ECG monitoring after ischemic stroke of TIA of unknown source with an insertable monitor ?

YES

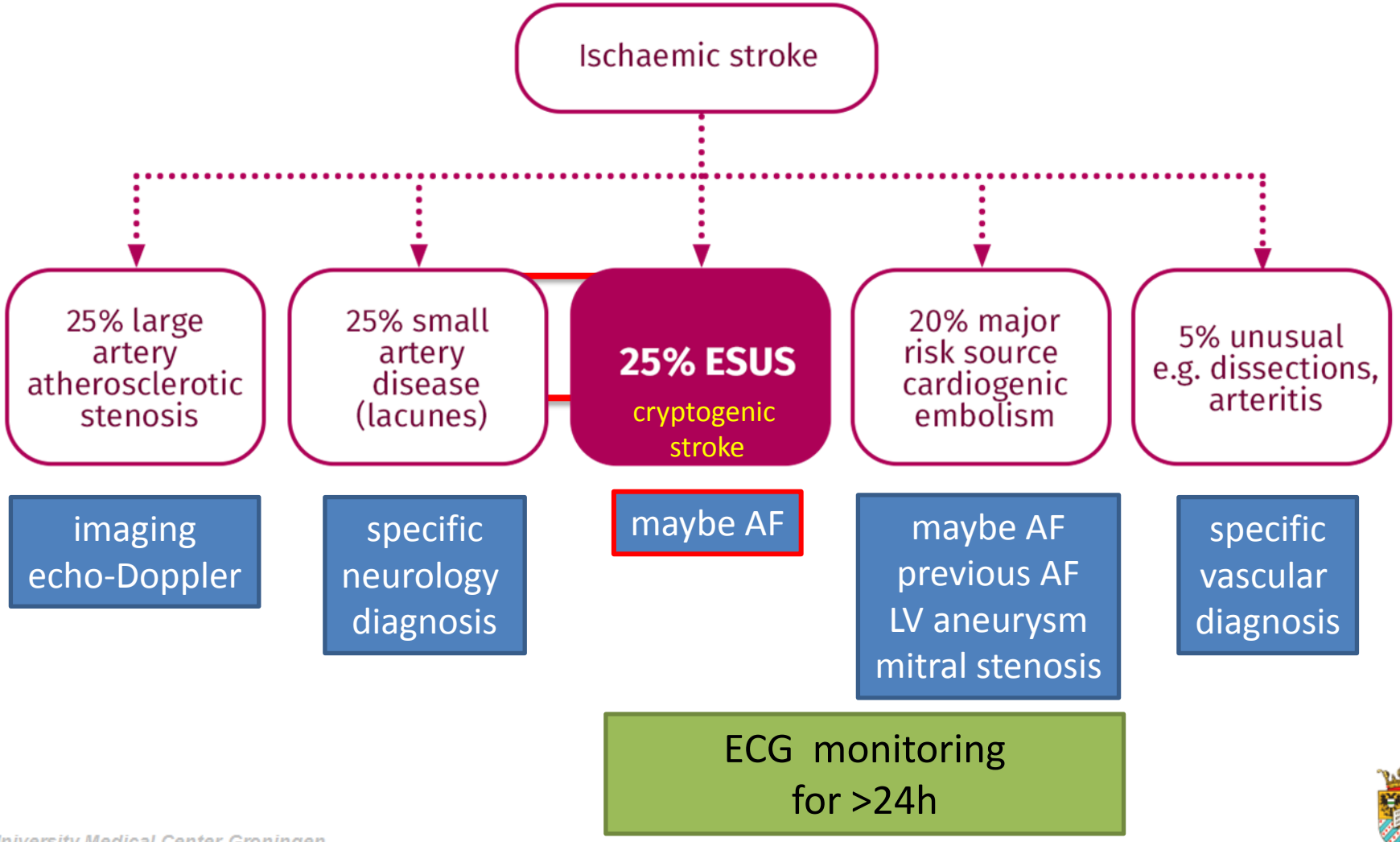
Isabelle C Van Gelder

University Medical Center Groningen

The Netherlands

funded by the dutch heart foundation

The problem:
25% of ischemic strokes is cryptogenic



ESUS

- Embolic Stroke of Unknown Sorce (ESUS) occurs frequently
- Now 24 hour Holter monitoring recommended
- But detection of AF has important therapeutic implications
- And not that this is secondary prevention !!

