

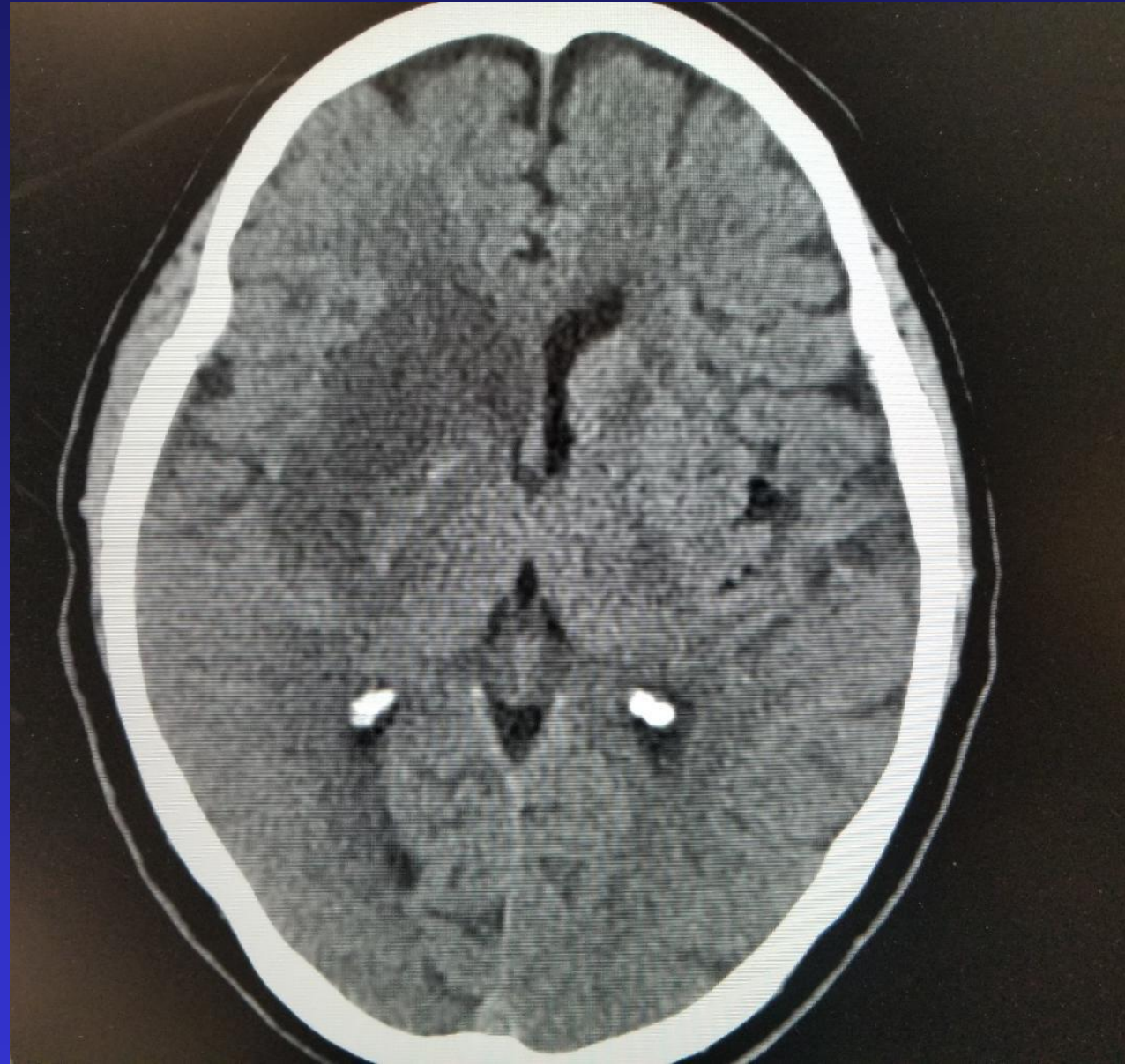
Finding the Silent Danger: Who, When and How for AF Screening

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History

- 72-year-old man
- Known HT, DM and gout
- Found lying on floor by son in the morning, left sided weakness and slurred speech
- 1/5 power on left side
- Limb power worsened to 0/5 and remained the same after rehabilitation

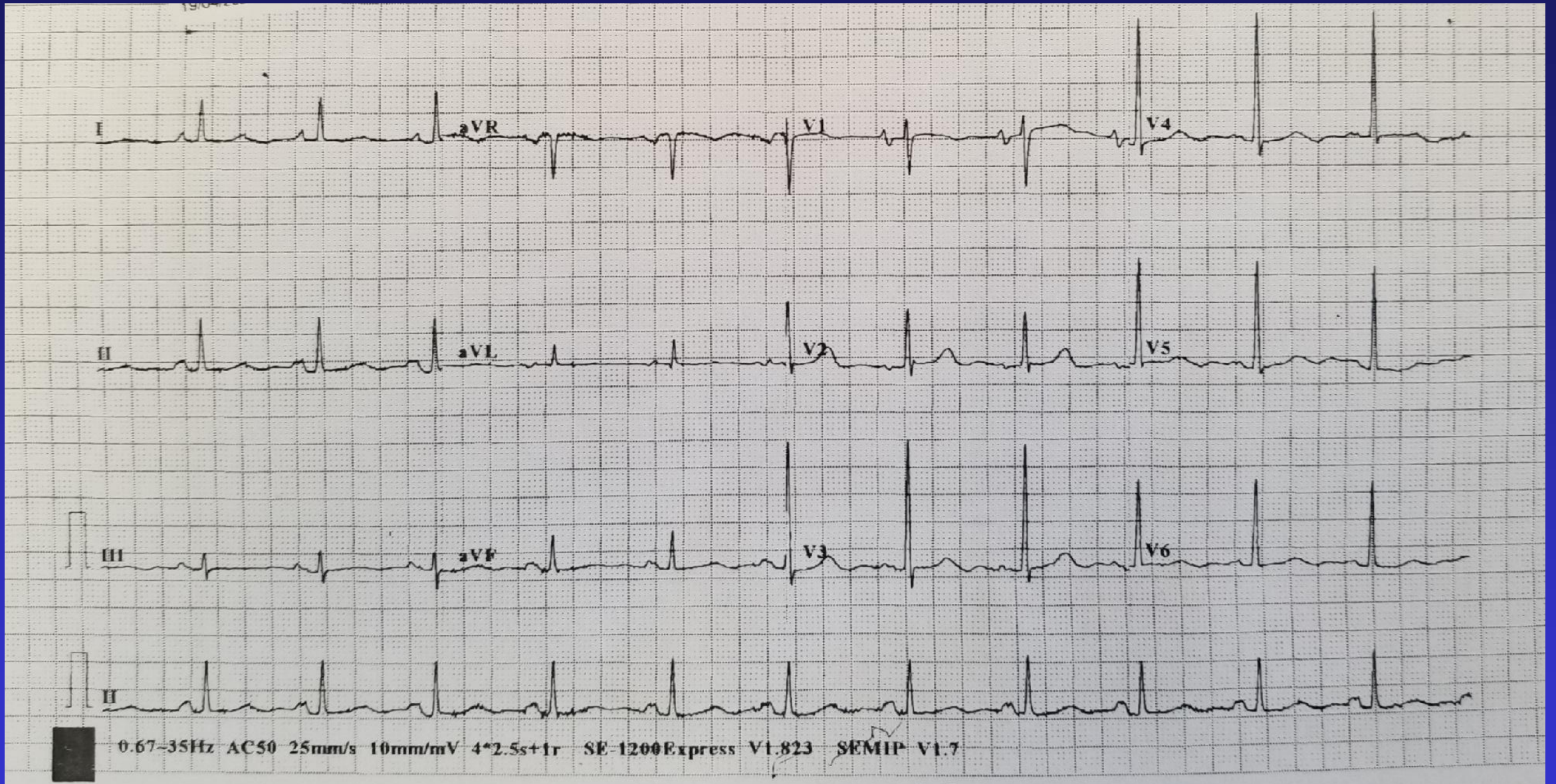
CT Brain



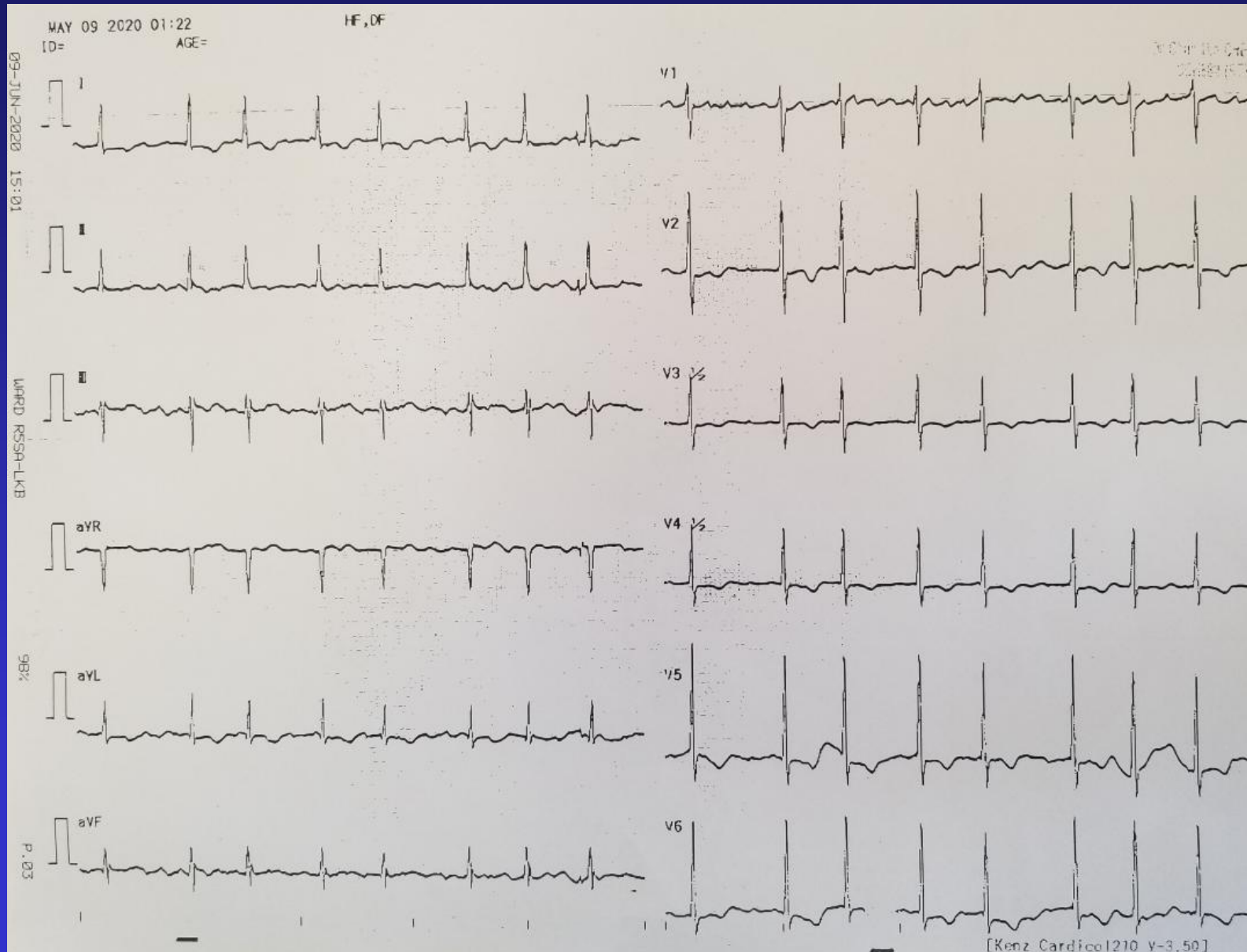
CT Brain



1st ECG



ECG Documented AF 19 days After Admission

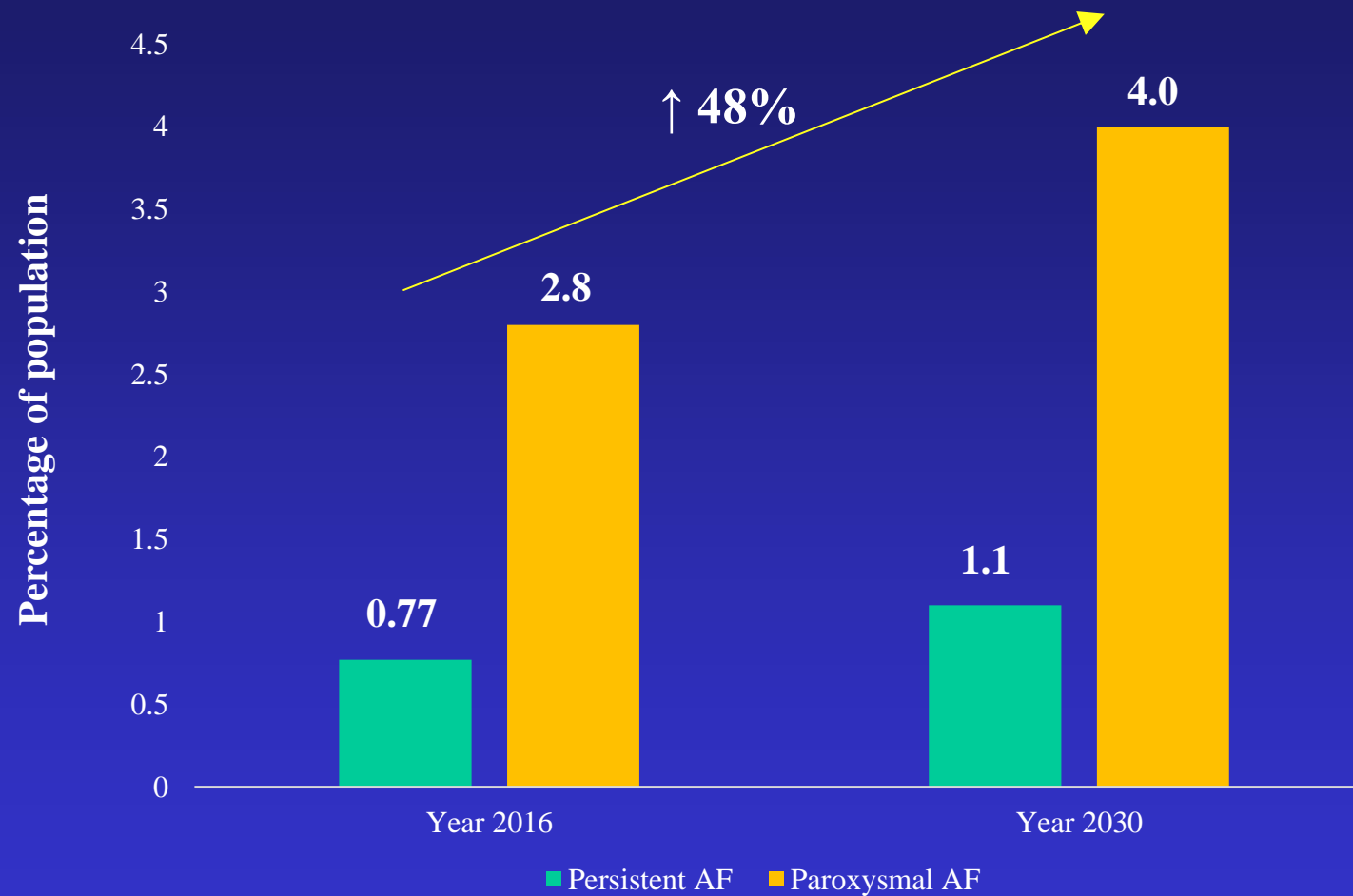


Atrial Fibrillation is Evasive

- 1/3 of patients with AF are asymptomatic¹
- 1/3 of patients with AF-related stroke were not aware of having AF before stroke²

1. Siontis K et al. Typical, atypical and asymptomatic presentations of new-onset atrial fibrillation in the community: characteristics and prognostic implications. *Heart Rhythm* 2016;13:1418-24.
2. Soo Y et al. Age-specific trends of atrial fibrillation-related ischaemic stroke and transient ischaemic attack, anticoagulant use and risk factor profile in Chinese population: a 15-year study. *J Neurol Neurosurg Psychiatry* 2017;88:744-8.

Prevalence of Atrial Fibrillation With an Ageing Population



Chan NY. Systematic screening for atrial fibrillation in the community: evidence and obstacles. *Arrhythm Electrophysiol Rev* 2018;7(1):39-42.

Chan NY et al. Screening for atrial fibrillation in 13122 Hong Kong citizens with smartphone electrocardiogram. *Heart* 2017;103(1):24-31

Is Atrial Fibrillation Suitable for Screening?

Table 1: Suitability of Atrial Fibrillation for Screening According to World Health Organization Criteria

Criteria	Suitability
Important health problem with an accepted treatment	+
Facilities for diagnosis and treatment	+
Latent and symptomatic stage	+
Natural history is understood	±
Agreed policy on whom to treat	+
Cost of finding the condition is economically balanced with overall health benefits of treatment	±
Case-finding is a continuous process	+
Screening test is suitable and acceptable to the population	+

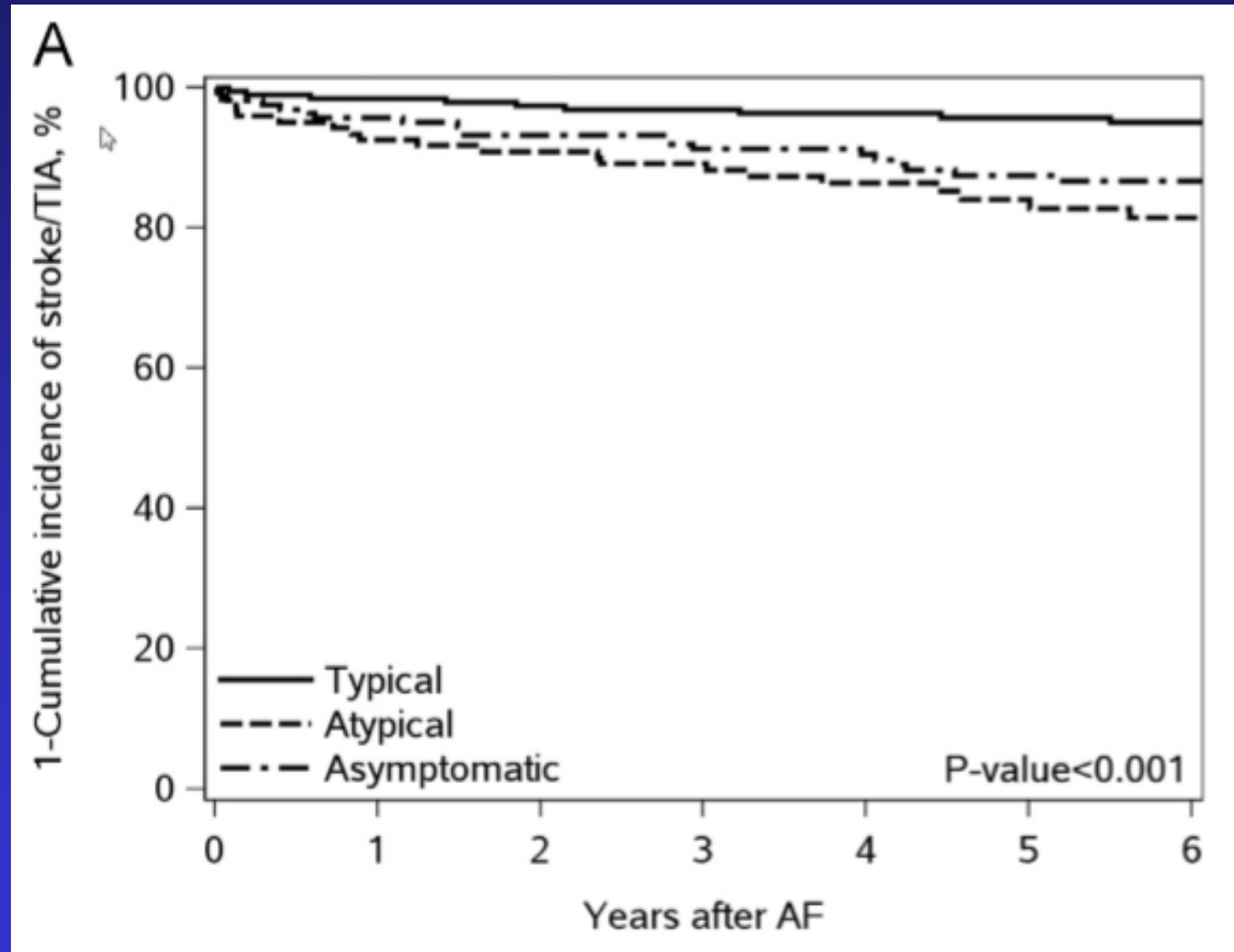
+ = suitable; ± = uncertain.

