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HERZ-KREISLAUFFORSCHUNG E.V.



Monitoring von Vorhofflimmern - welche Patienten? Wann ergibt sich eine Behandlungskonsequenz?

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Conflict of Interest – Disclosure

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

Affiliation/Financial Relationship

1. Honoraria for lectures

Company

Bayer, Berlin Chemie, Boehringer Ingelheim, CVRx, Medtronic, Novartis, Pfizer, Servier

2. Honoraria for advisory board activities

Boehringer Ingelheim, Novartis

3. Participation in clinical trials

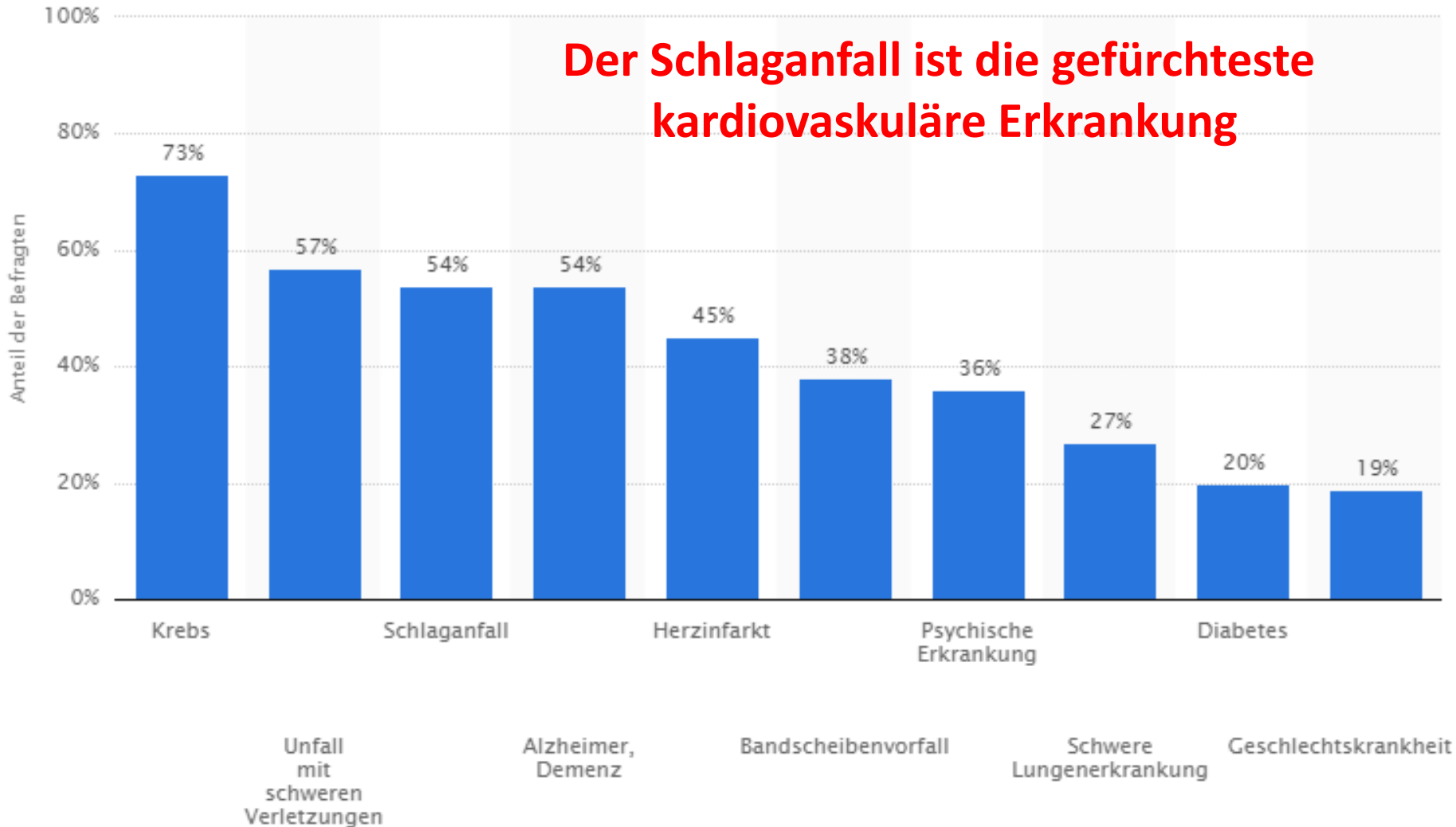
Bayer, Boston Scientific, Celladon, CVRx, Johnson&Johnson, Medtronic, Novartis, Pfizer, Servier

4. Research funding

BMBF (Kompetenznetz Herzinsuffizienz und DZHK), European Union (Horizon 2020) and Boehringer Ingelheim

Wovor fürchten sich die Menschen?

