When and How to Detect AF?

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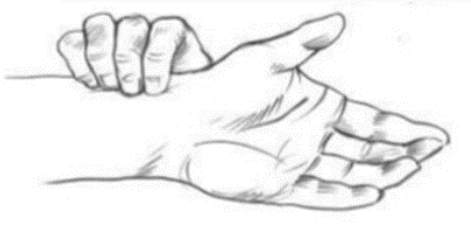
Declaration of Interests: Dr. J. Healey

Research Grants and Speaking Fees from

- Boston Scientific
- Medtronic
- BMS/Pfizer

AF Screening in 2025

Field driven by technology to detect AF, and safety/efficacy of oral anticoagulation…

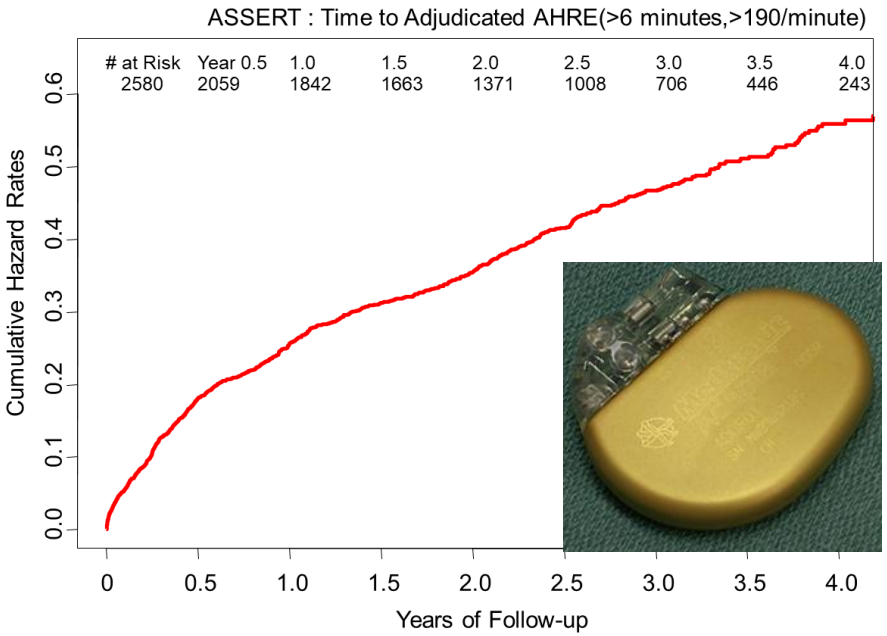


1. **Opportunistic Case-Finding (vs. Screening)**
    a. Pacemaker and ICD interrogation
    b. Cardiac monitors (ED, ICU, etc.)
    c. Medical visits for other reasons

2. **Who to screen?**
    Elderly, cardiovascular disease, other risks?

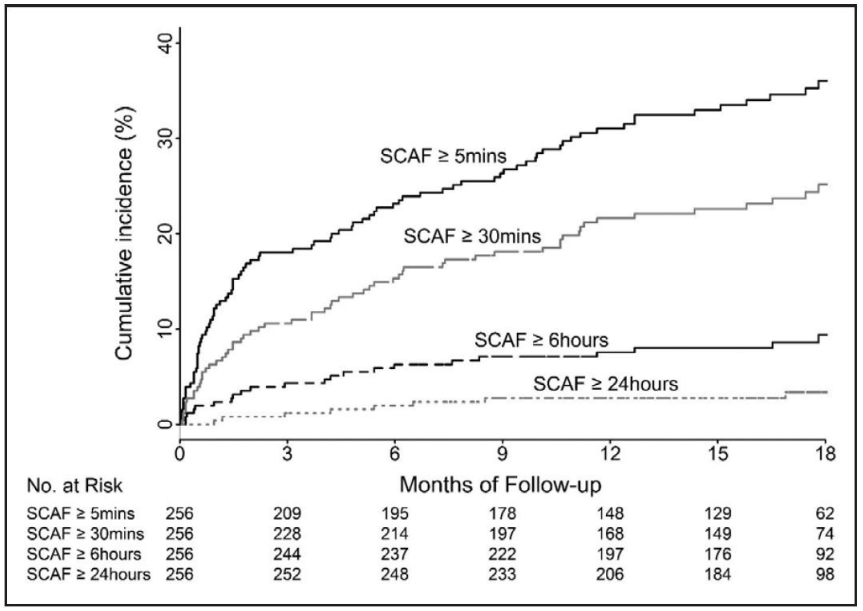
3. **How and when to screen?**
    a. Single time-point vs. continuous monitoring?
    b. How long? How often?
4. **Is screening worthwhile?**
    a. Can we detect enough AF? Stroke risk high enough?
    b. Does treatment prevent stroke? Will patients accept?
    c. Is AF screening cost-effective?

