




“Waar de blanke top der duinen”

over het afwegen van de benefit/risk ratio

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Amphia ziekenhuis / Julius Clinical

Stroke prevention in atrial fibrillation

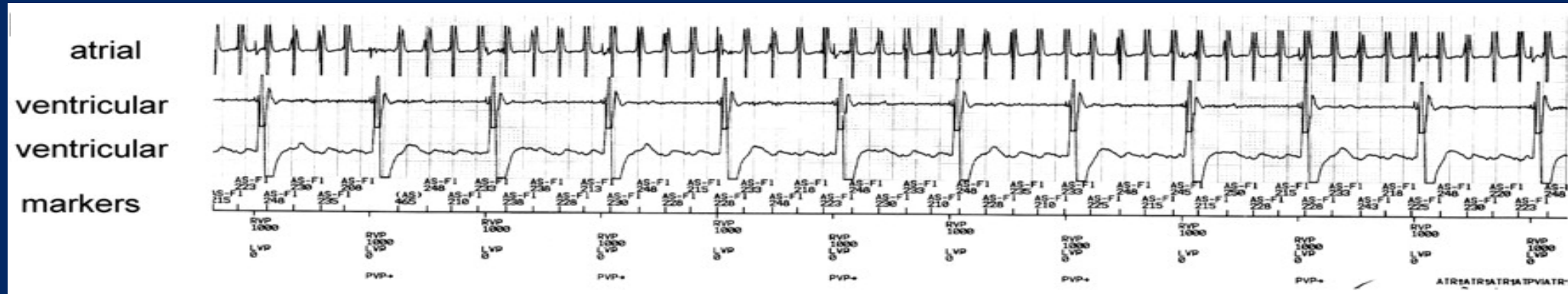
 European Heart Journal (2016) 37, 2893–2962	
OAC for SPAF is recommended in male AF patients with CHADSVASc ≥ 2 , and in female AF patients with CHADSVASc ≥ 3	I
OAC for SPAF should be considered in male AF patients with CHADSVASc 1, and in all female AF patients with CHADSVASc 2	IIa
When OAC is indicated a NOAC is preferred to VKA	I

*that which we call a rose
by any other name would smell as sweet*

subclinical atrial fibrillation (SCAF)

(device detected) atrial high rate electrograms (AHRE)
excessive atrial ectopic activity (ESVEA)

SCAF: (how) does it differ from AF?



SCAF is a variant of clinical AF but differs in that SCAF:

- would not be detected by means other than an implanted device with 24/7 recording
- is often asymptomatic; episodes short in duration

Is the cardiovascular risk with SCAF the same as with AF?

TRENDS: is SCAF associated with stroke?

- prospective, 2486 pacemaker-patients, ≥ 1 CHADS₂ risk score
- SCAF = AT >175 bpm, ≥ 20 sec

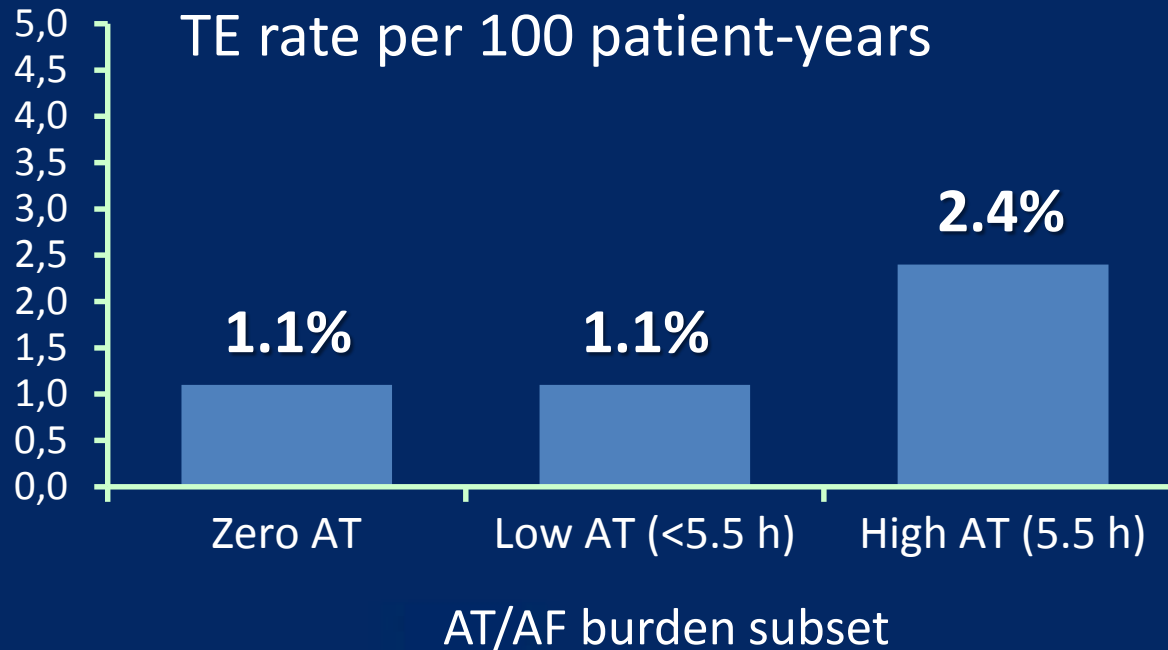
Objective:

