Supplementary Online Content

Vinson DR, Warton EM, Durant EJ, et al. Decision support intervention and anticoagulation for emergency department atrial fibrillation: the O'CAFÉ stepped-wedge cluster randomized clinical trial. *JAMA Netw Open*. 2024;7(11):e2443097. doi:10.1001/jamanetworkopen.2024.43097

This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Management Recommendations Provided in the Clinical Decision Support Application RISTRA-AF to Improve Care of Emergency Department Patients with Primary Atrial Fibrillation or Flutter

Major Recommendations in Electronic Clinical Decision Support Application	Rationale for Recommendation
1. Sustained rate reduction	
Administer long-acting rate-reducing medications early in the ED encounter, either in addition to or in lieu of standard intravenous bolus medications	Medications with sustained effect on rapid ventricular response have been central to multifaceted ED interventions associated with reduced hospitalization.
2. Effective cardioversion	
2A. Electrical	
Start with maximal joules and consider manual pressure augmentation, especially for obese patients	These measures improve first-shock success and may reduce sedation duration and risk.
2B. Pharmacologic	
Consider efficiency in addition to effectiveness, safety, and ease of administration when selecting medications	For example, medications with a shorter time to effect, e.g., intravenous procainamide (median 30-40 min), facilitate ED operational efficiencies, unlike intravenous amiodarone, which does not distinguish itself from placebo for 6-8 hours.
3. Stroke prevention	
A. Identify patients at risk using auto-populating validated scoring system	Stroke risk stratification is the essential preparatory step for any subsequent stroke prevention action.
B. Print risk-specific handout for eligible patients and review with patient and family at bedside	The handout helps initiate a shared decision-making conversation on stroke prevention that can continue with outpatient physicians following discharge to home.
C1. Initiate outpatient anticoagulation at the time of ED discharge to home	Oral anticoagulation with DOACs or warfarin significantly reduces ischemic stroke and death in patients with AFF. Prescription on ED discharge can be associated with higher long-term use than when prescribing is left to post-discharge outpatient care.
C2. Or electronically consult the Anticoagulation Management Service to request they contact patients who want to learn more about stroke prevention before initiating anticoagulation	Following discharge to home, anticoagulation pharmacists can call interested patients to provide in-depth education on benefits and risks of anticoagulation for stroke prevention.
4. Timely Follow-up	
a. Encourage or request close follow-up (<7d) with outpatient physicians	Transferring care to outpatient physicians who can oversee longitudinal care of AFF and related conditions is key to long-term management

eTable 1. Management Recommendations Provided in the Clinical Decision Support Application RISTRA-AF to Improve Care of Emergency Department Patients with Primary Atrial Fibrillation or Flutter

Major Recommendations in Electronic Clinical Decision Support Application	Rationale for Recommendation
	success. Moreover, follow-up of these patients within a week of discharge has been associated with a reduction in the rate of death and hospitalization within 1 year.

AFF, atrial fibrillation or atrial flutter; DOAC, direct oral anticoagulant; ED, emergency department