ASSERT-1
Age > 65 with CV risk factors and pacemaker



J. Healey, NEJM 2012

ASSERT-2
Age > 65 with CV risk factors



J. Healey, Circulation 2017

ASSERT: Clinical Outcomes

Healey JS, NEJM 2012

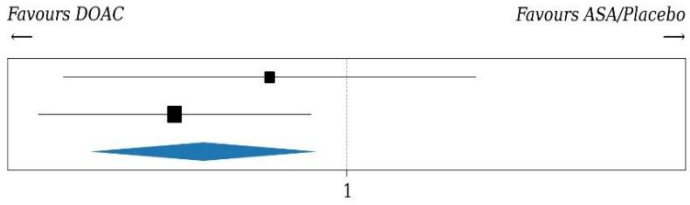
Both absolute and relative risks of stroke with SCAF are lower than with clinical AF

Event	Device-Detected Atrial Tachyarrhythmia				Device-Detected Atrial Tachyarrhythmia Present vs. absent		
	Absent N=2319		Present N= 261				
	events	%/year	events	%/ year	RR	95% CI	p
Ischemic Stroke or Systemic Embolism	40	0.69	11	1.69	2.49	1.28 – 4.85	0.007
Vascular Death	153	2.62	19	2.92	1.11	0.69 – 1.79	0.67
Stroke / MI / Vascular Death	206	3.53	29	4.45	1.25	0.85 – 1.84	0.27
Clinical Atrial Fibrillation or Flutter	71	1.22	41	6.29	5.56	3.78 – 8.17	<0.001

META-ANALYSIS OF ARTESIA AND NOAH EFFICACY OUTCOMES (ITT) MCINTYRE WF. CIRCULATION 2023

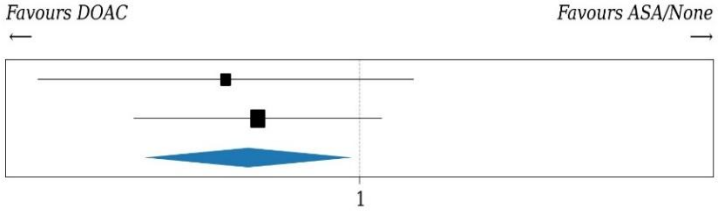
Ischemic Stroke

Study	DOAC	(%)	ASA/Placebo	(%)	Weight	RR [95% CI]
NOAH-AFNET 6	22/1,270	(1.7%)	27/1,266	(2.1%)	30.4%	0.81 [0.47, 1.42]
ARTESiA	45/2,015	(2.2%)	71/1,997	(3.6%)	69.6%	0.63 [0.43, 0.91]
Pooled Estimate	67/3,285	(2.0%)	98/3,263	(3.0%)	I^2: 0%	0.68 [0.5, 0.92]
Mantel-Haenszel, DerSimonian-Laird Random Effects	*p=0.01, z=2.47 τ²=0.00*					*RR: Risk Ratio CI: Confidence Interval*



