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Net clinical benefits of guidelines and decision tool recommendations for oral anticoagulant use among patients with atrial fibrillation

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Abstract

BACKGROUND—The 2012 CHEST, the 2012 European Society of Cardiology (ESC) and the 2014 American Heart Association guidelines and published decision tools by LaHaye and Casciano offer oral anticoagulant (OAC) recommendations for patients with atrial fibrillation (AF). The aim of our study was to compare the net clinical benefit (NCB) of OAC prescribing that was concordant with these decision aids.

METHODS—A cohort study of the 2001–2013 Lifelink claims data was used. NCB of concordance with each decision aid was defined as adverse events (thromboembolic and major bleed events) prevented per 10,000 person-years. Cox proportional hazard models were used to assess the relative risk of AF adverse events associated with concordance with each decision aid adjusted for potential confounders.

FINDINGS—The study included 15,129 AF patients, contributing 33,512 person-years. The NCB of the CHEST guidelines was the highest (NCB=30.07; 95%CI=28.66, 31.49) and the ESC guidelines the lowest (NCB=7.38; 95%CI=5.97, 8.80). Significant unadjusted decreases in the risk of AF adverse events associated with concordant OAC use/non-use were found for the CHEST guidelines (HR=0.825; 95%CI=0.695, 0.979), Casciano tool (HR=0.838; 95%CI=0.706, 0.995),

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and LaHaye tool (HR=0.841; 95%CI=0.709, 0.999), however none were significant after multivariate adjustment.

CONCLUSION—Concordant OAC use with any of the decision aids except the aggressive LaHaye tool led to a positive NCB. The decision aids based on CHA₂DS₂VASc algorithm did not consistently improve the NCB compared to CHADS₂ based aids. Recommending OAC use when CHA₂DS₂–VASc=1 resulted in a lower NCB when all other factors guiding recommendations were held constant.

Keywords

Atrial fibrillation; guideline; decision tool; concordance; Net clinical benefit

INTRODUCTION

Atrial fibrillation (AF) is a cardiac arrhythmia that increases the risk of ischemic stroke (IS) or thromboembolism (TE).¹ Oral anticoagulants are often prescribed in these patients to reduce the risk of IS/TE events. Warfarin and newer oral anticoagulants (OAC) are more effective than aspirin in reducing the IS/TE risk, but are also associated with an increased bleeding risk.² Therefore, evaluation of both stroke and bleeding risk are critical when considering anticoagulation of patients with AF.

The treatment recommendations of contemporary AF treatment guidelines are mainly based on ischemic stroke risk; only a few consider or formally incorporate bleeding risk when recommending OAC despite the availability of bleeding risk algorithms that accurately predict major bleed events.³ Widely accepted guidelines such as the 2012 American College of Chest Physicians' Evidence-Based Clinical Practice (CHEST) Guidelines and the 2014 American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society (AHA/ACC/HRS hereafter "AHA") guidelines do not incorporate bleeding risk algorithms when making OAC treatment recommendations in AF patients.^{4,5} Likewise, the 2012 European Society of Cardiology (ESC) guidelines for the management of atrial fibrillation considers the HAS-BLED bleeding risk but only recommends caution when prescribing anticoagulants in patients with a HAS-BLED score greater than or equal to 3.⁶ To address this problem, various clinical decision support tools have been developed which incorporate both the ischemic stroke risk and the bleeding risk.^{7–10}

Currently there is limited evidence documenting the overall benefit to patients in routine care when different guidelines are followed. The impact of inadequate adherence to the AF guideline recommendations was studied by Saarinen et al in 2014, however, they only assessed the AHA and ESC guidelines recommendations on 3-month mortality due to ischemic and hemorrhagic strokes using a small study sample (n=102).¹¹ In this study, we compared two decision tools developed and published by Casciano et al. and LaHaye et al. along with the three AF guidelines: the 2012 CHEST guidelines, the 2012 ESC guidelines and the 2014 AHA guidelines (decision tools and guidelines hereafter referred "decision aids").^{4–6,9,10} To our knowledge, no epidemiological study has been conducted to compare the clinical benefit of decision tools to AF guidelines.