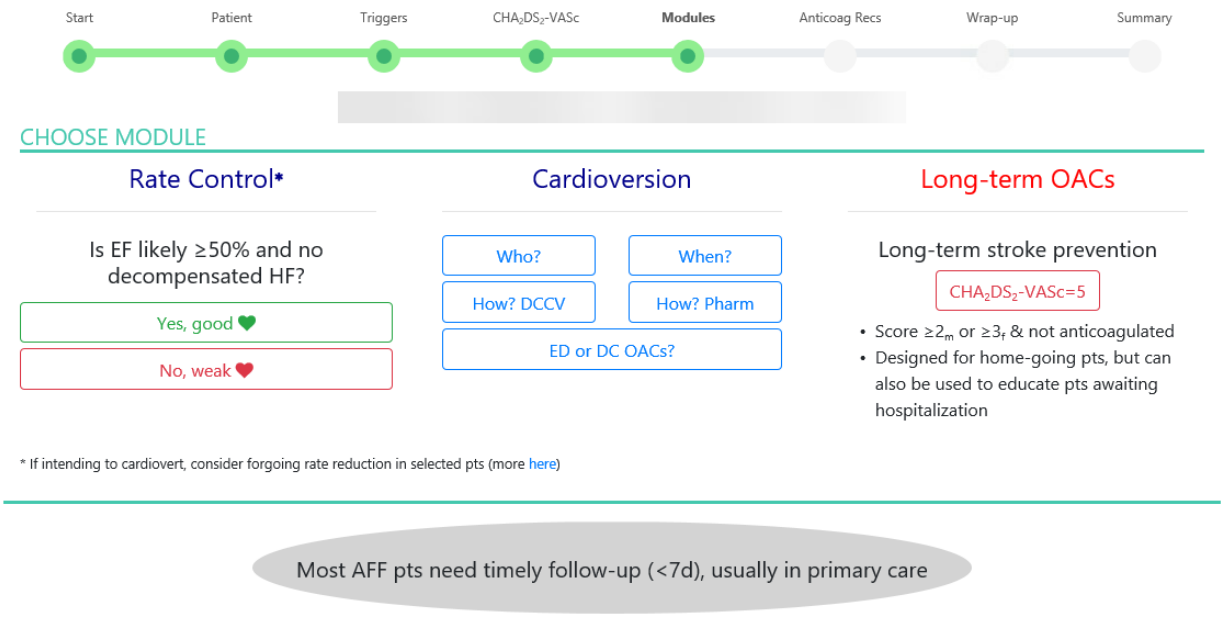
eMethods 1. Explanation of Open Cohort Design

The Stroke Prevention Aim of the O'CAFÉ trial was designed as an open-cohort study so that patients could technically have multiple eligible encounters during the study period. Patients who had only a single encounter would be counted as "churned", including patients who received the intervention, adhered to oral anticoagulation and thus were no longer eligible at subsequent AFF encounters. For this analysis we expected a high churn rate, with low numbers of patients with multiple eligible encounters. Among 1,203 eligible encounters in the study period, excluding washout periods, 1,149 patients had only 1 eligible ED encounter for a churn rate of 95.5%. The remaining 54 encounters included 47 patients with 2 eligible encounters and 7 patients with 3 or more encounters. We suspected these patients would be less likely to initiate recommended oral anticoagulation treatment, so we performed a sensitivity analysis including only the first encounter per patient. This resulted in minimal change to the odds ratio estimate and no change to the inference.

eMethods 2. Details of Decision Support Leading up to the Stroke Prevention Recommendations

Once activated, RISTRA-AF provided decision support on the leading clinical questions surrounding ED AFF management, e.g., rate control, cardioversion, and stroke prevention (**eTable 1; eFigure 1**). On the CHA_2DS_2-VASc screen (**eFigure 2**), demographic and clinical variables were pre-populated if available from the electronic health record. Clinician users reviewed the pre-populated entries and confirmed or edited as needed. The patient's CHA_2DS_2-VASc score was reported on this screen as well as the modules screen (**eFigure 1**). The stroke prevention module was not accessible if the physician had denoted earlier in RISTRA-AF that the patient was already on oral anticoagulation, if the patient had 1 of the 3 exclusions listed on the CHA_2DS_2-VASc screen (**eFigure 2**), or if the CHA_2DS_2-VASc score was below the thromboprophylaxis threshold (2 in men and 3 in women, as per U.S. guidelines).[2]

eFigure 1. Modules Screen of the RISTRA-AF Clinical Decision Support System



EF, ejection fraction; HF, heart failure; OAC, oral anticoagulation; pts, patients; ♥, heart.