Composite of All-cause Stroke, Peripheral Arterial Embolism, Myocardial Infarction, Pulmonary Embolism or Cardiovascular Death

Study	DOAC	(%)	ASA/None	(%)	Weight	RR [95% CI]
NOAH-AFNET 6	83/1,270	(6.5%)	101/1,266	(8.0%)	30.4%	0.82 [0.62, 1.08]
ARTESiA	189/2,015	(9.4%)	218/1,997	(10.9%)	69.6%	0.86 [0.71, 1.03]
Pooled Estimate	272/3,285	(8.3%)	319/3,263	(9.8%)	I^2: 0%	0.85 [0.73, 0.99]
Mantel-Haenszel, DerSimonian-Laird Random Effects	*p=0.03, z=2.11 τ²=0.00*					*RR: Risk Ratio CI: Confidence Interval*



2020 ESC Guidelines for DDAF

Six-month incidence of transition to higher AHRE burden[a]
(*n* = 6580, pooled from three prospective studies)[469]

	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_2VASc category
(*n* = 21 768 device patients not taking OAC)[1466]

	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%

Efficacy vs. Safety at 3.5 years for Apixaban vs. ASA
Lopes RD. JACC 2024

	Proportion of ARTESiA Patients	Strokes Prevented per 100 patients	Major Bleeds per 100 patients
CHA_2DS_2-VASc < 4	39%	0.04 (NNT = 2500)	1.28 (NNH = 78)
CHA_2DS_2-VASc = 4	34%	2.25 (NNT = 44)	0.05 (NNH = 2000)
CHA_2DS_2-VASc > 4	27%	3.95 (NNT = 25)	1.70 (NNH = 59)

All NNHs (number needed to harm) for major bleeding events are not statistically significant.
NNT (number needed to treat) for stroke in patients with CH_2ADS_2-VASc <4 is not statistically significant

