Circulation

ORIGINAL RESEARCH ARTICLE

Development and Validation of the DOAC Score: A Novel Bleeding Risk Prediction Tool for Patients With Atrial Fibrillation on Direct-Acting Oral Anticoagulants

Rahul Aggarwal, MD; Christian T. Ruff, MD, MPH; Saverio Virdone, MSc; Sylvie Perreault, BPharm, PhD; Ajay K. Kakkar, MBBS, PhD; Michael G. Palazzolo, MPH; Marc Dorais, MSc; Gloria Kayani, BSc; Daniel E. Singer, MD; Eric Secemsky, MD; Jonathan Piccini, MD, MHS; Usman A. Tahir, MD, MBI; Changyu Shen, PhD; Robert W. Yeh, MD, MSc

Background

- When deciding to initiate anticoagulation, clinicians must balance the tradeoffs of decreasing the risk of antithrombotic events against increasing the risk of bleeding.
- The most popular and predictive clinical tool for determining bleeding risk in patients with AF is the HAS-BLED score.
- This risk score, however, has demonstrated limited accuracy in multiple studies and was developed for patients taking warfarin, whereas many patients are now treated with direct-acting oral anticoagulants (DOACs).

AIM of the study

- To develop and validate a clinical risk score to personalize estimates of bleeding risk for individuals with atrial fibrillation taking DOACs.

Methods

- The bleeding risk prediction tool was initially developed in the RE-LY trial (Randomized Evaluation of Long-Term Anticoagulation Therapy) (N=18 113) dabigatran 150 mg group.
- Then, the model was further developed among GARFIELD-AF individuals, because GARFIELD-AF included a large proportion of patients on apixaban and rivaroxaban.
- Finally, external validation was conducted in 2 different cohorts: the COMBINE-AF clinical trial and the RAMQ administrative database.
- The primary outcome was major bleeding at 1 year; the secondary outcome was life-threatening bleeding at 1 year, a subset of major bleeding.

