Enhanced Monitoring For Atrial Fibrillation Following Cardiac Surgery

Primary Results of The SEARCH-AF CardioLink Trial

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- Is the NC for DAPA-HF, DELIVER-HFpEF, EMPEROR-Preserved, EMPEROR-Reduced, SOLOIST, and SELECT
- Is on the SEC for EMPEROR-Reduced, EMPEROR-Preserved, DETERMINE-A and DETERMINE-B
- Is the Co-PI for ACE, CAMRA, ENABLE-Chiropody, EMPA-HEART, EMPA-HEART 2, NEWTON-CABG, and SEARCH-AF
- Is President of the Canadian Medical and Surgical Knowledge Translation Research Group
- Is on the SC of CIRT and BELIEVE

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Background - 1

Early post-operative atrial fibrillation (POAF) occurs in **30–50%** of patients, **peaking at 3–5 days** and declining afterwards

The **natural history of POAF after discharge from cardiac surgery is not well defined** because the observation period in most studies have been limited to the hospitalization phase

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Background - 2

Unclear if the risk of POAF persists in post-surgical patients, especially those without AF pre-operatively or during hospitalization

Guidelines provide little or no direction on optimal duration of monitoring post cardiac surgery particularly if they are in SR at discharge

Randomized data guiding detection and management of POAF after hospitalization for cardiac surgery are lacking

AF, atrial fibrillation; POAF, post-operative atrial fibrillation.

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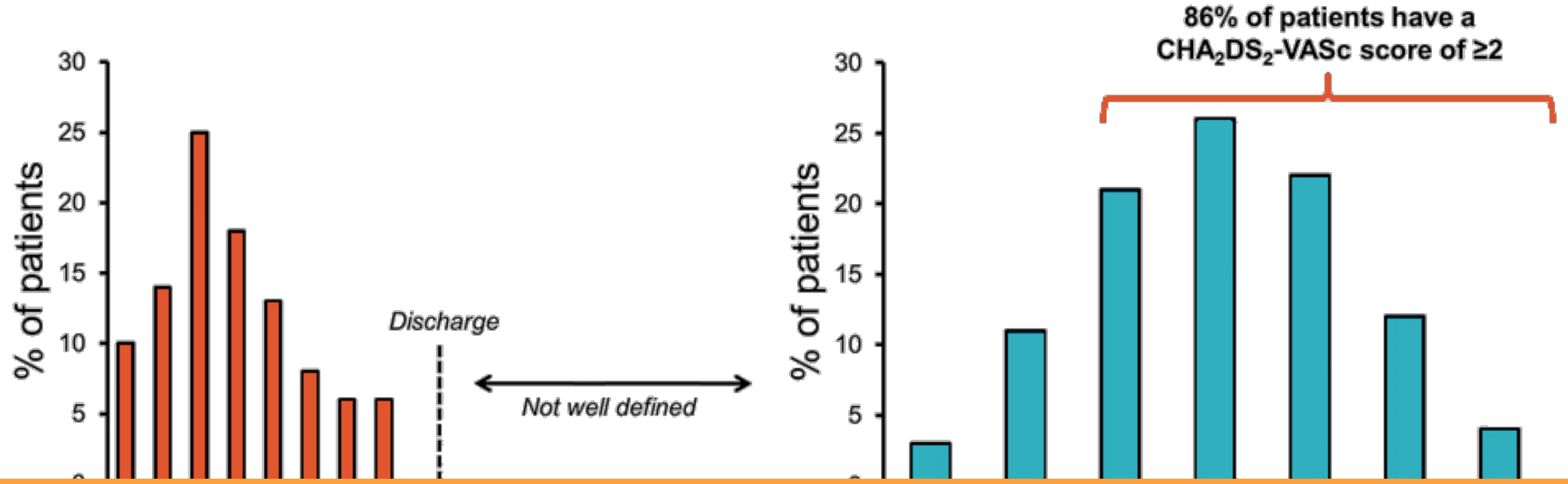
Rationale Behind SEARCH-AF

POAF after cardiac surgery is associated with
adverse short- and long-term outcomes (e.g. death, stroke)



A strategy to enhance our ability to detect POAF during the subacute post-operative phase (e.g. after discharge) could incrementally identify patients who might benefit from therapeutic interventions (e.g. oral anticoagulation)

POAF, post-operative atrial fibrillation.

Aranki S et al. Circulation 1996;94:390-397; Gialdini G et al. JAMA 2014;312:616-622.

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Primary Objective

To determine whether **enhanced cardiac rhythm monitoring** with an adhesive, continuous monitoring device results in **higher rates of atrial fibrillation/flutter (AF/AFL) detection** during the subacute, post-discharge period of cardiac surgical patients who are at risk of stroke and developing post-operative atrial arrhythmias

AF, atrial fibrillation; AFL, atrial flutter; POAF, post-operative atrial fibrillation.

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Study Hypothesis

A strategy of enhanced cardiac rhythm monitoring will result in an increase in AF/AFL when compared to usual care within 30 days after randomization among post-cardiac surgical patients without a previous history of AF/AFL and at high risk of stroke

AF, atrial fibrillation; AFL, atrial flutter; POAF, post-operative atrial fibrillation.