Is AT burden over a 30-day period an independent predictor for stroke?

- mean age 71 yr, mean follow-up 1.4 yr, CHADS₂ 2.2
- 53% of patients had no AT/AF at any time
- median duration of AT/AF burden in 30 day windows : 5.5 h

Glötzer TV et al. *Circulation Arrhythm Electrophys* 2009;2:474–80.

TRENDS: is SCAF associated with stroke?



AT/AF burden	HR for TE high vs zero burden
Low <5.5 h	0.98 [0.34, 2.82]
High ≥5.5 h	2.20 [0.96, 5.05]

- TE rate was low compared to clinical AF
- TE risk seems to be related to AT/AF burden

ASSERT: is SCAF associated with stroke?

- 2580 new PM/ICD pts; ≥ 65 years + hypertension; no history of AF, no VKA
- SCAF = atrial rate >190 bpm, >6 min



- **Primary outcome:** ischaemic stroke or systemic embolism

	SCAF before 3 month visit		Event %/yr		HR	95% CI	<i>p</i>
	No (n=2319)	Yes (n=261)	SCAF no (n=2319)	SCAF yes (n=261)			
Age (yr)	76	77	Stroke / SE	0.69 1.69	2.49	1.28 - 4.85	0.007
CHADS ₂	2.3	2.2	Clinical AF/AFL	1.22 6.29	5.56	3.78 - 8.17	<0.001

Healey JS et al. *N Engl J Med.* 2012;366:120–9.