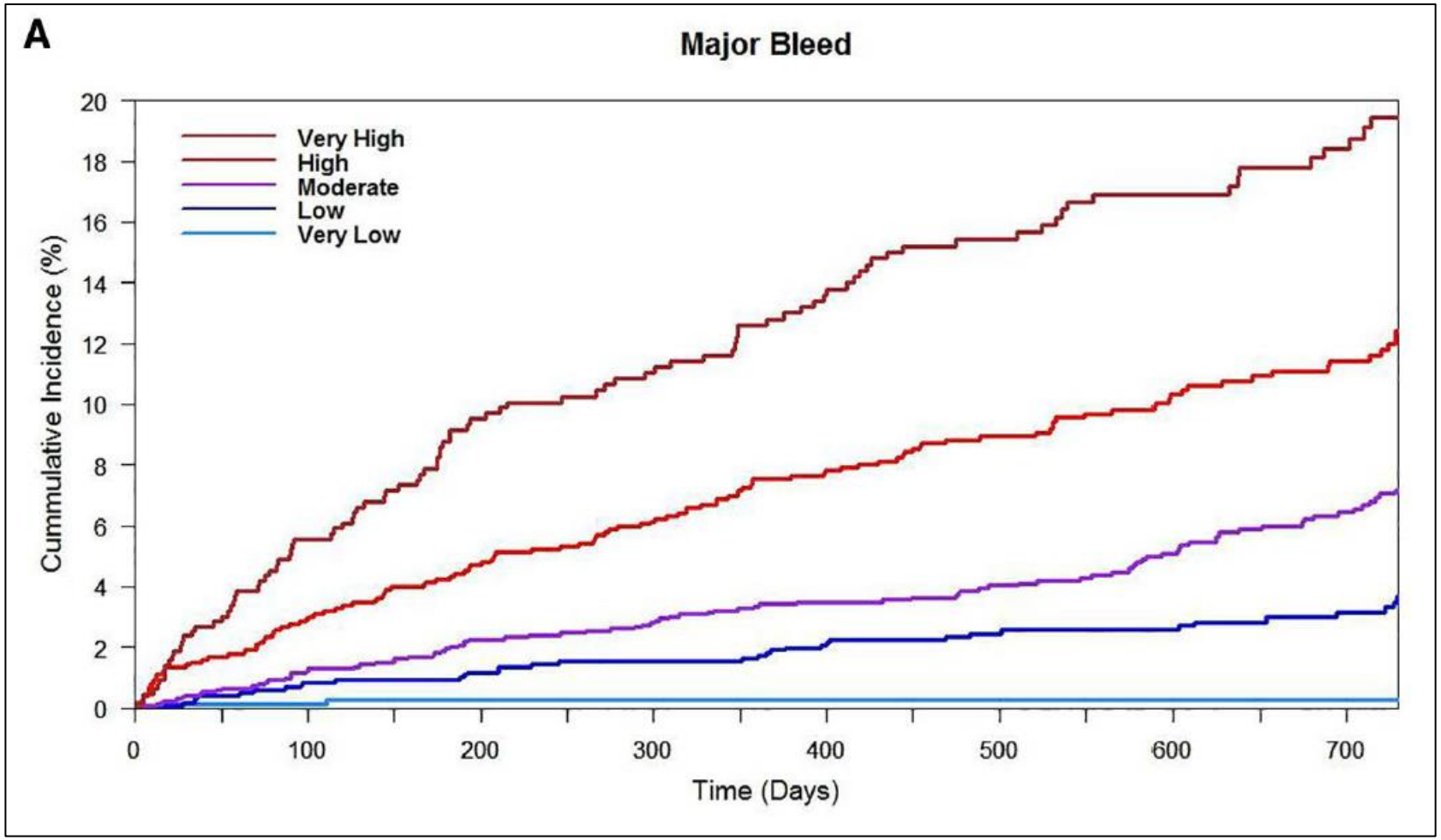
Results

- The final clinical risk prediction scoring system was named the DOAC Score.
- The score consists of 11 final predictors, including age, creatinine clearance/glomerular filtration rate, body mass index, smoking history, stroke/transient ischemic attack/embolism history, diabetes, hypertension, antiplatelet use, and nonsteroidal antiinflammatory use, in addition to bleeding history and liver disease.
- Point assignments were based on the coefficients of the variables in a Cox regression model for the outcome of major bleeding.
- Risk scores were 0 to 10, with risk categories assigned as very low (score 0–3), low (score 4–5), moderate (score 6–7), high (score 8–9), and very high (score 10).
- The maximum number of allocated points for an individual is 10 points.Individuals with scores >10 were assigned a score of 10.

Table 2. DOAC Score

Clinical risk prediction tool	Points
Age, y	
65–69	2
70–74	3
75–79	4
≥80	5
Creatinine clearance/estimated glomerular filtration rate (mL/min)	
30–60	1
<30	2
Underweight (body mass index <18.5 kg/m^2)	1
Stroke/transient ischemic attack/embolism history	1
Diabetes	1
Hypertension	1
Antiplatelet use	
Aspirin	2
Dual-antiplatelet	3
Nonsteroidal anti-inflammatory (NSAID) use	1
Bleeding history	3
Liver disease*	2
Total score range: 0–10 (Maximum 10 points – individuals with scores ≥ 10 are assigned a score of 10)	

Figure 1. **Cumulative incidence for major bleeding outcomes by predicted risk category in the development cohorts: RE-LY (A) and GARFIELD-AF (B).**