Prognosis of Asymptomatic Atrial Fibrillation

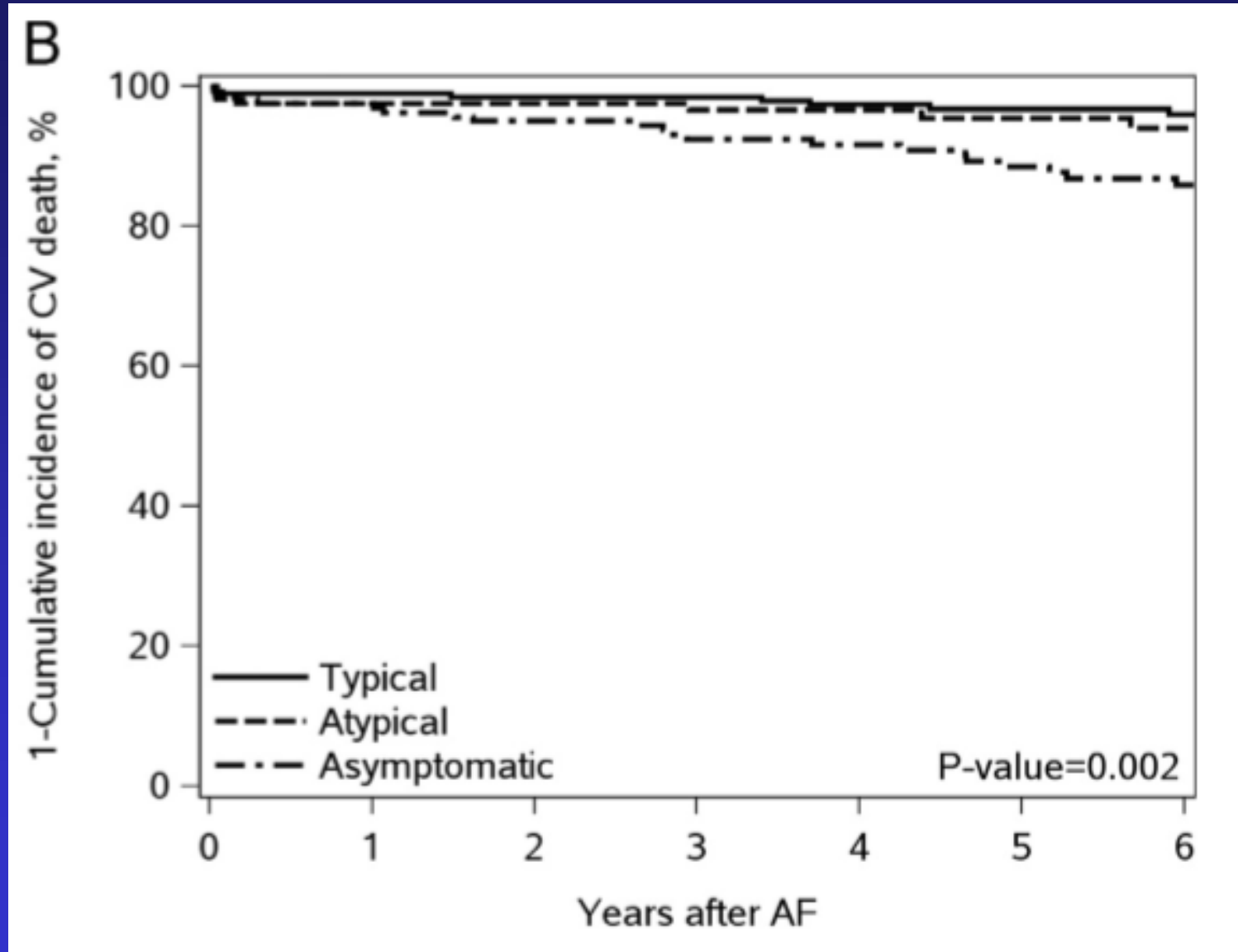
N=476 with incident AF in Olmsted County, Minnesota randomly selected (2000-10)

193 had typical, 122 had atypical and 161 had no symptoms

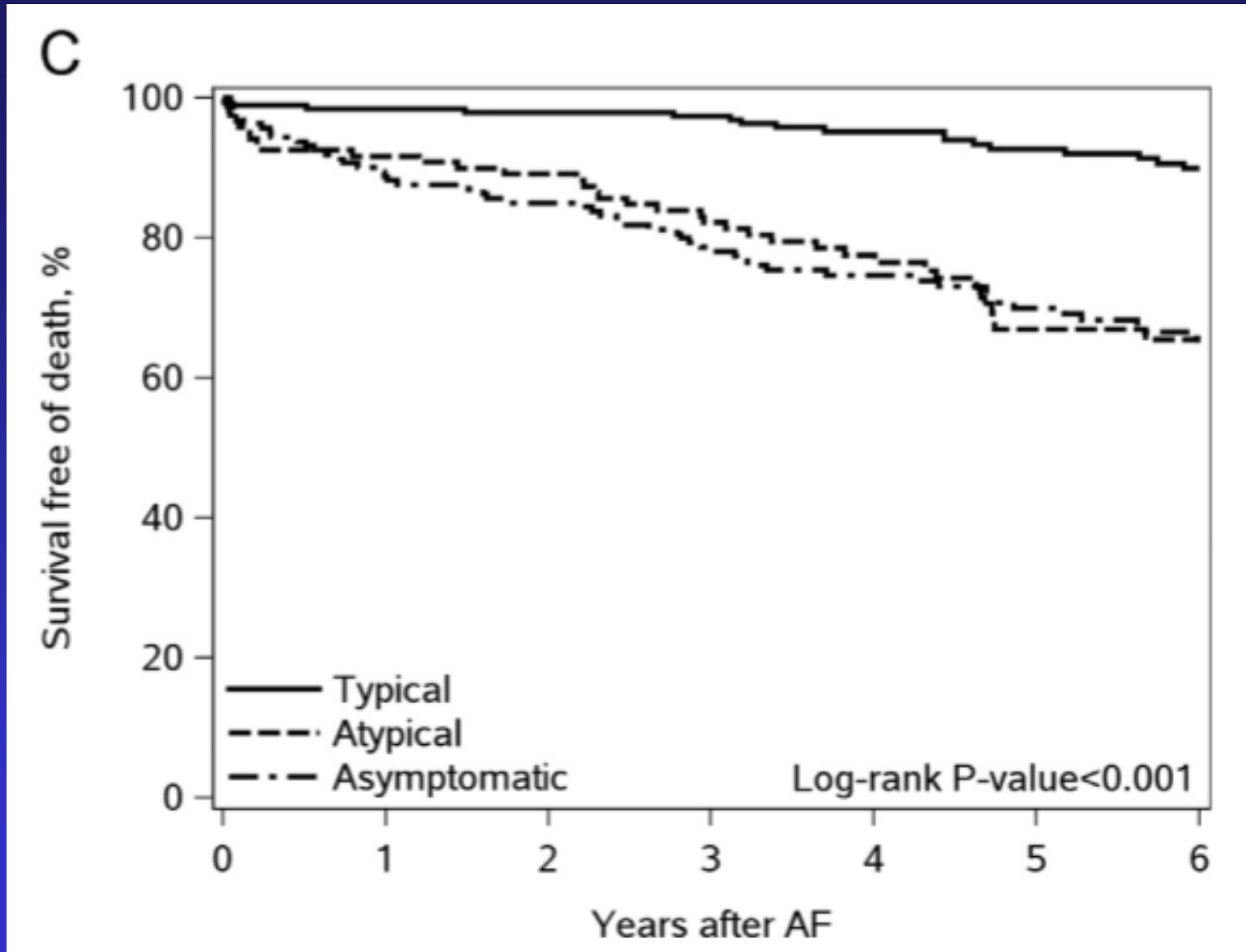
Adjustment for CHA₂DS₂VASc score, age, warfarin use and comorbidities



Prognosis of Asymptomatic Atrial Fibrillation

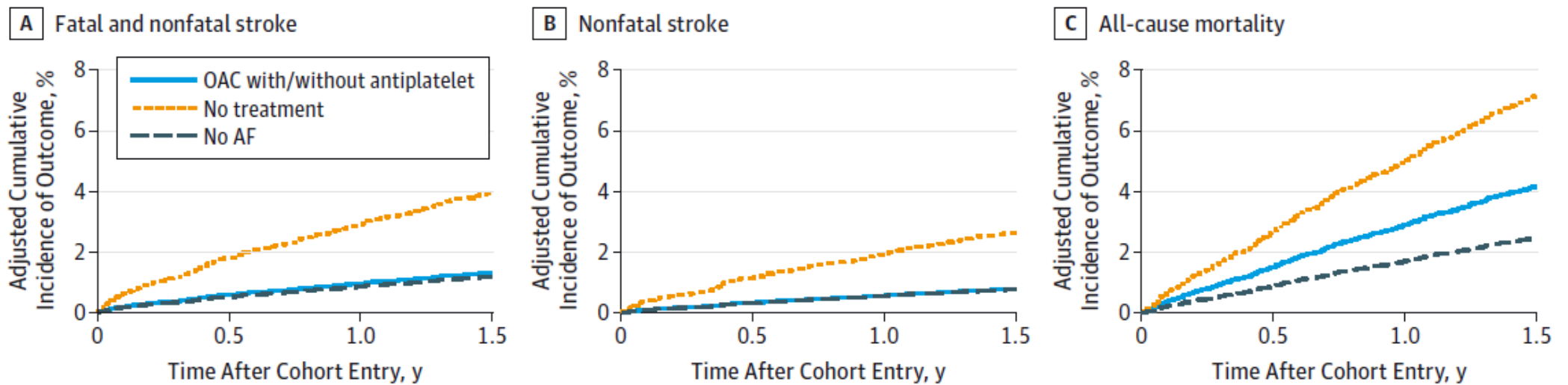


Prognosis of Asymptomatic Atrial Fibrillation



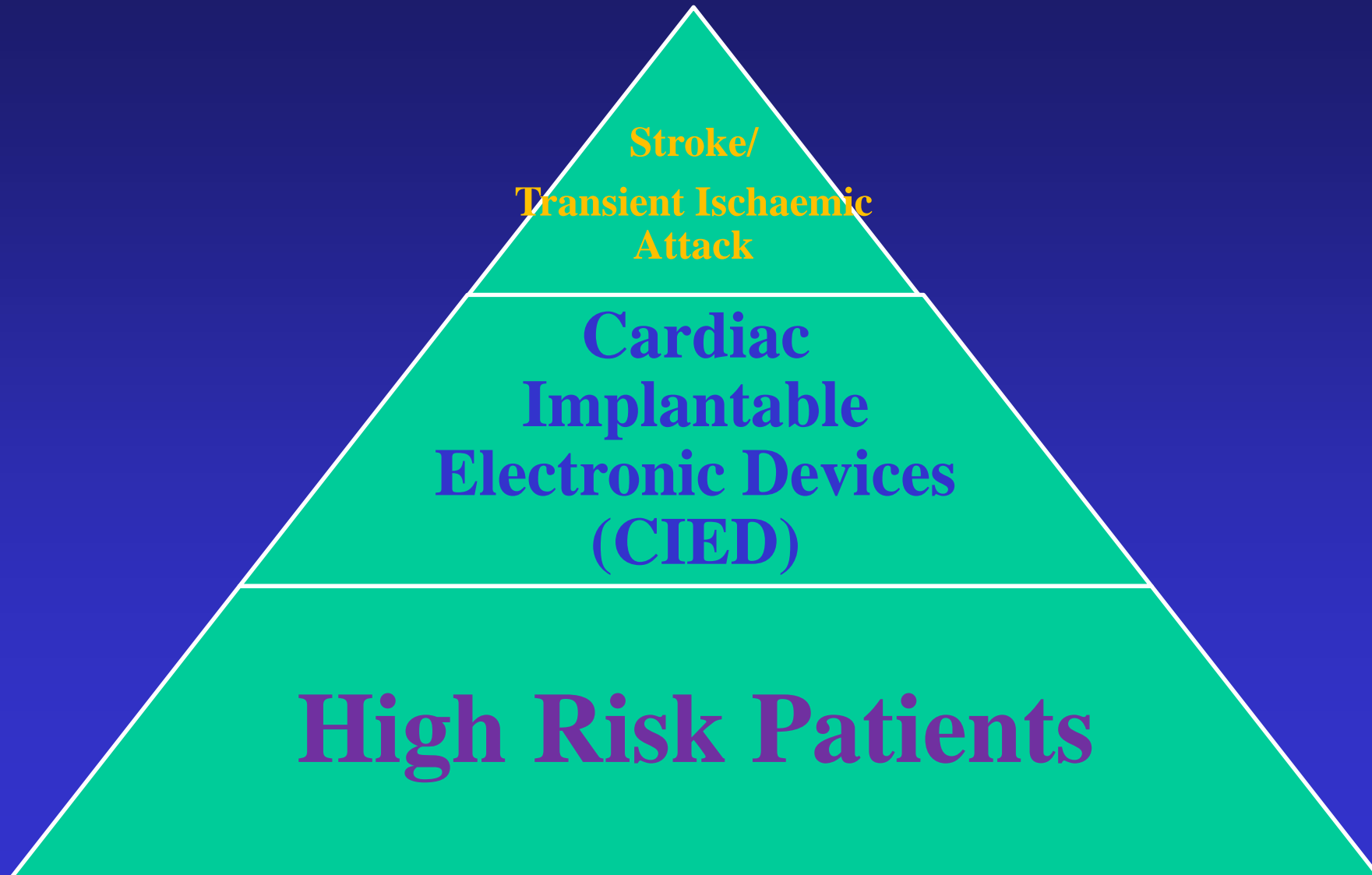
Prognosis and Response to Treatment of Incidentally Detected Ambulatory AF

Data from UK Clinical Practice Research Datalink re-analyzed
 5555 patients with incidentally detected ambulatory AF: 2492 receiving warfarin, 1603 received an antiplatelet and 1460 received no antithrombotic
 Compared with 24705 age and sex matched cohort patients without AF seen in general practice on the same day



No. at risk	0	0.5	1.0	1.5	0	0.5	1.0	1.5	0	0.5	1.0	1.5
AF: OAC with/without antiplatelet	552	881	642	492	552	881	642	492	552	893	653	499
AF: No treatment	2712	926	674	552	2712	926	674	552	2712	928	675	553
No AF	24705	24086	23401	22317	24705	24086	23401	22317	24705	24171	23544	22499

Screening for Atrial Fibrillation



Recommendations	Class ^a	Level ^b	Ref ^c
Opportunistic screening for AF is recommended by pulse taking or ECG rhythm strip in patients >65 years of age.	I	B	130, 134, 155
In patients with TIA or ischaemic stroke, screening for AF is recommended by short-term ECG recording followed by continuous ECG monitoring for at least 72 hours.	I	B	27, 127
It is recommended to interrogate pacemakers and ICDs on a regular basis for atrial high rate episodes (AHRE). Patients with AHRE should undergo further ECG monitoring to document AF before initiating AF therapy.	I	B	141, 156
In stroke patients, additional ECG monitoring by long-term non-invasive ECG monitors or implanted loop recorders should be considered to document silent atrial fibrillation.	IIa	B	18, 128
Systematic ECG screening may be considered to detect AF in patients aged >75 years, or those at high stroke risk.	IIb	B	130, 135, 157

Current Guidelines

Kirchhof P et al. 2016 ESC guidelines for the management of AF developed in collaboration with EACTS. EHJ 2016;37:2893-962.

International Guidelines

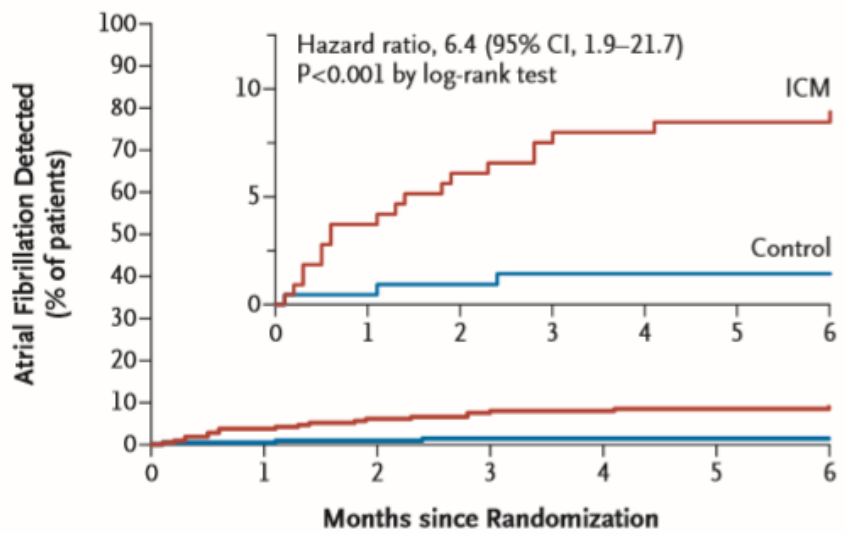
Guidelines	Screening approach	Screening method	Recommendations
NICE	N/A	N/A	N/A
NHFA/CSANZ	Opportunistic	Pulse palpation or Point-of-care ECG (ECG preferred)	≥65 years
KHRS	Opportunistic/ systematic	Pulse palpation/ ECG	Opportunistic for age >65 years Systematic may be considered for age >75 years or high stroke risk
ACC/AHA/HRS	N/A	N/A	N/A

USPSTF-Screening for AF With ECG

Population	Older adults
Recommendation	No recommendation. Grade: I (insufficient evidence)

Risk Assessment	Atrial fibrillation is strongly associated with older age and obesity. Other risk factors include high blood pressure, diabetes, heart failure, prior cardiothoracic surgery, current smoking, prior stroke, sleep apnea, alcohol and drug use, and hyperthyroidism.
Screening Tests	The USPSTF found inadequate evidence to assess whether screening with electrocardiography identifies older adults with previously undiagnosed atrial fibrillation more effectively than usual care.
Treatments and Interventions	Treatment of atrial fibrillation has 2 components: managing arrhythmia and preventing stroke. In general, these treatment goals are independent of each other. Arrhythmia can be managed by controlling the heart rate to minimize symptoms (usually through medication) or by restoring a normal rhythm. Treatment with anticoagulant therapy reduces the incidence of stroke in patients with symptomatic atrial fibrillation and high stroke risk.
Other Relevant USPSTF Recommendations	The USPSTF has made recommendations on many factors related to stroke prevention, including screening for high blood pressure, use of statins, counseling on smoking cessation, counseling to promote healthful diet and physical activity, and use of low-dose aspirin for certain persons at increased risk of cardiovascular disease.

A Detection of Atrial Fibrillation by 6 Months



No. at Risk

Control	220	214	200	198	197	197	194
ICM	221	205	198	195	194	193	191

AF Screening in Cryptogenic Stroke

N=441 patients with cryptogenic stroke randomized to ICM for AF screening and control

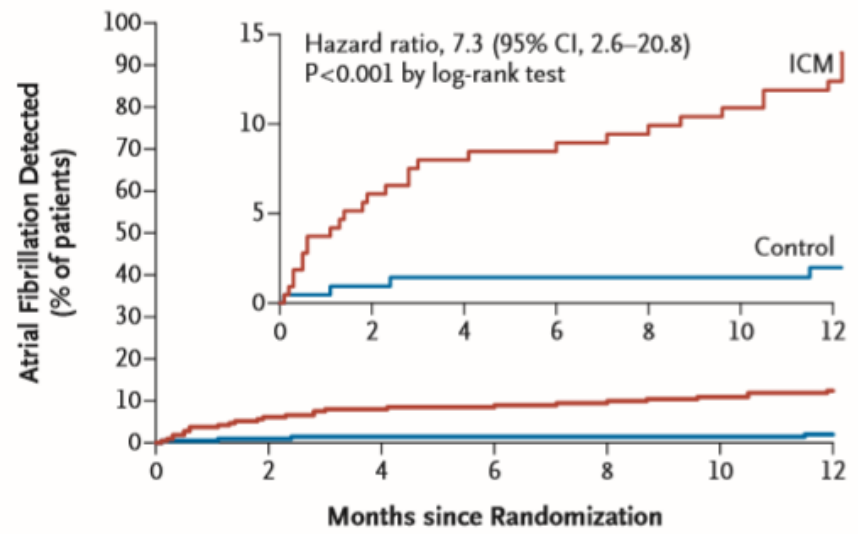
Primary endpoint: time to 1st AF detection (lasting >30s) within 6 months

6 months: 8.9 vs 1.4%

12 months: 12.4 vs 2%

36 months: 30 vs 3%

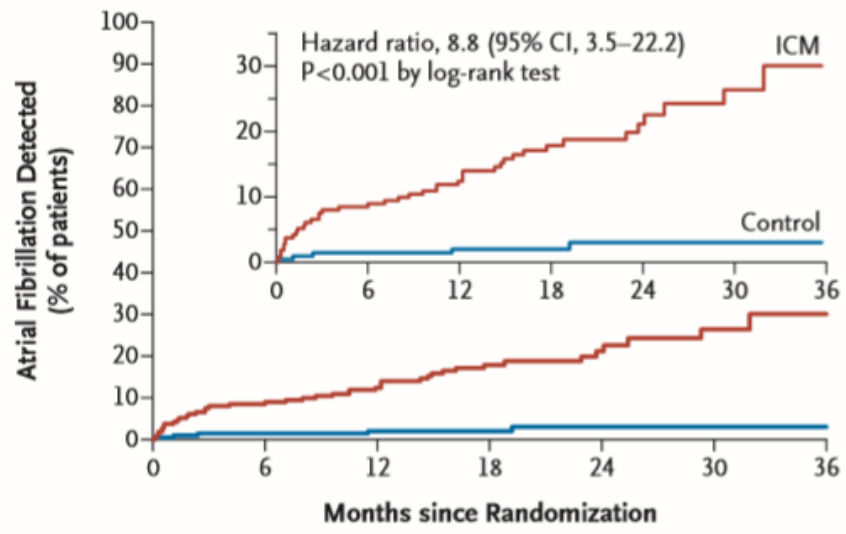
B Detection of Atrial Fibrillation by 12 Months



No. at Risk

Control	220	200	197	194	184	184	167
ICM	221	198	194	191	186	182	173

C Detection of Atrial Fibrillation by 36 Months



No. at Risk

Control	220	194	167	114	72	36	7
ICM	221	191	173	102	57	29	8

Sanna T et al. Cryptogenic stroke and underlying atrial fibrillation. NEJM 2014;370:2478-86

