



## **CIED Detected AF and Stroke Risk?**



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# Korean Heart Rhythm Society

## COI Disclosure

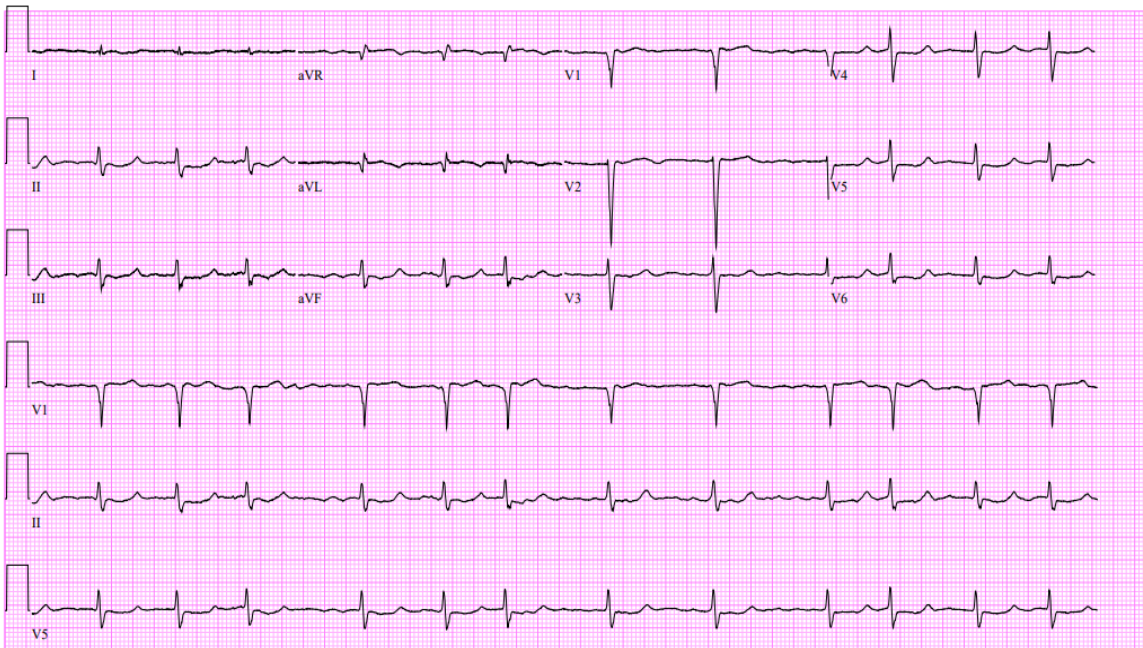
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The authors have no financial conflicts of interest  
to disclose concerning the presentation



# Clinical Atrial fibrillation

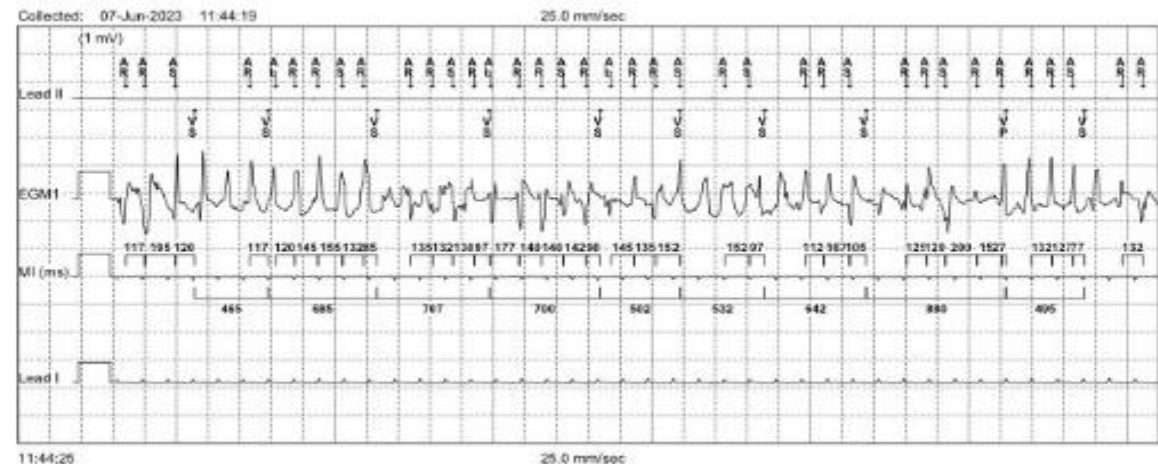
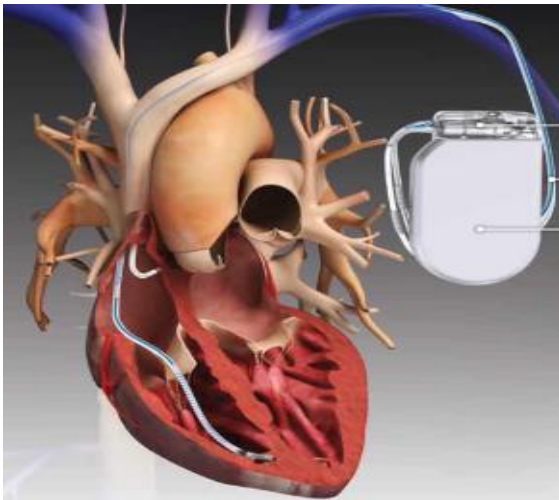
- Traditionally been defined by documentation of the arrhythmia on surface ECG
- Independent of the duration of the arrhythmia or the associated symptoms



# Atrial high-rate episodes(AHRE)

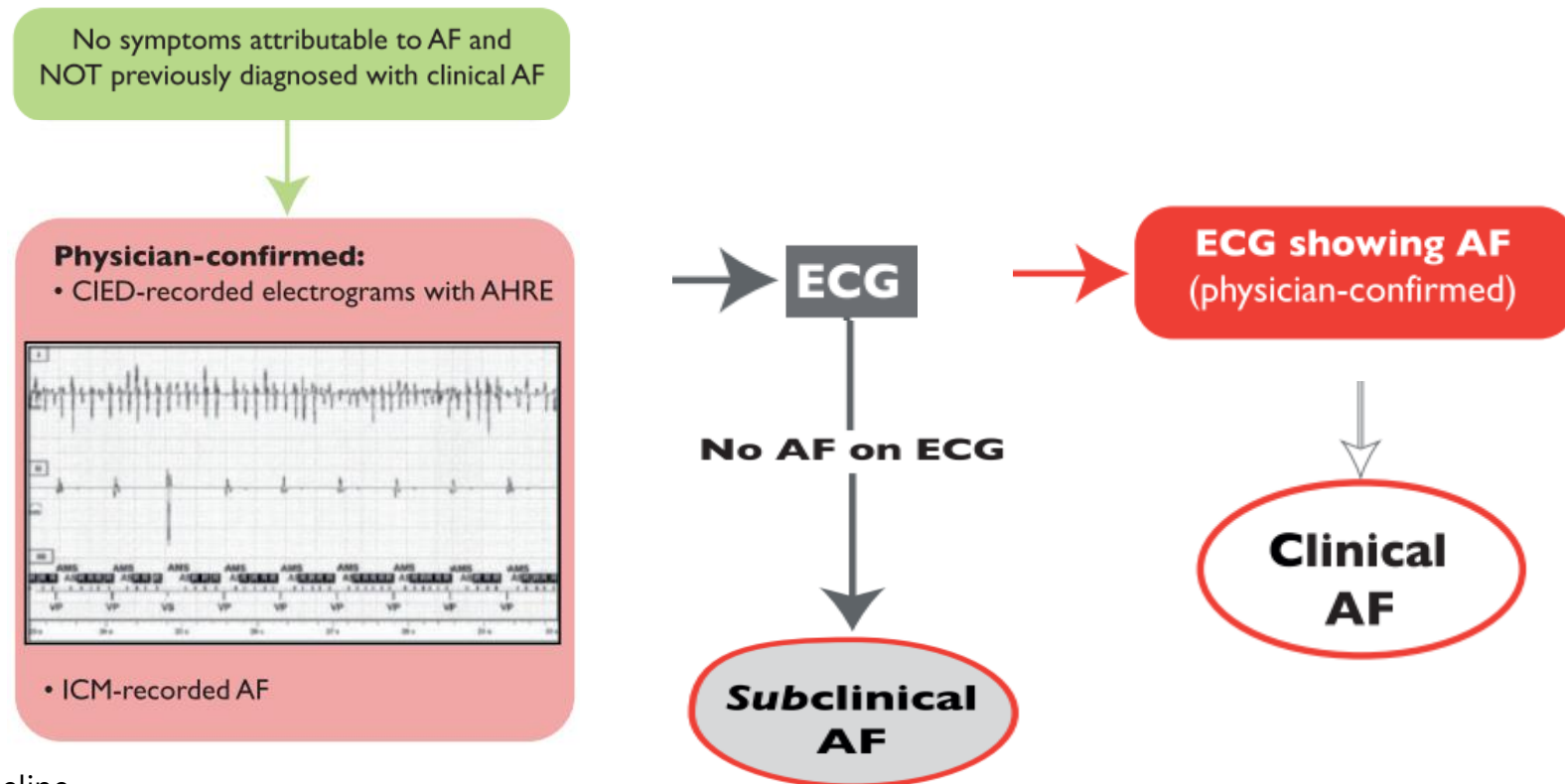
Programmed or specified criteria for AHRE that are detected by CIEDs with an atrial lead allowing automated continuous monitoring of atrial rhythm and tracings storage.

CIED-recorded AHRE need to be visually inspected because some AHRE may be electrical artefacts/false positives.