Population Health Research Institute
HEALTH THROUGH KNOWLEDGE

Stroke/SE Risk by AF Type: AVERROES/ACTIVE

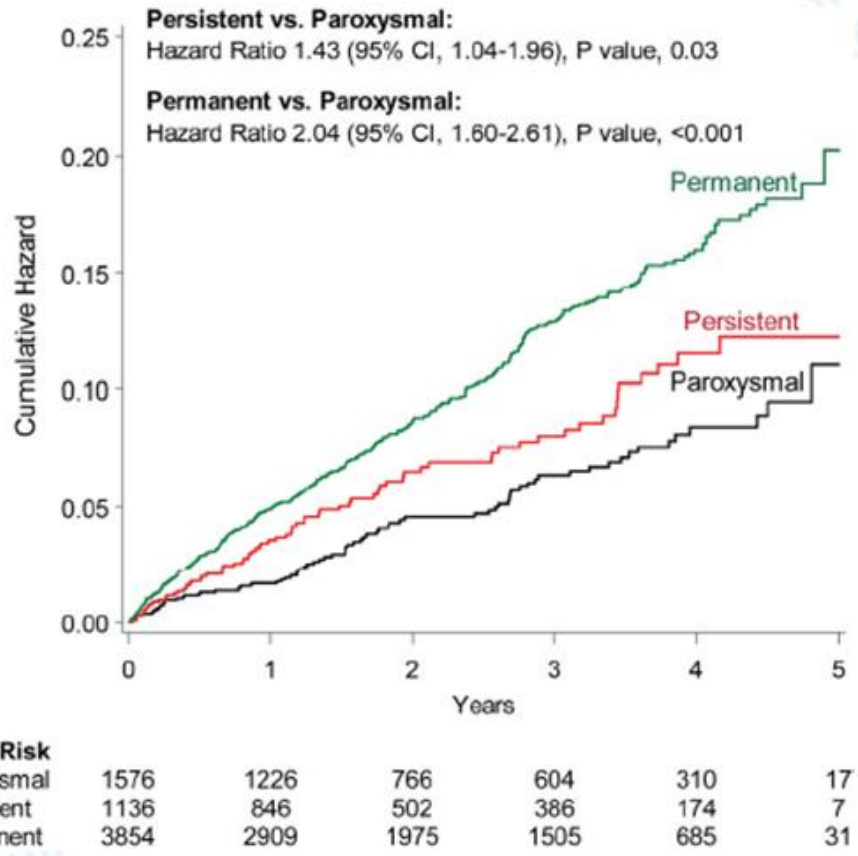


Figure 1. Kaplan-Meier cumulative hazard rates of embolic events according to pattern of AF occurence.

4.2% per year

3.0% per year

2.1% per year

- **Venassche T, Eur Heart J 2014**
- **N=6563**
- **ASA-Treated**

Circulation. 2017 May 9;135(19):1851-1867

Randomized Trials of AF Screening

	Country	Status	N	Screening method
AF-CATCH	China	Follow-up	7641	ALIVECOR; ECG 1x/yr vs 4x/yr vs 1x/wk in 1st month
D2AF study	Netherlands	Complete	19200	MyDiagnostik, Watch BP Single time-point
DANCAVAS	Denmark	Complete	35K	Single-time, 3-lead ECG
Danish Loop Study	Denmark	Complete	6K	ICM
MonDAFIS	Germany	Complete	3,470	Post-stroke, hospital ECG
MSTOPS	USA	Complete	6000	Ziopatch
REHEARSE-AF	UK/Wales	Complete	1K	Alivecor
SAFER	UK	Ongoing	120K	Zenicor
SCREEN-AF	Canada	Complete	822	Ziopatch
STROKESTOP	Sweden	Complete	7,173	Zenicor, BID for 14 days
STROKESTOP II	Sweden	Complete	8K	Zenicor, BID for 14 days
VITAL-AF	USA	Complete	30, 715	Single time-point
GUARD-AF	USA	Complete	5,684	ZioXT

2021 US Guidelines

Clinical Review & Education

JAMA | US Preventive Services Task Force | RECOMMENDATION STATEMENT

Screening for Atrial Fibrillation
US Preventive Services Task Force Recommendation Statement

US Preventive Services Task Force

POPULATION Adults 50 years or older without a diagnosis or symptoms of AF and without a history of transient ischemic attack or stroke.

EVIDENCE ASSESSMENT The USPSTF concludes that evidence is lacking, and the balance of benefits and harms of screening for AF in asymptomatic adults cannot be determined.

RECOMMENDATION The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for AF. (I statement)