Empirical Rivaroxaban Treatment for Embolic Stroke of Undetermined Source

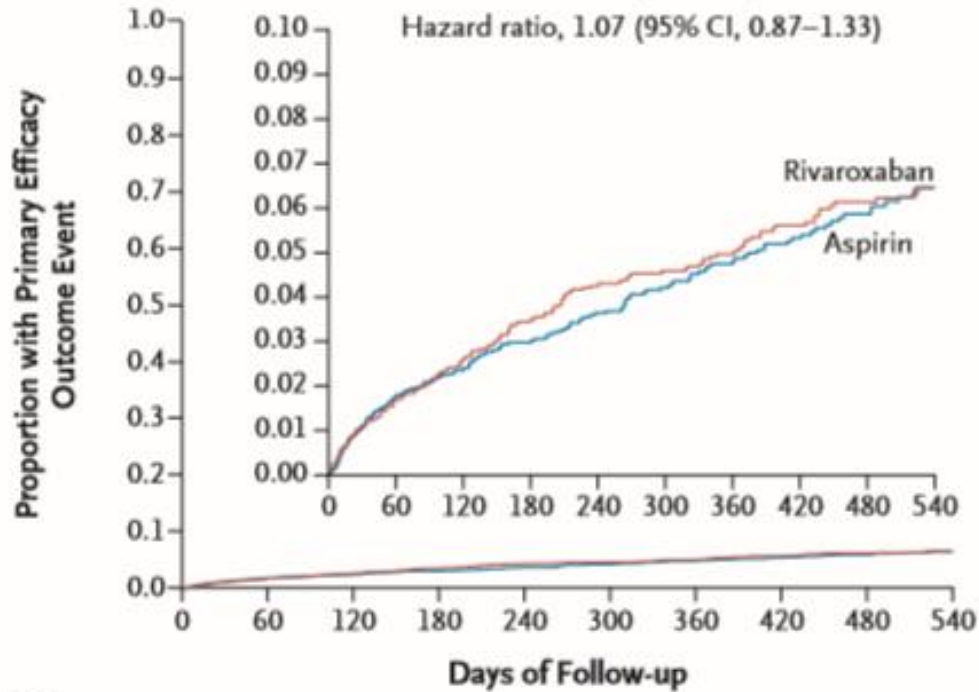
N=7213 patients randomized to receive Rivaroxaban (15mg daily) or Aspirin (100mg daily)

Prematurely terminated because of lack of effect

Primary efficacy outcome: 1st recurrence of ischaemic or haemorrhagic stroke or systemic embolism

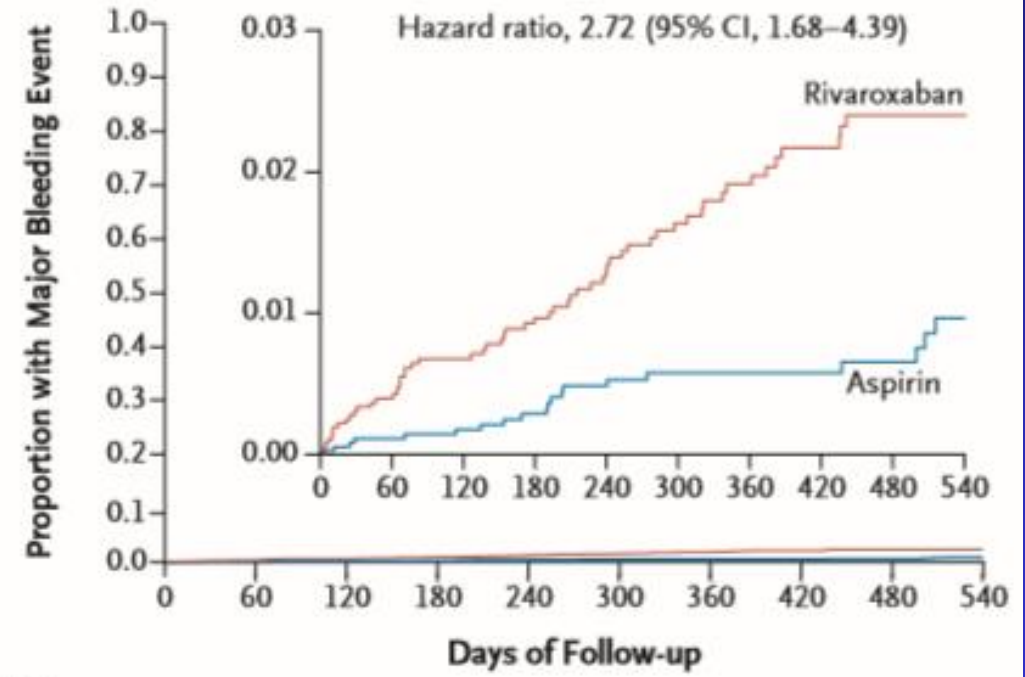
Primary safety outcome: rate of major bleeding

A Kaplan–Meier Curves for Time to Event in the Primary Efficacy Outcome



No. at Risk	0	60	120	180	240	300	360	420	480	540
Rivaroxaban	3609	3211	2854	2525	2156	1874	1584	1306	1046	786
Aspirin	3604	3205	2858	2531	2166	1880	1579	1319	1036	779

B Kaplan–Meier Curves for Time to Major Bleeding Event



No. at Risk	0	60	120	180	240	300	360	420	480	540
Rivaroxaban	3609	3249	2906	2582	2206	1911	1615	1342	1071	807
Aspirin	3604	3254	2918	2597	2231	1939	1637	1371	1083	822

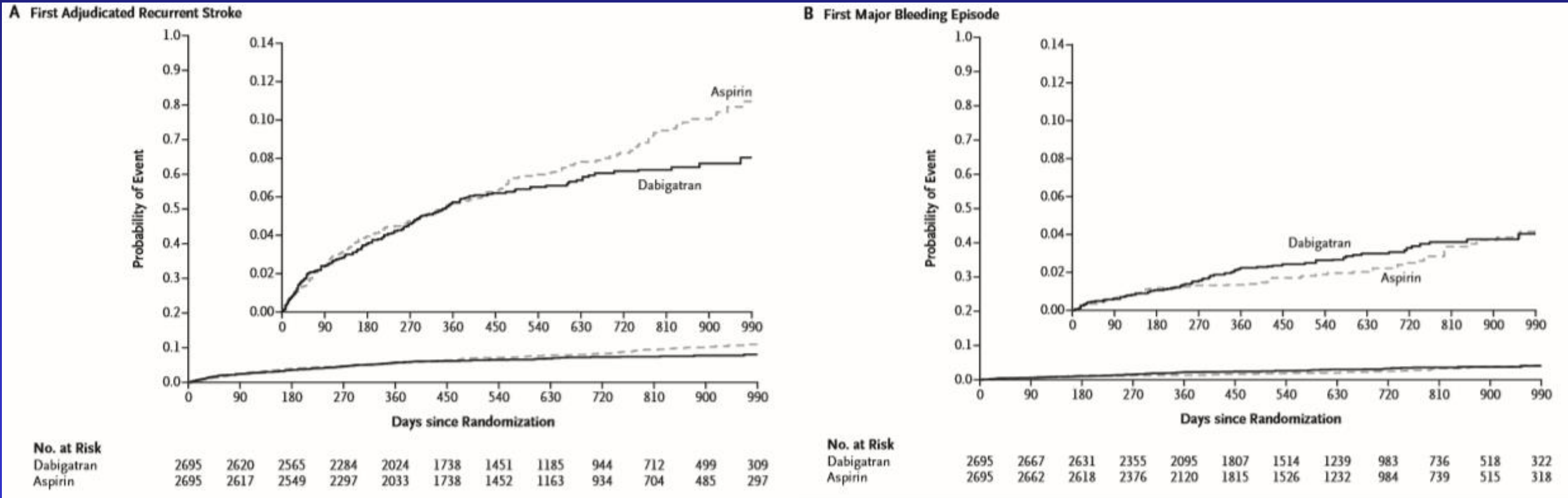
Empirical Dabigatran Treatment for Embolic Stroke of Undetermined Source

N=5390 patients randomized to receive Dabigatran (150 or 110mg BD) or Aspirin (100mg daily)

Prematurely terminated because of lack of effect

Primary outcome: Recurrent stroke

Primary safety outcome: rate of major bleeding

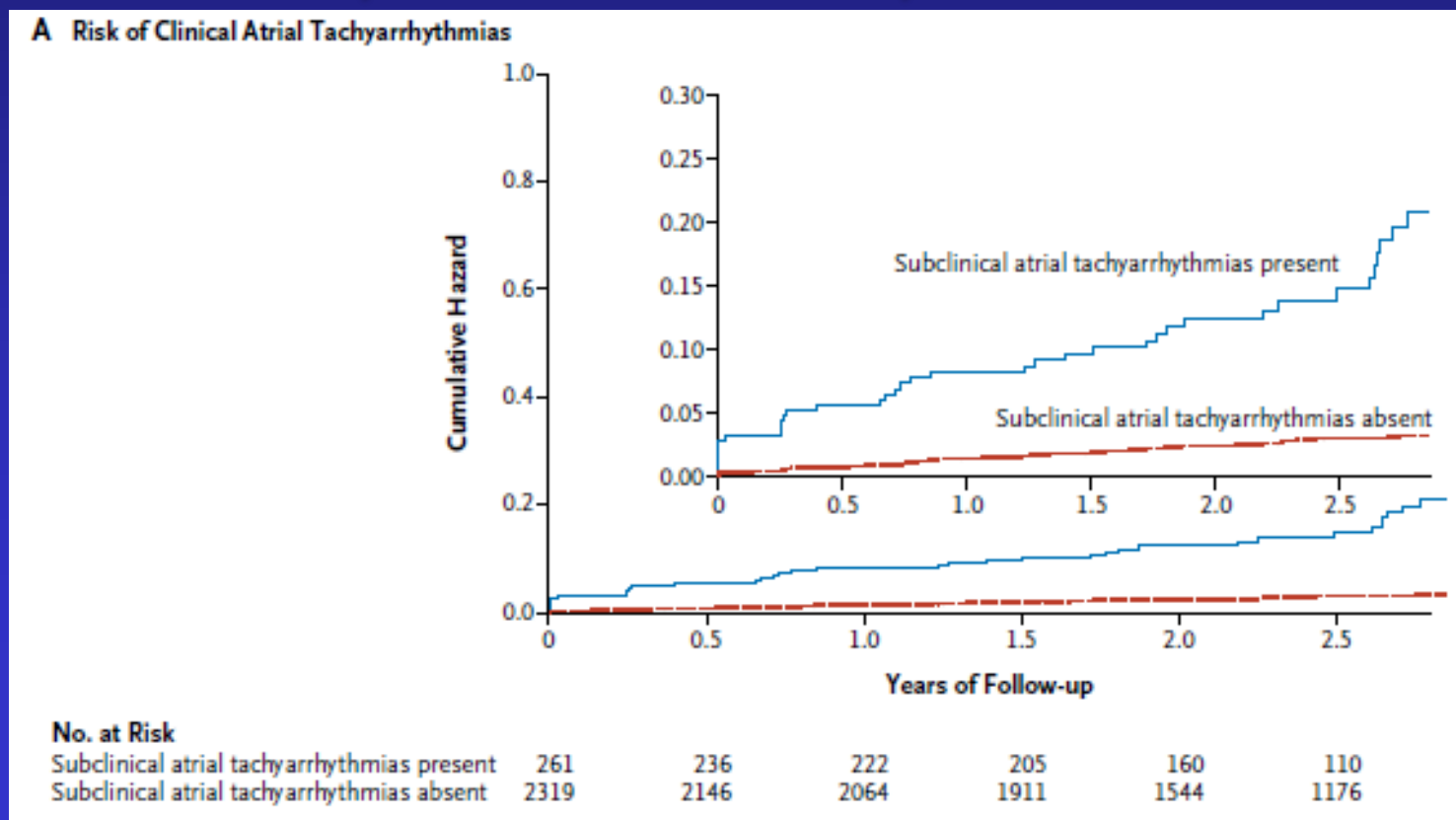


Significance of CIED-detected Subclinical Atrial Tachyarrhythmias

N=2580 patients with hypertension and no history of AF, with a pacemaker or ICD recently implanted
Patients were monitored for 3 months to detect subclinical atrial arrhythmias (episodes of atrial rate >190 beats per minute for more than 6 minutes)

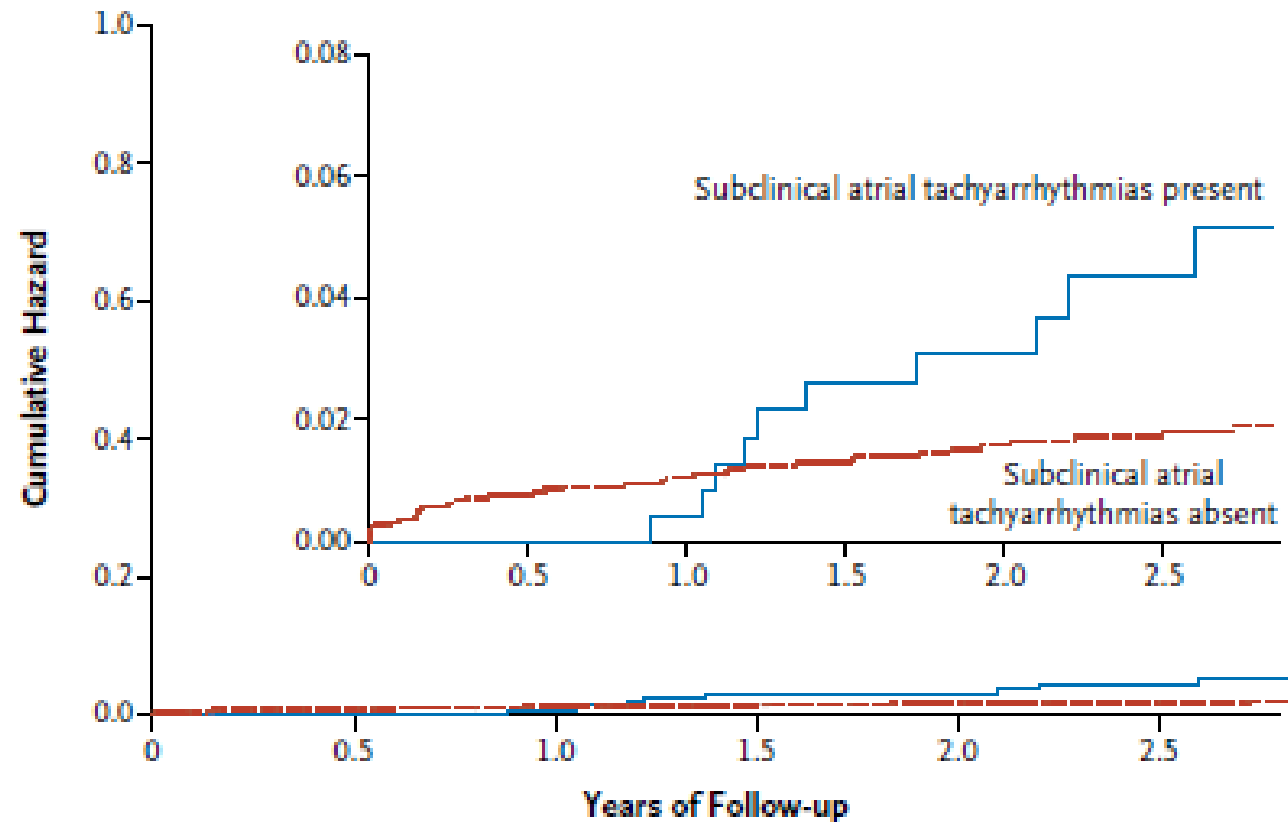
FU for a mean of 2.5 years

Primary outcome: Ischemic stroke or systemic embolism



Significance of CIED-detected Subclinical Atrial Tachyarrhythmias

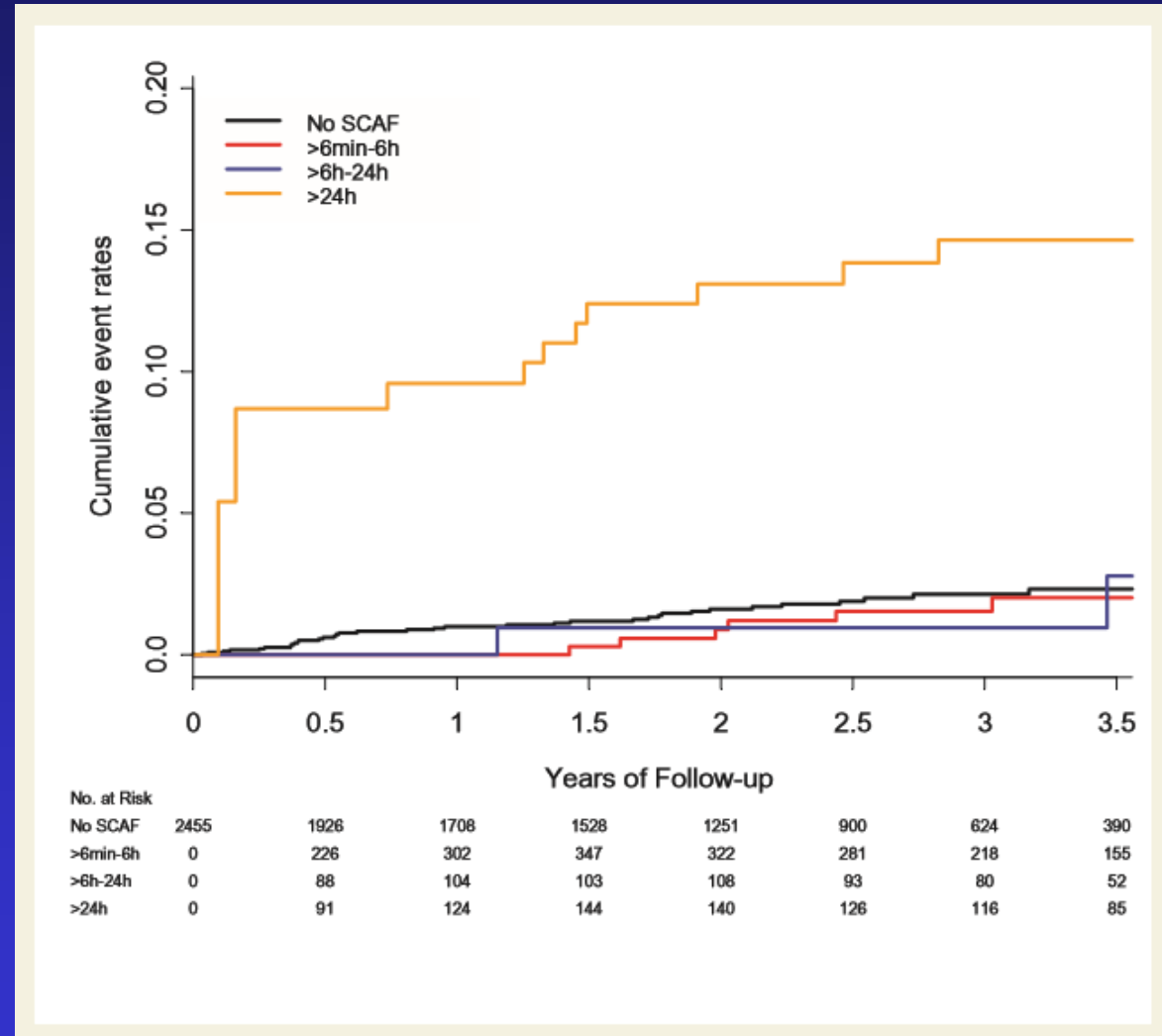
B Risk of Ischemic Stroke or Systemic Embolism



