The Case for Screening for Unknown Atrial Fibrillation to Prevent Stroke

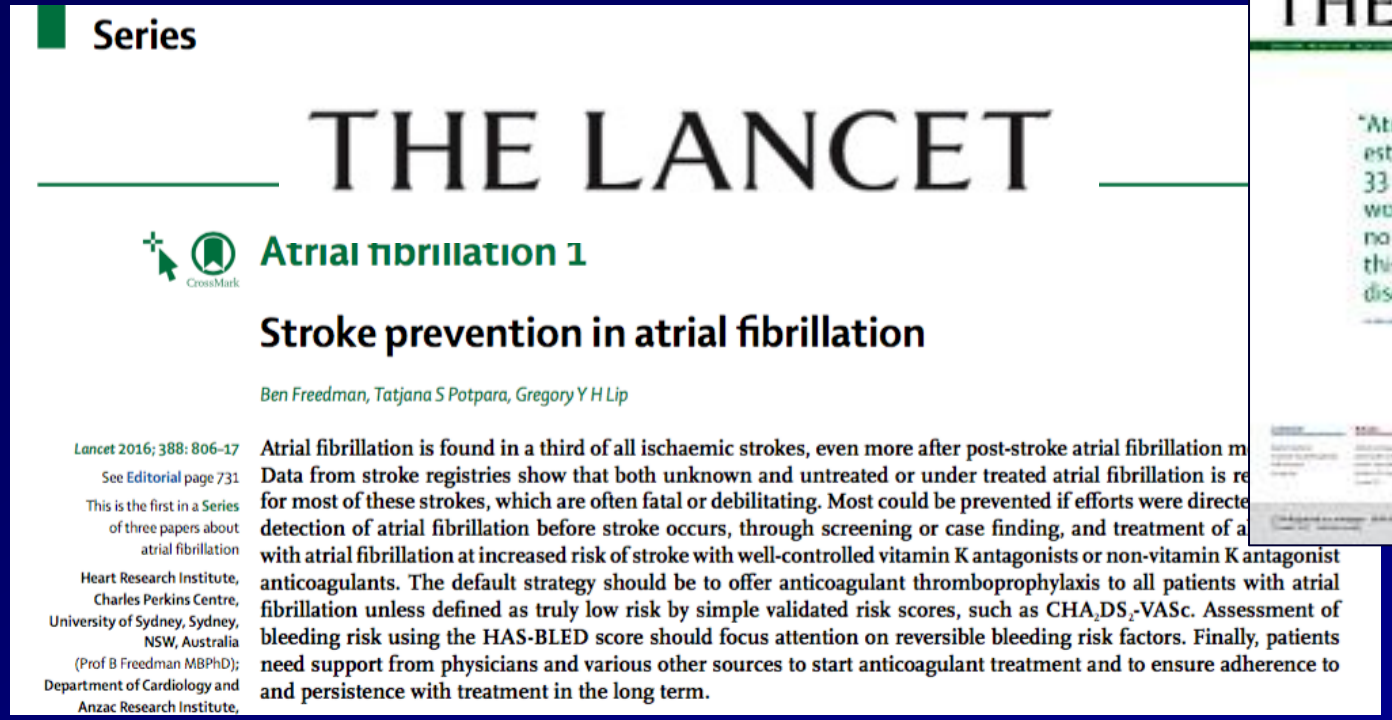
Jeff Healey MD, MSc, FRCP, FHRS
Senior Scientist
Population Health Research Institute
McMaster University, Canada

Disclosures

- Research grants from:
  - Boston Scientific, Medtronic, St. Jude
  - Bayer, Boehringer-Ingelheim, Bristol-Meyers-Squibb
- Director of Canadian Stroke Prevention Intervention Network
- Career Award from the Heart and Stroke Foundation of Ontario

Why might AF screening be effective?

- Many new screening technologies have shown promise
- NOACs have made treatment easier
- Aging population; AF-stroke a major problem
- Early work suggest a large number of AF patients can be identified.