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Key Inclusion and Exclusion Criteria

INCLUSION

- Isolated CABG or valve replacement/repair ± CABG
- Sinus rhythm at the time of randomization
- No intent to initiate oral anticoagulation at the time of discharge
- CHA_2DS_2-VASC ≥4 or ≥2 with ≥1 of the following:
  COPD | sleep apnea | eGFR <60 mL/min/1.73m² | ≥mild left atrial dilatation | BMI ≥30 kg/m²

EXCLUSION

- Known previous history of AF/AFL
- AF/AFL for ≥24 hours post-operatively
- Subjects who will be treated with OAC due to POAF/AFL
- Mechanical valve
- Hospitalization for ≥10 days (Day #0 = day of surgery)
- Received ≥5 g of IV/oral amiodarone

AF, atrial fibrillation; AFL, atrial flutter; BMI, body mass index; CABG, coronary artery bypass graft surgery; COPD, chronic obstructive pulmonary disease; eGFR, estimated glomerular filtration rate; OAC, oral anticoagulant; POAF, post-operative atrial fibrillation.

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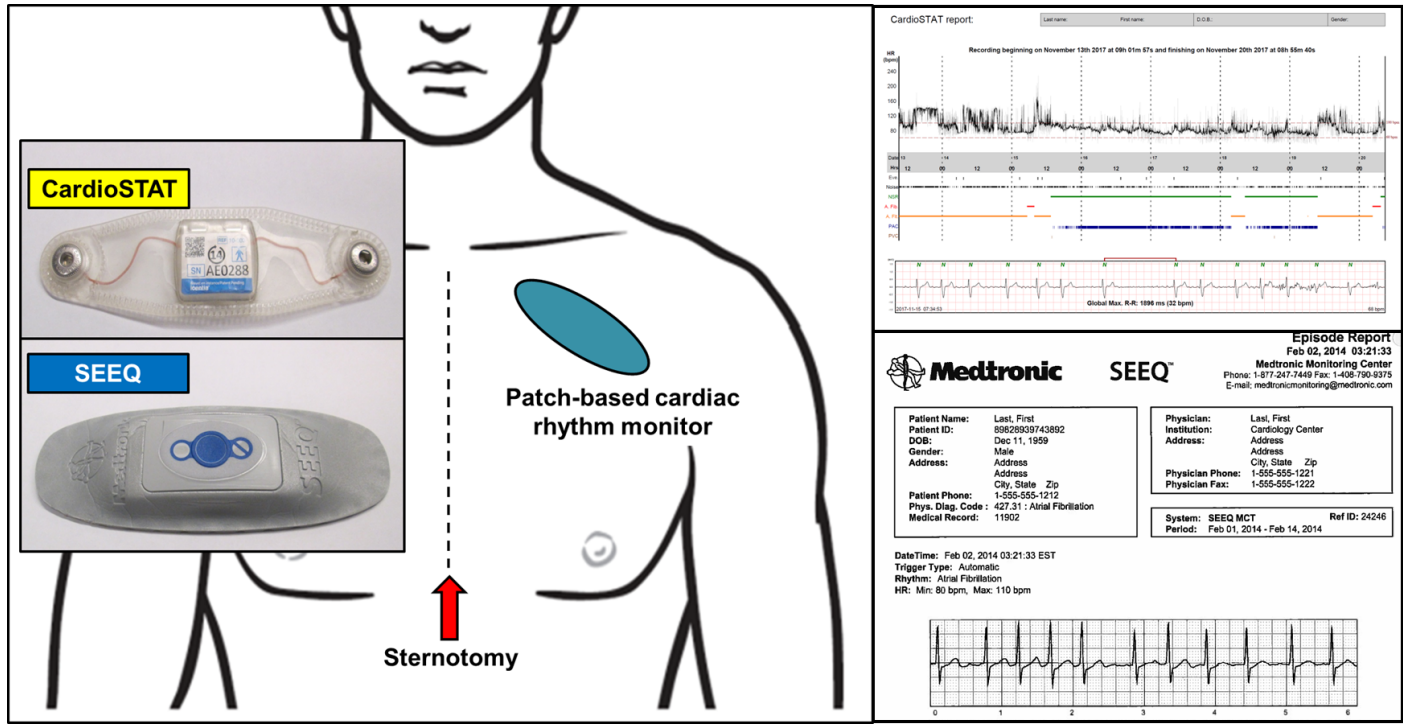
Study Groups

Enhanced Cardiac Rhythm Monitoring (Intervention)

Continuous cardiac rhythm monitoring
with SEEQ™ (Medtronic) or CardioSTAT® (Icentia Inc.)
within the first 30 days after randomization



Usual Care (Control)

No protocol-mandated continuous cardiac rhythm monitoring ECG and/or Holter monitoring at the discretion of the treating physicians

