Les défis de l'anticoagulation en rythmologie

Modération : Dr Maxime Guenoun (Marseille)

Prise en charge précoce de la fibrillation atriale : pour qui ? Comment ?

Pr Jean Claude Deharo (Marseille)

T**raitement de l'anticoagulation : traitement à vie ?**

Pr Laurent Fauchier (Tours)

Prise en charge précoce de la fibrillation atriale

Les défis de l'anticoagulation en rythmologie

Jean-Claude Deharo

Assistance Publique Hôpitaux de Marseille

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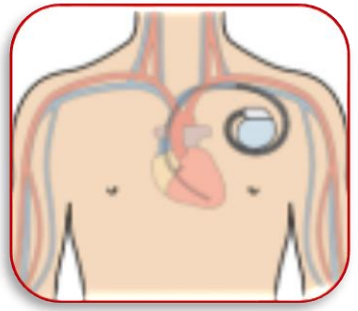
Liens d’intérêt

- Liens d’intérêt :

Honoraires pour présentations à des congrès; bourses de recherche

- Abbott
- Medtronic
- Boston Scientific
- Biotronik
- Bewys
- Viatris
- Bayer
- BMS Pfizer

Silent (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.

From AF ESC guidelines 2020

ESC European Society of Cardiology

Europace (2022) **00**, 1–27
https://doi.org/10.1093/europace/euac038

POSITION PAPER
EHRA practical guide

How to use digital devices to detect and manage arrhythmias: an EHRA practical guide

Emma Svennberg [1], Fleur Tjong[2], Andreas Goette[3,4], Nazem Akoum[5], Luigi Di Biaise[6], Pierre Bordachar[7], Giuseppe Boriani[8], Haran Burri[9], Giulio Conte[10], Jean-Claude Deharo[11,12], Thomas Deneke[13], Inga Drossart[14,15], David Duncker[16], Janet K. Han[17], Hein Heidbuchel[18,19], Pierre Jais[20], Marcio Jansen de Oliviera Figueiredo[21], Dominik Linz[22], Gregory Y.H. Lip[23,24], Katarzyna Malaczynska-Rajpold[25], Manlio Márquez[26], Corrette Ploem[27], Kyoko Soejima[28], Martin K. Stiles[29], Eric Wierda[30], Kevin Vernooy[31], Christophe Leclercq[32]

Consensus statement

Systematic screening by intermittent ECG[a] is beneficial to detect AF in individuals aged ≥75 years

Systematic screening by intermittent ECG[a] may be beneficial to detect AF in individuals aged ≥65 years with comorbidities increasing the risk of stroke

Opportunistic screening for AF may be beneficial in patients aged ≥65 years without comorbidities or <65 years with comorbidities

PPG-based or ECG-based devices are preferred to pulse palpation for AF screening

In systematic screening for AF, PPG-based or ECG-based devices can be used

If PPG screening is indicative of AF, an ECG-based method should be used to confirm the diagnosis of AF

If AF is diagnosed during screening, patients should be informed, appraised for OAC treatment, and AF risk factors managed

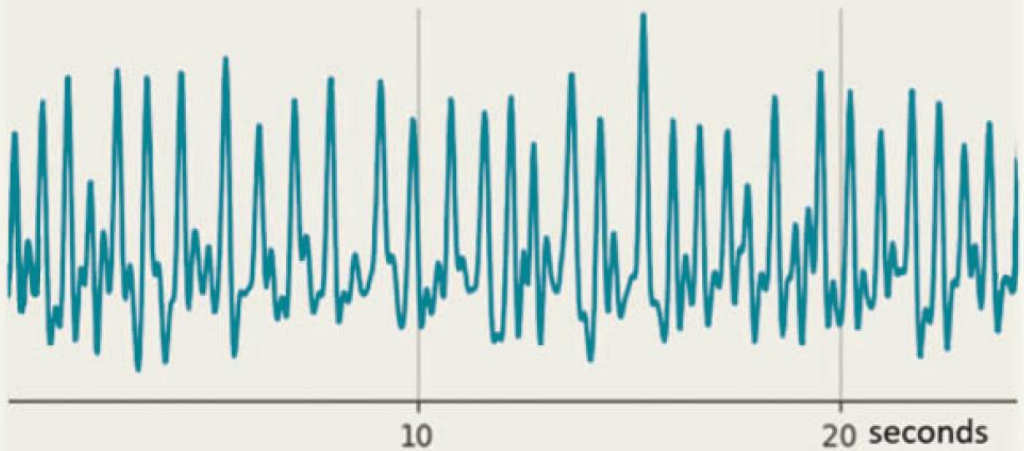
Screening for AF at multiple time points or over a prolonged time should be preferred over single time-point screening to increase the diagnostic yield regardless of symptoms

The term 'screening-detected AF' should be used for AF diagnosed in a screening setting and the diagnosis should be confirmed by a physician

Svennberg E et al. Europace 2022

PPG

- Sensor-based light source & photodetector
- Measures changes in tissue blood volume based on reflected light
- Generates *pulse waveform*
- Heart *rate* is derived
- Abnormal heart *rhythm* can be detected by embedded algorithms

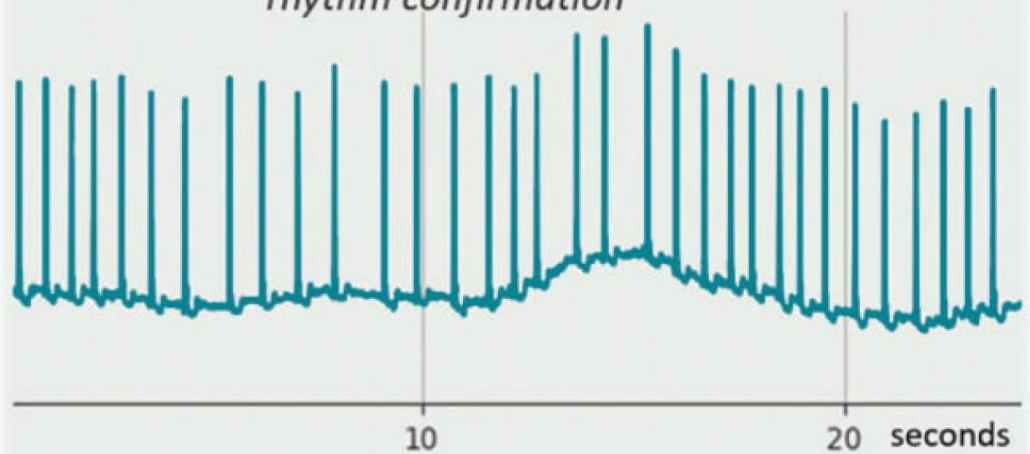


ECG

- Electrode-based
- Generates an electrocardiographic (ECG) tracing
- Allows direct analysis/diagnosis of heart *rhythm*

Can be diagnostic

- Clinician oversight is required for *rhythm confirmation*



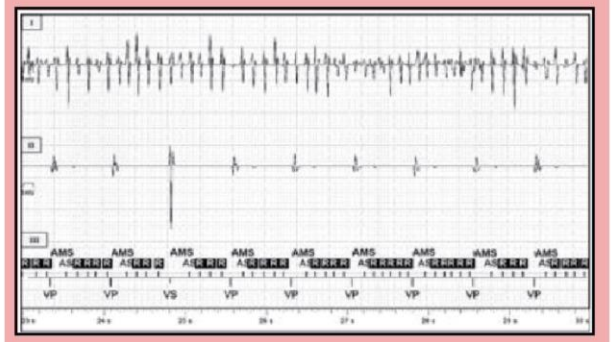
Svennberg E et al. Europace 2022

Strategy	Definition	Examples
Opportunistic screening	Screening performed as a part of clinical contacts for any other reason than screening	• During a routine GP consultation • Including during cardiovascular risk factor management • Screening of pharmacy customers • Screening during vaccination appointments • In contact with healthcare personnel where pulse palpation might be performed
Systematic screening	Screening programme performed continuously irrespective of medical contacts or need	• Population-based screening programme • Systematic screening during health campaigns
Screening in risk groups	Screening performed in individuals who sustained a prior stroke or transient ischaemic attack	• In-hospital screening • Monitoring post-discharge

Svennberg E et al. Europace 2022

No symptoms attributable to AF and NOT previously diagnosed with clinical AF

Physician-confirmed:
- CIED-recorded electrograms with AHRE



- ICM-recorded AF

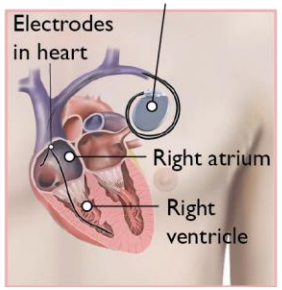
ECG

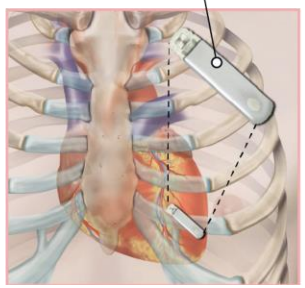
No AF on ECG

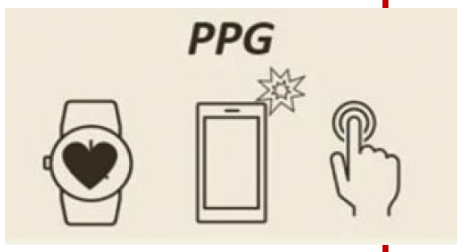
***Sub*clinical AF**

Pacemaker/implantable defibrillator inserted under the skin

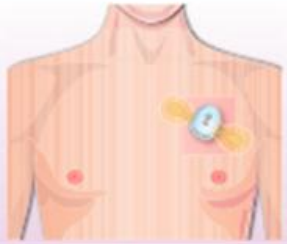
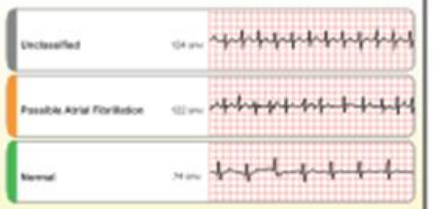
Insertable Cardiac Monitor (ICM)