thus: SCAF is associated with stroke

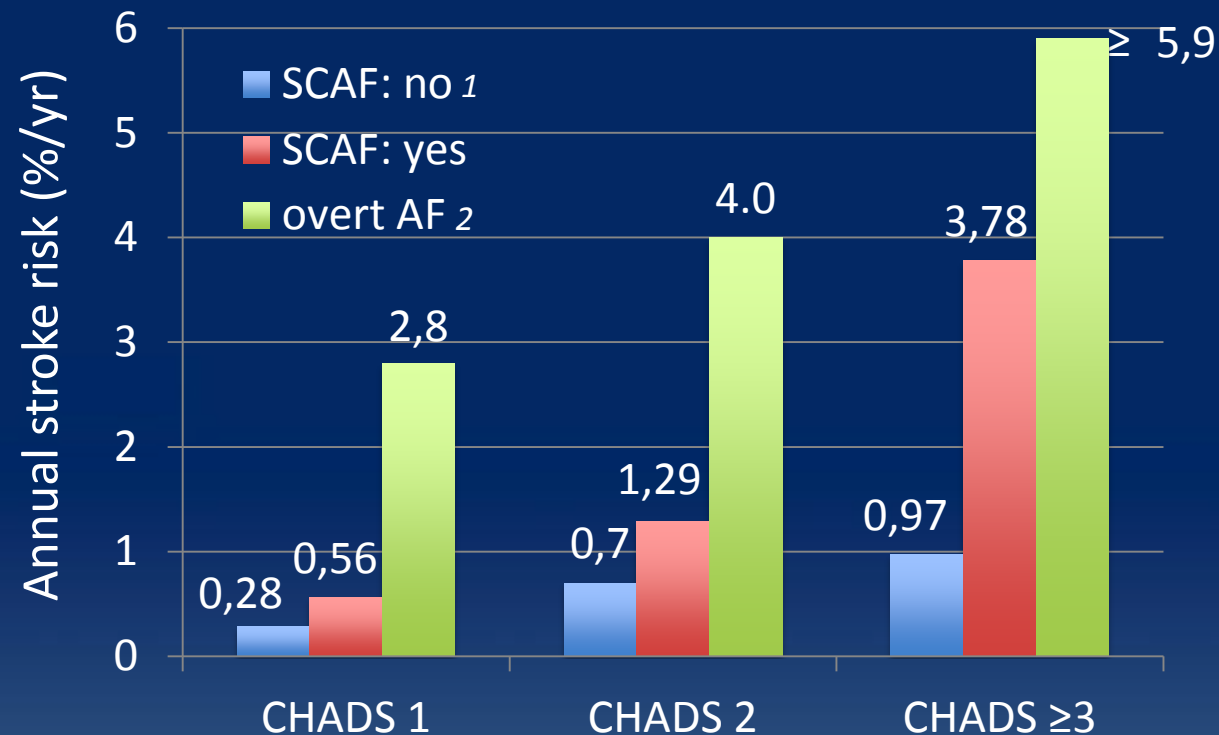
Is stroke risk in SCAF similar as in overt AF?



Healey JS et al. N Engl