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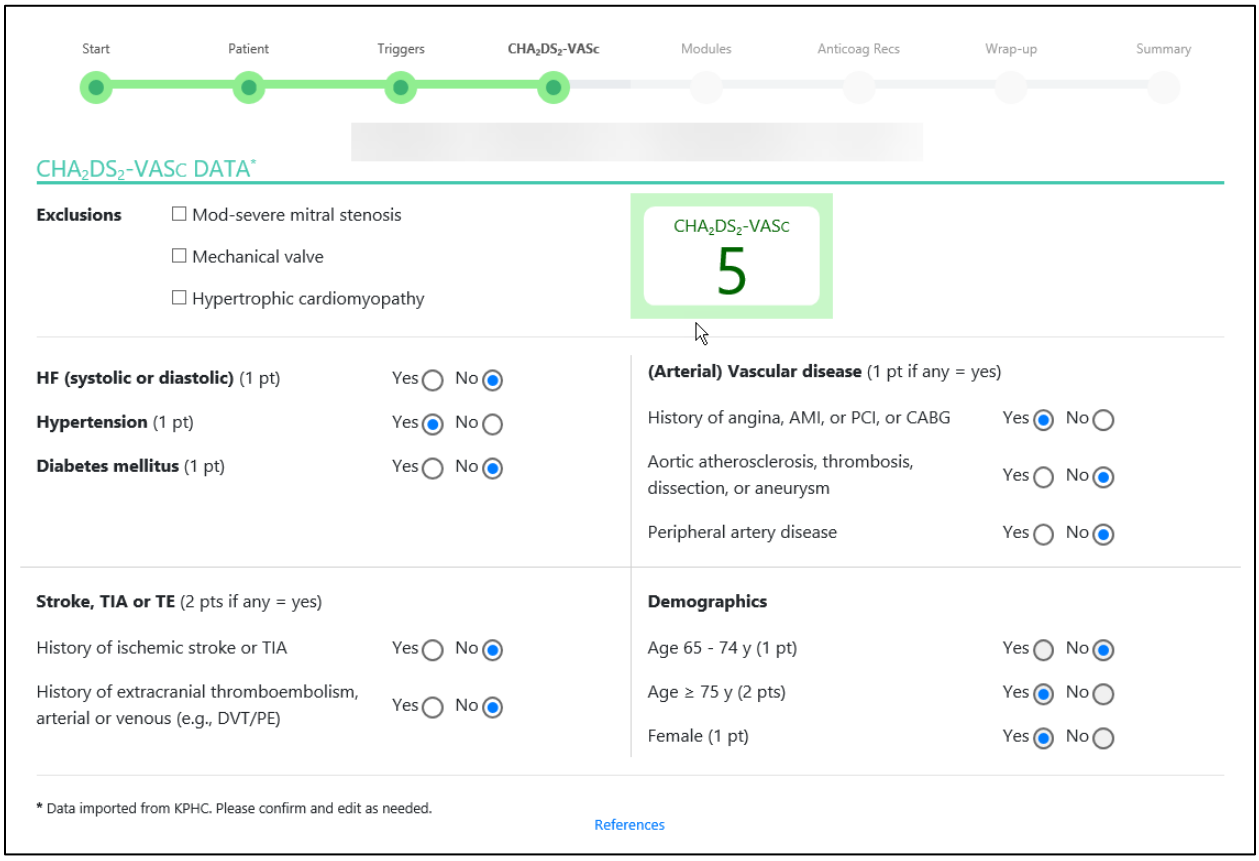
eFigure 2. The CHA_2DS_2-VASc Screen of the RISTRA-AF Clinical Decision Support Application



AMI, acute myocardial infarction; CABG, coronary artery bypass graft; DVT, deep vein thrombosis; HF, heart failure; PCI, percutaneous coronary intervention; PE, pulmonary embolism; pts, points; TE, thromboembolism; TIA, transient ischemic attack.