JAMA. 2022;327(4):360-367. doi:10.1001/jama.2021.23732

AF-SCREEN/AFFECT-EU Meta-Analysis

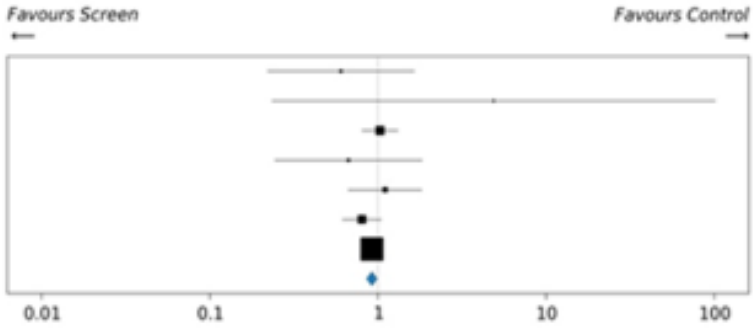
AF-SCREEN SRMA

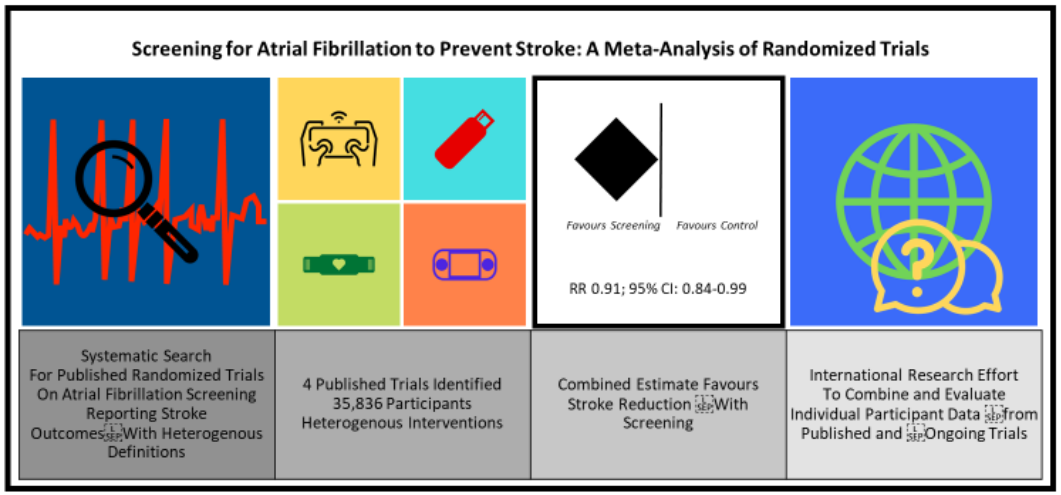
Study	Screen	(%)	Control	(%)	Weight	RR [95% CI]
REHEARSE-AF 2017	6/500	(1%)	10/501	(2%)	0.6%	0.6 [0.22, 1.64]
SCREEN AF 2021	2/434	(0%)	0/422	(0%)	0.1%	4.86 [0.23, 100.98]
MonDAFIS 2021	121/1714	(7%)	118/1717	(7%)	9.9%	1.03 [0.8, 1.31]
PerDIEM 2021	6/150	(4%)	9/150	(6%)	0.6%	0.67 [0.24, 1.83]
AF-CATCH 2021	30/3244	(1%)	30/3562	(1%)	2.3%	1.1 [0.66, 1.82]
LOOP 2021	67/1501	(4%)	251/4503	(6%)	8.6%	0.8 [0.62, 1.04]
STROKESTOP II 2021	903/13979	(6%)	985/13996	(7%)	78.0%	0.92 [0.84, 1.0]
Pooled Estimate	1135/21522	(5%)	1403/24851	(6%)	I^2: 0%	0.92 [0.85, 0.99]