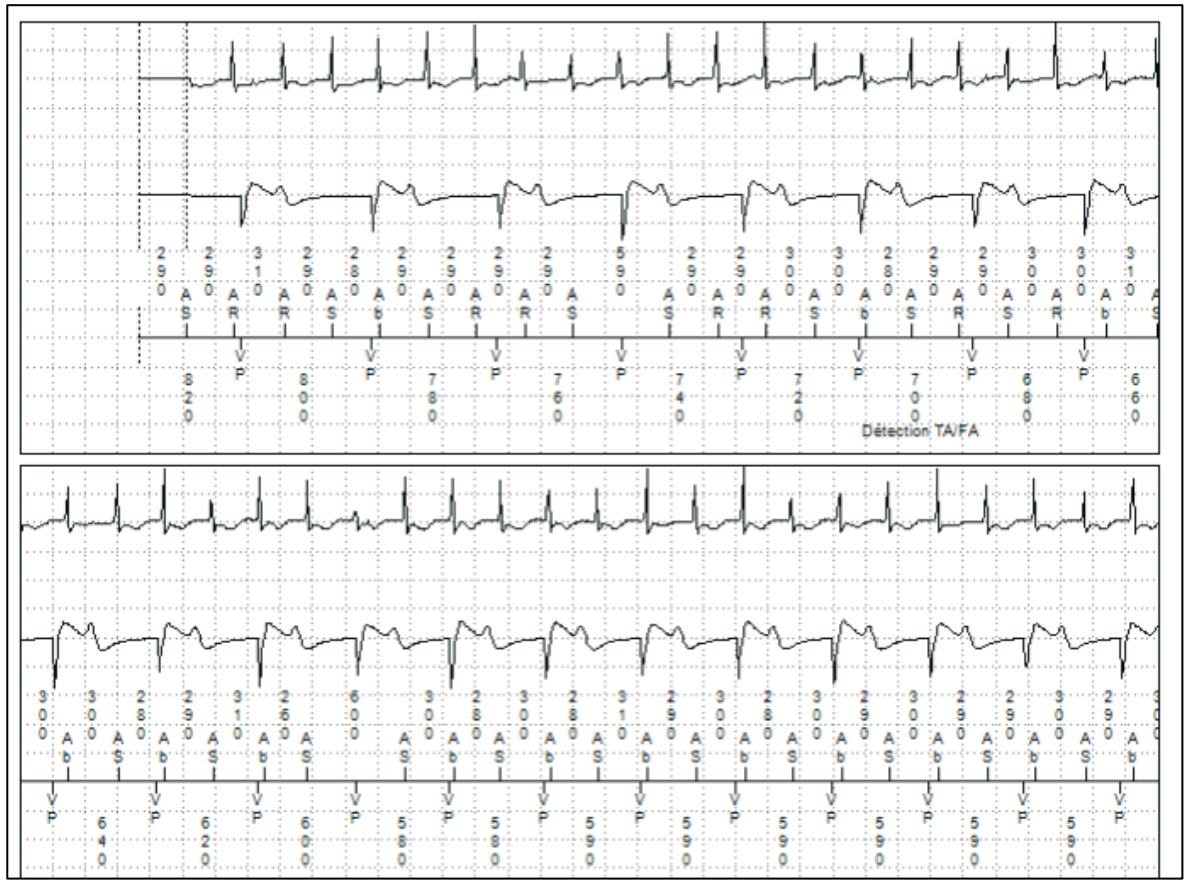


From AF ESC guidelines 2020

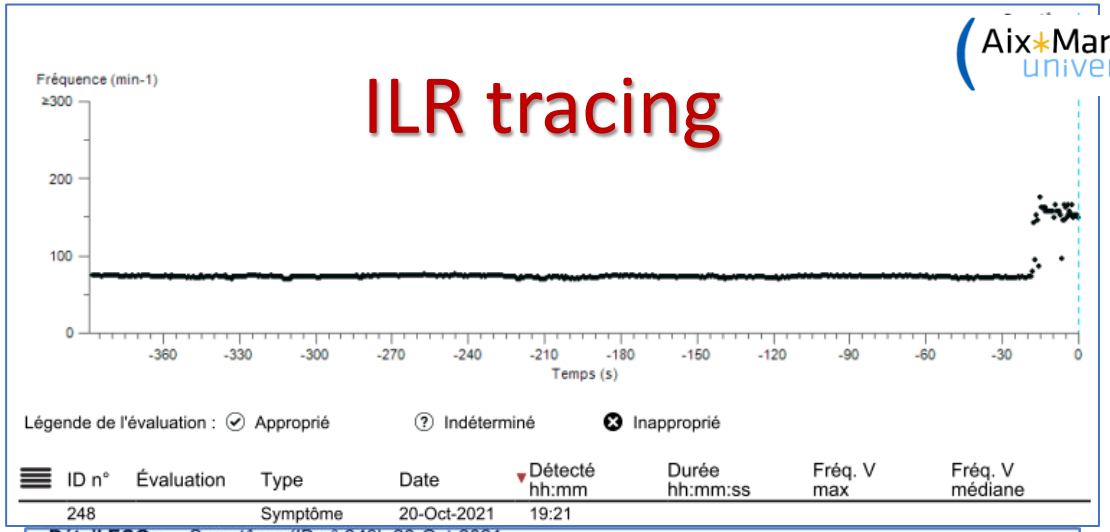
Device name	Device	Atrial fibrillation recording
Photoplethysmography via smartwatch or watch e.g. AppleWatch		 On screen message can alert wearer to suspected arrhythmia
Patch ECG monitors, e.g. Zio patch Zio (iRhythm), Cardiostat (Icentia) and Nuvant (Corventis)		
Smartphone compatible ECG recorder e.g. Alivecor Kardia		
WatchBP		Watch BP uses an inbuilt algorithm to detect an irregular heart beat and highlights this to the patient and healthcare professional via an 'AFIB' symbol displayed on screen.
Handheld device e.g. MyDiagnostick (Applied Biomedical Systems BV)		