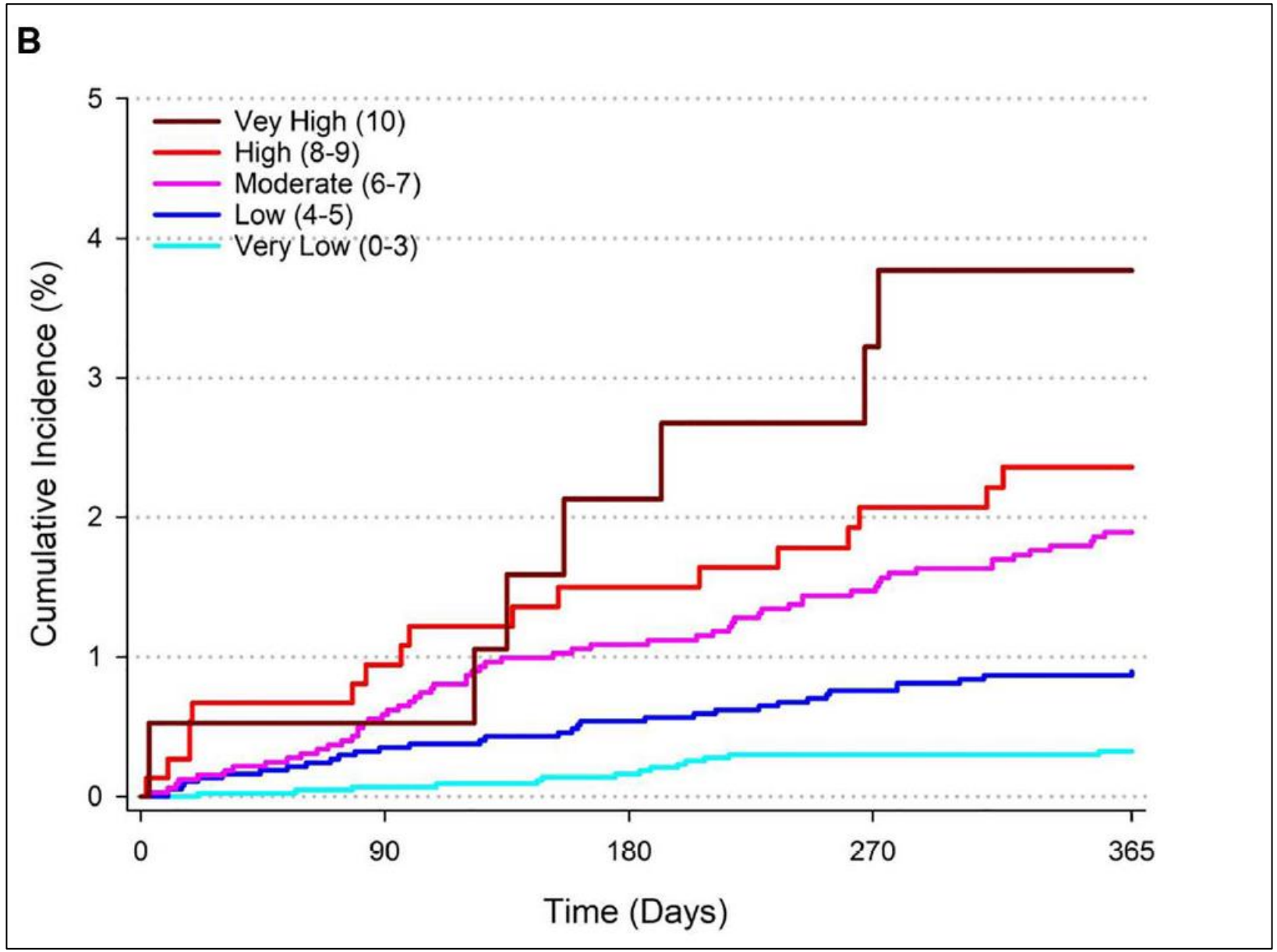
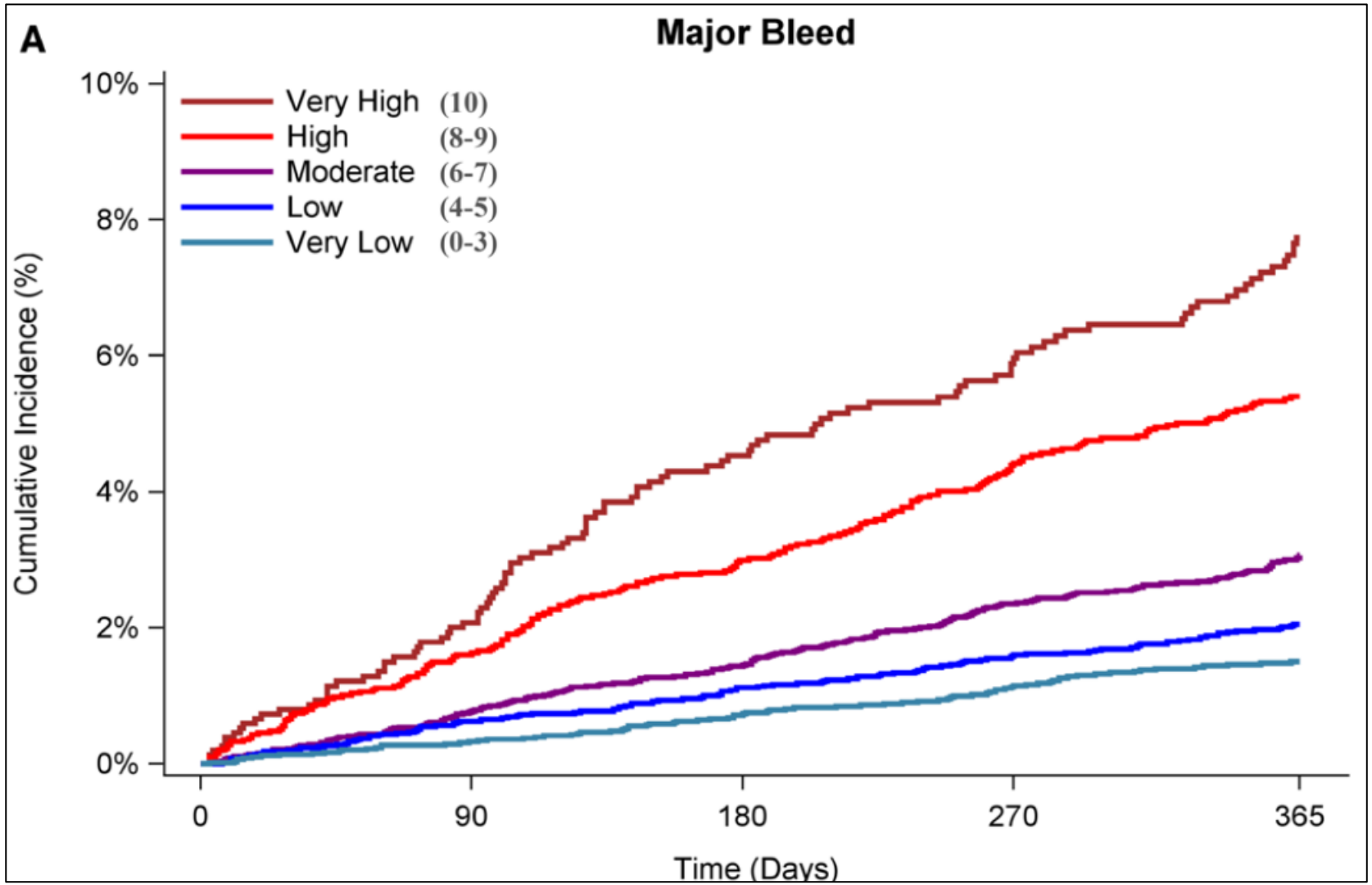