# Device detected AF = Subclinical AF

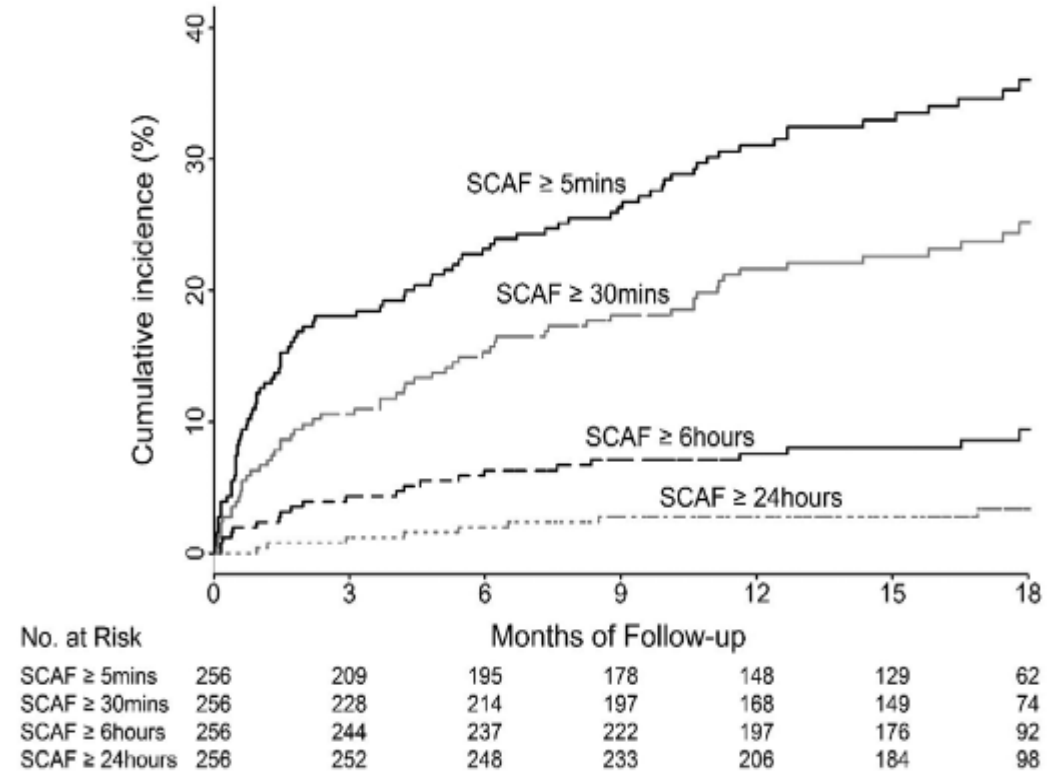
AHRE confirmed to be AF, AFL, or an AT, or AF episodes detected by insertable cardiac monitor or wearable monitor and confirmed by visually reviewed intracardiac electrograms or ECG-recorded rhythm



# ASSERT II: SCAF incidence

:256 patients over 65 yrs with risk factors, without known AF, implant ILR

	Overall (n=256)	SCAF (n=90)	No SCAF (n=166)	P Value
Age, y (SD)	73.9 (6.2)	75.3 (6.9)	73.1 (5.7)	0.008
Female sex, n (%)	88 (34.4)	33 (36.7)	55 (33.1)	0.57
White, n (%)	246 (96.1)	89 (98.9)	157 (94.6)	0.17
History of hypertension, n (%)	188 (73.4)	62 (68.9)	126 (75.9)	0.23
Systolic blood pressure, mm Hg (SD)	137.9 (19.2)	134.6 (18.5)	139.7 (19.4)	0.043
Resting sinus rate, bpm (SD)	64.6 (10.2)	65.7 (9.6)	64.0 (10.5)	0.19
History of heart failure, n (%)	22 (8.6)	3 (3.3)	19 (11.4)	0.027
Diabetes mellitus, n (%)	64 (25.0)	16 (17.8)	48 (28.9)	0.049
Prior stroke, TIA, or systemic embolism, n (%)	123 (48.0)	47 (52.2)	76 (45.8)	0.33
Vascular disease, n (%)	82 (32.0)	22 (24.4)	60 (36.1)	0.06
Sleep apnea, n (%)	29 (11.3)	9 (10.0)	20 (12.0)	0.62
BMI, kg/m <sup>2</sup>	28.7 (4.6)	28.6 (5.3)	28.8 (4.3)	0.79

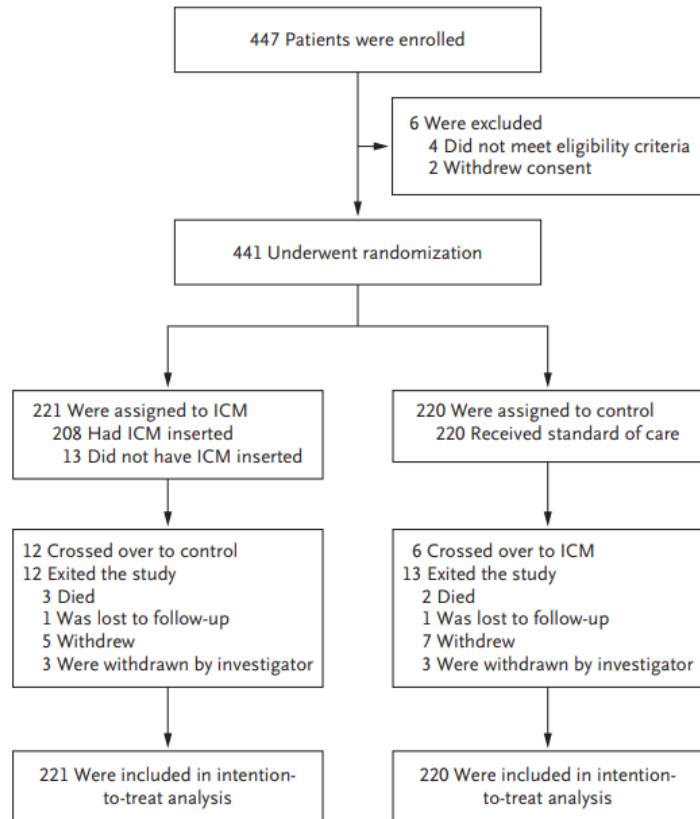


- Baseline age was 74 years, mean CHA2DS2-VASc score was  $4.1 \pm 1.4$
- SCAF  $\geq 5$  minutes was detected in 90 patients (detection rate, 34.4%/y)
- Baseline predictors of SCAF were increased, left atrial dimension, and blood pressure

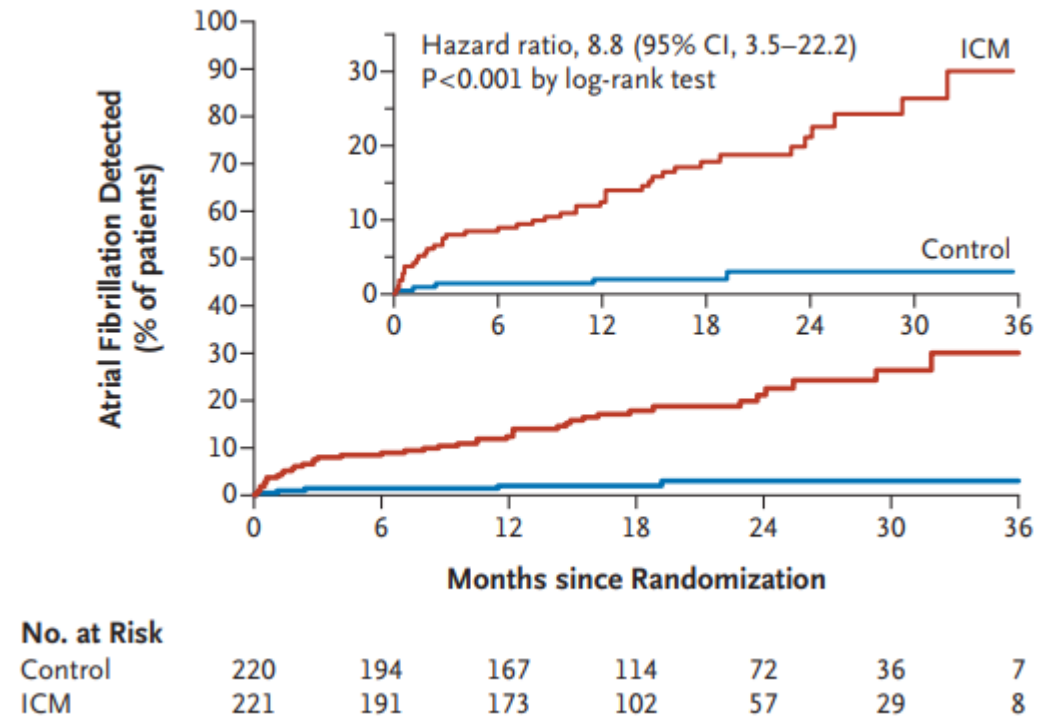


# CRYSTAL AF: SCAF incidence

:441 patients with cryptogenic stroke. >40 yrs without known AF, implant ILR



C Detection of Atrial Fibrillation by 36 Months

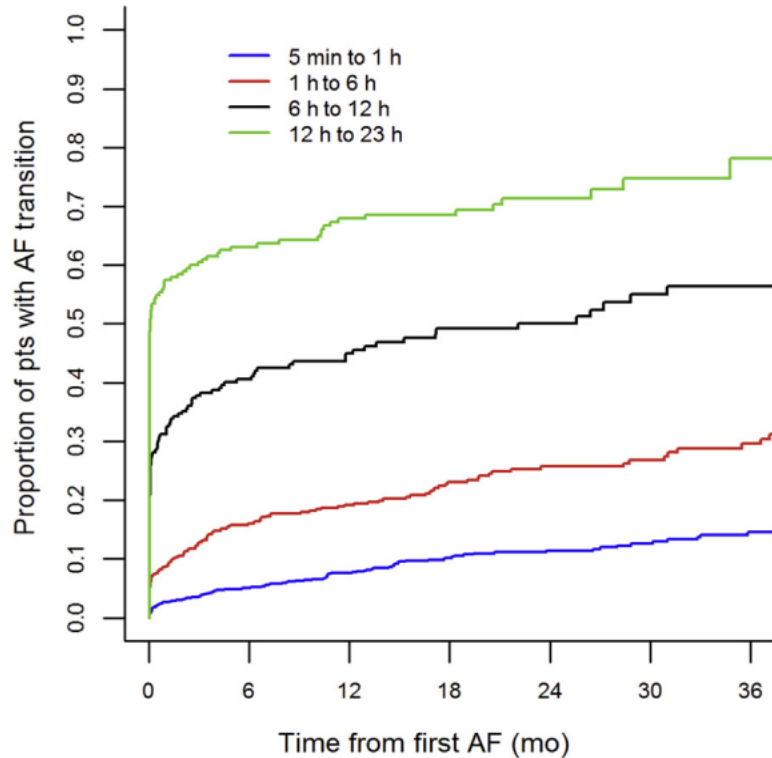


- By 36 months, atrial fibrillation had been detected in 30.% of patients in the ICM group (42 patients) versus 3.0% of patients in the control group (5 patients)