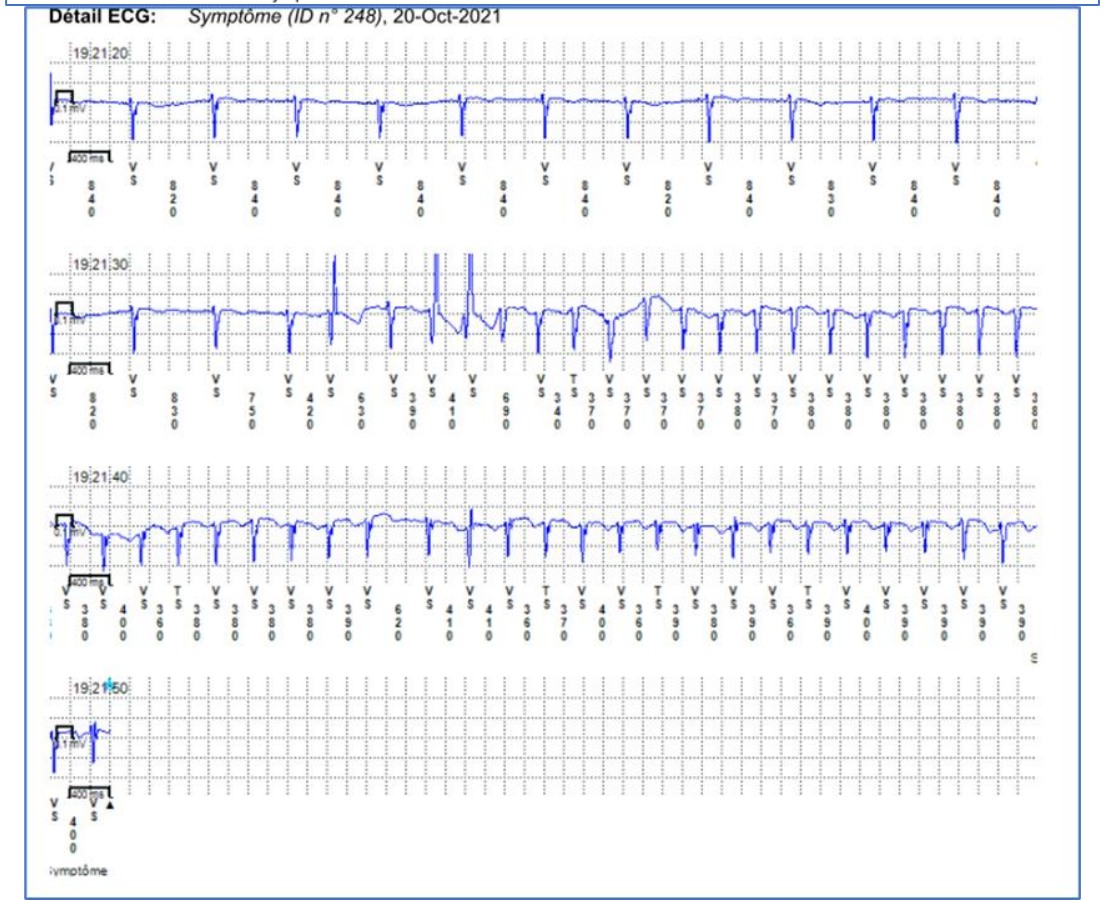
From Jones NR et al., Europace 2020

ICD tracing

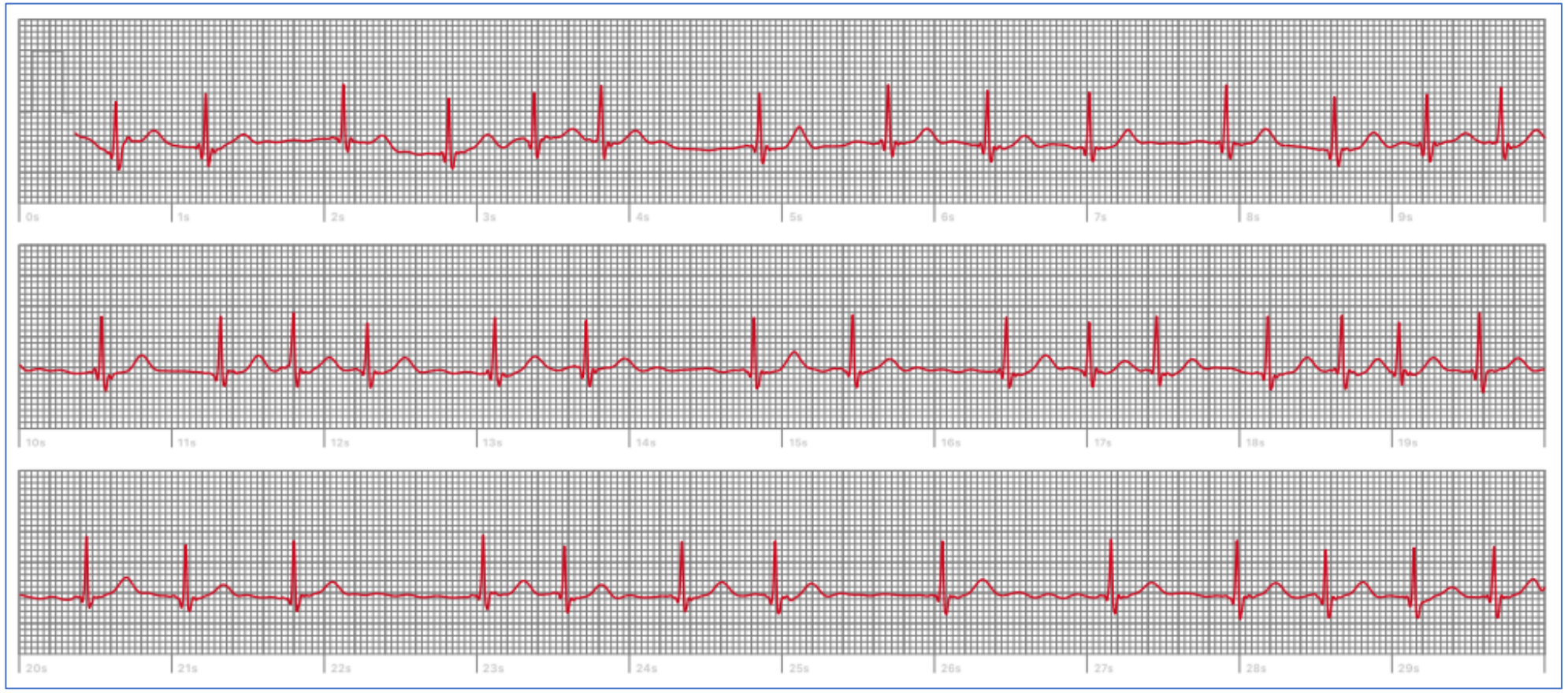


ILR tracing



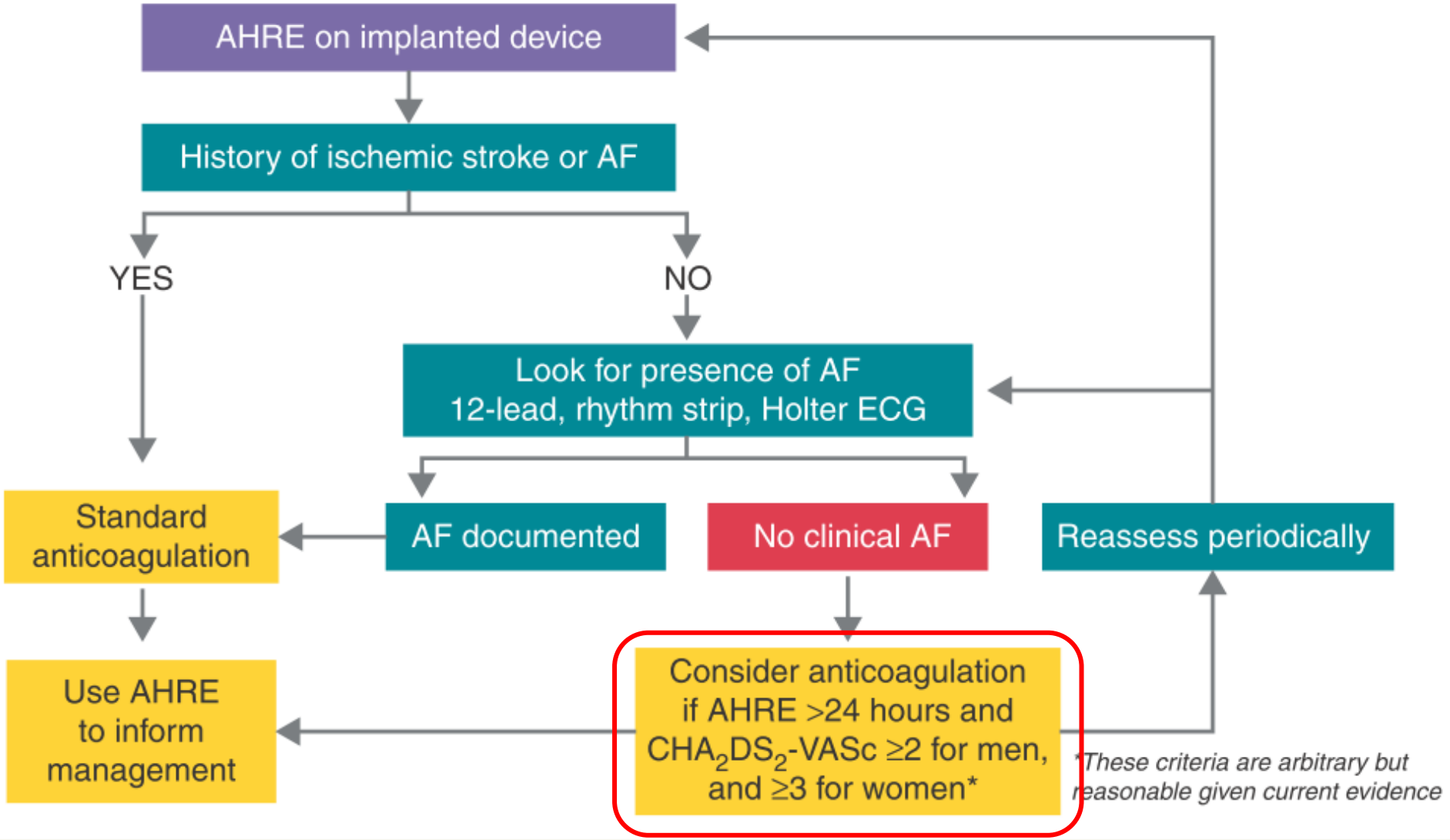


Smartwatch ECG



« AF » detected by CIEDs (AHRE) and risk of stroke

Author	# pts (Setting)	*Risk*
Glotzer Circulation , 2003	312 (SSS)	***Death or stroke x 2.5***
Capucci Clinical Research in Cardiology, 2020	725 (PAF)	***AT/AF > 24 h → risk of embolism x 3.1***
Glotzer Circ Arrythm Electrophysiol, 2009	2486 (≥1 RFS)	***Daily AF burden > 5.5 h in the 30 previous days → risk of stroke x 2***
Ziegler Stroke, 2010	163 (Stroke)	***New AF in 28% of pts with stroke***
Healey New Engl J Med, 2016	2580 (>65, HTN)	***Risk of stroke or embolism x 2.5***
Shanmugan Europace, Feb 2012	560 (CRT)	***AF burden > 3.8 h → increased risk of TE***