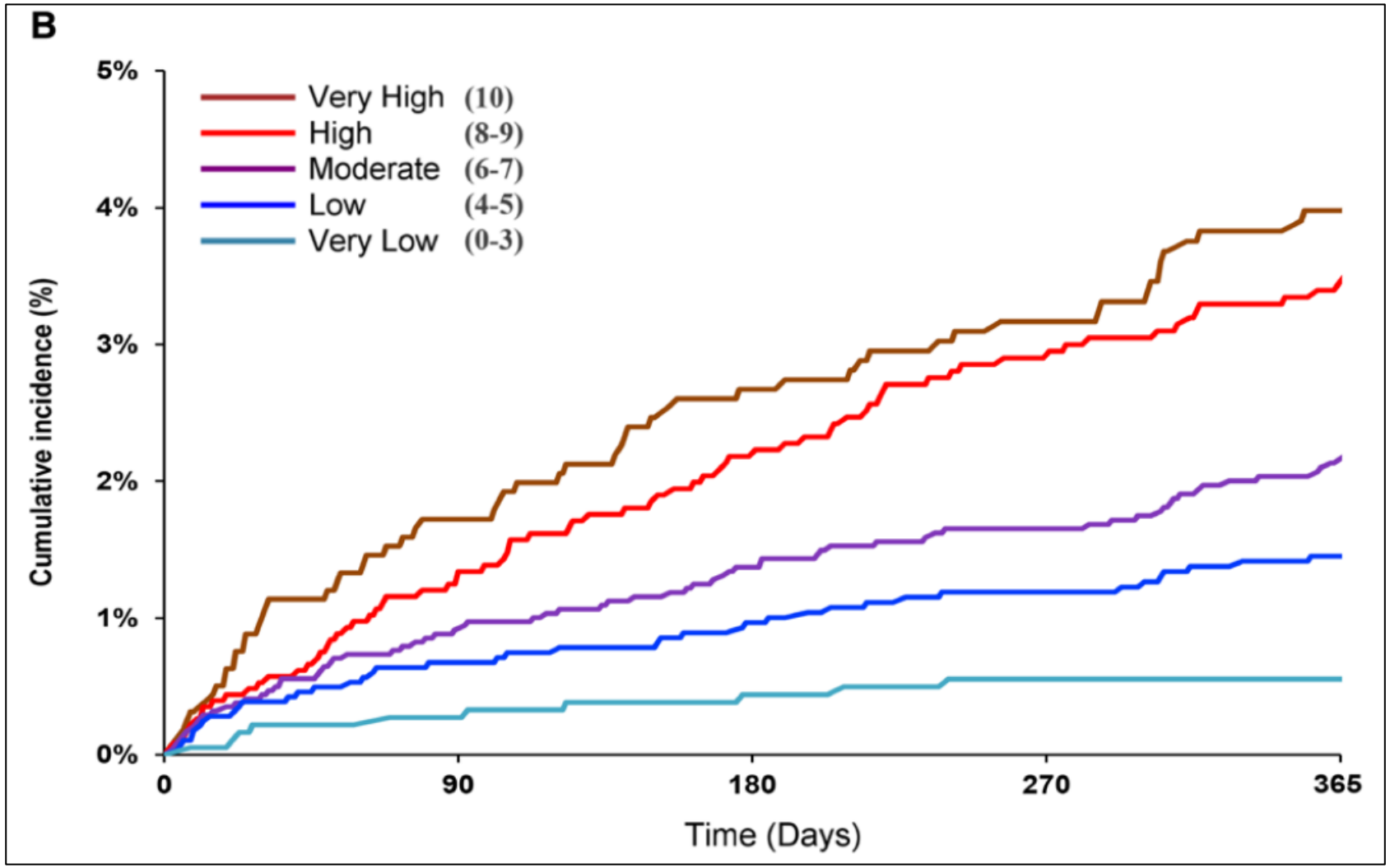