# SCAF progression

:5580 CIED patients without AF



Parameter	Univariate		Multivariate*	
	HR (95% CI)	P value	HR (95% CI)	P value
Male sex <sup>†</sup>	1.78 (1.42-2.22)	<.001	1.77 (1.41-2.21)	<.001
Age ≥ 75 y	1.32 (1.10-1.58)	.003		
Diabetes	1.09 (0.88-1.33)	.430		
Prior stroke	1.13 (0.73-1.75)	.586		
Hypertension	1.26 (1.04-1.52)	.017		
Heart failure	1.19 (0.99-1.42)	.060		
CHADS <sub>2</sub> ≥ 2 <sup>†</sup>	1.45 (1.21-1.73)	<.001	1.44 (1.20-1.72)	<.001
CRT	1.26 (1.06-1.50)	.008		

- AF burden of 5 minutes, was detected in 2244 patients (34%)
- 1091 (49.8%) transitioned to a higher AF-burden threshold during follow-up



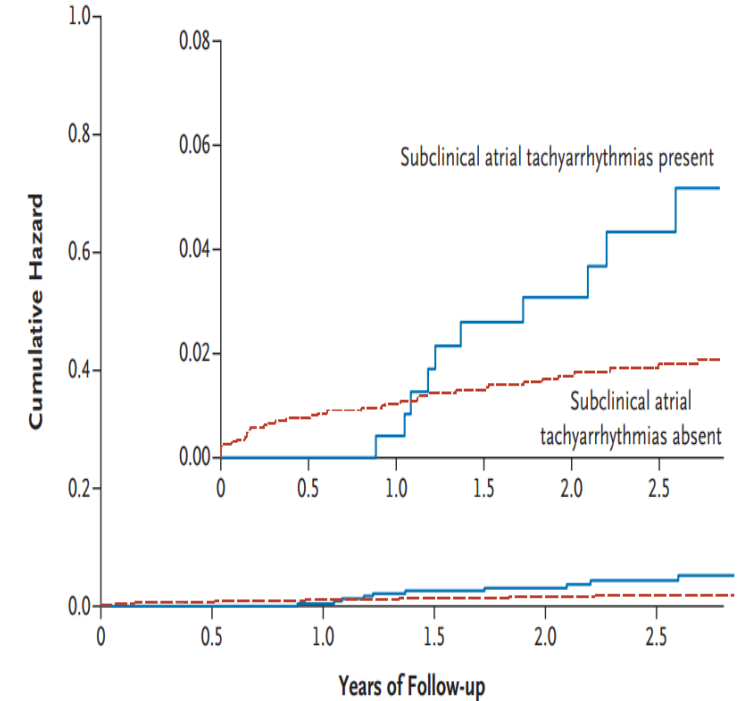


# ASSERT: SCAF and stroke

:2580 pacemaker patients over 65 yrs with HTN, without known AF

**Table 1. Baseline Characteristics of the Patients.\***

Characteristic	Device-Detected Subclinical Atrial Tachyarrhythmia		P Value
	Yes (N=261)	No (N=2319)	
Age — yr	77±7	76±7	0.13
Male sex — no. (%)	147 (56.3)	1359 (58.6)	0.48
Systolic blood pressure while sitting — mm Hg	137±20	138±19	0.38
Heart rate — beats/min	68±12	70±12	0.001
Body-mass index‡	28±5	27±5	0.43
Risk factors for stroke — no. (%)			
Prior stroke	18 (6.9)	168 (7.2)	0.84
Prior transient ischemic attack	13 (5.0)	113 (4.9)	0.94
History of heart failure	39 (14.9)	335 (14.4)	0.83
Diabetes mellitus	59 (22.6)	674 (29.1)	0.03
Prior myocardial infarction	32 (12.3)	427 (18.4)	0.01
CHADS <sub>2</sub> score§	2.2±1.1	2.3±1.0	0.47
Sinus-node disease, with or without atrioventricular-node disease — no. (%)	130 (49.8)	964 (41.6)	0.01
Atrioventricular-node disease, without sinus-node disease — no. (%)	132 (50.6)	1279 (55.2)	0.16
Atrial lead in septal position — no. (%)	101 (38.7)	972 (41.9)	0.32
Duration of hypertension >10 yr — no. (%)	115 (44.1)	965 (41.6)	0.45
Left ventricular hypertrophy on ECG — no. (%)	6 (2.3)	105 (4.5)	0.09
Time from implantation of pacemaker or ICD to enrollment — days	25±22	29±40	0.04



**No. at Risk**

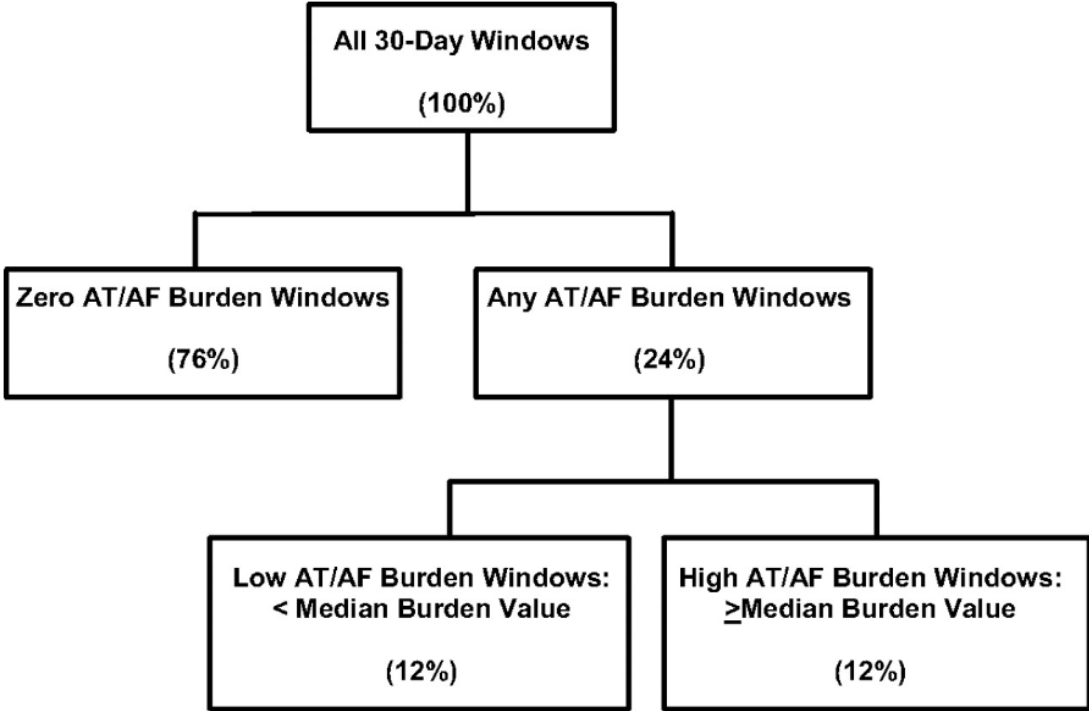
Subclinical atrial tachyarrhythmias present	261	249	238	218	178	122
Subclinical atrial tachyarrhythmias absent	2319	2145	2070	1922	1556	1197

- By 3 months, SCAF detected in 261 patients (10.1%)
- Subclinical atrial tachyarrhythmias were associated with an increased risk of ischemic stroke or systemic embolism (HR 2.49)



# TRENDS: SCAF and stroke

:2486 CIED patients with 1 stroke risk factor( HF, HTN, age≥65 yrs, DM, prior stroke)



Category	Variable	Hazard Ratio (95% CI)*	P Value
AT/AF burden	Low burden vs zero burden	0.98 (0.34, 2.82)	0.97
	High burden vs zero burden	2.20 (0.96, 5.05)	0.06

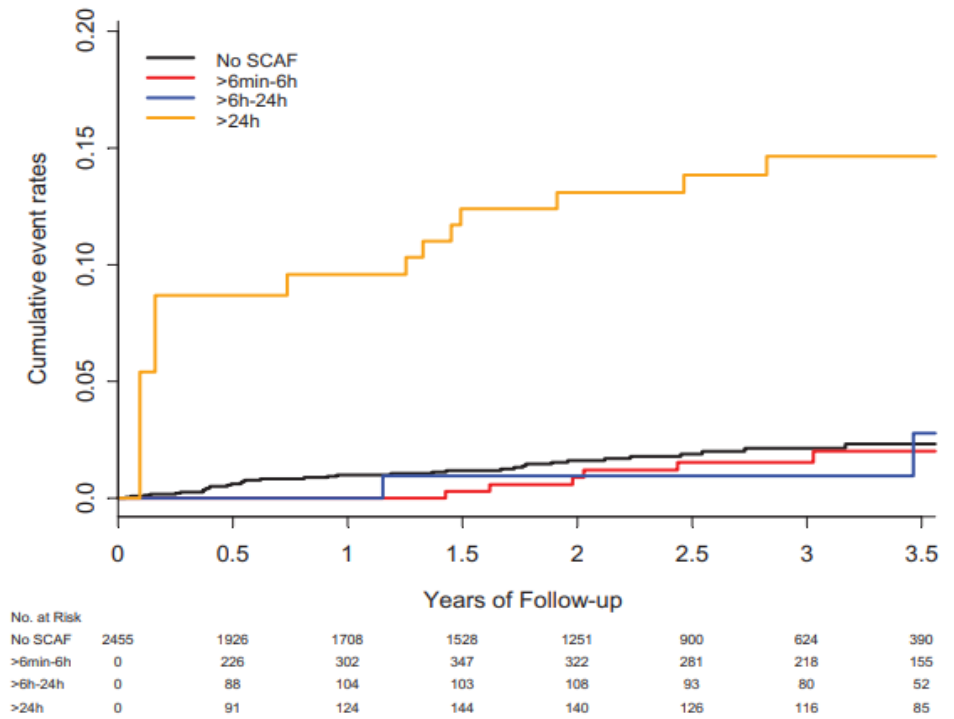
- 47% of study patients had AT/AF observed during study.
- During a mean follow-up of 1.4 years, annualized TE risk was 1.1% for zero, 1.1% for low, and 2.4% for high burden subsets of 30-day windows
- AT/AF burden ≥5.5 hours on any of 30 prior days appeared to double TE risk