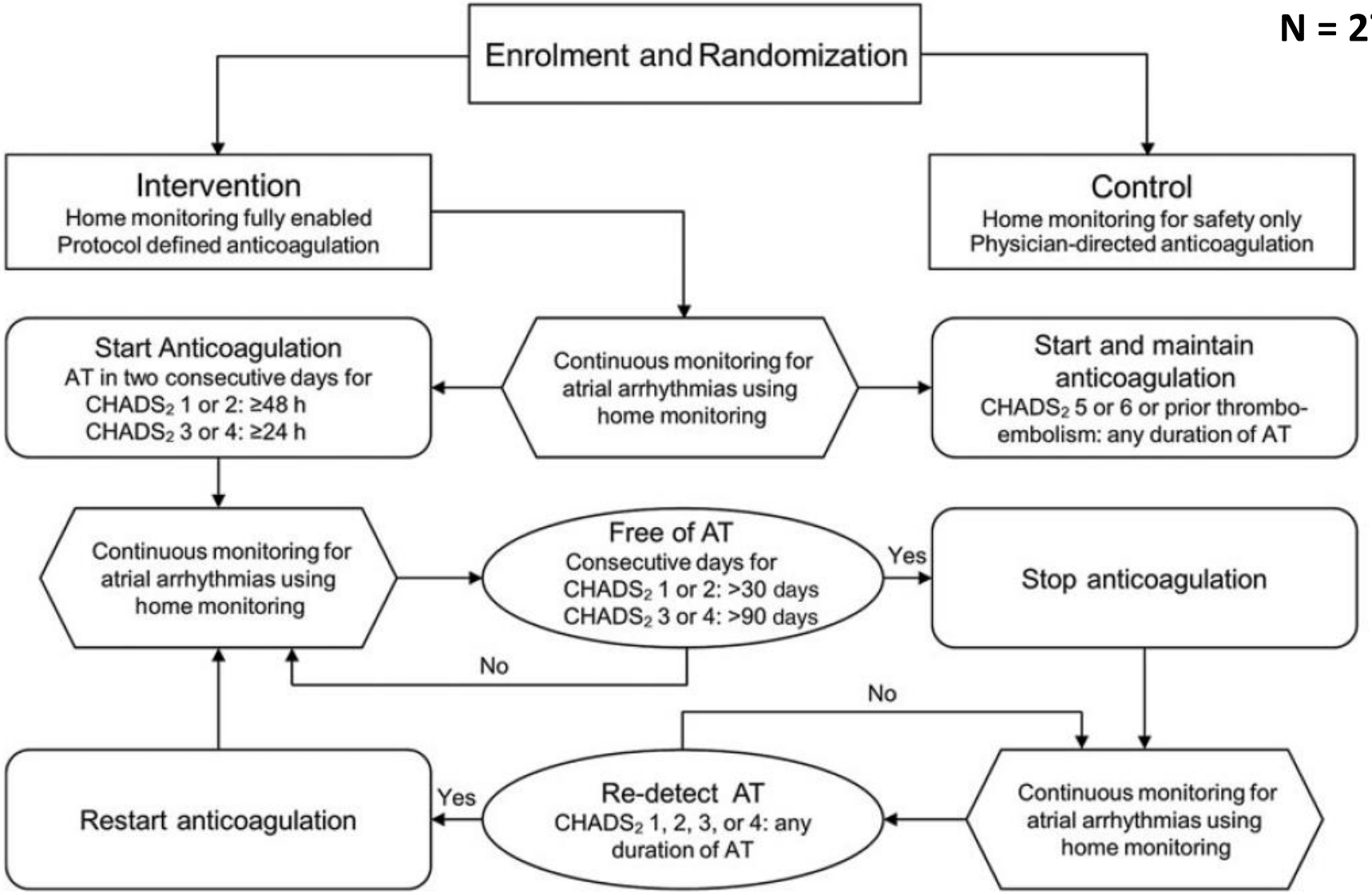


Suggested treatment algorithm for management of patients with AHREs. Adapted from Kirchhof *et al.*[70]