Der Schlaganfall ist die gefürchtetste kardiovaskuläre Erkrankung

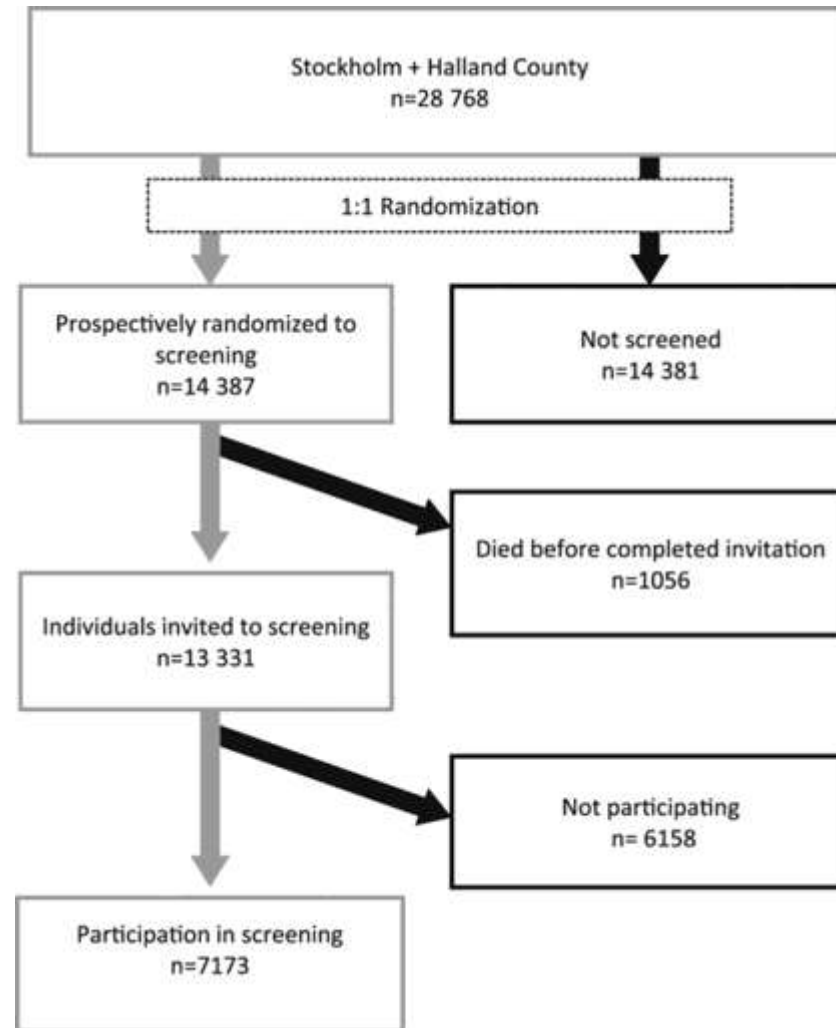


Monitoring auf Vorhofflimmern

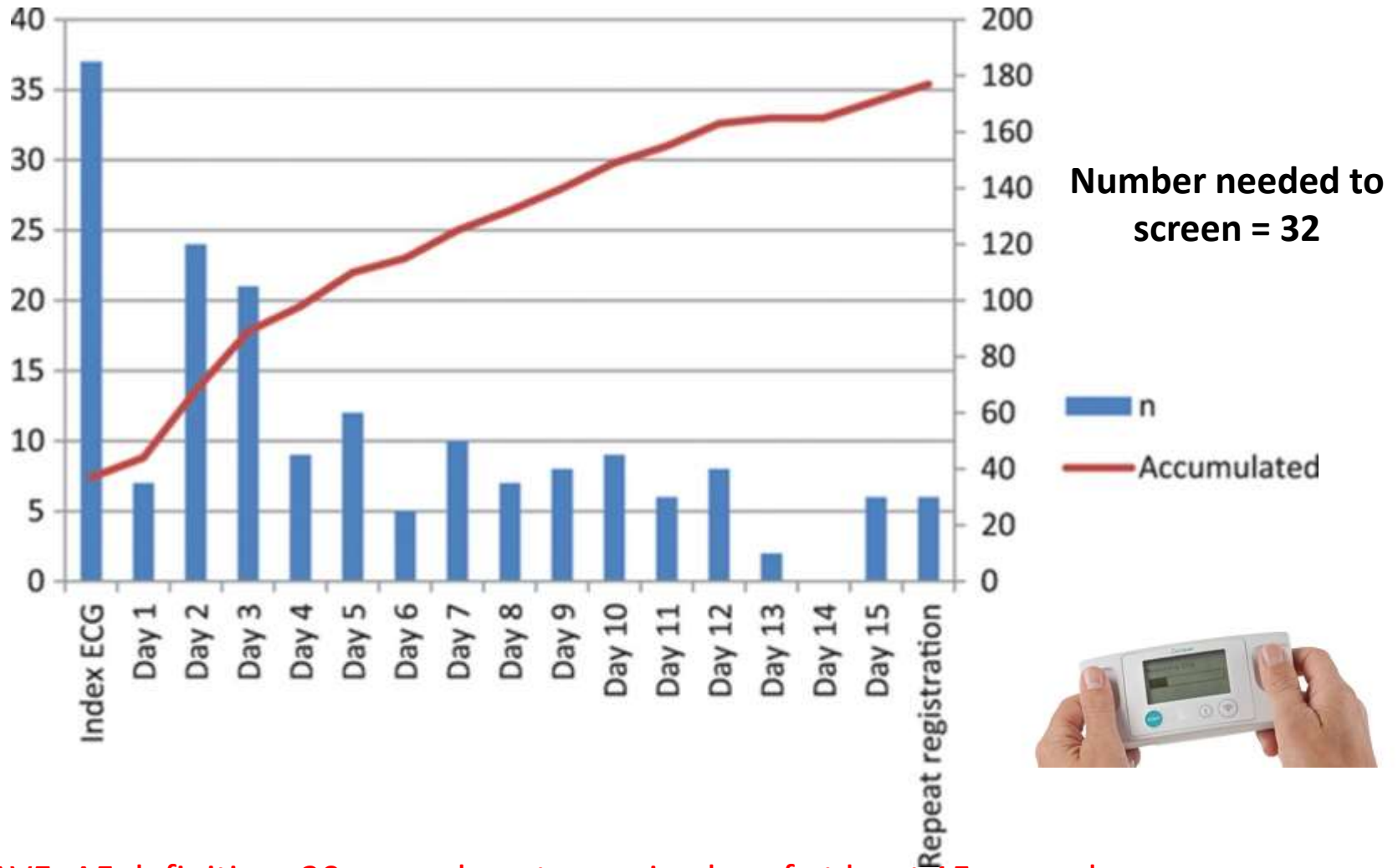
1. Primärprophylaxe: Detektion von Vorhofflimmern als Schlaganfallspräventionsmaßnahme

2. Sekundärprophylaxe: Detektion von Vorhofflimmern zur Verhinderung eines erneuten Schlaganfalles

Stepwise screening in primary prevention: STOPSTROKE



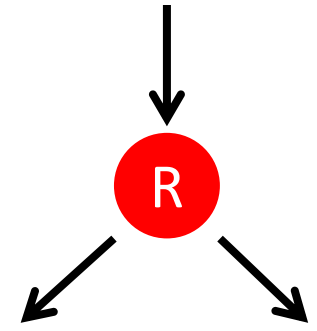
Time to first detection of atrial fibrillation among participants undergoing intermittent ECG registrations.