What are the data ?

- High risk patients without clinical AF

ASSERT II

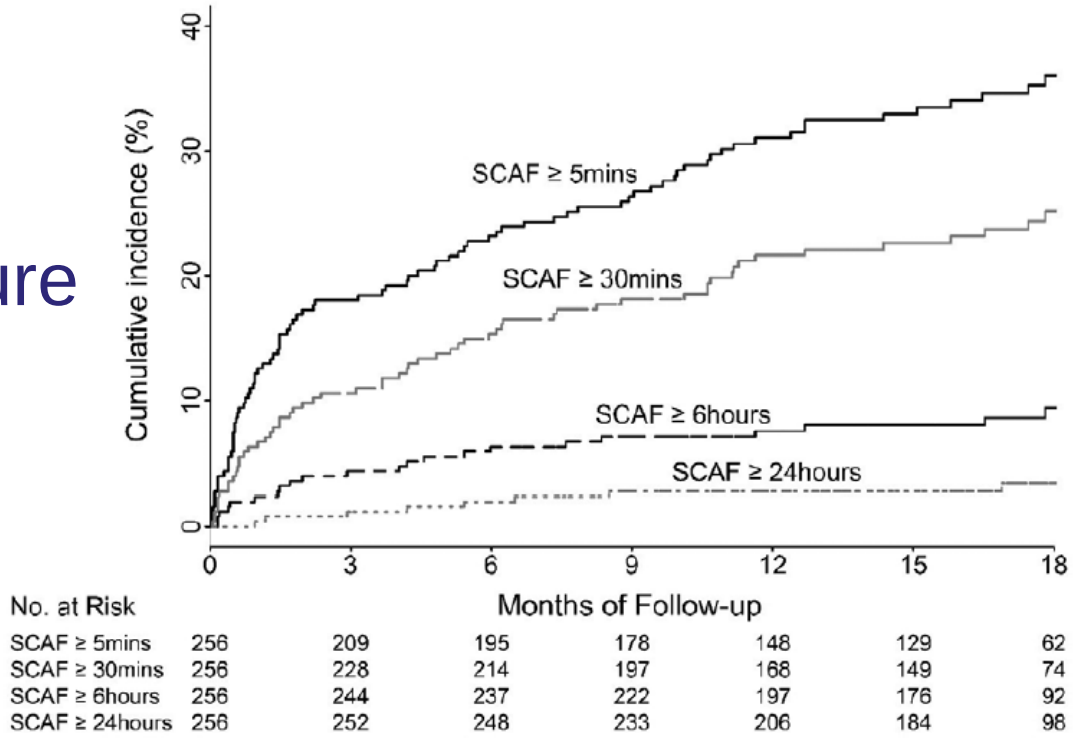
- Patients ≥ 65 years at cardiology or neurology department but NO history of AF
- Inclusion if:
  - CHA_2DS_2-VASc ≥ 2, or
  - OSAS, or
  - BMI > 30 kg/m^2, or
- And LA ≥ 44mm or LAV≥ 58 mL, or
- NT-proBNP ≥290 pg/ml
- Primary endpoint: SCAF ≥ 5 min

ASSERT II

- 256 patients
- Mean age 74 years
- CHA_2DS_2-VASc = 4
- LA 47 mm
- 48% prior stroke or TIA or embolism

ASSERT II

- SCAF occurred in 90 pts :34% per year
- 39% per year if previous stroke
- Baseline predictors:
  - Age
  - LA size
  - Blood pressure



No. at Risk							
SCAF ≥ 5mins	256	209	195	178	148	129	62
SCAF ≥ 30mins	256	228	214	197	168	149	74
SCAF ≥ 6hours	256	244	237	222	197	176	92
SCAF ≥ 24hours	256	252	248	233	206	184	98

Healey for the ASSERT II Investigators Circulation 2017

REVEAL AF study

Objectives

GOAL:

- To determine the incidence of previously undiagnosed AF with ICM* monitoring in a high-risk population.