The aim of our study was to compare the predictive ability of these aids by contrasting the net clinical benefit when OAC use is concordant and discordant with each of the aids. Since AF anticoagulant decisions are not based on single event rates such as ischemic stroke or major bleed, the standard measures of model performance such as model discrimination could not be used directly. Instead, we compared composite stroke/bleed event rates of these tools when anticoagulant prescribing is concordant and when it is discordant with the treatment recommendations. This will allow clinicians to identify the differences between these aids and offer insights on which decision aid may have more clinical value in rendering anticoagulant recommendations when followed in routine care.

METHODS

Study Design and Study Measures

A cohort study design using the 2001–2013 Pharmetrics Lifelink claims data was used to compare the net clinical benefit (NCB) of AF patients who were concordant versus discordant with the decision aids. Pharmetrics Lifelink is representative of the commercially insured population of the US with respect to age, gender, geographic location and the type of insurance coverage. The database includes inpatient claims, outpatient claims, prescription claims and eligibility data. The study subjects were incident AF cases without any AF related claims the year prior to their first primary AF diagnosis. For each subject, we calculated the CHADS₂¹², CHA₂DS₂–VASc¹³, HAS-BLED¹⁴, ATRIA¹⁵ scores and other measures necessary for the 2012 CHEST, the 2012 ESC, the 2014 AHA guidelines, and LaHaye and Casciano tools to render an OAC recommendation. Because the AHA guidelines do not offer clear guidance when the CHA₂DS₂–VASc = 1 we constructed two scenarios; AHA aggressive which recommended OAC when CHA₂DS₂–VASc = 1 and AHA conservative which recommended withholding OAC when CHA₂DS₂–VASc = 1. In order to operationalize recommendations of the ESC guidelines which incorporate bleeding risk, when CHA₂DS₂–VASc = 1 and HAS-BLED ≥ 3 we defined that as a recommendation to withhold OAC and when CHA₂DS₂–VASc = 1 and HAS-BLED < 3 we defined that as an OAC recommendation. Bleeding risk was not considered for any other levels of CHA₂DS₂–VASc scores. OAC exposure was determined within the first 90 days after the index AF diagnosis using both prescription fills (for warfarin, dabigatran, apixaban or rivaroxaban) and inpatient/outpatient claims data (for INR testing). We compared those recommendations with actual OAC exposures to determine concordant and discordant OAC use/non-use. When patient's OAC exposure status was consistent with decision aid recommendation (OAC recommended and OAC exposed, OAC not recommended and OAC unexposed), that patient was considered to be concordant with the treatment recommendation of the respective decision aid and vice versa for discordant use. More details of the data source, incident AF study subjects, definitions of OAC exposure based on prescription fills (warfarin, dabigatran, apixaban or rivaroxaban), INR testing, details in determining decision aid recommendations, and other study measures are described in our previous work.¹⁶

Outcome measures

The adverse outcome events included ischemic stroke (IS), other thromboembolic events, and both intracranial (ICH) and extracranial bleeding (ECH) events based on the ICD-9-CM codes which were previously validated.^{10,17} Inpatient claims data is a more accurate source to identify “major” adverse events, inasmuch as major adverse events would invariably lead to hospitalization. We considered only the primary diagnosis to increase our certainty that the hospitalization was due to one of our adverse events and not as a secondary complication or a record of a prior complication. For each outcome, a patient was followed after the OAC exposure period (90 days after initial AF diagnosis) until the date of his/her first event (stroke or major bleed event), the study end date, or disenrollment, whichever came first.

