European Heart Journal Supplements (2025) **27** (Supplement 1), i162–i166
The Heart of the Matter
https://doi.org/10.1093/eurheartjsupp/suae088

ESC European Society of Cardiology

Subclinical atrial fibrillation/atrial high-rate episodes: what significance and decision-making?

Giuseppe Boriani [1]*, Enrico Tartaglia [1], Paola Trapanese[1], Francesco Tritto[1], Luigi Gerra[1], Niccolò Bonini [1], Marco Vitolo [1], Jacopo F. Imberti [1,2], and Davide A. Mei [1,2]

[1]Cardiology Division, Department of Biomedical, Metabolic and Neural Sciences, Italy University of Modena and Reggio Emilia, Policlinico di Modena, Modena 41124, Italy; and [2]Clinical and Experimental Medicine PhD Program, University of Modena and Reggio Emilia, Modena 41124, Italy

KEYWORDS
Anticoagulants;
Atrial cardiomyopathy;
Atrial fibrillation;
Defibrillator;
Pacemaker;
Stroke

Subclinical atrial fibrillation (AF) and atrial high-rate episodes (AHREs) are often detected incidentally through cardiac implantable electronic devices or wearables, especially in asymptomatic patients. These episodes pose a clinical challenge as they are associated with an increased risk of stroke, albeit at a lower rate compared with clinical AF. This review discusses the evolving understanding of AHRE, highlighting the uncertainties regarding optimal management, particularly the use of oral anticoagulants. Two key trials, ARTESiA and NOAH-AFNET 6, investigated anticoagulation in patients with device-detected AHRE. ARTESiA found that apixaban significantly reduced stroke or systemic embolism, but with an increased risk of major bleeding. In contrast, NOAH-AFNET 6, which tested edoxaban, did not demonstrate a significant benefit in reducing cardiovascular events but also observed higher bleeding rates. A meta-analysis of these trials confirmed the efficacy of oral anticoagulants in lowering ischaemic stroke risk, though with an elevated bleeding risk. Given these findings, clinical decision-making in patients with AHRE must be individualized, taking into account stroke risk, bleeding risk, and patient preferences. Shared decision-making is crucial to balance the benefits and risks of anticoagulation, especially in the context of progression to clinical AF and its associated stroke risk. Moreover, it is essential to educate patients about the risk of bleeding complications and emphasize the importance of close monitoring. Future research may further clarify optimal anticoagulation strategies and better define high-risk subgroups that would most benefit from therapy.

Sub-clinical atrial fibrillation and atrial high-rate episodes: from the definition to the clinical implications

Atrial fibrillation (AF) is a complex condition that can present as symptomatic arrhythmia or, quite frequently, as an asymptomatic event.[1,2] It is often detected incidentally through a 12-lead electrocardiogram (ECG), Holter monitoring, or even via modern technology like smartphones and smartwatches, referred to as wearables.[3-5]

A diagnosis of 'clinical AF'[6,7] is established when AF is documented on a 12-lead ECG or through an ECG rhythm strip that shows at least 30 s of AF.

Cardiac implantable electronic devices (CIEDs) with atrial sensing capabilities[6,7] provide extensive options for monitoring cardiac rhythm. These devices—including

*Corresponding author. Tel: 0594225463, E-mail: giuseppe.boriani@unimore.it

pacemakers, implantable cardioverter-defibrillators, cardiac resynchronization therapy devices, and implantable loop recorders—have significantly enhanced our understanding of the temporal dynamics of atrial tachyarrhythmias.

The term *atrial high-rate episodes* (AHREs) can be applied when a CIED detects an atrial tachyarrhythmia in a patient with no prior history of AF, absence of symptoms typical of AF, and no detection of AF at a conventional 12-lead ECG, provided that noise or artefacts are excluded by analysis of the recorded tracing. The term *subclinical AF* has been used, like a synonym, when the arrhythmic nature of AHRE is confirmed by visually revision of intra-cardiac electrograms or ECG-recorded rhythm strips.[5,6] Most recently, the term *device-detected subclinical AF* has been proposed for AF detected through continuous monitoring devices, including CIEDs and consumer-based wearable monitors.