Mantel-Haenszel, DerSimonian-Laird Random Effects

p=0.03, z=2.17
τ^2=0.00

RR: Risk Ratio
CI: Confidence Interval





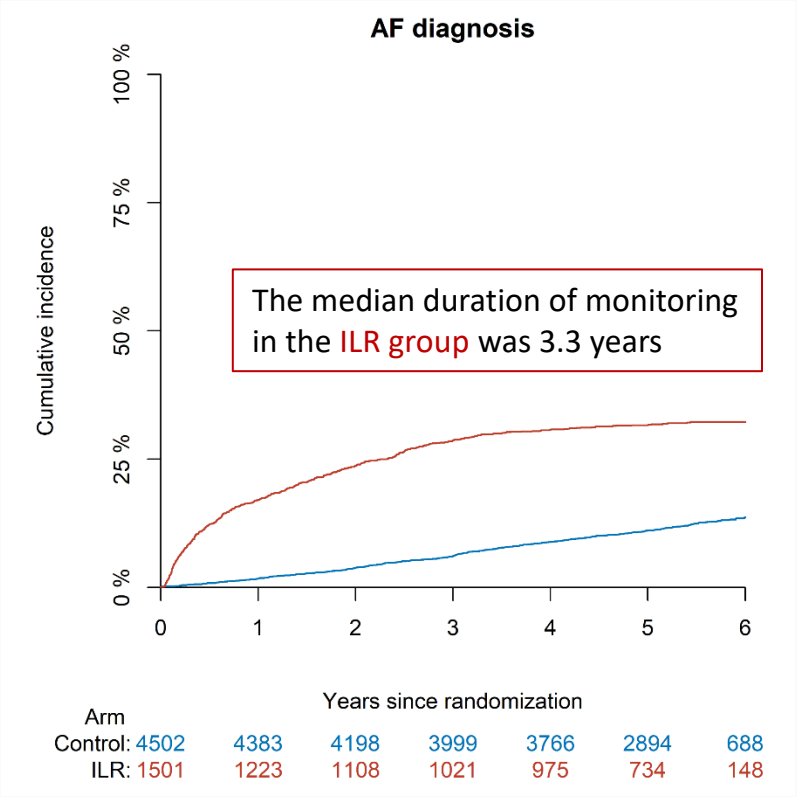
McIntyre et al EHJ Open 2022

Results – AF Diagnosis

AF was diagnosed in 1,027 participants;

477 (32%) in the ILR group vs. 550 (12%) in the Control group

HR 3.17; 95% CI 2.81-3.59; P<0.001



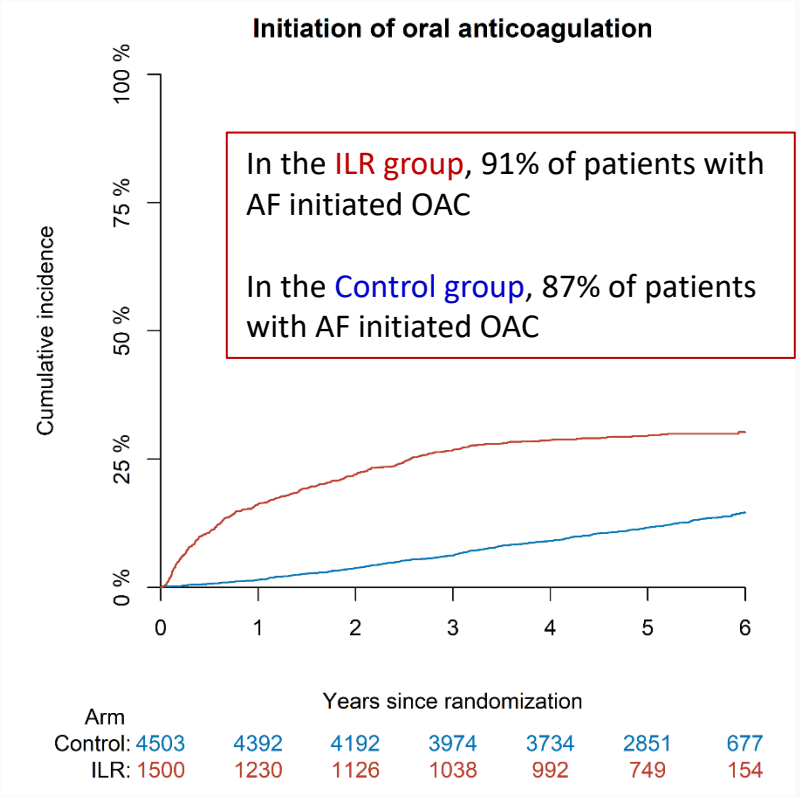
Diederichsen SZ. Lancet 2021

Results – Oral Anticoagulation

Oral anticoagulation (OAC) was initiated in 1,036 participants;