J Med. 2012;366:120–9.

thus: SCAF is associated with stroke

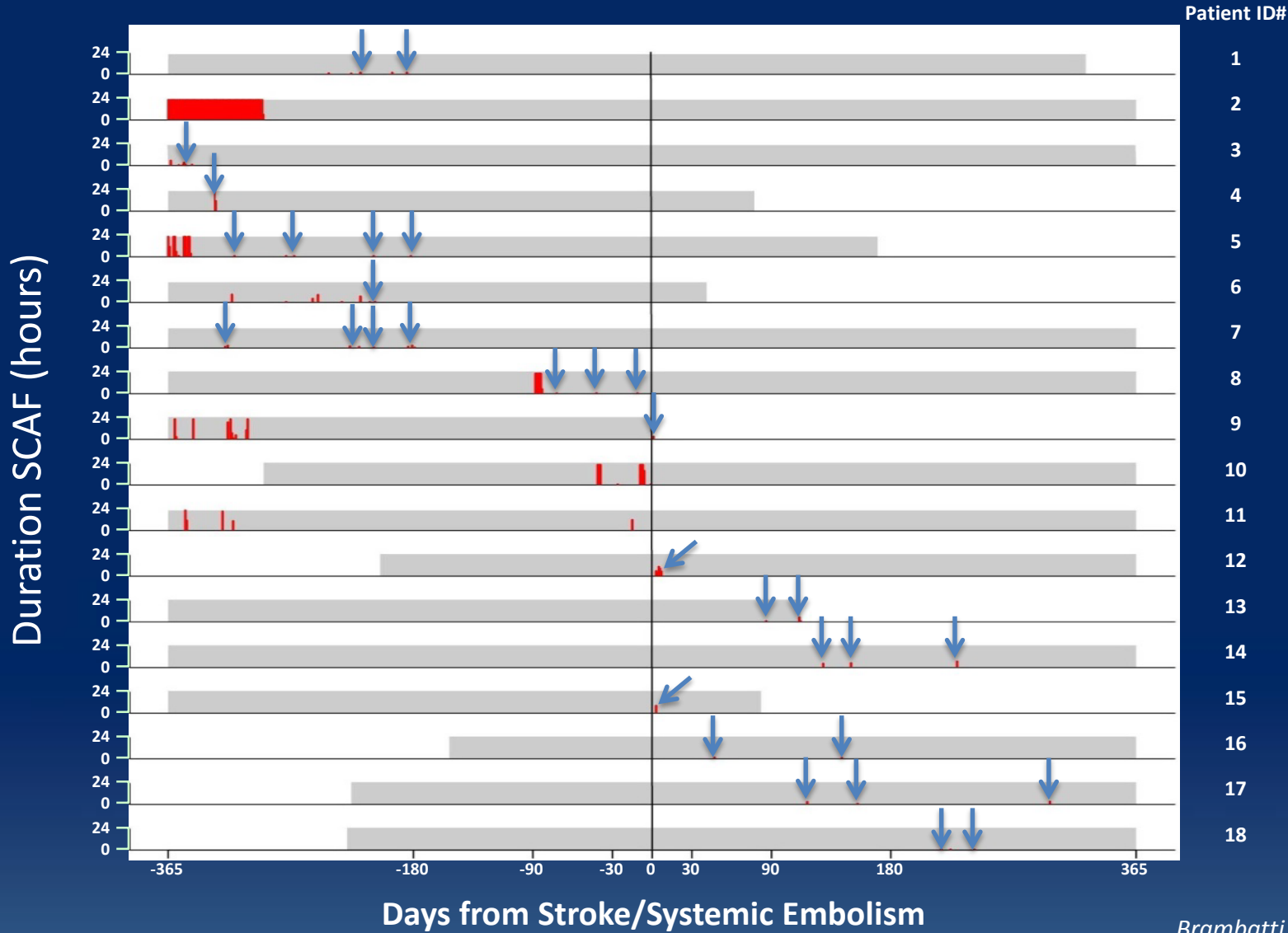
Is stroke risk in SCAF similar as in overt AF?