The characterization of AHRE was analysed in the last 15 years by a series of observational studies that showed that AHRE/subclinical AF are quite common, especially in elderly patients, with up to 30% of patients experiencing AHRE $\geq$ 5–6 min during follow-up ranging from 1 to 3 years. Atrial high-rate episodes $\geq$5–6 min are associated with around a two-fold increased risk of stroke, thus differing from the five-fold increase reported for clinical AF.[6] The risk of stroke/systemic embolism increases according to AF burden and CHA_2DS_2-VASc. However, the precise cut-off of a single AF episode duration or daily AF burden associated with a substantial increase in the risk was not established in observational studies since thresholds ranging from 5–6 min to 1 h, to 5.5 h or even 24 h were identified.[5,6]

What implications for anticoagulation after ARTESiA and NOAH-AFNET 6 trials?

In patients with AHRE, the lack of clear indications to anticoagulation and the need to assess the possible risk-benefit ratio of oral anticoagulants in this setting led 8–10 years ago to plan two randomized controlled trials, the Apixaban for the Reduction of Thrombo-Embolism in Patients with Device-detected Subclinical AF (ARTESiA) trial and the Non-vitamin K Antagonist Oral Anticoagulants in Patients with Atrial High-Rate Episodes (NOAH-AFNET 6) trial[7–10] (*Table 1*). These two studies differed for the entry criteria for AHRE (between 6 min and 24 h in ARTESiA, >6 min in NOAH-AFNET 6 without an upper limit of AHRE duration), for the oral anticoagulant tested in the intervention arm (apixaban in ARTESiA and edoxaban in NOAH-AFNET 6), and also for the control arm (aspirin 81 mg in ARTESiA),[10] aspirin or placebo, at the discretion of investigators, in NOAH-AFNET 6, which however included aspirin in around half of enrolled patients.[9] As shown in *Table 1*, the primary endpoint differed significantly between the two trials: in NOAH-AFNET 6, cardiovascular mortality was included in a composite with stroke and systemic embolism, whereas in ARTESiA, the endpoint was limited to stroke and systemic embolism alone.

The NOAH-AFNET 6 trial recruited 2536 subjects with an average age of 78 years and subclinical AF episodes with an average duration of 2.8 h, randomized to receive either edoxaban or placebo.[9] The primary endpoint of the study consisted of death from cardiovascular causes, stroke, or systemic embolism. The study was stopped prematurely after a mean follow-up of 21 months based on recommendations from the data and safety monitoring board and the steering committee, owing to safety concerns, and based on the results of an informal assessment of futility for the efficacy of edoxaban.[9]

At the conclusion of the trial, the primary endpoint was observed in 3.2% of the treated group and 4% of the placebo group [hazard ratio (HR) 0.81; 95% confidence interval (CI): 0.60–1.08; $P = 0.15$]. The incidence of stroke was ~1% per patient-year in both the groups. The decision to include cardiovascular death as a primary endpoint in this trial is debatable, as cardiovascular death is largely influenced by underlying heart disease and comorbidities, and fewer than 10% of all deaths may be related to stroke. As a matter of fact, this diminishes the likelihood of demonstrating a positive effect of anticoagulants.

The composite endpoint of total mortality and major bleeding was observed in 5.9% of the edoxaban group compared with 4.5% in the placebo group (HR 1.31; 95% CI 1.02–1.67; $P = 0.03$). Patients receiving edoxaban experienced a doubled risk of major bleeding (*Table 1*), with an average of 0.06 ± 0.35 events per patient-year. There was no significant difference in all-cause mortality between edoxaban and placebo groups. Clinical AF developed in 18.2% of the enrolled patients (8.7% per patient-year). The authors of the NOAH-AFNET 6 trial concluded that in patients with AHRE treated with edoxaban, the incidence of composite outcome of cardiovascular death, stroke, or systemic embolism did not differ from placebo, but treatment with edoxaban led to a higher incidence of the composite endpoint of death or major bleeding.[9]

A secondary pre-specified analysis of the NOAH-AFNET 6 trial by Becher *et al.*[11] examined interactions between AHRE duration at baseline, with a specific focus on AHRE > 24 h and anticoagulation with edoxaban compared with placebo. Atrial high-rate episode >24 h were present at baseline in 259/2389 patients, with clinical characteristics non-different from patients with shorter AHRE. The primary outcome occurred in 9/132 patients with AHRE > 24 h (2 strokes) treated with anticoagulation and in 14/127 patients treated with placebo (2 strokes). The small number of events indicates that the statistical power of this analysis was very low.