B
Vey High (10)
High (8-9)
Moderate (6-7)
Low (4-5)
Very Low (0-3)
Cumulative Incidence (%)
0
1
2
3
4
5
0
90
180
270
365
Time (Days)

Figure 2. **Cumulative incidence for bleeding outcomes by predicted risk category in the validation cohorts: COMBINE-AF (A) and RAMQ (B).**




B
5%
4%
3%
2%
1%
0%
Cumulative incidence (%)
Very High (10)
High (8-9)
Moderate (6-7)
Low (4-5)
Very Low (0-3)
0
90
180
270
365
Time (Days)

Results (II)

- The score had superior performance to the HAS-BLED score in RE-LY (C statistic, 0.73 versus 0.60; *P* for difference <0.001) and among 12 296 individuals in GARFIELD-AF (C statistic, 0.71 versus 0.66; *P* for difference = 0.025).
- The DOAC Score had stronger predictive performance than the HAS-BLED score in both validation cohorts, including 25 586 individuals in COMBINE-AF (C statistic, 0.67 versus 0.63; *P* for difference <0.001) and 11 945 individuals in RAMQ (C statistic, 0.65 versus 0.58; *P* for difference <0.001).

Table 3. Predictive Performance of the DOAC Score Compared With HAS-BLED

	N	No. of events	DOAC Score, C statistic (95% CI)	HAS-BLED, C statistic (95% CI)	*P* value
RE-LY	5684	386	0.72 (0.71–0.74)	0.60 (0.58–0.62)	<0.001
GARFIELD-AF	12 296	131	0.71 (0.67–0.75)	0.66 (0.62–0.71)	0.025
COMBINE-AF	25 586	692	0.67 (0.64–0.69)	0.63 (0.61–0.65)	<0.001
RAMQ	11 945	258	0.65 (0.61–0.68)	0.58 (0.55–0.62)	<0.001

Conclusions

- In this study, the DOAC Score was developed, a novel bleeding risk score to stratify bleeding risk among patients with AF who are prescribed a DOAC.
- The DOAC Score consistently outperformed the HASBLED score in every cohort and was able to stratify patients by levels of bleeding risk across both randomized trials and observational populations.
- Its adoption by clinicians will depend on its endorsement by Atrial Fibrillation Guideline Committees both in the United States and in Europe with global implications.