No. at Risk

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

Significance of CIED-detected Subclinical Atrial Tachyarrhythmias

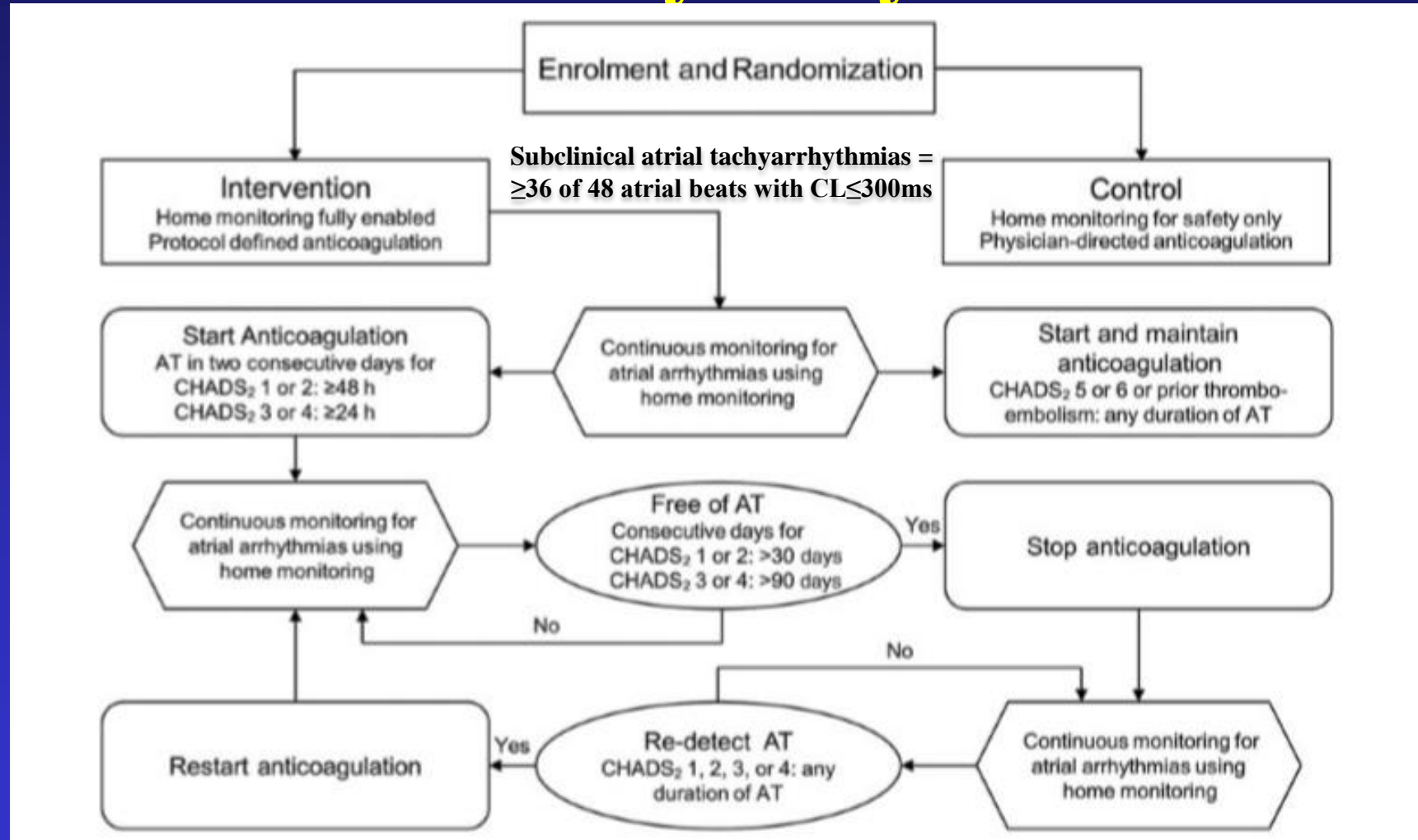


Significance of CIED-detected Subclinical Atrial Tachyarrhythmias

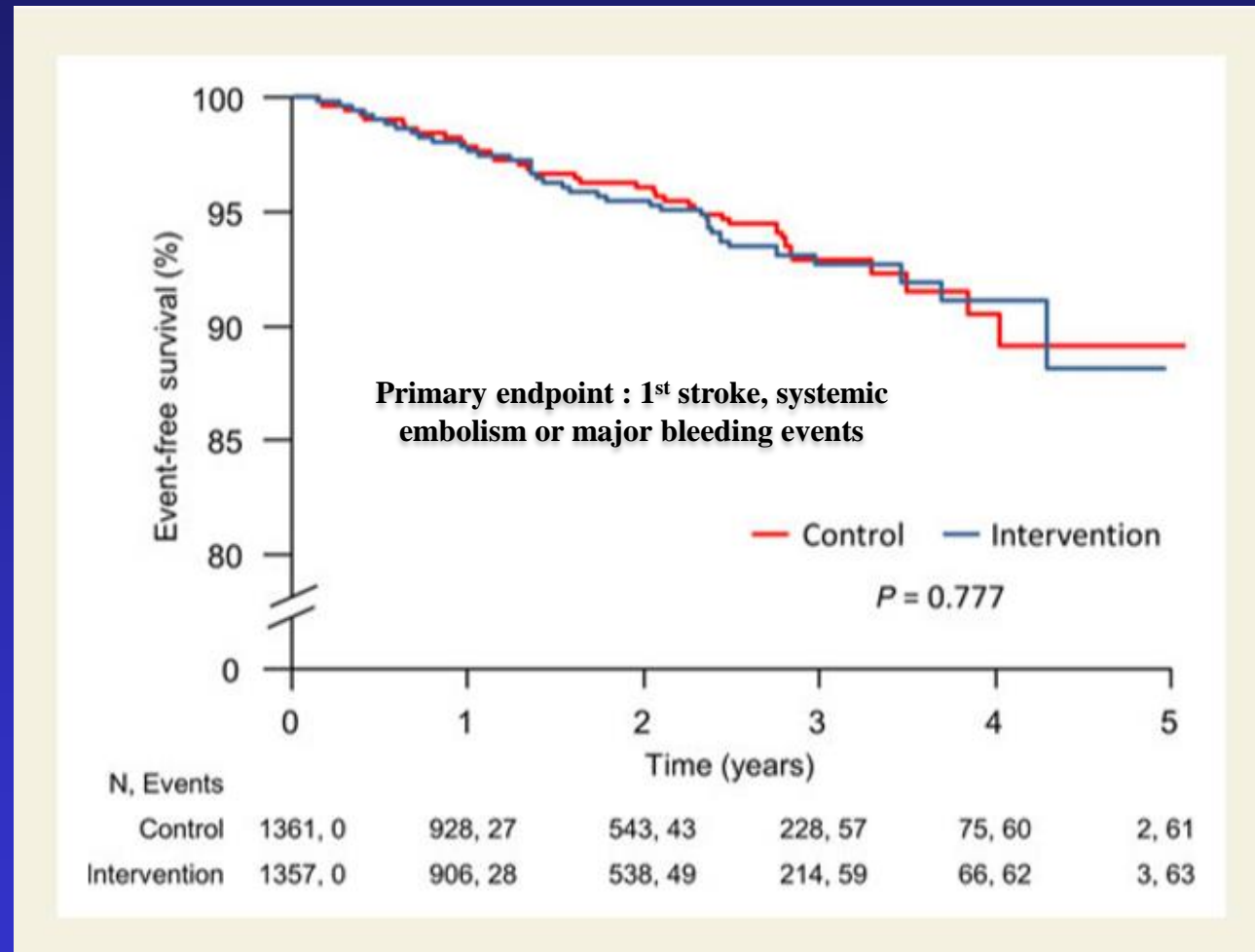
AT/AF=atrial rate >175/min lasting \geq 20s

AT/AF Burden Subset	Annualized TE Rate (95% CI), %	Annualized TE Rate Excluding TIAs (95% CI), %
Zero AT/AF burden	1.1 (0.8–1.6)	0.5 (0.3–0.9)
Low AT/AF burden (<5.5 h)	1.1 (0.4–2.8)	1.1 (0.4–2.8)
High AT/AF burden (\geq 5.5 h)	2.4 (1.2–4.5)	1.8 (0.9–3.8)

Treatment Response of CIED-detected Subclinical Atrial Tachyarrhythmias

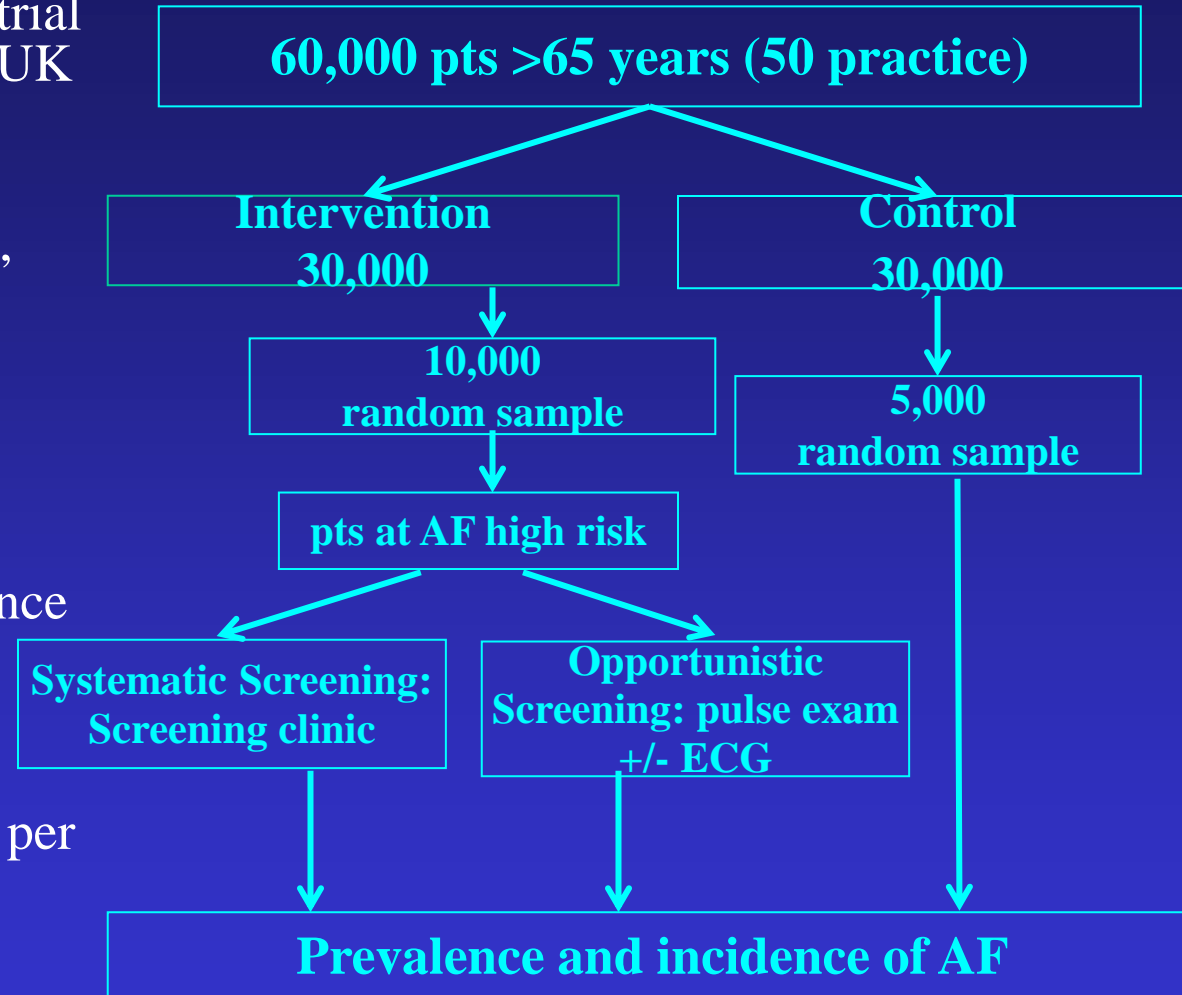


Treatment Response of CIED-detected Subclinical Atrial Tachyarrhythmias



Atrial Fibrillation Screening at Primary Care in UK: SAFE Study

- A randomized controlled trial at primary care setting in UK
- 50 primary care centers across the West Midlands, UK.
- Patients > 65 years
- To determine baseline prevalence and the incidence of AF
- To compare 2 screening strategies in terms of cost per case identified



Atrial Fibrillation Screening at Primary Care in UK: SAFE Study

- Baseline prevalence of AF: 7.2%
- Incidence of AF/year
 - Opportunistic: 1.64%
 - Systematic: 1.62%
 - Control: 1.04%
- AF screening program in patients >65, the only strategy that improved on routine practice was opportunistic screening
- Annual opportunistic screening was cost-effective

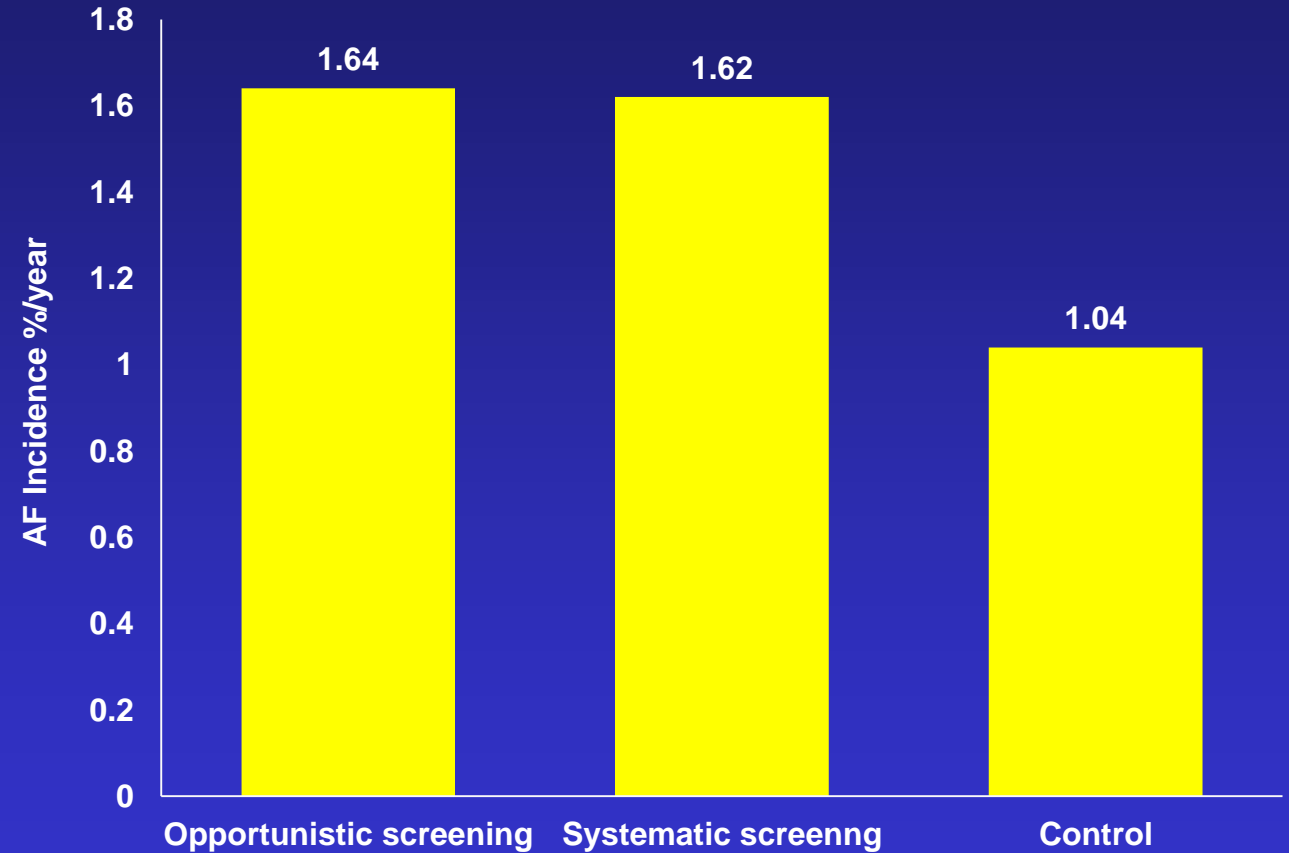
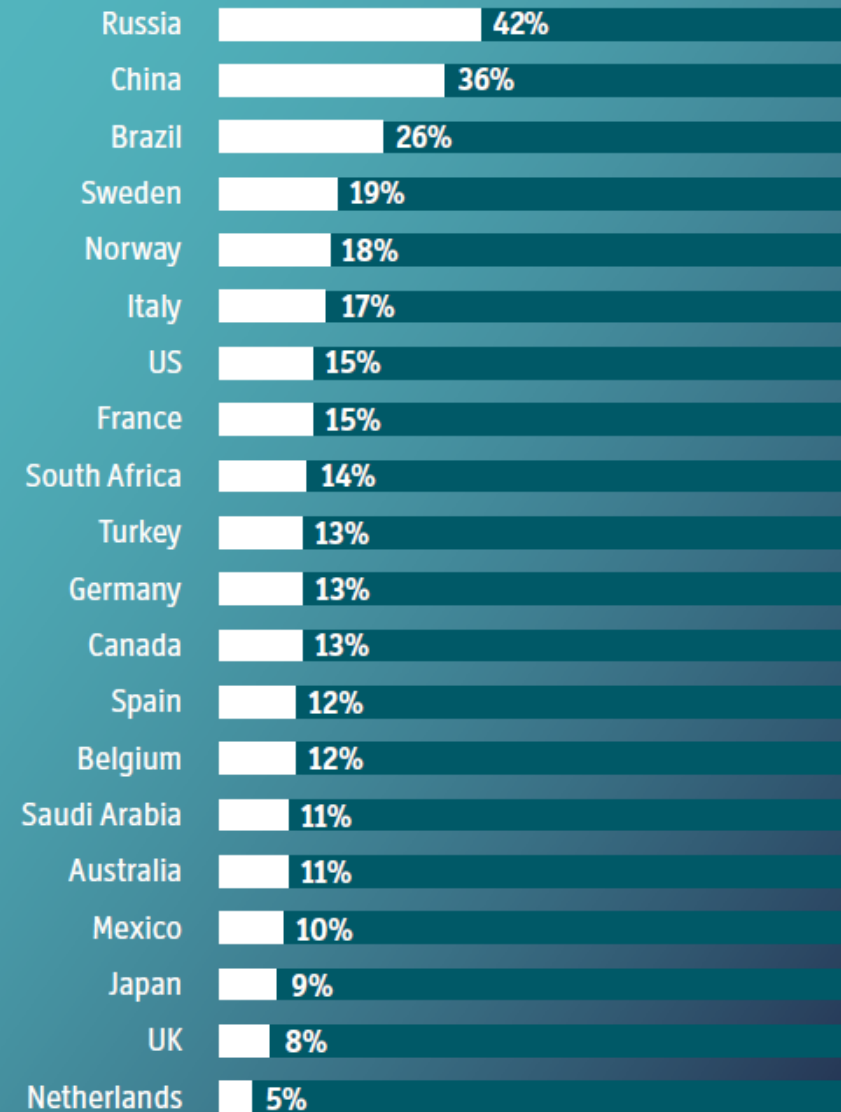


Chart 6: Atrial fibrillation screening in clinical settings

Percent of patients aged 65 and over screened for atrial fibrillation by pulse palpation or electrocardiogram in clinical practice during the previous two weeks who were not already being monitored for AF.



Source: Economist Intelligence Unit Healthcare survey of 1,000 physicians across 20 studied countries

Real-World Compliance to Opportunistic Screening for Atrial Fibrillation

Impact of a Large-scale Territory-wide Social Media-based Program on Atrial Fibrillation Awareness and Screening Behaviour

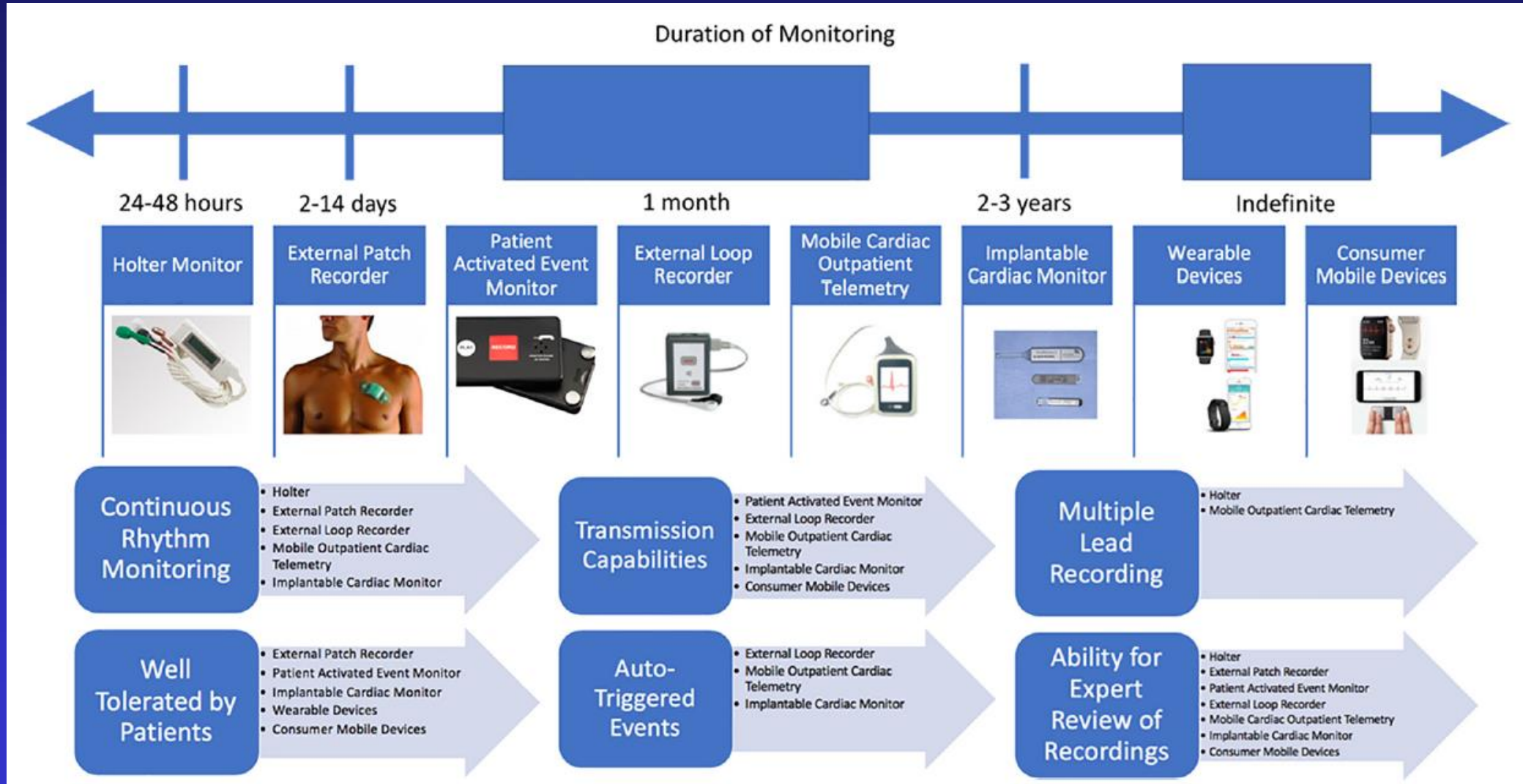
Aims: To study the impact of a large-scale, territory-wide and social media-based program (AFAP) on awareness and compliance to guideline-recommended opportunistic screening for AF.↵