Analyses

Currently, there are no standards to compare clinical decision support tools and guidelines when multiple outcomes (major bleeds and ischemic strokes) are simultaneously considered. To assess the appropriateness of treatment recommendations by each decision aid, we compared the number of adverse events prevented per 10,000 person years calculated as the difference between the adverse events rates of discordant and concordant subjects. A positive number indicates that the stroke/bleed event rate is higher among the treatment discordant group compared to the treatment concordant group. The number of stroke events and bleed events prevented were assessed individually first for each decision tool. To compare the overall performance of the decision aid, the net clinical benefit (NCB) was then calculated as a composite measure incorporating both stroke and bleed events prevented. The NCB was calculated using two approaches: 1) we determined the NCB as the number of all AF adverse events prevented which includes all thromboembolic events (TE) including IS and all major bleed events, 2) we determined NCB as the number of major AF adverse events prevented, which only included IS and ICH. A higher NCB indicates fewer adverse events among concordant use compared to discordant use.

Unadjusted and adjusted Cox proportional hazards models¹⁸ were used to assess the risk of all AF adverse (including thromboembolic and major bleed) events between patients who were concordant versus those who were discordant with the recommendations of each decision aid. The adjusted models controlled for the following factors not incorporated in the CHADS₂ that have been shown to be prognostic for major bleed or thromboembolic events: age, gender, diabetes, heart failure, vascular diseases, anemia, renal failure, liver failure, prior stroke, prior bleed, alcohol abuse and other medication use (anti-platelet, GI protectants, NSAIDs heparin, immunosuppressant, corticosteroids) and also included geographic region, year of diagnosis to control for potential regional and temporal differences. It was hypothesized that the hazard ratio for concordant OAC use for each decision aid that confers the highest NCB will have a lower relative risk (lower hazard ratio) of AF adverse events.

Sensitivity Analyses

To assess the robustness of our analysis, we conducted four additional sensitivity analyses. 1) The OAC exposure definition was restricted to the prescription claims data exclusively and did not consider INR/PT lab tests to define OAC exposure. 2) The LaHaye tool

recommendations for OAC use can vary depending on the treatment threshold, cost threshold and bleed ratio preferences selected. Thus, we considered two extremes of the LaHaye tool to produce the most conservative (fewest OAC recommendations) and aggressive (most OAC recommendations) scenarios. These two alternative scenarios were obtained by using fixed values of the treatment threshold, the cost threshold and bleed ratio (Table S1 and Table S2 in Appendix). 3) A weighting factor of 1.5, adopted by Singer et al.¹⁹ was used to adjust for the severity of intracranial events relative to ischemic stroke in the approach that only considered IS and ICH events to calculate NCB. 4) To assess the impact of changes in exposure status over time, a patient was censored when a previously OAC unexposed patient was exposed to OAC or if an OAC exposed patient discontinued OAC (defined as a gap in OAC therapy of more than 90 days). 5) Accounting for stroke and bleeding risk factors in the adjusted Cox models could result in over-adjusting of the models as the decision aid recommendations already incorporate some or all of these factors. To address this issue, we conducted two sub-analyses; i) adjusted Cox models without accounting for CHADS₂ factors and ii) adjusted Cox models without accounting for any of the stroke and bleeding risk factors used in CHADS₂, CHA₂DS₂-VASc, HAS-BLED and ATRIA algorithms. All analyses were performed using SAS version 9.3 (SAS Institute Inc., Cary, NC). The study was approved by the University of Arkansas for Medical Sciences Institutional Review Board.

RESULTS

A total of 15,129 AF patients with a median follow up time of 1.84 years (IQR: 3.17 – 0.92) contributing 33,512 person-years met the study inclusion criteria. The demographic characteristics of the study cohort and concordance of OAC use with each of the decision aids have been previously reported.¹⁶ The rates of ischemic stroke were lower for those who were OAC exposed (56.62 vs. 68.69 events per 10,000 person-years) whereas intracranial hemorrhagic event rates (26.23 vs. 16.12 events per 10,000 person-years) and major extra-cranial event rates (71.55 vs. 56.75 events per 10,000 person-years) were higher for those who were OAC exposed compared to OAC unexposed (Table #1).