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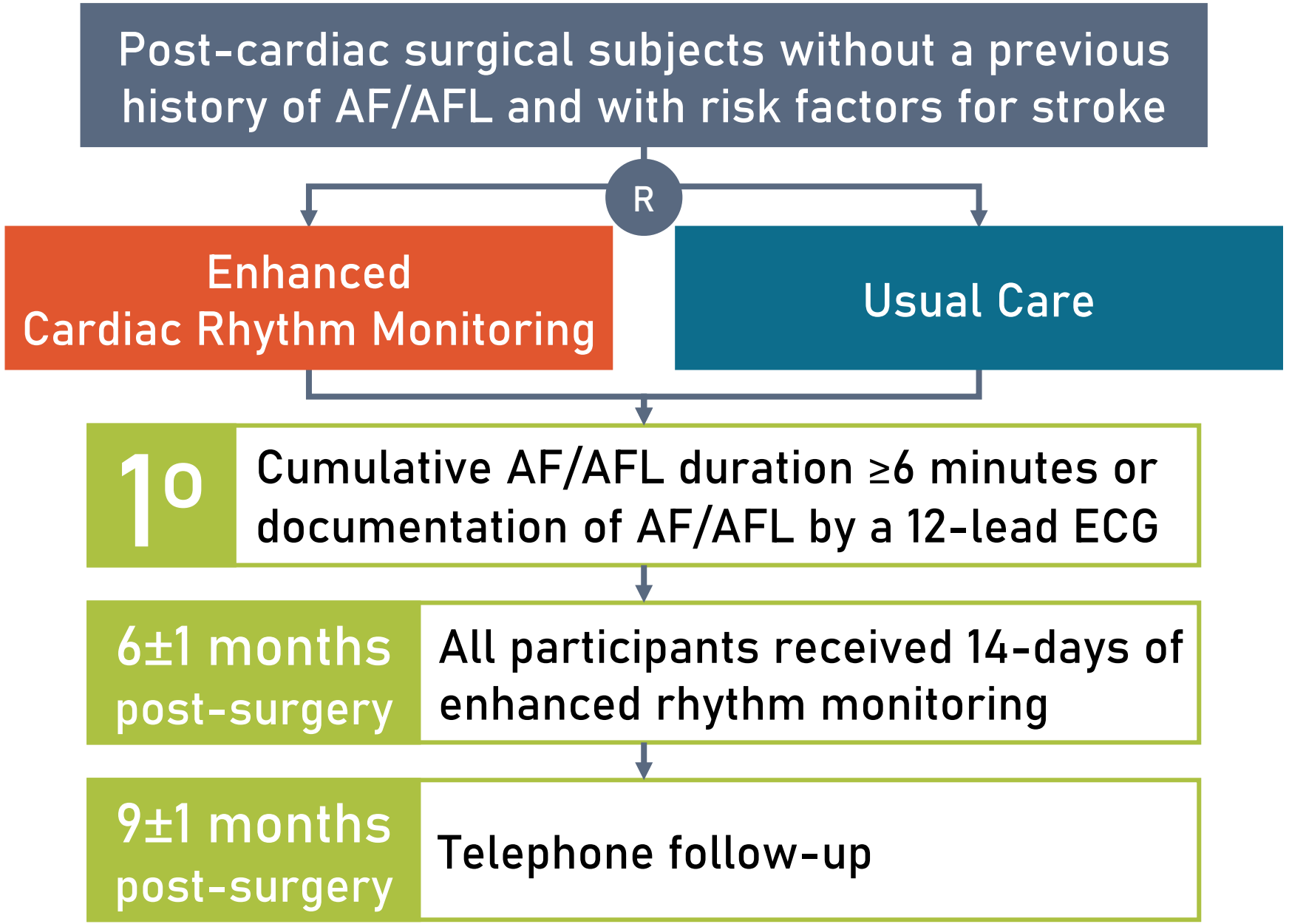
Study Design

- Multicenter
- Parallel group (2-arm)
- Open-label
- Randomized

- Blinded adjudication of outcomes (PROBE design)



AF, atrial fibrillation; AFL, atrial flutter.