Methods: AFAP was conducted from November 2017 to May 2018 in Hong Kong. A dedicated website was established, short videos and printed booklets on AF were made. A Guinness record-breaking activity for AF screening was organized. Emphasis was placed on promotion via social media and the theme was on AF screening and stroke prevention. Professional educational sessions were also organized. Telephone survey was conducted on elderly citizens above 65 years of age before and 4 months after AFAP.↵

Impact of a Large-scale Territory-wide Social Media-based Program on Atrial Fibrillation Awareness and Screening Behaviour

	Pre-AFAP (n=844)	Post-AFAP (n=813)	p-value
Sex (women %)	69.2	66	0.270
Age	73.9±7.2	74.8±7.2	0.019
Heard of AF before? (Yes %)	41.5	45	0.301
AF can be asymptomatic? (Yes %)	14.5	14	0.801
Stroke is a complication? (Yes %)	53.1	50.2	0.238
Heart failure is a complication? (Yes %)	40	39.5	0.153
Oral anticoagulation is a treatment? (Yes %)	23.1	21.4	0.405
Pulse check or ECG performed on consultation in past 12 months? (Yes %)	65	52.3	<0.001

Screening Tools for Atrial Fibrillation



Screening Tools for Atrial Fibrillation

Device	Method of Interpretation	Sensitivity (%)	Specificity (%)	Reference
Pulse palpation		94 (84–97)	72 (69–75)	Cooke et al ⁵⁵
Handheld single-lead ECGs				
AliveCor (Kardia) heart monitor	Algorithm only (based on presence of P wave and RR irregularity)	98 (89–100)	97 (93–99)	Lau et al ⁵⁶
Merlin ECG event recorder	Cardiologist interpretation	93.9	90.1	Kearley et al ⁵⁷
Mydiagnostick	Algorithm only (based on RR irregularity)	94 (87–98)	93 (85–97)	Tieleman et al ⁵⁸
				Vaes et al ⁵⁹
Omron HCG-801	Algorithm only (based on RR irregularity)	98.7 (93.2–100)	76.2(73.3–78.9)	Kearley et al ⁵⁷
Omron HCG-801	Cardiologist interpretation	94.4	94.6	Kearley et al ⁵⁷
Zenicor EKG	Cardiologist interpretation	96	92	Doliwa et al ⁶⁰
Modified blood pressure monitors				
Microlife BPA 200 Plus	Algorithm only (based on pulse irregularity)	92	97	Marazzi et al ⁶¹
Microlife BPA 200	Algorithm only (based on pulse irregularity)	97 (81.4–100)	90 (83.8–94.2)	Wiesel et al ⁶²
Omron M6	Algorithm only (based on pulse irregularity)	100	94	Marazzi et al ⁶¹
Omron M6 comfort	Algorithm only (based on pulse irregularity)	30 (15.4–49.1)	97 (92.5–99.2)	Wiesel et al ⁶²
Microlife WatchBP	Algorithm only (based on pulse irregularity)	94.9 (87.5–98.6)	89.7 (87.5–91.6)	Kearley et al ⁵⁷
Plethysmographs				
Finger probe	Algorithm only (based on pulse irregularity)	100	91.9	Lewis et al ⁶³
iPhone photo-plethysmograph	Algorithm only (based on pulse irregularity)	97.0	93.5	McManus et al ^{64*}

Facial PPG for AF Screening

Each participant sat in front of an iPhone placed upright on a desk around 30cm away

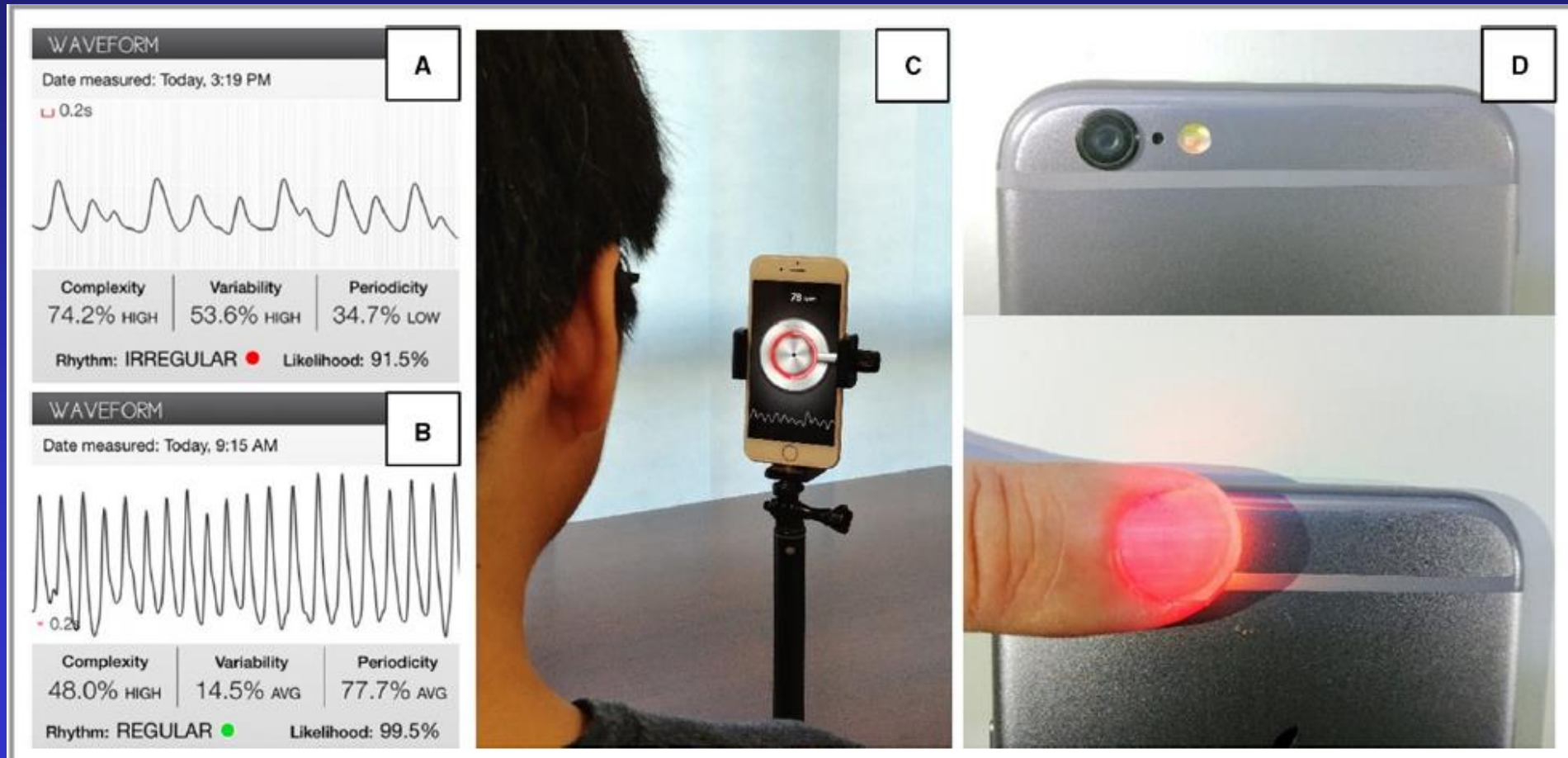
A large circle displaced on the front camera's field of view

The participant was instructed to position his/her entire face within the circle during measurement session

Continuous pulsatile PPG signal from the face was obtained during measurement

3 consecutive 20-second measurements were performed

Sensitivity 95%, specificity 96%, PPV 92%, NPV 97%



Number-Needed-To-Screen for One Newly Diagnosed Atrial Fibrillation

Study	Number of participants	Target population	Mean age (years)	Response rate (%)	Screening tool	Confirmation with 12-lead ECG	Total AF detected, n (%)	Previously undiagnosed AF detected, n (%)	Patients* indicated and given OAC, n (%)	NNS
Furberg et al. 1994 ¹⁰	5,151	Random sample of citizens from Medicare eligibility lists from four US communities	N/A (≥65)	57.6	12-lead ECG	N/A	277 (5.4)	77 (1.49)	N/A	67
Meschia et al. 2010 ¹¹	29,861	Black Americans and residents of the southeastern 'stroke belt region' in the US	74.0 (median)	49.0	7- or 12-lead ECG	N/A	432 (1.4)	174 (0.58)	85 (48.9)	172
Schnabel et al. 2012 ¹²	5,000	Persons aged 35–74 from the city of Mainz and Mainz-Bingen region in Germany	52.2	60.4	12-lead ECG	N/A	161 (3.2)	25 (0.5)	N/A	200
Frewen et al. 2013 ¹³	4,890	Community-dwelling citizens aged ≥50 years in the Republic of Ireland	63.8	37.1	3-lead ECG	No	118 (2.4)	45 (0.92)	N/A	109

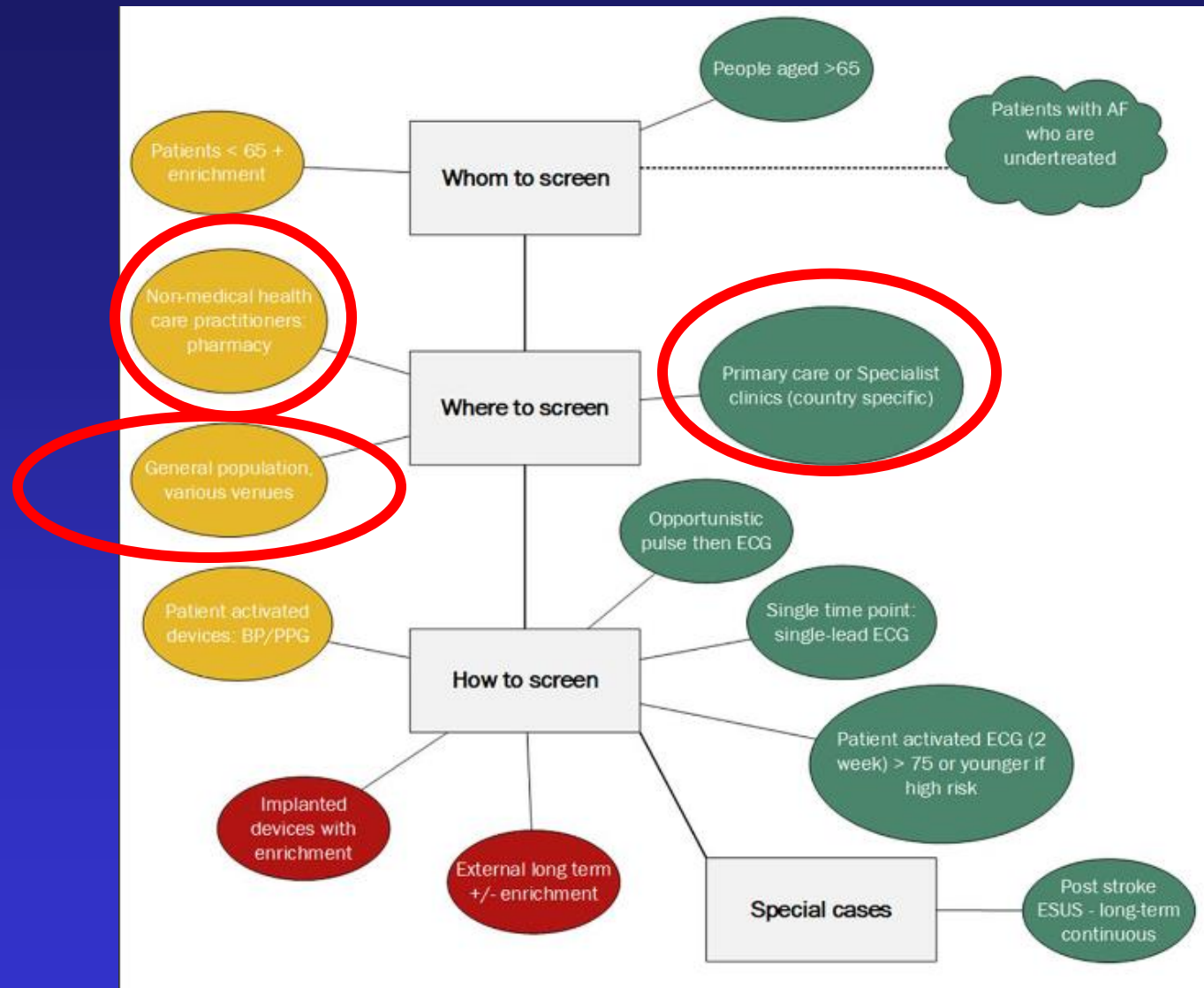
Number-Needed-To-Screen for One Newly Diagnosed Atrial Fibrillation

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Svennberg et al. 2015 ¹⁴	7,173	75–76-year-old population in Stockholm county or the Halland region in Sweden	N/A	53.8	1-lead ECG	No	884 (12.3) with history plus ECG	218 (3)	203 (93)	Single ECG: 200 Twice daily ECG for 2 weeks: 33
Chan et al. 2016 ²	13,122	Untargeted voluntary participation by Hong Kong citizens aged ≥18 years	64.7	N/A	1-lead ECG	No	239 (1.8)	101 (0.8)	N/A	129
Proietti et al. 2016 ¹⁵	65,747	Untargeted voluntary participation by Belgian citizens	58.0 (median)	N/A	1-lead ECG	Yes when 1-lead ECG unclear	911 (1.4)	603 (0.92)	N/A	109
Chan et al. 2017 ¹⁶	10,735	Untargeted voluntary participation by Hong Kong citizens aged ≥50 years	78.6	N/A	1-lead ECG	No	244 (2.3)	74 (0.69)	17 (24)	145

CA Colon Screening Program in Hong Kong

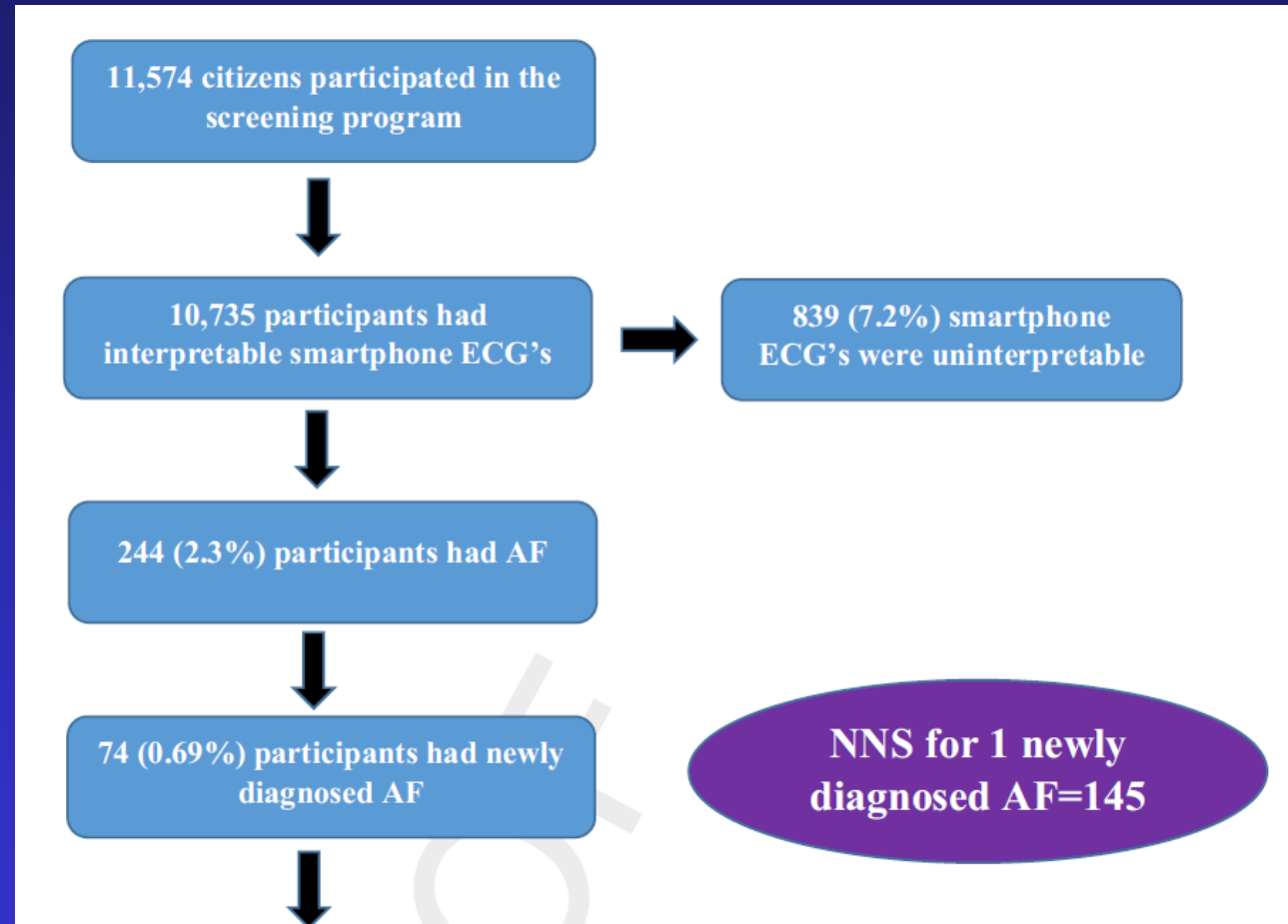
- Started in August 2018
- Phase I: age 61-75; phase II: age 56-75, phase II: age 50-75
- Till September 2019
 - 166,000 screened with FOB
 - 19500 (12.6%) FOB+ve
 - 11900 (66.7%) colonic adenoma (<5% will progress to CA colon over 7-10 years)
 - 1170 (6.6%) CA colon
- NNS for detecting one CA colon: 142
 - NNS for detecting one colonic adenoma: 14
- Recommended bi-annual screening