# SCAF duration and stroke: ASSERT trial analysis

:2580 pacemaker patients over 65 yrs with HTN, without known AF

	No SCAF (N=1562)	SCAF >6 min-6 h (N=462)	SCAF >6 h-24 h (N=169)	SCAF >24 h (N=262)
Age (years), mean ± SD	76.0 ± 6.7	76.9 ± 6.5	76.2 ± 6.9	77.2 ± 7.0
Male, n (%)	887 (56.8)	254 (55.0)	104 (61.5)	183 (69.8)
Systolic blood pressure (sitting, mmHg), mean ± SD	137.8 ± 19.4	139.0 ± 19.5	139.5 ± 19.8	136.3 ± 19.1
Heart rate (bpm), mean ± SD	70.0 ± 11.7	70.1 ± 12.0	68.7 ± 10.3	67.7 ± 11.2
BMI (kg/m <sup>2</sup> ), mean ± SD	27.3 ± 4.8	27.5 ± 4.9	27.4 ± 5.2	28.3 ± 5.0
Prior stroke, n (%)	116 (7.4)	30 (6.5)	15 (8.9)	16 (6.1)
Prior TIA, n (%)	77 (4.9)	21 (4.5)	9 (5.3)	13 (5.0)
History heart failure, n (%)	222 (14.2)	70 (15.2)	27 (16.0)	43 (16.4)
Diabetes mellitus, n (%)	470 (30.1)	110 (23.8)	48 (28.4)	77 (29.4)
Prior MI, n (%)	300 (19.2)	68 (14.7)	30 (17.8)	48 (18.3)
CHADS <sub>2</sub> score, mean ± SD	2.3 ± 1.0	2.2 ± 1.0	2.3 ± 1.0	2.3 ± 1.0
CHA <sub>2</sub> DS <sub>2</sub> -VAsC score, mean ± SD	4.0 ± 1.3	3.9 ± 1.3	4.0 ± 1.4	4.0 ± 1.2
Sinus node disease with or without atrioventricular-node disease, n (%)	668 (42.8)	194 (42.0)	74 (43.8)	120 (45.8)
Atrioventricular node disease without sinus-node disease, n (%)	776 (49.7)	240 (51.9)	87 (51.5)	129 (49.2)
Atrial lead septal position, n (%)	66 (4.2)	25 (5.4)	3 (1.8)	10 (3.8)
Duration hypertension >10 years, n (%)	629 (40.3)	208 (45.0)	72 (42.6)	119 (45.4)
Aspirin, n (%)	987 (63.2)	267 (57.8)	102 (60.4)	168 (64.1)
Beta-blocker, n (%)	599 (38.3)	138 (29.9)	67 (39.6)	104 (39.7)
Statin, n (%)	773 (49.5)	200 (43.3)	87 (51.5)	124 (47.3)

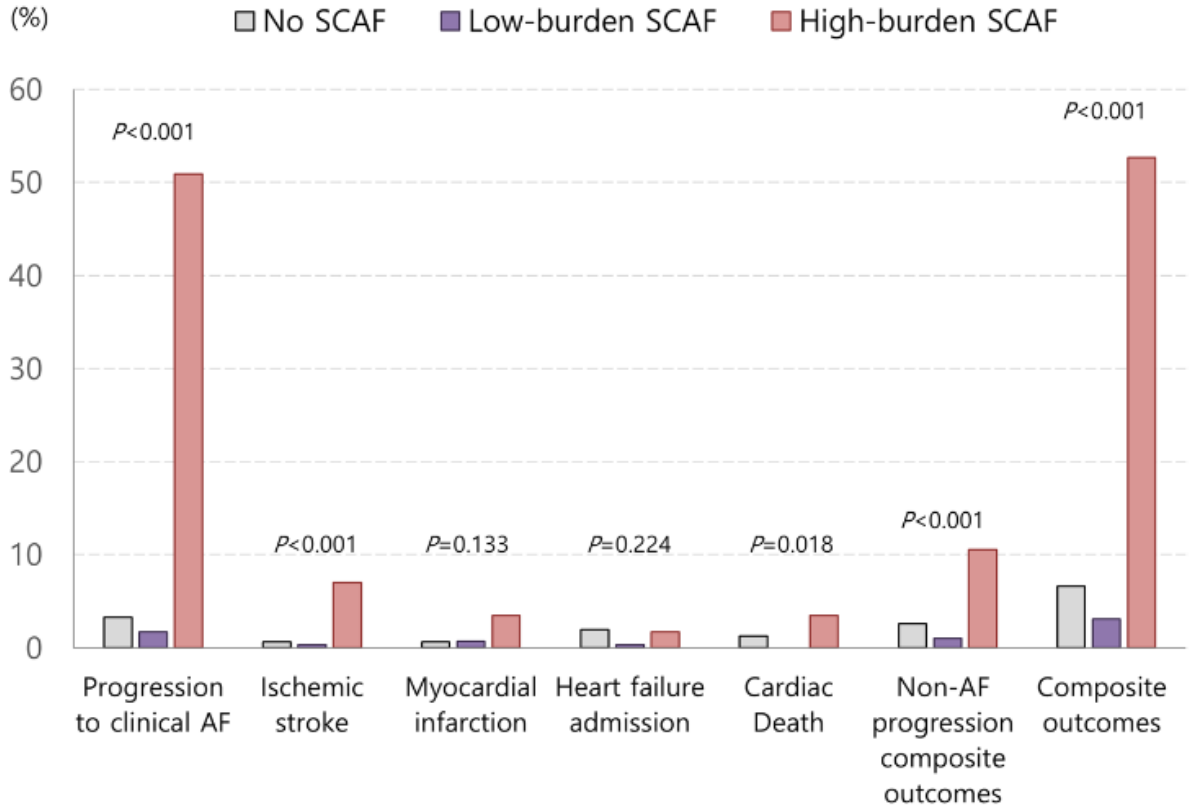
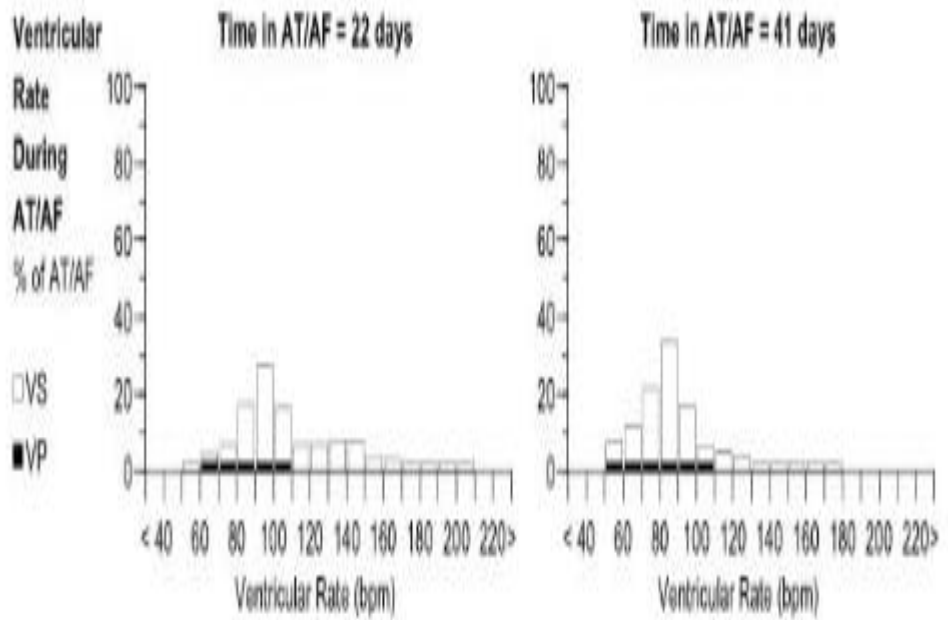


- SCAF duration >24 h was associated with a significant increased risk of subsequent stroke or systemic embolism (HR 3.2)
- SCAF between 6 min and 24 h was not significantly different from patients without SCAF