Series

THE LANCET

Atrial fibrillation 1

Stroke prevention in atrial fibrillation

Ben Freedman, Tatjana S Potpara, Gregory Y H Lip

Lancet 2016; 388: 806–17

See Editorial page 731

This is the first in a Series of three papers about atrial fibrillation

Heart Research Institute, Charles Perkins Centre, University of Sydney, Sydney, NSW, Australia (Prof B Freedman MBPhD); Department of Cardiology and Anzac Research Institute,

Atrial fibrillation is found in a third of all ischaemic strokes, even more after post-stroke atrial fibrillation m
Data from stroke registries show that both unknown and untreated or under treated atrial fibrillation is re
for most of these strokes, which are often fatal or debilitating. Most could be prevented if efforts were directe
detection of atrial fibrillation before stroke occurs, through screening or case finding, and treatment of a
with atrial fibrillation at increased risk of stroke with well-controlled vitamin K antagonists or non-vitamin K antagonist anticoagulants. The default strategy should be to offer anticoagulant thromboprophylaxis to all patients with atrial fibrillation unless defined as truly low risk by simple validated risk scores, such as CHA_2DS_2-VASc. Assessment of bleeding risk using the HAS-BLED score should focus attention on reversible bleeding risk factors. Finally, patients need support from physicians and various other sources to start anticoagulant treatment and to ensure adherence to and persistence with treatment in the long term.

THE LANCET

"Atrial fibrillation is estimated to affect 33 million people worldwide....There are no excuses to ignore this common cardiac disorder."

Atrial fibrillation and stroke: unrecognised and undertreated

When did you or your primary care physician last palpate your wrist to check for a regular heart rate? This simple action, followed by an electrocardiogram if the heart rate is irregular, might be crucial in preventing death and disability from ischaemic stroke, heart failure, or myocardial infarction ….

… any people do not know that they have atrial fibrillation until they develop symptoms or present with an ischaemic thromboembolic stroke or systemic thromboembolism.

The Lancet

Lancet 2016; 388: 806–17

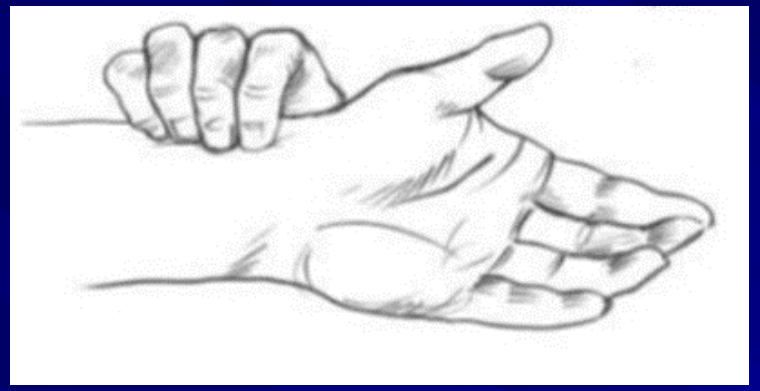
Screening the General Population

1. Population-based Screening
2. Opportunistic Screening
3. Screen Based on Age ± Risk Factors
4. Screening for paroxysmal vs. persistent/permanent AF

WHO attributes of a good screening program

- Important health problem
- Available treatment
- Facilities for diagnosis and treatment
- Asymptomatic phase of disease
- Test for condition; acceptable to public
- Natural history understood; agreement on policy
- Cost of case finding balanced with overall costs
- Test should be sensitive
- Screening should be a continuous process

