | | |
|---|---|---|---|---|---|---|---|
| | Absent N=2319 | | Present N= 261 | | | | |
| | events | %/year | events | %/ year | RR | 95% CI | p |
| Ischemic Stroke or Systemic Embolism | 40 | 0.69 | 11 | 1.69 | 2.49 | 1.28 – 4.85 | 0.007 |
| Vascular Death | 153 | 2.62 | 19 | 2.92 | 1.11 | 0.69 – 1.79 | 0.67 |
| Stroke / MI / Vascular Death | 206 | 3.53 | 29 | 4.45 | 1.25 | 0.85 – 1.84 | 0.27 |
| Clinical Atrial Fibrillation or Flutter | 71 | 1.22 | 41 | 6.29 | 5.56 | 3.78 – 8.17 | <0.001 |

# Clinical Outcomes in ASSERT

| $CHADS_2$ Score | Total Pts. | Sub-clinical Atrial Tachyarrhythmia between enrollment and 3 months | | | | | | Sub-clinical Atrial Tachyarrhythmia Present vs. absent | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Present | | | Absent | | | | | |
| | | Pts. | events | %/year | Pts. | events | %/year | HR | 95% CI | P trend |
| 1 | 600 | 68 | 1 | 0.56 | 532 | 4 | 0.28 | 2.11 | 0.23 – 18.9 | 0.35 |
| 2 | 1129 | 119 | 4 | 1.29 | 1010 | 22 | 0.77 | 1.83 | 0.62 – 5.40 | |
| >2 | 848 | 72 | 6 | 3.78 | 776 | 18 | 0.97 | 3.93 | 1.55 – 9.95 | |

# Relation between AF and Stroke

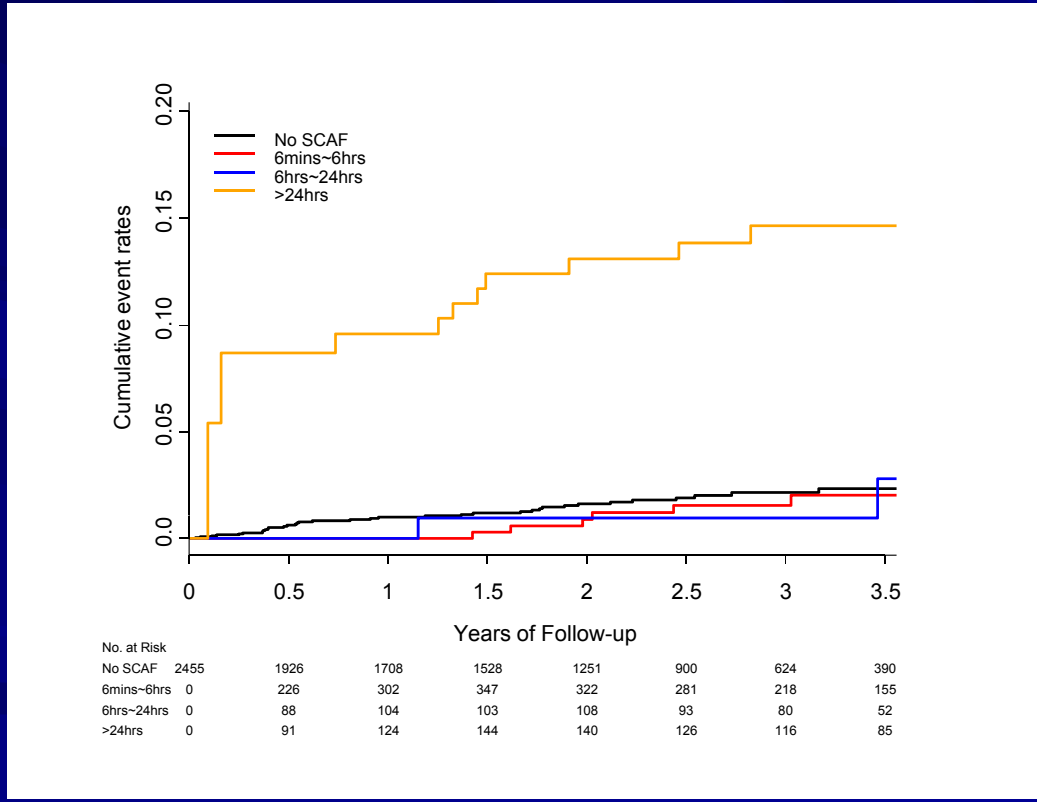



M. Brambatti
Circulation 2014

# SCAF, Stroke Sub-Type and Severity in ASSERT

| | Patients without SCAF | Patients with SCAF | P-value |
|---|---|---|---|
| | | | |
| Stroke Sub-Type | | | |
| Cardio-embolic | 6.7% | 35.7 | |
| Large Artery | 3.3% | 7.1% | |
| Lacunar | 56.7% | 35.7% | |
| Undetermined | 33.4% | 21.4% | 0.30 |
| Stroke Severity | | | |
| 7-day Rankin | 3.1 ± 1.8 | 3.7 ± 2.0 | 0.37 |
| 30-day Rankin | 2.6 ± 1.8 | 3.0 ± 2.0 | 0.64 |

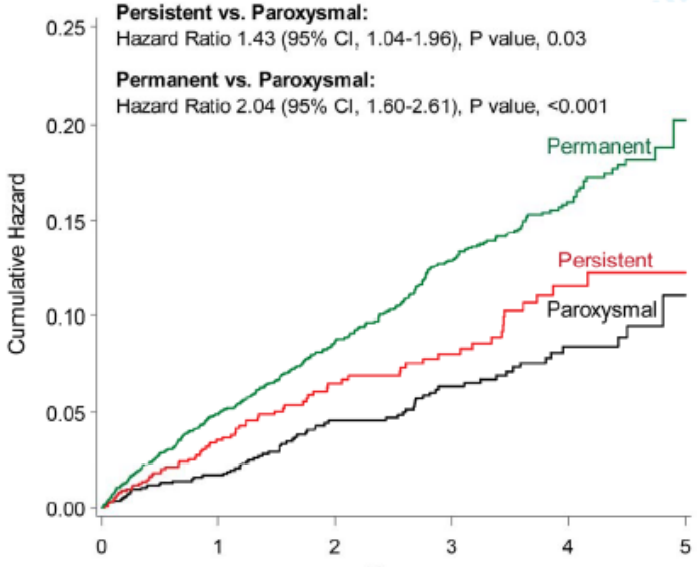
# Risk of ischemic stroke or systemic embolism according to duration of SCAF




Unpublished from ASSERT

# ACTIVE-AVERROES

N=6563, ASA-treated

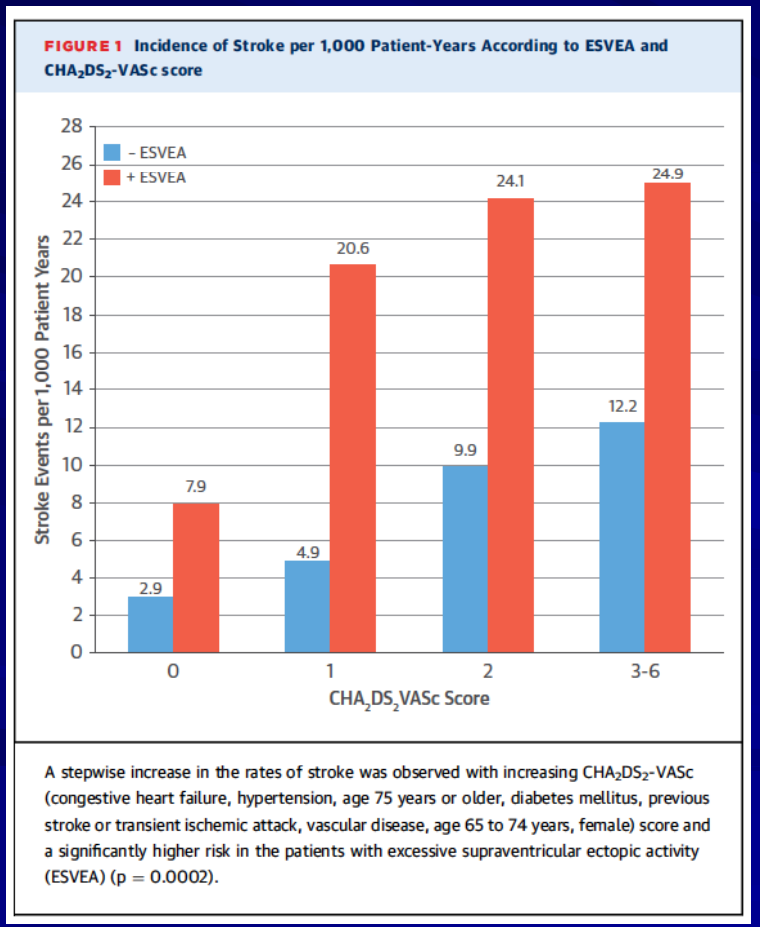



| No. at Risk | | | | | | |
|---|---|---|---|---|---|---|
| Paroxysmal | 1576 | 1226 | 766 | 604 | 310 | 17 |
| Persistent | 1136 | 846 | 502 | 386 | 174 | 7 |
| Permanent | 3854 | 2909 | 1975 | 1505 | 685 | 31 |

Figure 1. Kaplan-Meier cumulative hazard rates of embolic events according to pattern of AF occurence.