¹Healey JS et al. *N Engl J Med.* 2012;366:120–9

²Gage BF et al. *JAMA.* 2001;285:2864–70

ASSERT: temporal relation of SCAF and stroke



Brambatti M et al. Circulation. 2014;129:2094–9

in pacemaker recipients SCAF is associated with stroke, given the lower absolute stroke risk when compared to overt AF and absence of a temporal relation with stroke, SCAF may be a marker of risk rather than the cause of stroke

What is the prevalence of SCAF in healthy patients , i.e. non device recipients, with riskfactors for stroke?

What is prevalence of SCAF in older pts (w.o. pacemaker)?

ASSERT-II

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

Jeff S Healey; Marco Alings; Jacob de Graaf; David Birnie; Michel Freericks; Andrew Ha; Atul Verma; Darryl Leong; Hisham Dokainish; Francois Philippon; Walid Barake; Kim Simek; Michael Hill; Jia Wang; Mark Carlson; William F McIntyre; Stuart J Connolly



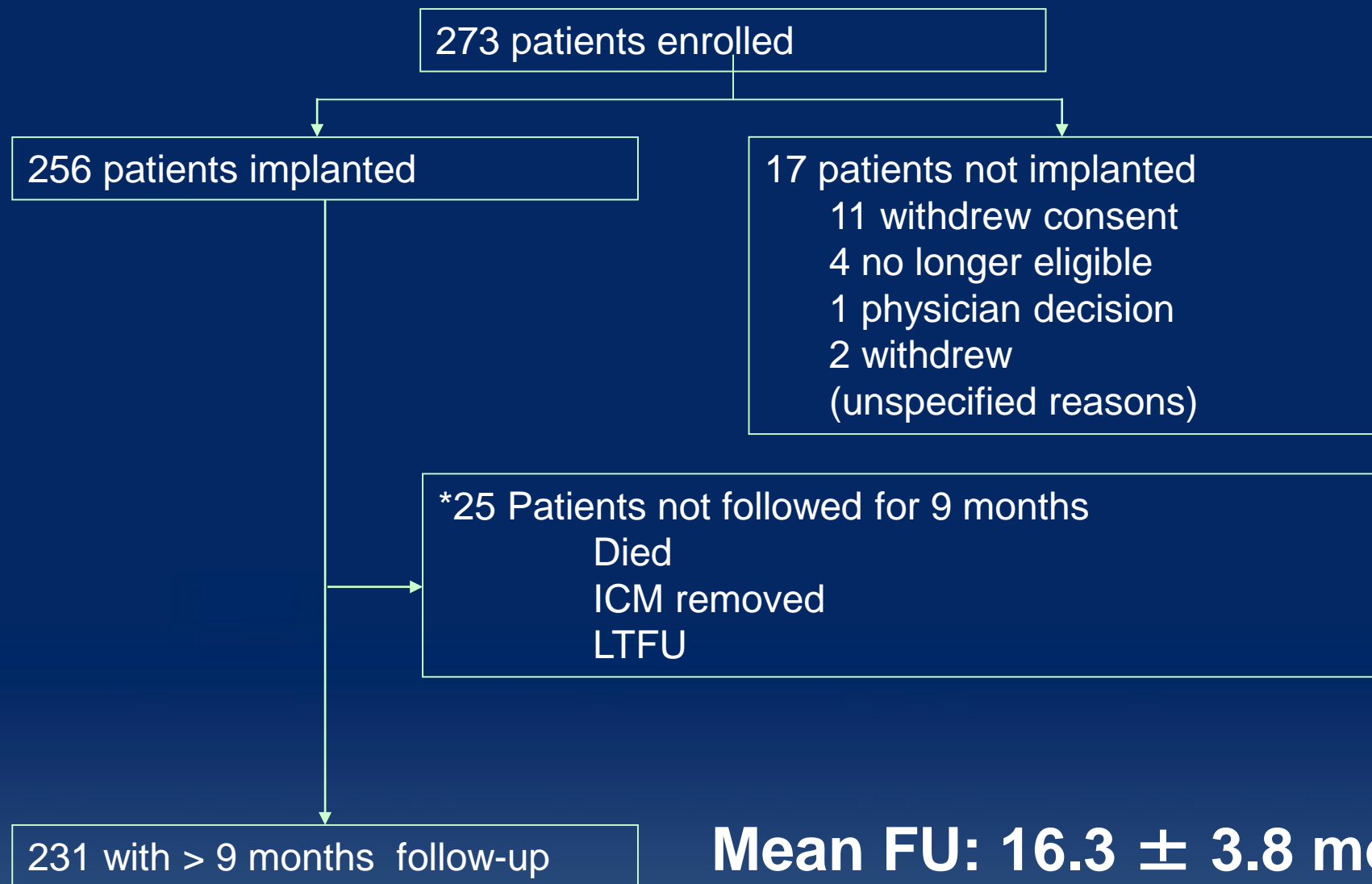
ASSERT II

Study	Phase IV – Cohort study
Population	Elderly patients with cardiovascular risk and risk of AF
Intervention	SJM Confirm®
Objective	incidence of SCAF \geq 5 minutes
Sites	20 Sites in Canada + 10 in the Netherlands; 250 participants total

Inclusion criteria

1. Age \geq 65, plus:
 - a) **CHA₂DS₂-VASc \geq 2**
or
 - b) **OSAS**
or
 - c) **BMI $>$ 30**
2. evidence of AF risk:
 - a) **LA \geq 58ml or \geq 4.4cm)**
or
 - b) **NT-pro-BNP \geq 290 pg/mL (34 pmol/l)**