CAVE: AF definition: 30 seconds or two episodes of at least 15 seconds



Hausärztliche Patienten, 75 Jahre und älter
mit medikamentös behandeltem arteriellen Hypertonus



Standard of care

2 weeks of monitoring
(ZioPatch) + BP-monitor +
Standard of care

Primary endpoint: Newly diagnosed AF within 6 months

n=822

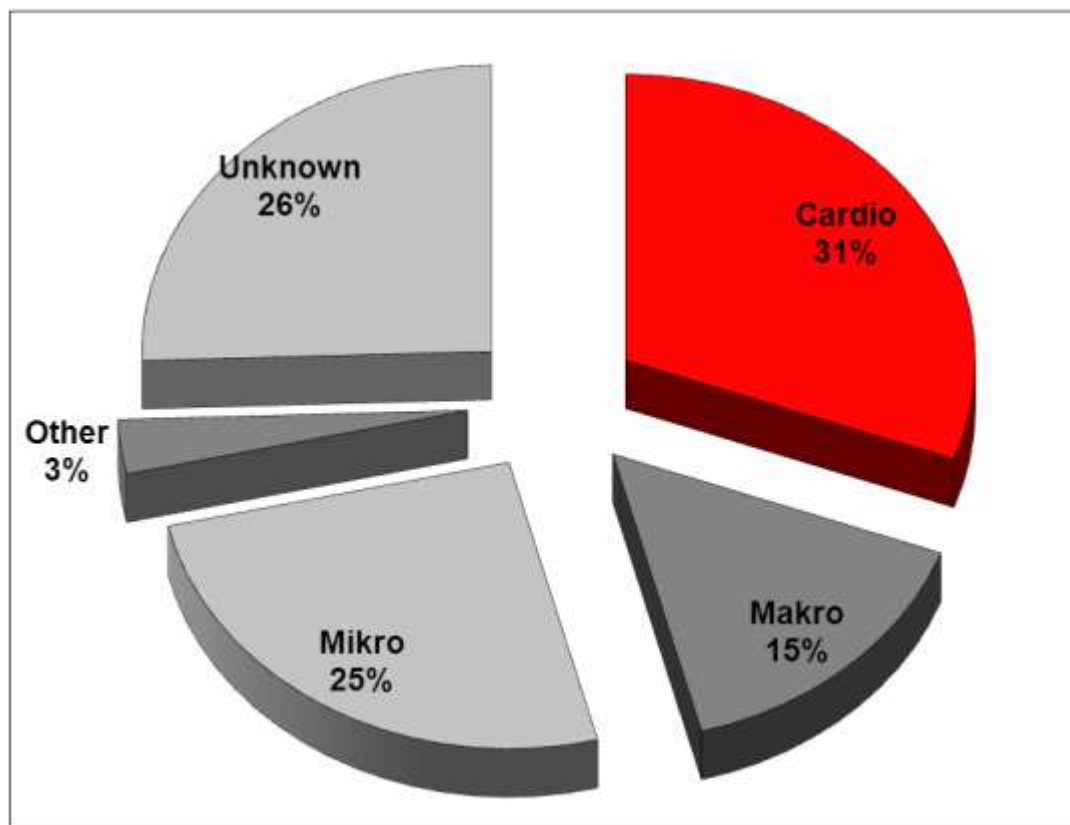
Study sites in Germany: 45 GPs around Frankfurt, Göttingen and Hamburg

Monitoring auf Vorhofflimmern

1. Primärprophylaxe: Detektion von Vorhofflimmern als Schlaganfallspräventionsmaßnahme
- 2. Sekundärprophylaxe: Detektion von Vorhofflimmern zur Verhinderung eines erneuten Schlaganfalles**

Prevalence of different stroke subtypes

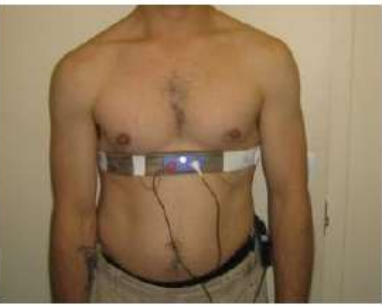
TOAST Classification of Subtypes of Acute Ischemic Stroke (Trial of Org 10172 in Acute Stroke Treatment)