**Venassche T. Eur Heart J. 2014**

# Copenhagen Heart Study

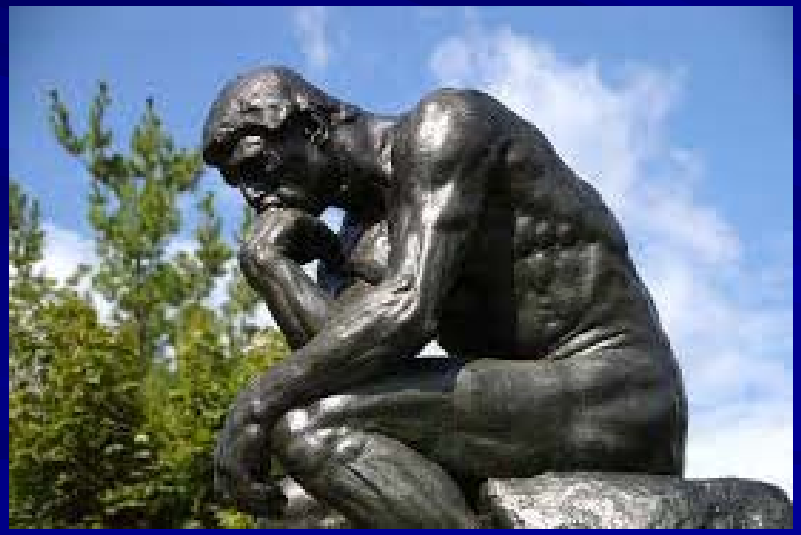



- JACC 2015;66:232-41
- n=678, age 55-75 yrs
- Median f/u 14 years
- ESVEA on baseline Holter defined as:
  - ≥30 APBs/h (≥720 APBs/d) or atrial runs ≥20 beats

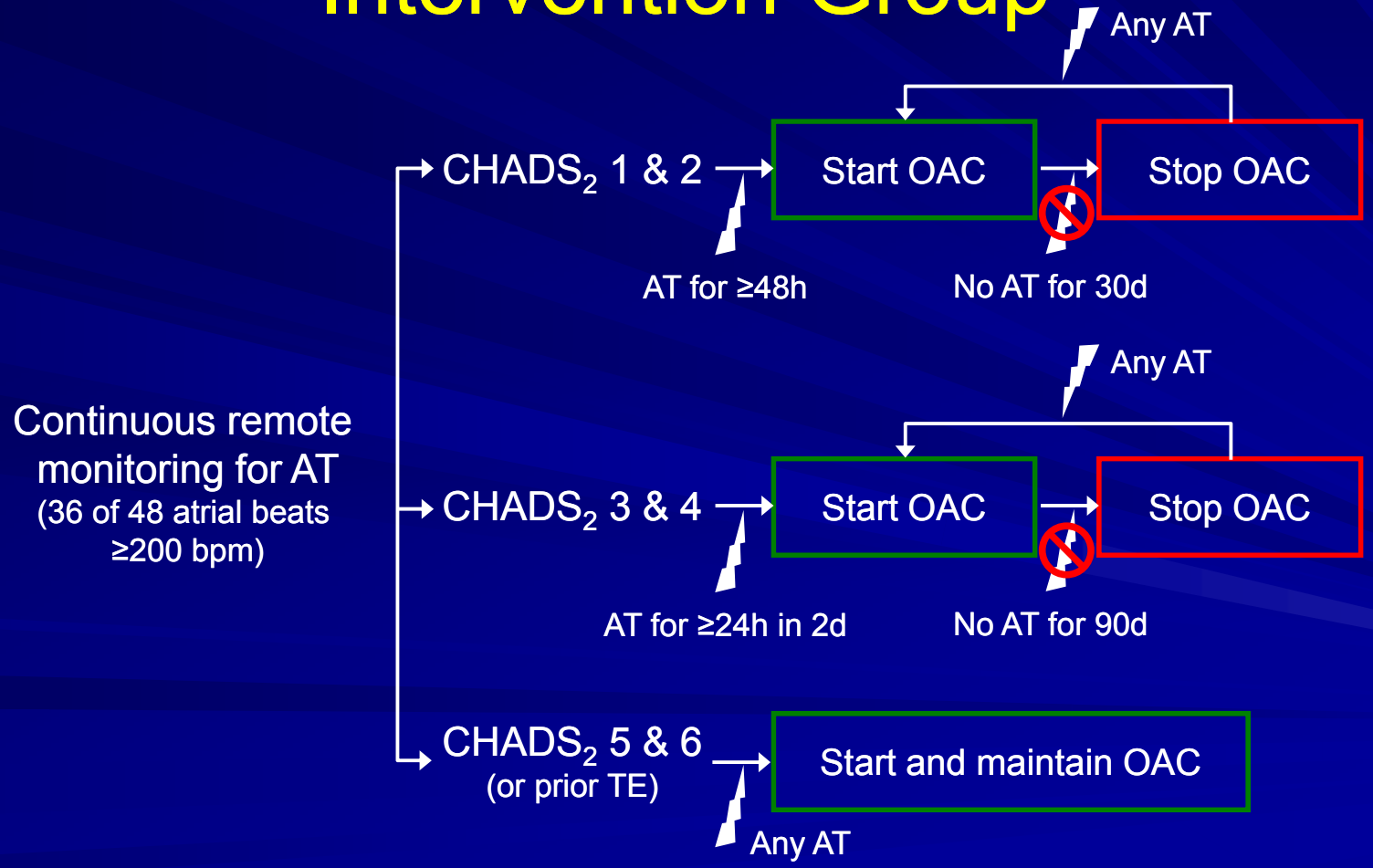
# Atrial Fibrillation and Stroke

- Relative risk for ischemic stroke appears increased for all types of AF and SCAF
- Appears to be a stepwise increase in ABSOLUTE risk with greater AF burden
- Further insights may come from large administrative datasets linking pacemaker or cardiac monitoring data with stroke

# Should I use oral anticoagulation to treat patients with sub-clinical AF?



# Anticoagulation Protocol Intervention Group



# Clinical Outcomes

| | Control Group N = 1,361 | | Intervention Group N = 1,357 | | Hazard Ratio | *p* |
|---|---|---|---|---|---|---|
| | N | rate | N | rate | | |
| Primary endpoint | 61 | 2.3 | 63 | 2.4 | 1.06 | 0.732 |
| Mortality | 140 | 5.1 | 147 | 5.4 | 1.07 | 0.662 |
| Thromboembolism | 37 | 1.4 | 32 | 1.2 | 0.88 | 0.586 |
| Ischemic stroke | 28 | 1.0 | 22 | 0.8 | 0.79 | 0.417 |
| Systemic embolism | 2 | | 0 | | - | 0.969 |
| TIA | 8 | | 10 | | 1.27 | 0.619 |
| Hemorrhagic stroke | 3 | 0.1 | 3 | 0.1 | 1.03 | 0.973 |
| Other major bleed | 32 | 1.2 | 43 | 1.6 | 1.39 | 0.145 |

Rates are expressed as the number of events per 100 patient-years.

# ARTESiA

APIXABAN FOR THE REDUCTION OF THROMBO-EMBOLISM DUE TO SUB-CLINICAL ATRIAL FIBRILLATION

**Patients with:**
- **SCAF (at least 1 episode ≥ 6 min but none > 24 hrs)**
- **$CHA_2DS_2$-VASc score ≥ 3**

CONSENT and RANDOMIZE

Double-blind, double-dummy design

| Active aspirin 81mg OD + Placebo apixaban bid | Placebo aspirin OD + Active apixaban 5mg or 2.5mg* bid |
|---|---|

**Follow-up Visits at 1 month and every 6 months until 248 primary efficacy outcomes (est. avg 3 yrs)**

Primary Efficacy Outcomes:
Stroke (including TIA with imaging)
Systemic Embolism

Primary Safety Outcomes:
Major Bleeding (ISTH)

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* 2.5 mg if either of the following:

- At least 2 of 3 of:
  - Age ≥ 80
  - Weight ≤ 65 kg
  - Serum Creatinine ≥ 133 µmol/L (1.5 mg/dL)
- Ongoing need for inhibitor of both CYP3A4 and P-glycoprotein