# SCAF burden and stroke: SMC data

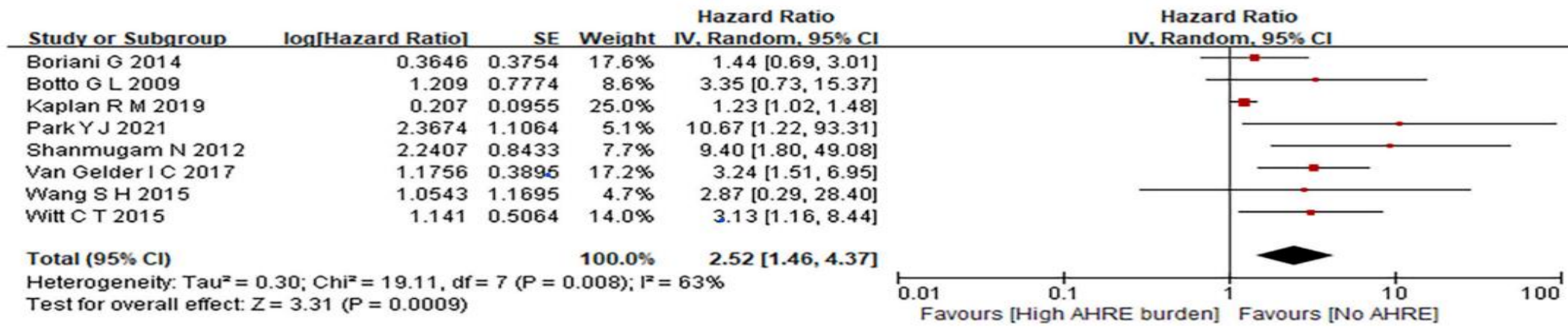
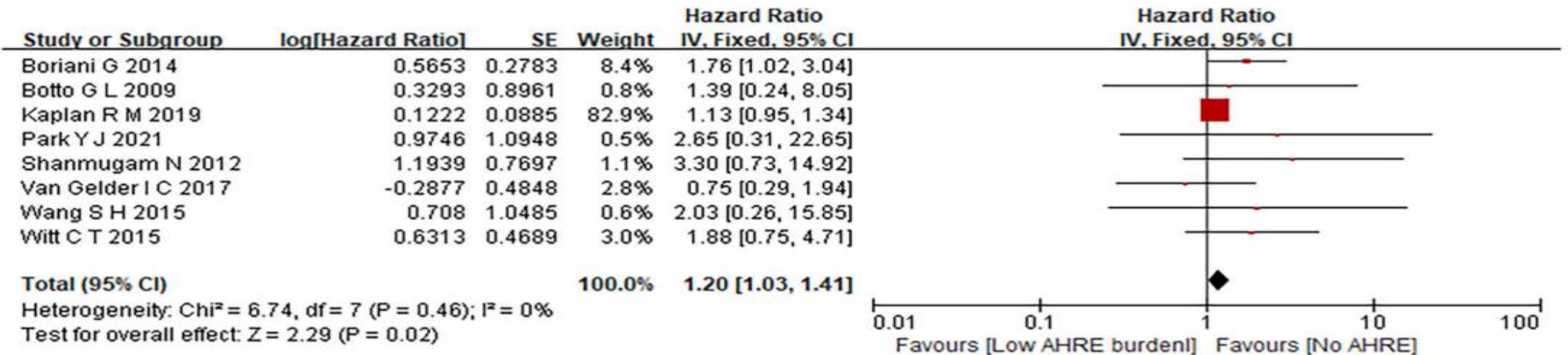
:496 pacemaker patients without known AF



- For 5.2 years, 344/496(69%) patients observed SCAF.
- High-burden SCAF(>24hr) associated risk of progression to clinical AF, ischemic stroke, cardiac death.



# SCAF duration and stroke: meta-analysis



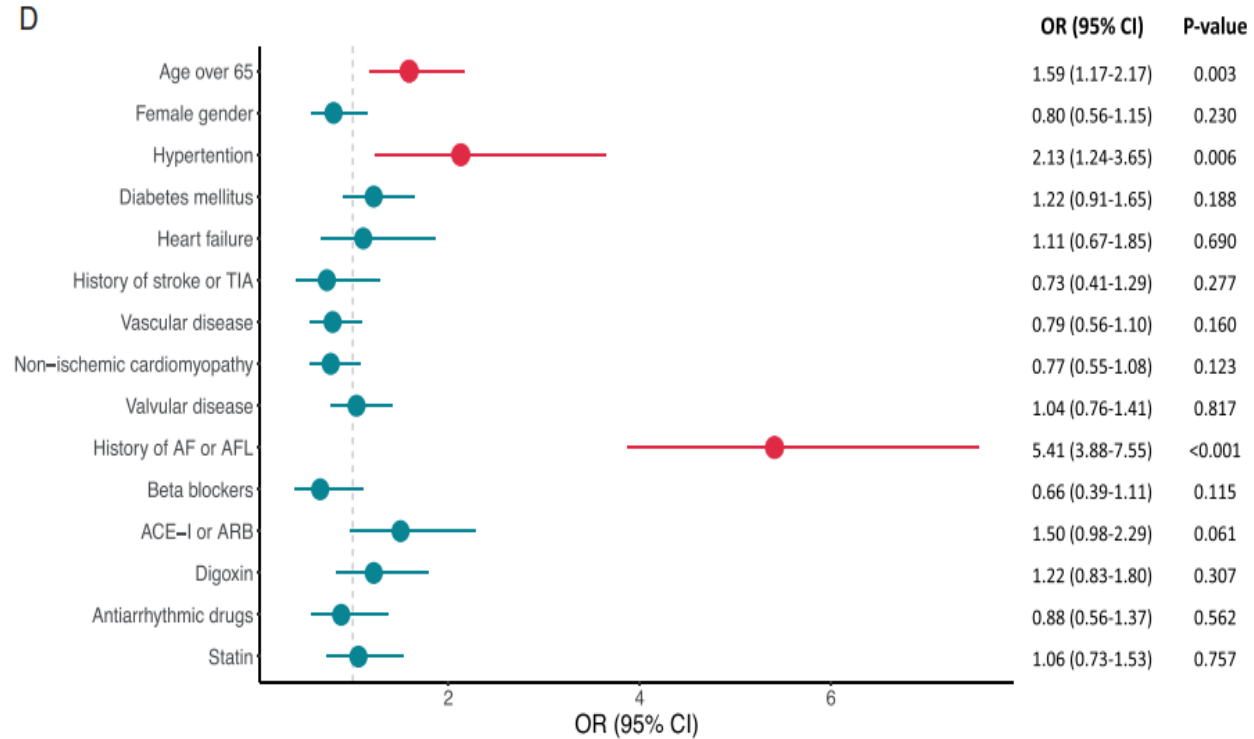
- Low SCAF was not increase risk of stroke.
- High SCAF was significantly associated with stroke[HR 2.52]



# SCAF risk factor

:2718 CIED patients with  $\geq 1$  CHA2DS2-VASc

	Overall		Low-risk group (CHA <sub>2</sub> DS <sub>2</sub> = 1 or 2)		High-risk group (CHA <sub>2</sub> DS <sub>2</sub> $\geq$ 3)		RR (95% CI) <sup>a</sup>
	Number of patients	Incidence rate (100 patient-years)	Number of patients	Incidence rate (100 patient-years)	Number of patients	Incidence rate (100 patient-years)	
AHRE $\leq$ 6 min	292	5.364	167	5.60	125	5.076	0.906 (0.73–1.13)
6 min < AHRE $\leq$ 6 h	653	11.995	341	11.439	312	12.669	1.11 (0.97–1.27)
6 h < AHRE $\leq$ 24 h	369	6.778	182	6.105	187	7.593	1.24 (1.03–1.50)
AHRE > 24 h	182	3.343	82	2.751	100	4.061	1.48 (1.11–1.96)

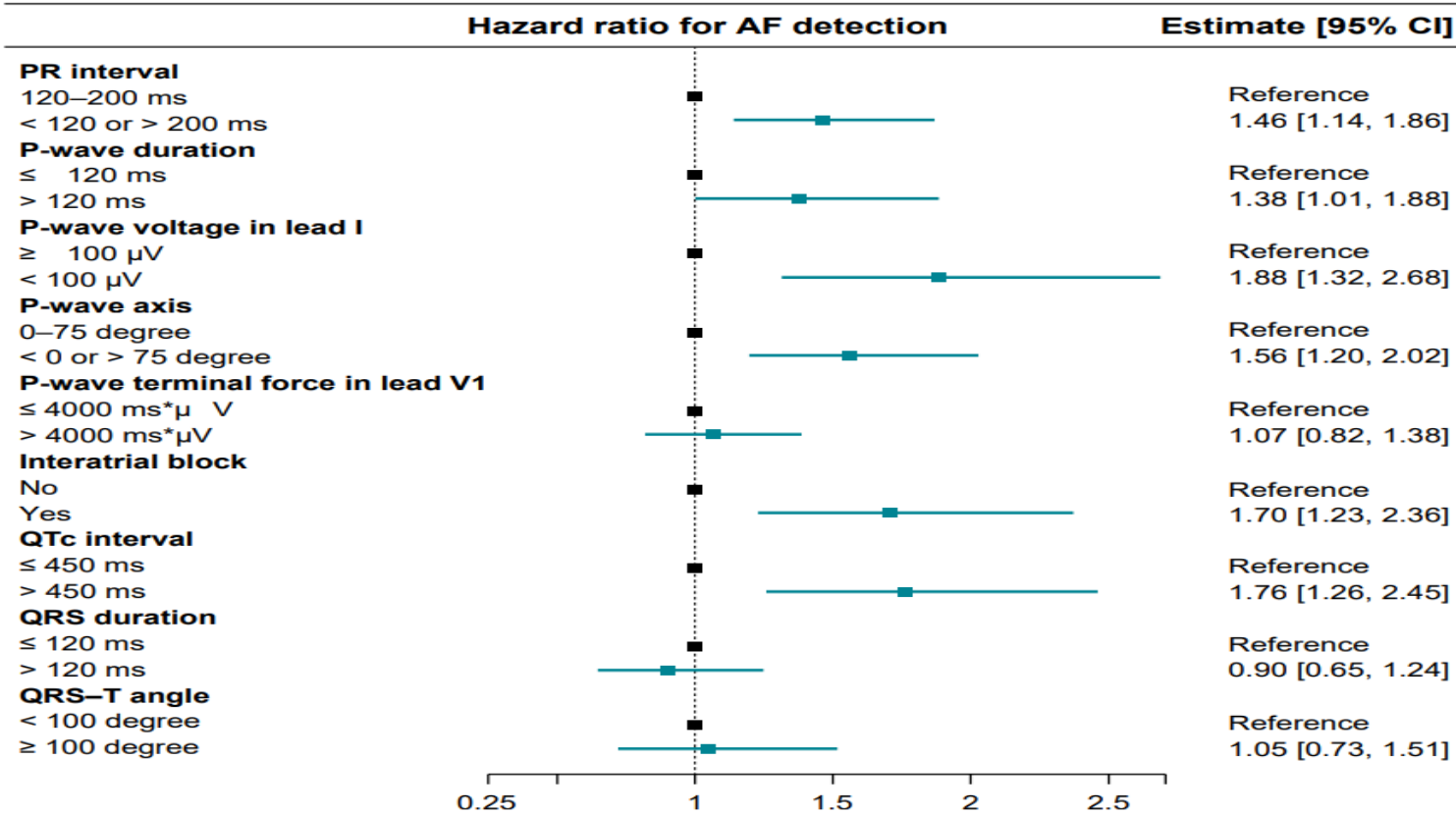


- The incidence rates of AHRE >6 h were significantly higher in patients at high risk of thromboembolism (CHA<sub>2</sub>DS<sub>2</sub> score  $\geq$  3) compared to those at low risk.
- Older age, hypertension, history of AF/AFL was associated with AHRE >24 h