The results of the ARTESiA trial may appear at first look quite conflicting when compared with the results of the NOAH-AFNET 6 trial.[10] In the ARTESiA, 4012 patients (mean age 77 years) with device-detected subclinical AF lasting from 6 min to 24 h (with a median longest episode duration of 1.5 h) were randomized to receive either apixaban (2.5 or 5 mg twice daily) or aspirin (81 mg daily). In patients with AF lasting more than 24 h or developing clinical AF, trial medications were discontinued, and oral anticoagulants were initiated as open-label treatment; this occurred in around 24% of the patients, after a median time after randomization of 18.3 months.[10] Stroke or systemic embolism (*Table 1*) was the primary endpoint. After a mean follow-up of 3.5 years, the primary endpoint occurred in 55 patients in the apixaban group compared with 86 in the aspirin

Table 1 Summary of the main characteristics and results of the NOAH-AFNET 6[9] and ARTESiA[10] randomized controlled trials and results of the study-level meta-analysis based on these two trials

	NOAH-AFNET 6 trial	ARTESiA trial	Study-level meta-analysis including NOAH-AFNET 6 and ARTESiA trials
Patients characteristics according to eligibility criteria	Patients with age ≥65 year and >1 additional CHA_2DS_2-VASc risk factor (except sex) or age ≥75 year and with SCAF episodes ≥6 min detected on CIEDs	Patients with age ≥55 year, CHA_2DS_2-VASc score ≥3, and SCAF episodes ≥6 min to <24 h detected on CIEDs	
Duration of AHRE/SCAF episodes required for enrolment in the study	At least one episode (atrial rate ≥170/min) ≥6 min, no upper limit	At least one episode (atrial rate ≥175/min) ≥6 min, but no single episode ≥24 h	
Tested treatment with oral anticoagulation	Edo 60 mg (30 mg with pre-specified dose reduction criteria) once daily	Api 5 mg (2.5 mg with pre-specified dose reduction criteria) twice daily	DOAC (Edo or Api)
Control treatment	Pla or Asa 100 mg once daily (when clinically indicated)	Asa 81 mg once daily	Pla or Asa
Open-label prescription of aspirin	In 54% of the Pla group	In 57% of the patients as open label	
Number of enrolled patients	2536 1270 Edo analysed 1266 Pla analysed	4012 2015 Api analysed 1997 Asa analysed	6548
Follow-up duration	Median 21 months	Mean 3.5 ± 1.8 years	
Primary efficacy endpoint	Composite of stroke or systemic embolism or CV death	Composite of stroke or systemic embolism	
Primary safety endpoint	Composite of death from any cause or major bleeding	Major bleeding	
Ischaemic stroke No. of patients (% or % per patient-year)	22 Edo (0.9%), 27 Pla (1.1%) (% per patient-year) HR 0.79 (0.45–1.39)	45 Api (0.64%), 71 Asa (1.02%) (% per patient-year) HR 0.62 (0.43–0.91)	67 DOAC (2.0%), 98 Pla/Asa (3.0%) RR 0.68 (0.50–0.92)
All-cause stroke or systemic embolism No. of patients (%)	23 Edo (1.8%), 33 Pla (2.6%) RR 0.69 (0.41–1.18)	55 Api (2.7%), 86 Asa (4.3%) RR 0.63 (0.45–0.88)	78 DOAC (2.4%), 119 Pla/Asa (3.6%) RR 0.65 (0.49–0.86)
Major bleeding No. of patients (% or % per patient-year)	53 Edo (2.1%), 25 Pla (1.0%) (% per patient-year) HR 2.10 (1.30–3.38)	106 Api (1.53%), 78 Asa (1.12%) (% per patient-year) HR 1.36 (1.01–1.82)	159 DOAC (4.8%), 103 Pla/Asa (3.2%) RR 1.62 (1.05–2.50)
Fatal bleeding No. of patients (%)	2 Edo (0.2%), 1 Pla (0.1%) RR 1.99 (0.18–21.96)	10 Api (0.5%), 14 Asa (0.7%) RR 0.7 (0.32–1.59)	12 DOAC (0.4%), 15 Pla/Asa (0.5%) RR 0.79 (0.37–1.69)
All-cause death No. of patients (% or % per patient-year)	111 Edo (4.3%), 94 Pla (3.7%) (% per patient-year) HR 1.16 (0.88–1.53)	362 Api (5.06%), 341 (4.82%) (% per patient-year) HR 1.04 (0.90–1.21)	473 DOAC (14.4%), 435 Pla/Asa (13.3%) RR 1.08 (0.96–1.21)