The NCB considering all thromboembolic and major bleed events was highest when OAC use/non-use was concordant with recommendations of the CHEST guidelines (NCB=30.07; 95%CI=28.66, 31.49), followed by the Casciano tool (NCB= 27.36; 95%CI=25.94, 28.78), the LaHaye tool (NCB=26.56; 95%CI=25.14, 27.97), AHA Conservative guidelines (NCB=21.65; 95%CI=20.23, 23.07), the AHA Aggressive guidelines (NCB=8.81; 95%CI=7.39, 10.22) and ESC guidelines (NCB=7.38; 95%CI=5.97, 8.80) (Table # 2). Concordance with treatment recommendations across the decision aids resulted in fewer strokes (0.58–25.91 events prevented/ 10,000 person-years). The risk of major bleed events, however, was higher when OAC use/non-use was concordant with the AHA aggressive (–8.98 events/10,000 person-years) and ESC guideline (–10.30 events/10,000 person-years) compared to their discordant counter groups. The NCB considering only IS and ICH events was highest for patients concordant with the CHEST guidelines (NCB=25.31; 95%CI=24.01, 26.62) followed by the Casciano tool (NCB=23.46; 95%CI=22.16, 24.76), AHA Conservative guidelines (NCB=21.86; 95%CI=20.56, 23.16), the AHA Aggressive

guidelines (NCB=15.37; 95%CI=14.07, 16.67), the ESC guidelines (NCB=15.26; 95%CI=13.96, 16.55) and the LaHaye tool (NCB=11.41; 95%CI=10.12, 12.71) (Table #3).

Concordance with OAC use/non-use resulted in lower risk of any AF adverse events with the CHEST guideline (HR=0.825; 95%CI=0.695, 0.979), Casciano tool (HR=0.838; 95%CI=0.706, 0.995), and LaHaye tool (HR=0.841; 95%CI=0.709, 0.999), however, concordance with the two AHA guideline scenarios or ESC guidelines did not confer a significant risk reduction (Table # 4). After adjusting for all potential confounders, there was no significant decrease in the risk of AF adverse events associated with concordant OAC use/non-use for any of the decision aids.

A sensitivity analysis in which the definition of OAC exposure was restricted to prescription claims exclusively largely preserved the rank order of decision aids with respect to NCB values except the LaHaye tool produced the highest NCB which originally ranked 3rd in the base case analysis (Table S3 in Appendix). However, altering the definition of the LaHaye tool recommendations led to a negative NCB estimate with OAC aggressive recommendations and a positive NCB estimate with the OAC conservative recommendations (Table S4 in Appendix). The rank order of the first 3 decision aids (CHEST guidelines, Casciano tool and AHA Conservative) for NCB estimates was consistent when ICH events were weighted by the factor of 1.5 (Table S5 in Appendix). When time to event was censored at the time of a change in exposure status, the rank order for the NCB estimates changed where the LaHaye tool had the highest NCB (52.94; 95%CI=51.52, 54.36) followed by the Casciano tool (32.80; 95%CI=31.38, 34.22), AHA Conservative guidelines (23.11; 95%CI=21.69, 24.53), CHEST guidelines (22.54; 95%CI=21.12, 23.96), AHA Aggressive guidelines (-11.80; 95%CI=-13.22, -10.38) and ESC guidelines (-12.02; 95%CI=-13.44, -10.60; Table# 5). Although all the decision aid recommendations were associated with stroke risk prevention in the sensitivity analysis that censored based on OAC status (8.14–31.28 events/ 10,000-person years), only the Casciano (1.51 events/ 10,000 person-years) and LaHaye (44.80 events/ 10,000 person-years) tool recommendations led to bleed prevention when the treatment concordant groups were compared against treatment discordant groups. Excluding CHADS₂ factors from the adjusted Cox models did not significantly alter the findings, however, excluding all the factors accounted for in the stroke and bleed algorithms showed that the CHEST, Casciano and Lahaye tools significantly reduced the risk of AF adverse events (Table S6 in Appendix).