# Electrocardiographic marker of SCAF

## :LOOP trial subgroup analysis(1370 ILR patients)



Ful 3.19 years  
 Mean age 74.7 yrs  
 Male 53.4%  
 419(30.6%) developed AF

- P-wave duration (PWD), P-wave terminal force in Lead V1, and interatrial block (IAB) further demonstrated significant associations with SCAF



# AF guideline

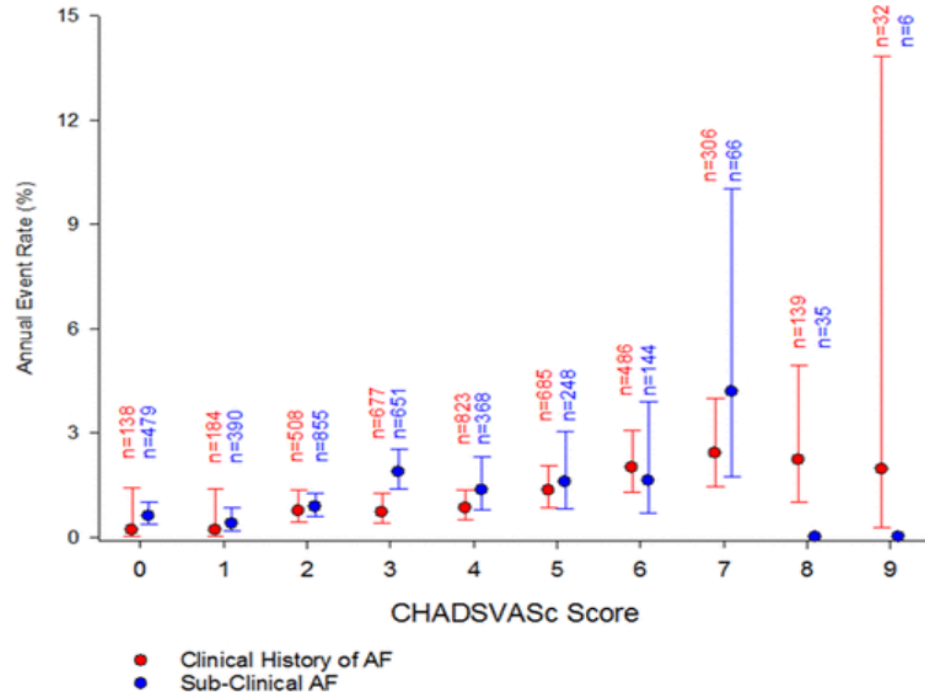
Recommendations	Class	Level
For stroke prevention in AF patients who are eligible for OAC, NOACs are recommended in preference to VKAs (excluding patients with mechanical heart valves or moderate-to-severe mitral stenosis).	I	A
For stroke risk assessment, a risk-factor-based approach is recommended, using the CHA <sub>2</sub> DS <sub>2</sub> -VASc clinical stroke risk score to initially identify patients at 'low stroke risk' (CHA <sub>2</sub> DS <sub>2</sub> -VASc score = 0 in men, or 1 in women) who should not be offered antithrombotic therapy.	I	A
OAC is recommended for stroke prevention in AF patients with CHA <sub>2</sub> DS <sub>2</sub> -VASc score $\geq 2$ in men or $\geq 3$ in women.	I	A





# SCAF burden, CHA2DS2-VASc and stroke

:21768 CIED patients



		CHA <sub>2</sub> DS <sub>2</sub> -VASc Score				
		0	1	2	3-4	≥5
Maximum Daily AF Duration		n=2922 (13.4%)	n=2151 (9.9%)	n=4554 (20.9%)	n=7164 (32.9%)	n=4977 (22.9%)
	No AF n=16815 (77.2%)	0.33% 40 events	0.62% 46 events	0.70% 95 events	0.83% 139 events	1.79% 157 events
	AF 6 min–23.5 h n=3381 (15.5%)	0.52% 11 events	0.32% 4 events	0.62% 17 events	1.28% 42 events	2.21% 36 events
	AF >23.5h n=1572 (7.2%)	0.86% 4 events	0.50% 3 events	1.52% 19 events	1.77% 28 events	1.68% 13 events

- Age 68.6 year, 63% male.
- AF duration and CHA<sub>2</sub>DS<sub>2</sub>-VASc score were significantly associated with stroke.

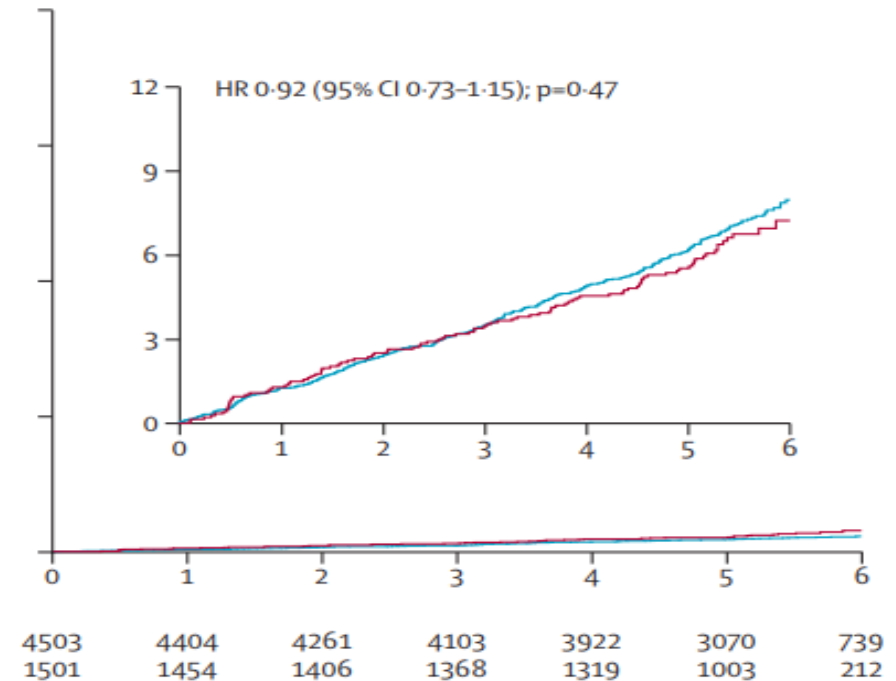


# SCAF and anticoagulation

:6004 patients, 70-90 years with 1 additional stroke risk factor

- 1: 3 ratio randomly assigned ILR to control.
- Atrial fibrillation was diagnosed in 477 (31.8%) in the ILR group versus 550 (12.2%) in the control group.
- Anticoagulation was recommended if atrial fibrillation episodes lasted **6 min or longer**
- Oral anticoagulation was initiated in 1036 participants: 445 (29.7%) in the ILR group versus 591 (13.1%) in the control group

B Ischaemic stroke, systemic arterial embolism, or transient ischaemic attack



- Stroke or systemic arterial embolism occurred in 67 (4.5%) in the ILR group versus 251 (5.6%) in the control group (HR 0.80; p=0.11)



# SCAF and anticoagulation

:10212 CIED patients with  $\geq 2$  CHA2DS2-VASc

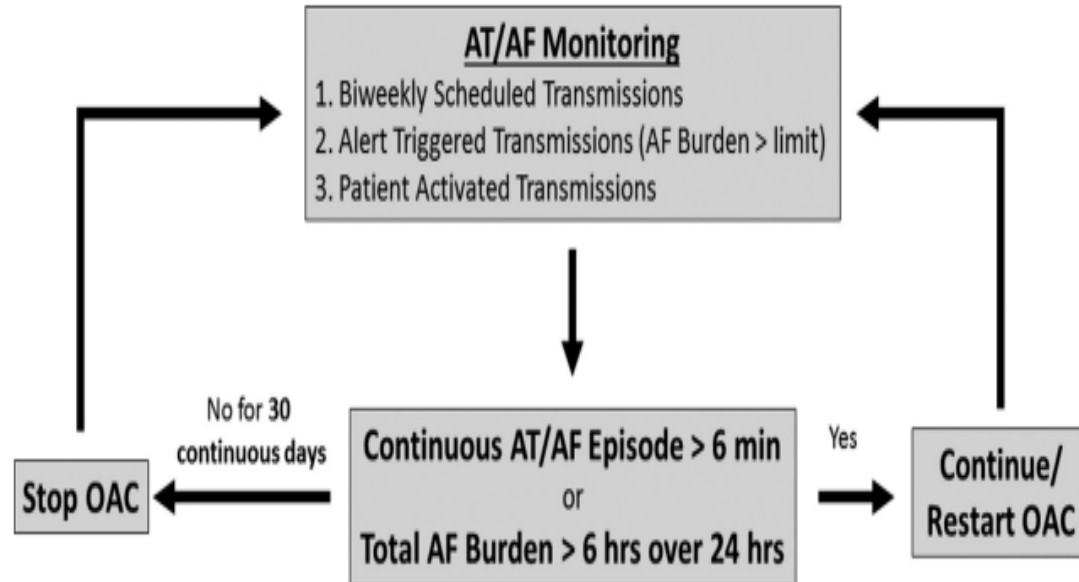
Device-Detected AF Burden	Total		No OAC*		OAC*		P Value†
	n/N (%)	IR (95% CI)	n/N (%)	IR (95% CI)	n/N (%)	IR (95% CI)	
AF >6 min‡							
Stroke	72/2101 (3.4)	9.9 (7.8–12.4)	66/1829 (3.6)	10.3 (8.1–13.1)	6/272 (2.2)	6.6 (2.9–14.6)	0.28
Death	587/2101 (27.9)	92.5 (85.3–100.3)	518/1829 (28.3)	93.3 (85.6–101.7)	69/272 (25.4)	87.1 (68.6–110.3)	0.60
AF >1 h‡							
Stroke	58/1712 (3.4)	9.8 (7.6–12.7)	51/1439 (3.5)	10.2 (7.8–13.5)	7/273 (2.6)	7.7 (3.7–16.2)	0.50
Death	503/1712 (29.4)	99.4 (91.1–108.5)	429/1439 (29.3)	100.4 (91.3–110.3)	74/273 (27.1)	94.4 (75.1–118.5)	0.63
AF >6 h‡							
Stroke	47/1279 (3.7)	10.7 (8.1–14.3)	41/1016 (4.0)	11.7 (8.6–15.8)	6/263 (2.3)	6.9 (3.1–15.5)	0.23
Death	395/1279 (20.9)	106.1 (96.1–117.1)	324/1016 (31.9)	108.7 (97.5–121.2)	71/263 (27.0)	95.8 (75.9–120.9)	0.34
AF >24 h‡							
Stroke	35/818 (4.3)	12.5 (9.0–17.4)	31/594 (5.2)	14.9 (10.5–21.2)	4/224 (1.8)	5.6 (2.1–14.8)	0.04
Death	297/818 (36.3)	129.0 (115.1–144.5)	234/594 (39.4)	139.3 (122.5–158.3)	63/224 (28.1)	101.1 (79.0–129.4)	0.02