Api, apixaban; Asa, acetylsalicylic acid; CIED, cardiac implantable electronic device; CV, cardiovascular; DOAC, direct oral anticoagulant; Edo, edoxaban; HR, hazard ratio; Pla, placebo; RR, relative risk; SCAF, subclinical atrial fibrillation.

group (corresponding to 0.78 and 1.24% per patient-year, HR 0.63; 95% CI 0.45–0.88, $P = 0.007$). Notably, the incidence of moderately disabling to fatal strokes, as evaluated by the modified Rankin Scale (scores 3–6), was reduced by half in those treated with apixaban. In patients with CHA2DS2-VASc > 4, the benefits of treatment with apixaban in preventing stroke or systemic embolism were greater than the risk of major bleeds.[12] Apixaban prevented 0.12 (95% CI: −0.38 to 0.62) strokes or systemic embolism per 100 patient-years and caused 0.33 (95% CI: −0.27 to 0.92) major bleeds, the opposite was true for patients with CHA2DS2-VASc < 4.[12] No significant differences were observed in mortality rates. Major bleeding, evaluated through an on-treatment analysis, was more common in the apixaban group (HR 1.81; 95% CI 1.26–2.57, $P = 0.04$). A similar trend was observed for gastrointestinal bleeding (HR 1.76, 95% CI 1.13–2.74). However, there were no significant differences in the rates of fatal bleeding or symptomatic intracranial haemorrhages. Most cases of major bleeding responded promptly to supportive care, and haemodynamic instability was uncommon.

A key finding from both the ARTESiA and NOAH-AFNET 6 trials is that the risk of stroke or systemic embolism associated with AHRE/subclinical AF is ∼1–1.2% per patient-year, which is lower than that seen with clinical AF. However, this should not understate the impact on patient outcomes, as 43% of strokes occurring in the aspirin group of the ARTESiA trial resulted in significant disability or death. When evaluating the risk–benefit ratio of anticoagulants for patients with AHRE or subclinical AF, it is crucial to differentiate between the reduction in stroke risk and the increase in major bleeding risk. Studies have shown discrepancies in how stroke and bleeding risks are perceived by patients vs. physicians. Physicians often view bleeding risks as more significant, while patients tend to prioritize the risk of stroke more strongly when compared with physicians.

According to AF guidelines, the threshold for stroke incidence that justifies oral anticoagulation is set at ∼1% per year and this corresponds to the actual risk of stroke found in AHRE/subclinical AF under placebo or aspirin in NOAH-AFNET 6 and ARTESiA.

In numerical terms and in an intention-to-treat approach, the results of ARTESiA suggest that oral anticoagulation results in 4.6 fewer strokes/embolic events per thousand patient-years, despite resulting in 4.1 additional major bleeding events per thousand patient-years. However, we should carefully consider, from the perspective of patient values, that the significant reduction in disabling strokes vs. aspirin of ARTESiA is far more meaningful for patients, their families, and the community, than the clinical implications of increased major bleeding by apixaban. Most of these bleeding events (90%) were managed conservatively, using transfusions when needed, and without increase in fatal bleedings or deaths.[10]

Any interpretation of the apparent discrepancies between ARTESiA and NOAH-AFNET 6 trials must consider that the conclusions of the latter study were significantly influenced by its premature termination, which adversely affected the trial's statistical power.

However, an important clarification is provided by the study-level meta-analysis based on ARTESiA and NOAH-AFNET 6, published by McIntyre *et al.*[13] that involved authors of both trials. This meta-analysis, incorporating data from NOAH-AFNET 6 (2536 participants) and ARTESiA (4012 participants; *Table 1*), demonstrated consistent results regarding the reduction of ischaemic stroke with oral anticoagulants [relative risk (RR) 0.68, 95% CI 0.50–0.92, I^2 statistic for heterogeneity = 0%; high-quality evidence]. Furthermore, the analysis revealed that oral anticoagulation was found to reduce the composite endpoint of cardiovascular death, all-cause stroke, peripheral arterial embolism, myocardial infarction, or pulmonary embolism (RR 0.85, 95% CI 0.73–1.00, $I^2 = 0\%$; moderate-quality evidence). The meta-analysis found no significant differences in rates of cardiovascular death (RR 0.95, 95% CI 0.76–1.17, $I^2 = 0\%$; moderate-quality evidence) or all-cause mortality (RR 1.08, 95% CI 0.96–1.21, $I^2 = 0\%$; moderate-quality evidence). It also noted that oral anticoagulation was associated with an increased risk of major bleeding (RR 1.62, 95% CI 1.05–2.5, I^2=61%; high-quality evidence), but no significant difference was observed in fatal bleeding rates (RR 0.79, 95% CI 0.37–1.69, $I^2 = 0\%$, moderate-quality evidence).[13]