Settings for AF Screening

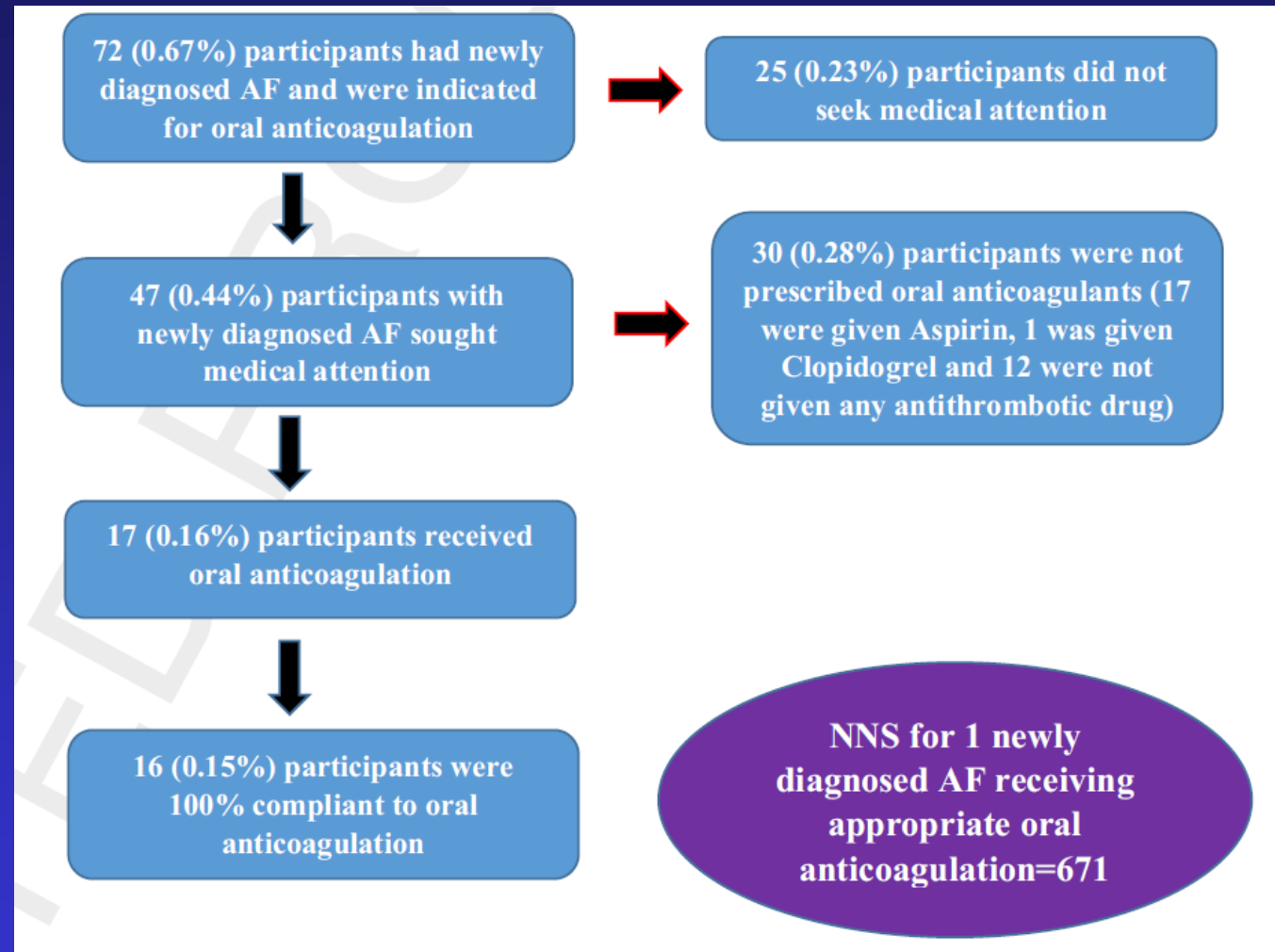


AFinder Program

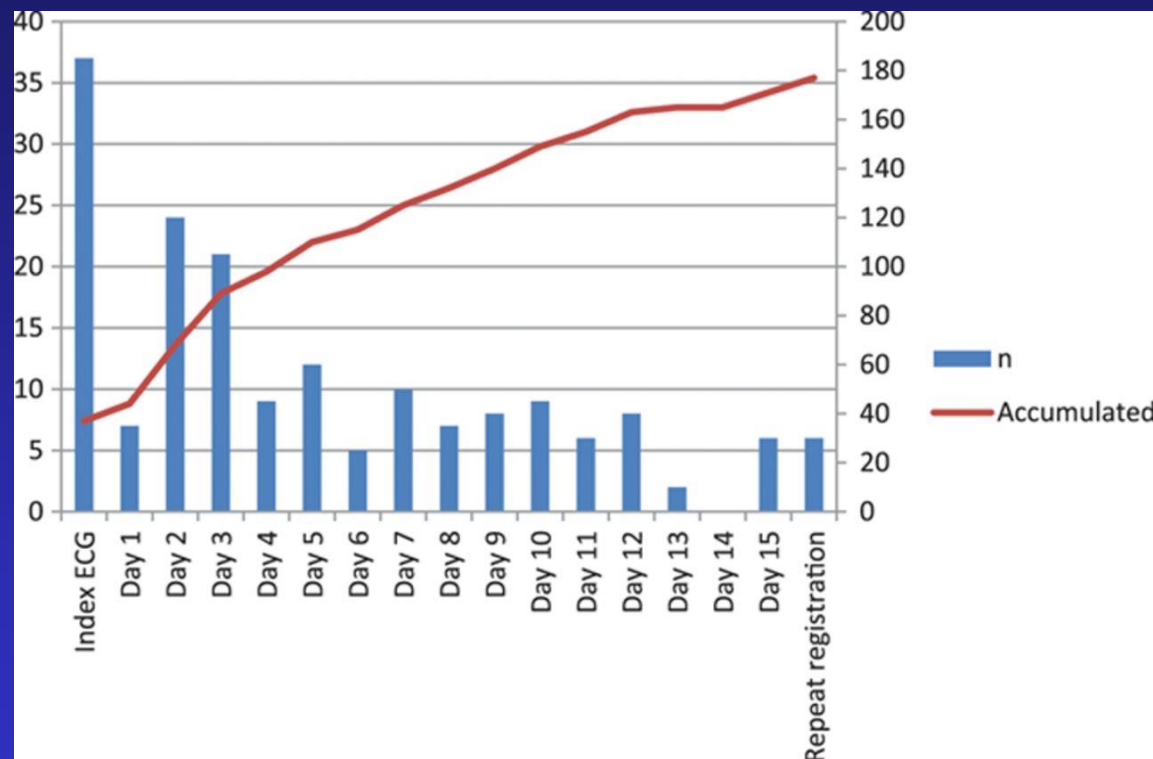
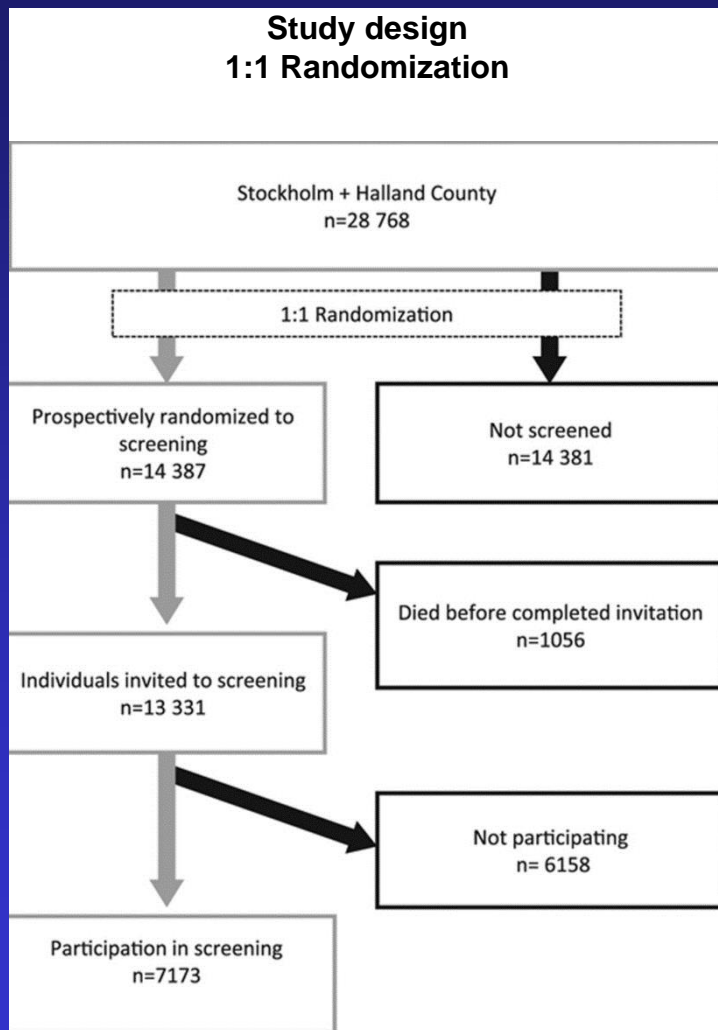
- N=10,735 (8564 [79.8%] female, mean age 78.6 ± 8.1) participants
- 244 participants (172 [70.5%] female, mean age 79.5 ± 7.9) had atrial fibrillation



AFinder Program

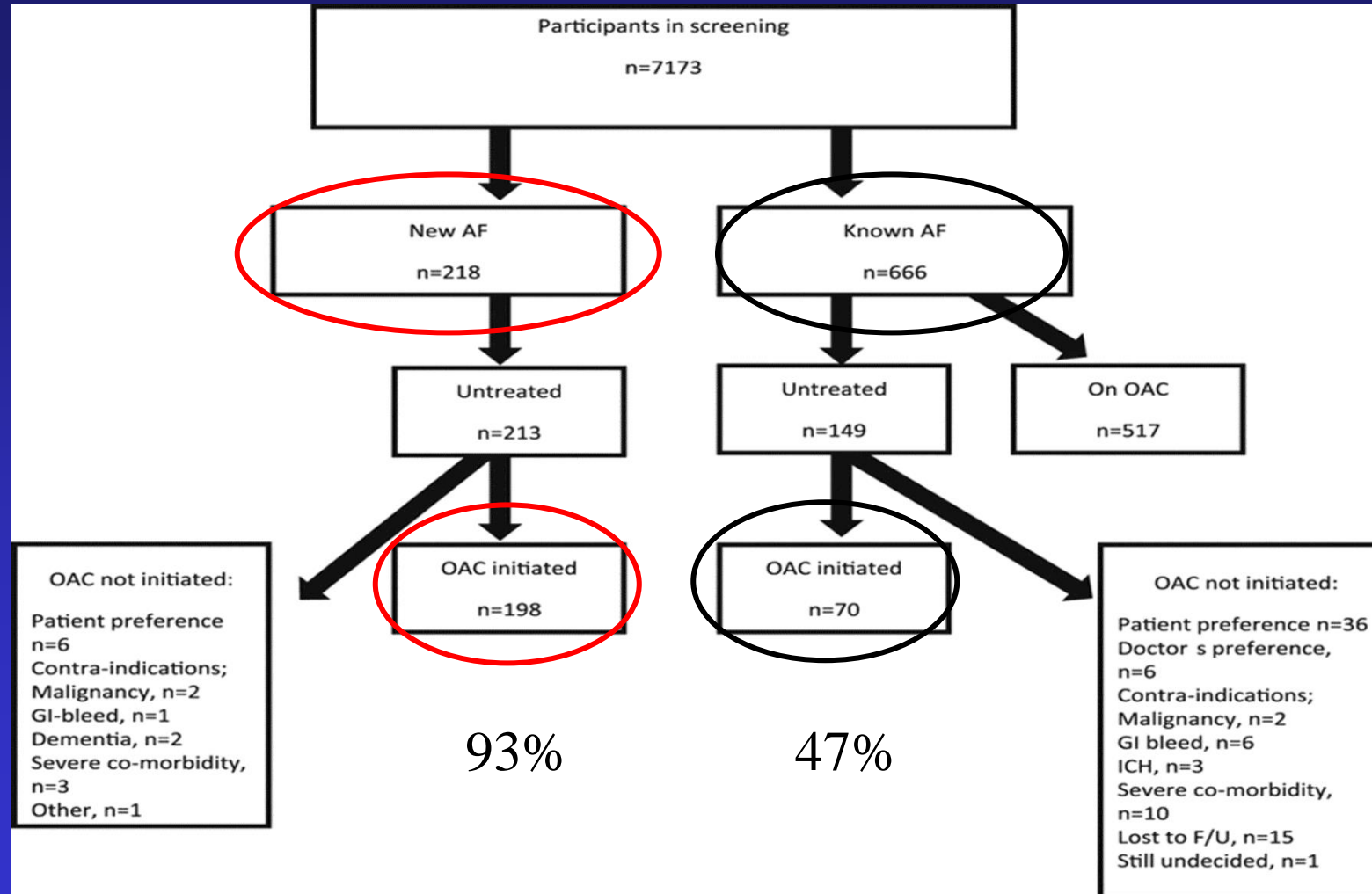


Population Atrial Fibrillation Screening in 75-76 years old in Sweden: STROKESTOP study

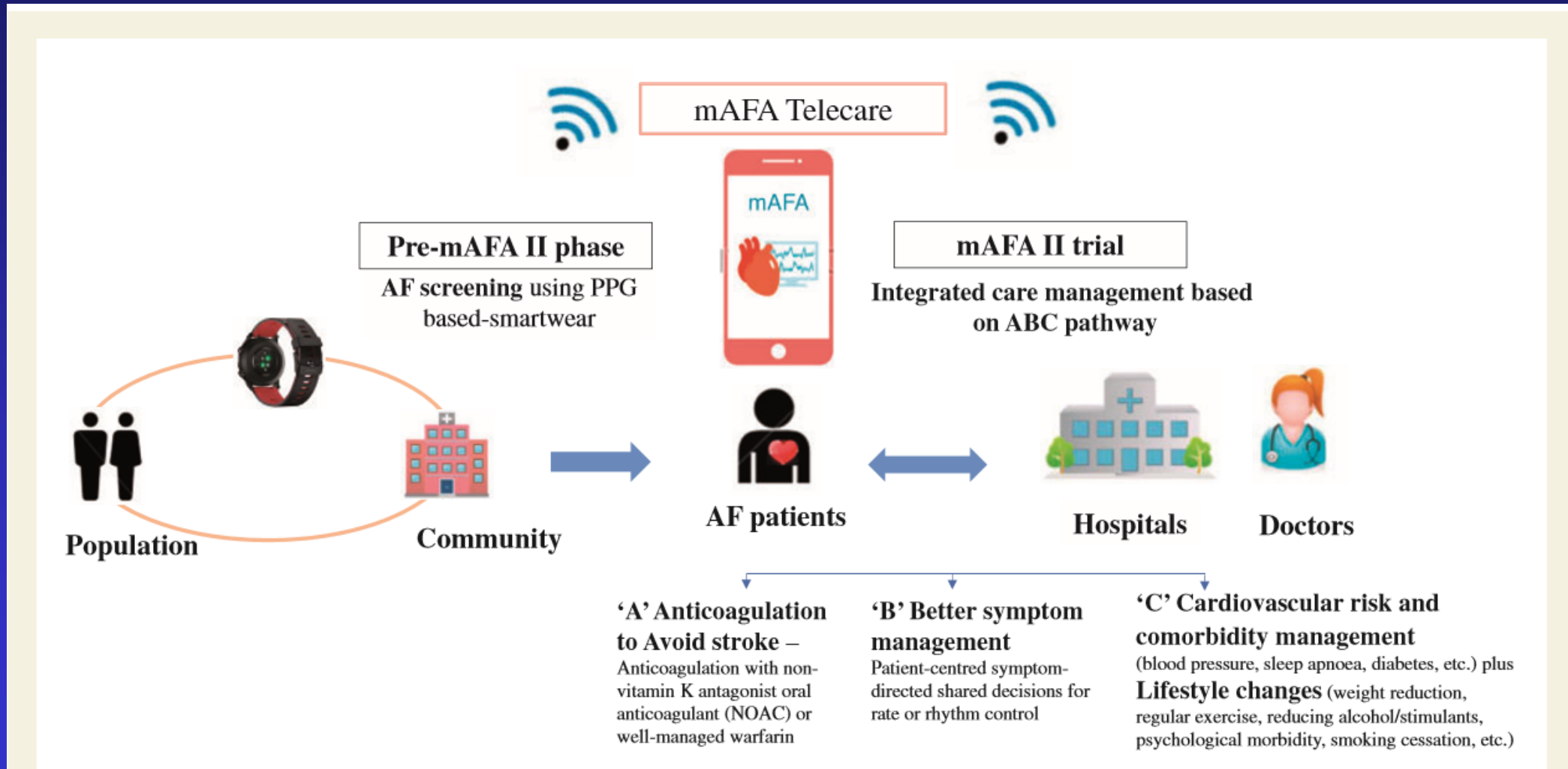


Time to first AF detection by intermittent ECG registrations using AliveCor

Community Atrial Fibrillation Screening in 75-76 years old in Sweden: STROKESTOP study



Mobile Health Technology for Integrated Care in Patients with AF

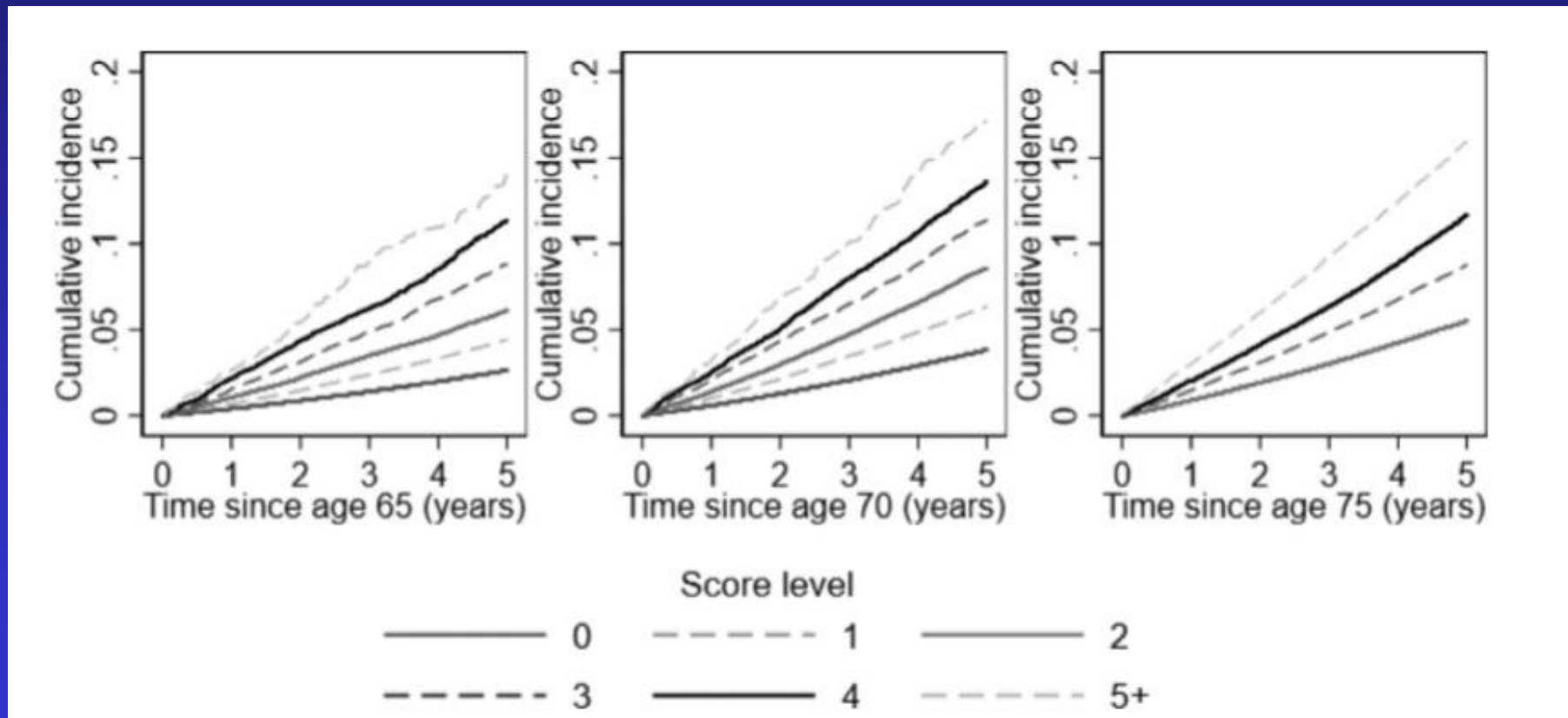


Mobile Health Technology for Integrated Care in Patients with AF

	mAFA group	Usual care group	P-value
No. of patients	1646	1678	
Mean age (years)	67	70	
Female sex n (%)	625 (38)	637 (38)	
Mean FU (months)	262	291	
Ischaemic stroke/systemic thromboembolism/death/Rehospitalization (%)	1.9	6	<0.05
Rehospitalization (%)	1.2	4.5	<0.05

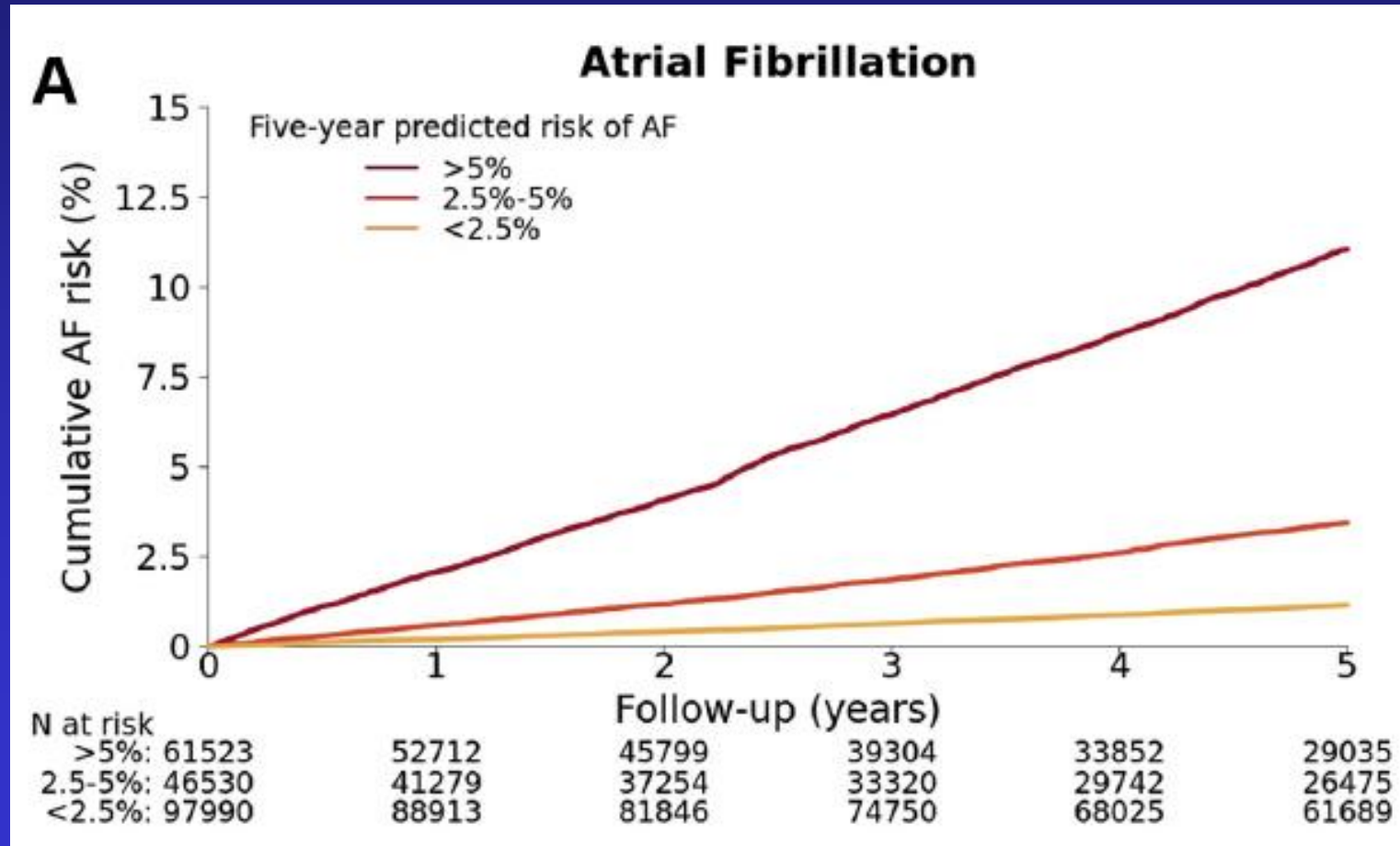
C₂HEST Risk Score

C₂: CAD/COPD; H: Hypertension; E: Elderly (Age \geq 75, doubled); S: Systolic HF (doubled); T: Thyroid disease (hyperthyroidism)