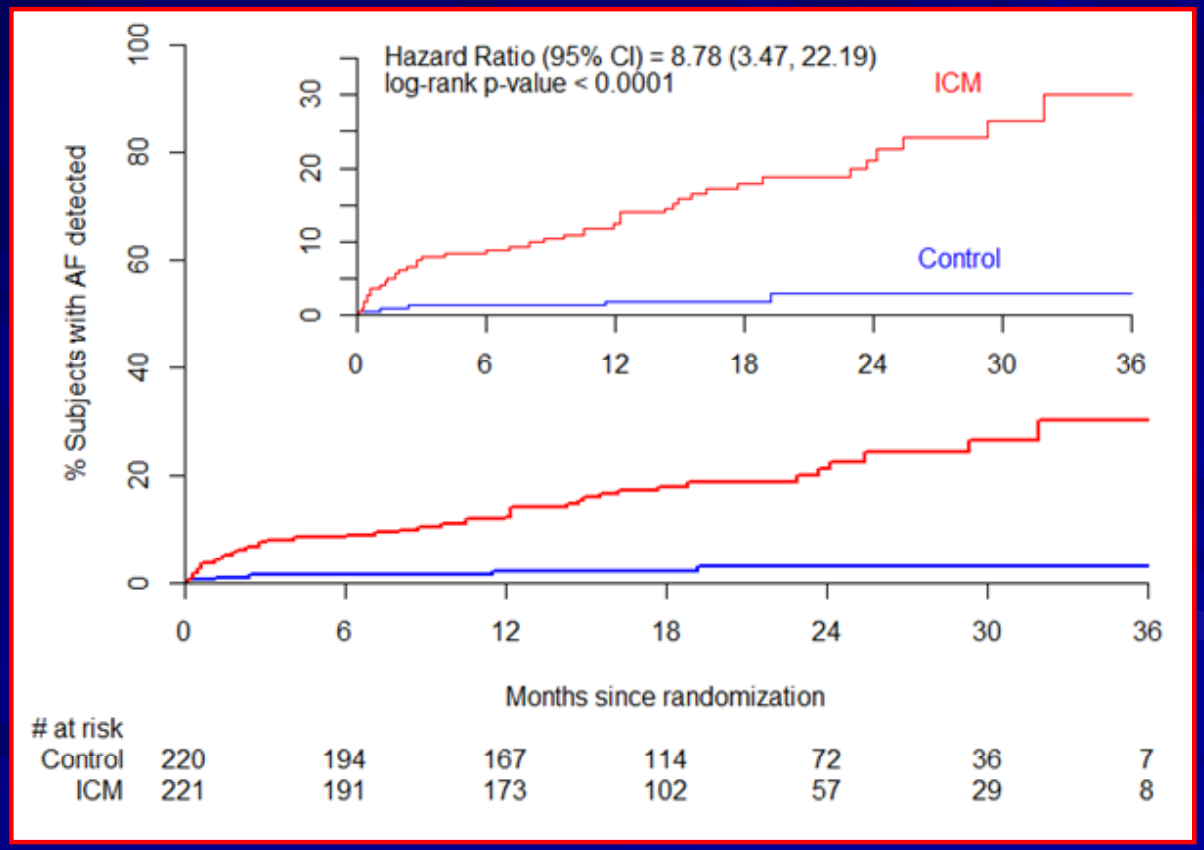
# How hard must one look for AF after an embolic stroke?

## Embolic strokes of undetermined source: the case for a new clinical construct

Robert G Hart, Hans-Christoph Diener, Shelagh B Coutts, J Donald Easton, Christopher B Granger, Martin J O'Donnell, Ralph L Sacco, Stuart J Connolly, for the Cryptogenic Stroke/ESUS International Working Group

Lancet Neurology 2014

# CRYSTAL-AF Trial: AF at 3 years
## R. Bernstein 2014




Rate of detection in ICM arm was 30.0% vs 3.0% in control arm

# EMBRACE Trial: AF Detection at 90 Days
## D. Gladstone 2013

| | Repeat Holter (n=285) | 30-day Monitor (n=287) | p-value | Absolute Detection Difference (95% CI) | NNS |
|---|---|---|---|---|---|
| **Primary Outcome** | | | | | |
| AF ≥30 seconds | 3% | 16% | <0.001 | 13% (9%-18%) | 8 |
| AF ≥30 sec (study monitors only) | 2% | 15% | <0.001 | 13% (9%-18%) | 8 |
| **Secondary Outcomes** | | | | | |
| AF ≥2.5 min | 2% | 10% | <0.001 | 8% (4%-12%) | 13 |
| Any AF | 4% | 20% | <0.001 | 16% (10%-21%) | 6 |

# Embolic Stroke of Unknown Source: ESUS

- RCT of DOAC vs. ASA in patients with ESUS
- Exclude AF by 12-lead and a single 24 hour Holter
- Then, just treat empirically

- Dabigatran: C. Diener
- Rivaroxaban: R. Hart; S. Connolly

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# How common is AF in the general population?

# CSPIN: PIAAF Program

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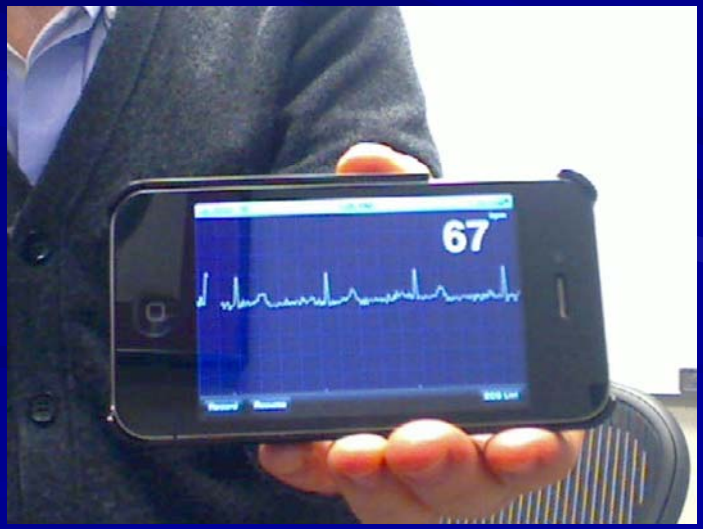

# PIAAF Pharmacy: Subgroup Analyses

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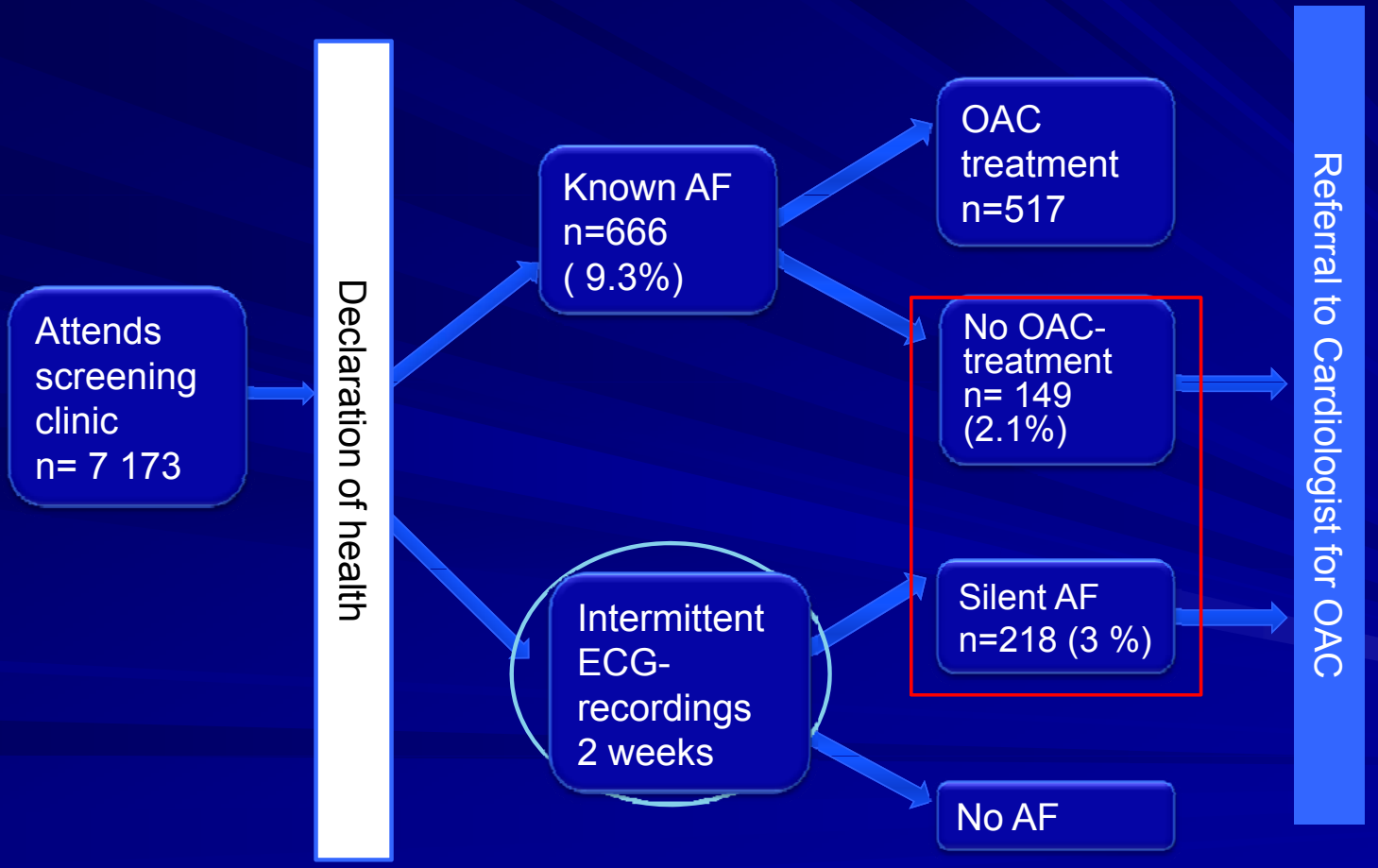
| Age Groups (years) | Total N (%) | 'Actionable' AF N (%) | No AF N (%) |
|---|---|---|---|
| **65-74** | 620 (54.8) | 11 (1.8) | 609 (98.2) |
| **75-85** | 422 (37.3) | 9 (2.1) | 413 (97.9) |
| **>85** | 89 (7.9) | 7 (7.9) | 82 (92.1) |

# 3 % new AF, total AF prevalence increase >30 %




Svennberg et al, Circulation 2015

Europace
doi:10.1093/europace/euv083

CLINICAL RESEARCH

# Cost-effectiveness of mass screening for untreated atrial fibrillation using intermittent ECG recording

**Mattias Aronsson[1]*, Emma Svennberg[2], Mårten Rosenqvist[2], Johan Engdahl[3], Faris Al-Khalili[2,4], Leif Friberg[2], Viveka Frykman-Kull[2], and Lars-Åke Levin[1]**

[1]Department of Medical and Health Sciences, Centre for Medical Technology Assessment, Linkoping University, SE-581 83 Linkoping, Sweden; [2]Karolinska Institutet, Department of Clinical Science, Cardiology Unit, Danderyd University Hospital, Stockholm, Sweden; [3]Department of Medicine, Halland Hospital, Halmstad, Sweden; and [4]Stockholm Heart Centre, Stockholm, Sweden