ASSERT II



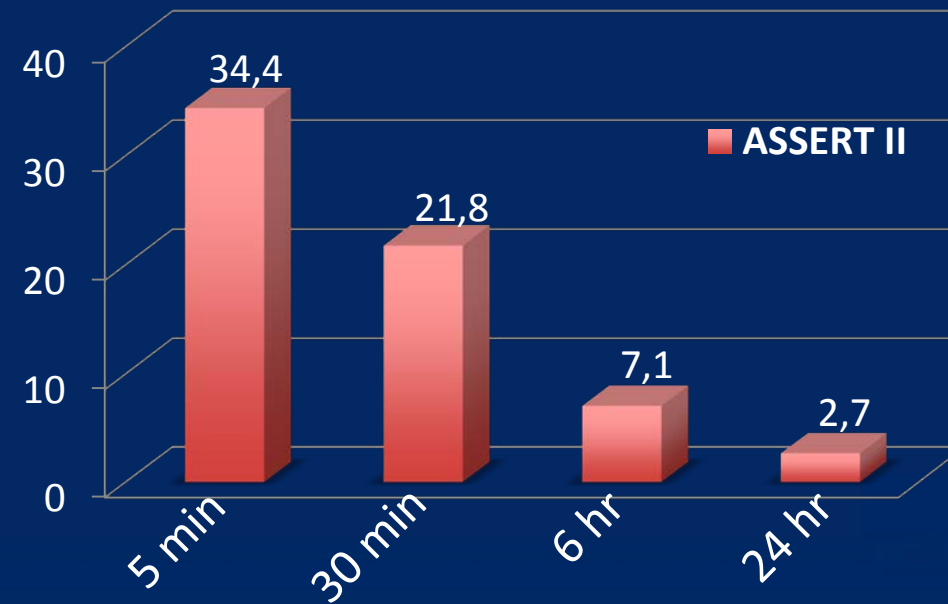
Mean FU: 16.3 ± 3.8 months

ASSERT II: baseline

	overall (n=256)	SCAF (n=90)	no SCAF (n=166)	p Value
Age, mean±SD	73.8±6.2	75.3±6.9	73.1±5.7	0.008
Hx. HTN, n(%)	188 (73.4)	62 (68.9)	126 (75.9)	0.225
Systolic BP (mmHg) ± SD	138±19	135±19	140±19	0.043
Hx. HF, n(%)	22 (8.6)	3 (3.3)	19 (11.4)	0.027
Diabetes, n(%)	64 (25.0)	16 (17.8)	48 (28.9)	0.049
Prior stroke, TIA or SE, n(%)	123 (48.0)	47 (52.2)	76 (45.8)	0.325
Vascular Disease, n(%)	82 (32.0)	22 (24.4)	60 (36.1)	0.055
Sleep Apnea, n(%)	29 (11.3)	9 (10.0)	20 (12.0)	0.622
BMI	28.9±4.6	28.6±5.3	28.75±4.3	0.786
Valve Disease, n(%)	37 (14.5)	12 (13.3)	25 (15.1)	0.708
CHA ₂ DS ₂ -VASc, mean±SD	4.1±1.4	4.1±1.4	4.18±1.36	0.483

ASSERT II: rate of incident SCAF

	n	Rate per year
Patients	256	
≥ 5 min (primary)	90	34.4%
≥ 30 min	63	21.8%
≥ 6 hours	23	7.1%
≥ 24 hours	9	2.7%
Clinical AT/AF	26	7.9%



Prevalence of Sub-Clinical Atrial Fibrillation Using an Implantable Cardiac Monitor in Patients With Cardiovascular Risk Factors: ASSERT II
AHA 2016

ASSERT II: conclusions

SCAF is common in older individuals with risk factors for stroke

- similar or greater frequency than in ICD and pacemaker population
- similar or greater than in patients with cryptogenic stroke:

- *CRYSTAL AF; n = 441; looprecorder vs conventional follow up*
- *End point: AF >30 sec*
- *@6 months: 8.9% vs 1.4% @12 months: 12.4% vs 2.0%*
- ***Mean duration AF/day 4.3 min (0.7-34.5 min)***

NEJM 2014;370:2478-2486

**“as SCAF is associated with stroke,
recommendations for stroke prevention
in AF should be followed”**



Should we? Is benefit/risk ratio the same?