Intermittent AF Screening



Pattern of AF and Stroke Risk

N=6563, ASA-treated from ACTIVE/AVERROES

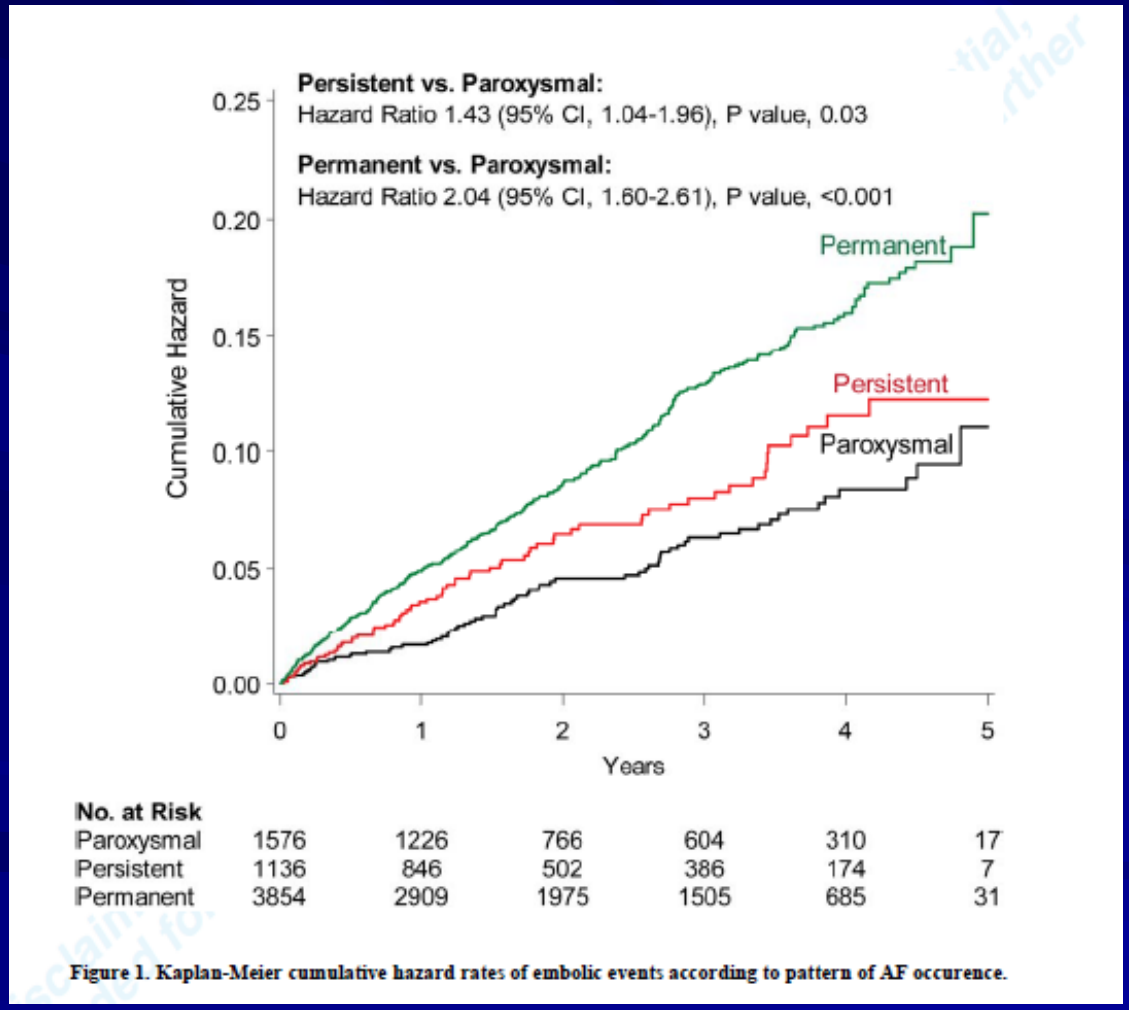


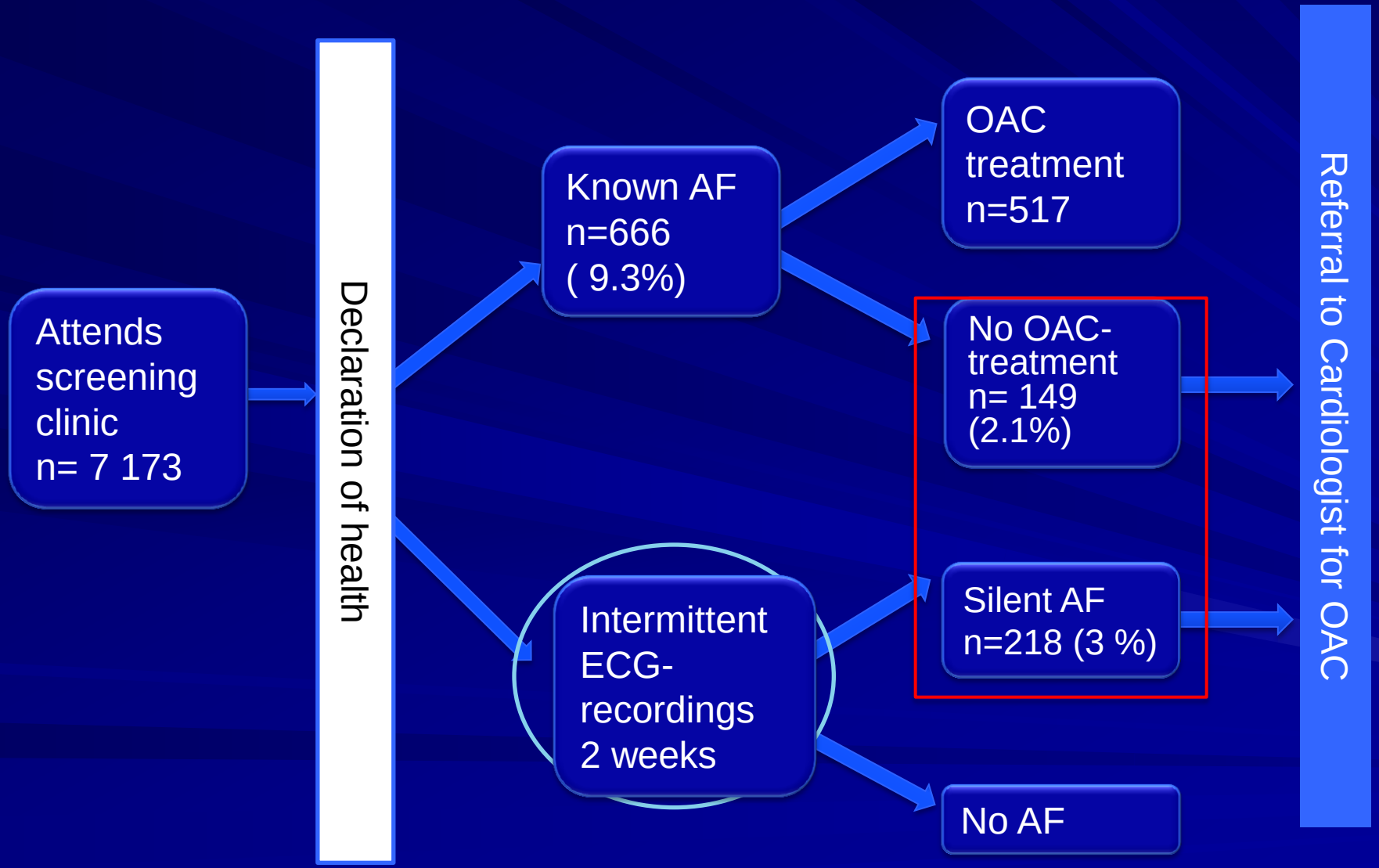
Figure 1. Kaplan-Meier cumulative hazard rates of embolic events according to pattern of AF occurence.

Venassche T. Eur Heart J. 2014

How common is undetected AF in individuals > age 65 years?

- A. 0.5%
- B. 1.0%
- C. 2.0%
- D. 4.0%
- E. 20%

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

AF-SCREEN

Single time-point screening vs patient activated

	Author	n	Age	Single Time	Intermittent
SINGLE TIME - POINT					
Pulse/ECG	Lowres et al	18 189	>65	1.4 %	
ECG	Engdahl et al	848	75	1%	
	Svennberg et al	7137	75/76	0.5%	
PATIENT ACTIVATED 2 weeks BID					
Zenicor	Svennberg et al	7137	75/6		3.0%
Zenicor	Engdahl	403	75 + 1 non-age $CHADS_2$ RF		7.8%

PIAAF Pharmacy

C-SPIN
Canadian Stroke Prevention Intervention Network

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)

Approximately 50% of patients had a BP > 140/90 at screening
Only 50% of screen-positive patients receiving OAC 3 months later

Value of combined screening

- Possible synergies:
  - HTN
  - Diabetes
  - Influenza vaccine
  - Polypill
- Improved efficiency, reduce costs
- Increase acceptability in primary care

Current Challenges for AF Screening

- Stroke prevention is assumed/modelled, not measured
  - Government agencies, high-impact journals demanding more…
- Screening strategy must be adapted for each country and setting
- Some difficulties translating AF detection into delivery of stroke prevention therapy
  - particularly in community settings