Camm et al., Europace 2017

The IMPACT study

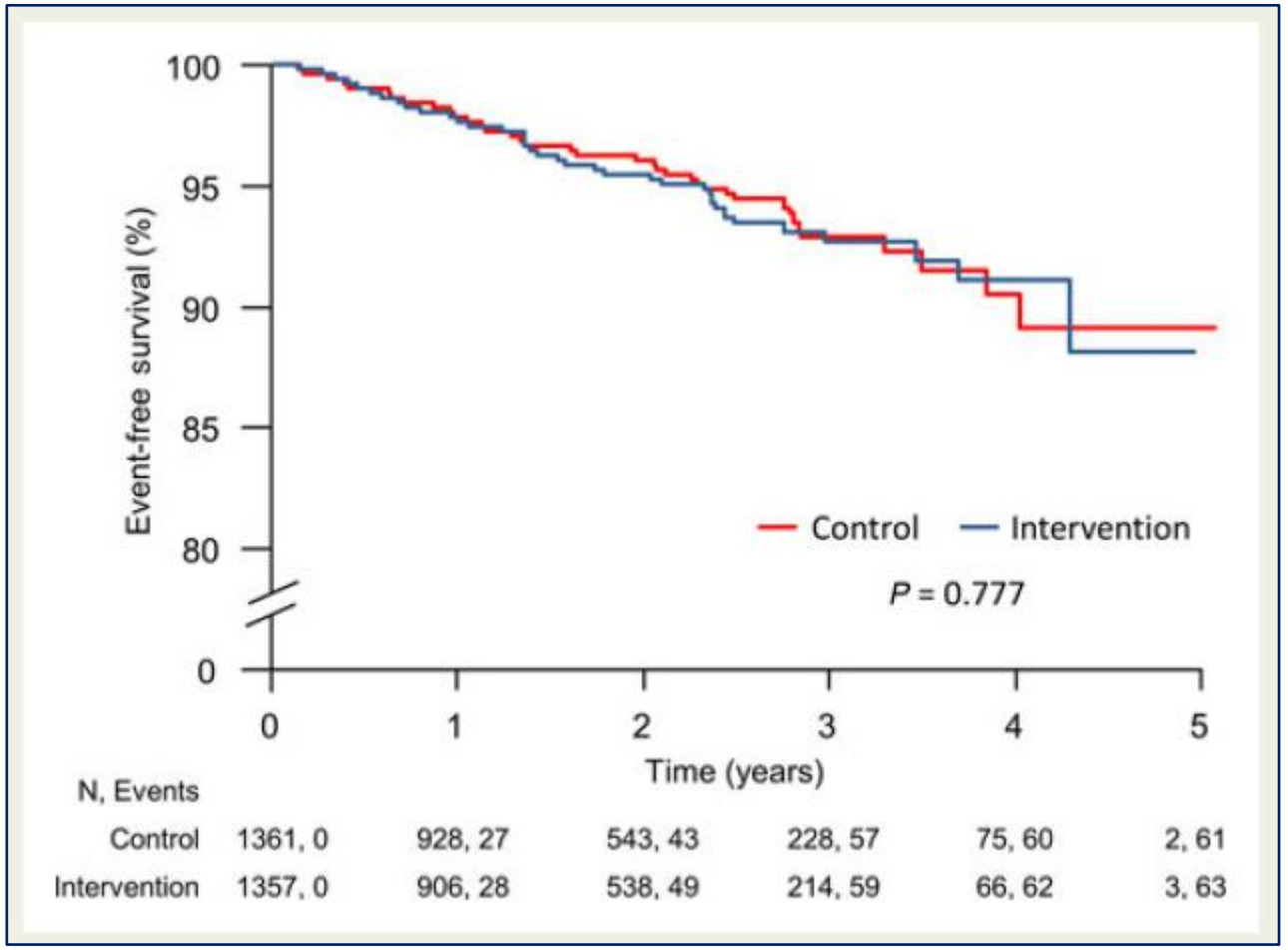
N = 2718 patients



DT Martin et al., EHJ 2015

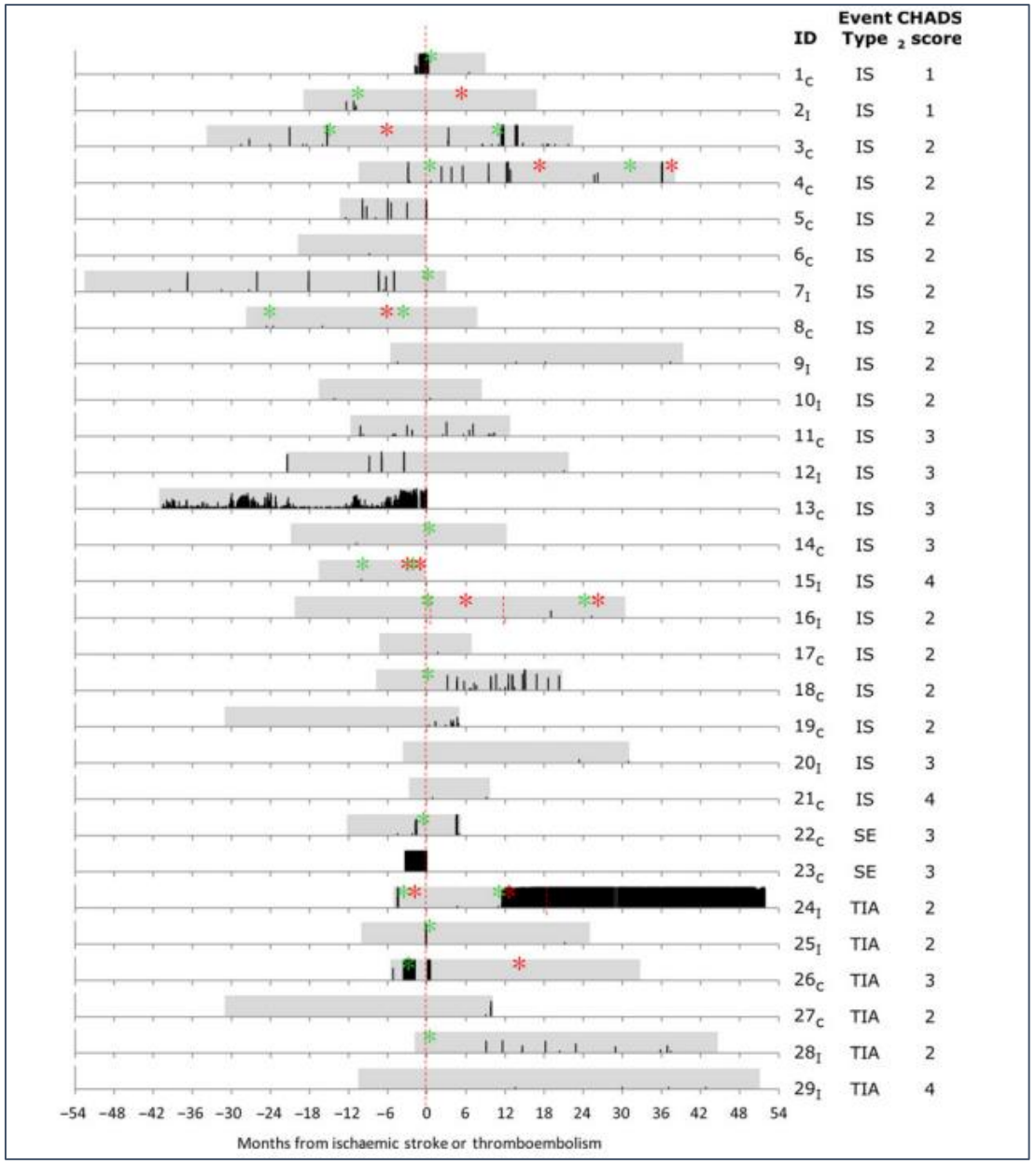
Primary events: first stroke, systemic embolism, or major bleeding (intention-to-treat analysis)

N = 2718 patients



DT Martin et al., EHJ 2015

Temporal relationship between daily atrial tachyarrhythmia burden and clinical thromboembolism

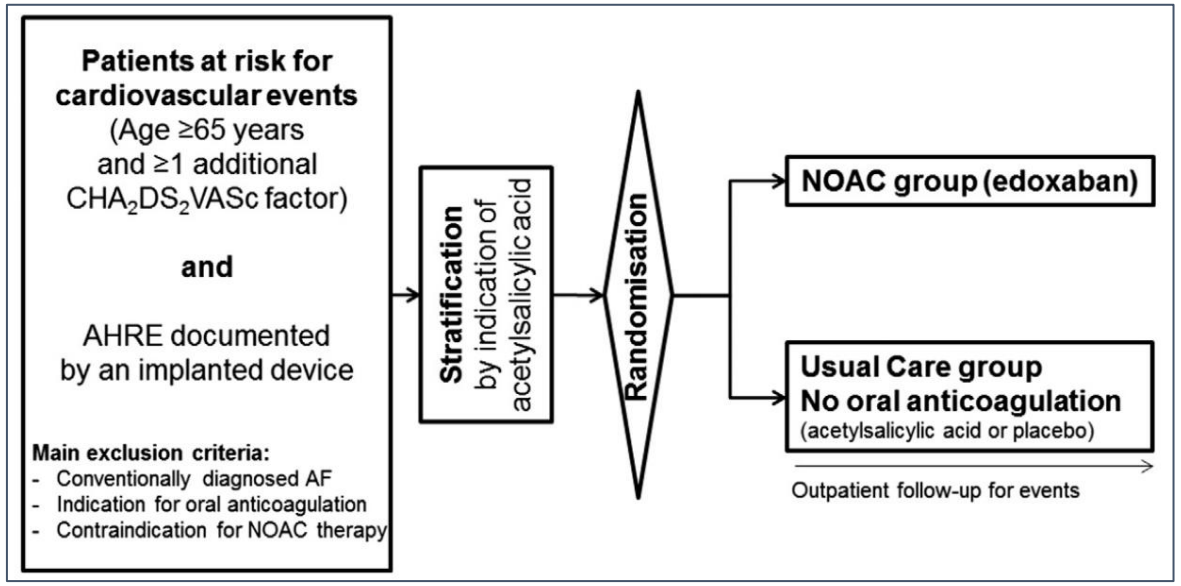


N = 69 ischemic events

DT Martin et al., EHJ 2015

Non–vitamin K antagonist Oral anticoagulants in patients with Atrial High rate episodes (NOAH–AFNET 6) trial

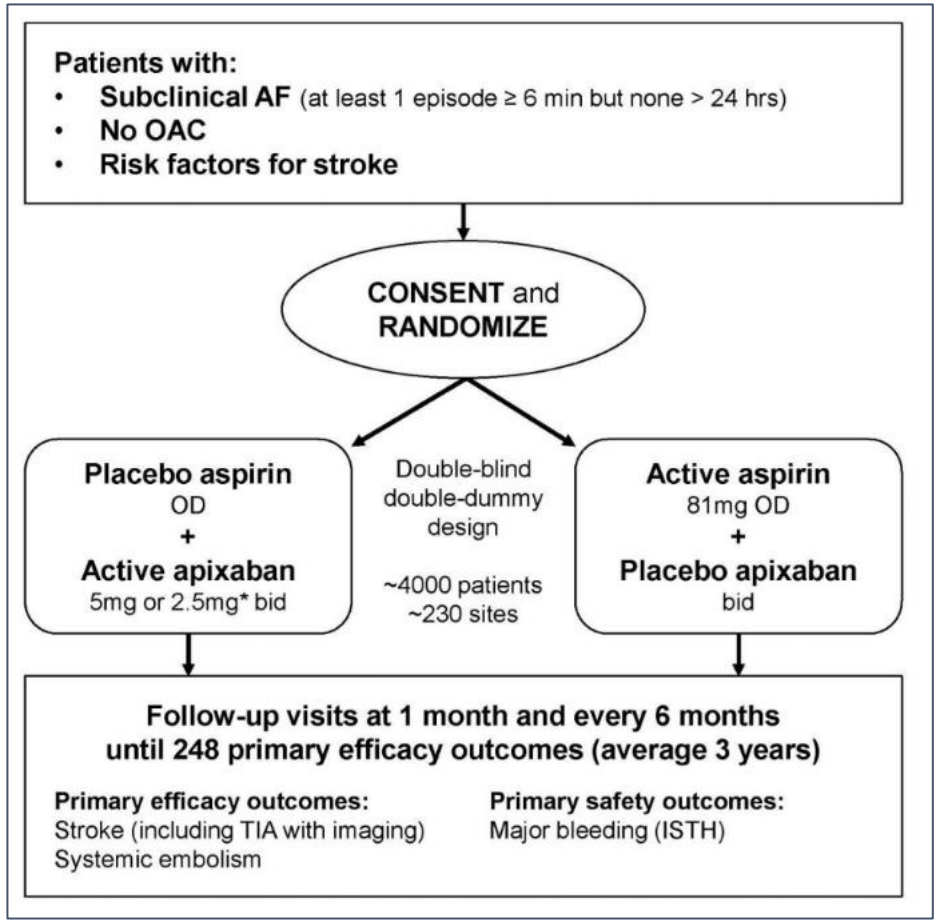
Kirchhof P et al. Am Heart J. 2017 Aug; 190: 12–18



N=2600

Apixaban for the Reduction of Thrombo-Embolism in Patients With Device-Detected Sub-Clinical Atrial Fibrillation (ARTESiA) trial

Lopes R et al. Am Heart J 2017;189:137-45.