- 4570 (45%), 3969 (39%), 3263 (32%), and 2469 (24%) had device-detected AF >6 minutes, >1 hour, >6 hours, and >24 hours
- OAC prescription after device-detected AF >24 hours was associated with reduced stroke risk (HR 0.28)



# SCAF and tailored anticoagulation

:48 CIED patients with  $\leq 3$  CHA2DS2-VASc, current DOAC use

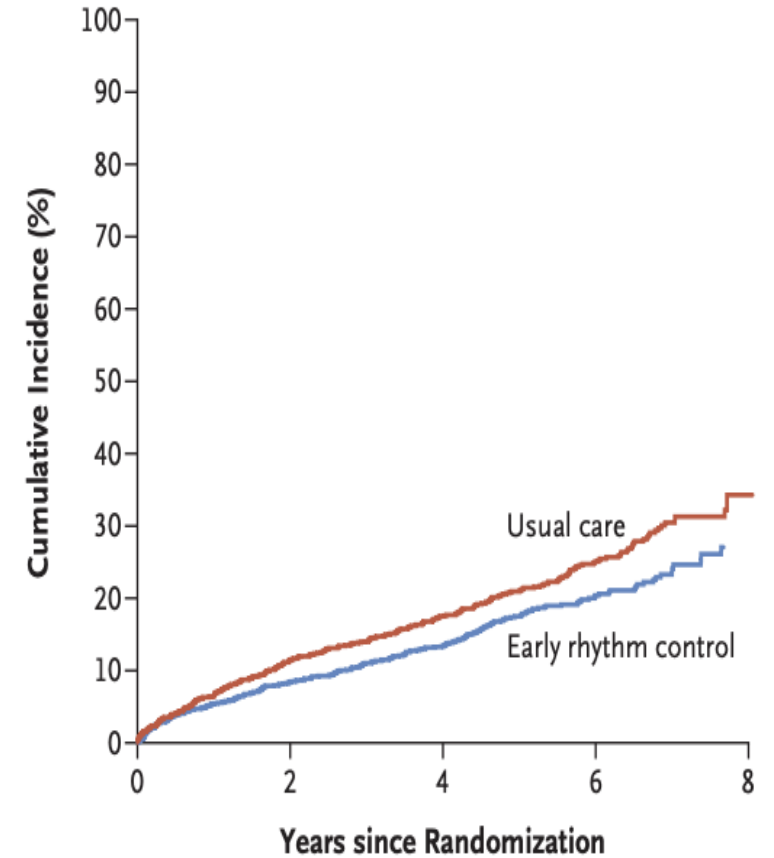
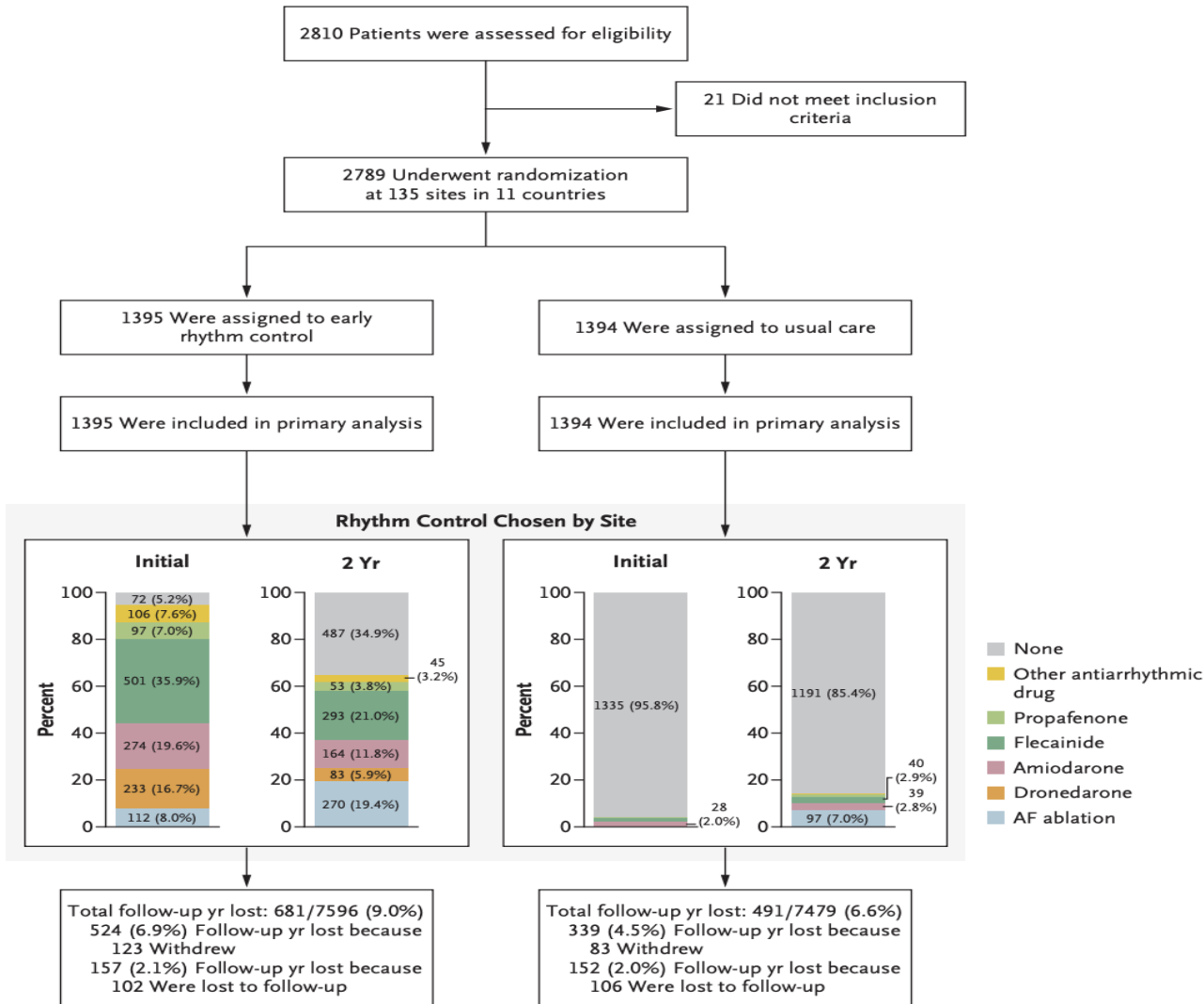


Reason for restarting/ continuing DOAC	Total days on DOAC	Study time on DOAC (%)	Total time on DOAC (%)
Days on DOAC after first 30 days	1777	12.0	47.2
AT/AF episode $\geq 6$ min	1317	8.8	35.0
Total AT/AF $\geq 6$ hr/day and AT/AF episode $\geq 6$ min	283	1.9	7.5
Total AT/AF $\geq 6$ hr/day	209	1.4	5.6
Perioperative management	117	0.8	3.1
Unable to transmit/travel	59	0.4	1.6
Transmitter malfunction	1	0.0	0.0
<b>Total days on DOAC</b>	<b>3763</b>	<b>25.4</b>	<b>100</b>

- Low-to moderate stroke risk, PM/ICD-guided DOAC administration is feasible and decreased anticoagulation utilization by 75% OAC with few adverse events and no thromboembolic events.