AF-SCREEN

Screening High-Risk Populations

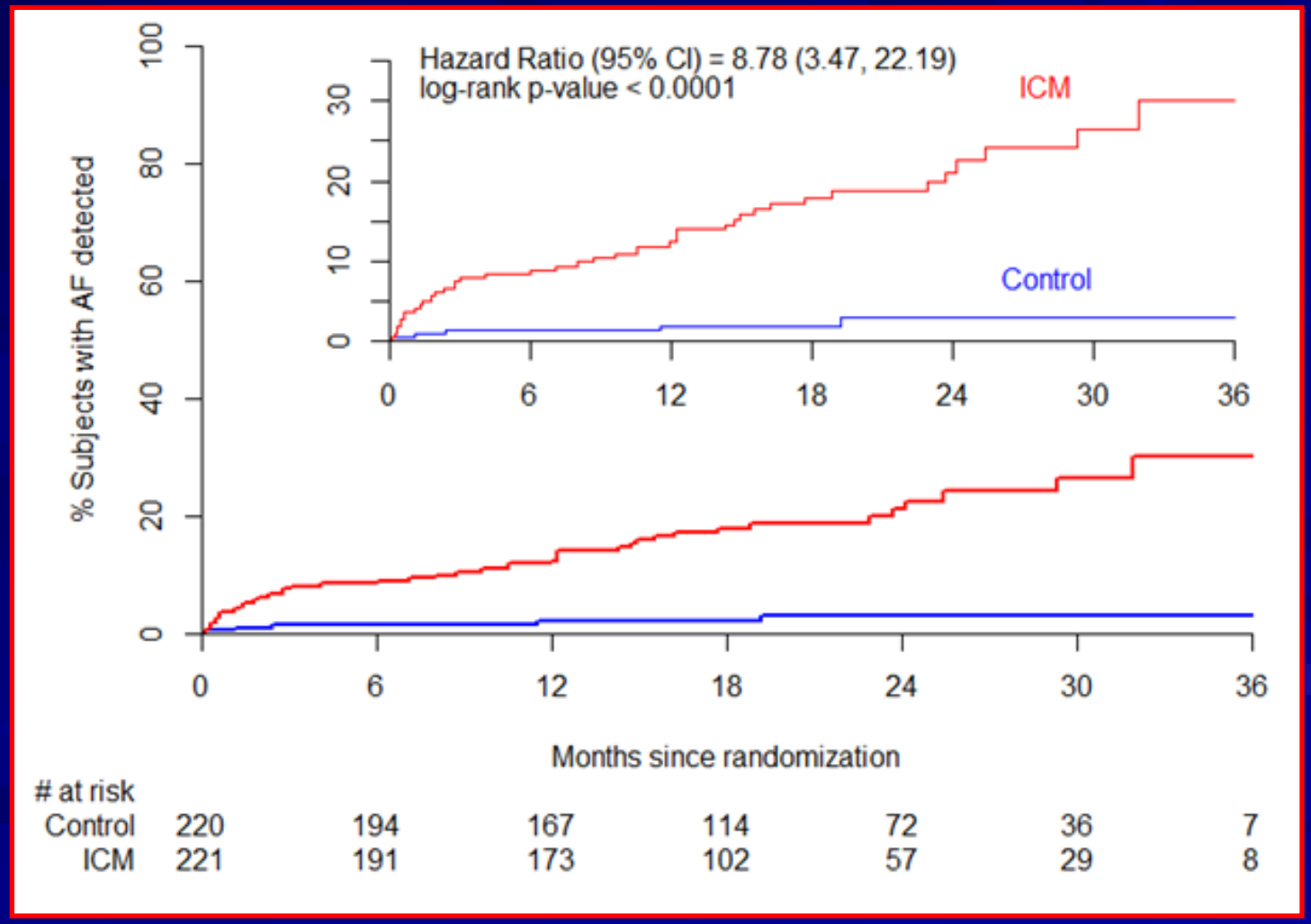
1. Patients following ESUS
2. Patients with a Pacemaker or ICD
3. Elderly at High Risk for AF