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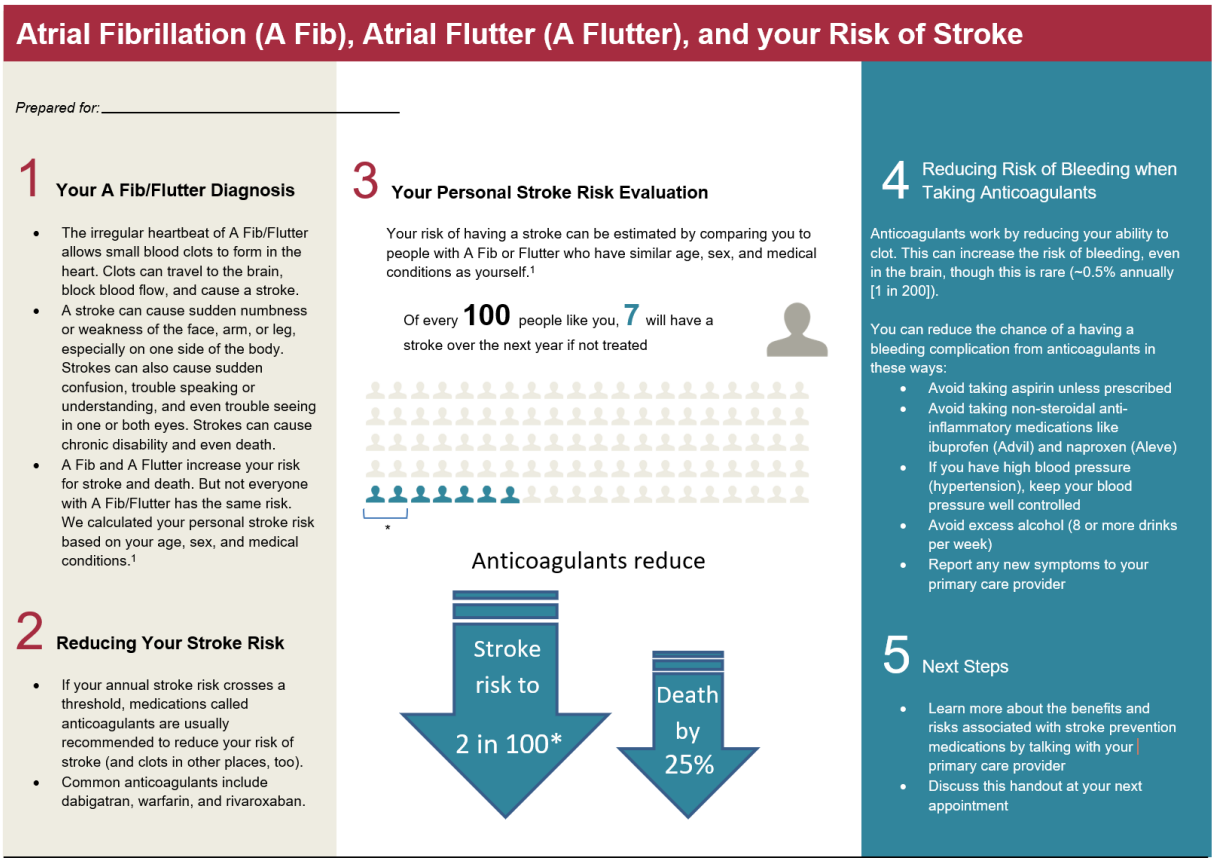
eFigure 3. Patient-Specific Handout Used in Shared Decision-Making on Stroke Prevention With At-Risk Emergency Department Patients With Atrial Fibrillation or Atrial Flutter



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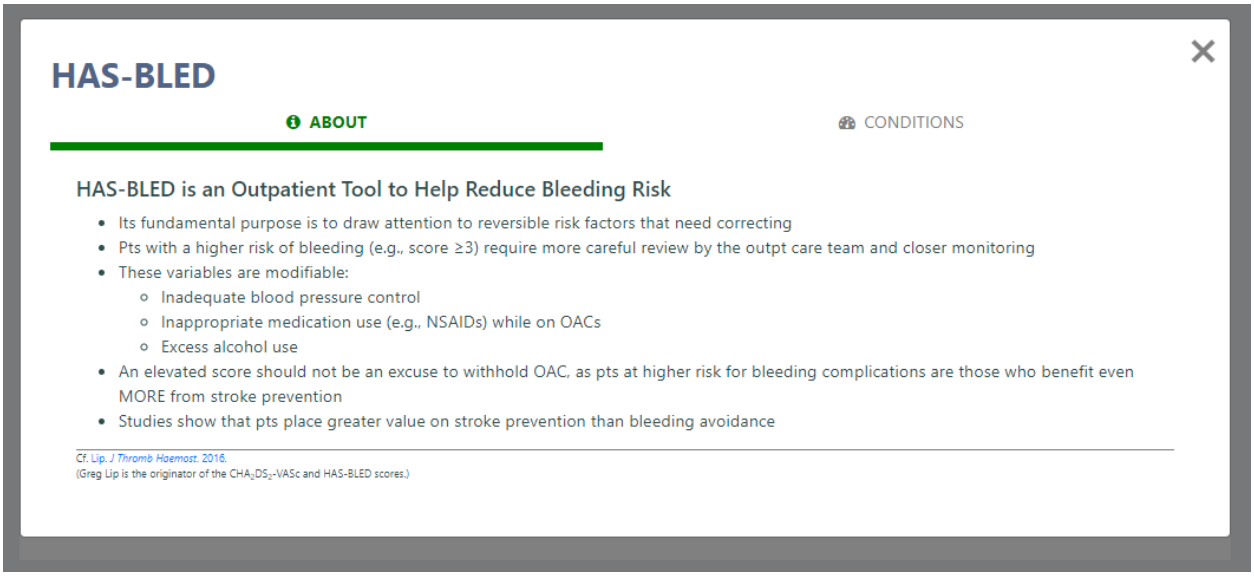
eFigure 4. The Screen in RISTRA-AF That Explains the HAS-BLED Tool



NSAIDs, non-steroidal anti-inflammatory drugs; OACs, oral anticoagulants; outpt, outpatient; pts, patients.