- 8 fewer strokes/1000 screened
- 12 QALYs / 1000 screened
- € 4313/QALY

# ASSERT-3: Study Design

- Cohort study, 7 FP clinics and 1 general medical clinic
- ≥ 80 years old, no prior AF, no PM/ICD
  - History of: hypertension and ≥ 1 additional risk factor (diabetes, BMI ≥ 30, sleep apnea, smoking, coronary disease, heart failure or LVH

| Duration of AF | N = 100 |
|---|---|
| < 30 seconds | 47 |
| 30 seconds – 6 minutes | 4 |
| ≥ 6 minutes | 15 |
| ≥ 6 hours | 7 |

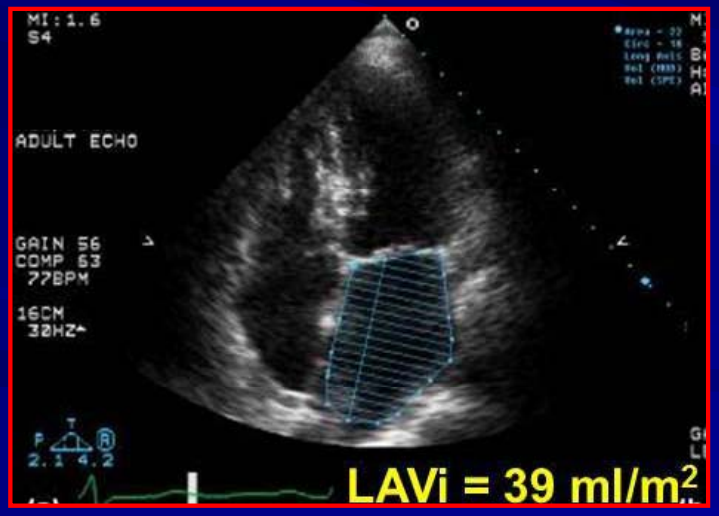
J1

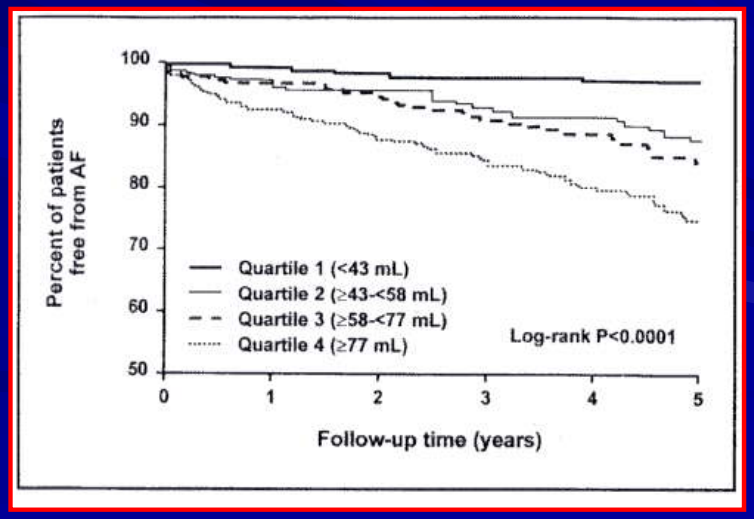
# ASSERT-II

Prevalence of Sub-Clinical Atrial Fibrillation Using an Implantable Cardiac Monitor in Patients with Cardiovascular Risk Factors

## Rationale and design of REVEAL AF: A prospective study of previously undiagnosed atrial fibrillation as documented by an insertable cardiac monitor in high-risk patients

James Reiffel, MD,[a] Atul Verma, MD,[b] Jonathan L. Halperin, MD,[c] Bernard Gersh, MB, ChB, DPhil,[d] Selcuk Tombul, DO,[e] John Carrithers, PhD,[f] Lou Sherfesee, PhD,[f] and Peter Kowey, MD[g] *New York, NY; Ontario, Canada; Rochester, and Minneapolis, MN; Chattanooga, TN; and Wynnewood, PA*




Tsang Mayo Clinic Proc. 2001

## Slide 31

**J1** Linnea to provide slides on device and programming

Jeff-PC2012, 6/26/2012

# Does it make sense to screen the population for AF?

# Does the AF itself cause stroke?

Does elimination of AF reduce risk of stroke?

# Drug-Based AF Rhythm Control

**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 |

*Percentages were derived from a Kaplan–Meier analysis. P values were derived from the log-rank statistic.

†The P value in the case of death was based on the square root of the log-rank statistic, adjusted for 10 interim monitoring analyses.

‡One patient had crossed over to the rhythm-control group and was taking quinidine, and one patient had torsade de pointes 72 hours after mitral-valve replacement.

§Information on warfarin therapy was missing for two patients in the rate-control group and three patients in the rhythm-control group. Information on the presence of atrial fibrillation with the event was missing for 16 patients in the rate-control group and 13 patients in the rhythm-control group.

AFFIRM: G. Wyse, NEJM 2002

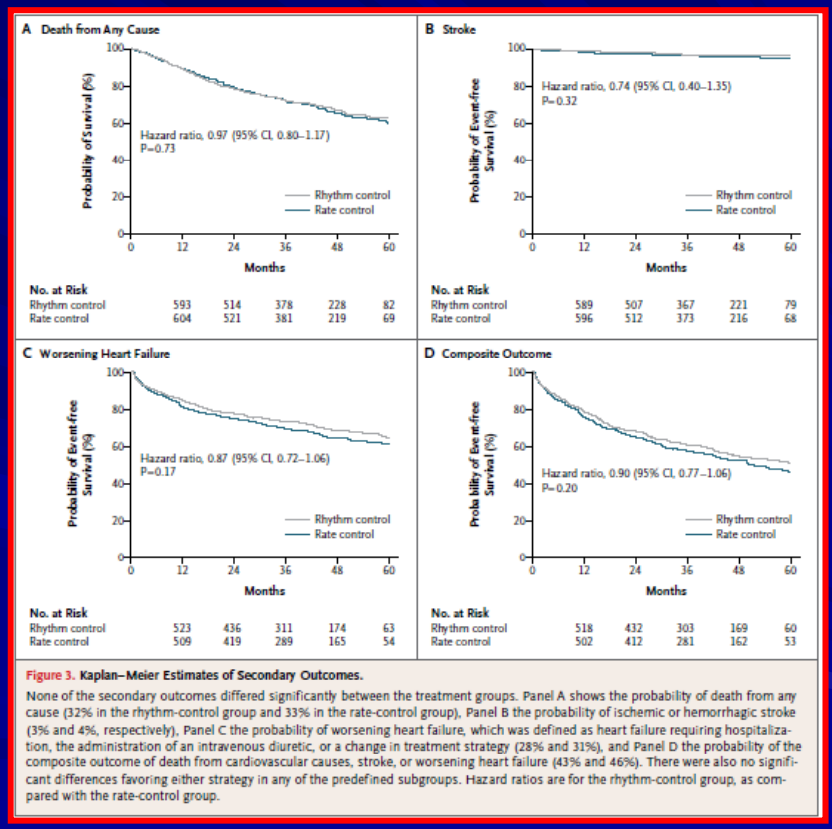



**Figure 3. Kaplan–Meier Estimates of Secondary Outcomes.**

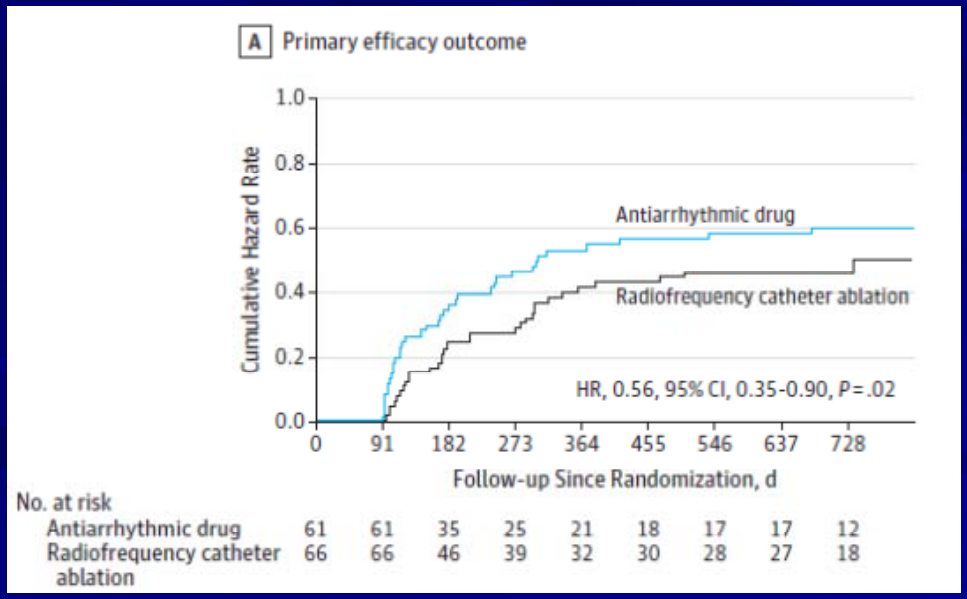
None of the secondary outcomes differed significantly between the treatment groups. Panel A shows the probability of death from any cause (32% in the rhythm-control group and 33% in the rate-control group), Panel B the probability of ischemic or hemorrhagic stroke (3% and 4%, respectively), Panel C the probability of worsening heart failure, which was defined as heart failure requiring hospitalization, the administration of an intravenous diuretic, or a change in treatment strategy (28% and 31%), and Panel D the probability of the composite outcome of death from cardiovascular causes, stroke, or worsening heart failure (43% and 46%). There were also no significant differences favoring either strategy in any of the predefined subgroups. Hazard ratios are for the rhythm-control group, as compared with the rate-control group.