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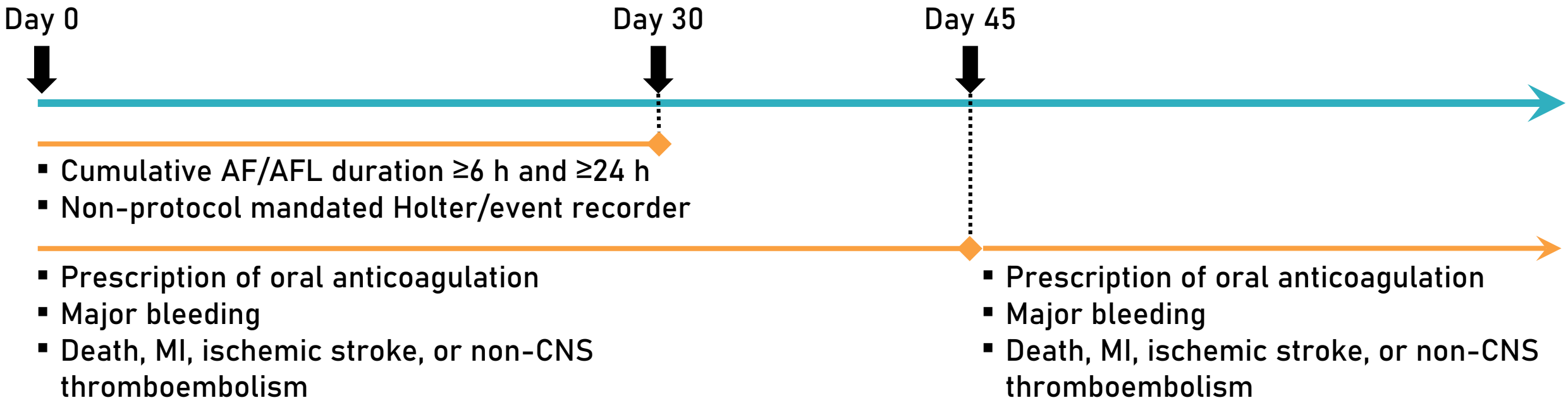
Outcome Measures

PRIMARY Outcome

Cumulative AF/AFL duration ≥6 min or documentation of AF/AFL by a 12-lead ECG

SECONDARY Outcomes



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Impact of COVID-19

March 19, 2020

- Enrollment suspended
- 336 subjects had been randomized (85% of the planned sample of 396)

July 17, 2020

- Enrollment of additional subjects was stopped

Analysis of outcomes is based on results from the 336 subjects randomized into the trial

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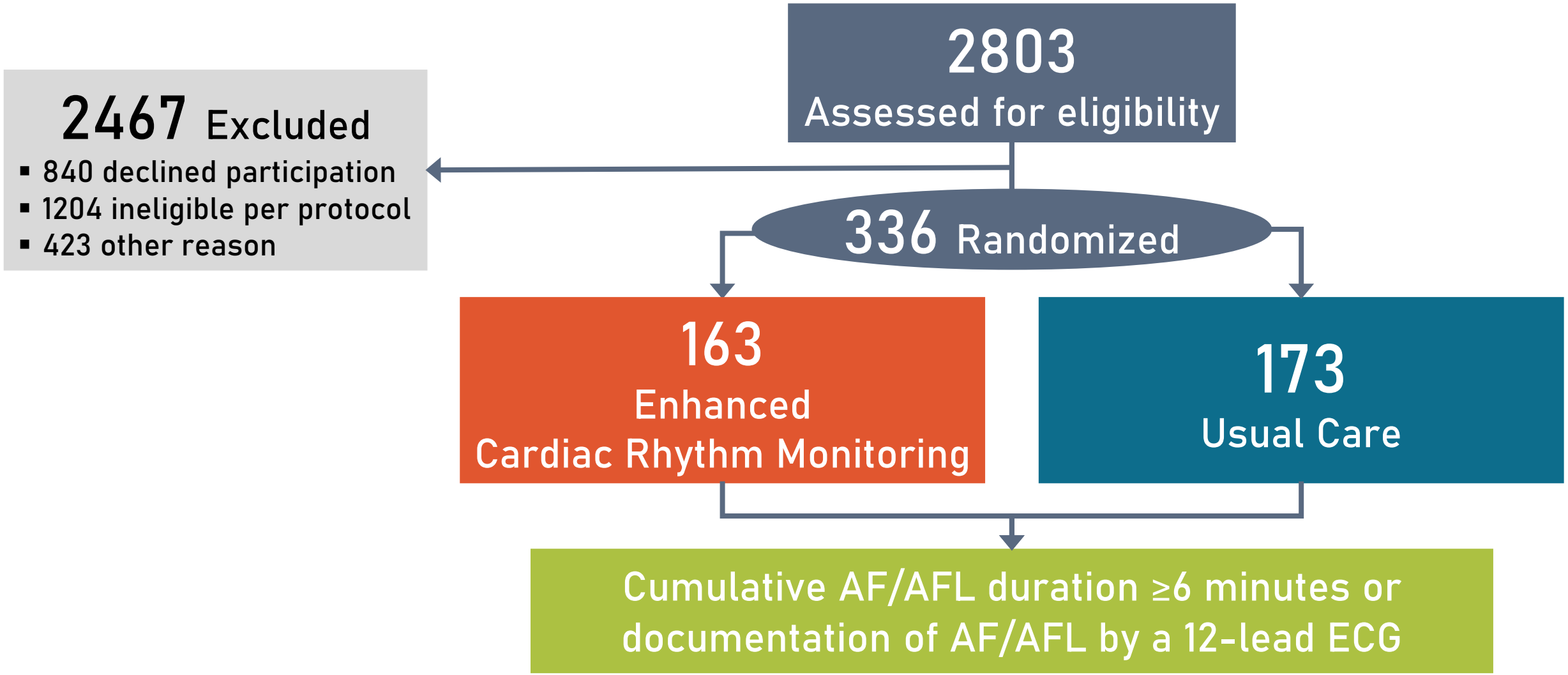
Abbreviated CONSORT Diagram