PRIMARY ENDPOINT:

- Incidence of AF (*adjudicated, ≥6 minutes*) at 18 months *in patients at high risk for, but without previously known AF.*

* ICM = insertable cardiac monitor with AF detection capabilities

REVEAL AF study

Methods

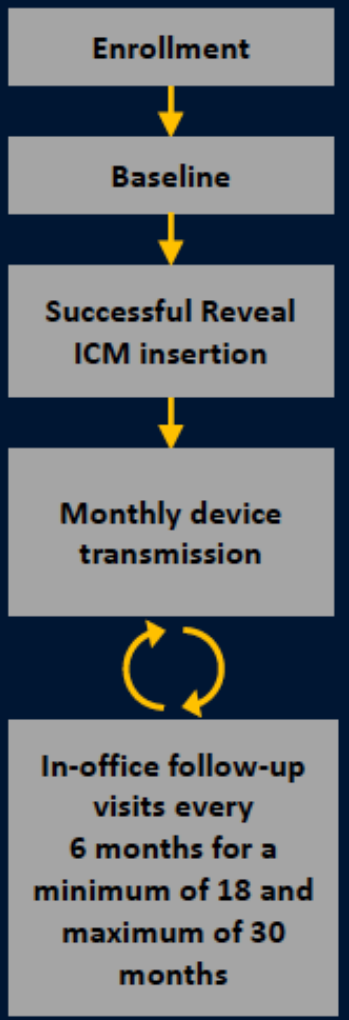
DESIGN:

- Prospective, single-arm, open-label, multi-center, post-market study.

INCLUSION CRITERIA:

- $CHADS_2$ score of ≥ 3 or $CHADS_2$ = 2 and at least 1 of the following:
  - Coronary artery disease
  - Renal impairment (GFR 30-60 ml/min)
  - Sleep apnea
  - Chronic obstructive pulmonary disease

[At least 70 pts were required for each $CHADS_2$ group (2, 3, ≥4)]



Reiffel for the REVEAL AF Investigators JAMA Cardiology 2017

REVEAL AF study

Baseline Demographics

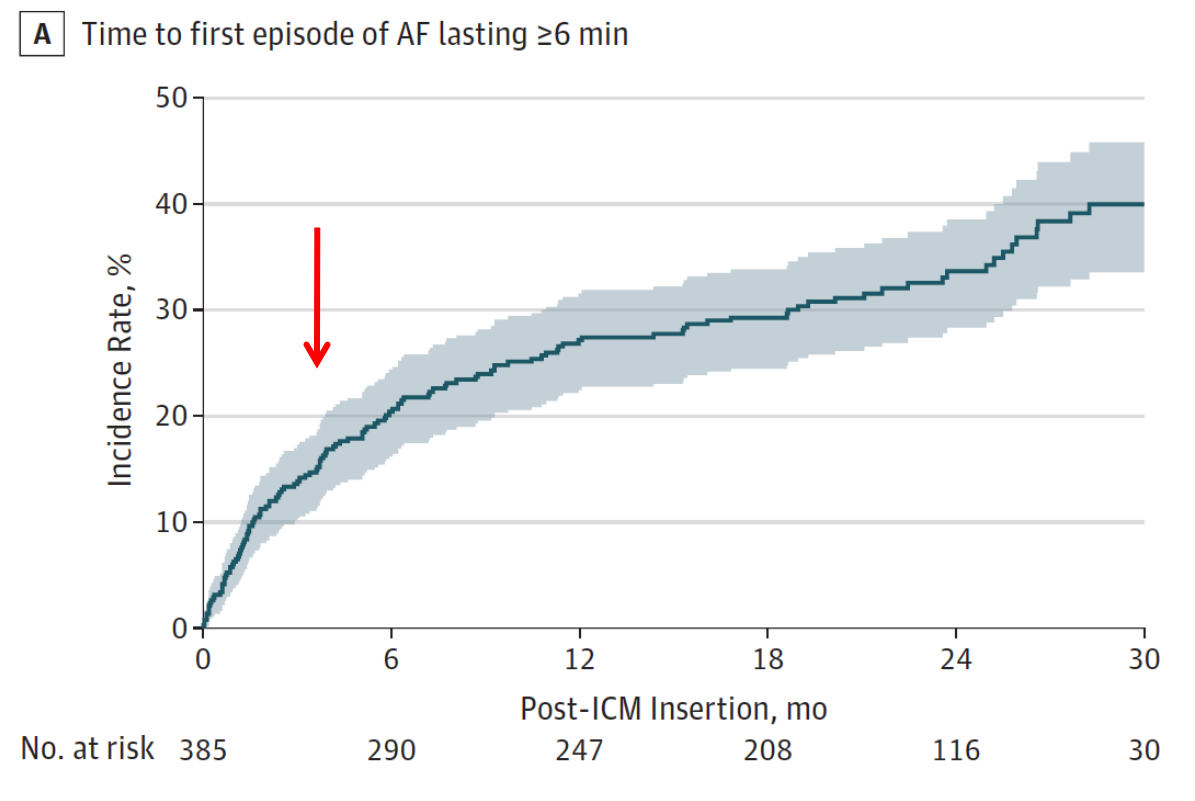
- The study population represents a common group of patients encountered in clinical practice.