AF-CHF: D. Roy, NEJM 2008

# Catheter Ablation: Ongoing Trials

**Radiofrequency Ablation vs Antiarrhythmic Drugs as First-Line Treatment of Paroxysmal Atrial Fibrillation (RAAFT-2)**
A Randomized Trial

Carlos A. Morillo, MD, FRCPC; Atul Verma, MD, FRCPC; Stuart J. Connolly, MD, FRCPC; Karl H. Kuck, MD, FHRS; Girish M. Nair, MBBS, FRCPC; Jean Champagne, MD, FRCPC; Laurence D. Sterns, MD, FRCPC; Heather Beresh, MSc; Jeffrey S. Healey, MD, MSc, FRCPC; Andrea Natale, MD; for the RAAFT-2 Investigators




JAMA 2014

- General AF population
  - CABANA (n=2200)
  - EAST (n=2745)
- AF-Heart Failure population
  - RAFT-AF (n=1000)
  - CASTLE (n=420)

# Asymptomatic or silent AF following AF Ablation: DISCERN AF

ORIGINAL INVESTIGATION

ONLINE FIRST

## Discerning the Incidence of Symptomatic and Asymptomatic Episodes of Atrial Fibrillation Before and After Catheter Ablation (DISCERN AF)

*A Prospective, Multicenter Study*

*Atul Verma, MD, FRCPC; Jean Champagne, MD; John Sapp, MD; Vidal Essebag, MD, PhD; Paul Novak, MD; Allan Skanes, MD; Carlos A. Morillo, MD; Yaariv Khaykin, MD; David Birnie, MD*

**Background:** The DISCERN AF study (Discerning Symptomatic and Asymptomatic Episodes Pre and Post Radiofrequency Ablation of Atrial Fibrillation) monitored atrial fibrillation (AF) using an implantable cardiac monitor (ICM) to assess the incidence and predictors of asymptomatic AF before and after catheter ablation.

**Methods:** Patients with symptomatic AF underwent implantation of an ICM with an automated AF detection algorithm 3 months before and 18 months after ablation. Patients kept a standardized diary to record symptoms of arrhythmia, and ICM data were downloaded every 3 months. All episodes were blindly adjudicated and correlated with the diary. Asymptomatic recurrences were ICM episodes of 2 minutes or longer with no associated diary symptoms.

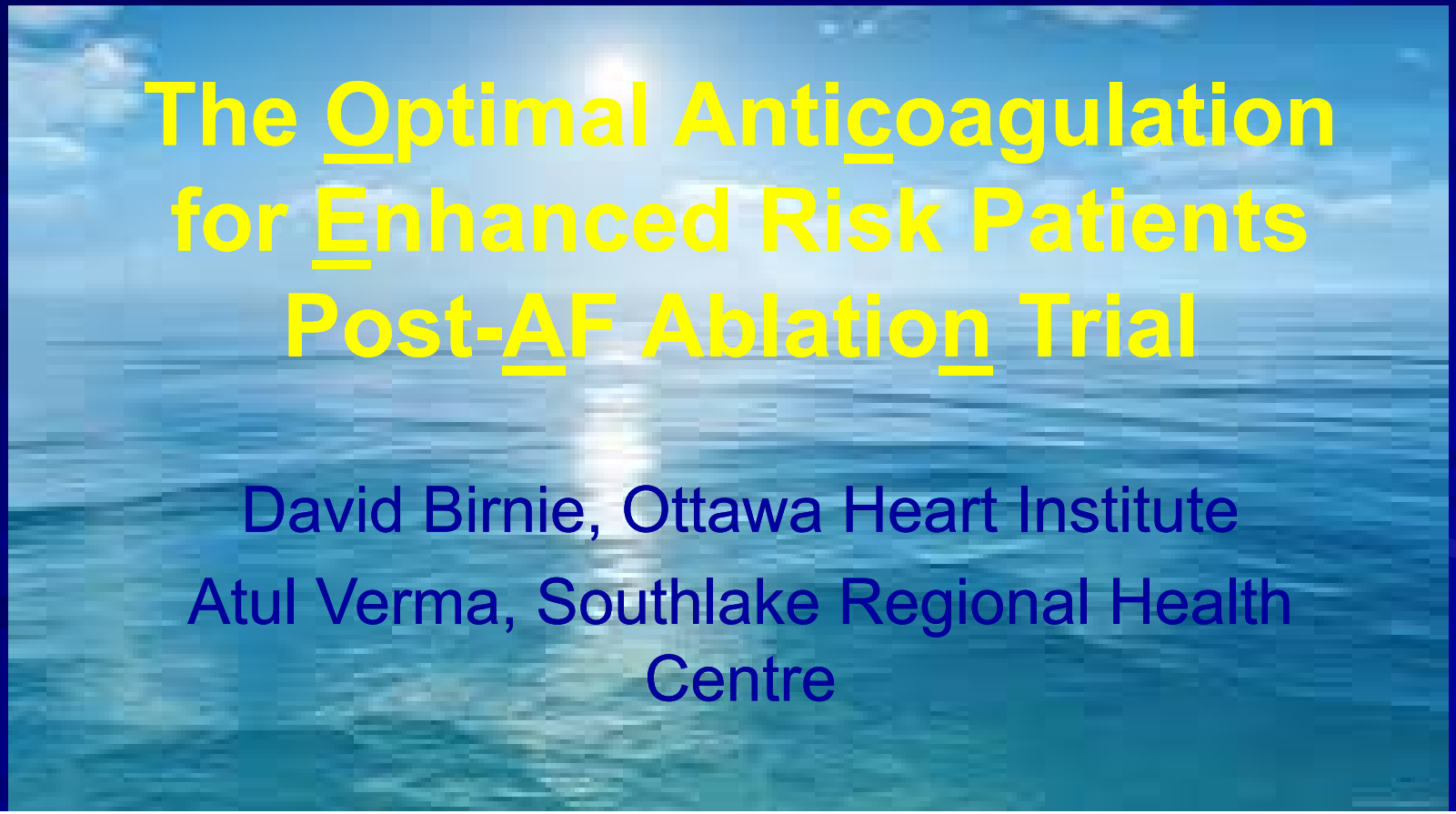
**Results:** Fifty patients had 2355 ICM episodes. Of these, 69.0% were true AF/atrial flutter (AFL)/atrial tachycardia (AT); 16.0%, sinus with extrasystoles; 11.0%, artifact; and 4.0%, sinus arrhythmia. Total AF/AFL/AT burden was reduced by 86% from a mean (SD) of 2.0 (0.5) h/d per patient before to 0.3 (0.2) h/d per patient after ablation ($P<.001$), and 56.0% of all episodes were asymptomatic. The ratio of asymptomatic to symptomatic AF episodes increased after ablation from 1.1 to 3.7 ($P=.002$). By symptoms alone, 29 of 50 patients (58%) were free of AF/AFL/AT after ablation compared with 23 of 50 (46%) using ICM-detected AF/AFL/AT recurrence. Asymptomatic episodes were more likely AFL/AT and were significantly shorter and slower, with lower heart rate variability. However, the postablation state was the strongest independent predictor of asymptomatic AF.

**Conclusions:** The ratio of asymptomatic to symptomatic AF episodes increased from 1.1 before to 3.7 after ablation. Postablation state is the strongest predictor of asymptomatic AF. Symptoms alone underestimate postablation AF burden, with 12% of patients having asymptomatic recurrences only.

**Trial Registration:** clinicaltrials.gov Identifier: NCT00745706

*Arch Intern Med.*
*Published online December 24, 2012.*
*doi:10.1001/jamainternmed.2013.1561*

# O C E A N



## The Optimal Anticoagulation for Enhanced Risk Patients Post-AF Ablation Trial

David Birnie, Ottawa Heart Institute

Atul Verma, Southlake Regional Health Centre

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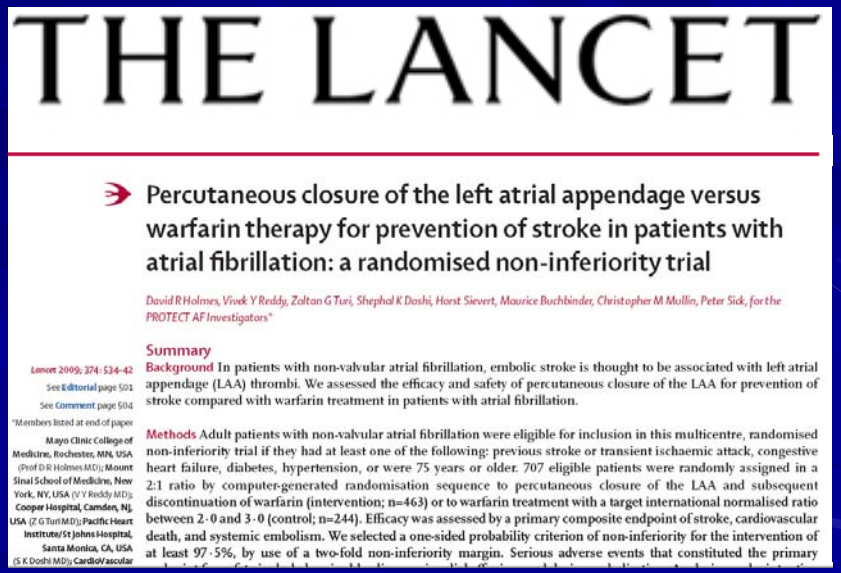
# OCEAN: Long-Term AF Monitoring

- Use of an implantable AF monitor in subset of patients to assess for silent AF
- Correlate silent AF to occurrence of new embolic events

Do most strokes in patients with AF come from clots in the LA Appendage?