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Baseline Characteristics

n (%) unless otherwise stated	Enhanced Cardiac Rhythm Monitoring (n=163)	Usual Care (n=173)
Age (mean±SD), years	67.5 ± 8.1	67.4 ± 8.2
Female	35 (21.5)	38 (22.0)
Hypertension	151 (92.6)	162 (93.6)
Diabetes	90 (55.2)	86 (49.7)
Heart failure	10 (6.1)	13 (7.5)
Stroke or Transient Ischemic Attack	17 (10.4)	18 (10.4)
Myocardial infarction	65 (39.9)	60 (34.7)
COPD	11 (6.7)	16 (9.2)
CHA_2DS_2-VASc (median, IQR)	4.0 (3.0, 4.5)	4.0 (3.0, 4.0)
HAS-BLED (median, IQR)	2.0 (2.0, 3.0)	2.0 (2.0, 3.0)
CABG only	124 (76.1)	131 (75.1)
Valve repair or replacement only	17 (10.4)	22 (12.7)
CABG and valve surgery	22 (13.5)	20 (11.6)
Ejection fraction (mean±SD) (%)	55.1 ± 10.4	57.4 ± 9.8
AF (<24 hours) during hospitalization after cardiac surgery)	6 (3.7)	12 (6.9)

AF, atrial fibrillation; CABG, coronary artery bypass graft surgery.

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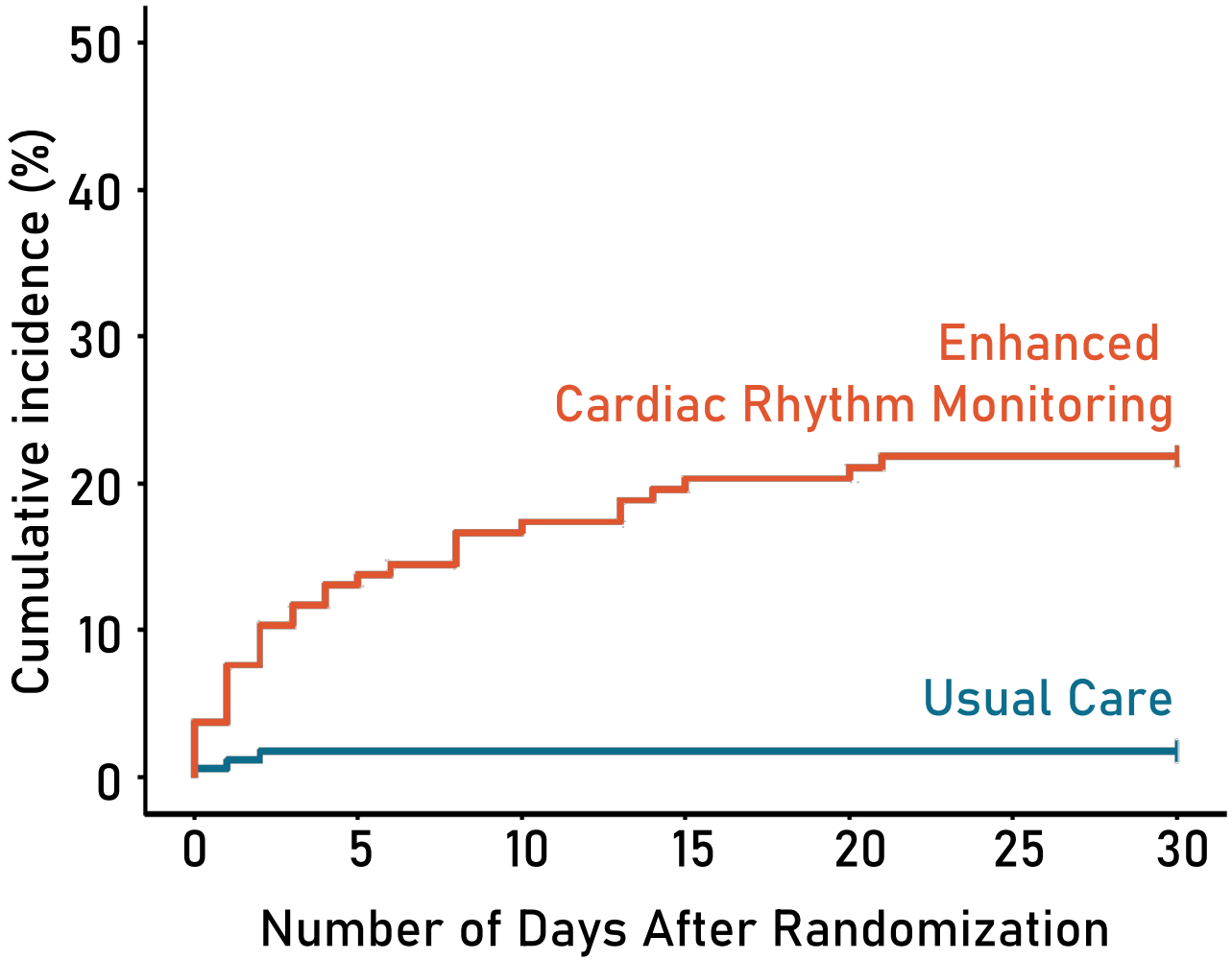
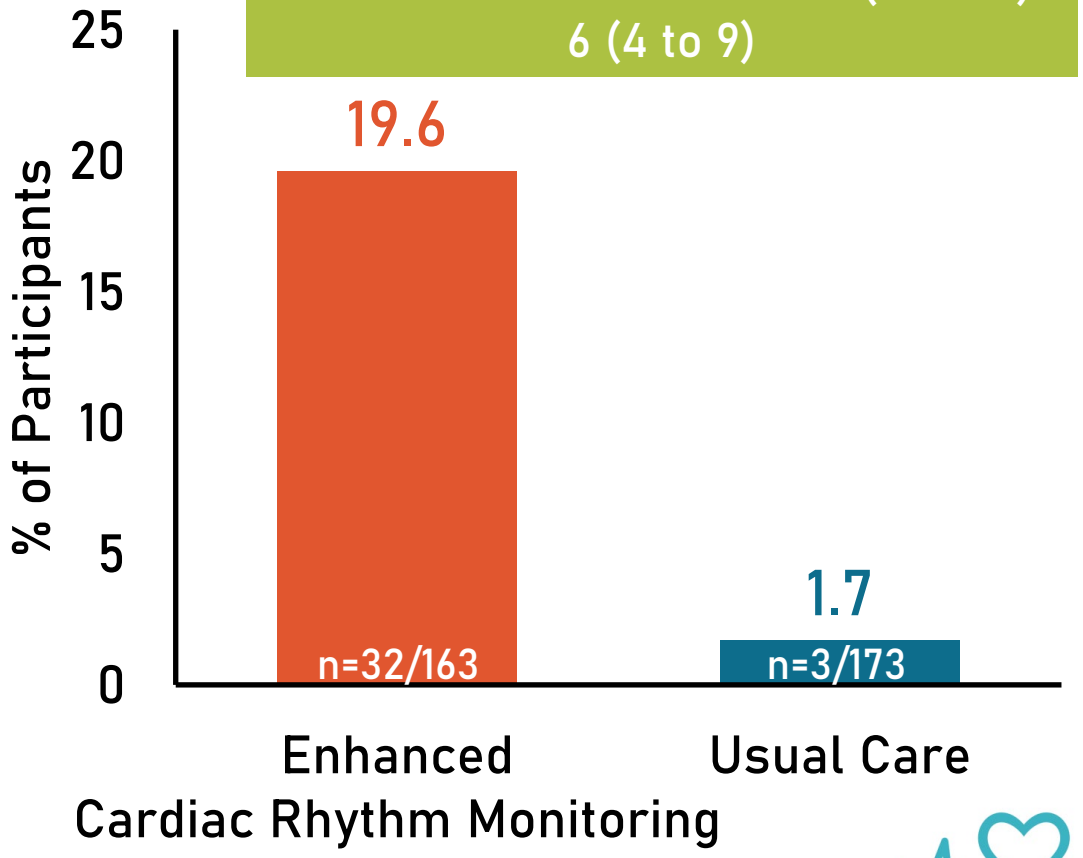
Primary Outcome: Cumulative AF/AFL duration ≥6 min or documentation of AF/AFL by a 12-lead ECG