Two large randomised multicenter trials in cryptogenic stroke

EMBRACE: 572 patients randomised to 30-day monitoring or 24h Holter ECG

CRYSTAL-AF: 441 patients randomised to implantable loop recorder or usual care



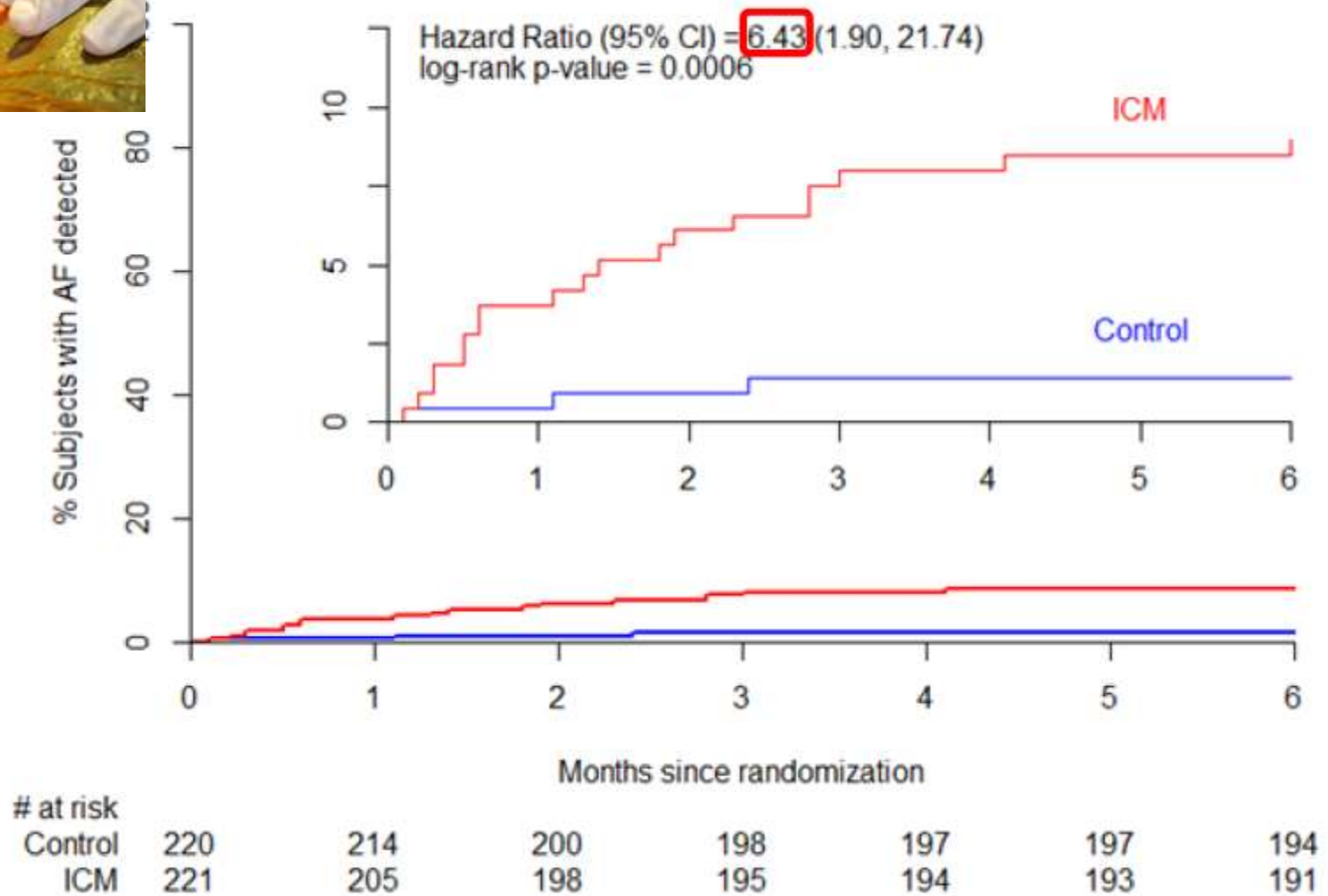
EMBRACE

Detection Between-Group Comparison

	Repeat Holter (n=285)	30-day Monitor (n=287)	p-value	Absolute Detection Difference (95% CI)	NNS
Primary Outcome					
AF \geq 30 seconds (within 90 days)	3%	16%	<0.001	13% (9%-18%)	8
AF \geq 30 sec (study monitors only)	2%	15%	<0.001	13% (9%-18%)	8
Secondary Outcomes					
AF \geq 2.5 min	2%	10%	<0.001	8% (4%-12%)	13
Any AF	4%	20%	<0.001	16% (10%-21%)	6



CRYSTAL-AF



Embolic stroke of unknown source (ESUS)

Embolic strokes of undetermined source: the case for a new clinical construct



Robert G Hart, Hans-Christoph Diener, Shelagh B Coutts, J Donald Easton, Christopher B Granger, Martin J O'Donnell, Ralph L Sacco, Stuart J Connolly, for the Cryptogenic Stroke/ESUS International Working Group

Cryptogenic (of unknown cause) ischaemic strokes are now thought to comprise about 25% of all ischaemic strokes. Advances in imaging techniques and improved understanding of stroke pathophysiology have prompted

Lancet Neurol 2014; 13: 429-38

See [Comment](#) page 344

Panel 2: Criteria for diagnosis of embolic stroke of undetermined source*

- Stroke detected by CT or MRI that is not lacunar†
- Absence of extracranial or intracranial atherosclerosis causing $\geq 50\%$ luminal stenosis in arteries supplying the area of ischaemia
- No major-risk cardioembolic source of embolism‡
- No other specific cause of stroke identified (eg, arteritis, dissection, migraine/vasospasm, drug misuse)