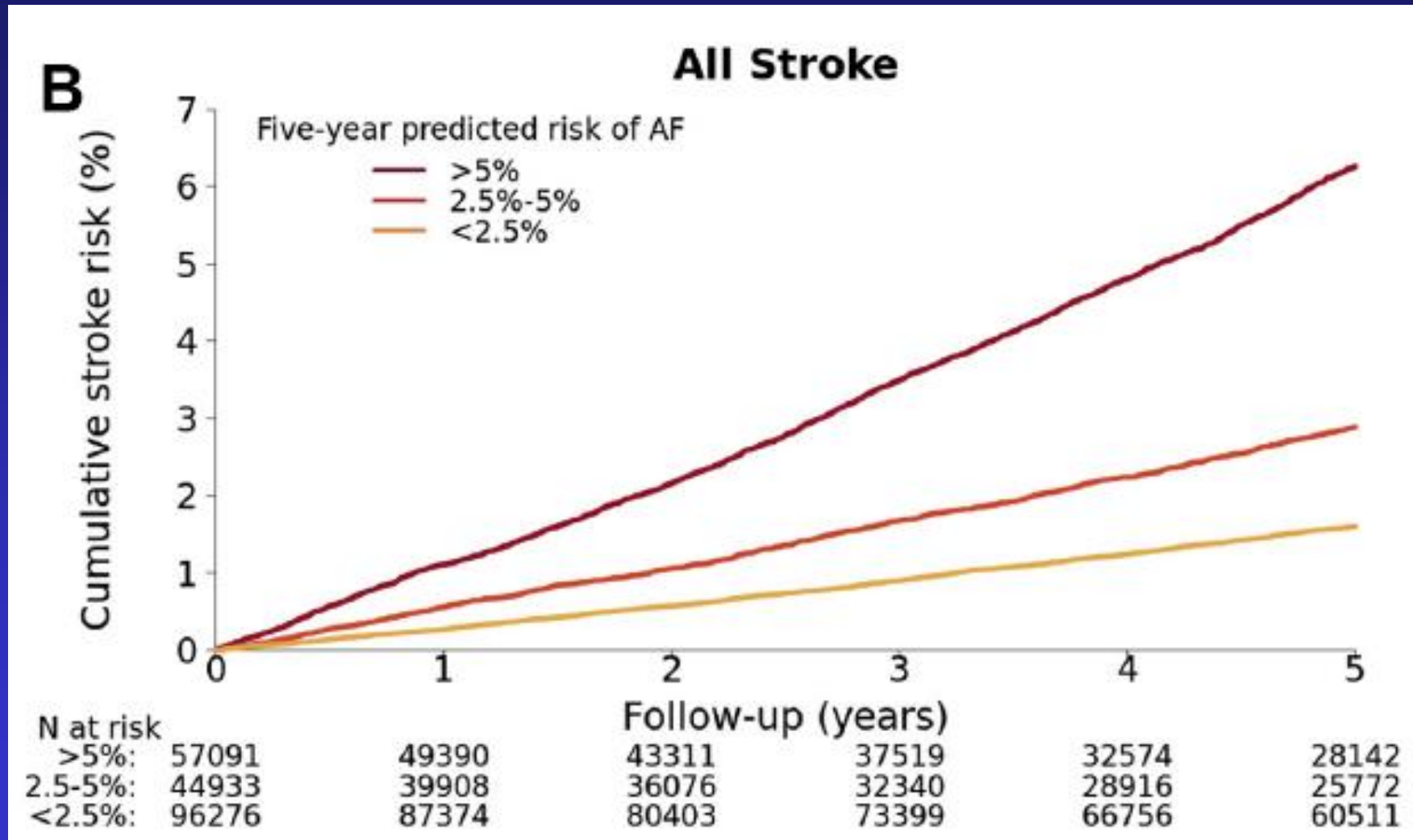


Electronic Health Record Score

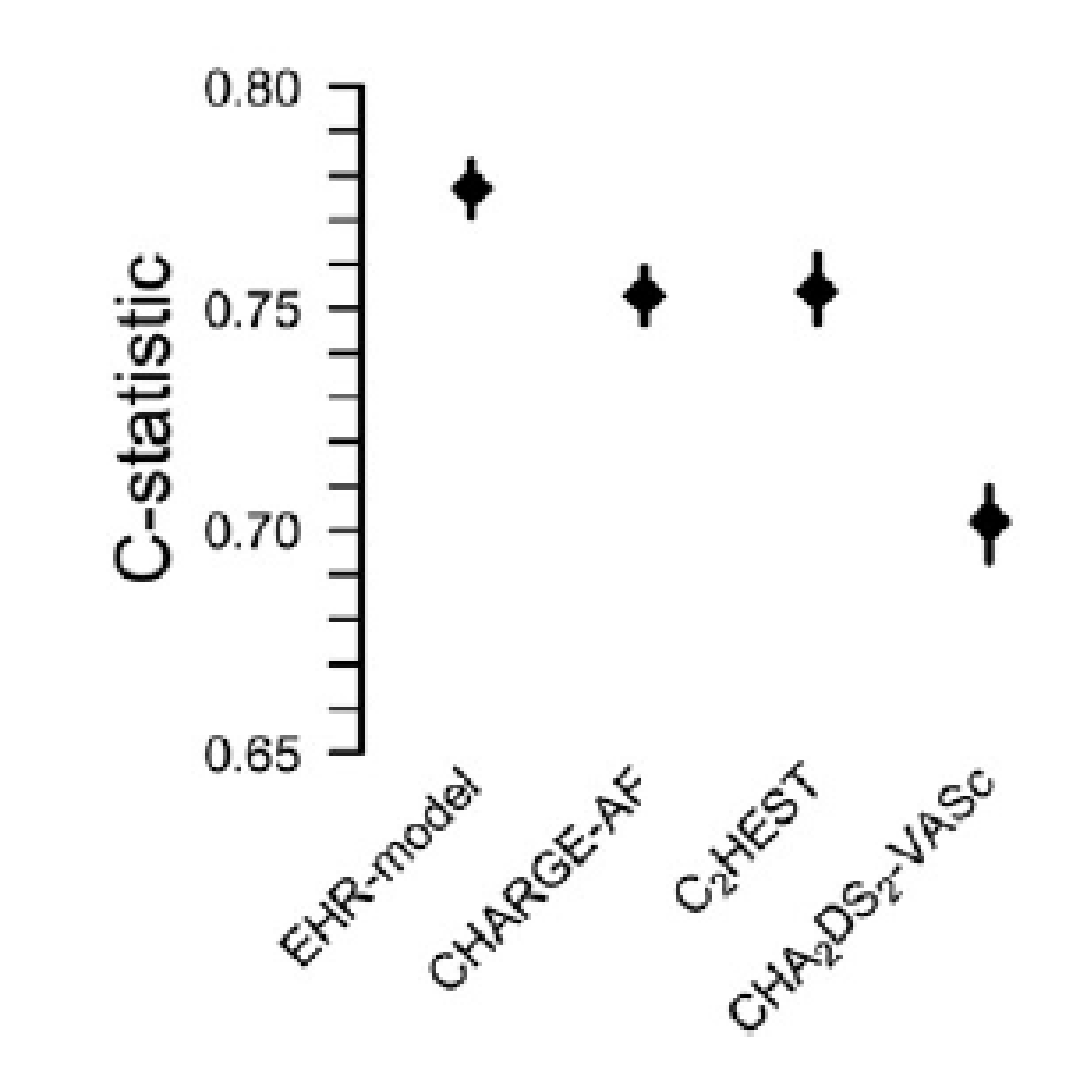
The optimal risk model included sex, age, race, smoking, height weight, DBP, HT, hyperlipidaemia, heart failure, CHD, VHD, prior stroke, PAD, chronic kidney disease, hypothyroidism and quadratic terms for height, weight and age



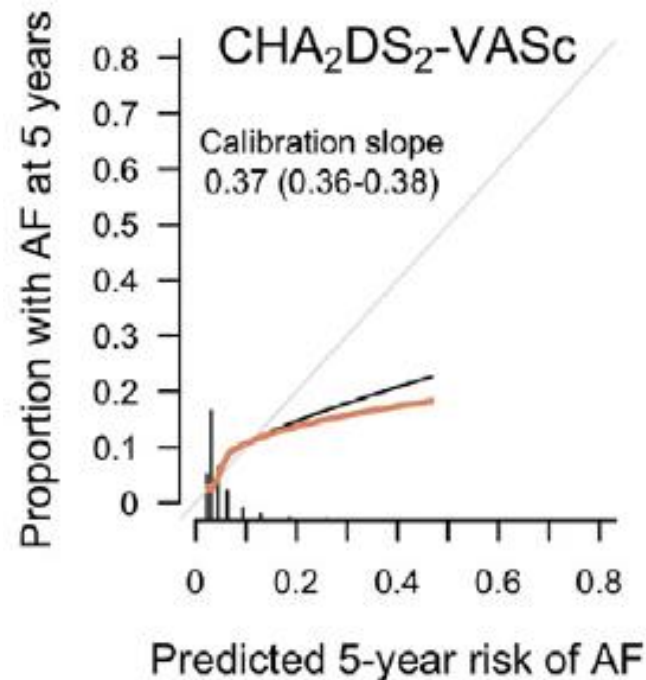
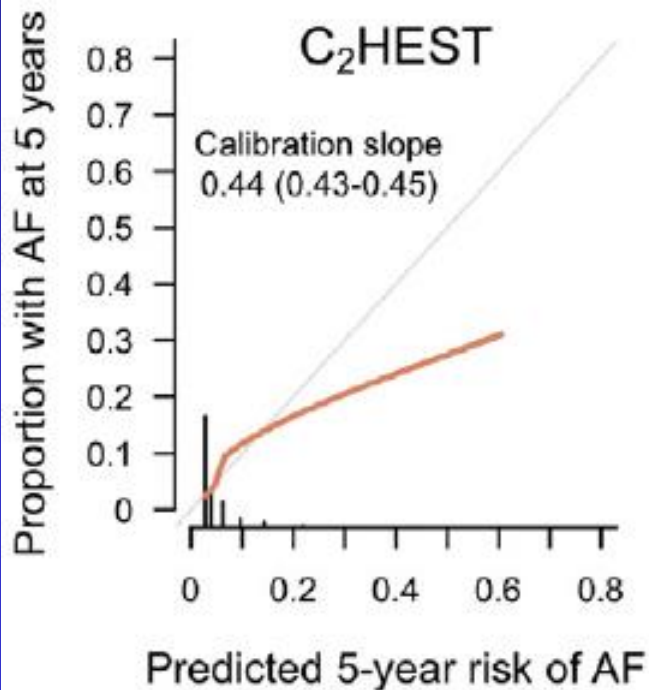
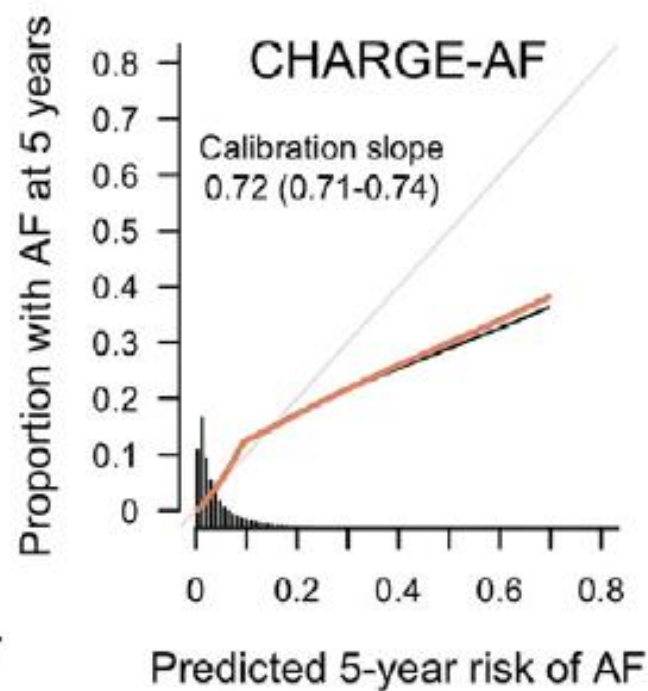
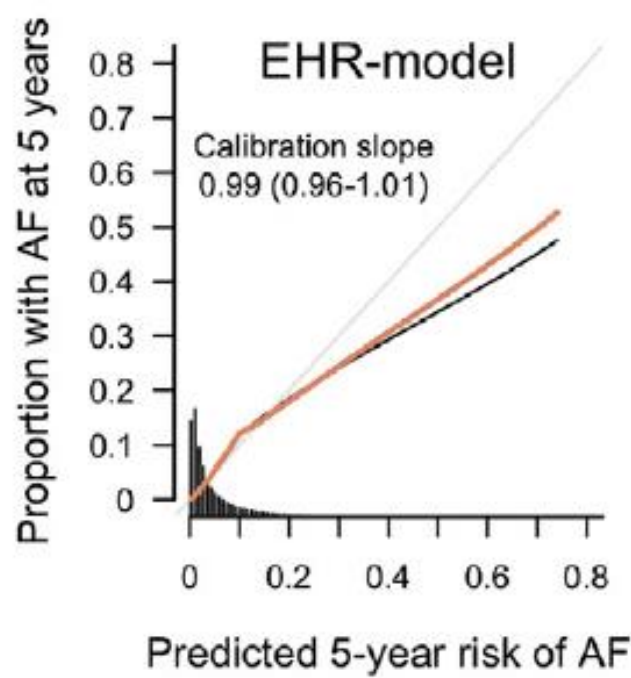
Electronic Health Record Score