# Protect-AF: Key Events

| | Watchman N=463 | | Warfarin N=244 | | Rel. Risk | 95%CI |
|---|---|---|---|---|---|---|
| | events | Rate/yr | events | Rate/yr | | |
| Total Stroke | 16 | 2.3 | 12 | 3.2 | 0.71 | 0.35-1.64 |
| Ischemic | 15 | 2.2 | 6 | 1.6 | 1.34 | 0.60-4.39 |
| Hemorrhagic | 1 | 0.1 | 6 | 1.6 | 0.09 | 0.0-0.45 |
| Systemic Embolism | 2 | | 0 | | - | - |
| Stroke + SEE | 18 | (2.5) | 12 | (3.3) | | |
| Ischemic Stroke+SEE | 17 | (2.4) | 6 | (1.7) | | |



THE LANCET

Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators*

Lancet 2009; 374: 534-42

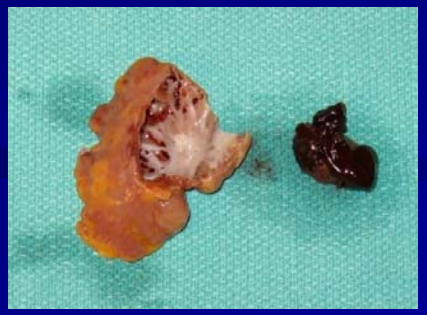
Summary

Background In patients with non-valvular atrial fibrillation, embolic stroke is thought to be associated with left atrial appendage (LAA) thrombi. We assessed the efficacy and safety of percutaneous closure of the LAA for prevention of stroke compared with warfarin treatment in patients with atrial fibrillation.

Methods Adult patients with non-valvular atrial fibrillation were eligible for inclusion in this multicentre, randomised non-inferiority trial if they had at least one of the following: previous stroke or transient ischaemic attack, congestive heart failure, diabetes, hypertension, or were 75 years or older. 707 eligible patients were randomly assigned in a 2:1 ratio by computer-generated randomisation sequence to percutaneous closure of the LAA and subsequent discontinuation of warfarin (intervention; n=463) or to warfarin treatment with a target international normalised ratio between 2·0 and 3·0 (control; n=244). Efficacy was assessed by a primary composite endpoint of stroke, cardiovascular death, and systemic embolism. We selected a one-sided probability criterion of non-inferiority for the intervention of at least 97·5%, by use of a two-fold non-inferiority margin. Serious adverse events that constituted the primary

# LAA Thrombus and Stroke

- Most strokes (70%) in AF patients are cardio-embolic originating from the LAA
- At least 90% of the clots are in the LAA in AF patients



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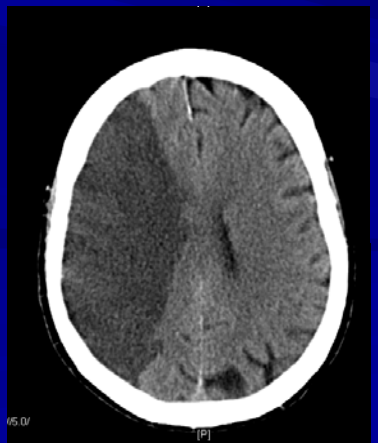
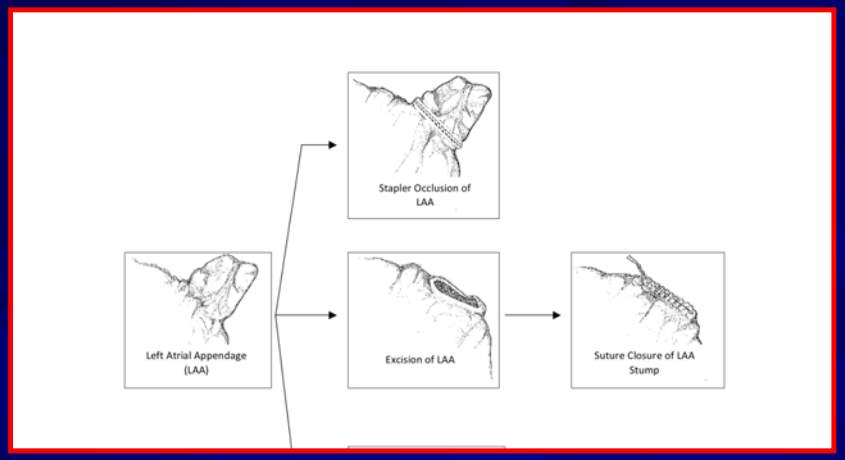
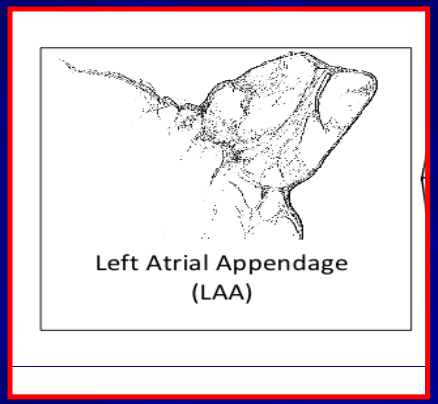


# LAAOS-III Trial




VS.




- Ongoing RCT (n=3700)
- Patients coming for routine CABG or valve surgery
- History of AF; on or off anticoagulation
- Randomized to LAA removal or control
- Currently, over 1000 patients, 25% not on anticoagulation

# What is a stroke?

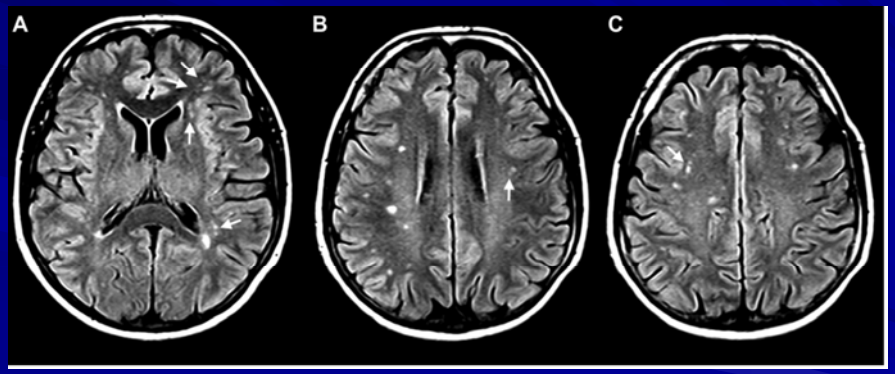
Does AF cause dementia?

Should young, low-risk AF patients receive OAC?

# OAC for Low-Risk Patients and Covert Stroke

Prevalence of Silent Cerebral Ischemia (SCI) in Paroxysmal and Persistent Atrial Fibrillation and Correlation With Cognitive Function

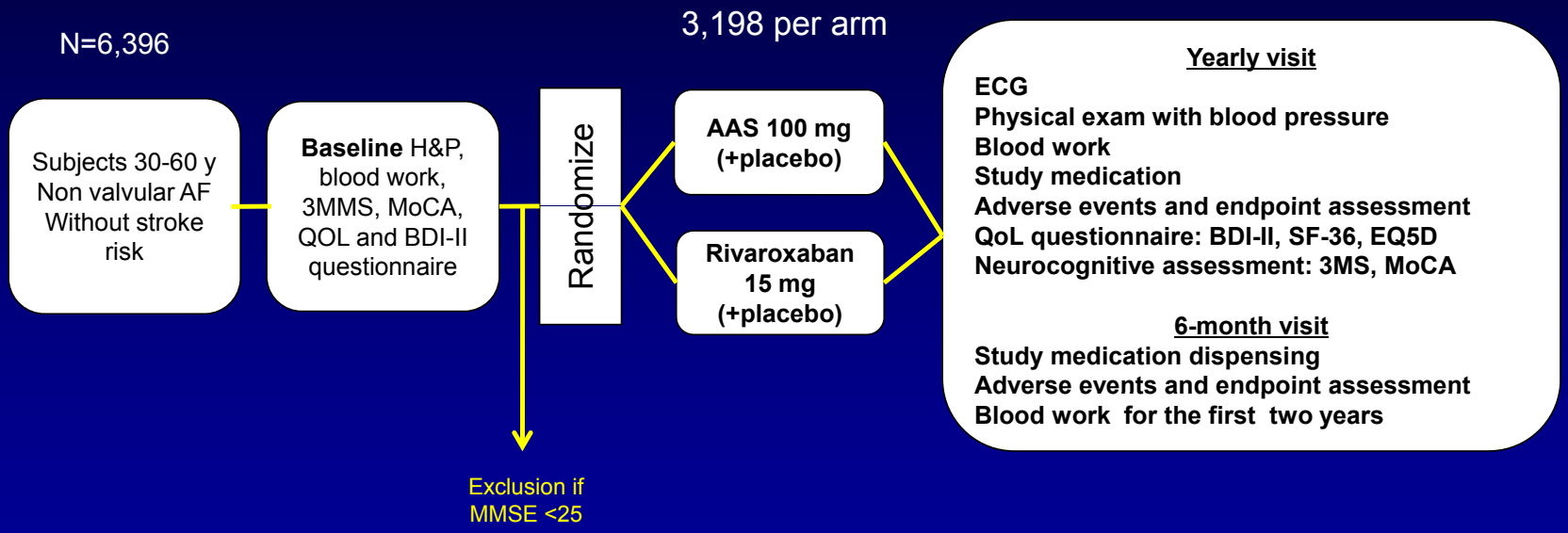
- 180 AF pts (60.5% with CHADs Vasc 0/1) and 90 controls in SR.
- Higher prevalence of SCI (OR=11.2; 95% CI 6 to 21; *P*<0.01) in AF patients vs. patients in SR with a worse cognitive performance.
- Higher number of areas of SCI per pt in AF patients vs. subjects in SR.
- Higher number of areas of SCI per pt in persistent AF patients vs. paroxysmal AF patients.