DISCUSSION

The NCB of a decision aid highlights the increased stroke risk associated with underuse of OACs and an increase in the bleeding risk associated with overuse of OACs. All of the tools, except for the LaHaye OAC aggressive recommendations in our base case analyses, lead to a significant positive NCB. Studies have shown that incorporation of these decision aids into clinical practice could result in more appropriate prescribing of anticoagulants by recommending against anticoagulation in low stroke/high bleeding risk patients and promoting use of anticoagulants in patients who are at high risk of stroke.^{10,20,21} These decision aids incorporate patient characteristics and medical history to render treatment

recommendations thereby promoting evidence-based practice rather than physician's perception-driven decision-making.²² All the algorithms used to develop these decision aids have proven prognostic for AF adverse events,^{12,23–25} therefore use of all but the LaHaye OAC aggressive recommendations may provide additional benefit over physician driven anticoagulant decisions.

Our study also offers some insights regarding the classification of stroke risk using either the CHA₂DS₂–VASc or the CHADS₂ algorithm. The decision aids that are based on the newer CHA₂DS₂–VASc algorithm did not consistently offer an additional benefit over the decision aids that are based on the CHADS₂ algorithm. The NCB values of the CHADS₂ based decision aids (the CHEST guideline and Casciano tool) were either significantly higher or non-inferior compared to the decision aids that are based on CHA₂DS₂–VASc algorithm in our base case analysis. However, this finding was sensitive to some of our key approaches. When patients' time to event were censored at a change in OAC exposure based exclusively on prescription claims, the ranking of NCB was mixed between those based on CHA₂DS₂–VASc and CHADS₂ algorithms. In both of those sensitivity analyses, the LaHaye tool (based on the CHA₂DS₂–VASc algorithm) outperformed other decision aids; however, the CHADS₂ based CHEST guidelines and Casciano tool were still ranked in the top 4 among all decision tools. The most direct difference between CHADS₂ and CHA₂DS₂–VASc can be observed by comparing the two AHA guidelines and the CHEST guidelines, neither of which considered bleeding risk but differed primarily on IS risk assessment. We found that the CHADS₂ based CHEST guidelines yielded a higher NCB than either of the AHA guideline scenarios in our base case analysis and all but one of our sensitivity analyses. Our finding that the CHA₂DS₂–VASc algorithm did not offer a consistent benefit corroborates a recent systematic review that recommended the use of CHADS₂ score until stronger evidence is available in favor of CHA₂DS₂–VASc algorithm.²⁶ Although the CHA₂DS₂–VASc algorithm was developed in 2010, the 2012 CHEST guideline recommends CHADS₂ score due to lack of evidence supporting the use of CHA₂DS₂–VASc score over CHADS₂ score.⁵

The 2014 AHA guidelines do not offer a clear recommendation for anticoagulation in patients with CHA₂DS₂–VASc score=1, and our data could be used to inform OAC recommendations at this level of stroke risk. By comparing our AHA conservative (recommend withholding OAC when CHA₂DS₂–VASc score=1) and AHA aggressive (recommend OAC when CHA₂DS₂–VASc score=1) recommendations our data offer a direct comparison holding all other factors constant. We found that the AHA aggressive recommendations had a lower NCB than the AHA conservative approach which was consistent across all of our sensitivity analyses. Utilizing the AHA conservative guidelines instead of the AHA aggressive would prevent about 13 major bleeding or thromboembolic adverse events per 10,000 person-years. Our data suggest that patients with CHA₂DS₂–VASc score =1 have more potential for harm from the increased risk of bleeding than potential benefit from decreased risk of stroke when anticoagulated which is consistent with a recently conducted epidemiological study.²⁷

Another issue in rendering OAC recommendations is whether to consider and quantify bleeding risk in addition to ischemic stroke risk.^{28,29} Three of the aids we compared

quantified bleeding risk (Casciano, LaHaye, ESC), however only the Casciano and LaHaye tools incorporate bleeding risk as a factor across the entire spectrum of ischemic stroke risk but also incorporate other factors such as quality of life adjustments and cost information.^{6,9,10} The NCB estimates of these two tools were somewhat mixed. In our base case analysis, neither of these tools had the highest NCB, however, the Casciano tool had the second highest NCB which was not significantly different than the CHEST guidelines, which had the highest NCB. In two of our sensitivity analyses the LaHaye tool was the highest ranked tool, and the Casciano tool was among the top three with the highest NCB. This may suggest that under certain situations, quantification of bleeding risk may result in improved OAC recommendations than guidelines that do not incorporate bleeding risks. , However, additional study is warranted because the NCB differences of these tools with other guidelines could be attributed to other factors besides quantification of bleeding risk.