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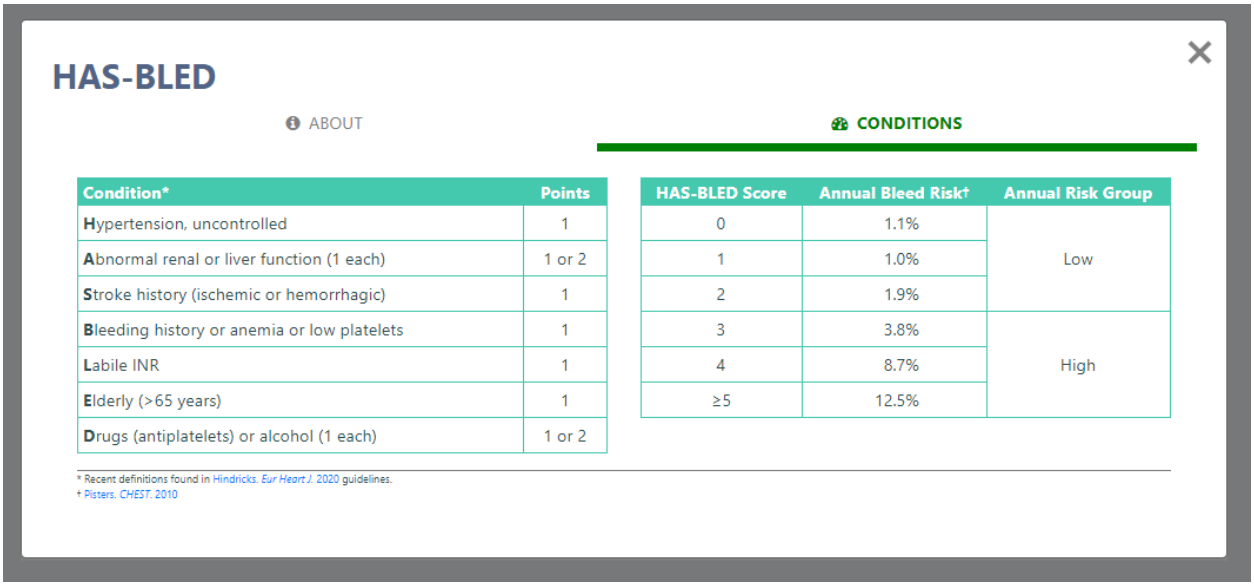
eFigure 5. The Screen in RISTRA-AF that Enumerates the Variables of the HAS-BLED Tool



INR, international normalized ratio.

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eMethods 3. Explanation of Power Calculation for the Larger O'CAFÉ Trial and the Stroke Prevention Aim (excerpted from our methods paper published in *Trials*[1] with additional references)

We estimate that our stepped-wedge design (with 9 clusters and 10 steps) will include approximately 3,420 adult ED encounters with primary and 972 (30%) with isolated AF or atrial flutter during the 10-month roll-out period. Based on pilot data, we expect at least 567 patients in the usual care condition and 460 patients in the intervention condition with isolated AF or atrial flutter during the 10-month roll-out period. Using preliminary data at the pilot sites and the trial sites, baseline initial hospitalization rate was 26.6%. We estimate a minimally detectable 8% absolute difference in initial hospitalization rate (Aim 1) at a level of 90% power and a 2-sided test at the 2.5% significance level.

We estimated the minimum number of clusters needed to achieve 90% power based on pilot data using the National Institutes of Health Stepped-wedge Group Randomized Trial Calculator.[3-9] We present our most conservative estimates here. For the hospitalization outcome, we assume an average of 11 eligible encounters per cluster, intraclass correlation of 0.01, the cluster autocorrelation of 0.47, and the individual autocorrelation of 0.9 with a discrete-time decay, a churn-rate of 0.942 and adjustment for 1 cluster-level variable (annual ED census) with R^2 of 0.07. We would need only 3 clusters to see a decrease of 8% in hospitalization rates at 90% power, so we believe that we have adequate power in this analysis, given data from 9 clusters over the course of the trial.