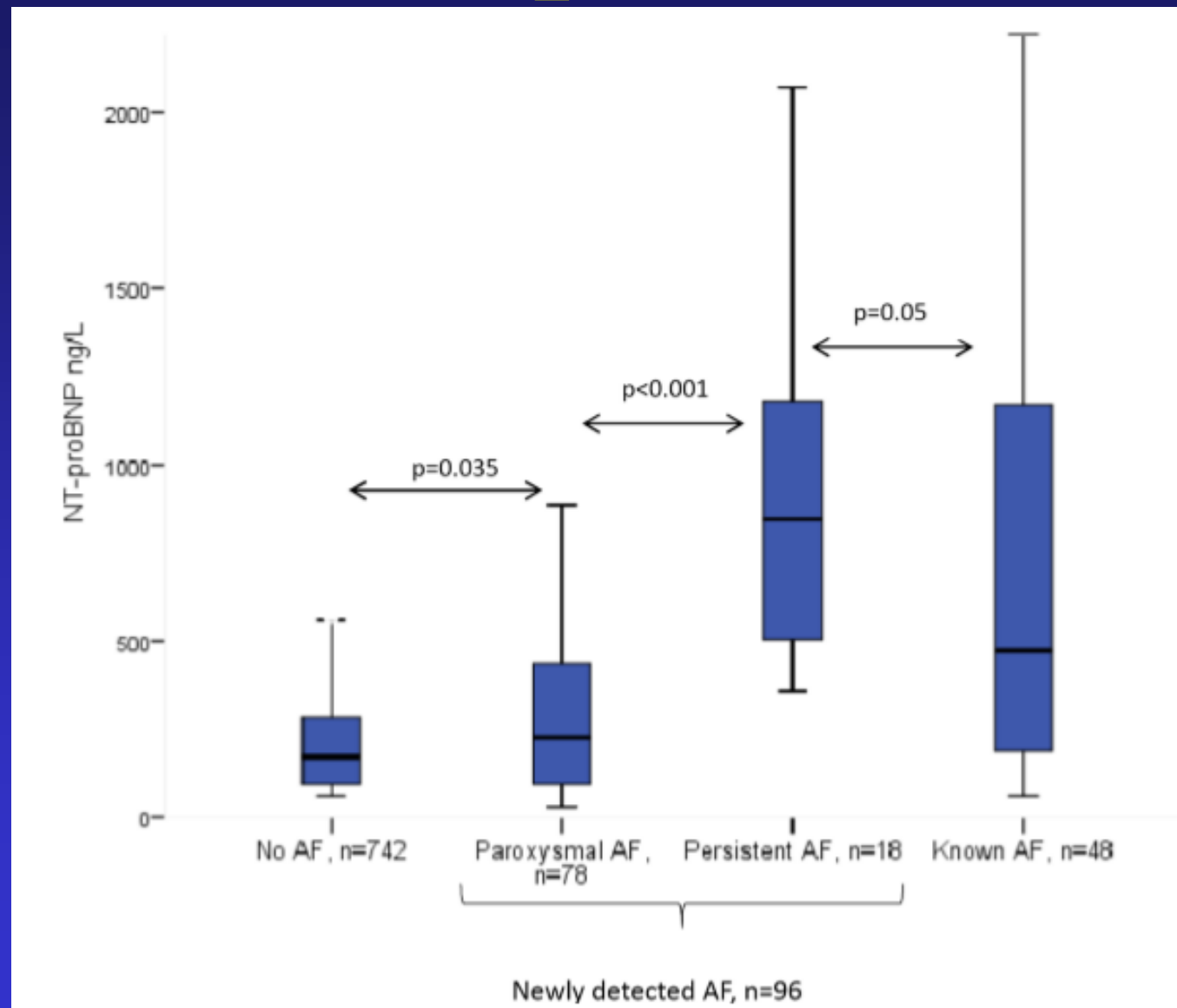
Electronic Health Record Score



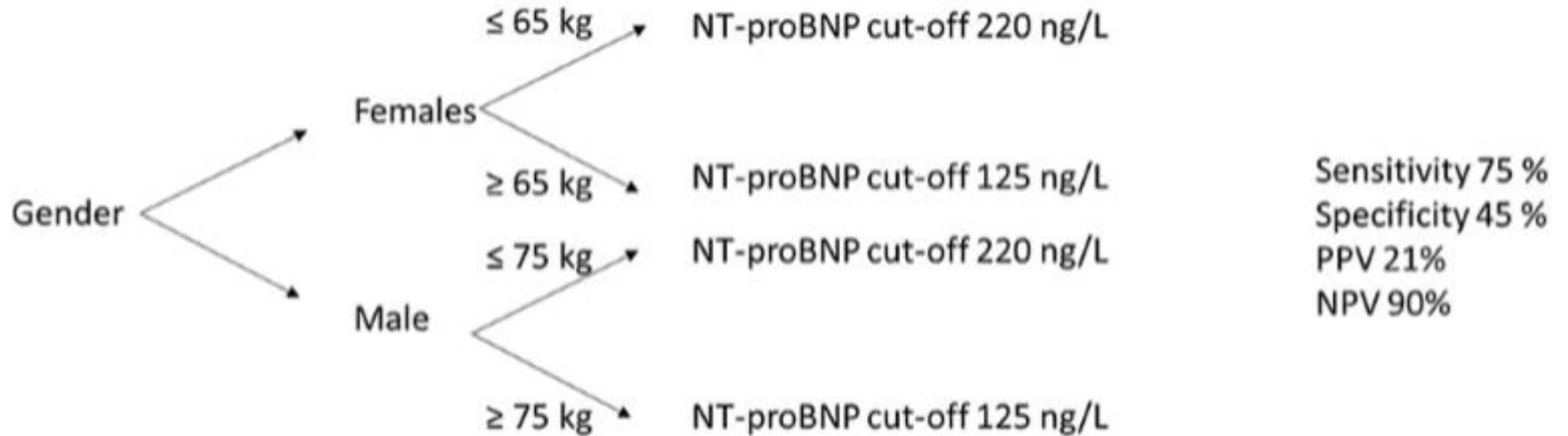
Electronic Health Record Score



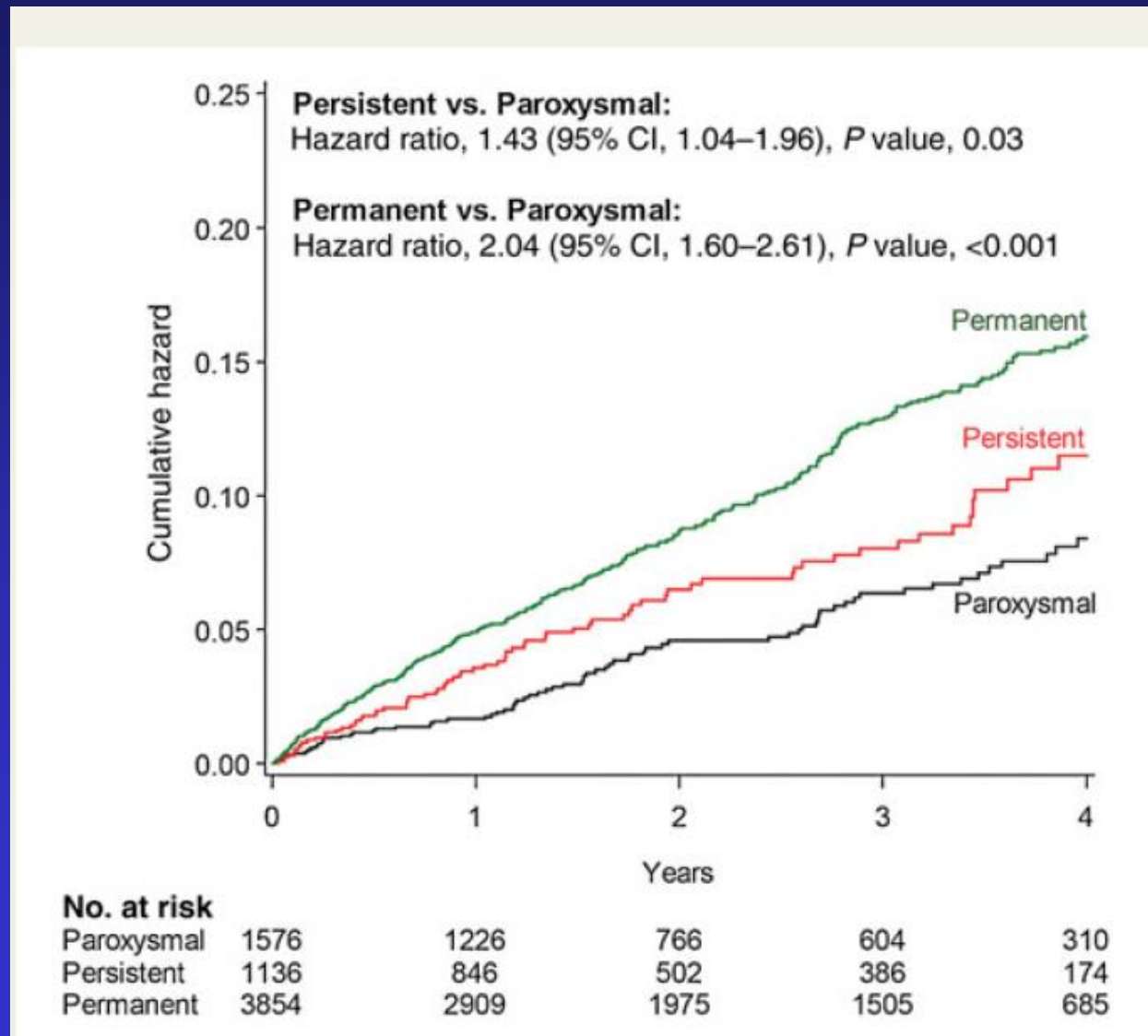
NT-proBNP



NT-proBNP and Weight



Embolic Events According to the Pattern of AF



N=6563 aspirin-treated patients with AF from ACTIVE-A and AVERROES databases

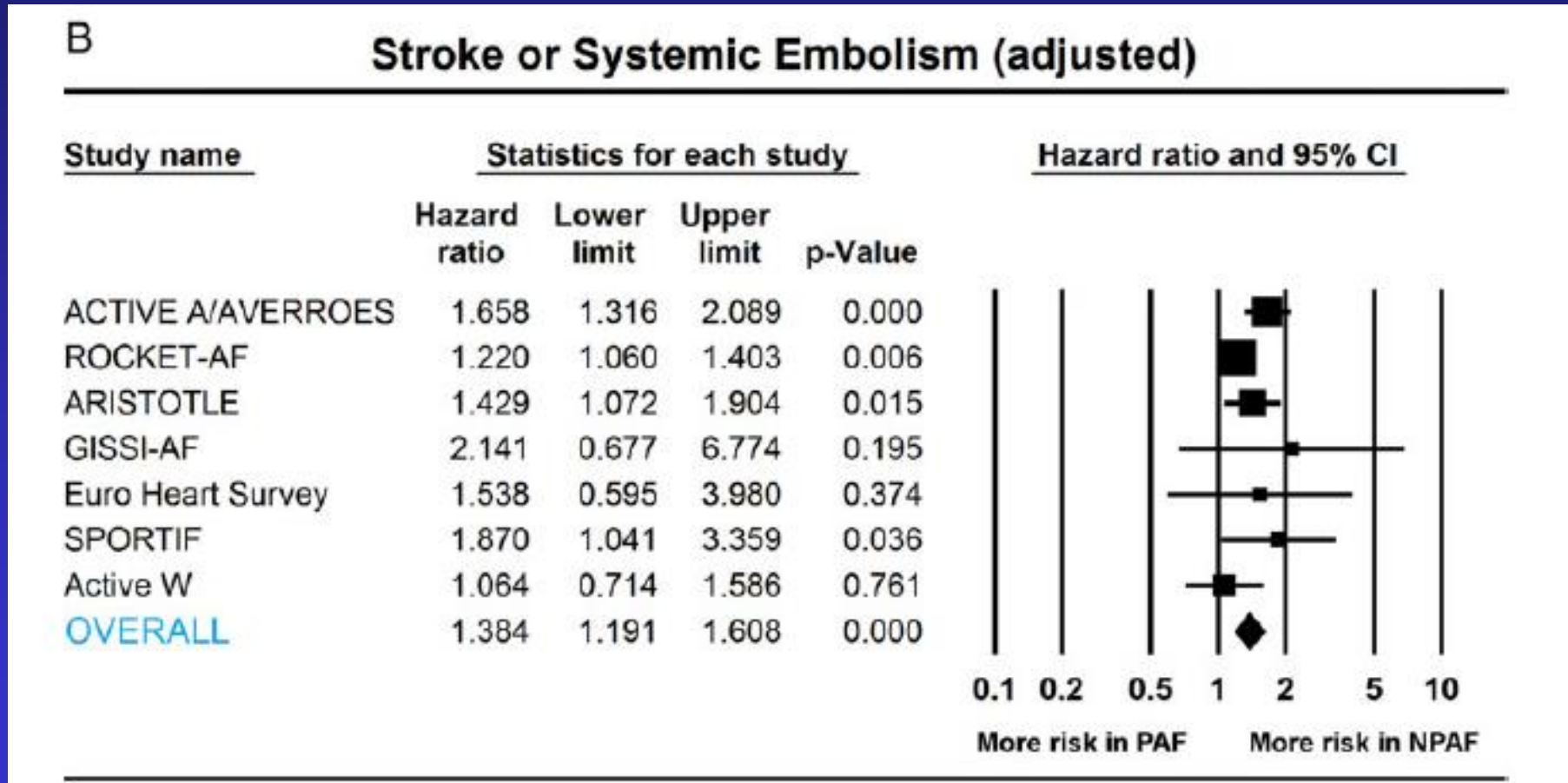
Rates of stroke and systemic embolism analysed

Annualized ischaemic stroke rates were 2.1, 3.0 and 4.2% for paroxysmal, persistent and permanent AF respectively

Age ≥ 75 years, sex, history of stroke/TIA and AF pattern are independent predictors, with AF pattern ranked the 2nd

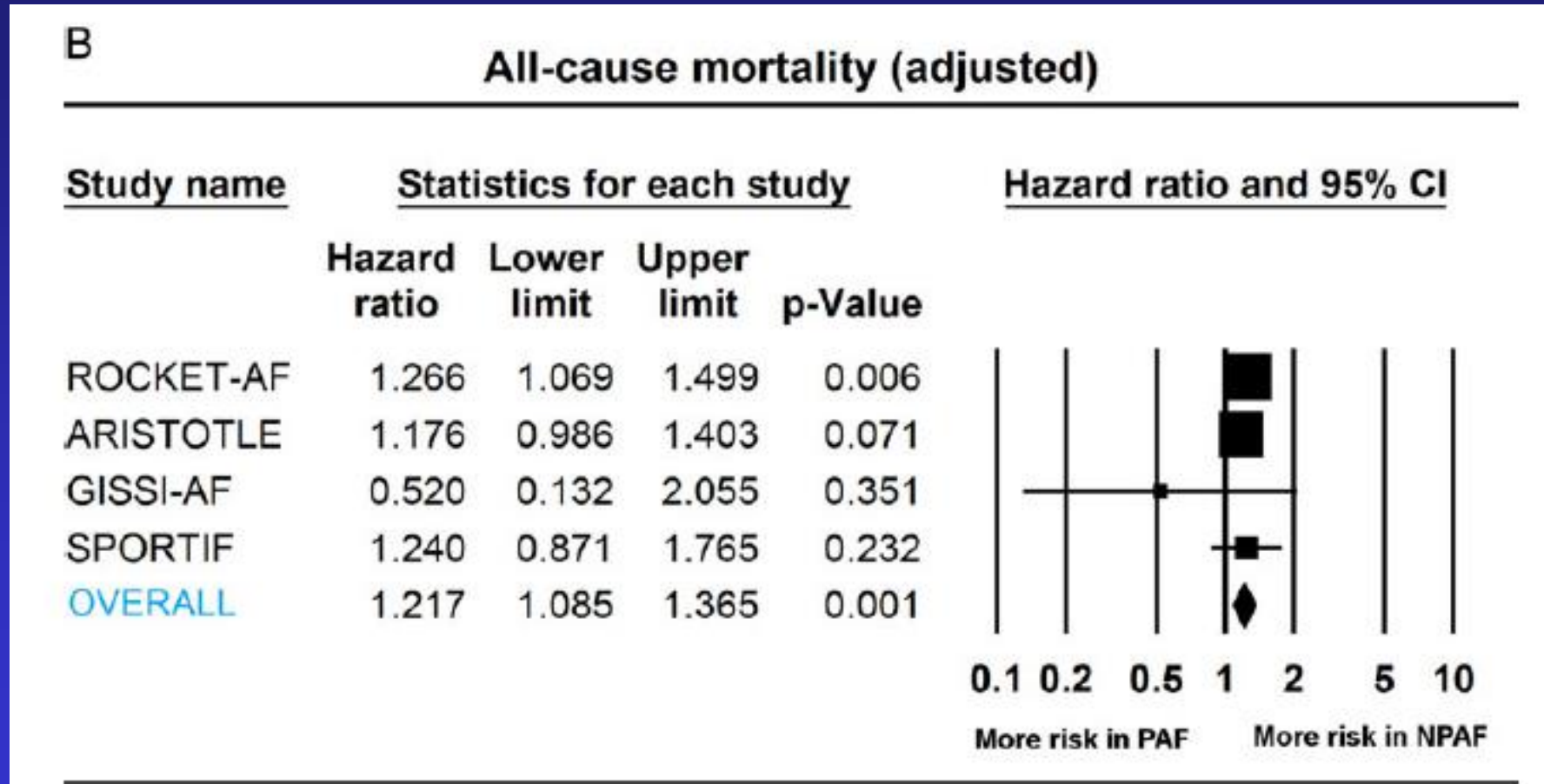
Risk of Thromboembolism and Mortality According to the Pattern of AF

AF clinical outcome data were extracted from 12 studies containing 99,996 patients

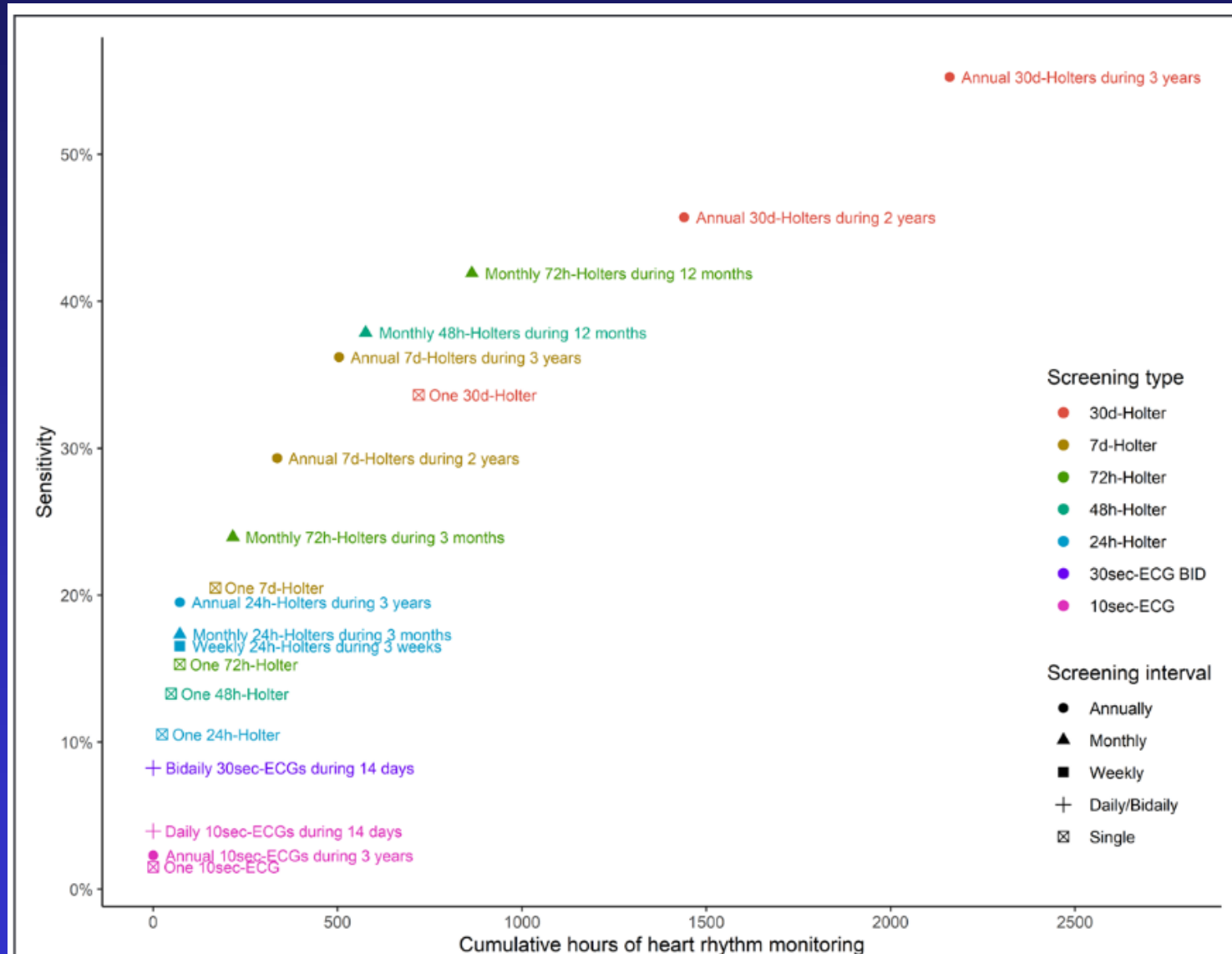


Risk of Thromboembolism and Mortality According to the Pattern of AF

AF clinical outcome data were extracted from 12 studies containing 99,996 patients



How Frequent and How Long Shall we Screen?



590 individuals with stroke risk factors but without AF recruited from general population

Screening with an ILR
New onset AF lasting ≥ 6 minutes adjudicated

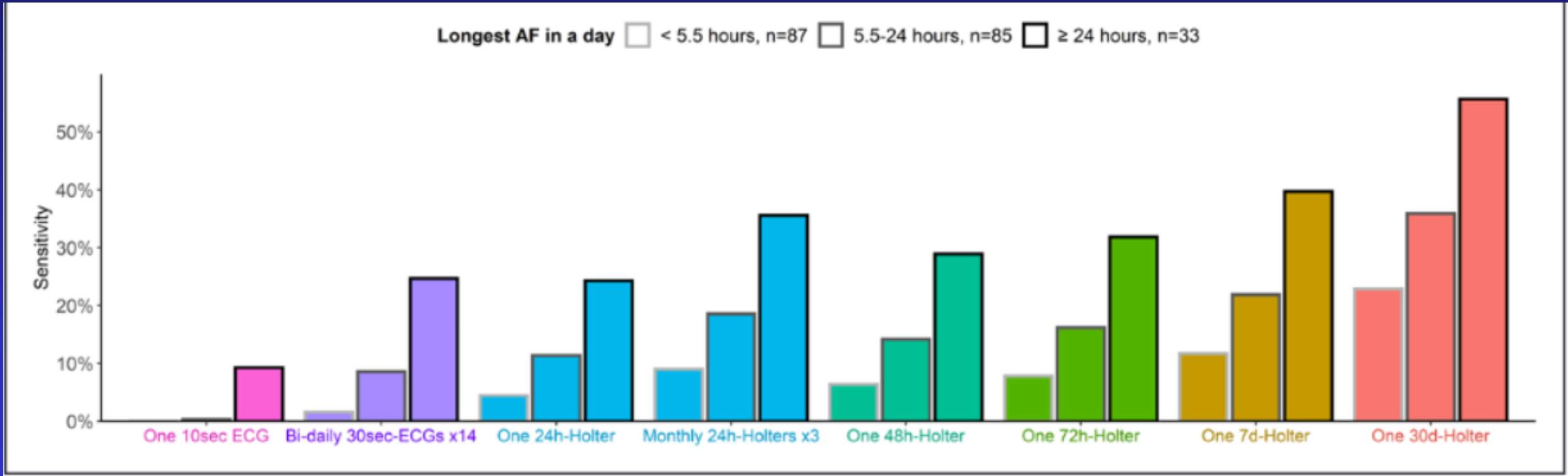
Continuous monitoring for >3 years

Random sampling applied to assess sensitivity and NPV of screening with various simulated screening strategies

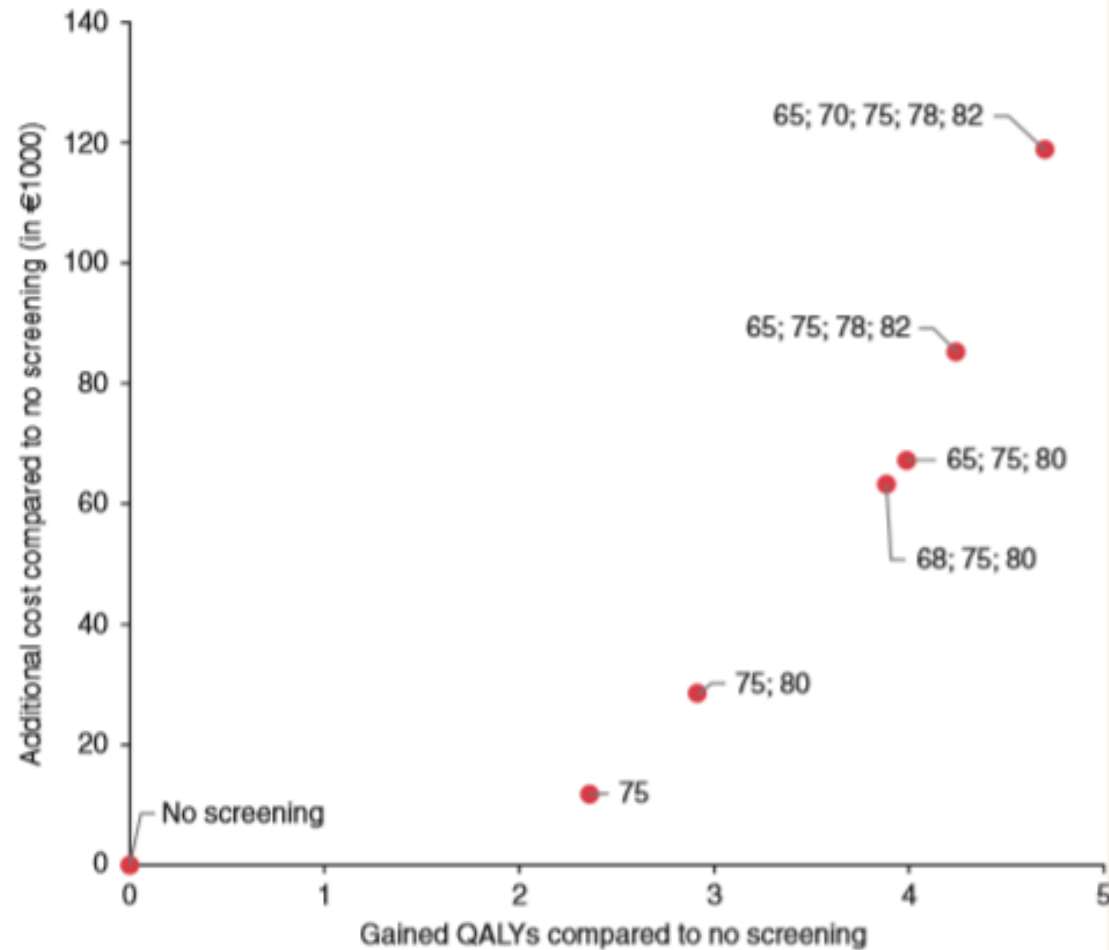


Zoga S et al. Comprehensive evaluation of rhythm monitoring strategies in screening for atrial fibrillation: insights from patients at risk monitored long term with an implantable loop recorder. *Circulation* 2020;141:1510-22.

How Frequent and How Long Shall we Screen?



Cost Effectiveness of AF Screening



Based on a decision-analytic simulation model

Mathematical Markov model was built to simulate how different designs of screening affected a population of 55-year-olds

Data used in the model was mainly from STROKESTOP study and supplemented with inputs from other studies

Cost Effectiveness of AF Screening

Age when screening is conducted (years)	Cost per gained QALY compared to no screening (€)	The design is the best option when a QALY is worth between (€)	Prevented stroke per 1000 simulated 55-year-olds (Cost per stroke €)
All			
No screening	–	<4 800	
75	4 800	4 800*–31 000	3.1 (7 300)
75, 80	9 500	31 000–37 000	4.1 (13 200)
68, 75, 80	15 800	37 000–40 000	4.7 (21 000)
65, 75, 80	16 400	40 000–74 000	4.7 (20 600)
65, 75, 78, 82	19 500	74 000–77 000	5.1 (23 900)
65, 70, 75, 78, 82	24 500	77 000–10 0000	5.3 (31 600)

Conclusions

- Patients with asymptomatic AF or screen-detected AF likely have a poorer prognosis than patients without
- Guidelines and expert opinion on AF screening vary and this remains a controversial topic
- The longer the period to screen AF, the higher the yield in patients with cryptogenic stroke; yet empirical oral anticoagulation treatment for embolic stroke of undetermined source has not been shown to be beneficial

Conclusions

- Subclinical atrial tachyarrhythmias detected by CIED predicts both occurrence of clinical AF and thromboembolic events; significant subclinical atrial tachyarrhythmias appear to be of a duration >24 hours or daily burden ≥ 5.5 hours; whether oral anticoagulation treatment can improve the prognosis remains to be shown

Conclusions

- Opportunistic AF screening, although shown to be more cost effective than systematic screening; it is seldomly practised in the real world
- With technological advancement, the cost-effectiveness equation becomes more favourable for systematic screening for AF
- A structured and comprehensive downstream management is crucial for any AF screening program to be effective
- AF burden is probably related to the level of stroke risk

Conclusions

- Increasing frequency, duration and dispersion of AF screening identifies patients with low AF burden and thus probably with low level of stroke risk
- Different risk prediction models have been developed to increase the detection rate for AF screening and at the same time, its cost effectiveness
- Depending on the cost effectiveness threshold acceptable by the country, a suitable design of an AF screening program can be implemented to make it cost effective