Characteristic	Subjects with device insertion (N = 394)	
Device inserted/attempted		
Reveal LINQ™ ICM	272 (69.0%)	
Reveal™ XT ICM	122 (31.0%)	
Gender: male	206 (52.3%)	
Age		
Years (mean ± standard deviation)	71.6 ± 9.8	
Under 65	88 (22.3%)	
65 to 75	131 (33.3%)	
75 and older	175 (44.4%)	
Medical history		
Renal dysfunction	64 (16.2%)	
Congestive heart failure	81 (20.6%)	
Coronary artery disease	233 (59.1%)	
Hypertension	369 (93.7%)	
COPD	76 (19.3%)	
Sleep apnea	104 (26.4%)	
Diabetes	248 (62.9%)	
Vascular disease		
Remote cerebrovascular accident (stroke)	80 (20.3%)	36.5%
Remote transient ischemic attack	76 (19.3%)	

Reiffel for the REVEAL AF Investigators JAMA Cardiology 2017

REVEAL AF study

Incidence of AF Lasting ≥ 6 Minutes



Median time to detection: 123 [IQR 41-330] days.

Detection rate at:

- **18 months (primary endpoint): 29.3%.**
- 30 days: 6.2%.
- 30 months: 40.0%.

AF may have gone undetected in over three-quarters of patients had monitoring been limited to 30 days.

University Medical Center Groningen

Reiffel for the REVEAL AF Investigators JAMA Cardiology 2017

What are the data ?

- Thus subclinical AF in patients at risk for stroke is high
- 30% per year

Monitoring in ESUS patients without known AF

- What show the studies in ESUS patients who are monitored for > 24 hours?

Long term monitoring in cryptogenic stroke EMBRACE-AF

- 572 patients > 55 years with cryptogenic stroke
- No prior AF
- Randomized to 30 days event triggered monitoring (irregular rhythm) versus repeat 24 hour Holter monitoring
- Primary outcome: SCAF > 30 seconds detected during first 6 months