Based on current knowledge, we believe that in patients with AHRE/subclinical AF detected through an implanted device, decision-making should be individualized. This approach should consider that in patients at risk of stroke, as indicated by the CHA_2DS_2-VASc score, anticoagulants significantly lower the risk of stroke, especially the risk of disabling or fatal stroke. This favourable effect is associated with an increased risk of major bleeding that can be managed conservatively in 90% of cases with no increase in fatal bleeding or death.

In this context, patients with AHRE/subclinical AF should be adequately informed about the expected benefit and the risk–benefit ratio of anticoagulation. Shared decision-making between clinicians and patients is crucial, taking into account individual values and preferences as well as an appropriate management of associated conditions and comorbidities with the correction of modifiable risk factors for bleeding.

Additionally, clinical decision-making should also consider that, on average, around one of five patients with device-detected AF (traditionally named AHRE or subclinical AF) will progress to clinical AF or long-duration AHRE (>24 h) within a 2 year follow-up. This progression inherently increases risk of stroke, particularly in patients with a higher $CHADS_2$ or CHA_2DS_2-VASc and/or a higher baseline AF burden. Data from the NOAH-AFNET 6 trial confirm that progression to clinical AF is more frequent when device-detected AHRE lasts more than 24 h, with the rate of progression to clinical AF doubling (17% per patient-year) compared with shorted AHRE.[11]

Remote monitoring of CIEDs offers detailed notifications regarding the presence and duration of AHREs/subclinical AF episodes, providing tracings with arrhythmia electrograms. This capability has significantly enhanced its clinical value for both patients with and without heart failure.[14,15]

Future analyses of ARTESiA and NOAH-AFNET 6 data are anticipated to provide additional information on other specific patients' subgroups with a higher likelihood of progression to clinical AF, as well as identifying those patients who can achieve the maximal net benefit from

anticoagulation, based on clinical characterization at baseline.[16,17] From a clinical perspective, examining the relationship between AHRE/subclinical AF and atrial cardiomyopathy is essential. Understanding how the degree of dysfunction in atrial structure and function correlates with stroke risk could greatly enhance predictive accuracy. Furthermore, exploring the progression from brief episodes of AHRE or subclinical AF to longer durations of clinical AF will offer valuable insights into patient risk and inform management strategies.

Conclusions

The NOAH-AFNET 6 and ARTESiA trials offer significant insights for clinical decision-making in everyday practice. In patients with AF and in patients with subclinical AF/AHRE, reduction of strokes, especially disabling strokes, through effective treatment with oral anticoagulants is a primary objective, in the perspective of the patient and of the community. Recent evidence indicates that this crucial aim can be achieved also in patients with AF identified through the extended diagnostics of CIEDs. Achieving this goal necessitates a clinically focused, patient-centred approach that includes tailored assessments of the risks and benefits of oral anticoagulants, which should be communicated with well-informed and empowered patients.

Funding

None declared.

Conflict of interest: G.B. reported small speaker fees from Bayer, Boehringer Ingelheim, Boston, Daiichi Sankyo, Janssen, and Sanofi outside of the submitted work. G.B. is the Principal Investigator of the Applying ARtificial Intelligence to define clinical trajectorieS for personalized predicTiOn and early deTEction of comorbidity and muLtimorbidity pattErnS project (ARISTOTELES) that received funding from the European Union within the Horizon 2020 research and innovation programme (grant no. 101080189). The other authors did not report conflicts of interest to disclose outside of the submitted work.

Data availability

There are no new data associated with this article.