445 (30%) in the ILR group vs. 591 (13%) in the Control group

HR 2.72; 95% CI 2.41-3.08; P<0.001

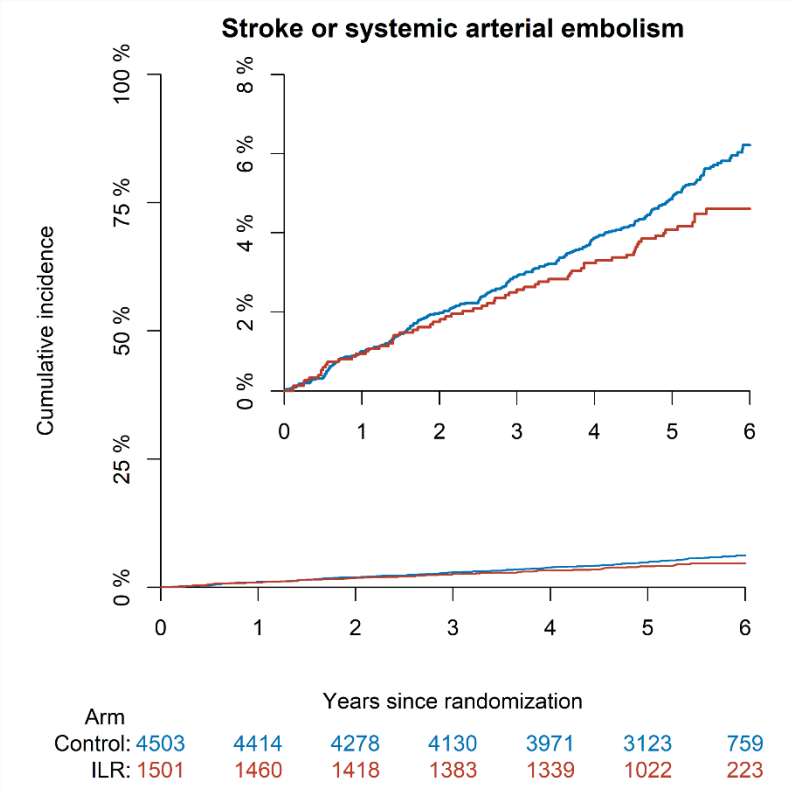


Results – Primary outcome

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

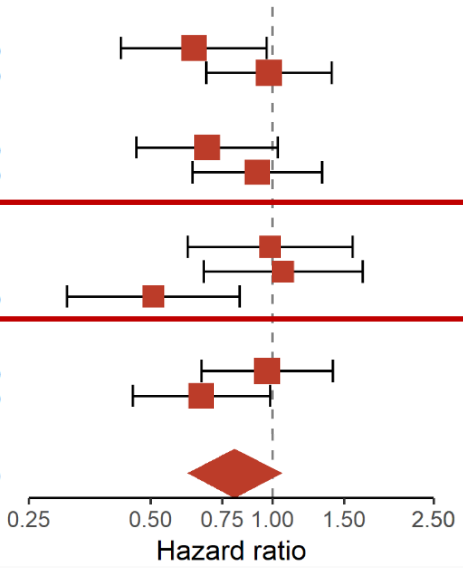
67 (4.5%) in the ILR group vs. 251 (5.6%) in the Control group

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



Results – Primary outcome, Subgroups

Subgroup	ILR group	Control group	Hazard ratio (95% CI)	P-value	P-value for interaction
	no. of events / total no. (%)				
BMI, kg/m2					0.18
≤ 27	27/706 (3.82%)	131/2207 (5.94%)	0.64 (0.42-0.97)	0.03	
> 27	40/794 (5.04%)	120/2296 (5.23%)	0.98 (0.68-1.40)	0.90	
Pulse rate, beats/min					0.94
≤ 70	29/747 (3.88%)	128/2312 (5.54%)	0.69 (0.46-1.03)	0.07	
> 70	37/746 (4.96%)	121/2178 (5.56%)	0.91 (0.63-1.32)	0.63	
Systolic blood pressure, mmHg					0.01
< 141	23/472 (4.87%)	74/1481 (5.00%)	0.99 (0.62-1.57)	0.95	
141-156	25/478 (5.23%)	76/1518 (5.01%)	1.06 (0.68-1.67)	0.80	
≥ 157	19/549 (3.46%)	101/1499 (6.74%)	0.51 (0.31-0.83)	0.01	
Diastolic blood pressure, mmHg					0.09
< 85	36/751 (4.79%)	116/2328 (4.98%)	0.97 (0.67-1.41)	0.86	
≥ 85	31/748 (4.14%)	135/2170 (6.22%)	0.67 (0.45-0.98)	0.04	
Overall	67/1501 (4.46%)	251/4503 (5.57%)	0.80 (0.61-1.05)	0.11	