# Early rhythm control in clinical AF



No. at Risk	0	2	4	6	8
Usual care	1394	1169	888	405	34
Early rhythm control	1395	1193	913	404	26



# SCAF management

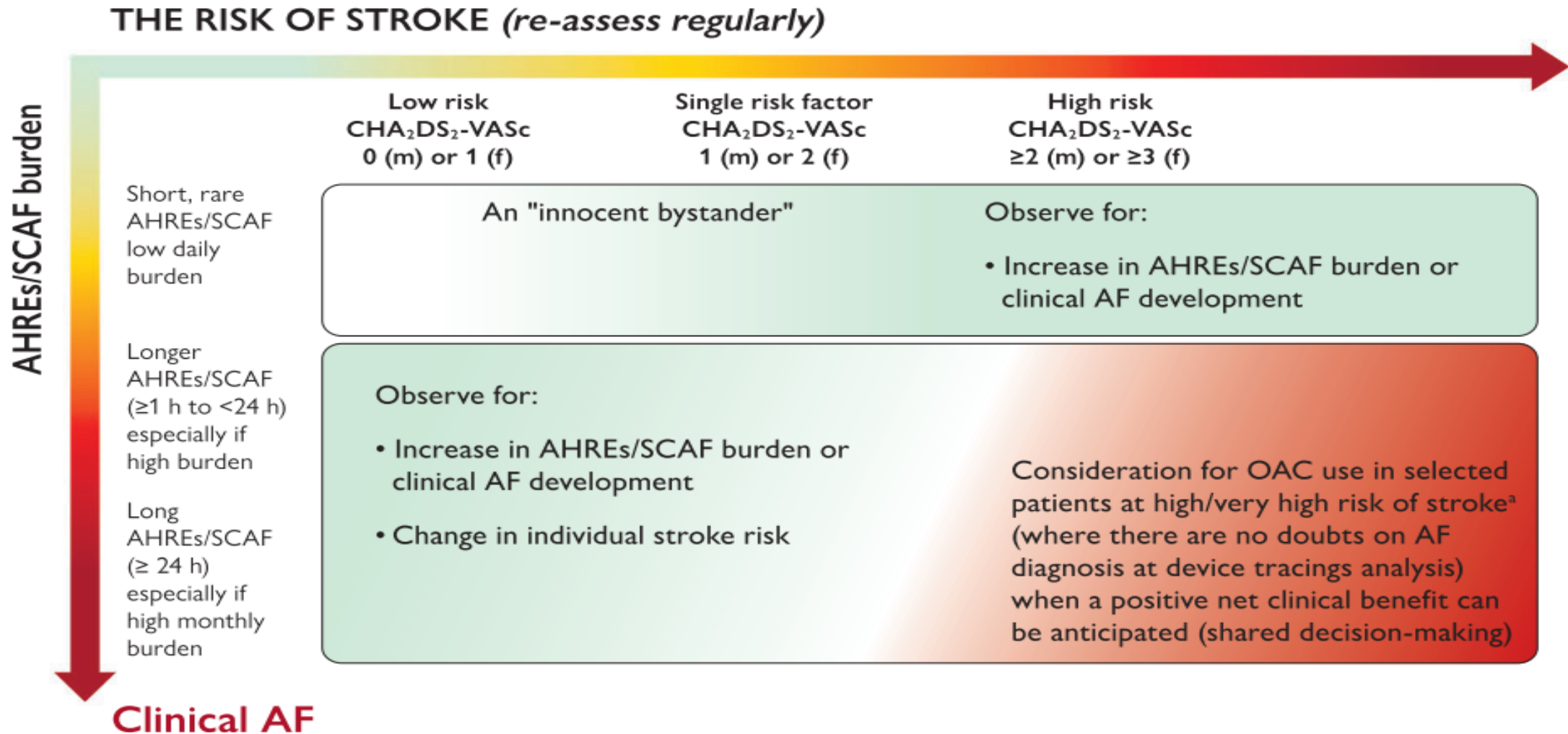
:ESC 2020 AF guideline

Recommendations	Class	Level
<p>In patients with <u>AHRE/subclinical AF</u> detected by CIED or insertable cardiac monitor, it is recommended to conduct:</p> <ul style="list-style-type: none"><li>• Complete <u>cardiovascular evaluation</u> with ECG recording, clinical risk factors/comorbidity evaluation, and thromboembolic risk assessment using the CHA<sub>2</sub>DS<sub>2</sub>-VASc score.</li><li>• Continued <u>patient follow-up and monitoring</u> (preferably with the support of remote monitoring) to detect progression to clinical AF, monitor the AHRE/subclinical AF burden (especially transition to ≥24 hours), and detect changes in underlying clinical conditions.</li></ul>	I	B



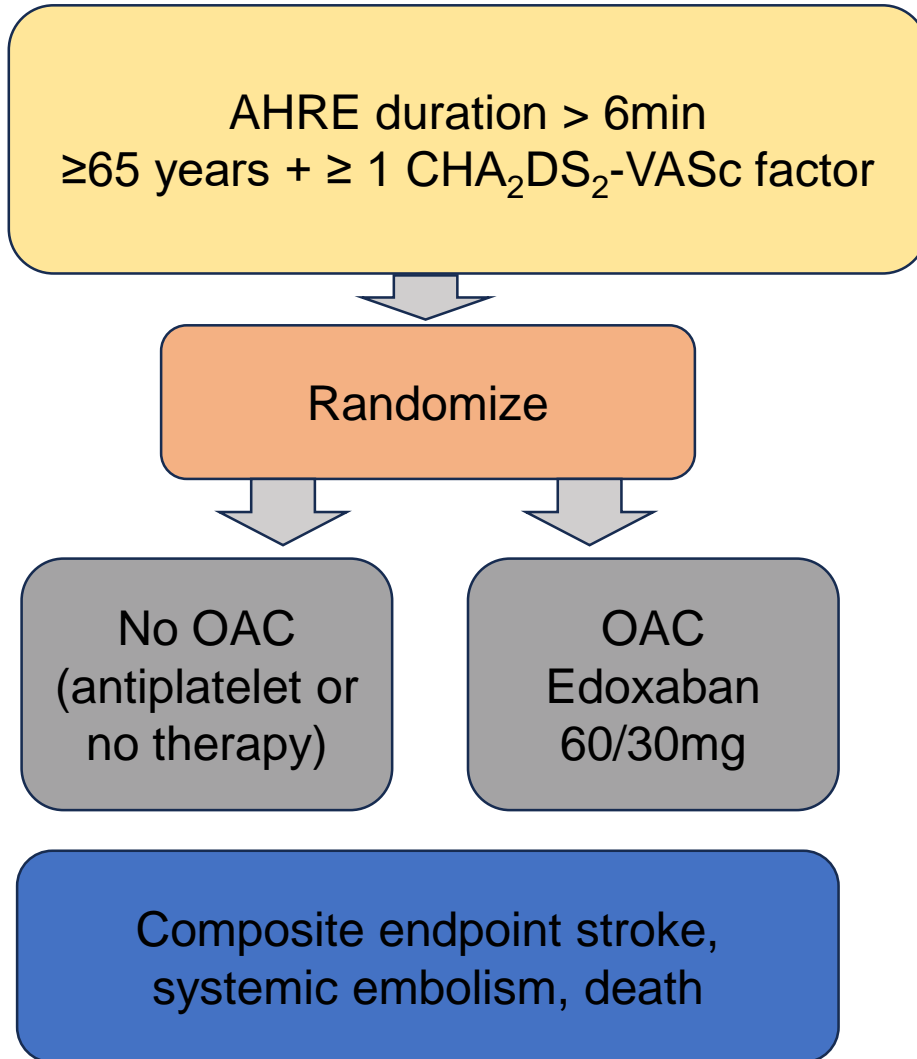
# SCAF management

:ESC 2020 AF guideline

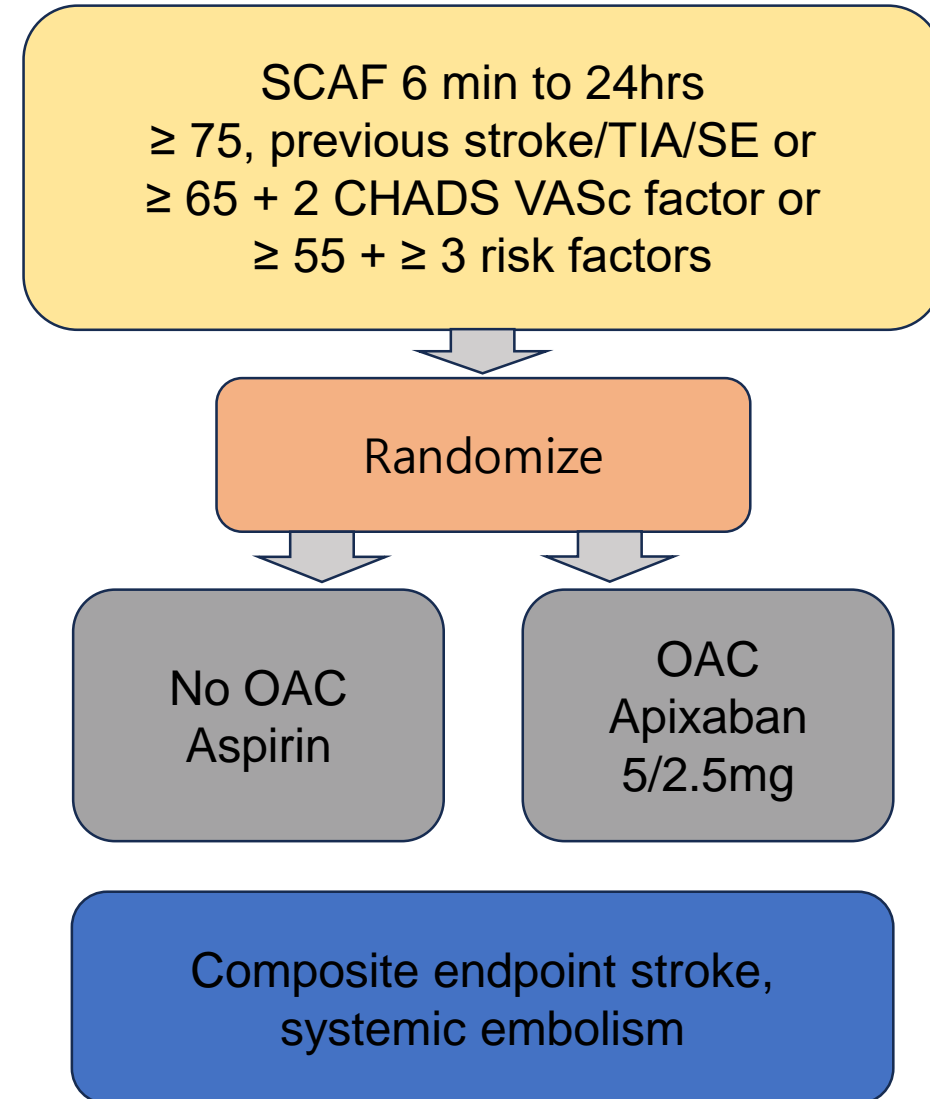


# Ongoing RCT

## NOAH-AFNET 6



## ATRESiA





# Summary

- Subclinical AF is common
- SCAF is associated with stroke in high burden(duration, risk factor)
- SCAF is progressive, periodic evaluation is essential
- Individualized anticoagulation according to the SCAF burden is required
- Outcome of SCAF anticoagulation trial has major implications for AF screening