GLADSTONE for the EMBRACE-AF Investigators New Engl J Med 2014

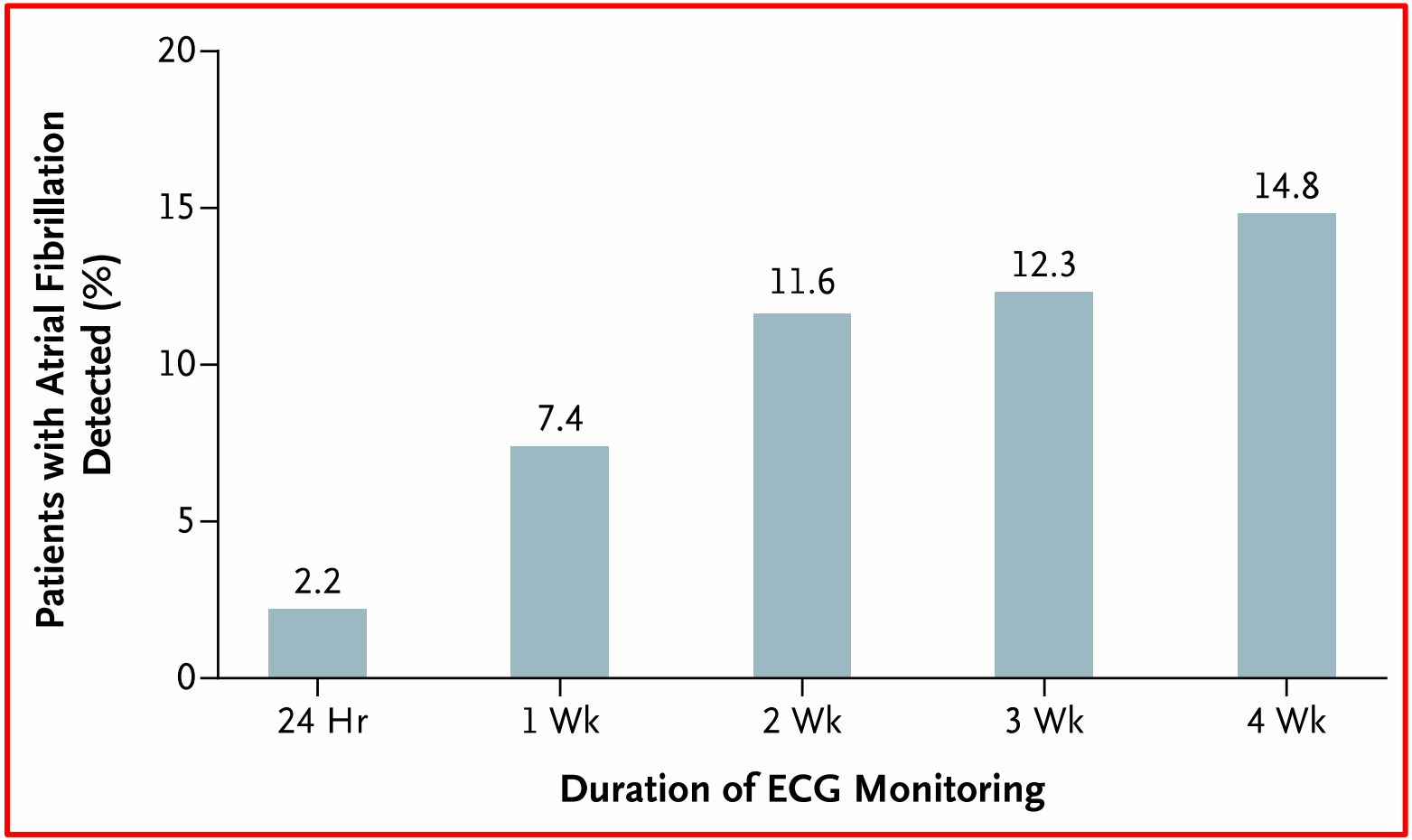
ESH AHA JSH


microlife
10:00
138
86
N=
85
WatchBPhome


START
2007-01-08 20:08
00:7200
21
HANDHELD ECG MONITOR


67

Long term monitoring in cryptogenic stroke EMBRACE-AF



GLADSTONE for the EMBRACE-AF Investigators New Engl J Med 2014

Long term monitoring in cryptogenic stroke EMBRACE-AF

	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
Secondary Outcomes					
AF ≥2.5 min	2%	10%	<0.001	8% (4%-12%)	13
Any AF	4%	20%	<0.001	16% (10%-21%)	6