N=4000

Progression of atrial high-rate episode burden (left panel) and stroke rates according to AHRE daily burden and CHA_2DS_2-VASc score (right panel)

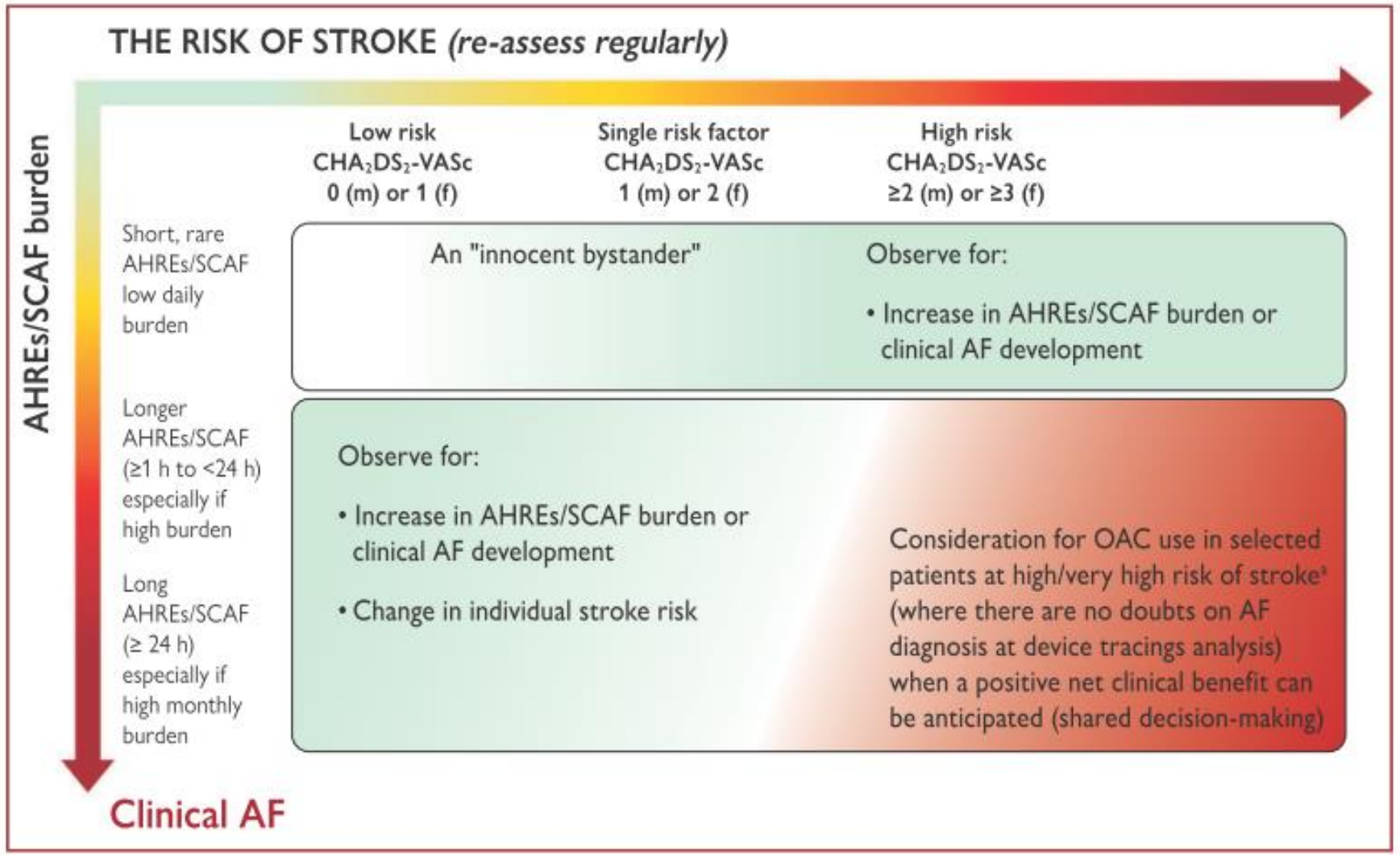
Six-month incidence of transition to higher AHRE burden[a]
(*n* = 6580, pooled from three prospective studies)

	Baseline burden			
6-month progression	5 min to <1 h	1 h to <6 h	6 h to <12 h	12 h to <23 h
Transition to ≥1 h	33.5%			
Transition to ≥6 h	15.3%	42.2%		
Transition to ≥12 h	8.9%	27.5%	55.8%	
Transition to ≥23 h	5.1%	16.0%	40.6%	63.1%

Stroke rates[b] per AHRE burden and CHA_2DS_2-VASc category
(*n* = 21 768 device patients not taking OAC)

	Baseline maximum daily burden		
CHA_2DS_2-VASc score	No AF	AF 6 min–23.5 h	AF >23.5 h
0	0.33%	0.52%	0.86%
1	0.62%	0.32%	0.50%
2	0.70%	0.62%	1.52%
3-4	0.83%	1.28%	1.77%
≥5	1.79%	2.21%	1.68%

[a]The higher the burden at diagnosis, the greater the incidence of progression in the next 6 months and thereafter. [b]Stroke rates above the threshold for OAC are shown in red.



ESC Guideline AF 2020

10,212 CIED patients
24–45% AHRE

Device-Detected AF Burden	Total		No OAC*		OAC*		
	n/N (%)	IR (95% CI)	n/N (%)	IR (95% CI)	n/N (%)	IR (95% CI)	*P* Value†
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

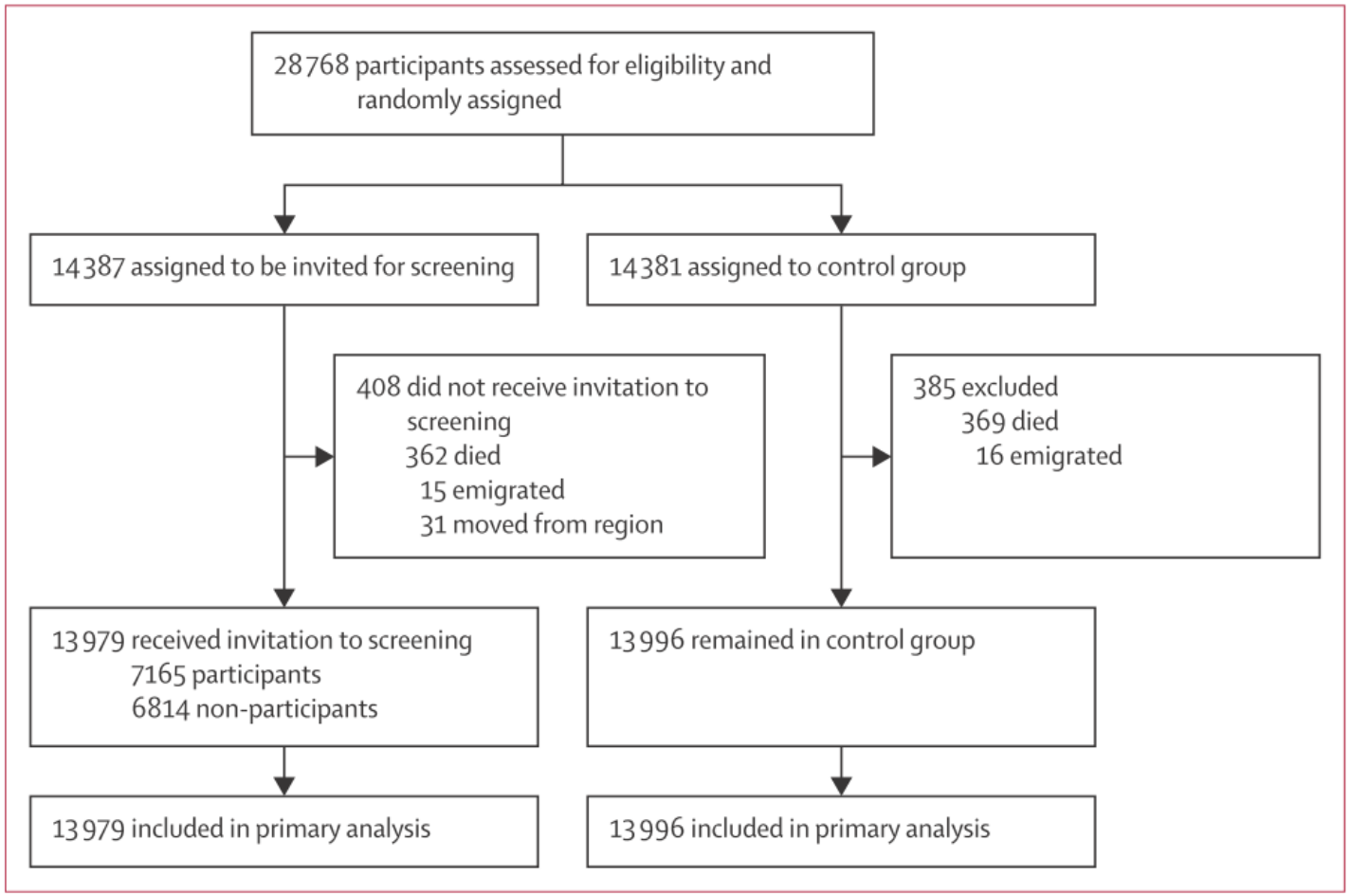
AC Perino et al. Circulation 2019

Recommendations	Class[a]	Level[b]
In patients with AHRE/subclinical AF detected by CIED or insertable cardiac monitor, it is recommended to conduct: • Complete cardiovascular evaluation with ECG recording, clinical risk factors/comorbidity evaluation, and thrombo-embolic risk assessment using the CHA_2DS_2-VASc score.[469] • Continued patient follow-up and monitoring (preferably with the support of remote monitoring) to detect progression to clinical AF, monitor the AHRE/subclinical AF burden (especially transition to ≥24 h), and detect changes in underlying clinical conditions.[469]	I	B

ESC Guideline AF 2020

Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial

Emma Svennberg, Leif Friberg, Viveka Frykman, Faris Al-Khalili, Johan Engdahl, Mårten Rosenqvist**