Absolute rate difference (95% CI)
17.9% (11.5%, 24.3%) P<0.001

Number needed to screen (95% CI)
6 (4 to 9)



AF, atrial fibrillation; AFL, atrial flutter.

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Primary Outcome and Its Components

n (%) unless otherwise stated	Enhanced Cardiac Rhythm Monitoring (n=163)	Usual Care (n=173)	Rate Difference (95% CI)
Primary Outcome			
Cumulative AF/AFL duration ≥6 min or documentation of AF/AFL by a 12-lead ECG within first 30 days	32 (19.6)	3 (1.7)	17.9* (11.5 to 24.3)
Components of the Primary Outcome			
Cumulative AF/AFL duration ≥6 min within first 30 days	30 (18.4)	0 (0.0)	18.4* (12.5 to 24.4)
Documentation of ≥1 episode of AF/AFL by a 12-lead ECG within first 30 days	6 (3.7)	3 (1.7)	1.9 (-1.5 to 5.4)

AF, atrial fibrillation; AFL, atrial flutter.
* P <0.001.

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Secondary Outcomes

n (%) unless otherwise stated	Enhanced Cardiac Rhythm Monitoring (n=163)	Usual Care (n=173)	Rate Difference (95% CI)
Cumulative AF/AFL duration ≥6 hours within first 30 days	14 (8.6)	0 (0.0)	8.6 (4.3 to 12.9)
Cumulative AF/AFL duration ≥24 hours within first 30 days	5 (3.1)	0 (0.0)	3.1 (0.4 to 5.7)
Non-protocol mandated Holter/event recorder within first 30 days	5 (3.1)	4 (2.3)	0.8 (-2.7 to 4.2)
Prescription of oral anticoagulation within first 45 days	7 (4.3)	4 (2.3)	2 (-1.9 to 5.8)
Prescription of oral anticoagulation after 45 days	6 (3.7)	4 (2.3)	1.4 (-2.3 to 5)
Major bleeding within first 45 days	0 (0.0)	1 (0.6)	-0.6 (-1.7 to 0.6)
Major bleeding after 45 days	1 (0.6)	3 (1.7)	-1.1 (-3.4 to 1.2)
Death, MI, ischemic stroke, or non-CNS thromboembolism within the first 45 days	1 (0.6)	1 (0.6)	0 (-1.6 to 1.7)
Death, MI, ischemic stroke, or non-CNS thromboembolism after 45 days	1 (0.6)	3 (1.7)	-1.1 (-3.4 to 1.2)

AF, atrial fibrillation; AFL, atrial flutter; MI, myocardial infarction.
* P <0.001.

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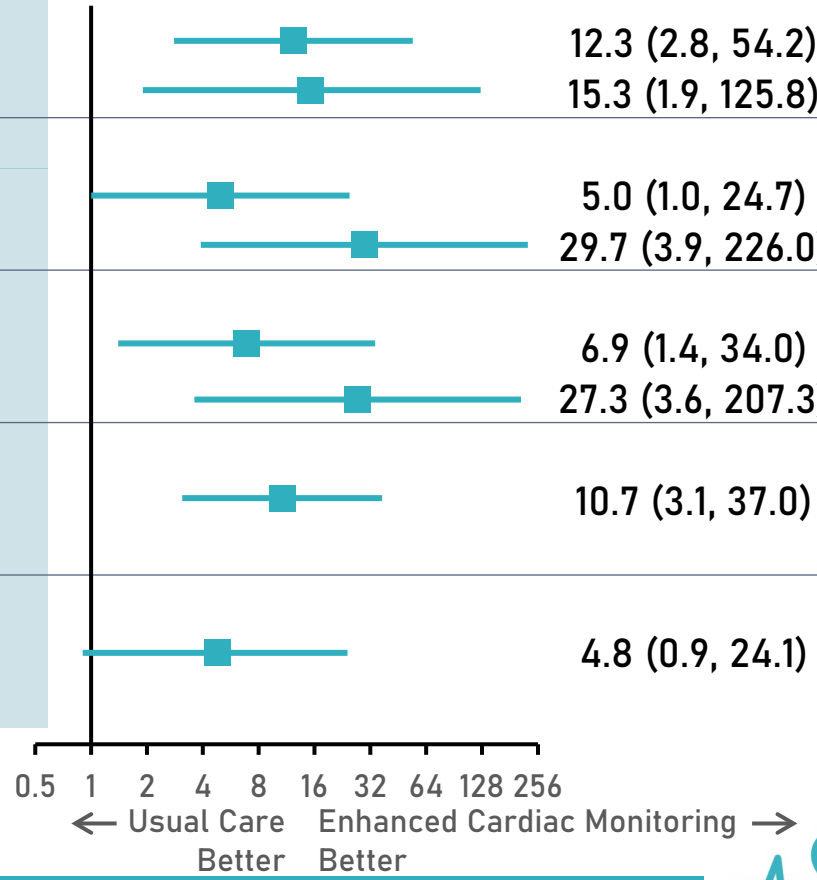
Primary Outcome
Stratified by Pre-specified Subgroups

Subgroup	No. of patients with events/Total No.		Adjusted Odds Ratio (95% CI)
	Enhanced Cardiac Rhythm Monitoring	Usual Care	
Isolated CABG			
Yes	20/124	2/131	12.3 (2.8, 54.2)
No	12/39	1/42	15.3 (1.9, 125.8)
Age			
<67 years	9/64	2/70	5.0 (1.0, 24.7)
≥67 years	23/99	1/103	29.7 (3.9, 226.0)
CHA_2DS_2-VASc score			
<4	8/56	2/80	6.9 (1.4, 34.0)
≥4	24/107	1/93	27.3 (3.6, 207.3)
Sex			
Male	26/128	3/135	10.7 (3.1, 37.0)
Female	6/35	0/38	
Large atrial enlargement			
Yes	8/63	2/64	4.8 (0.9, 24.1)
No	9/28	0/32	