University Medical Center Groningen

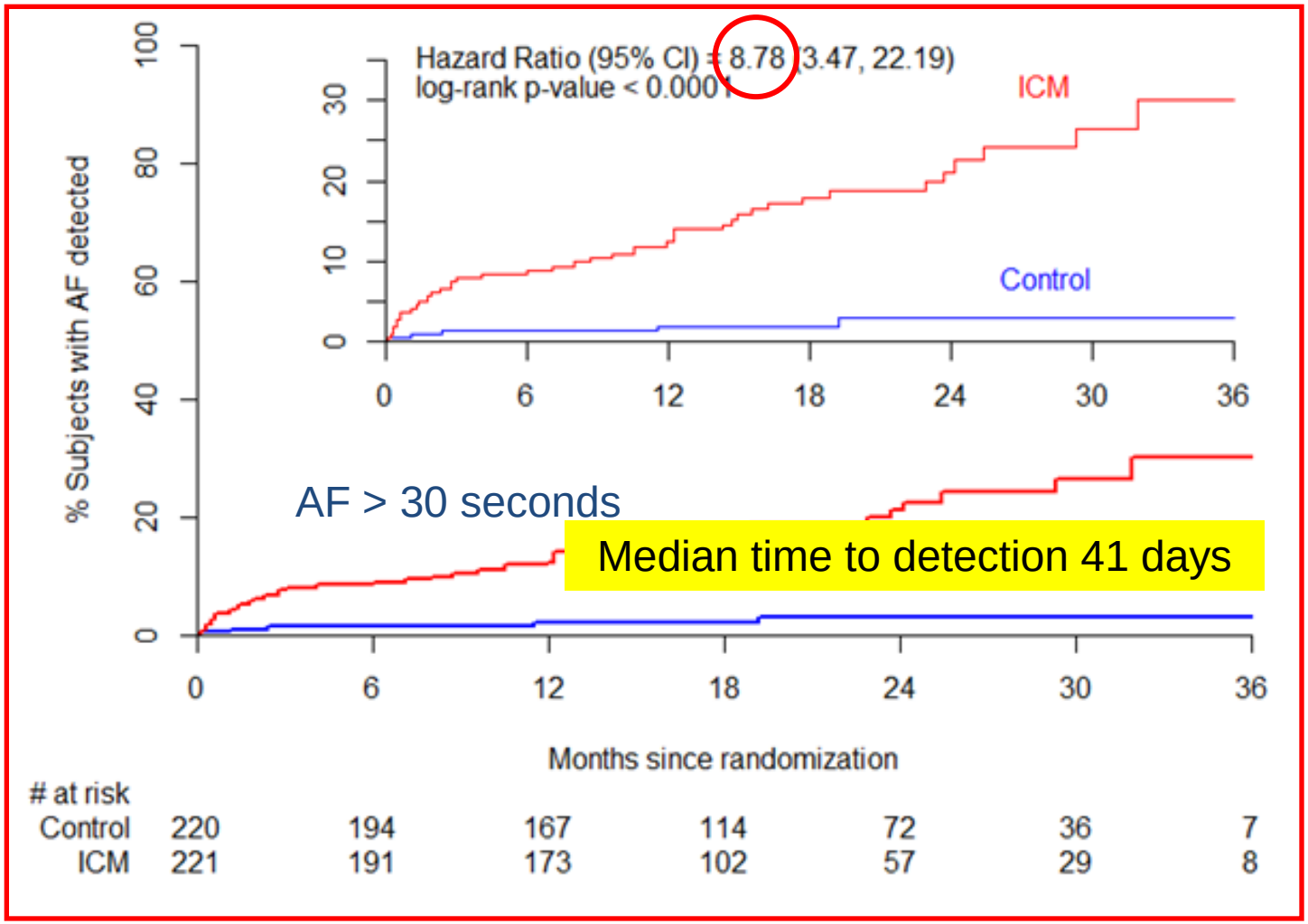
GLADSTONE for the EMBRACE-AF Investigators New Engl J Med 2014

Long term ILR in ESUS patients CRYSTAL-AF

- 441 patients > 40 years with ESUS
- No prior AF
- Randomized to implantable loop recorder versus routine clinical care
- Primary endpoint: AF > 30 seconds detected < 6 months

Sanna for the CRYSTAL-AF Investigators New Engl J Med 2014

Long term monitoring in cryptogenic stroke CRYSTAL-AF



Rate of detection in ICM arm was 30.0% vs 3.0% in control arm after 36 months

University Medical Center Groningen

Sanna for the CRYSTAL-AF Investigators New Engl J Med 2014

Conclusion

ECG monitoring after ischemic stroke/ TIA of unknown source with an insertable monitor ?

YES

Safety and benefit of ILR

- Infection: 1.4%
- ILR remained inserted in 97% at 1 year
- Number needed to implant to detect 1st episode AF 14 for 6 months, 4 for 36 months

Sanna for the CRYSTAL-AF Investigators New Engl J Med 2014

High risk patients

AF can also occur asymptomatic: ‘silent AF’

Recommendations	Class[a]	Level [b]
Opportunistic screening for AF in patients ≥65 years of age using pulse-taking followed by an ECG is recommended to allow timely detection of AF.	I	B