2X/j pdt 2 semaines
≥1 FA>30 s ou
≥2 FA 10-29 s

The Lancet, 2021

Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial

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	Randomly assigned groups		Within the invited to screening group		
	Invited to screening (n=13 979)	Control group (n=13 996)	Participants (n=7165)	Non-participants (n=6814)	p value*
Demographic and socioeconomic factors					
Age, years	76·0 (75·5–76·6)	76·0 (75·5–76·6)	75·8 (75·3–76·3)	76·2 (75·7–76·8)	<0·0001
Women	7637 (54·6%)	7636 (54·6%)	3863 (53·9%)	3774 (55·4%)	0·081
Living alone	7125 (51·0%)	7095 (50·7%)	3222 (45·0%)	3903 (57·3%)	<0·0001
Born outside of Sweden	2865 (20·5%)	2857 (20·4%)	1076 (15·0%)	1789 (26·3%)	<0·0001
Income in highest quartile	3552 (25·4%)	3522 (25·2%)	2256 (31·5%)	1296 (19·0%)	<0·0001
University or college education	3964 (28·4%)	3937 (28·1%)	2465 (34·4%)	1499 (22·0%)	<0·0001
Alcohol index†	352 (2·5%)	378 (2·7%)	88 (1·2%)	264 (3·9%)	<0·0001
Medical history					
CHA_2DS_2VASC‡ score	3·5 (1·3)	3·5 (1·3)	3·3 (1·1)	3·7 (1·4)	<0·0001
Ischaemic stroke, transient ischaemic attack, or systemic embolism	1557 (11·1%)	1513 (10·8%)	634 (8·8%)	923 (13·5%)	<0·0001
Heart failure	1045 (7·5%)	1098 (7·8%)	341 (4·8%)	704 (10·3%)	<0·0001
Hypertension	4963 (35·5%)	4980 (35·6%)	2262 (31·6%)	2701 (39·6%)	<0·0001
Vascular disease§	1632 (11·7%)	1686 (12·0%)	649 (9·1%)	983 (14·4%)	<0·0001
Diabetes	2115 (15·1%)	2107 (15·1%)	829 (11·6%)	1286 (18·9%)	<0·0001
Chronic kidney disease	303 (2·2%)	356 (2·5%)	77 (1·1%)	226 (3·3%)	<0·0001
Cancer¶	1767 (12·6%)	1864 (13·3%)	898 (12·5%)	869 (12·8%)	0·70
Dementia	465 (3·3%)	408 (2·9%)	72 (1·0%)	393 (5·8%)	<0·0001
Drugs dispensed within preceding 6 months‖					
Oral anticoagulant	1282 (9·2%)	1313 (9·4%)	574 (8·0%)	708 (10·4%)	<0·0001
Aspirin	3525 (25·2%)	3702 (26·5%)	1634 (22·8%)	1891 (27·8%)	<0·0001
β blocker	4752 (34·0%)	4764 (34·0%)	2154 (30·1%)	2598 (38·1%)	<0·0001
ACE inhibitor or angiotensin receptor blocker	5476 (39·2%)	5361 (38·3%)	2632 (36·7%)	2844 (41·7%)	<0·0001
Statin	4183 (29·9%)	4238 (30·3%)	2042 (28·5%)	2141 (31·4%)	<0·0001

The Lancet, 2021

Clinical outcomes in systematic screening for atrial fibrillation (STROKESTOP): a multicentre, parallel group, unmasked, randomised controlled trial

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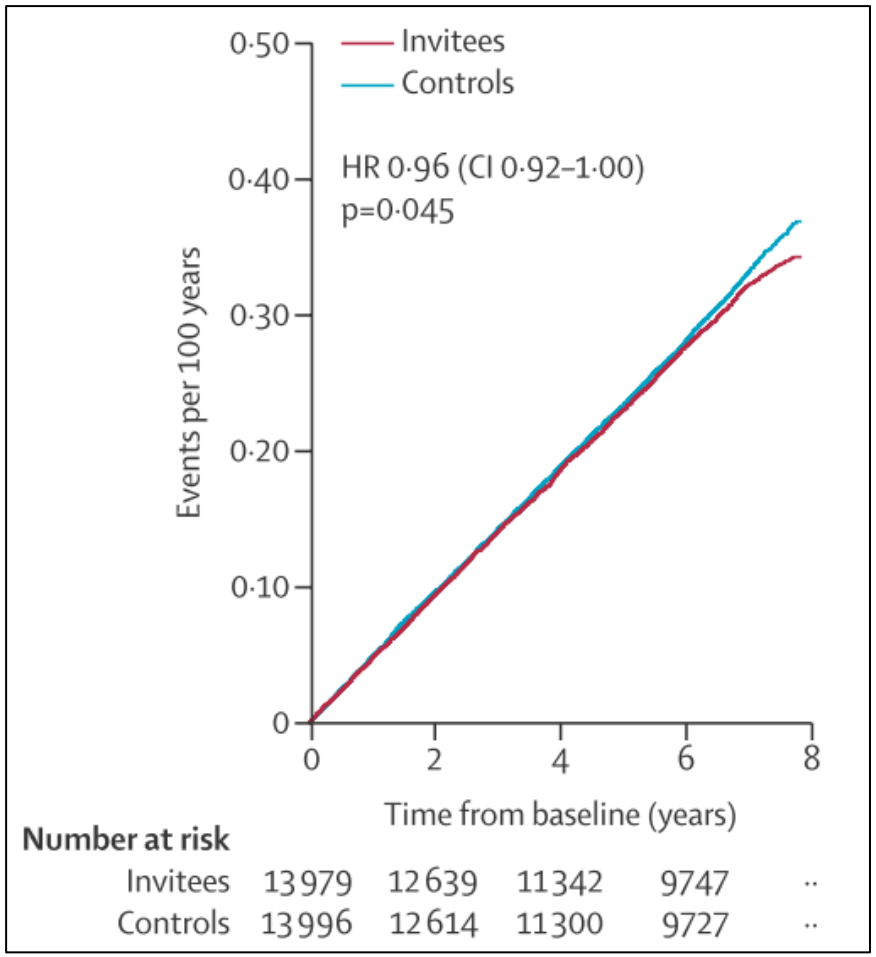


Primary endpoint:

Ischaemic or haemorrhagic stroke, systemic embolism, major bleeding leading to hospitalisation, or death from any cause in all randomly assigned individuals (regardless of participation)

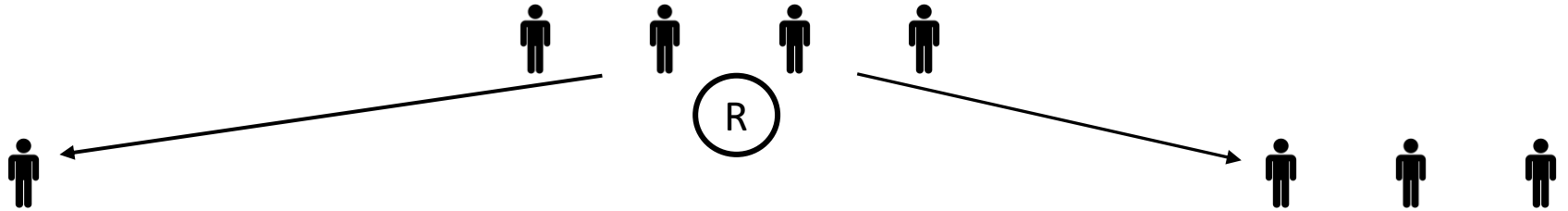
The Lancet, 2021

Implantable loop recorder detection of atrial fibrillation to prevent stroke (The LOOP Study): a randomised controlled trial

Jesper H Svendsen, Søren Z Diederichsen, Søren Højberg, Derk W Krieger, Claus Graff, Christian Kronborg, Morten S Olesen, Jonas B Nielsen, Anders G Holst, Axel Brandes, Ketil J Haugan, Lars Køber

The LOOP Study, an investigator-initiated Randomized Controlled Trial

- Participants identified via registries, recruited at 4 centres in 3 of 5 Danish regions
- Inclusion criteria: Age ≥70 yrs and ≥1 of hypertension, diabetes, heart failure, previous stroke
- Exclusion criteria: AF, pacemaker, anticoagulation, or contraindication to anticoagulation
- Eligible participants were randomized 1:3 to ILR vs control



ILR group
Received **I**mplantable **L**oop **R**ecorder (Reveal LINQ™, Medtronic) with continuous remote monitoring
- AF episodes were adjudicated by ≥2 senior cardiologist
- AF episodes ≥6 min gave indication for oral anticoagulation

Control group
Received usual care

The Lancet, 2021

Methods

The LOOP Study, an investigator-initiated Randomized Controlled Trial

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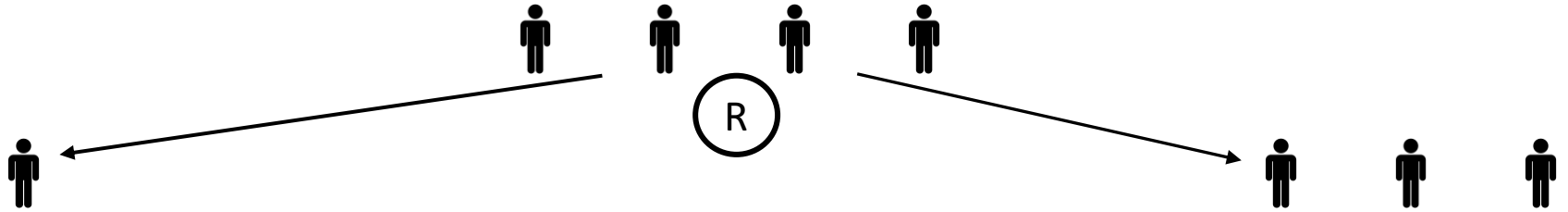