Brain MRI of a 55-year-old man with paroxysmal AF without other risk factor

Gaita et al. JACC 2013

# BRAIN-AF: Study Schema




Phase I: 500 patient in 50 centers in Canada

Phase II: Expansion to international sites

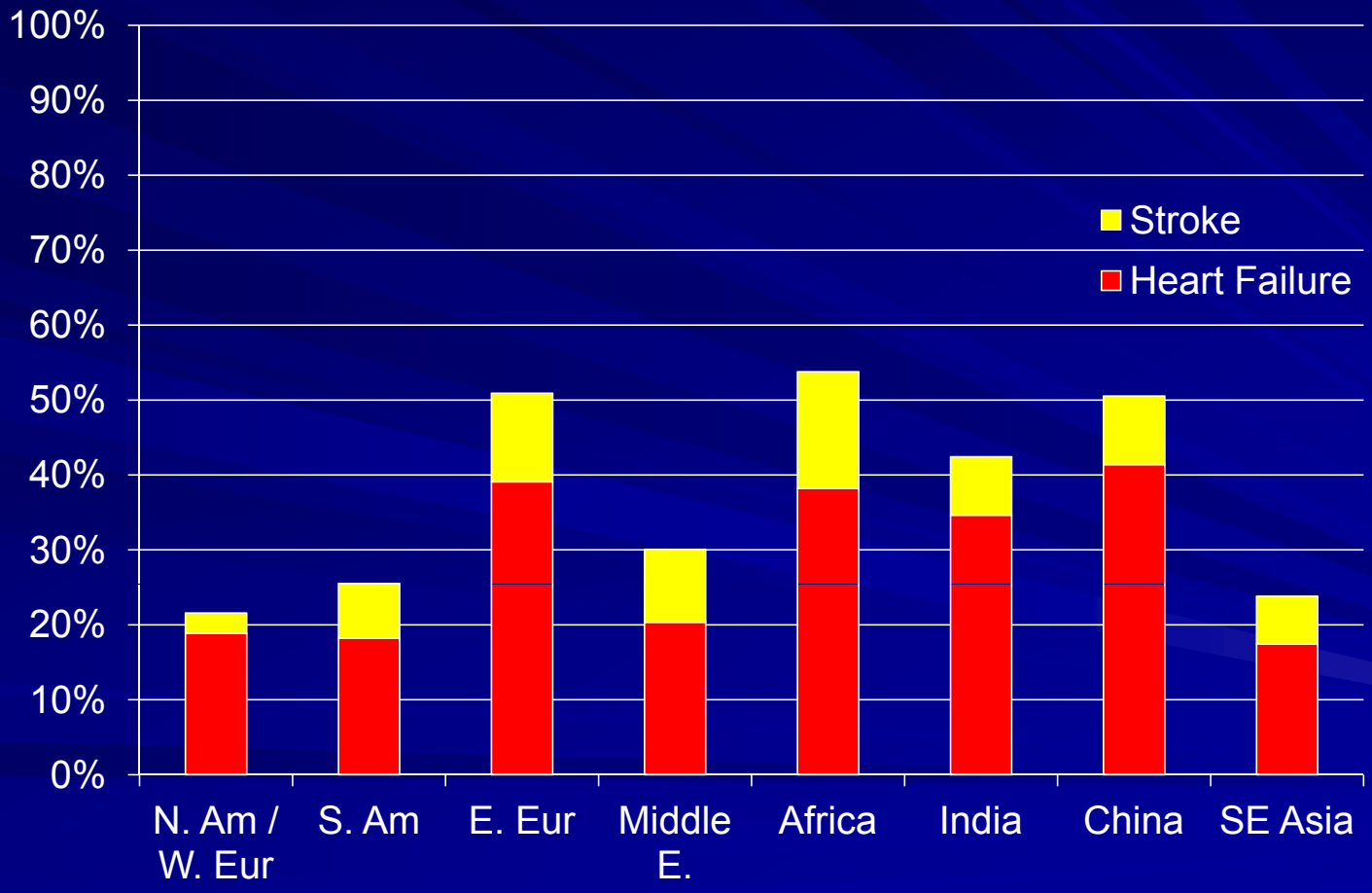
BDI-II =Beck Depression Inventory-II

# Can we prevent AF and stroke due to AF by treating risk factors?

Can we prevent other AF-related complications?

WS19

# Proportion of Causes of Death by Region




Circulation 2015

## Slide 47

**WS19** N. Am and W. Eur were combined.
Wang, Steven, 1/15/2015

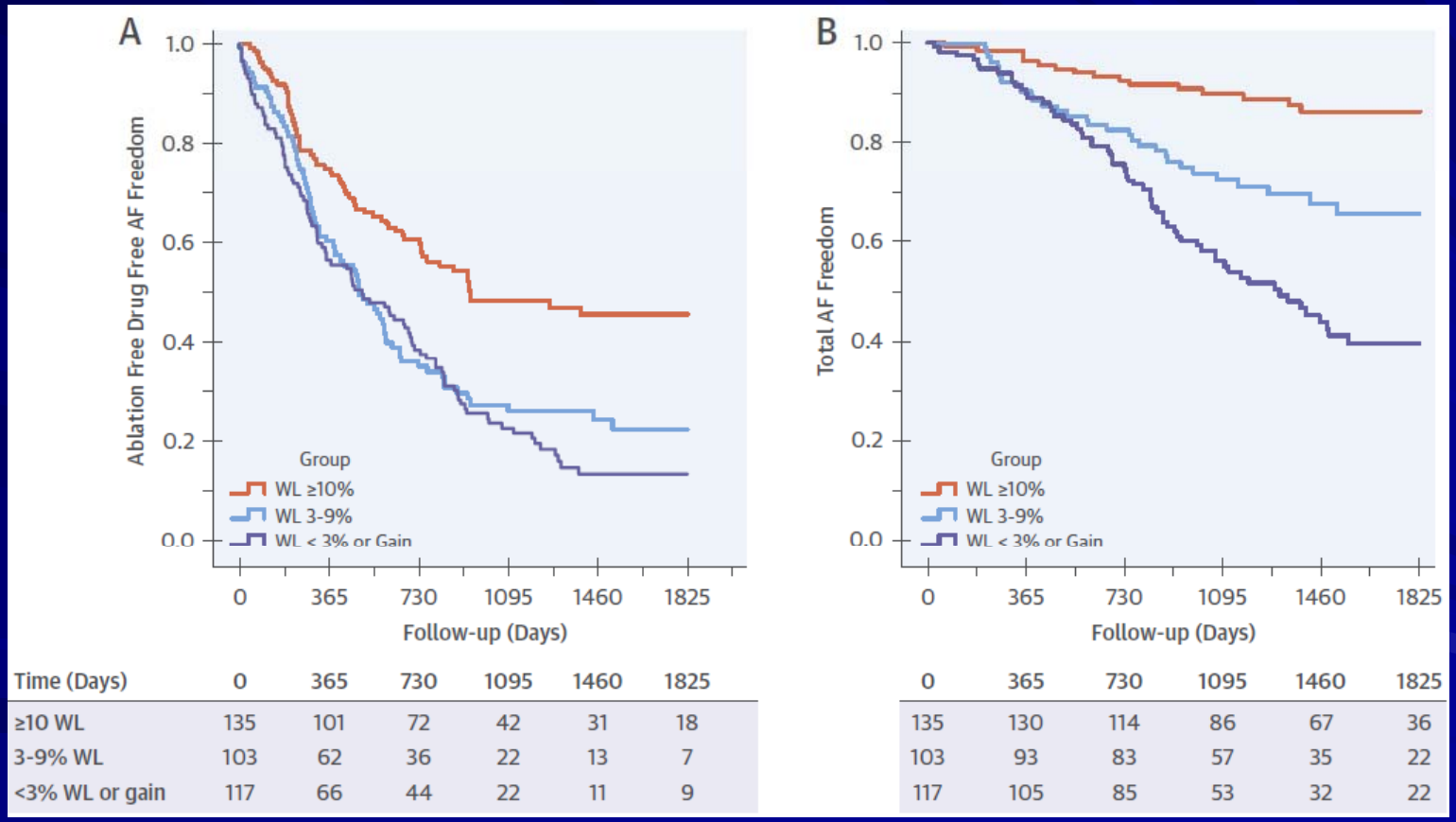
# ARIC

## Huxley, Circulation 2011

**Table 4. Incidence Rate, Relative Hazard (95% Confidence Intervals), and Population-Attributable Fractions for Atrial Fibrillation for Risk Factors in the Atherosclerosis Risk in Communities Study, 1987 to 2007**