Camm et al. ESC focussed update AF guidelines Eur Heart J 2012

And cryptogenic ischemic strokes may be associated with AF

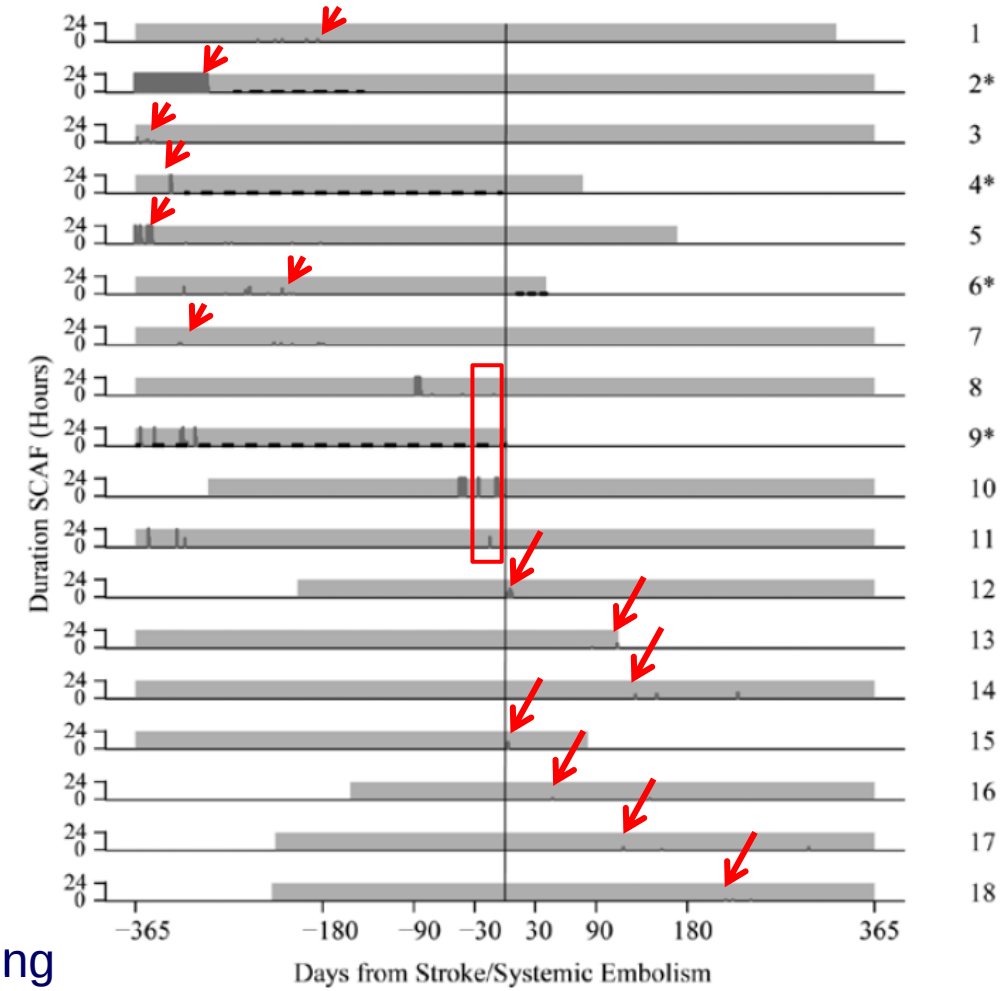
- 123 patients with ESUS using ILR
- AF in 23 patients (20%)
- First detection after 4 months

Risk of ischemic stroke or embolism in SCAF

- 2580 patients with hypertension, > 65 yrs
- no AF, pacemaker or ICD
- Follow-up: 2.5 years
- Subclinical AF: > 6 min > 190 bpm