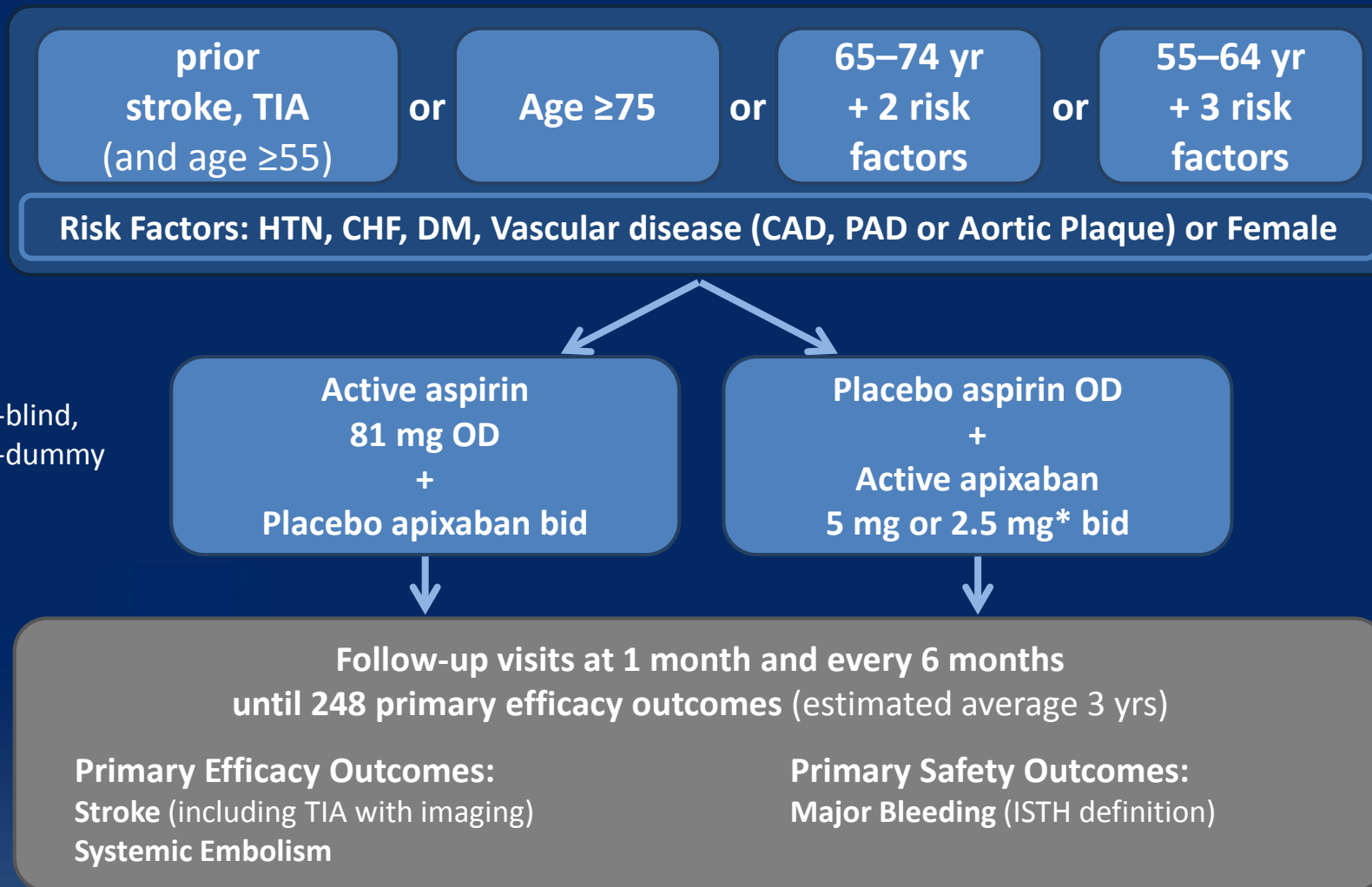
“as SCAF is associated with stroke, recommendations for stroke prevention in AF should be followed”

[...] it is unclear whether AHRE imply the same therapeutic requirements as overt AF, and the benefit of OAC in patients with AHRE is tested in ongoing clinical trials [ARTESiA and NOAH]

[...] in rare individual circumstances, oral anticoagulation may be considered in patients with AHRE but without diagnosed AF



double-blind,
double-dummy
design



ARTESiA: rationale

SCAF

<6 min

“low risk”

no OAC

(some with background
aspirin)

SCAF

6 min – 24 hr

ARTESiA

blinded therapy
(apixaban or aspirin)