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

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

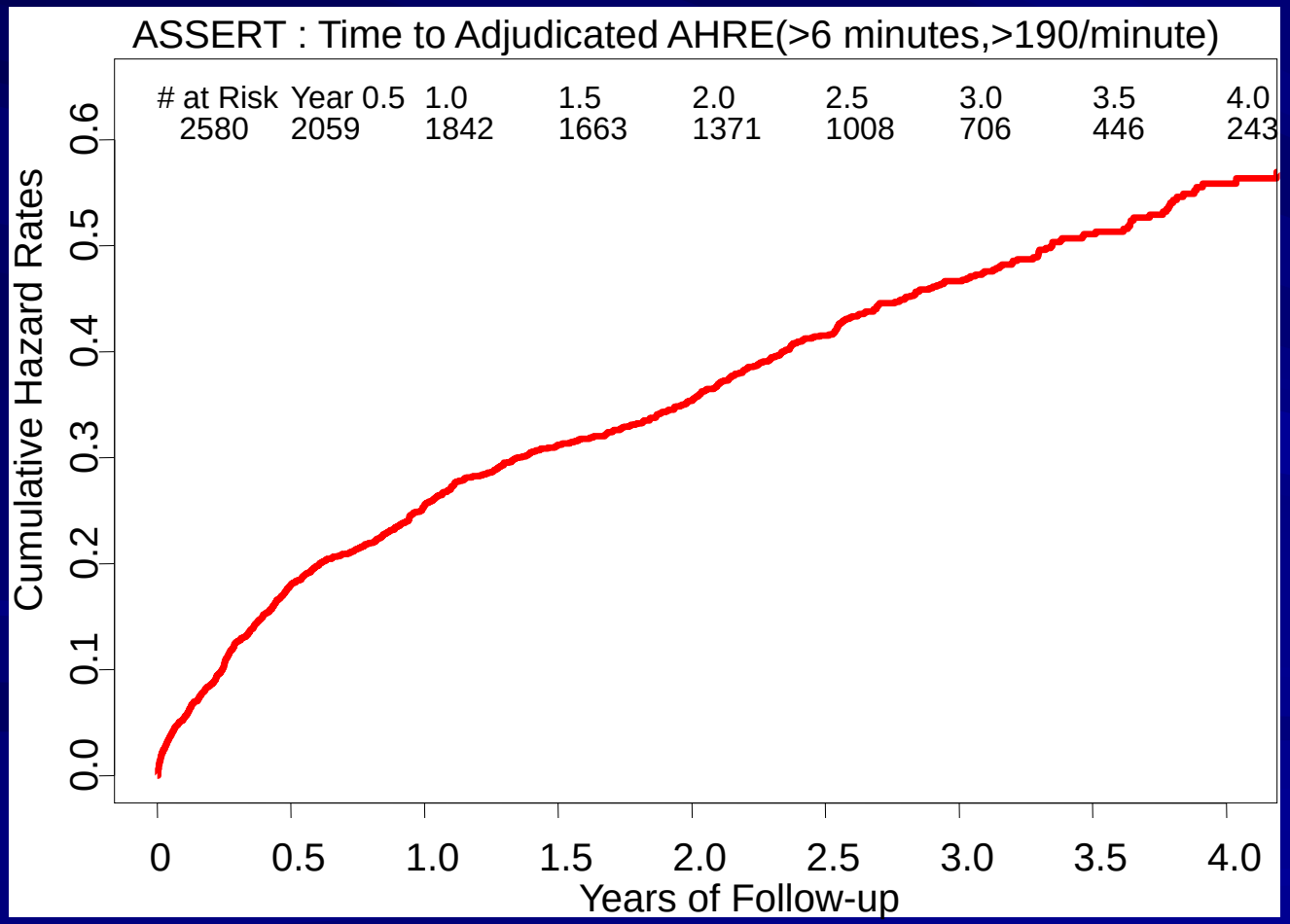
Embolic Stroke of Unknown Source: ESUS

- 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

C-SPIN
Canadian Stroke Prevention Intervention Network

ASSERT: NEJM 2012
SCAF > 6 min, >190 bpm



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"**

Active aspirin 81mg OD + Placebo apixaban bid

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

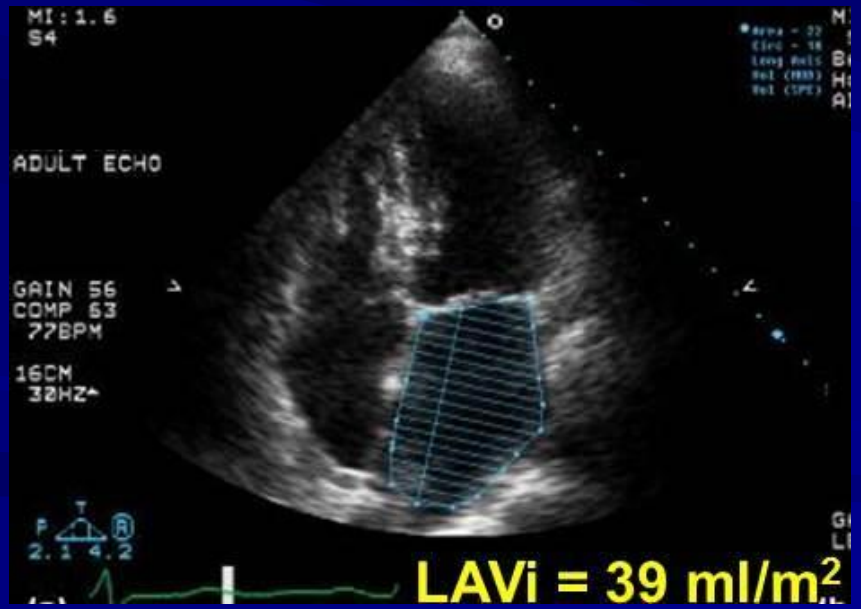
Primary Outcome of Stroke or Systemic Embolism

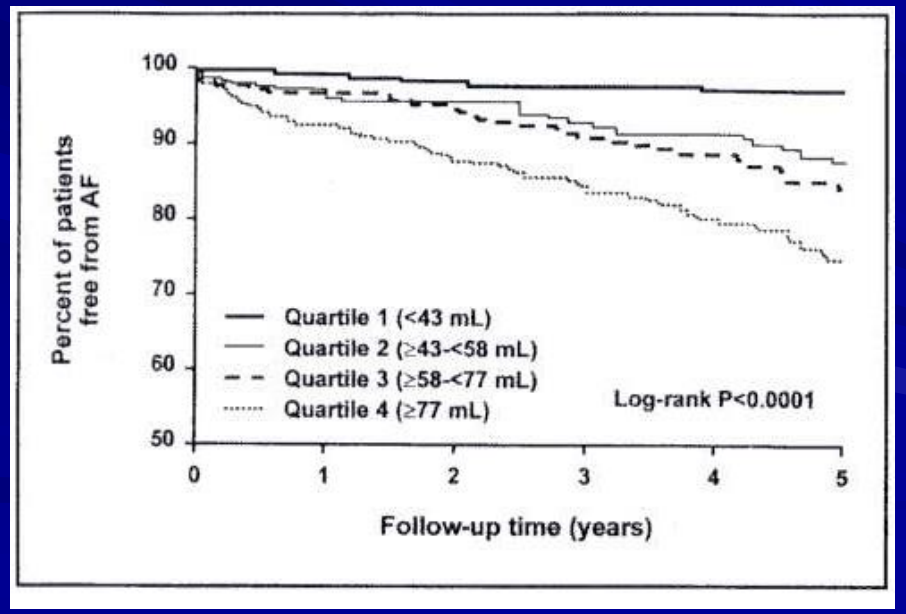
Is SCAF common in non-PM patients?

Study	Sample Size	Device	Inclusion
ASSERT-II	250	SJM Confirm	Age>65, AND CHADS-VASc≥2, or OSA, or BMI> 30; AND LA> 58mL, or NT-ProBNP > 290 pg/mL
GRAF	200	MDT REVEAL-XT	Age ≥ 18 CHADS-VASc≥4
REVEAL-AF	450	MDT REVEAL-XT	Age ≥ 18 CHADS≥3, or CKD/COPD/OSA/CAD

ASSERT-II

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





Tsang Mayo Clinic Proc. 2001

Conclusions

- Unrecognized AF appears very common
  - Particularly in the elderly and those with AF/stroke risk factors
- Many tools now available to detect AF
- Further research needed to define optimal screening strategies:
  - Which individuals
  - Which tools
  - How to do in a cost-effective fashion that is acceptable to patients and healthcare providers