ILR group
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- AF episodes were adjudicated by ≥2 senior cardiologist
- AF episodes ≥6 min gave indication for oral anticoagulation

Control group
Received usual care

The Lancet, 2021

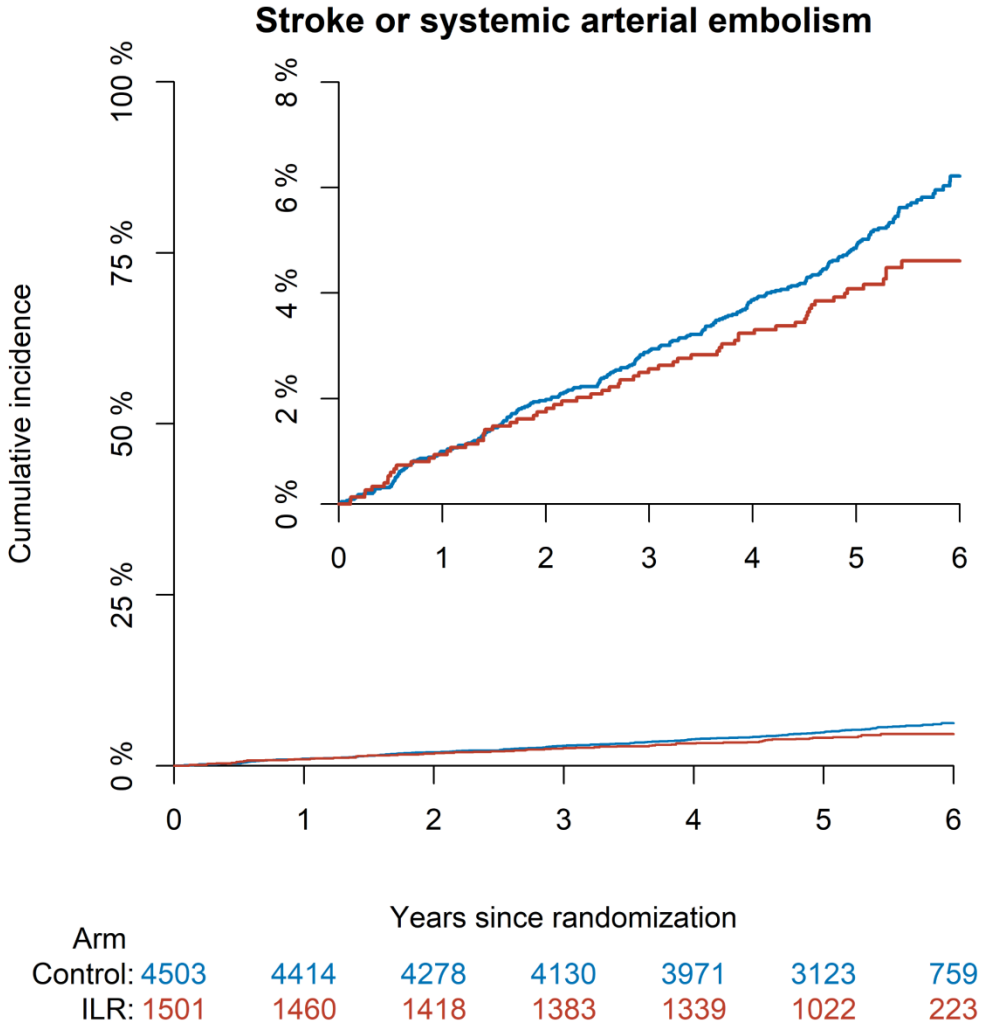
Baseline characteristics	ILR n=1501	Control n=4503
Sex		
Female	702 (47.2)	2128 (47.3)
Male	792 (52.8)	2375 (52.7)
Age, years	74.7 ± 4.1	74.7 ± 4.1
Comorbidities		
Hypertension	1378 (91.8)	4066 (90.3)
Diabetes	422 (28.1)	1288 (28.6)
Heart failure	67 (4.5)	199 (4.4)
Previous stroke	262 (17.5)	794 (17.6)
CHA_2DS_2-VASc score	4 [3, 4]	4 [3, 4]
Medication		
Beta blockers	354 (23.6)	1172 (26.0)
Calcium channel blockers	562 (37.4)	1684 (37.4)
Renin-angiotensin inhibitors	991 (66.0)	2999 (66.6)
Statins	879 (58.6)	2621 (58.2)
Platelet inhibitors	702 (46.8)	2204 (48.9)
Systolic blood pressure, mmHg	150.6 ± 19.2	149.8 ± 19.5
Diastolic blood pressure, mmHg	84.7 ± 11.1	83.9 ± 11.3
Pulse rate, beats/min	71.6 ± 12.1	71.3 ± 12.5
Body mass index, kg/m2	27.8 ± 4.7	27.6 ± 4.5
eGFR, mL/min	76 ± 19.2	75.4 ± 19.4

Results – Primary outcome

The primary outcome occurred in 318 participants (315 stroke, 3 systemic arterial embolism);

67 (4.5%) in the ILR group vs.
251 (5.6%) in the Control group

HR 0.80; 95% CI 0.61-1.05;
P=0.11

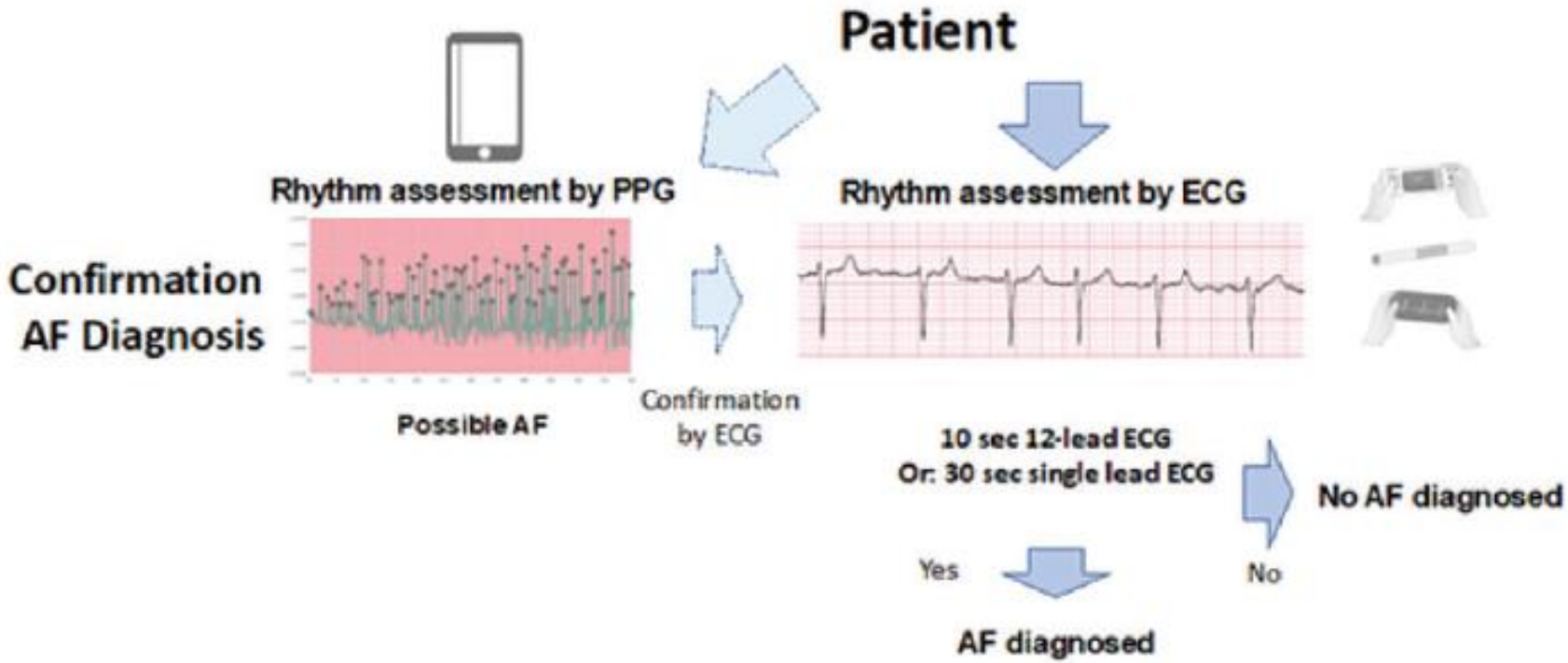


The Lancet, 2021

Recommendation	Class[a]	Level[b]	
Opportunistic screening for AF by pulse taking or ECG rhythm strip is recommended in patients ≥65 years of age.	I	B	?
It is recommended to interrogate pacemakers and implantable cardioverter defibrillators on a regular basis for AHRE.	I	B	? ARTESIA / NOAH AFNET
Systematic ECG screening should be considered to detect AF in individuals aged ≥75 years, or those at high risk of stroke.	IIa	B	√

ESC Guidelines on Atrial Fibrillation 2020

The digital AF patient journey



AF work-up & education

Anticoagulation?

Better symptom control?

Concomitant conditions?

ABC approach supported by app-based evaluation of

- Stroke risk by the CHA_2DS_2-VASc
  - Confirmation by a physician
- Symptom burden by the EHRA score
  - Symptom-rhythm correlation?
- Risk factor management

Svennberg E et al. Europace 2022