Limitations

The exposure cohort consisted primarily of patients who were taking warfarin as the newer OACs were not available during most of the time periods for which data are available. Hence, we could not calculate the NCB between warfarin and the novel anticoagulants. Furthermore, the data do not completely capture OTC use of aspirin, those that we defined as OAC unexposed may represent a mixture of persons taking and not taking aspirin. The anticoagulant exposure definition in our base-case analysis was based on anticoagulant use within first 90 days after index AF diagnosis and could change over time. We conducted a sensitivity analysis that censored the patient time when OAC exposure changed to address this limitation and we found that 27 stroke and 61 bleed events were not accounted as the time during which these events occurred was censored due to change in exposure. This resulted in a substantial change in NCB estimated for LaHaye tool. Although this sensitivity analysis addresses changing OAC status, it does not incorporate updated bleeding and stroke risk such as new diagnoses of hypertension over time. Our OAC exposure definition relied on the receipt of OAC or two or more INR/PT claims which may misclassify some persons as receiving OAC; however, our results were largely robust to a more restrictive OAC definition relying solely on prescription claims. Although we used administrative claims data which can introduce measurement error in to identifying the outcome events, the ICD-9 codes used to identify outcomes were previously used by Casciano et al.¹⁷ and were validated by Go et al.³⁰ using the medical records. The outcome event rates found in our study were similar to the rates reported by Go et al.³⁰

Though our unadjusted Cox-models largely corroborated our NCB findings, the fully adjusted Cox-model results did not find a significant reduction in the risk of adverse events when OAC status was concordant with any of decision aids we examined. This may be due to a true null association, the moderate sample size, or over-adjusting the data. When we excluded factors used in quantifying stroke or bleeding risk that are already incorporated in the decision aids, concordance with the CHEST, Casciano and Lahaye tools significantly reduced AF adverse events. The NCB values associated with the base case analysis of the LaHaye tool recommendations should be considered as one of many possible scenarios of the LaHaye tool and not an assessment of the entire LaHaye approach given that recommendations are flexible and can vary with the patient preference for treatment

threshold, bleed ratio and cost threshold. Also, we assumed that the ESC guideline recommends non-OAC in patients with patients with $\text{CHA}_2\text{DS}_2\text{-VASc}$ score=1 and HAS-BLED = 3. However, the two scenarios of AHA guideline could be viewed as a sensitivity analysis for alternative definitions of ESC guideline recommendations which did not consider bleeding risk when $\text{CHA}_2\text{DS}_2\text{-VASc}$ score=1. Lastly, the data are representative of a commercially insured population which we found to have a lower mean age than other AF studies and the study findings may not be applicable to other populations.

Conclusion

We found that use of any of the decision aids we tested except the aggressive LaHaye tool led to a positive NCB. The decision aids which were based on the new stroke risk algorithm ($\text{CHA}_2\text{DS}_2\text{-VASc}$) did not consistently improve the NCB compared to the decision aids which are based on CHADS_2 score. A recommendation in favor of OAC use in persons with a $\text{CHA}_2\text{DS}_2\text{-VASc}$ =1 resulted in a lower NCB. Incorporating bleeding risk algorithm along with stroke risk may improve the NCB of the decision aid. Our study findings are important for building upon the evidence base demonstrating implications of guideline/decision tool recommendations in real world settings, particularly highlighting that adherence to different decision aid recommendations could result in improved outcomes. Our findings offers some initial insights as to which decision aids that might outperform others when followed, however larger epidemiologic studies are warranted before any one of the decision aids can be recommended over others to routinely guide OAC treatment decisions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Adverse event rate among OAC exposed and unexposed patients:

AF adverse events	OAC exposed		OAC unexposed		Total population	
	N	Event rate	N	Event rate	N	Event rate
Total events	278	165.75	248	148.14	526	156.96
<i>Ischemic stroke</i>	100	56.62	115	68.69	215	64.15
<i>Other thromboembolic events</i>	14	8.34	11	6.57	25	7.46
<i>Intracranial haemorrhage</i>	44	26.23	27	16.12	71	21.19
<i>Major Extra-cranial bleed events</i>	120	71.55	95	56.75	215	64.15
<i>Total person-years</i>	16771		16741		33512	

Note: Event rates are expressed in events per 10,000 person-years.

Table 2

Net clinical benefit of TE and any major bleed event prevention by being concordant with decision aid recommendations:

Decision aid	Concordant status	TE events	Bleed events	Person-years	TE events prevented	Bleed events prevented	NCB (CIs)
AHA Aggressive	Concordant	114	161	17988			
	Discordant	126	125	15523	17.79	-8.98	8.81 (7.39, 10.22)
AHA Conservative	Concordant	118	156	18598			
	Discordant	122	130	14913	18.36	3.29	21.65 (20.23, 23.07)
Casciano	Concordant	117	160	19080			
	Discordant	123	126	14431	23.91	3.45	27.36 (25.94, 28.78)
CHEST guidelines	Concordant	115	159	19032			
	Discordant	125	127	14479	25.91	4.17	30.07 (28.66, 31.49)
ESC guidelines	Concordant	114	162	17976			
	Discordant	126	124	15535	17.69	-10.30	7.38 (5.97, 8.80)
LaHaye	Concordant	121	123	16963			
	Discordant	119	163	16549	0.58	25.98	26.56 (25.14, 27.97)

Note: NCB estimate includes both thromboembolic and major bleed events prevented by being concordance with decision aid recommendations. AF adverse events: Thromboembolic events (including ischemic stroke), Bleed events: Any type of major bleed event, TE prevented: Number of TE events prevented per 10,000 person years by being concordant with decision aid recommendations, Bleed prevented: Number of bleed events prevented per 10,000 person years by being concordant with decision aid recommendations. AHA Aggressive: AHA guidelines (assuming that guideline recommends OAC at CHA₂DS₂-VASC =1), AHA Conservative: AHA guidelines (assuming that guideline recommends withholding OAC at CHA₂DS₂-VASC =1), Casciano: Casciano tool, CHEST: CHEST guidelines, ESC: ESC guidelines, LaHaye: LaHaye tool.

Table 3

Net clinical benefit of IS and ICH event prevention by being concordant with decision aid recommendations:

Decision aid	Concordant status	IS events	ICH events	Person-years	IS events prevented	ICH events prevented	NCB (CIs)
AHA Aggressive	Concordant	103	43	18169			
	Discordant	121	29	15668	20.53	-5.15	15.37 (14.07, 16.67)
AHA Conservative	Concordant	108	38	18778			
	Discordant	116	34	15058	19.51	2.34	21.86 (20.56, 23.16)
Casciano	Concordant	108	41	19259			
	Discordant	116	31	14578	23.49	-0.02	23.46 (22.16, 24.76)
CHEST guidelines	Concordant	106	41	19208			
	Discordant	118	31	14629	25.47	-0.155	25.31 (24.01, 26.62)
ESC guidelines	Concordant	103	43	18157			
	Discordant	121	29	15679	20.44	-5.19	15.26 (13.96, 16.55)
LaHaye	Concordant	113	27	17107			
	Discordant	111	45	16729	0.30	11.12	11.41 (10.12, 12.71)

Note: NCB estimate includes ischemic stroke and intracranial hemorrhage events prevented by being concordant with decision aid recommendations. IS events: Ischemic stroke events, ICH events: Intracranial hemorrhage, IS events prevented: Number of IS events prevented per 10,000 person years by being concordant with decision aid recommendations, ICH events prevented: Number of ICH events prevented per 10,000 person years by being concordant with decision aid recommendations. AHA Aggressive: AHA guidelines (assuming that guideline recommends OAC at CHA₂DS₂-VASC = 1), AHA Conservative: AHA guidelines (assuming that guideline withholding OAC at CHA₂DS₂-VASC = 1), Casciano: Casciano tool, CHEST: CHEST guidelines, ESC: ESC guidelines, LaHaye: LaHaye tool.