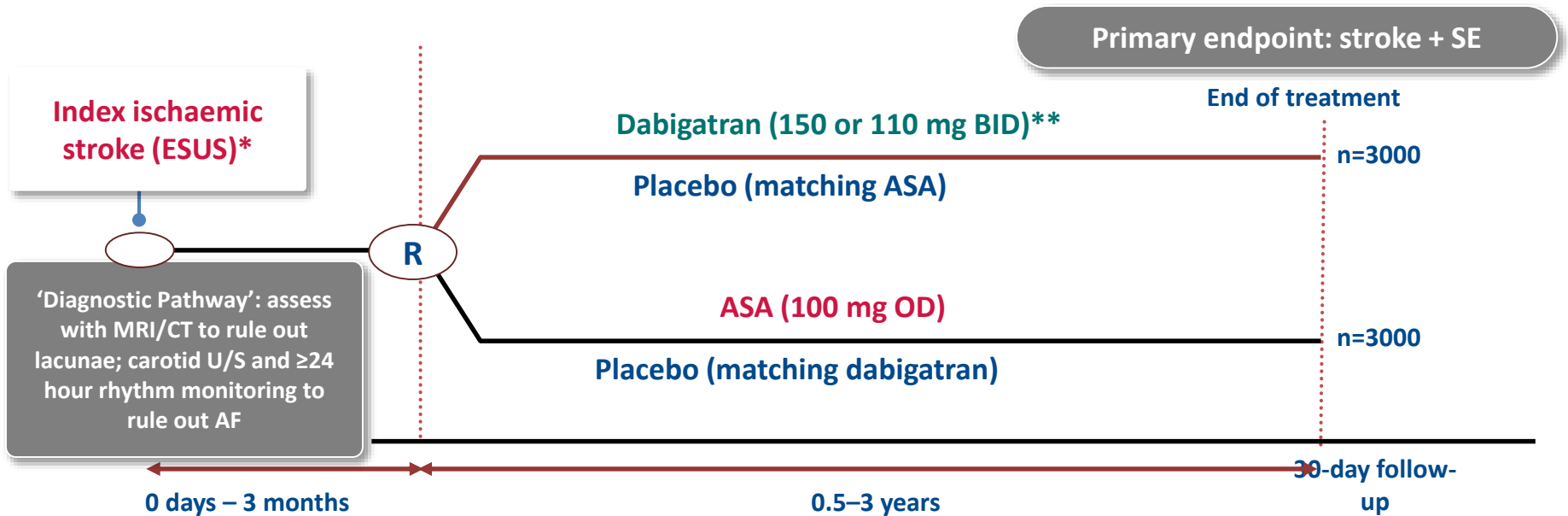
* Requires minimum diagnostic assessment (panel 3). † Lacunar defined as a subcortical infarct smaller than or equal to 1.5 cm (< 2.0 cm on MRI diffusion images) in largest dimension, including on MRI diffusion-weighted images, and in the distribution of the small, penetrating cerebral arteries; visualisation by CT usually needs delayed imaging greater than 24–48 h after stroke onset. ‡ Permanent or paroxysmal atrial fibrillation, sustained atrial flutter, intracardiac thrombus, prosthetic cardiac valve, atrial myxoma or other cardiac tumours, mitral stenosis, recent (< 4 weeks) myocardial infarction, left ventricular ejection fraction less than 30%, valvular vegetations, or infective endocarditis.

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RE-SPECT ESUS

Randomized Evaluation in Secondary stroke Prevention Comparing the Thrombin inhibitor dabigatran etexilate versus ASA in Embolic Stroke of Undetermined Source (ESUS)

- ~20% of ischaemic strokes have been categorized in recent studies as ESUS



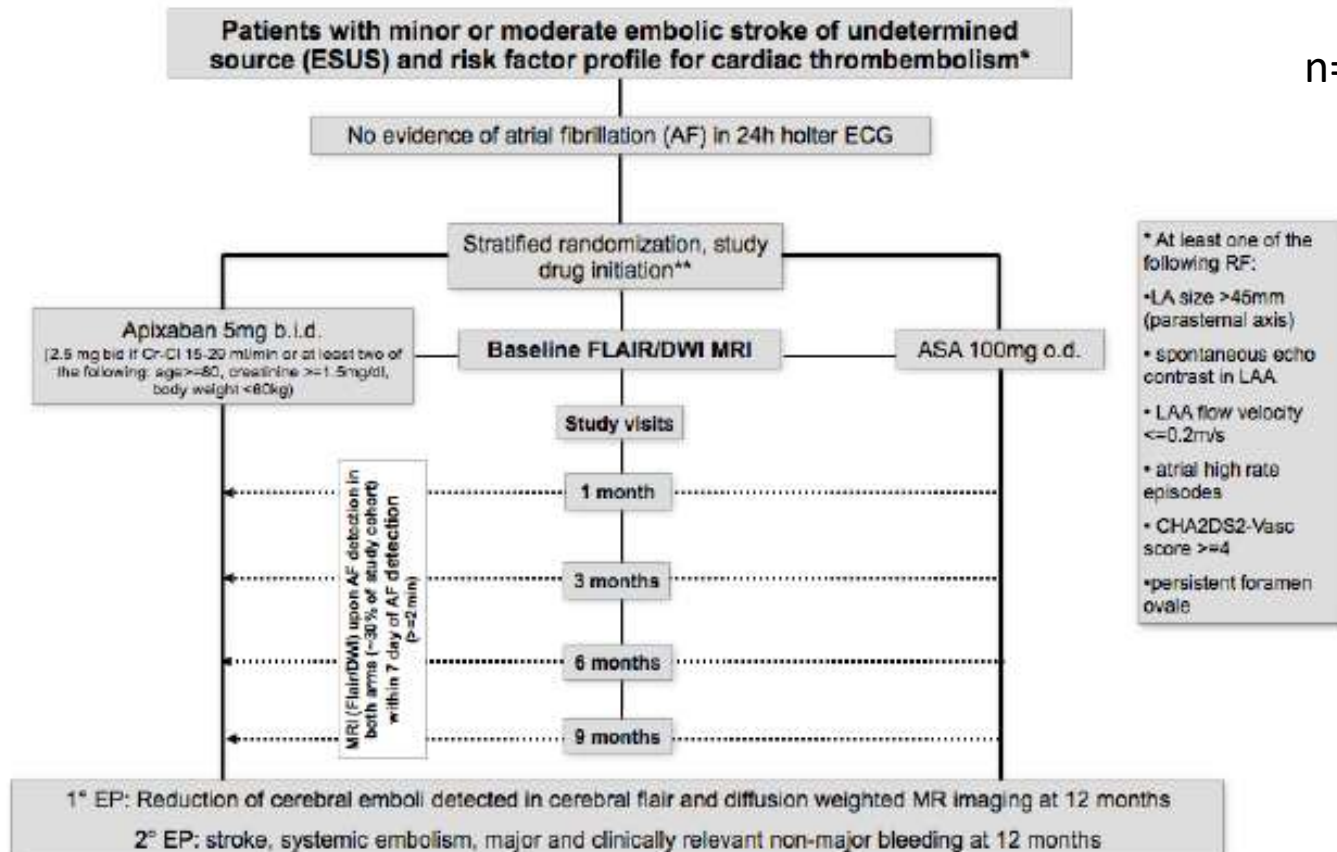
*mRS ≤3, age ≥60 or 50–59 with additional risk factors. Includes TIA with pathological imaging evidence.**All patients receive dabigatran 150 mg BID, unless ≥75 years or CrCl <50 mL/min. These patients receive dabigatran 110 mg BID