| | At Risk, n | Incident AF, n | IR | RH (95% CI)* | PAF, % | 95% CI |
|---|---|---|---|---|---|---|
| History of cardiac disease, % | | | | | | |
| Optimal | 13 398 | 1259 | 5.00 | 0.54 (0.46–0.62) | 0.00 | … |
| Elevated | 1200 | 261 | 12.17 | 1 (Reference) | 5.35 | 3.32–7.45 |
| Blood pressure, % | | | | | | |
| Optimal | 5626 | 381 | 3.93 | 0.55 (0.48–0.63) | 0.00 | … |
| Borderline | 3317 | 304 | 4.72 | 0.65 (0.56–0.74) | 2.89 | −0.11–5.64 |
| Elevated | 5655 | 835 | 7.65 | 1 (Reference) | 21.6 | 16.8–26.7 |
| BMI, % | | | | | | |
| Optimal | 4889 | 389 | 4.27 | 0.65 (0.56–0.74) | 0.00 | … |
| Borderline | 5767 | 591 | 5.28 | 0.70 (0.62–0.79) | 5.16 | 0.93–9.26 |
| Elevated | 3942 | 531 | 7.36 | 1 (Reference) | 12.7 | 9.30–16.3 |
| Diabetes mellitus, % | | | | | | |
| Optimal | 7558 | 645 | 4.68 | 0.67 (0.58–0.78) | 0.00 | … |
| Borderline | 5491 | 617 | 5.83 | 0.71 (0.61–0.82) | 0.78 | −3.52–4.84 |
| Elevated | 1533 | 253 | 8.77 | 1 (Reference) | 3.08 | 0.91–5.30 |
| Smoking, % | | | | | | |
| Optimal | 6077 | 510 | 4.23 | 0.55 (0.48–0.62) | 0.00 | … |
| Borderline | 4769 | 550 | 5.76 | 0.60 (0.52–0.68) | 2.06 | −2.05–6.05 |
| Elevated | 3752 | 460 | 7.45 | 1 (Reference) | 9.78 | 6.74–12.9 |

# Weight Loss Maintenance and AF

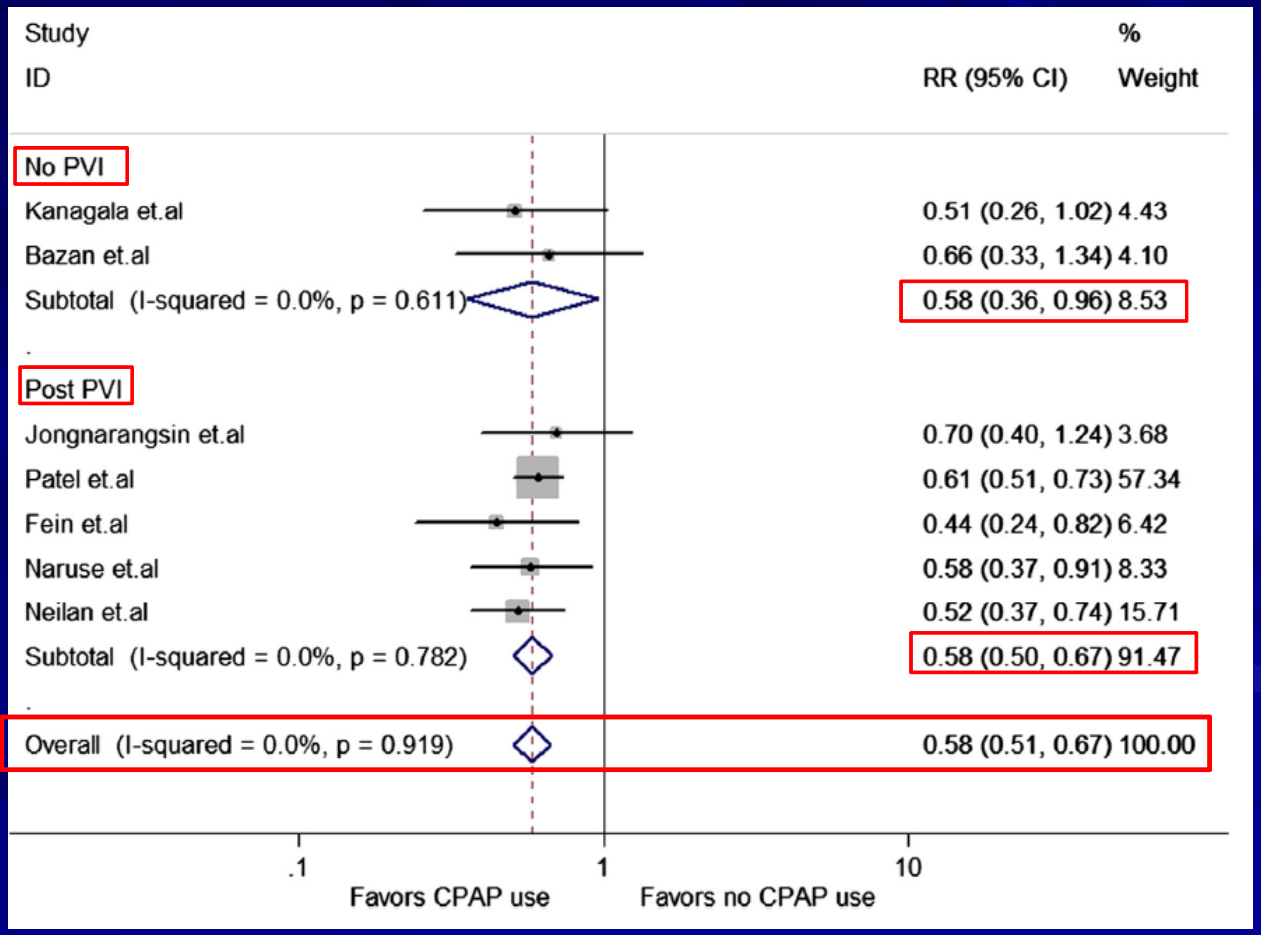



| Time (Days) | 0 | 365 | 730 | 1095 | 1460 | 1825 |
|---|---|---|---|---|---|---|
| ≥10 WL | 135 | 101 | 72 | 42 | 31 | 18 |
| 3-9% WL | 103 | 62 | 36 | 22 | 13 | 7 |
| <3% WL or gain | 117 | 66 | 44 | 22 | 11 | 9 |

| 0 | 365 | 730 | 1095 | 1460 | 1825 |
|---|---|---|---|---|---|
| 135 | 130 | 114 | 86 | 67 | 36 |
| 103 | 93 | 83 | 57 | 35 | 22 |
| 117 | 105 | 85 | 53 | 32 | 22 |

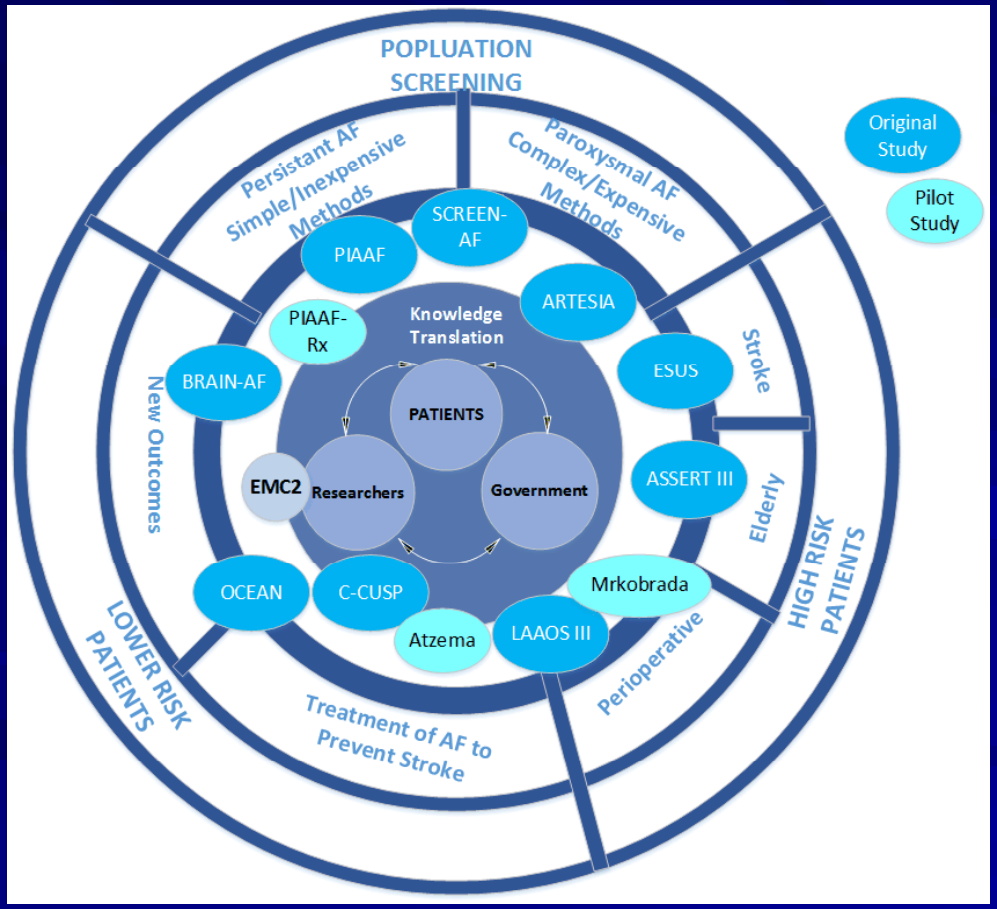
Pathak et al. JACC 2015

# CPAP Use in Sleep Apnea and AF




Shukla et al. JACC Clinical Electrophysiology 2015

# Synergies Across Network




C-SPIN

Canadian Stroke Prevention Intervention Network

# Canadian AF Research: Gen 2.0

C-SPIN
Canadian Stroke Prevention Intervention Network