References

1. Boriani G, Bonini N, Vitolo M, Mei DA, Imberti JF, Gerra L *et al.* Asymptomatic vs. symptomatic atrial fibrillation: clinical outcomes in heart failure patients. *Eur J Intern Med* 2024;**119**:53–63.
2. Schnabel RB, Marinelli EA, Arbelo E, Boriani G, Boveda S, Buckley CM *et al.* Early diagnosis and better rhythm management to improve outcomes in patients with atrial fibrillation: the 8th AFNET/EHRA consensus conference. *Europace* 2023;**25**:6–27.
3. Svennberg E, Tjong F, Goette A, Akoum N, Di Biase L, Bordachar P *et al.* How to use digital devices to detect and manage arrhythmias: an EHRA practical guide. *Europace* 2022;**24**:979–1005.
4. Svennberg E, Caiani EG, Bruining N, Desteghe L, Han JK, Narayan SM *et al.* The digital journey: 25 years of digital development in electrophysiology from an Europace perspective. *Europace* 2023;**25**: euad176.
5. Kalarus Z, Mairesse GH, Sokal A, Boriani G, Średniawa B, Casado-Arroyo R *et al.* Searching for atrial fibrillation: looking harder, looking longer, and in increasingly sophisticated ways. An EHRA position paper. *Europace* 2023;**25**:185–198.
6. Imberti JF, Bonini N, Tosetti A, Mei DA, Gerra L, Malavasi VL *et al.* Atrial high-rate episodes detected by cardiac implantable electronic devices: dynamic changes in episodes and predictors of incident atrial fibrillation. *Biology (Basel)* 2022;**11**:443.
7. Toennis T, Bertaglia E, Brandes A, Dichtl W, Fluschnik N, de Groot JR *et al.* The influence of atrial high-rate episodes on stroke and cardiovascular death: an update. *Europace* 2023;**25**:euad166.
8. Lip GYH, Proietti M, Potpara T, Mansour M, Savelieva I, Tse HF *et al.* Atrial fibrillation and stroke prevention: 25 years of research at EP Europace journal. *Europace* 2023;**25**:euad226.
9. Kirchhof P, Toennis T, Goette A, Camm AJ, Diener HC, Becher N *et al.* Anticoagulation with edoxaban in patients with atrial high-rate episodes. *N Engl J Med* 2023;**389**:1167–1179.
10. Healey JS, Lopes RD, Granger CB, Alings M, Rivard L, McIntyre WF *et al.* Apixaban for stroke prevention in subclinical atrial fibrillation. *N Engl J Med* 2024;**390**:107–117.
11. Becher N, Toennis T, Bertaglia E, Blomström-Lundqvist C, Brandes A, Cabanelas N *et al.* Anticoagulation with edoxaban in patients with long atrial high-rate episodes ≥24h. *Eur Heart J* 2024;**45**:837–849.
12. Lopes RD, Granger CB, Wojdyla DM, McIntyre WF, Alings M, Mani T *et al.* Apixaban vs aspirin according to CHA_2DS_2VASc score in subclinical atrial fibrillation: insights from ARTESiA. *J Am Coll Cardiol* 2024;**84**:354–364.
13. McIntyre WF, Benz AP, Becher N, Healey JS, Granger CB, Rivard L *et al.* Direct oral anticoagulants for stroke prevention in patients with device-detected atrial fibrillation: a study-level meta-analysis of the NOAH-AFNET 6 and ARTESiA trials. *Circulation* 2024;**149**:981–988.
14. Varma N, Braunschweig F, Burri H, Hindricks G, Linz D, Michowitz Y *et al.* Remote monitoring of cardiac implantable electronic devices and disease management. *Europace* 2023;**25**:euad233.
15. Boriani G, Burri H, Svennberg E, Imberti JF, Merino JL, Leclercq C. Current status of reimbursement practices for remote monitoring of cardiac implantable electrical devices across Europe. *Europace* 2022;**24**:1875–1880.
16. Imberti JF, Mei DA, Vitolo M, Bonini N, Proietti M, Potpara T *et al.* Comparing atrial fibrillation guidelines: focus on stroke prevention, bleeding risk assessment and oral anticoagulant recommendations. *Eur J Intern Med* 2022;**101**:1–7.
17. Mei DA, Imberti JF, Bonini N, Romiti GF, Corica B, Proietti M, *et al.* Performance of HAS-BLED and DOAC scores to predict major bleeding events in atrial fibrillation patients treated with direct oral anticoagulants: a report from a prospective European observational registry. *Eur J Intern Med.* 2024;**128**:63–70. http://dx.doi.org/10.1016/j.ejim.2024.06.022