ASA = acetylsalicylic acid; BID = twice daily; CrCl = creatinine clearance; CT = computed tomography; ESUS= embolic stroke of undetermined source; MRI = magnetic resonance imaging; mRS = modified Rankin score; OD = once daily; SE = systemic embolism; TIA = transient ischaemic attack

ATTICUS-Studie

ATTICUS – Randomized, active controlled, blinded (PROBE), multicentre Clinical Trial

n=500



** Study drug initiation at day 3 to 7 after minor or moderate stroke onset, depending on individual stroke related bleeding risk. A low risk of HTI is likely determined by small area of brain infarction (<30% of MCA territory), absence of HTI at the time of anticoagulation, blood pressure <140 mmHg systolic, and normal blood glucose and platelet counts

A shift in paradigm



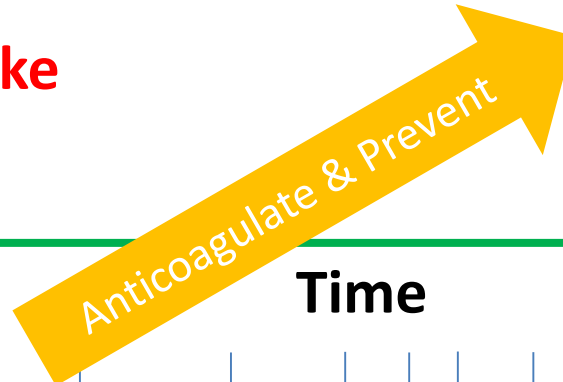
Retrospection
(Cryptogenic stroke,
ESUS)

Why did this stroke happen? Can I find an explanation? Is it cryptogenic? Does it look embolic? Should I anticoagulate?

Cerebral events
(stroke, TIA)



1st stroke



2nd stroke



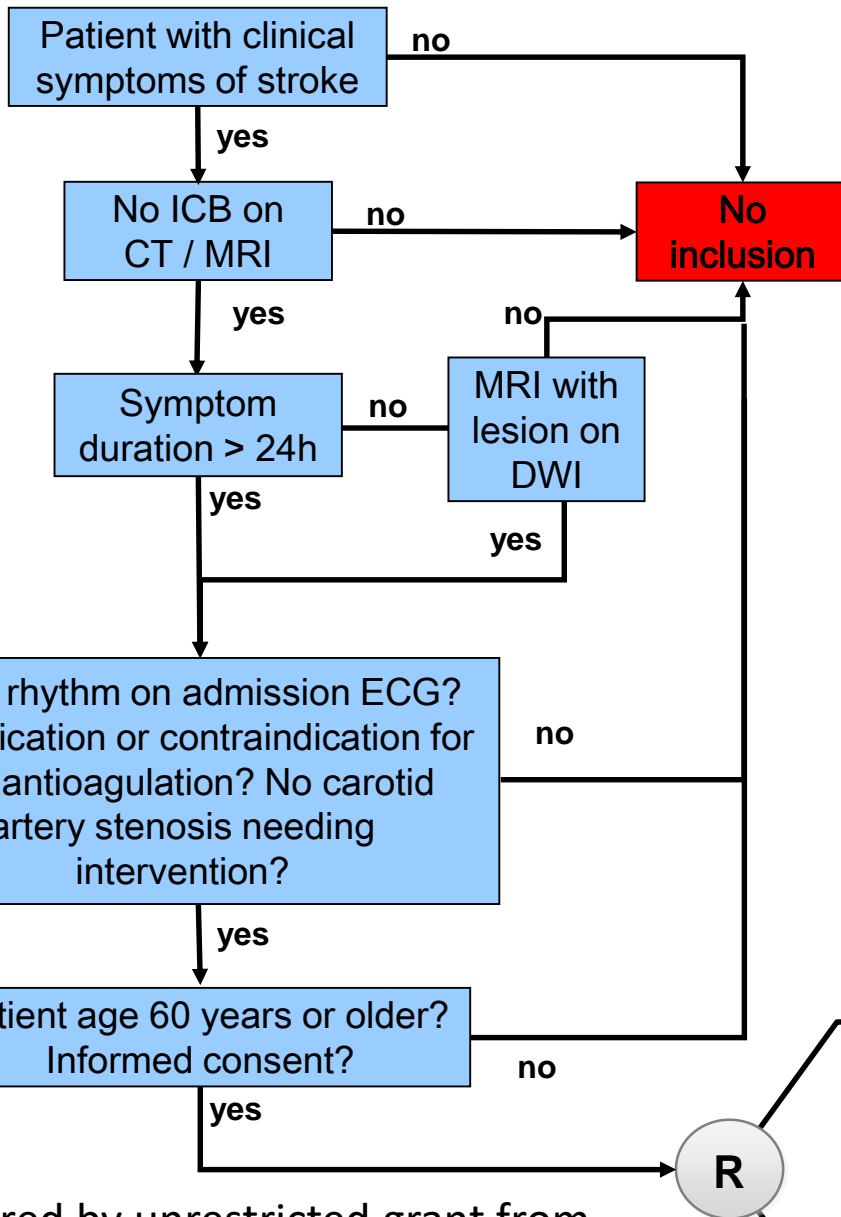
AF cluster



Look ahead
(Find-AF randomised)



Stroke patients have a high risk of underlying AF irrespective of stroke etiology and should be anticoagulated if AF is detected



Primary endpoint:
First detection of AF at 6 months

Prolonged Holter-monitoring (10 days and 2x10 days)