Given that only 18% of ED encounters are eligible for stroke prevention action (discharged to home, current KP member, not currently or recently taking oral anticoagulants, and at high risk for stroke), the overall numbers of eligible encounters for the stroke-prevention related outcomes are much smaller. For the primary Aim 2 outcome (any prescription ordered for oral anticoagulation medications within 30 days of the index visit), power is still adequate in this study design to identify changes in rates of prescriptions ordered as small as 5% in the eligible subgroup. Based on pilot data and assuming an average of 7 eligible encounters per cluster, intraclass correlation of 0.006, the cluster autocorrelation of 0.356, and the individual autocorrelation coefficient of 0 with a discrete-time decay, a churn-rate of 0.984 with no adjustments for cluster-level variables, our 9-cluster design will allow us to identify a 4.9% change in rates of anticoagulant prescription with 80% power.

eMethods 4. Explanation of Marginal Model

We used the PROC GLIMMIX procedure in SAS to fit a marginal model that is similar to a generalized estimating equations model in that it accounts for correlation within clusters and generates robust standard errors.[10] We specified R-side random effects to model the correlation within clusters and used the MBN method to adjust for potential bias in the empirical sandwich estimator due to small numbers of patients with repeated measures. The outcome was modeled as a binary distribution using a logit link and accounting for clustering by study cluster and individual patient. We assumed a covariance structure of compound symmetry for correlation within clusters.

eResults. Intraclass Correlation and Churn Rates

We used mixed model regression methods, examining within and between cluster correlation over time to see if time-decay correlation might apply.[3-9] In this smaller subset of encounters where the patient was eligible for oral anticoagulation intervention, the inter-cluster correlation was 0.019 for the trial period, and correlations between clusters, study time period, and the outcome were all small ($P<0.05$) and not statistically significant (all P values >0.16).

The intra-cluster correlation coefficient was low at 0.025 for study clusters but very high for repeated patients, as expected (0.96 with 54 out of 1203 patients with more than 1 eligible encounter). Review of intra- and inter-cluster correlation by study month did not indicate any time trends, and so compound symmetry was chosen to account for clustering by patient and study cluster in the analysis.

As expected, churn in the open cohort was quite high, with only 4.5% of patients having more than one eligible encounter during the trial period. Churn ranged from a low of 89.2% in month 8 of the trial period to 100% in 4 out of 22 trial months.

With the cohort split between 9 clusters over 22 trial months, mixed models for monthly intraclass correlation calculations did not have positive Hessian matrices. Summarizing into 3 time periods of 7 months each, intraclass correlation for study clusters were all low: 0.006, 0.003, and 0.102 for beginning, middle and ending periods. Intraclass correlations for patient clustering in these same 3 study periods were 0.96, 0.99, and 0.90, respectively.

eTable 2. Emergency Department Patients with Primary Atrial Fibrillation or Atrial Flutter Eligible for Anticoagulation Initiation on Intervention Condition, Stratified by Oral Anticoagulation Initiation on Discharge or Within 30 Days