SCAF

>24 hr

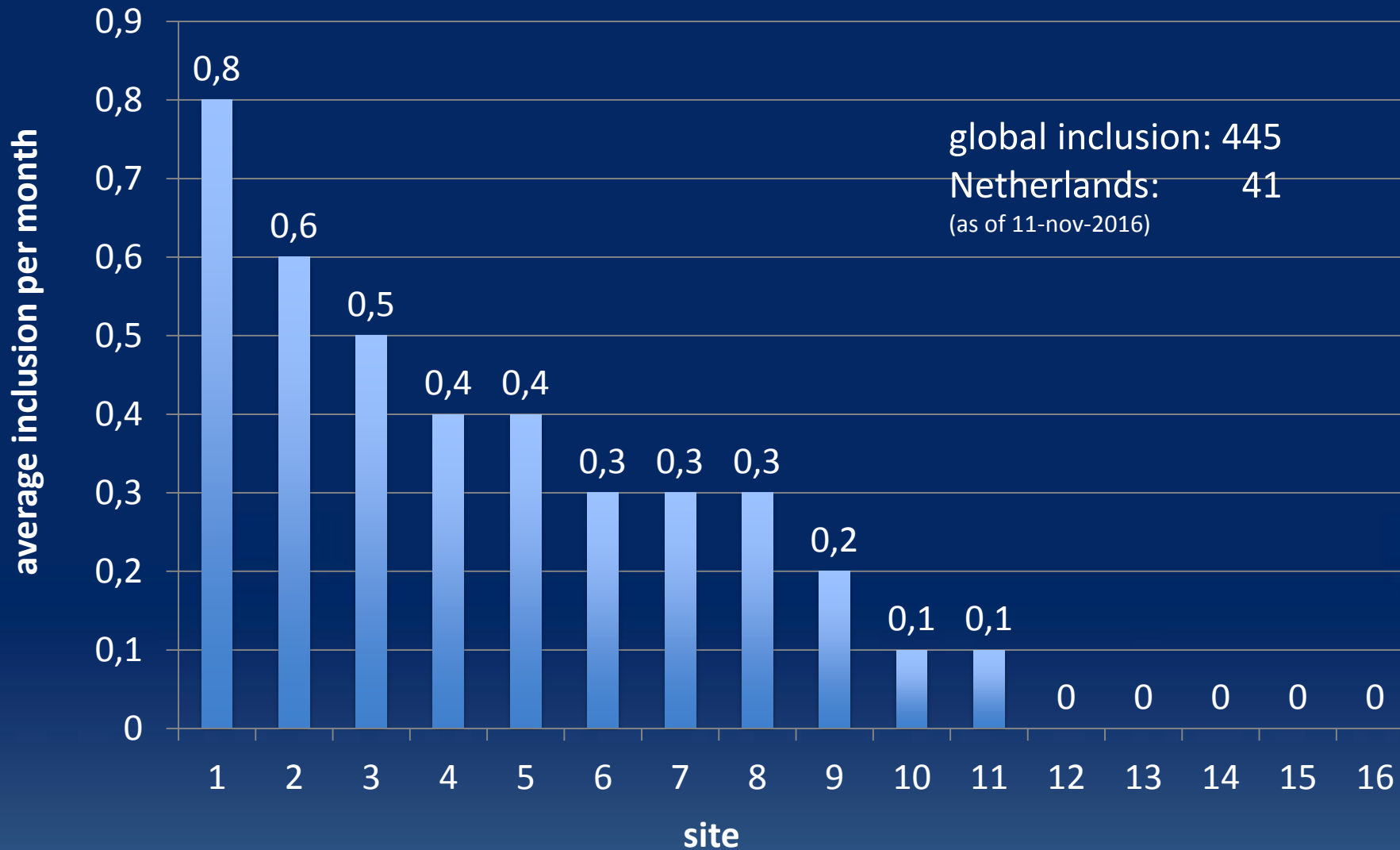
“high
risk”

In rare individual circumstances, oral anticoagulation may be considered in patients with SCAF, but without diagnosed AF. This clearly needs discussion with the patient and careful evaluation of perceived benefit and risk¹

¹Eur Heart J (2016) 37, 2893–2962

ARTESiA: clinicaltrials.gov/ct2/show/NCT01938248.

ARTESiA: average inclusion per month NL



conclusions

- SCAF is very common
- SCAF is associated with stroke
- absolute risk of stroke in SCAF << overt AF
- no temporal relation between SCAF and stroke
- benefit/risk ratio of oral anticoagulation in SCAF is unknown
- ARTESIA will test the benefit of OAC in patients with SCAF



If you are interested to participate please mail: secretariaat@wcnnnet.nl