1:1 randomisation, 400 patients

usual stroke-unit care

Sponsored by unrestricted grant from



Find-AF randomised



Vorhofflimmern

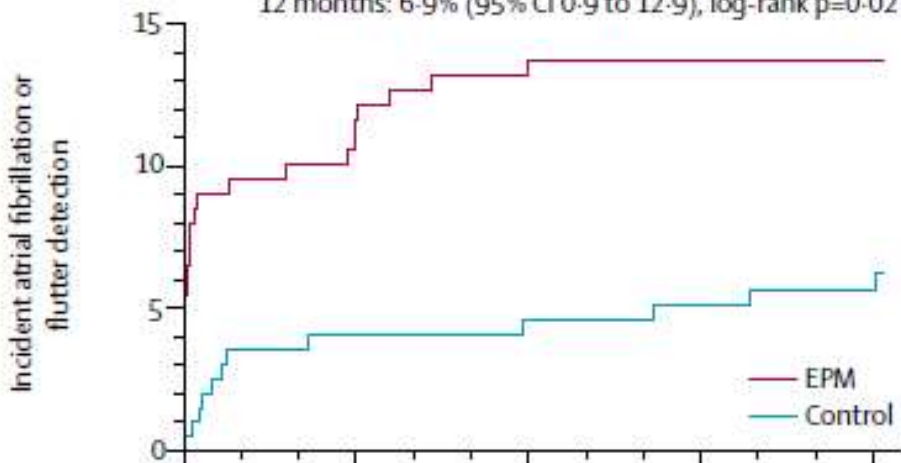
Schlaganfälle

A

Difference of cumulative event rates

6 months: 9.1% (95% CI 3.5 to 14.8), log-rank p=0.002

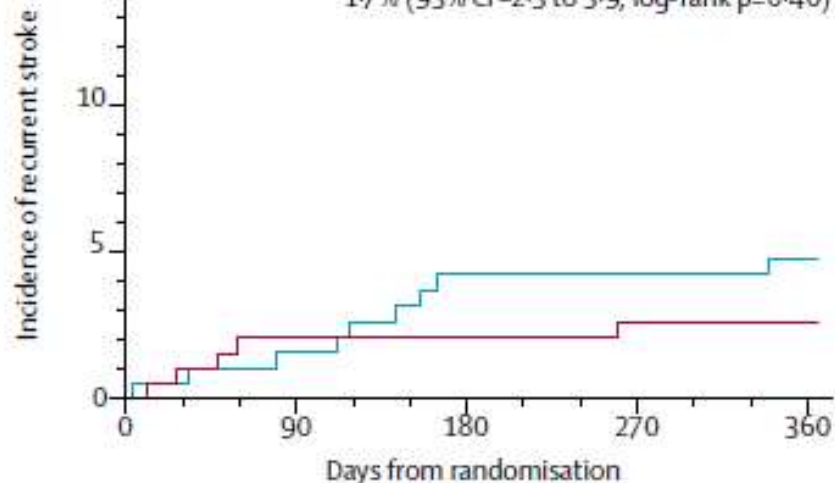
12 months: 6.9% (95% CI 0.9 to 12.9), log-rank p=0.02