Characteristics	Total (N=816) n (%)	Oral Anticoagulation Initiation		*P* value
		Yes (n=558) n (%)	No (n=258) n (%)	
Age, y				
Mean (SD)	74.5 (10.3)	74.4 (9.2)	74.6 (12.2)	0.80
Median (IQR)	74.0 (68.0-81.0)	75.0 (69.0-81.0)	73.0 (67.0-84.0)	0.84
Range	38.0-101.0	39.0-101.0	38.0-99.0	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	
Category				**0.04**
<65	109 (13.4)	63 (11.3)	46 (17.8)	
65-74	309 (37.9)	215 (38.5)	94 (36.4)	
≥75	398 (48.8)	280 (50.2)	118 (45.7)	
Female	406 (49.8)	278 (49.8)	128 (49.6)	0.96
Male	410 (50.2)	280 (50.2)	130 (50.4)	
Race/ethnicity, self-reported[a]				**0.03**
African American	60 (7.4)	36 (6.5)	24 (9.3)	
Asian	109 (13.4)	74 (13.3)	35 (13.6)	
Hispanic or Latinx	79 (9.7)	63 (11.3)	16 (6.2)	
White	533 (65.3)	356 (63.8)	177 (68.6)	
Other/Multi/Unknown[a]	35 (4.3)	29 (5.2)	6 (2.3)	
Index atrial arrhythmia				0.42
Atrial fibrillation	683 (83.7)	471 (84.4)	212 (82.2)	
Atrial flutter or both	133 (16.3)	87 (15.6)	46 (17.8)	
Comorbidities				
History of prior AFF	469 (57.5)	265 (47.5)	204 (79.1)	**<0.001**
Hypertension	677 (83.0)	469 (84.1)	208 (80.6)	0.23
Vascular disease	577 (70.7)	377 (67.6)	200 (77.5)	**0.004**
Diabetes	261 (32.0)	185 (33.2)	76 (29.5)	0.29
Congestive heart failure	113 (13.8)	55 (9.9)	58 (22.5)	**<0.001**
Ischemic stroke, transient ischemic attack, or thromboembolic disease	72 (8.8)	43 (7.7)	29 (11.2)	0.10
CHA_2DS_2-VASc Score				
Mean (SD)	4.0 (1.5)	4.0 (1.4)	4.1 (1.7)	0.35
Median (IQR)	4.0 (3.0-5.0)	4.0 (3.0-5.0)	4.0 (3.0-5.0)	0.87
Range	2.0-9.0	2.0-9.0	2.0-9.0	

eTable 2. Emergency Department Patients with Primary Atrial Fibrillation or Atrial Flutter Eligible for Anticoagulation Initiation on Intervention Condition, Stratified by Oral Anticoagulation Initiation on Discharge or Within 30 Days

Characteristics	Total (N=816) n (%)	Oral Anticoagulation Initiation		*P* value
		Yes (n=558) n (%)	No (n=258) n (%)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	
Category				**0.001**
2-3	345 (42.3)	229 (41.0)	116 (45.0)	
4-5	334 (40.9)	248 (44.4)	86 (33.3)	
≥6	137 (16.8)	81 (14.5)	56 (21.7)	
Decision Support Use				**0.008**
Yes	217 (26.6)	164 (29.4)	53 (20.5)	
No	599 (73.4)	394 (70.6)	205 (79.5)	

AFF, atrial fibrillation or atrial flutter.
[a]Other race/ethnicity includes Native American and Hawaii and Pacific Islander.

P values bold if <0.05.

eTable 3. Emergency Department Patients With Primary Atrial Fibrillation or Atrial Flutter Eligible for Anticoagulation Initiation During Intervention Phase, Stratified by Clinical Decision Support Use

Characteristics	Total (N=816) n (%)	Clinical Decision Support Use		*P* value
		Yes (n=217) n (%)	No (n=599) n (%)	
Age, y				
Mean (SD)	74.5 (10.3)	73.5 (10.2)	74.8 (10.3)	0.11
Median (IQR)	74.0 (68.0-81.0)	74.0 (68.0-79.0)	75.0 (68.0-82.0)	0.20
Range	38.0-101.0	39.0-99.0	38.0-101.0	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	
Category				0.34
<65	109 (13.4)	33 (15.2)	76 (12.7)	
65-74	309 (37.9)	87 (40.1)	222 (37.1)	
≥75	398 (48.8)	97 (44.7)	301 (50.3)	
Female	406 (49.8)	100 (46.1)	306 (51.1)	0.21
Male	410 (50.2)	117 (53.9)	293 (48.9)	
Race/ethnicity, self-reported[a]				0.76
African American	60 (7.4)	16 (7.4)	44 (7.3)	
Asian	109 (13.4)	31 (14.3)	78 (13.0)	

eTable 3. Emergency Department Patients With Primary Atrial Fibrillation or Atrial Flutter Eligible for Anticoagulation Initiation During Intervention Phase, Stratified by Clinical Decision Support Use