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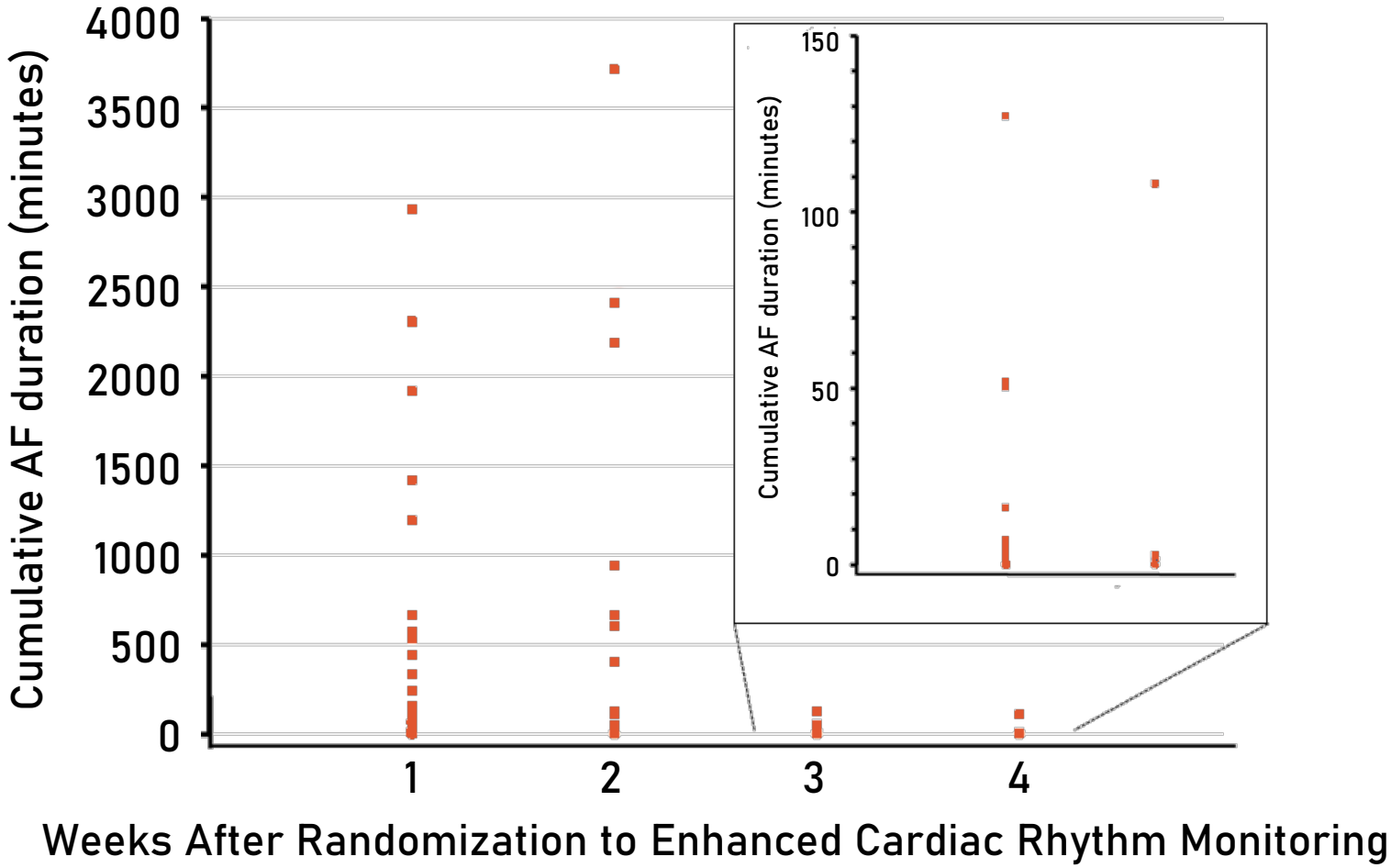
Cumulative AF Duration Per Patient in the Intervention Arm During the First 30 Days



AF, atrial fibrillation.
Each square represents a single patient who had AF detected within the first 30 days with continuous monitoring.

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Summary

In post-cardiac surgical patients at high risk of stroke and with little or no AF during index hospitalization, continuous rhythm risk of AF (by a factor of 10) vs. usual care.

Similar findings were seen for longer durations of detected AF include ≥6 hours and ≥24 hours

While incidence of POAF decreased over the 4 weeks of monitoring, it was much higher than a normal matched population (prior studies report an AF incidence of ~1-1.5 per 100 patient years in a general population with similar CHA_2DS_2-VASc score vs. 20% 30-day incidence observed in this trial)

The rates of oral anticoagulation were lower than the rates of detected AF

AF, atrial fibrillation; POAF, post-operative atrial fibrillation.

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Limitations

The primary endpoint was limited to 30 days with repeat monitoring at 6-months

This may have underestimated the long-term, ongoing risk of POAF

Only individuals with no/minimal AF burden in hospital were included

Those with prolonged stay were excluded

Both criteria could have underestimated POAF and CV events

SEARCH-AF was not powered to detect differences in stroke and whether oral anticoagulation would alter risk

AF, atrial fibrillation; CV, cardiovascular; POAF, post-operative atrial fibrillation.

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Conclusions and Implications

In patients who have undergone cardiac surgery (isolated CABG, valve, or CABG+valve) and have an elevated risk of stroke with no history of pre-operative or pre-discharge AF, a strategy of continuous rhythm monitoring unveiled a significant persistent burden of unrecognized and potentially actionable AF

POAF after cardiac surgery is not confined to the hospitalization period per se

These data should help inform on clinical practice guidelines on monitoring for POAF in such patients

AF, atrial fibrillation; CABG, coronary artery bypass graft surgery; POAF, post-operative atrial fibrillation.

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