PIAAF Pharmacy

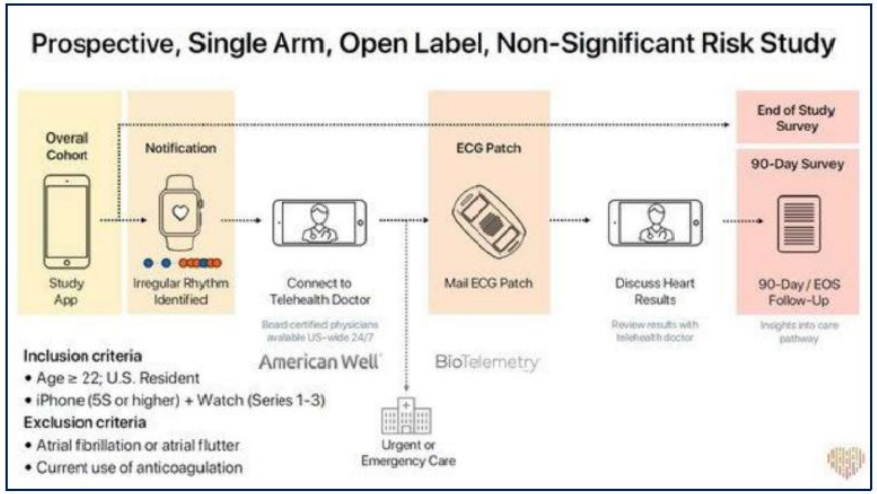
Age Groups (years)	Total N (%)	'Actionable' AF N (%)	No AF N (%)
65-74	620 (54.8)	11 (1.8)	609 (98.2)
75-85	422 (37.3)	9 (2.1)	413 (97.9)
>85	89 (7.9)	7 (7.9)	82 (92.1)

Approximately 50% of patients had a BP > 140/90 at screening
Only 50% of screen-positive patients receiving OAC 3 months later

Apple Heart Study

- The Apple Heart Study used a novel study design of self-enrollment.

- 419,297 people self-enrolled in the study within an **8-month enrollment period**.



- **Apple Watch had moderate accuracy in AF detection.**

Turakhia et al. Presented at ACC 2019.

AFFECT-EU: Horizon's 2020 Grant. R. Schnable

AF-detection results: Sept 1st 3:15 in Paris-4. Dr. L. Xing

AF-SCREEN

Randomized clinical studies:

- D2AF (n=18,744)
- STROKESTOP I (n=27,975)
- STROKESTOP II (n=28,712)
- MonDAFIS (n=3,431)
- mSToPS (n=2,659)
- SCREEN-AF (n=856)
- LOOP (n=6,004)

Non-randomized studies:

- RITMO-OK (n=2,814)
- AF-STROKE (n=7,107)
- STROKESTOP Pilot (n=1,330)
- AFRICAT Phase I and II (n=359)

- *Single-lead ECG device*
- *Single-lead ECG patch*
- *Holter*
- *Implantable cardiac monitor*

AFFECT-EU

Who and How to Screen for AF?

- 1. Prevalence of AF increases with age and CV risk factors: CHADS-VASc, LA enlargement, NT-ProBNP
- 2. Higher-burden AF has greater stroke risk
- 3. Although single time-point (STP) screening detects less AF, such AF confers a higher-risk of stroke
- 4. Screening a general, older population (>70 or 75 years) using STP has appeal?
- 5. Continuous monitoring methods for individuals with greater risk of AF and stroke?
- 6. Patient-level meta-analysis coming soon….