Characteristics	Total (N=816) n (%)	Clinical Decision Support Use		*P* value
		Yes (n=217) n (%)	No (n=599) n (%)	
Hispanic or Latinx	79 (9.7)	18 (8.3)	61 (10.2)	
White	533 (65.3)	140 (64.5)	393 (65.6)	
Other/Multi/Unknown[a]	35 (4.3)	12 (5.5)	23 (3.8)	
Index atrial arrhythmia				0.73
Atrial fibrillation	683 (83.7)	180 (82.9)	503 (84.0)	
Atrial flutter or both	133 (16.3)	37 (17.1)	96 (16.0)	
Comorbidities				
History of prior AFF	469 (57.5)	106 (48.8)	363 (60.6)	**0.003**
Hypertension	677 (83.0)	179 (82.5)	498 (83.1)	0.83
Vascular disease	577 (70.7)	147 (67.7)	430 (71.8)	0.26
Diabetes	261 (32.0)	70 (32.3)	191 (31.9)	0.92
Congestive heart failure	113 (13.8)	27 (12.4)	86 (14.4)	0.48
Ischemic stroke, transient ischemic attack, or thromboembolic disease	72 (8.8)	21 (9.7)	51 (8.5)	0.85
CHA_2DS_2-VASc Score				
Mean (SD)	4.0 (1.5)	3.9 (1.5)	4.1 (1.5)	0.16
Median (IQR)	4.0 (3.0-5.0)	4.0 (3.0-5.0)	4.0 (3.0-5.0)	0.17
Range	2.0-9.0	2.0-8.0	2.0-9.0	
Missing	0 (0.0)	0 (0.0)	0 (0.0)	
Category				0.15
2-3	345 (42.3)	90 (41.5)	255 (42.6)	
4-5	334 (40.9)	98 (45.2)	236 (39.4)	
≥6	137 (16.8)	29 (13.4)	108 (18.0)	

AFF, atrial fibrillation or atrial flutter.

[a]Other race/ethnicity includes Native American and Hawaii and Pacific Islander

P values bold if <0.05.

eDiscussion 1. Results in the Context of Our Power Calculations

The power calculations for this trial estimated 63 anticoagulation- eligible patients per month or 1,386 patients for the entire study period. Additional power calculation assumptions included a churn rate of 0.984, inter cluster correlation (ICC) of 0.006, cluster autocorrelation of 0.356, and an individual autocorrelation coefficient of zero assuming a discrete-time decay. Our power calculation estimated that we could identify a 4.9% increase in OAC action taken with 80% power.

During the study, only 1,203 OAC-eligible patients were identified —87% of what was anticipated, thus reducing power to detect our targeted difference. Our assumption of a low ICC was reasonable, with the ICC for the study period being slightly higher at 0.025, potentially reducing power slightly. However, our assumed cluster autocorrelation was incorrect. We checked for autocorrelation in each cluster using an autoregression model and found no evidence of autocorrelation within any of the study clusters during the study period. This lack of autocorrelation likely reduced power to detect a difference as the actual autocorrelation could not increase the precision of our estimate. We assumed an individual autocorrelation of zero and very high churn, with few patients contributing multiple measures in this open cohort. Our actual churn rate of 0.955 was slightly lower than anticipated, and the individual autocorrelation was quite high at 0.96, among the 54 patients with multiple measures. The high individual autocorrelation should increase power to detect a difference, but only slightly. Overall, we expect that the combination of these factors decreased our power to detect a difference of 4.9%, and so, although we identified a 5.4% increase, it failed to reach statistical significance (P=0.07 unadjusted, P=0.13 adjusted).

We also performed a sensitivity analysis using only the first eligible encounter for each patient to remove the impact of individual autocorrelation and the resulting estimate changed only minimally and still did not reach statistical significance.

eDiscussion 2. Pre-to-Post Studies of Anticoagulation-Focused Decision Support Interventions in the Emergency Department

Several pre-post studies of OAC-focused CDSS interventions in the ED have demonstrated improvements in OAC initiation among eligible patients with AF at and following discharge.[11-13] Comparisons between these studies and the O'CAFÉ trial are complicated by significant differences in study design (e.g., pre-post with lack of controls[12,13] or controls without randomization[11]), setting (e.g., university vs community), anticoagulation eligibility criteria (e.g., excluding patients >80 years,[12] who were included in O'CAFÉ), baseline ED OAC initiation rates (e.g., 15%[12] vs 49% in O'CAFÉ), the nature of interventions (e.g., providing post-ED follow-up in cardiology clinic[11-12]), and timing of OAC ascertainment (e.g., nothing beyond the ED[13] or 90 days beyond the ED[11]).

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