Table 4

Unadjusted and Fully Adjusted Hazard Ratios of Concordant OAC use/non-use of OAC decision aids:

Decision aid	Unadjusted HR (CIs)	Adjusted HR (CIs)
AHA Aggressive	0.943 (0.795, 1.120)	0.955 (0.803, 1.136)
AHA Conservative	0.870 (0.733, 1.032)	0.931 (0.783, 1.107)
Casciano	0.838 (0.706, 0.995)	0.911 (0.767, 1.082)
CHEST guidelines	0.825 (0.695, 0.979)	0.909 (0.765, 1.081)
ESC guidelines	0.952 (0.802, 1.130)	0.963 (0.809, 1.146)
LaHaye	0.841 (0.709, 0.999)	0.931 (0.783, 1.106)

Note: Data represent the risk of adverse (thromboembolic and all major bleed) events when patients are concordant with decision aid recommendations. AHA Aggressive: AHA guidelines (assuming that guideline recommends OAC at CHA₂DS₂-VASc =1), AHA Conservative: AHA guidelines (assuming that guideline withholding OAC at CHA₂DS₂-VASc =1), Casciano: Casciano tool, CHEST: CHEST guidelines, ESC: ESC guidelines, LaHaye: LaHaye tool. The adjusted models accounted for age, gender, geographic region, year of diagnosis, diabetes, heart failure, hypertension, vascular diseases, anemia, renal failure, liver failure, prior stroke, prior bleed, alcohol consumption and other medication use (anti-platelet, GI protectants, NSAIDs heparin, immunosuppressant, corticosteroids)

Table 5

Net clinical benefit of any thromboembolic and major bleed event prevention by being concordant with decision aid recommendations when person times were censored at the change of OAC use status:

Decision aid	Concordant status	TE events	Bleed events	Person-years	TE events prevented	Bleed events prevented	NCB (CIs)
AHA Aggressive	Concordant	101	142	14829			
	Discordant	112	83	12824	19.22	-31.03	-11.80 (-13.22, -10.39)
AHA Conservative	Concordant	104	130	15763			
	Discordant	109	95	11891	25.69	-2.57	23.11 (21.69, 24.53)
Casciano	Concordant	97	124	15367			
	Discordant	116	101	12286	31.29	1.52	32.80 (31.38, 34.22)
CHEST guidelines	Concordant	103	134	15925			
	Discordant	110	91	11729	29.10	-6.56	22.54 (21.12, 23.96)
ESC guidelines	Concordant	101	142	14820			
	Discordant	112	83	12833	19.11	-31.14	-12.02 (-13.44, -10.61)
LaHaye	Concordant	106	87	14491			
	Discordant	107	138	13163	8.13	44.80	52.94 (51.52, 54.36)

Note: NCB estimate includes both thromboembolic and major bleed events prevented by being concordance with decision aid recommendations. AF adverse events: Thromboembolic events (including ischemic stroke), Bleed events: Any type of major bleed event, TE prevented: Number of TE events prevented per 10,000 person years by being concordant with decision aid recommendations, Bleed prevented: Number of bleed events prevented per 10,000 person years by being concordant with decision aid recommendations. AHA Aggressive: AHA guidelines (assuming that guideline recommends OAC at CHA₂DS₂-VAsC = 1), AHA Conservative: AHA guidelines (assuming that guideline recommends withholding OAC at CHA₂DS₂-VAsC = 1), Casciano: Casciano tool, CHEST: CHEST guidelines, ESC: ESC guidelines, LaHaye: LaHaye tool.