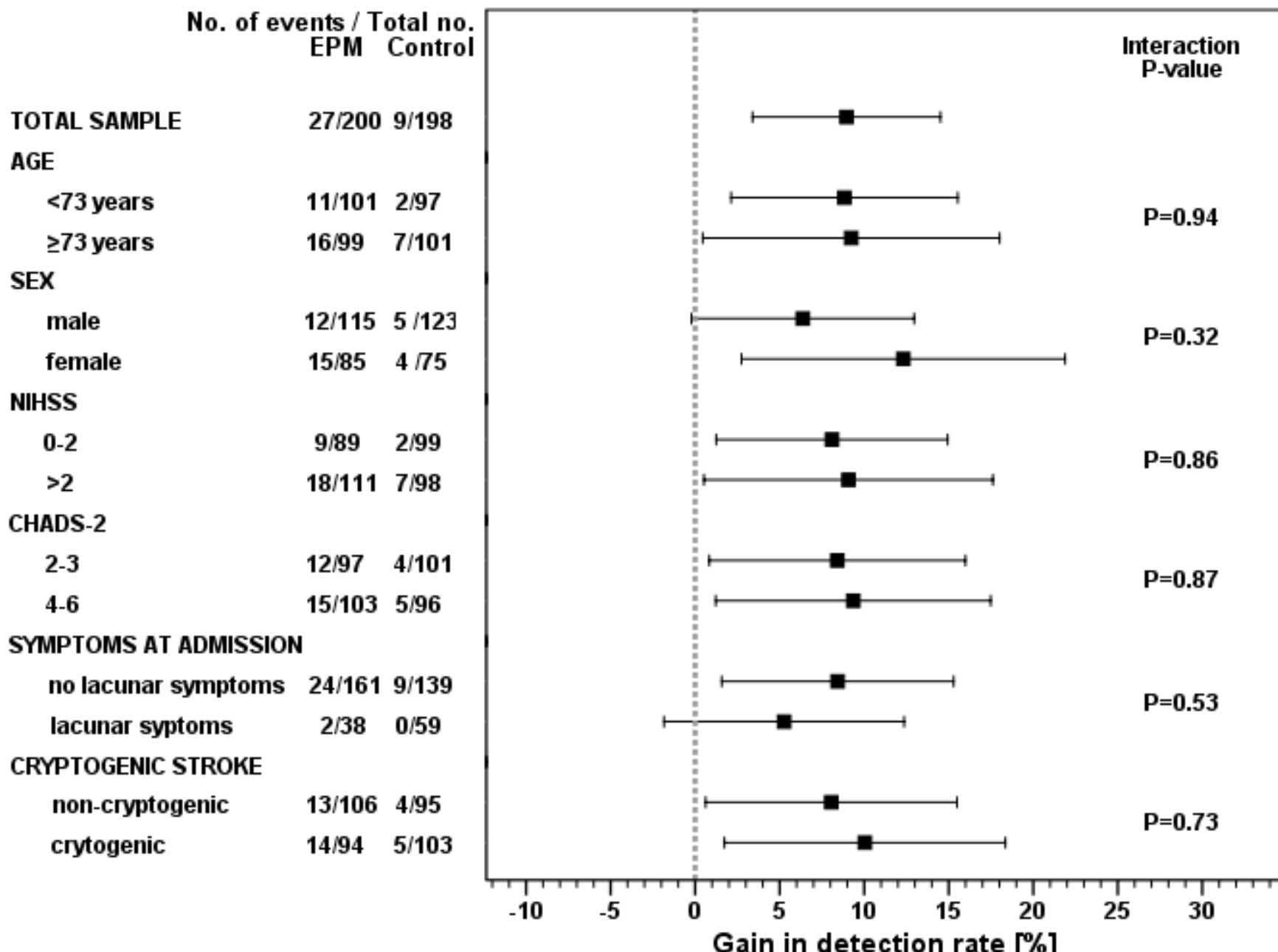
B

Difference of cumulative event rates

1.7% (95% CI -2.5 to 5.9, log-rank p=0.46)

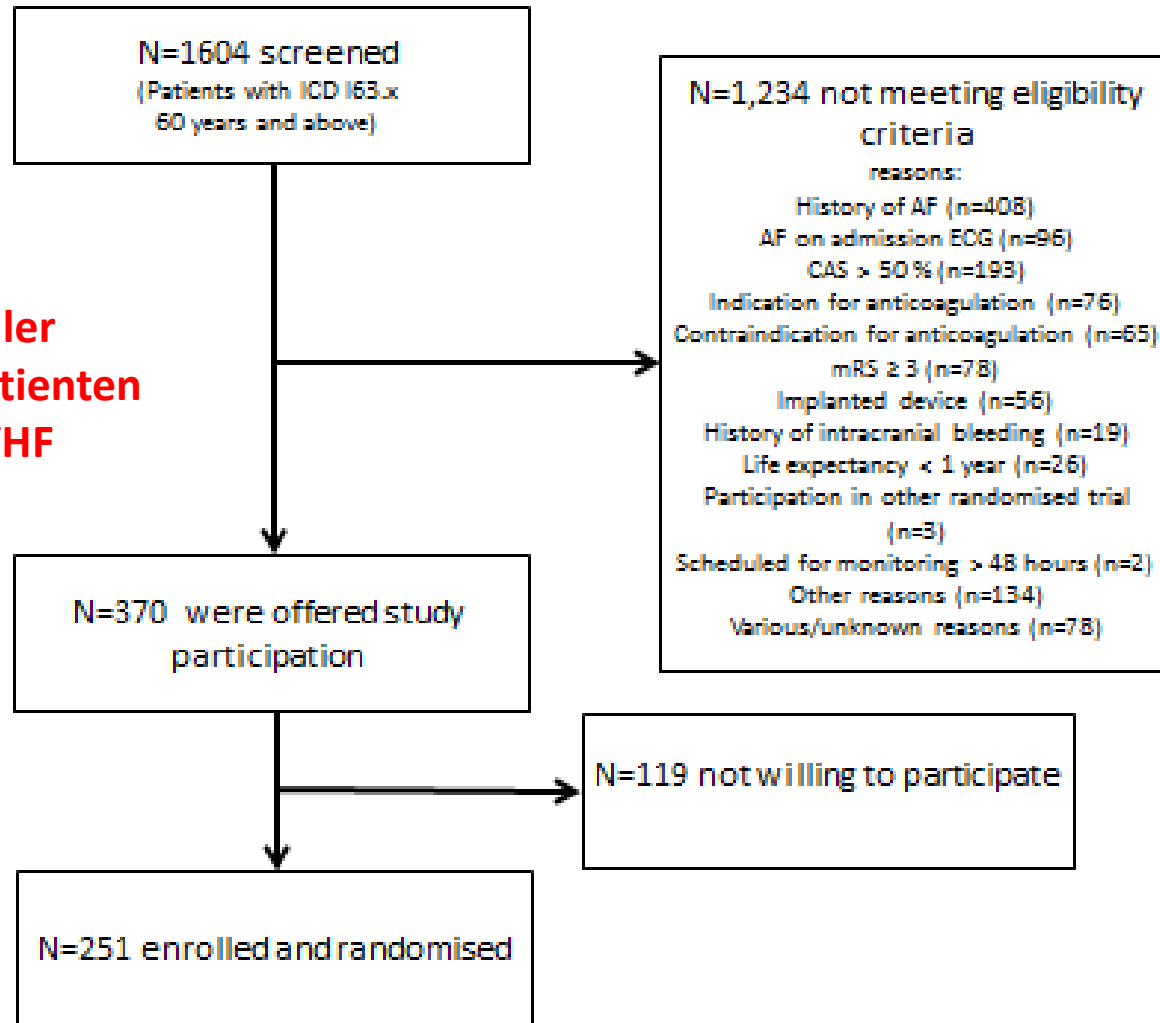


Primary Endpoint in Subgroups



Kandidaten für verlängertes Monitoring

**30-50 % aller
Schlaganfallpatienten
frei von VHF**



Zusammenfassung

- Früherkennung von Vorhofflimmern als Primärpräventionsmassnahme gegen Schlaganfälle
- EMBRACE, CRYSTAL-AF: Jeder 8. Patient mit kryptogenem Schlaganfall hat unentdecktes Vorhofflimmern!
- Find-AF randomised: Unabhängig vom Schlaganfallsubtyp profitieren Patienten vom Monitoring auf Vorhofflimmern
- ESUS: Neue Entität. Alle gleich antikoagulieren? Oder alle monitorieren?