Healey New Engl J Med 2012 ASSERT Study

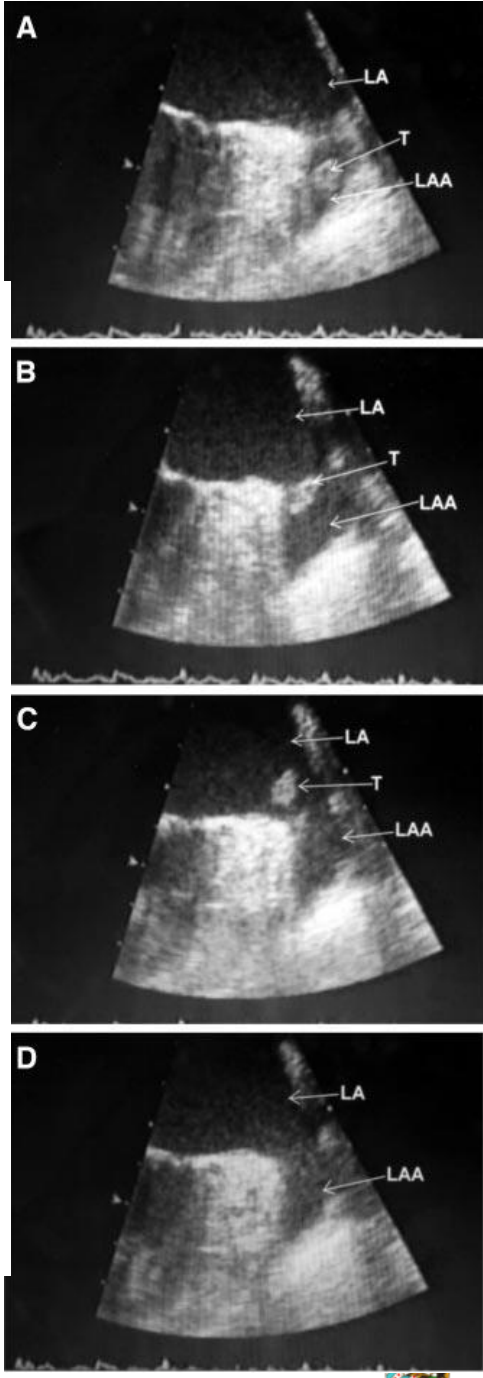
Temporal disconnect



monitoring

VKA therapy

stroke



Brambatti for the ASSERT Investigators Circulation 2014

Parekh et al. Circ 2006

University Medical Center Groningen

AF: mechanism or marker for stroke ?

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

Continuous rhythm monitoring RACE V

Medtronic Advisa Pacemaker

Medtronic Reveal LINQ

CareLink system

FOCUSON™

Medtronic
When Life Depends on Medical Technology
funded by the
dutch heart foundation
Hartstichting

RACE V

Medtronic

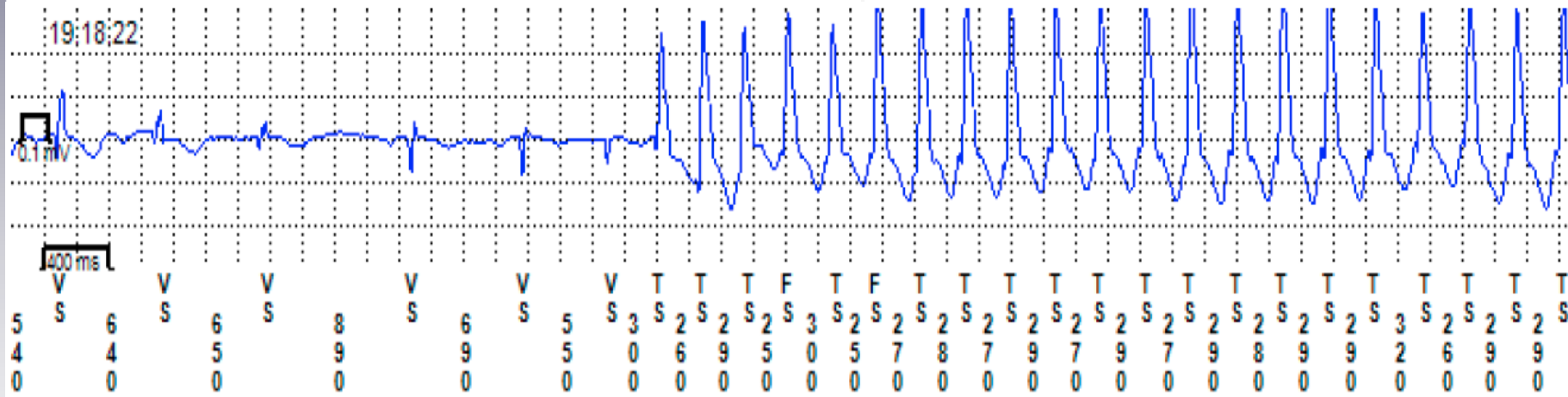
FOCUSON™

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 tachycardieen zichtbaar max duur 20 seconden (#9) mogelijk VT, SVT/AT aberrante geleiding niet uitgesloten.

- 65 year old female
- Symptomatic atrial fibrillation
- Risk factor for AF hypertension
- Near collaps ~19.15 h



- 35 year old male
- Symptomatic atrial fibrillation
- Obesity, BMI 31, no other risk factors

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 FOCUS**ON**™ 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

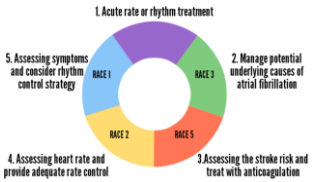
funded by the
dutch heart foundation

Hartstichting

University Medical Center Groningen

ESC COUNCIL Stroke

cohfar
Center for Translational Molecular Medicine
a ctmm project



atrialfibrillationresearch.nl